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The role of CT in predicting the need for surgery in patients diagnosed with mesenteric phlebosclerosis

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Abstract

To determine if imaging findings on computed tomography (CT) can predict the need of surgery in patients with idiopathic mesenteric phlebosclerosis (IMP).

This retrospective study included 28 patients with IMP. Abdominal CT images were reviewed to determine the extent and severity of mesenteric calcifications and the presence of findings related to colitides. We compared the number of colonic segments with mesenteric venous calcification, a total calcification score, and the rate of colonic wall thickening, pericolic fat stranding, and bowel loop dilatation between patients undergoing surgery (surgery group) and patients without surgery (nonsurgery group). Comparisons were made using the Mann–Whitney *U* test and Fisher exact test. Receiver operating characteristic analysis was also performed. Inter-reader agreement for the calcification scores was analyzed using kappa statistics.

The number of colonic segments with mesenteric venous calcification and the total calcification scores were both significantly higher in the surgery group than the nonsurgery group (4.33 vs 2.96, $P=0.003$; and 15.00 vs 8.96, $P<0.001$). The areas under the receiver operating characteristics to identify patients who need surgery were 0.96 and 0.92, respectively. The prevalence of bowel loop dilatation in the surgery group was also significantly higher than that in the nonsurgery group (16% vs 100%, $P=0.011$).

Evaluation of the severity and extent of IMP based on the total mesenteric venous calcification score, number of involved colonic segments, and the presence bowel loop dilatation on CT may be useful to indicate the outcomes of conservative treatment and need for surgery.

Abbreviations: CT = computed tomography, IMP = idiopathic mesenteric phlebosclerosis.

Keywords: calcification score, computed tomography, mesenteric phlebosclerosis, surgery

1. Introduction

Idiopathic mesenteric phlebosclerosis (IMP) refers to the non-thrombotic stenosis and/or occlusion of mesenteric veins that may cause chronic ischemic colitis.[1,2] It is difficult to accurately make the diagnosis of IMP based solely on clinical symptoms, as many patients are asymptomatic during the initial phase of the disease and symptomatic patients present with nonspecific signs and symptoms that vary from abdominal pain to nausea and vomiting, to diarrhea and bloody stool.[3,4] While the etiology of the disease remains unclear,[5] several colonoscopic and imaging findings that are associated with IMP have been described.[6,7] The typical colonoscopic finding is dark purple mucosa, but features of other forms of colitides, for example, mucosal edema, erosion, and ulcerations could also be found with or without dark purple mucosa. And some patients may even have a negative colonoscopy.[4,8] As with colonoscopy, many imaging findings of IMP are common to other forms of chronic colitides, for example, colonic wall thickening, pericolic edema, and fibrotic stenosis, and are easily visualized with computed tomography (CT). The most characteristic finding, however, is that of tortuous thread-like venous calcifications arranged perpendicular to the wall of the affected bowel.[6]

The treatment of IMP is dependent on the severity of the disease, but is usually conservative and focused on symptoms management.[2,7,9] Surgery is typically reserved for patients in whom the symptoms persist or recur after conservative treatment, patients who develop postischemic stricture and bowel obstruction, and patients who develop bowel wall infarction or perforation.[1,10] Failure of conservative therapy, however, delays definitive treatment of patients and increases their risk of developing the more ominous complications of IMP. Furthermore, elective surgical therapy is always preferred to emergent procedures. Unfortunately, so far no methods to predict response to conservative treatment have been developed. Since CT can detect the degree of blood supply deprivation, the extent of IMP,

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associated bowel changes, and the rare complications of IMP, the purpose of this study was to determine if imaging findings on CT can predict the need of surgery in patients with IMP.

2. Materials and methods

Our institutional review board approved this retrospective study with a waiver of consent form.

2.1. Patients and clinical data collection

We searched of our hospital electronic medical records and retrospectively identified all patients diagnosed with IMP who had CT scans between the years 2003 and 2015. A total of 28 patients (14 men, 14 women; mean age: 64.0 ± 9.8 years) were identified, 3 of who underwent surgical interventions (surgery group). The other patients were treated conservatively (nonsurgery group). The following data was collected: age, gender, clinical presentation (e.g., abdominal pain), management details, pathology, and outcome.

