Seasonal variation in occurrence of ischemic colitis: a retrospective study

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Abstract

Objectives: We aimed to identify the clinical characteristics of ischemic colitis (IC) and to investigate the occurrence of seasonal variation.

Methods: From January 2008 to December 2014, 368 had IC as the reason for their admission. A total of 364 patients were enrolled in this study. We investigated patient characteristics and seasonal variations in incidence.

Results: The mean age (±standard deviation) of patients with IC at diagnosis was 66.8 (±16.9) years. Most patients had abdominal pain (341 cases), hematochezia (337 cases), and diarrhea (199 cases) as their chief complaints. The clinical courses of the disease were classified as transient (294 cases), stricture (17 cases), gangrenous (2 cases), and indeterminate types (51 cases). Although IC tended to occur less frequently in winter, the seasonal difference was not significant.

Conclusion: There is currently no evidence for seasonal variation in hospital admissions for IC.

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Introduction

Ischemic colitis (IC) is the most common form of ischemic injury of the gastrointestinal tract,[1] with abdominal pain, hematochezia, and diarrhea being among the most frequent presenting features.[2,3] Marston classified the disease clinically into transient, stricture, and gangrenous types.[4] Numerous risk factors have been reported for IC, including cerebrovascular disease, hypertension, diabetes mellitus, past history of abdominal surgery, irritable bowel syndrome (IBS), and constipation.[5] IC therefore usually occurs in elderly individuals with multiple comorbidities, but it may also occur in young or middle-aged individuals.

Based on our experience in routine clinical practice, more IC patients seemed to be admitted in the spring compared with in the winter. Seasonal variation in disease incidence is a well-known phenomenon, and we therefore aimed to identify any seasonal variation in the occurrence of IC. For example, acute myocardial infarction and heart failure occur most frequently in the winter,[6-9] possibly associated with low-temperature-induced stimulation of sympathetic nerves and reduced insensible perspiration.[10,11]

Seasonal variation in some gastrointestinal diseases has also been reported,[12] such as peptic ulcer diseases, which are more common in colder seasons.[13] Cold stress stimulates sympathetic nerve activity and increases catecholamine secretion from the adrenal medulla, causing blood vessel contraction. Contraction of the celiac artery and the resulting decreased blood supply to the gastroduodenal mucosa are expected to increase the risk of developing gastroduodenal ulcers. Seasonal variation, especially during the winter, may also occur in other gastrointestinal diseases with a pathogenetic relationship to decreased blood supply. This suggests that there may be seasonal variation in the occurrence of IC, though there is currently no evidence to support this hypothesis.

We aimed to identify the clinical characteristics of IC and to investigate the presence of seasonal variation in the occurrence of IC.

Methods

Data sources and definitions

This study involved a retrospective analysis of the medical charts of patients who were admitted to the gastroenterology wards of Shimane Prefectural Central Hospital from January 2008 to December 2014. Shimane Prefectural Central Hospital has the largest emergency department in Izumo city, and approximately half of all patients requiring emergency care in the Izumo area are admitted to this hospital. Most patients with IC are admitted for treatment in Shimane Prefectural Central Hospital. The diagnosis of IC was confirmed based on typical medical history supported by colonoscopic, histopathological, and radiologic findings. An absence of antibiotic administration prior to the clinical diagnosis and negative stool cultures were mandatory for a diagnosis of IC.[5,14]

Meteorological characteristics and data

The city of Izumo has a temperate, humid climate (Köppen–Geiger Climate Classification; Cfa), with a wide seasonal temperature range. It has a high rainfall under the influence of monsoons in June and July, and a relatively cold, dry climate in the winter. Weather parameters (monthly mean temperature, diurnal temperature difference, mean humidity, mean atmospheric pressure, daylight hours, and precipitation) were obtained from the Japan Meteorological Agency (http://www.data.jma.go.jp/risk/obsdl/). Seasons were defined as follows: winter (December–February); spring (March–May); summer (June–August); and fall (September–November).

Study ethics

This study protocol (R14-086) was reviewed and approved by the Shimane Prefectural Central Hospital Ethics Committee, and all patients provided written informed consent.

Statistical analysis

We assessed differences between proportions using χ^2 or Fisher's exact tests and differences between means using Mann–Whitney U tests. Comparisons of disease occurrences among different months and seasons were tested by single-factor analysis of variance (ANOVA). We investigated characteristics according to age group by cluster analysis (Ward method). All analyses were performed using IBM SPSS Statistics 21. All values of $P < 0.05$ were considered significant.

