Clinical Importance, Incidence and Risk Factors for the Development of Postoperative Ileus Following Adult Spinal Deformity Surgery

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Abstract

Study Design: Retrospective observational study of a cohort of consecutive patients.

Objectives: Postoperative ileus (POI) is associated with a variety of adverse effects. Although the incidence of and risk factors for POI following spinal surgery have been reported, the frequency and pathology of POI after spinal corrective surgery for adult spinal deformity (ASD) are still largely unknown. The study objectives were to: (1) clarify the prevalence and clinical significance of POI, (2) elucidate the risk factors for POI, (3) determine radiographically which preoperative and/or postoperative spinal parameters predominantly influence the risk of POI after spinal corrective surgery for ASD.

Methods: We included data from 144 consecutive patients who underwent spinal corrective surgery. Perioperative medical complications and clinical information were extracted from patient electronic medical records. Preoperative radiographic parameters and changes in radiographic parameters after surgery were compared between patients with and without POI. Multivariate logistic regression analyses were performed to clarify potential risk factors for POI.

Results: POI developed in 25/144 (17.4%) patients and was the most common complication in the present study. The frequencies of smoking, gastroesophageal reflux disease, and lateral lumbar interbody fusion (LLIF), as well as the duration of surgery were significantly greater in the group with POI versus the group without POI. Among radiographic parameters, only the change in thoracolumbar kyphosis (TLK) from before to after surgery was significantly larger in the group with POI. Multivariate logistic regression analysis showed that male sex, LLIF and large changes in TLK from before to after surgery were significantly associated with the development of POI.

Conclusions: These results suggested that LLIF and large corrections in TLK were independent risk factors for POI after ASD surgery. When patients with ASD have large TLK preoperatively, and it is determined that a large correction is needed, physicians must be aware of the potential for occurrence of POI.

Keywords
adult spinal deformity, postoperative ileus, thoracolumbar kyphosis, surgical spinal correction, perioperative complications, lateral lumbar interbody fusion

Introduction

Despite having a crucial role to improve the health-related quality of life (HRQoL) of patients with adult spinal deformity (ASD), spinal corrective surgery for ASD often requires extensive dissection, with a large number of exposed spinal levels, osteotomy, blood transfusion, and extended hospitalization. Over the last few decades, the ability to treat ASD has advanced, including improvements in minimally invasive...
techniques, such as lateral lumbar interbody fusion (LLIF), and other surgical strategies.\textsuperscript{1-4} However, surgical treatment of spinal deformities for elderly patients remains challenging because of the high rates of surgical and medical complications.\textsuperscript{5,6} Therefore, many investigators have tried to determine the incidence of and risk factors for perioperative complications associated with the surgical treatment of ASD. In those studies, infections, neurologic deficits, cardiopulmonary complications, cerebrovascular accident and deep venous thrombosis were identified as major complications. We recently noted that many patients with ASD complain of abdominal symptoms after spinal corrective surgery (Supplemental Table).

Postoperative ileus (POI) is defined as the temporary obstruction of the gastrointestinal (GI) tract and overall disruption of normal peristalsis in response to surgical stress, manifested clinically by nausea, vomiting, inability to tolerate an oral diet, abdominal distention, and/or delayed passage of flatus or stool for 3 or more days after surgery.\textsuperscript{7} POI is associated with a variety of adverse effects, such as increased postoperative pain, increased pulmonary morbidity and infectious complications, poor wound healing, delayed postoperative mobilization, prolonged hospitalization, decreased patient satisfaction, and increased health care costs.\textsuperscript{8} Although POI is a well-known complication after intra-abdominal surgery, it has also been known to develop after orthopedic surgery.\textsuperscript{9} To date, the incidence of and risk factors for POI following spinal surgery have been reported.\textsuperscript{10,11} However, the frequency and pathology of POI after spinal corrective surgery for ASD are still largely unknown.

The purposes of present study were (1) to clarify the prevalence and clinical significance of POI, (2) to elucidate the risk factors for POI, and (3) to determine radiographically which preoperative and/or postoperative spinal parameters predominantly influence the risk of POI after spinal corrective surgery for ASD.

