

## Favorable surgical treatment outcomes for chronic constipation with features of colonic pseudo-obstruction

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### Abstract

**AIM:** To determine long-term outcomes of surgical treatments for patients with constipation and features of colonic pseudo-obstruction.

**METHODS:** Consecutive 42 patients who underwent surgery for chronic constipation within the last 13 years were prospectively collected. We identified a subgroup with colonic pseudo-obstruction (CPO) features, with dilatation of the colon proximal to the narrowed transitional zone, in contrast to typical slow-transit constipation (STC), without any dilated colonic segments. The outcomes of surgical treatments for chronic constipation with features of CPO were analyzed and compared with outcomes for STC.

**RESULTS:** Of the 42 patients who underwent surgery for constipation, 33 patients had CPO with dilatation of the colon proximal to the narrowed transitional zone.

There were 16 males and 17 females with a mean age of  $51.2 \pm 16.1$  years. All had symptoms of chronic intestinal obstruction, including abdominal distension, pain, nausea, or vomiting, and the mean duration of symptoms was 67 mo (range: 6-252 mo). Preoperative defecation frequency was  $1.5 \pm 0.6$  times/wk (range: 1-2 times/wk). Thirty-two patients underwent total colectomy, and one patient underwent diverting transverse colostomy. There was no surgery-related mortality. Postoperative histologic examination showed hypoganglionosis or aganglionosis in 23 patients and hypoganglionosis combined with visceral neuropathy or myopathy in 10 patients. In contrast, histology of STC group revealed intestinal neuronal dysplasia type B ( $n = 6$ ) and visceral myopathy ( $n = 3$ ). Early postoperative complications developed in six patients with CPO; wound infection ( $n = 3$ ), paralytic ileus ( $n = 2$ ), and intraabdominal abscess ( $n = 1$ ). Defecation frequencies 3 mo after surgery improved to  $4.2 \pm 3.2$  times/d (range: 1-15 times/d). Long-term follow-up (median: 39.7 mo) was available in 32 patients; all patients had improvements in constipation symptoms, but two patients needed intermittent medication for management of diarrhea. All 32 patients had distinct improvements in constipation symptoms (with a mean bowel frequency of  $3.3 \pm 1.3$  times/d), social activities, and body mass index ( $20.5 \text{ kg/m}^2$  to  $22.1 \text{ kg/m}^2$ ) and were satisfied with the results of their surgical treatment. In comparison with nine patients who underwent colectomy for STC without colon dilatation, those in the CPO group had a lower incidence of small bowel obstructions (0% vs 55.6%,  $P < 0.01$ ) and less difficulty with long-distance travel (6.7% vs 66.7%,  $P = 0.007$ ) on long-term follow-up.

**CONCLUSION:** Chronic constipation patients with features of CPO caused by narrowed transitional zone in the left colon had favorable outcomes after total colectomy.

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**Key words:** Constipation; Total colectomy; Pseudo-obstruction; Surgical outcome; Hypoganglionosis

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## INTRODUCTION

Constipation is a common clinical problem with multiple etiologies, affecting approximately 16.5% of the population in South Korea<sup>[1]</sup> and 5%-20% of the Western world<sup>[2]</sup>. Most patients with constipation have various symptoms, representing different pathologic processes<sup>[3,4]</sup> and including infrequent or difficult evacuation, abdominal pain, and bloating, which are often resistant to medical therapy or dietary manipulation. Constipation is believed to be frequently observed in women, elderly people, and those of low socioeconomic status<sup>[5-7]</sup>. When chronic idiopathic constipation is diagnosed, a conservative treatment is generally conducted as a first-line treatment. If such a conservative treatment fails, surgical treatment is then considered<sup>[8-12]</sup>. The British surgeon Lane<sup>[13]</sup> first performed surgery for constipation in 1908. Since then, total colectomy (TC) with ileorectal anastomosis has been suggested as a standard option for the management of refractory chronic constipation. In our previous report, we demonstrated favorable surgical outcomes for patients with features of chronic pseudo-obstruction (CPO) with distinct transitional zone (TZ)<sup>[14]</sup>. The purpose of this study was to analyze the long-term surgical outcomes of patients with chronic idiopathic constipation and features of CPO, and compare these results with treatment of patients with slow-transit constipation (STC).

