ORIGINAL ARTICLE
Gastroenterology & Hepatology

JKMS

http://dx.doi.org/10.3346/jkms.2014.29.5.699 • J Korean Med Sci 2014; 29: 699-703

The Clinical Characteristics of Colonic Pseudo-obstruction and the Factors Associated with Medical Treatment Response: A Study Based on a Multicenter Database in Korea

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Received: 10 November 2013
Accepted: 26 February 2014

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This study was supported by 2011 KSNM (Korean Society of Neurogastroenterology and Motility) research funding.

Colonic pseudo-obstruction (CPO) is defined as marked colonic distension in the absence of mechanical obstruction. We aimed to investigate the clinical characteristics of CPO and the factors associated with the response to medical treatment by using a multicenter database in Korea. CPO was diagnosed as colonic dilatation without mechanical obstruction by using radiologic and/or endoscopic examinations. Acute CPO occurring in the postoperative period in surgical patients or as a response to an acute illness was excluded. CPO cases were identified in 15 tertiary referral hospitals between 2000 and 2011. The patients' data were retrospectively reviewed and analyzed. In total, 104 patients (53 men; mean age at diagnosis, 47 yr) were identified. Seventy-seven of 104 patients (74%) showed a transition zone on abdominal computed tomography. Sixty of 104 patients (58%) showed poor responses to medical treatment and underwent surgery at the mean follow-up of 7.4 months (0.5-61 months). Younger age at the time of diagnosis, abdominal distension as a chief complaint, and greater cecal diameter were independently associated with the poor responses to medical treatment. These may be risk factors for a poor response to medical treatment.

Keywords: Colonic Pseudo-obstruction; Abdominal Distension; Colonic Dilatation; Transition Zone

INTRODUCTION

Intestinal pseudo-obstruction is defined as marked intestinal distension in the absence of mechanical obstruction. Likewise, colonic pseudo-obstruction (CPO) is defined as marked colonic distension in the absence of mechanical obstruction. CPO may be either acute or chronic. Acute CPO is called Ogilvie's syndrome. It occurs in the postoperative period in surgical patients or as a response to an acute illness. Chronic CPO showing a relapsing and remitting pattern is rare. The pathogenesis, clinical manifestations, response to medical treatment, and prognosis of chronic CPO have not been fully elucidated (1, 2). Since most previous reports consist of a small number of case series, information on this disease is limited. CPO is known to mimic mechanical bowel obstruction without evidence of lesions occluding the bowel lumen (1, 2). There is confusion regarding the terms used for the disease, including CPO, Ogilvie's syndrome, false colonic obstruction, adult megacolon, functional obstruction, and idiopathic large bowel obstruction (3). CPO is usually treated conservatively; if that fails, pharmacologic treatment and colonic decompression are used. However, considerable numbers of patients with CPO, except those with an acute form occurring in the postoperative period or as a response to an acute illness, are presumed to follow the chronically recurrent course and require repeated interventions or surgery. However, clinical knowledge about CPO is mainly based on a small number of case series from the western countries (1-4). To our knowledge, CPO data from Asian countries are lacking.

Thus, in the present study, we aimed to investigate the clinical characteristics of CPO and the factors associated with the response to medical treatment by using a multicenter

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pISSN 1011-8934
eISSN 1598-6357

database in Korea.

MATERIALS AND METHODS

Identification of patients with CPO

Patients diagnosed with CPO in 15 tertiary referral hospitals between 2000 and 2011 were identified. CPO was defined as marked colonic distension in the absence of mechanical obstruction and diagnosed based on clinical, radiological, and/or endoscopic findings. Acute CPO occurring in the postoperative period in surgical patients or as a response to an acute illness was excluded. Abdominal radiographs showed a dilated large bowel. All patients underwent abdominal computed tomography (CT) on admission. Colonoscopy was performed to exclude mechanical obstruction or to decompress the dilated colon. The medical records were retrospectively reviewed for the demographic features, clinical symptoms, imaging studies performed, the response to medical treatment, and follow-up results.

CT evaluation

The presence or absence of a transition zone between the dilated and collapsed colon was determined on the CT images taken at the first admission. Transition zone was defined as the junction between the dilated and non-dilated colon, showing abrupt change in the colon diameter. The presence and location of the transition zone were evaluated. The diameters of the cecum and mid-transverse colon were measured with electronic calipers as the longest diameter on axial or coronal images. The diameter of the colon is different according to the segments. Accordingly, it seems to be rational that the degree of dilation should be compared in the same segment of the colon. In the present study, the diameters of the cecum and mid-transverse colon were compared between patients. The CT findings were evaluated by experienced gastrointestinal radiologists.