2.2. Imaging protocol

All scans were performed on multi-detector CT scanners (Brightspeed 16: n = 13, Lightspeed 16: n = 2, Lightspeed VCT 64: n = 3, and Optima 660: n = 6, GE Medical Systems, Milwaukee, WI) or single-slice CT scanners (n = 2, PQ 5000, Picker Medical Systems, Cleveland, OH; n = 2, TWIN, Elscint, Haifa, Israel). One patient received only unenhanced CT scan and 27 patients received CT studies before and after the intravenous administration of 100 mL of iodinated contrast medium. The protocol in 9 patients included the unenhanced and portal venous phases, while in 18 cases the protocol included an additional acquisition during the arterial phase of enhancement. The images were reconstructed in axial section with a slice thickness of 10 mm in 4 patients who received examinations on single-slice CT scanners and axial and coronal sections with a slice thickness of 5 mm in patients who received multidetector CT exams. Follow-up studies were not necessarily obtained in the same scanner utilized for baseline imaging.

2.3. Imaging interpretation

Two readers (CHL and WCL) with 2 and 8 years of experience reading abdominal CT scans independently reviewed all images on a Picture Archiving and Communication System workstation (Infinitt; Infinitt Healthcare, Phillipsburg, NJ).

2.4. Extent of mesenteric venous calcification

The extent and severity of mesenteric venous calcifications were evaluated in 2 different ways. First, the readers recorded the number of the colonic segments with mesenteric venous calcifications. The colon was divided into 5 segments: cecum, ascending colon, transverse colon (including both hepatic and splenic flexures), descending colon, and sigmoid colon. Next, a calcification score, which ranged between 1 and 4, was assigned to the ileocecal vein, the right colic vein, the middle colic vein, the left colic vein, and the sigmoid vein. A score of 1 was defined as calcifications limited to the straight vein of the colon. A score of 2 was given when the calcification extended to the paracolic marginal vein. A score of 3 was assigned to patients with calcifications extending to the main branch of the mesenteric vein, but without involving more than 50% of its proximal length. A score of 4 was given when the distal end of the main branch was also involved. Figure 1 depicts the calculation of the calcification score.

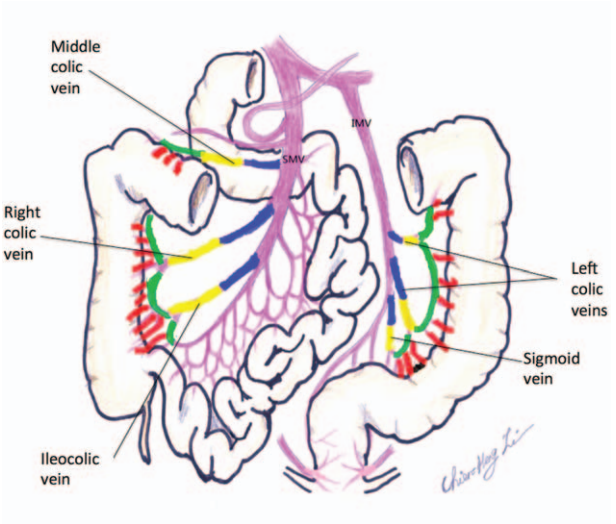

Figure 1. Color illustrations of how to calculate the calcification score. Mesenteric venous calcifications limited in the straight vein of the colon (marked in red) were scored as 1; when the calcification extended to the paracolic marginal vein (marked in green), the score was 2; when the calcification extended to the proximal half of main branch of mesenteric vein (marked in yellow), the score was 3; and when the distal end of the main branch was involved (marked in blue), the score was 4. The highest calcification score for each main mesenteric venous branch, including the ileocecal vein, the right colic vein, the middle colic vein, the left colic vein, and the sigmoid vein, was recorded and summed as a total calcification score.

Following this session, the calcification score of each individual branch was determined by consensus of both readers, and the total mesenteric venous calcification score was the sum of scores of each individual branch.