## MATERIALS AND METHODS

### Patients

Between 1998 and 2011, 47 consecutive patients with chronic intractable constipation underwent surgery by a single surgeon at the Department of Surgery, Seoul National University Hospital. Two patients were excluded from this study because they had secondary constipation due to amyloidosis, and three patients were excluded because they had Hirschsprung's disease (HD). The remaining 42 patients with chronic idiopathic constipation were enrolled in our study. All patients were subjected to a full history taking and physical examination. Prior to surgery, 40 (95.2%) patients were treated with various medications, such as bulking agents, stimulant laxa-

tives, and probiotics, specifically, 24 patients (57.1%) were treated with prokinetic agents (e.g., mosapride and itopride) and eight patients (19.0%) were treated with pyridostigmine. Suppositories or enemas were used in 40 patients (95.2%). Anorectal manometry and colon transit-time studies were selectively conducted as preoperative functional tests. Plain abdominal X-ray, abdominal computed tomography scan, and colonoscopy were selectively conducted when necessary. The preoperative and postoperative clinical symptoms, postoperative complications, defecation frequency after surgery, results of postoperative histologic examination, postoperative satisfaction, and postoperative activities were retrospectively analyzed by a medical chart review and phone survey. Postoperative satisfaction after surgery was divided into five grades: poor, unhappy, good/satisfied, improved, and very good, and was scored from 1 to 5 points. Surgery was considered successful if the score was 3 points or higher<sup>[15]</sup>.

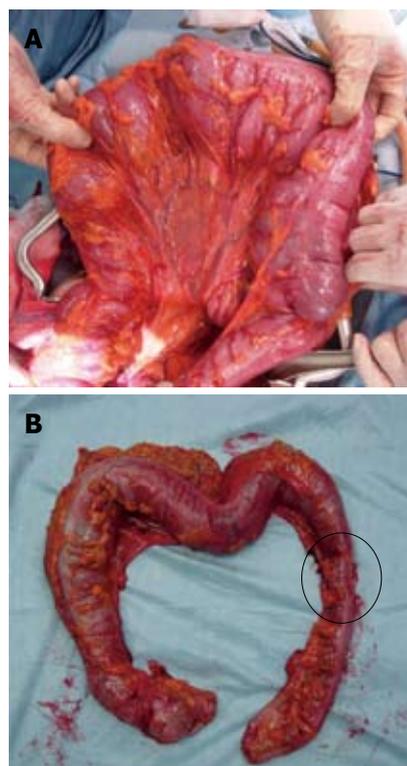
### Statistical analysis

Analysis were performed using the SPSS statistical software package (version 18.0; SPSS Inc, Chicago, IL). Comparisons were made between groups using the  $\chi^2$  and Mann-Whitney tests. *P* values of less than 0.05 were considered statistically significant.

## RESULTS

The patient group included 21 women and 21 men, with a mean age of  $51.2 \pm 16.1$  years (range: 18-75 years) and a median follow-up duration of 39.7 mo (range: 3-147 mo). Thirty-three patients (78.6%) presented with features of CPO with distinct TZ (the CPO group), whereas the remaining nine patients (21.4%) had STC without colon dilatation (the STC group; Figure 1). The preoperative characteristics of the CPO and STC groups are shown in Table 1. The patients complained of symptoms including abdominal pain, abdominal distension, vomiting, and weight loss before surgery. The mean duration of symptoms was  $67.1 \pm 72.8$  mo (range: 6-252 mo). Of the 42 patients, 26 (61.9%) experienced abdominal pain preoperatively, 21 (50.0%) complained of abdominal distention, and 15 (35.7%) experienced inadequate defecation. Nausea or vomiting was a chronic problem in six patients (14.3%), and three patients (7.1%) experienced weight loss preoperatively. Among the 42 patients, 40 patients (95.2%) received laxatives or enemas for treatment of chronic constipation. Three patients had a previous history of abdominal surgery in other hospitals; one patient underwent colostomy; one patient had ileostomy because of persistent intestinal obstruction after right hemicolectomy; and one patient underwent biopsy after exploration.

The surgical procedures performed in this study were as follows: 39 patients underwent TC with ileorectal anastomosis (92.9%); two patients underwent TC with end ileostomy (4.8%); and one patient underwent



**Figure 1** Operative findings and colectomy specimen from a 70-year-old female with chronic constipation. A: Operative findings; B: Colectomy specimen. A definite transitional zone (marked with a circle) with proximal dilatation and distal collapse can be seen.

transverse colostomy (2.3%). The patient who underwent transverse colostomy instead of TC was initially treated for severe bowel distension but refused further surgery. In 13 patients (30.9%), emergency surgery was performed because of impending perforation or toxic symptoms such as tachycardia, fever, hypotension, and marked dilatation of both the small intestine and colon.