Results

Patient characteristics

A total of 12,804 patients were admitted to Shimane Prefectural Central Hospital during the study period, of whom 368 had IC. Among these 368 patients, four who had IC as a result of laxative use for colonoscopic preparation were excluded from this study, and 364 patients (89 male and 275 female) were finally enrolled for evaluation of seasonal IC onset (Figure 1). The mean (±standard deviation [SD]) age at diagnosis was 66.8 (±16.9) years (interquartile range: 55–80). Women were approximately three times more likely than men to develop IC. However, IC could occur at any age, and its incidence increased with age in both sexes, with a small additional peak in women in their 30 s. Abdominal pain (341 cases, 93.7%), hematochezia (337 cases, 92.6%), and diarrhea (199 cases, 54.7%) were the major symptoms at diagnosis. IC was classified as transient type (294 cases), stricture type (17 cases), or gangrenous type (2 cases), while 51 cases could not be classified. There were no deaths, including deaths from comorbidities, during the study-observation period. The distribution of IC in terms of location was the cecum (0 cases), ascending colon (13 cases), hepatic flexure (11 cases), transverse
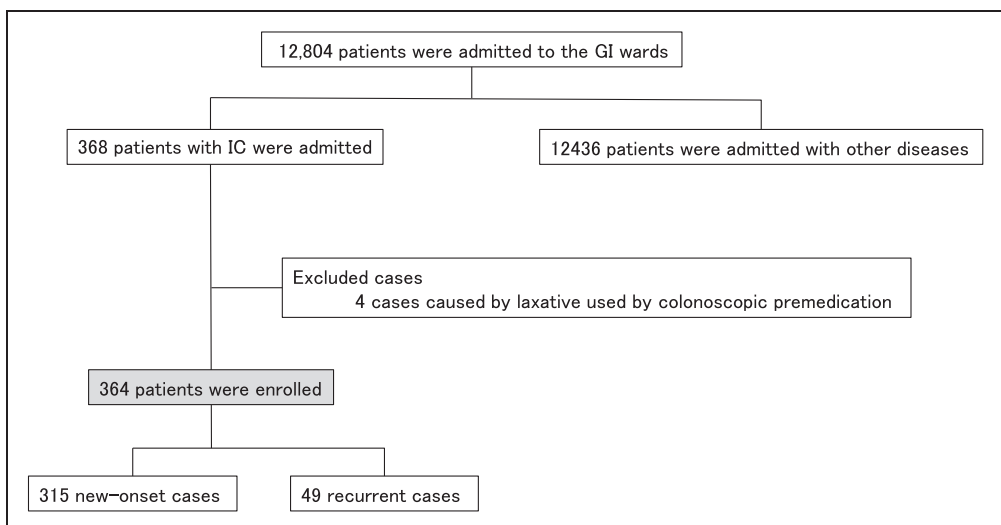

Figure 1. Patient flow.
GI, gastrointestinal; IC, ischemic colitis.

colon (79 cases), splenic flexure (109 cases), descending colon (303 cases), sigmoid colon (300 cases), and rectum (11 cases). These results indicated that IC frequently occurred in the descending colon and sigmoid colon, but rarely in the right-sided colon.

Monthly variation

There was no significant variation in the number of patients hospitalized for treatment of IC throughout the year, though small peaks were detected in March, June, and September to October ($P = 0.642$; Figure 2). The number of patients with IC tended to be lower in November and December, though the difference was not significant.