2.5. Other imaging features related to ischemic colitis

Images were reviewed in consensus by both radiologists for the presence of other imaging features related to ischemic colitis. These included colonic wall thickening, pericolic fat stranding, and bowel loop dilatation. Colonic wall thickening was considered present when a colonic segment had a luminal width greater than 2 cm and a wall thickness greater than 5 mm, or when a colonic segment had a luminal width greater than 4 cm and a wall thickness greater than 3 mm.[11] Pericolic fat stranding was subjectively assessed in a binary fashion (present or absent). Bowel loop dilatation was considered present when the diameters of the small intestine, cecum, and other portions of the colon were more than 3, 9, and 6 cm, respectively.[12,13]

2.6. Statistical analysis

The inter-reader agreement for the calcification scores was analyzed using kappa statistics. The agreement was defined excellent ($\kappa > 0.81$), good ($\kappa = 0.61$–0.80), moderate ($\kappa = 0.41$–0.60), fair ($\kappa = 0.21$–0.40), and poor ($\kappa \leq 0.20$).[14]

The number of the colonic segments with mesenteric venous calcifications, the total calcification scores, and the presence or absence of other imaging features related to colitis were compared between the surgery and nonsurgery groups. Ordinal

variables were expressed in mean ± standard deviation and tested with the Mann–Whitney *U* test. Fisher exact test was used to compare the categorized data.

Receiver operating characteristic analysis was performed to assess the ability of total calcification score and the number of the colonic segments with mesenteric venous calcifications to discriminate patients requiring surgical intervention from those only requiring conservative treatment, and quantified by using the area under the receiver operating characteristic curve (AUC). The optimal calcification score and number of the involved colonic segments were determined by the Youden index (J = Sensitivity + Specificity − 1)[15] that maximized the average of sensitivity and specificity to predict patients with mesenteric phlebosclerosis who need surgical intervention. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of the CT imaging features in predicting the need of surgery for IMP were also calculated. All the statistical analyses were performed using SPSS software (version 17.0; SPSS Inc, Chicago, IL). A *P* value less than 0.05 was considered statistically significant.

3. Results

3.1. Clinical characteristics, treatment, and outcomes

Seventeen patients presented with abdominal symptoms, including pain, fullness, diarrhea, nausea, and vomiting. Eleven patients were asymptomatic and the diagnosis was made incidentally on CT scans. Four of these asymptomatic patients had underlying chronic hepatitis and liver cirrhosis, and received CT exams for the evaluation of suspicious liver nodules seen on ultrasound. The other 7 asymptomatic patients underwent CT scans as part of surveillance of urological cancers (n = 4), fever of unknown origin, thrombocytopenia, and elevated liver function after liver transplantation.

None of these asymptomatic patients received any treatment for IMP, and all were followed as outpatients for at least 5 months (range of 5 months to 4 years). They remain have no abdominal symptoms that require surgical treatment. Among the 17 patients who were symptomatic, 14 received conservative treatment, and 3 underwent subtotal colectomy due to persistent symptoms after the conservative treatment. The specimens revealed IMP-induced transmural ischemic necrosis with fibrous thickening of the bowel submucosa, and fibrous thickening and calcifications of the walls of colonic and mesenteric veins.

There were 2 deaths not directly related to IMP; 1 patient died of respiratory failure secondary to an empyema, and the other died of sepsis due to a urinary tract infection. The remaining 26 patients continue under follow-up with a median duration of 3 years (range of 1 month to 11 years) and no 1 died of IMP or had an abdominal symptom that requires surgery.

3.2. CT imaging findings

There was excellent inter-readers agreement (κ = 0.91) for assessing the calcification score.

Mesenteric venous calcifications involved the cecum and ascending colon of all patients, and extended to the transverse colon in 18 patients, descending colon in 5 patients, and sigmoid colon in 1 patient. The number of colonic segments with mesenteric venous calcifications was significantly higher in the surgery group (4.33 ± 0.58 vs 2.96 ± 0.54, $P = 0.003$). The total calcification score was also significantly higher in patients who underwent surgery than in the nonsurgery group (15.00 ± 3.61 vs 8.96 ± 2.13, $P < 0.001$). These results are summarized in Table 1, and Figs. 2 and 3 show a representative case of each group.