## Methods

### Patients and Surgical Techniques

This study was approved by the institutional review board (IRB) of the authors’ affiliated institution. We carried out a retrospective observational study of a cohort of consecutive patients with a diagnosis of ASD who underwent spinal corrective surgery. Patients were considered candidates for thoracolumbar correction if fusion was indicated because of ASD and a full course of conservative care had been exhausted. The inclusion criteria were a radiographic diagnosis of ASD defined by at least one of the following parameters: a coronal Cobb angle $>30^\circ$; a C7 sagittal vertical axis (SVA, defined as the distance between the C7 plumb line and the posterolateral edge of S1) $>5$ cm; and/or a $>30^\circ$ pelvic tilt (PT), which is the orientation of the pelvis with respect to the femurs and the rest of the body. We only included cases of de novo degenerative spinal deformity to study, separate from secondary degenerative scoliosis superimposed on adolescent idiopathic scoliosis.

### Statistical Analyses

There were no significant differences between the groups for age, sex, body mass index (BMI), preoperative intake of medicine for constipation, preoperative intake of NSAIDs/opioids, smoking status, and history of gastroesophageal reflux disease (GERD). Evaluation of GERD was conducted within 2 weeks prior to surgery. GERD was diagnosed by a gastroenterologist based on the patient’s response to proton pump inhibitor (PPI) medication and/or a Frequency Scale for Symptoms of GERD (FSSG) score $>8$ points.\textsuperscript{13}

### Data Extraction

We extracted the following sociodemographic and clinical information from the patient electronic medical records: age, sex, body mass index (BMI), preoperative intake of medicine for constipation, preoperative intake of NSAIDs/opioids, smoking status, and history of gastroesophageal reflux disease (GERD). Evaluation of GERD was conducted within 2 weeks prior to surgery. GERD was diagnosed by a gastroenterologist based on the patient’s response to proton pump inhibitor (PPI) medication and/or a Frequency Scale for Symptoms of GERD (FSSG) score $>8$ points.\textsuperscript{13}

## Table 1. Patient Characteristics.

| Category                                      | N = 144 |
|-----------------------------------------------|---------|
| Age, years                                    | 71 ± 7  |
| Female/male, n                                | 127/17  |
| LLIF, n (%)                                   | 97 (67%)|
| SRS osteotomy classification, n (%)           |         |
| Grade 1-2                                     | 88 (61%)|
| Grade 3-5                                     | 56 (39%)|
| Location of UIV, n (%)                        |         |
| Th9-11                                        | 117 (81.3%)|
| Th8 ~                                         | 27 (18.8%)|
| Bleeding, ml                                  | 996 ± 838|
| Duration of surgery, min                      | 457 ± 84|

Interval and ratio values represent the mean ± standard deviation. LLIF, lateral lumbar interbody fusion; SRS, Scoliosis Research Society; UIV, upper instrumented vertebra.

Patients were excluded if they had a history of abdominal surgery, a rounded back because of Parkinson’s disease and a diagnosis of adolescent idiopathic scoliosis. We included data from 144 consecutive patients who underwent spinal corrective surgery between April 2012 and March 2019, as performed by 3 board-certified spinal surgeons at a single institution.

If it was judged to be valid by pre-operative radiographic flexibility evaluations, as previously reported,\textsuperscript{12} the surgeons used an anterior approach to LLIF from L1–L2 or L2–L3 to the level of the L4-5 disc to obtain adequate coronal and sagittal global spine alignment in patients with ASD (Table 1). Subsequently each patient was placed in a prone position to undergo a posterior lumbar interbody fusion (PLIF) at the level of the L5-S1 disc, and the spinal kyphosis was corrected using a cantilever force with bilateral S1 screws and bilateral single or dual iliac screws. All surgeries with LLIF were performed as single-staged lateral-posterior combined surgeries. Where flexibility of spinal motion was lost, we performed a suitable osteotomy, which was classified as grade 1–6 by Scoliosis Research Society–Schwab criteria14 (Table 1).