The response to medical treatment

Conservative treatment included diet restriction, nasogastric tube insertion, and intravenous fluid and electrolyte supplements. Laxatives and prokinetics were used as pharmacologic treatment. If needed, enema fluid was infused in the rectum, and colonoscopic decompression was performed. Non-responders were defined as patients with no improvement of bowel symptoms and bowel dilation after medical treatment, which were followed by surgical treatment.

Evaluation of myenteric ganglion cells

Pathological reports were obtained from each hospital. Data on the change of ganglion cells in the myenteric plexus were available in 36 out of 60 patients who underwent surgery. Myenteric ganglion cells were evaluated using hematoxylin and eosin (H&E). Ganglion cells characterized by large vesicular nuclei with prominent nucleoli and abundant amphiphilic granular cytoplasm were counted in the myenteric plexus.

Statistical analysis

All data were expressed as means ± standard deviations (SDs). Numeric and non-numeric parameters were compared between groups by using the Student's t-test and the chi-square test or Fisher's exact test, respectively. P values < 0.05 were considered statistically significant. The parameters that were significantly different in a univariate analysis were included in a multivariate logistic regression analysis. Statistical analysis was performed by using the SPSS statistical software version 14.0 (SPSS Inc., Chicago, IL, USA).

Ethics statement

This study was approved by the institutional review board of Ajou University Hospital (MED-MDB-11-286). The institutional review board of each participating hospital approved the treatment protocol before the initiation of investigation. Informed consent was not obtained because this study was performed by retrospective review of medical records.

RESULTS

Demographic and clinical characteristics

In total, 104 patients (53 men and 51 women) in 15 hospitals were identified. The mean age at diagnosis was 47 ± 17 yr (Range; 12-80 yr). The chief complaints at diagnosis were constipation (37%), abdominal pain (35%), abdominal distension (23%), nausea/vomiting (4%), dyspnea (1%), and diarrhea (1%). When the duration of constipation was 6 months or longer, chronic constipation was diagnosed. A history of chronic constipation was found in 31 of 104 patients (30%). The mean duration of chronic constipation was 4.5 ± 5.0 yr (range; 0.5-20 yr).

Radiological findings

Fig. 1 shows the radiological findings of a patient with CPO. The air-fluid levels were shown on simple abdominal radiographs or CT in all patients. The mean diameters of the cecum and mid-transverse colon at the first admission were 6.0 ± 2.6 cm (range, 1.9-15 cm) and 7.4 ± 2.5 cm (range, 2.6-15 cm), respectively. The small bowel was dilated in 21 patients (20%). The transition zone was observed in 77 patients (74%); 28 in sigmoid colon, 24 in descending colon, 16 in splenic flexure, and 9 in transverse colon. Twenty-seven patients (26%) did not show any transitional zone.

The response to medical treatment

Sixty of 104 patients (58%) were refractory to medical treatment. They finally underwent surgery at the mean follow-up of 7.4 months (0.5-61 months); total colectomy in 38 patients (63%), sub-