Table 1

Compare the CT imaging features of the nonsurgery group to the surgery group.

	Nonsurgery group (n = 25)	Surgery group (n = 3)	*P*
Colonic wall thickening	64%	100%	0.530
Pericolic fat stranding	48%	100%	0.226
Bowel loop dilatation	16%	100%	0.011
Colonic segments with mesenteric venous calcification	2.96 ± 0.54	4.33 ± 0.58	0.003
Total calcification score	8.96 ± 2.13	15.00 ± 3.61	<0.001

CT = computed tomography.

The AUC of the number of colonic segments with mesenteric venous calcification and the total calcification score to discriminate between patients who do and do not need surgery was 0.96 and 0.92, respectively. The appropriate cutoff value for the number of colonic segments with mesenteric venous calcification was 3.5 and it was 10.5 for the total calcification score in predicting the need of surgery. But when the total calcification score was 14, it achieved the highest accuracy. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of CT image features in predicting the need of surgery are shown in Table 2.

All 3 patients in the surgery group had the CT imaging findings of colonic wall thickening, pericolic fat stranding, and bowel loop dilatation. In the nonsurgery group, 16 patients had colonic wall thickening, 12 patients had pericolic fat stranding, and 4 patients had bowel loop dilatation on CT. No significant differences were seen in the prevalence of colonic wall thickening and pericolic fat stranding between the 2 groups. Bowel loop dilatation, however, was more common in the surgery group ($P = 0.01$).

Two patients in the surgery group and 10 patients in the nonsurgery group had at least 1 follow-up CT with a median follow-up period of 3 years (range of 1 month to 11 years). Changes in imaging features were seen in only 3 patients on the follow-up CT scans. The calcification score was upgraded in 1 patient and the distribution of mesenteric venous calcification was more extensive, but without changing of the calcification score in each main branch, in 2 patients on the 11, 3, and 3 years follow-up CT scan, respectively.

4. Discussion

The results of our study show that bowel loop dilatation, the number of colonic segments involved by mesenteric venous calcifications, and the total calcification score on CT scans may be helpful to determine who are the patients with IMP who might fail conservative therapy and require surgical intervention.

Due to its fibrotic, rather than thrombotic, nature, the treatment of IMP is mostly focused on maintenance of adequate hydration, or surgery when complications ensue.[1,2] CT is believed to be the most valuable imaging modality for the diagnosis of IMP and follow-up of patients.[6,7] And, it has been suggested that patients with more extensive venous calcifications have a higher probability of requiring surgical interventions and bowel resection.[2,3,16–19] The results of our study support this impression.

It should not be unexpected that patients with a greater number of veins with calcifications distributed more widely throughout