In the entire CPO group, intraoperative findings manifested as marked colonic dilatation proximally within the TZ and a normal or collapsed distal bowel lumen. The location of the TZ was near the left side of the descending colon in 20 patients (60.6%) and of the sigmoid colon in nine patients (27.3%) patients; four patients (12.1%) had TZ in the distal transverse colon.

Postoperative histologic examination in the CPO group showed hypoganglionosis (HG) or agangliosis (AG) in 23 patients, and HG combined with visceral neuropathy or myopathy in 10 patients. In contrast, histology in STC group revealed visceral neuropathy [intestinal neuronal dysplasia (IND) type B,  $n = 6$ ] and visceral myopathy ( $n = 3$ ) (Table 2).

Postoperative results are shown in Table 1. The patients in the CPO group passed the first flatus significantly earlier than did patients in the STC group, and their hospital stay tended to be shorter. Early postoperative complications developed in seven patients (16.7%): paralytic ileus ( $n = 3$ ), wound infection ( $n = 3$ ), and intraabdominal abscess ( $n = 1$ ). The incidence of early postoperative complications did not differ significantly

**Table 1** Preoperative clinical characteristics and postoperative results of patients with constipation

	CPO ( $n = 33$ )	STC ( $n = 9$ )	<i>P</i> value	
Preoperative clinical characteristics				
Sex (male/female)	21/21	16/17	5/4	0.43
Age (yr)	51.2 ± 16.1	50.7 ± 16.2	53.2 ± 16.6	0.23
Constipation duration (mo)	67.1 ± 72.8	38.3 ± 49.4	69.7 ± 75.1	0.34
Defecation frequency (times/wk)	1.6 ± 0.5	1.5 ± 0.3	1.6 ± 0.6	0.15
Postoperative results				
Gas passing (d)	4.2 ± 1.5	4.1 ± 1.0	5.1 ± 0.8	< 0.01
Postoperative hospital stay (d)	11.4 ± 4.7	10.7 ± 4.9	13.3 ± 3.2	0.07
Defecation frequency (times/d) at 3 mo postop	5.1 ± 3.6	4.2 ± 3.2	5.2 ± 3.1	0.56

CPO: Colonic pseudo-obstruction; STC: Slow-transit constipation.

**Table 2** Results of histologic examination in two groups

	CPO ( $n = 33$ )	STC ( $n = 9$ )
Hypogangliosis or agangliosis	23	0
Hypogangliosis with neuropathy or myopathy	10	0
Visceral neuropathy	0	6
Visceral myopathy	0	3

CPO: Colonic pseudo-obstruction; STC: Slow-transit constipation.

**Table 3** Early and late postoperative complications

Complications	CPO	STC	<i>P</i> value
Early complications ( $n = 7$ )			
Wound infection	3	0	0.47
Ileus	1	2	0.33
Intra-abdominal abscess	1	0	0.78
Late complications ( $n = 10$ )			
Small-bowel obstruction	0	5	< 0.01
Diarrhea	2	2	0.15

CPO: Colonic pseudo-obstruction; STC: Slow-transit constipation.

between the CPO and STC groups (Table 3). All of these early complications resolved after conservative care, and there was neither anastomotic leakage nor mortality.

In long-term follow-up (median: 40 mo), recurrent small bowel obstruction requiring hospitalization occurred in five patients (11.9%). The incidence of small bowel obstruction was significantly higher in the STC group (0% in CPO *vs* 55.6% in STC,  $P < 0.01$ ), and all patients in whom small bowel obstruction occurred had pathologic features of IND type B. These five patients in the STC group responded to conservative management. Postoperative diarrhea requiring intermittent medication occurred in four patients (9.5%); two in the CPO group and two in the STC group).