All patients received intravenous patient-controlled analgesia with droperidol, fentanyl citrate and lidocaine; oral administration of non-steroidal anti-inflammatory drugs (NSAIDs) was added for postoperative pain management at the request of the patient.
Perioperative (within 30 days of surgery) medical complications were also collected (Supplemental Table), and included the following: infection (pneumonia, urinary tract infection, sepsis, and surgical site infection), cardiopulmonary complications (deep venous thrombosis, pulmonary embolism, myocardial infarction, arrhythmia, congestive heart failure, pneumothorax, atelectasis, adult respiratory distress syndrome, electrolyte imbalance), neurologic deficit, symptomatic spinal epidural hematoma, renal complications (acute renal failure with and without hemodialysis) and POI. Patients were identified as having POI if they exhibited at least 2 of the following: the presence of gastrointestinal symptoms or signs, such as anorexia, nausea, vomiting, failure to pass stool or flatus for 3 days, and abdominal distension or radiographic findings of paralytic ileus within 30 days after spinal surgery.

**Radiographic Measurements**

Radiographic data consisted of full-length lateral radiographs obtained preoperatively and 4–6 weeks postoperatively, with the patients in a freestanding posture and their fingers placed on their clavicles. On pre- and postoperative coronal radiographs, the Cobb angle (the angle between the superior endplate of the most tilted vertebra cranially and the inferior endplate of the most tilted vertebra caudally) was measured. The following sagittal radiographic parameters were measured pre- and postoperatively using a lateral view: T5–T12 thoracic kyphosis (TK); T10-L2 thoracolumbar kyphosis (TLK); T12–S1 lumbar lordosis (LL) angles; pelvic incidence (PI); PT; sacral slope (SS); SVA; T1 pelvic angle (TPA), which is the angle between the line from the center of the femoral heads to the center of S1 and the line from the femoral head to the center of T1; and global tilt (GT), which is the angle formed by the intersection of 2 lines, the first line drawn from the center of C7 to the center of the sacral endplate and the second line drawn from the center of the femoral heads to the center of the sacral endplate. Radiographic measurements were made by 2 board certified spine surgeons (TO [author 1] and HO [author 3]) to determine interobserver error. We applied the mean values of these measurements to the analyses that followed. The intraclass coefficient was 0.880, indicating that the inter-rater reliability was almost perfect. These authors had >10 years of experience in spinal surgery and were blinded to patient data before the measurements were made.

**Statistical Analyses**

We report mean ± standard deviation (SD) for continuous variables and number (percentage) for categorical variables. We performed a Student t or Fisher exact test when we compared means between 2 groups statistically, assuming normal distributions for continuous variables. We used Prism (version 7.0; GraphPad Software, La Jolla, CA) to calculate summary statistics and perform the t tests. Multinvariate logistic regression analyses were performed with R software, version 3.2.3, to evaluate the odds ratio (OR) with a 95% confidence interval (95% CI) for potential risk factors for POI. Statistical significance was set at P < 0.05.

**Results**

**Patient Population and Overall Complications**

We included 144 eligible patients in this study; 88% were female, and the mean age was 71.1 ± 7.1 years. LLIF was used in 67% of patients, grade 2 osteotomy was used in 61%, and grade 3-5 osteotomy was used in 39%. Mean bleeding was 996 ± 838 ml, and mean duration of surgery was 457 ± 84 min (Table 1). A summary of perioperative complications is shown in supplemental Table 1. POI developed in 25/144 (17.4%) patients and was the most frequent complication in the present study. Additionally, the incidence of non-POI complications was significantly higher in the POI (+) group compared to the POI (−) group (Figure 1).

**Comparison of Patients With and Without Postoperative Ileus**

As shown in Table 2, there were no significant differences between groups in age, sex, BMI, frequency of preoperative constipation, frequency of NSAID and/or opioid use, preoperative Cobb angle, estimated blood loss, frequency of osteotomy or the period from surgery to the start of ambulation. In contrast, the frequency of smoking, the frequency of GERD, the duration of surgery and the frequency of LLIF were significantly greater in the group with POI than in the group without POI (Table 2).