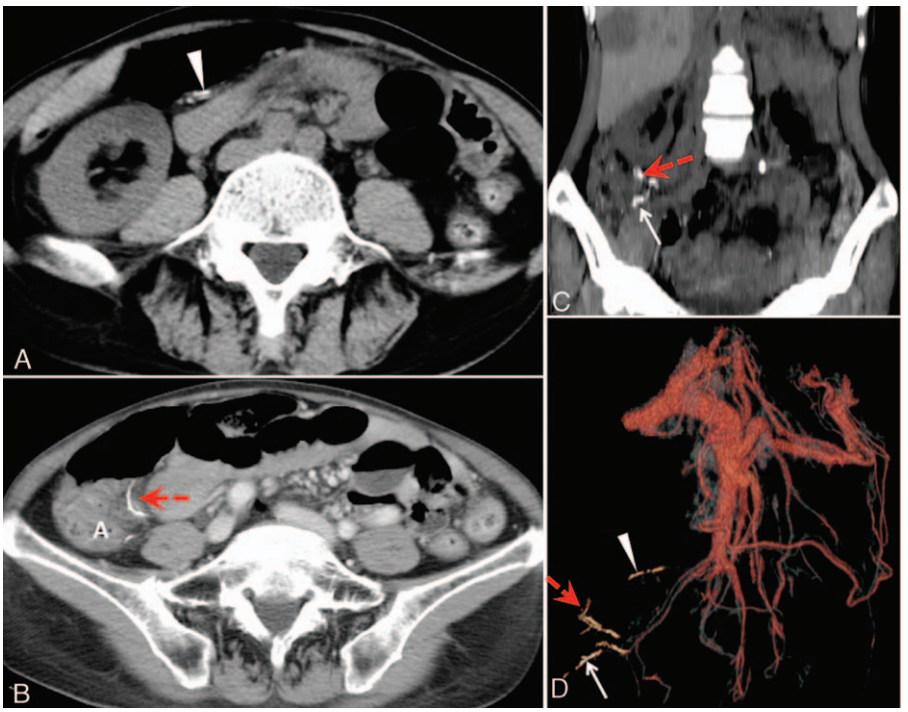

Figure 2. Idiopathic mesenteric phlebosclerosis in a 55-year-old woman presenting with epigastric pain. Unenhanced axial CT image at hepatic flexure level (A), enhanced axial image at ascending colon level (B), reconstructed maximum intensity projection coronal image (C), and postcontrast enhanced volume rendering image (D) show calcification in the ileocecal vein (white arrow), right colic vein (red arrow with dot line), and middle colic vein (white arrowheads). Note wall thickening at ascending colon (A). CT = computed tomography.

the colon are at greater risk of failing conservative therapy, as a greater extent of their colon is exposed to chronic vascular injury. The results of our study back this hypothesis and suggest that patients are very likely to fail conservative therapy when more than 3.5 segments of the colon are involved by IMP.

While collateral outflow may be able to protect the bowel in the presence of only a few affected veins within 1 or 2 colonic segments, this mechanism may not be adequate if most vessels within these segments are stenotic or occluded. This is illustrated by the role the total calcification score played in predicting the need of surgery in our population. Based on our results, surgical intervention should be promptly offered to symptomatic patients with a total calcification score higher than 14, while patients with a total calcification score between 10.5 and 14, in particular when presenting with bowel dilatation, are likely to benefit from close monitoring for symptom progression. Patients with a total calcification score less than or equal to 10.5 more likely only require conservative treatment and regular follow-up. As only 3 patients had progression of venous calcifications on the follow-up CT scans, none required surgical treatment, it remains to be determined if follow-up imaging can be used to detect progression of disease that requires a change in management, and the adequate follow-up interval. Notably, the total calcification score was determined in a subjective manner by the readers; yet, the inter-reader agreement was excellent suggesting it is a reliable and reproducible imaging parameter that can be easily applied.

Patients who required surgery had a significantly higher incidence of small bowel loop dilatation than patients treated conservatively. Interestingly, these dilatations were not associated with small bowel or colonic transition points. While the mechanism of small intestinal dilatation is unclear, it is most suggestive of a distal colonic pseudo-obstruction related to an absence of colonic peristalsis. Ischemic necrosis and marked submucosal fibrotic thickening could be the causes of pseudo-obstruction. Colonic wall thickening and pericolic fat stranding, however, did not help to identify the need for surgery. While this may be due to our small sample size, an alternative explanation is

Table 2

The sensitivity, specificity, PPV, NPV, and accuracy of CT image features in predicting the need of surgery.

	Sensitivity	Specificity	PPV	NPV	Accuracy
Colonic wall thickening	100.00	36.00	15.79	100.00	42.86
Pericolic fat stranding	100.00	52.00	20.00	100.00	57.14
Bowel loop dilatation	100.00	84.00	42.86	100.00	85.71
Number of involved colonic segments (cutoff value of 3.5)	100.00	88.00	50.00	100.00	89.29
Total calcification score (cutoff value of 10.5)	100.00	68.00	27.27	100.00	71.43
Total calcification score (cutoff value of 14)	66.67	100.00	100.00	96.15	96.43

CT = computed tomography, NPV = negative predictive value, PPV = positive predictive value.