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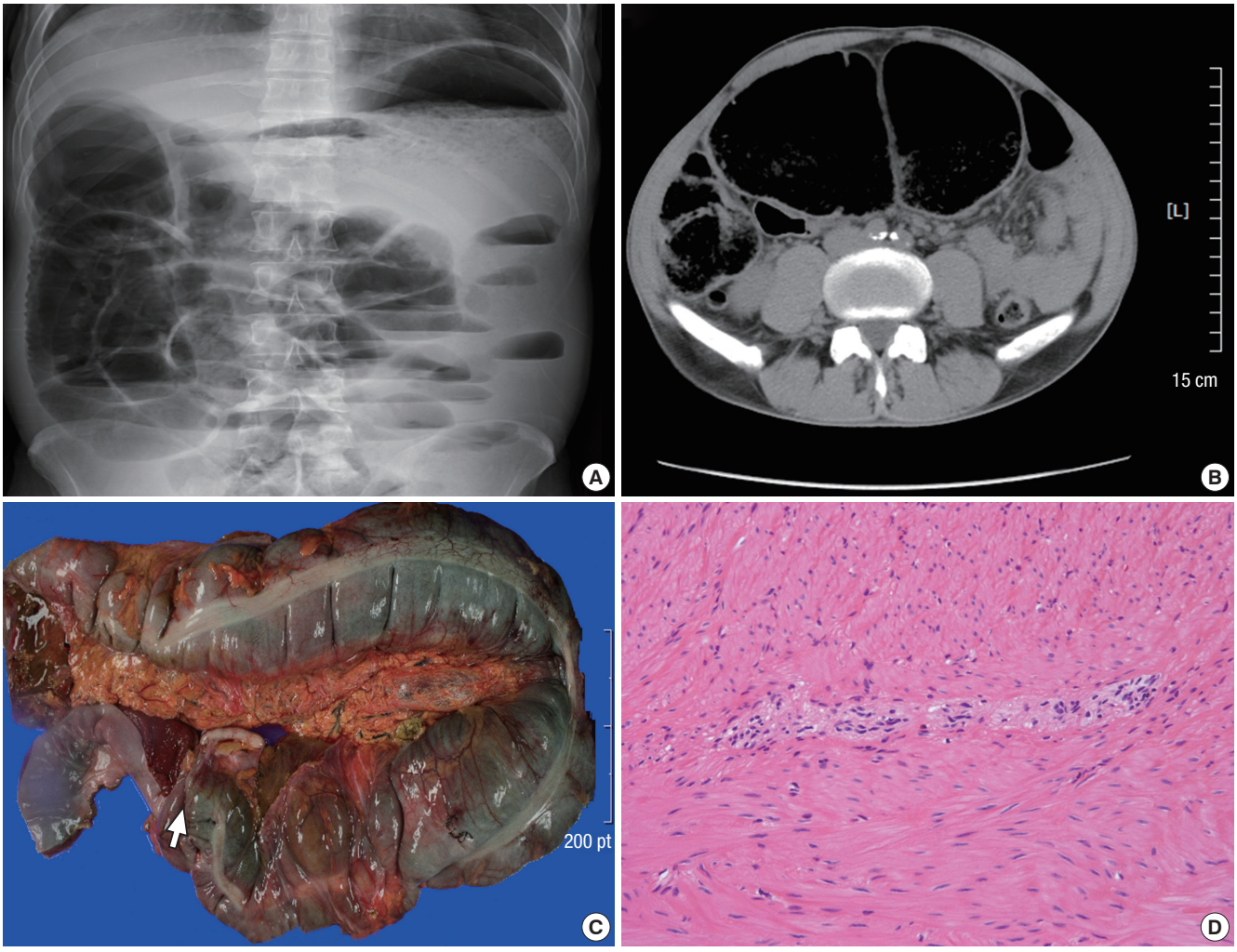

Fig. 1. An example of CPO associated with neuropathy. Simple abdominal radiograph (**A**) and computed tomography (**B**) reveal a dilated transverse colon without definite mechanical obstruction. On surgical specimens, the dilated and non-dilated colonic segments with a transition zone (arrow) are observed (**C**), and ganglion cells are not identified in the myenteric plexus by hematoxylin and eosin staining (×200) (**D**).

total colectomy in 11 patients (18%), hemicolectomy in 7 patients (12%), and colostomy in 4 patients (7%). In the univariate analysis between patients who were not responsive and those who were responsive to medical treatment, there were significant differences in the mean age at the time of diagnosis (42 ± 15 yr vs 53 ± 17 yr, $P = 0.001$) (Fig. 2), the proportion of women (60% vs 34%, $P = 0.009$), abdominal distension as a chief complaint (33% vs 9%, $P = 0.004$) (Fig. 3), the presence of a transition zone (83% vs 61%, $P = 0.012$) and cecal diameter on abdominal CT (6.7 ± 2.8 cm vs 5.1 ± 1.9 cm, $P = 0.005$) (Table 1). When the multivariate logistic regression analysis was conducted, younger age at the time of diagnosis, abdominal distension as a chief complaint, and greater cecal diameter were independently associated with the poor responsiveness to medical treatment (Table 2).