**Comparison of Spinopelvic Parameters With and Without Postoperative Ileus**

There were no significant differences between the groups for any of the preoperative spine radiographic parameters (Table 3). In contrast, only the change in TLK (ΔTLK) from before to after surgery was significantly larger in the group with POI.
Discussion

Among perioperative complications, POI was the most frequent complication after ASD surgery in the present study, and 2 patients required laparotomy because of intussusception and severe ileus (Supplemental Table). Additionally, we found that the development of POI might increase the incidence of secondary adverse events, such as deep vein thrombosis, pulmonary embolism, infectious complications and poor wound healing (Figure 1), as in previous reports.8,16 These results indicate that it has clinical significance to clarify the pathology of POI after spinal surgery for ASD. Actually, POI has been known as a relatively common complication after surgery that affects 3.5%–12% of patients undergoing all spinal procedures.10,17,18 In particular, ASD surgery has many risk factors that have been reported for POI development, such as use of an anterior approach, surgery in the prone position, scoliosis surgery and intraoperative opioid exposure.10,11,19-21 A recent study reported a high incidence (18.4%) of POI, and length of stay remains significantly longer in patients who develop POI after adult spinal surgery.22 However, there was insufficient evidence regarding the risk of development of POI after ASD surgery and the changes in spinal alignment caused by spinal corrective surgery.

Our multivariate analysis clarified that critical risk factors for POI after ASD surgery were LLIF and large changes in TLK value from before to after surgery were significantly associated with the development of POI (Table 4).

Risk Factors for Developing POI

A multivariate logistic regression analysis was conducted with parameters including age, sex, history of GERD, preoperative constipation, smoking status, duration of surgery, LLIF and TLK. Finally, the present study showed that male sex, LLIF and large changes in TLK value from before to after surgery were significantly associated with the development of POI (Table 4).

Table 2. Comparison of Patients With and Without Postoperative Ileus.

| Variables                        | Non-POI (n = 119) | POI (n = 25) | P value |
|----------------------------------|-------------------|-------------|---------|
| Age, years                       | 71.3 ± 7.3        | 72.3 ± 7.1  | NS      |
| Female/male, n                   | 107/12            | 19/6        | NS      |
| BMI, kg/m²                       | 24.0 ± 17.7       | 21.7 ± 2.6  | NS      |
| Preoperative constipation, n (%) | 52 (44)           | 14 (56)     | NS      |
| Preoperative NSAID/opioid use, n (%)| 65 (55)          | 12 (48)     | NS      |

Table 3. Comparison of Preoperative Spinopelvic Parameters in Patients With and Without Postoperative Ileus.

| Spinopelvic parameters | Non-POI (n = 119) | POI (n = 25) | P value |
|------------------------|-------------------|-------------|---------|
| TLK, °                 | 20.3 ± 18.9       | 27.5 ± 18.1 | NS      |
| TK, °                  | 25.9 ± 17.3       | 24.8 ± 17.8 | NS      |
| PT, °                  | 38.7 ± 10.5       | 35.3 ± 12.9 | NS      |
| SS, °                  | 15.1 ± 13.7       | 13.4 ± 13.3 | NS      |
| LL, °                  | 9.4 ± 22.2        | 5.1 ± 24.7  | NS      |
| SVA, mm                | 125 ± 71.8        | 130 ± 65.7  | NS      |
| GT, °                  | 54.2 ± 17.2       | 54.3 ± 21.1 | NS      |
| TPA, °                 | 42.7 ± 15.3       | 41.6 ± 14.5 | NS      |

Table 4. Multivariate Logistic Regression Analysis of Risk Factors for Developing Postoperative Ileus.