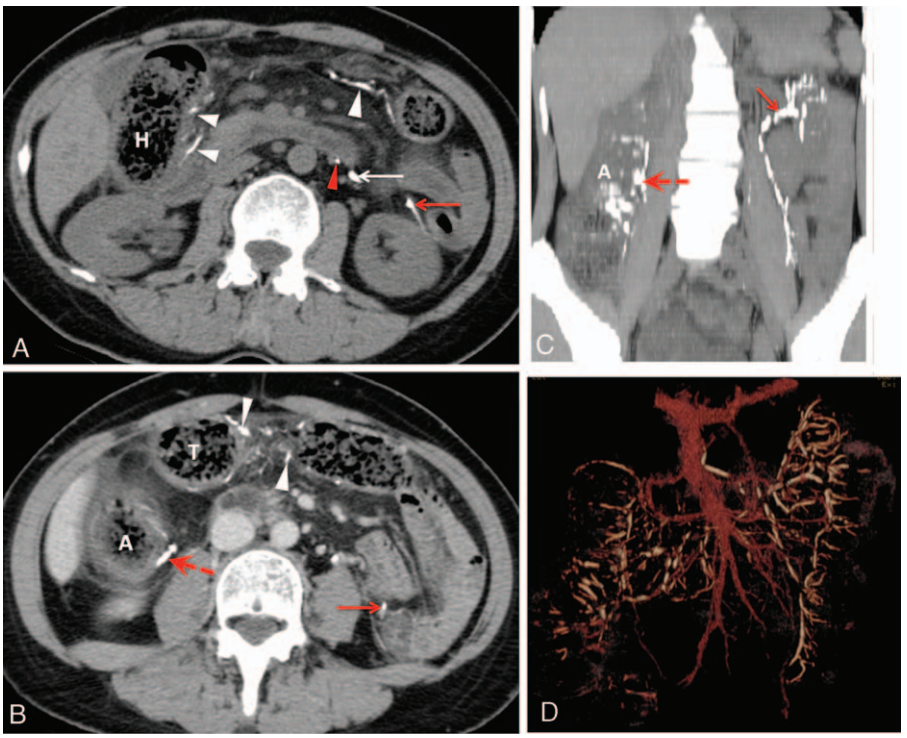

Figure 3. A 54-year-old female was diagnosed as idiopathic mesenteric phlebosclerosis suffered from abdominal pain, nausea, and vomiting. Unenhanced axial CT image at the level of hepatic flexure colon (H) (A), enhanced axial CT image at ascending colon (A) and transverse colon (T) level (B), and reconstructed maximum intensity projection coronal CT images (C) show calcification in the right colic vein (red arrow with dot line), middle colic vein (white arrowheads), left colic vein (red arrows), sigmoid vein (white arrow), and inferior mesenteric vein (red arrowhead). The post contrast enhanced volume rendering CT image (D) shows the extensive distribution of calcification along the mesenteric veins. Note the mild thick bowel wall of ascending colon and fat stranding around ascending colon (A) to transverse colon (T).

that these signs, which may be related to the fibrous thickening of the submucosa, adjacent tissue reaction, and ischemia, do not accurately represent the severity of colitis, as proposed by Cruz et al.[20] Complications of ischemic colitis, including definite infarction and perforation, are obvious indications of surgery;[1] but these features were not present on CT in our patients, nor were the focus of our study, which aims at preventing such complications.

Our study has limitations. First, it included only a limited number of patients. However, it must be noted that IMP is a rare disease with only 89 cases reported in the English literature.[5,18,21] Studies focused on imaging include even fewer subjects and are mostly case reports. Therefore, while a sample size of 28 patients is small when compared with other studies that investigate more common diseases, this is the largest study on this particular entity. Second, our search may not have identified all patients with IMP, as some may be asymptomatic or present with nonspecific clinical symptoms without typical colonoscopy or imaging features. Yet, the inclusion of these patients presumably would not have significantly influenced our results, as they would likely have only required conservative treatment. Third, this was a retrospective review study; hence, the timing and decision to proceed with surgical intervention varied and depended mainly on the surgeons' assessment of the patients' clinical conditions. And while imaging findings likely influenced these treatment decisions, the total calcification score we proposed had yet to be developed. Fourth, patients were identified over a long period of time (12 years), during which the CT technology continuously evolved. Variations on imaging quality and resolution may have impacted the detection of the disease features, in particular in older cases..