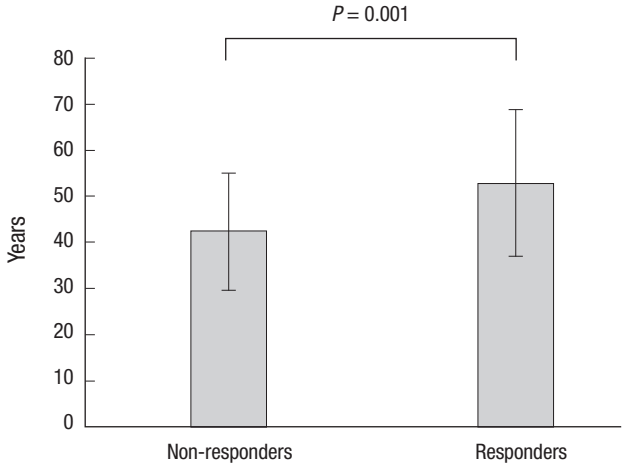

Fig. 2. Comparison of age between non-responders and responders. There is a significant difference in the mean age at the time of diagnosis between patients who were not responsive and those who were responsive to medical treatment (42±15 yr vs 53±17 yr, $P = 0.001$).

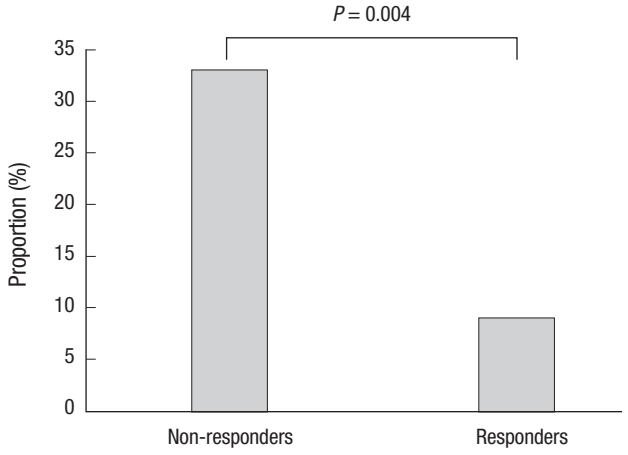

Fig. 3. The presence of abdominal distension as a chief compliant in non-responders and responders. There is a significant difference in the proportion of abdominal distension as a chief complaint between patients who were not responsive and those who were responsive to medical treatment (33% vs 9%, $P = 0.004$).

Table 1. Comparisons between patients who responded and those who did not respond to medical treatment

Parameters	Non-responders (n = 60)	Responders (n = 44)	*P* value
Age at diagnosis (yr)	42 ± 15	53 ± 17	0.001
Female gender	36 (60%)	15 (34%)	0.009
Chief complaints			0.001
Constipation	24 (40%)	14 (32%)	0.392
Abdominal distension	20 (33%)	4 (9%)	0.004
Abdominal pain	13 (22%)	23 (52%)	0.001
Nausea/vomiting	2 (3%)	2 (4%)	
Dyspnea	0 (0%)	1 (2%)	
Diarrhea	1 (2%)	0 (0%)	
History of chronic constipation	22 (37%)	9 (20%)	0.074
Small bowel dilation (No., %)	14 (23)	7 (16)	0.508
Transition zone (No., %)	50 (83)	27 (61)	0.012
Cecal diameter (cm)	7.3 ± 2.4	5.4 ± 2.5	0.001
Transverse colon diameter (cm)	7.2 ± 2.6	7.7 ± 2.4	0.368

Table 2. Logistic regression analysis for poor responsiveness to medical treatment

Parameters	Odds ratio	95% confidence interval	*P* value
Age at diagnosis	1.050	1.013-1.089	0.008
Female gender	2.153	0.716-6.471	0.172
Abdominal distension	4.256	1.299-13.947	0.017
Transition zone (+)	2.346	0.496-11.104	0.282
Cecal diameter (cm)	1.307	1.036-1.647	0.024

Pathological findings

Pathological reports including evaluation of ganglion cells in the myenteric plexus were available in 36 out of 60 patients who underwent surgery. Neuropathy showing hypoganglionosis or aganglionosis in the myenteric plexus was observed in 32 patients (89%).

DISCUSSION

CPO can be either acute or chronic. Acute CPO known as Ogilvie's syndrome is the most common intestinal pseudo-obstruction and was excluded from the present study. CPO that appears in either idiopathic or chronic disorders is a rare and heterogeneous clinical syndrome. Our findings revealed that 60 of 104 patients (58%) were refractory to medical treatment and finally underwent surgery at a mean follow-up of 7.4 months. Furthermore, younger age at the time of diagnosis, abdominal distension as a chief complaint, and greater cecal diameter were independently associated with poor responsiveness to medical treatment. Since CPO is a rare motility disorder, data on its response to conventional medical treatment are lacking. Particularly, reports of patients with CPO from Asian countries are very limited.