| Parameter                        | OR     | 95% CI    | P value |
|----------------------------------|--------|-----------|---------|
| Age                              | 1.029  | 0.955–1.114 | NS      |
| Female                           | 0.234  | 0.053–1.028 | <0.05   |
| History of GERD                  | 1.366  | 0.450–4.115 | NS      |
| Preoperative constipation         | 1.996  | 0.689–5.961 | NS      |
| Smoking (NSO/CS or FS), n        | 77/33  | 14/11     | NS      |
| Duration of surgery, min         | 466 ± 87.4 | 512 ± 81.2 | <0.05   |
| Estimated blood loss, ml         | 957.3 ± 818 | 1004 ± 631 | NS      |
| Use of LLIF, n (%)               | 75 (63) | 22 (88)   | <0.0001 |
| Use of osteotomy, G1-2/G3-5, n    | 73/46  | 16/9      | NS      |
| Period from surgery to the start of ambulation, days | 5.2 ± 1.2 | 5.7 ± 2.1 | NS      |
influence of surgical approach on developing POI. To our knowledge, this is the first study to show that alignment correction in the thoracolumbar curve during surgery was a risk factor for POI after ASD surgery. Recently, we reported that patients with ASD had a high frequency of GERD symptoms, and that TLK is a key spinal parameter involved in the pathology of GERD in patients with ASD.\textsuperscript{13,23} Considering these results, the thoracolumbar curve has significant effects on gastrointestinal function in patients with ASD. A limitation of the present study was that there was no consideration of the influence of postoperative narcotic medication on POI, because it was difficult to standardize the dose and frequency of postoperative narcotic medication. Involvement of POI pathogenesis caused by narcotic medication is well known, and recent studies have indicated that a decreasing incidence of POI after orthopedic surgery may be attributed to a reduction in postoperative narcotic use.\textsuperscript{24,25}

Conventional treatments for POI include nasogastric suction, prokinetic agents, early mobilization, early enteral feeding, and the use of less invasive surgical procedures.\textsuperscript{26} Unfortunately, insufficient evidence of the efficacy of individual conventional treatments has been reported.\textsuperscript{8} Further study is needed on how to prevent and/or treat POI. However, this study has a clinically significant result indicating that when patients with ASD have large TLK preoperatively, and it is determined that a large correction is needed, more attention might be paid to the occurrence of POI.