5. Conclusions

Evaluation of the severity and extent of IMP based on the total mesenteric venous calcification score, number of involved colonic segments, and the presence bowel loop dilatation on CT may be useful to indicate the outcomes of conservative treatment and the need for surgery. Despite these initial promising results, further investigation with a larger and independent patient population is warranted.

References

[1] Washington C, Carmichael JC. Management of ischemic colitis. Clin Colon Rectal Surg 2012;25:228–35.
[2] Iwashita A, Yao T, Schlemper RJ, et al. Mesenteric phlebosclerosis: a new disease entity causing ischemic colitis. Dis Colon Rectum 2003;46: 209–20.
[3] Konishi HHM, Akimoto S, Suzuki H, et al. Surgical treatment of idiopathic mesenteric phlebosclerosis: a case report. Jikeikai Med J 2014; 61:35–42.
[4] Lee SM, Seo JW. Phlebosclerotic colitis: case report and literature review focused on the radiologic findings in relation to the intake period of toxic material. Jpn J Radiol 2015;33:663–7.
[5] Fang YL, Hsu HC, Chou YH, et al. Phlebosclerotic colitis: a case report and review of the literature. Exp Ther Med 2014;7:583–6.
[6] Yao T, Iwashita A, Hoashi T, et al. Phlebosclerotic colitis: value of radiography in diagnosis—report of three cases. Radiology 2000;214: 188–92.

[7] Choi JM, Lee KN, Kim HS, et al. Idiopathic phlebosclerotic colitis: a rare entity of chronic ischemic colitis. Korean J Gastroenterol 2014;63: 183–6.
[8] Hiramatsu K, Sakata H, Horita Y, et al. Mesenteric phlebosclerosis associated with long-term oral intake of geniposide, an ingredient of herbal medicine. Aliment Pharmacol Ther 2012;36:575–86.
[9] Yu CJ, Wang HH, Chou JW, et al. Phlebosclerotic colitis with nonsurgical treatment. Int J Colorectal Dis 2009;24:1241–2.
[10] Kusanagi M, Matsui O, Kawashima H, et al. Phlebosclerotic colitis: imaging-pathologic correlation. AJR Am J Roentgenol 2005;185: 441–7.
[11] Wiesner W, Mortele KJ, Ji H, et al. Normal colonic wall thickness at CT and its relation to colonic distension. J Comput Assist Tomogr 2002; 26:102–6.
[12] Lappas JC, Reyes BL, Maglinte DD. Abdominal radiography findings in small-bowel obstruction: relevance to triage for additional diagnostic imaging. AJR Am J Roentgenol 2001;176:167–74.
[13] Krajewski K, Siewert B, Eisenberg RL. Colonic dilation. AJR Am J Roentgenol 2009;193:W363–72.
[14] Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics 1977;33:159–74.
[15] Youden WJ. Index for rating diagnostic tests. Cancer 1950;3:32–5.
[16] Oshitani N, Matsumura Y, Kono M, et al. Asymptomatic chronic intestinal ischemia caused by idiopathic phlebosclerosis of mesenteric vein. Dig Dis Sci 2002;47:2711–4.
[17] Guo F, Zhou YF, Zhang F, et al. Idiopathic mesenteric phlebosclerosis associated with long-term use of medical liquor: two case reports and literature review. World J Gastroenterol 2014;20:5561–6.
[18] Markos V, Kelly S, Yee WC, et al. Phlebosclerotic colitis: imaging findings of a rare entity. AJR Am J Roentgenol 2005;184:1584–6.
[19] Chang KM. New histologic findings in idiopathic mesenteric phlebosclerosis: clues to its pathogenesis and etiology—probably ingested toxic agent-related. J Chin Med Assoc 2007;70:227–35.
[20] Cruz C, Abujudeh HH, Nazarian RM, et al. Ischemic colitis: spectrum of CT findings, sites of involvement and severity. Emerg Radiol 2015;22: 357–65.
[21] Hu P, Deng L. Phlebosclerotic colitis: three cases and literature review. Abdom Imaging 2013;38:1220–4.