Preoperatively, the mean defecation frequency was 1.6 times/wk. The defecation frequencies were  $1.5 \pm 0.3$  times/wk (range: 1-2 times/wk) and  $1.6 \pm 0.6$  times/wk (range: 1-2 times/wk) in the CPO and STC groups, respectively (Table 1). At 3 mo after surgery, defecation

**Table 4** Quality of life scoring (questionnaire) and postoperative satisfaction *n* (%)

Scores	Quality of life scoring	CPO	STC
1	Poor	0 (0)	0 (0)
2	Unhappy	0 (0)	1 (11.1)
3	Good/satisfied	5 (15.6)	2 (22.2)
4	Improved	25 (78.1)	5 (55.6)
5	Very good	2 (6.3)	1 (11.1)
Scores of $\geq 3$		32/32 (100)	8/9 (89)

CPO: Colonic pseudo-obstruction; STC: Slow-transit constipation.

frequency increased in both groups (Table 1) but did not differ significantly between the two groups ( $P = 0.56$ ).

Informed consent for the questionnaire on satisfaction and quality of life after surgery was received from 41 of the 42 patients (97.6%) who were alive at the time of the review. Overall, 97.6% of the patients (40/41) were satisfied with the results of their surgery (Table 4). All 32 patients in the CPO group responded that they were satisfied with the results of the surgery. In comparison, one patient in the STC group gave 2 points and was not satisfied with the surgery because she had treatments for intermittent obstructive symptoms. Thirty-three patients (80.5%) indicated that they had no problems in their daily or leisure activities, housework, travel, and social activities. However, eight patients (19.5%) complained of difficulty with long-distance travel because of increased bowel frequency. In the CPO group, only two patients (6.7%) had difficulty with long-distance travel in contrast to six patients (66.7%) in the STC group ( $P = 0.007$ ). Body mass index increased from 20.5 kg/m<sup>2</sup> to 22.1 kg/m<sup>2</sup> in the CPO group, and from 19.9 kg/m<sup>2</sup> to 22.0 kg/m<sup>2</sup> in the STC group, which did not significantly differ between the two groups.

## DISCUSSION

Surgical treatment may be considered in patients with intractable constipation who are poorly responsive to conventional medical treatments. TC with ileorectal anastomosis is the most commonly performed surgical procedure for constipation<sup>[16-18]</sup>. The reasons for primarily performing TC in patients with chronic constipation are that it is difficult to precisely distinguish between normal bowel segments and pathologic lesions and that symptoms may recur if segmental resection alone is performed<sup>[19-21]</sup>. In our series of patients, one of the patients in CPO group had undergone right hemicolectomy at another hospital for chronic constipation as well as two more operations because of persistent symptoms within the previous 2 years. Subsequently, the patient visited our hospital and underwent TC. As a result, the patient enjoys good nutritional status without any evidence of recurrence to date. This case illustrates the importance of appropriate resection with pathologic lesions, using TC as a favorable example.

When evaluating the results of surgical treatments

for chronic constipation, it is important to assess patient satisfaction after surgical treatment, complications, and improvement in quality of life. All the patients in this study experienced difficulty in their daily lives due to symptoms of intestinal obstruction preoperatively. In severe cases, these symptoms prevented the patient from sufficient nutritional intake. However, almost all of the patients were satisfied with their surgery and had no problems in their daily lives afterwards.

Our study suggests that defecation frequency improved significantly after surgery. Postoperative diarrhea, when it occurred, was present for only a short time and did not require long-term therapy. Constipation symptoms in the preoperative period, such as abdominal distention or pain, disappeared in both groups. There were no serious early postoperative complications and late complications, especially recurrent small bowel obstruction, were more common in the STC group. All five patients with small bowel obstruction had pathologic findings of IND type B and were successfully managed with conservative therapy. In the STC group of patients with pathologic features of IND type B, the pathology may not be localized to the colon; thus, the possibility of small bowel involvement exists. This may account for intestinal obstructions after the surgery in the STC group of patients with IND type B pathology. None of the three patients with visceral myopathy in the STC group had a small bowel obstruction episode. On the other hand, pathologic changes of AG or HG associated with features of CPO are limited to a relatively short segment of the colon and probably account for the low rate of small bowel obstruction after TC.