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References
1. Park HY, Ha KY, Kim YH, et al. Minimally invasive lateral lumbar interbody fusion for adult spinal deformity: clinical and radiological efficacy with minimum two years follow-up. Spine (Phila Pa 1976). 2018;43(14):E813-E821. doi:10.1097/brs.0000000000002507
2. Ohba T, Ebata S, Oba H, Koyama K, Yokomichi H, Haro H. Predictors of poor global alignment and proportion score after surgery for adult spinal deformity. Spine (Phila Pa 1976). 2019;44(19):E1136-e1143. doi:10.1097/brs.0000000000003086
3. Ohba H, Ebata S, Takahashi J, et al. Loss of pelvic incidence correction after long fusion using iliac screws for adult spinal deformity: cause and effect on clinical outcome. Spine (Phila Pa 1976). 2018. doi:10.1097/brs.0000000000002775
4. Tanaka N, Ebata S, Oda K, Oba H, Haro H, Ohba T. Predictors and clinical importance of postoperative coronal malalignment after surgery to correct adult spinal deformity. Clin Spine Surg. 2020;33(7):E337-E341. doi:10.1097/BSS.0000000000000947
5. Soroceanu A, Burton DC, Oren JH, et al. Medical complications after adult spinal deformity surgery: incidence, risk factors, and clinical impact. Spine (Phila Pa 1976). 2016;41(22):1718-1723. doi:10.1097/BRS.0000000000001636
6. Smith C, Lamba N, Ou Z, et al. The prevalence of complications associated with lumbar and thoracic spinal deformity surgery in the elderly population: a meta-analysis. J Spine Surg. 2019;5(2):223-235. doi:10.21037/jss.2019.03.06
7. Bragg D, El-Sharkawy AM, Psaltis E, Maxwell-Armstrong CA, Lobo DN. Postoperative ileus: recent developments in pathophysiology and management. Clin Nutr (Edinburgh, Scotland). 2015;34(3):367-376. doi:10.1016/j.clnu.2015.01.016
8. Kehlet H, Holte K. Review of postoperative ileus. Am J Surg. 2001;182(5A suppl):3S-10S. doi:10.1016/s0002-9610(01)00781-4
9. Lee TH, Lee JS, Hong SJ, et al. Risk factors for postoperative ileus following orthopedic surgery: the role of chronic constipation. J Neurogastroenterol Motil. 2015;21(1):121-125. doi:10.5056/jnm14077
10. Fineberg SJ, Nandyala SV, Kurd MF, et al. Incidence and risk factors for postoperative ileus following anterior, posterior, and circumferential lumbar fusion. Spine J. 2014;14(8):1680-1685. doi:10.1016/j.spinee.2013.10.015
11. Al Maaieh MA, Du JY, Aichmair A, et al. Multivariate analysis on risk factors for postoperative ileus after lateral lumbar interbody fusion. Spine (Phila Pa 1976). 2014;39(8):688-694. doi:10.1097/brs.000000000000238
12. Ohba T, Ebata S, Ikegami S Oba H, Haro H. Indications and limitations of minimally invasive lateral lumbar interbody fusion without osteotomy for adult spinal deformity. Eur Spine J. 2020;29(6):1362-1370. doi:10.1007/s00586-020-06352-4
13. Ohba T, Ebata S, Koyama K, Haro H. Prevalence and key radiographic spinal malalignment parameters that influence the risk for gastroesophageal reflux disease in patients treated surgically for adult spinal deformity. BMC Gastroenterol. 2018;18(1):8. doi:10.1186/s12876-018-0738-6
14. Ryan DJ, Protopsaltis TS, Ames CP, et al. T1 pelvic angle (TPA) effectively evaluates sagittal deformity and assesses radiographic surgical outcomes longitudinally. Spine (Phila Pa 1976). 2014;39(15):1203-1210. doi:10.1097/BRS.0000000000000382
15. Obeid I, Boissiere L, Yilgor C, et al. Global tilt: a single parameter incorporating spinal and pelvic sagittal parameters and least affected by patient positioning. Eur Spine J. 2016;25(11):3644-3649. doi:10.1007/s00586-016-4649-3
16. Artinyan A, Nunoo-Mensah JW, Balasubramaniam S, et al. Prolonged postoperative ileus-definition, risk factors, and predictors after surgery. World J Surg. 2008;32(7):1495-1500. doi:10.1007/s00268-008-9491-2
17. Durand WM, Ruddell JH, Eltorai AEM, et al. Ileus following adult spinal deformity surgery. *World Neurosurg*. 2018;116: e806-e813. doi:10.1016/j.wneu.2018.05.099
18. Daniels AH, Ritterman SA, Rubin LE. Paralytic ileus in the orthopaedic patient. *J Am Acad Orthop Surg*. 2015;23(6):365-372. doi: 10.5435/jaaos-d-14-00162
19. Gifford C, Minnema AJ, Baum J, et al. Development of a postoperative ileus risk assessment scale: identification of intraoperative opioid exposure as a significant predictor after spinal surgery. *J Neurosurg Spine*. 2019;31(5):1-8. doi:10.3171/2019.5.spine19365
20. Bureta C, Tominaga H, Yamamoto T, et al. Risk factors for postoperative ileus after scoliosis surgery. *Spine Surg Relat Res*. 2018;2(3):226-229. doi:10.22603/ssrr.2017-0057
21. Oh CH, Ji GY, Yoon SH, et al. Paralytic ileus and prophylactic gastrointestinal motility medication after spinal operation. *Yonsei Med J*. 2015;56(6):1627-1631. doi:10.3349/ymj.2015.56.6.1627
22. Wright AK, La Selva D, Nkrumah L, et al. Postoperative ileus: old and new observations on prevention and treatment in adult spinal deformity surgery. *World Neurosurg*. 2019;132:e618-e622. doi:10.1016/j.wneu.2019.08.062
23. Ohba T, Ebata S, Obata H, et al. Key radiographic parameters that influence the improvement of postoperative gastroesophageal reflux disease in patients treated surgically for adult spinal deformity with a minimum 2-year follow-up. *Spine (Phila Pa 1976)*. 2020. doi:10.1097/brs.0000000000003459
24. Behm B, Stollman N. Postoperative ileus: etiologies and interventions. *Clin Gastroenterol Hepatol*. 2003;1(2):71-80. doi:10.1053/cgh.2003.50012
25. Nguyen BH, Bono OJ, Bono JV. Decreasing incidence of postoperative ileus following total knee arthroplasty: a 17-year retrospective review of 38,007 knee replacements at one institution. *J Knee Surg*. 2020;33(8):750-753. doi:10.1055/s-0039-1684013
26. Waldhausen JH, Schirmer BD. The effect of ambulation on recovery from postoperative ileus. *Ann Surg*. 1990;212(6):671-677. doi:10.1097/00000658-199012000-00004