A considerable proportion of the patients with CPO (70%) in the present study did not have a previous history of chronic constipation. These patients are most likely to have acquired idiopathic CPO. Acquired chronic intestinal pseudo-obstruction is associated with hypoganglionosis or aganglionosis (5). Idiopathic CPO occurs as a consequence of a primary abnormality of the gut such as a visceral myopathy or neuropathy. In the present study, the majority of the patients who underwent surgery had neuropathy showing hypoganglionosis or aganglionosis in the myenteric plexus. In fact, pathologic examinations of the surgical specimens show hypoganglionosis or intramural ganglionic damage in cases of chronic CPO (5, 6). Congenital chronic intestinal pseudo-obstruction is classified into more diverse etiological phenotypes including aganglionosis, hypoganglionosis, degenerative neuropathy, muscularis propria malformations, or degenerative leiomyopathy (5). Of the 104 patients with CPO, 31 patients (30%) had a history of chronic constipation. Slow transit constipation may be associated with CPO in these patients. Hypoganglionosis, lymphocytic ganglionitis, abnormal neurochemical coding, and abnormal interstitial cells of Cajal networks can play a role in the pathogenesis of CPO associated with slow transit constipation (5). Hypoganglionosis with a focally narrowed transition zone in adult patients has been reported, particularly from Korea (6, 7). In the present study, the majority of our patients with CPO (74%) had a transition zone. CPO is known to be characterized by a narrowed transition zone in the left side of the colon. The presence of transition zones can be used to differentiate CPO from paralytic ileus. There are fewer ganglion cells in the transition zone than in the proximal dilated colon (8). The myogenic contractions in the transition zone and the generation of Ca^{++} waves underlying contractions of longitudinal muscle and circular muscle have been studied in an aganglionic mouse model (9). Reduced neuronal nitric oxide synthase expression associated with impaired nitric oxide production may also play a role in generating pseudo-obstruction.

Conservative treatments for CPO include the insertion of a nasogastric tube with suction, enemas, and prokinetic agents.

http://dx.doi.org/10.3346/jkms.2014.29.5.699

The cecal diameter on abdominal CT influences the decision to perform colonic decompression. Acute pseudo-obstruction is a transient reversible form that occurs in severe medical illness and major surgical procedures (10, 11). However, the chronic form usually recurs or persists. The chronic form is presumed to be less responsive to medical treatment. In the present study, 60 of 104 patients (58%) were refractory to medical treatment. Finally, they underwent surgical treatment. Subtotal colectomy can provide symptomatic relief to patients with CPO (12, 13). Favorable outcomes after total colectomy were reported in CPO patients with a narrowed transitional zone in the left colon (13). The majority of the patients who were poorly responsive to medical treatments underwent total or subtotal colectomy (81%). The multivariate analysis demonstrated that younger age at the time of diagnosis, abdominal distension as a chief complaint, and greater cecal diameter were independently associated with the poor responsiveness to medical treatment. Since the pathogenesis of CPO is not completely understood, the reason why younger age is a risk factor for poor responsiveness to medical treatment cannot be clearly explained yet. The age-related differences in the clinical and pathological findings of CPO warrant further investigation. Abdominal distension as a chief complaint and greater cecal diameter are likely to indicate the more severe form of CPO.

This study has some limitations. First, the study design was based on a retrospective review of medical records. Because of this retrospective nature, the medical treatments were not standardized. However, the decision to surgically treat the patients was made after a period of medical treatment in all patients. Since the patients' data were collected from multiple hospitals, the timing of surgical treatment may have differed from hospital to hospital. Secondly, the evaluation of myenteric ganglion cells was based on the pathologic reports from each hospital. Thus, the methodology of pathologic examinations may not be standardized.

In conclusion, considerable numbers of CPO patients need surgical treatment. Younger age at the time of diagnosis, a chief complaint of abdominal distension, and greater cecal diameter are risk factors for a poor response to medical treatment. A prospective study in a larger number of patients is warranted.

DISCLOSURE

The authors have no conflicts of interest to disclose.

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