HG, a disease associated with a limited number of intestinal ganglion cells, is an intestinal neuronal dysganglionosis arising in the gastrointestinal tract<sup>[17]</sup>. HG is typified by a decreased number of ganglion cells, a reduced size of ganglia, and a wider distance between myenteric ganglia. The diagnostic criteria used for diagnosis of HG and IND type B have been previously discussed<sup>[14]</sup>. IND type B has also been described as one of the causes of chronic idiopathic constipation<sup>[22]</sup>. In the CPO group, HG and AG were confined to a short segment of the colon in most patients, resulting in a failure of segment relaxation and dilatation of the proximal colon, as is the case for HD in which the region of the colon proximal to the aganglionic segment becomes dilated. Segmental HG or AG may be considered a variant of HD. A finding similar to our study was recently described by Do *et al.*<sup>[23]</sup> in which the term adult-onset HD was used. However, clinically, radiologically, and histologically, there may be differences<sup>[24,25]</sup>. Clinically, HG shows later symptom onset and a better prognosis than HD. In addition, in abdominal computed tomography and barium enema studies, TZ ratio (the transverse diameter ratio of the most dilated colonic segment proximal to the TZ to the narrowed colonic segment distal to the TZ) was higher in HD than in HG<sup>[26]</sup>. Since our patients had symptom onset during adulthood, we suggest that our

patients with features of CPO have an acquired form of AG or HG, in contrast to typical HD, which manifests in early childhood. Additionally, various mechanisms for ganglion cell loss have been described<sup>[27-32]</sup>, and acquired loss of myenteric nerves may occur secondary to Chagas disease, multiple sclerosis, scleroderma, diabetes, amyloid disease, advanced malignancy, Crohn's disease, and in response to certain medications<sup>[8,33]</sup>.

In our STC patients, since there was no TZ, pathologic examinations were performed at random sites throughout the colon, thus reflecting the diffuse nature of the pathologic changes. As such, it is assumed that the CPO patients in our study have a zonal pathology that is responsible for their constipation compared to the diffuse pathologic changes observed in the STC patients. The persistent abdominal symptoms that include small bowel obstruction episodes after surgery may result from diffuse neurologic abnormalities of the gastrointestinal tract in IND type B patients. In the case of gastrointestinal dysmotility involving the small bowel, a careful approach is required for selecting surgical treatment because the role of surgery may be limited and recurrence is possible<sup>[34,35]</sup>.

In our study, the CPO group had better early postoperative results regarding gas passing and shortened hospital stays compared to the STC group. On long-term follow-up, all of the CPO patients had distinct improvements in constipation symptoms and were satisfied with the results of their surgical treatment. In comparison with the STC group, the CPO group had a lower incidence of small bowel obstructions and fewer difficulties with long-distance travel on long-term follow-up.

CPO in patients with chronic constipation is characterized by a narrowed TZ in the left side of the colon. Its pathologic features suggest that CPO is caused by acquired segmental HG or AG. Pathologic findings in the CPO group were quite different from patients in the STC group without a dilated colon, and the CPO group had outcomes that were more favorable after TC compared to those of STC patients.

## COMMENTS

### Background

Constipation is a common clinical problem with multiple etiologies and affects. When chronic idiopathic constipation is diagnosed, a conservative treatment is conducted as the first line treatment. If the conservative treatment has failed, surgical treatment is then considered

### Research frontiers

Because of diagnostic difficulty, hypoganglionosis (HG) is often considered to be a variant of Hirschsprung's disease (HD) or a subtype of intestinal neuronal dysplasia type B. But clinically, radiologically and histologically, there are differences between them. Clinically, HG shows later onset of symptoms and a better prognosis than HD. In abdominal computed tomography and barium enema studies, transition zone ratio (the transverse diameter ratio of the most dilated colonic segment proximal to the transitional zone (TZ) to the narrowed colonic segment distal to the TZ) is higher in HD than in HG.

### Innovations and breakthroughs

In the series of patients operated for intractable constipation, patients were divided into two groups; features of chronic pseudo-obstruction (CPO) with distinct transitional zone and slow-transit constipation (STC) without colonic dilata-

tion. Authors suggested that CPO group had more favorable outcome after total colectomy as compared to STC patients.

### Applications

By understanding pathophysiology of CPO, this study may represent a future strategy for surgical procedure in the treatment of patients with chronic idiopathic constipation.

### Terminology

HG has been associated with fewer intestinal ganglion cells. HG is one of an intestinal neuronal dysganglionosis arising in the gastrointestinal tract.

### Peer review

The authors provide evidence that patients with chronic constipation with CPO do have a better outcome from surgical resection than patients with slow transit dysmotility. Distinguishing the two groups of patients is not difficult and the article suggests that if CPO is identified with a normal caliber distal colon, that these patients have better outcome. While that authors suggest the aganglionosis in this segment of bowel is acquired, others believe that this disease is still a variant of HD. Nevertheless, it seems reasonable that such patients tend to have better outcomes with surgery than patients who have dysmotility.

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