Seasonal variation

The highest number of IC admissions occurred during the spring (n = 96, 26.4%) followed by the summer (n = 93, 25.5%), and autumn (n = 91, 25.0%), with the lowest number during winter (n = 84, 23.1%) (Figure 3). There was no significant difference in frequency of admissions between seasons, but there was a non-significant increasing trend from winter to spring ($P = 0.888$). There was also no significant difference in the seasonal occurrence of IC ($P = 0.490$) in male or female patients analyzed separately. The occurrence of IC in elderly male and female patients (≥ 50 years, n = 230) decreased in winter and increased in spring, while the occurrence in young female patients (< 50 years, n = 44) showed a different trend (data not shown). Young females more frequently had diarrhea ($P = 0.028$), while risk factors including diabetes mellitus ($P = 0.037$), hypertension ($P < 0.001$), hyperlipidemia ($P = 0.005$), and surgical history ($P = 0.011$) were less common. Young female patients thus
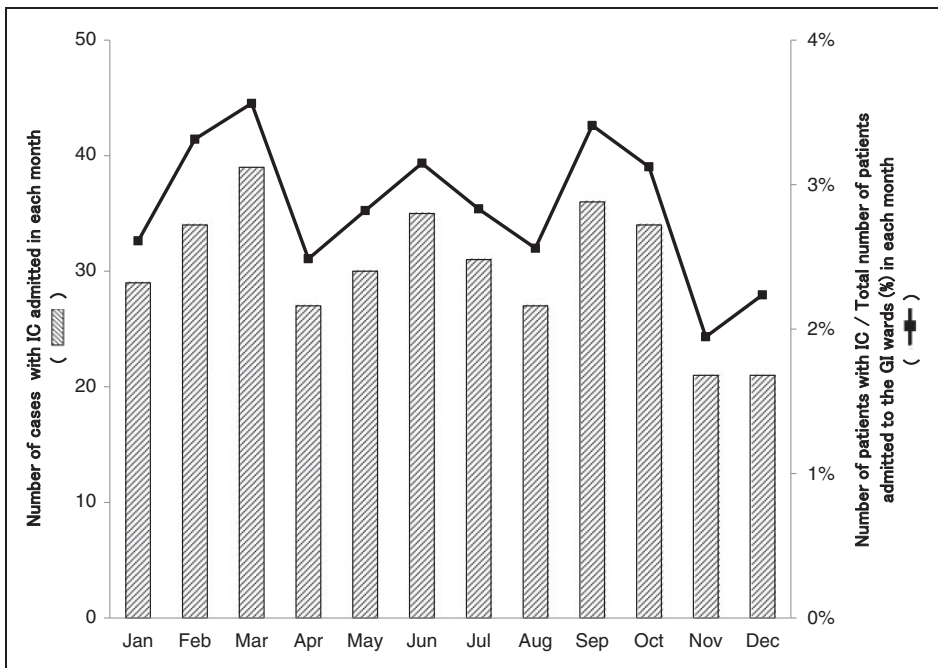

Figure 2. Number of patients with IC admitted in each month and number of patients with IC/total number of patients admitted to the gastroenterology wards (%) in each month.
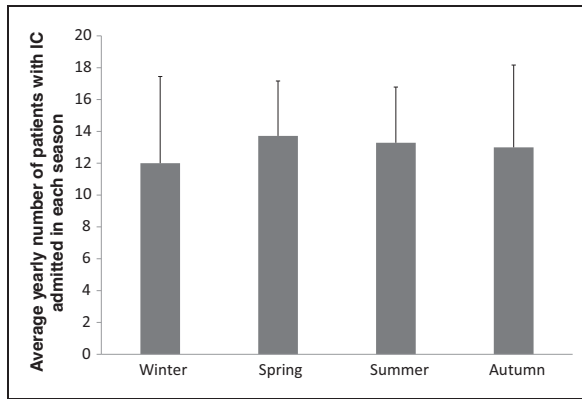
Figure 3. Number of patients with IC admitted in each season. Vertical lines indicate the SD.

demonstrated a different disease background compared with other groups.

Variations in onset day of the week and time of day

We also investigated the day of the week when IC occurred (Figure 4). There was no significant difference in the frequency of admissions for IC in relation to day of the week, though the number of admissions tended to be lower on Wednesdays ($P = 0.090$). We also examined the daily onset time of IC (Figure 5), and found that most admissions for IC occurred between 6 pm and midnight, though the difference was not significant ($P = 0.106$).

Meteorological data

The monthly mean temperature peaked in July–August, and the diurnal temperature change was greatest in March–May. The mean atmospheric pressure was lowest in June–August and highest in December–January. The mean humidity was lowest in March–April and increased rapidly in May. Monthly daylight hours were longer in the summer. There were large variations among years in terms of monthly precipitation, with no clear seasonal trend.

New-onset and recurrent IC

The study population included 315 new-onset and 49 recurrent cases. There was no significant difference in age, sex, form of disease, comorbidities, or drugs used at the time of IC occurrence between initial and recurrent cases (Table 1). Seasonal variations and biochemical data, such as peripheral leukocyte count and C-reactive protein, did not differ significantly between the two groups. Twenty of the 49 recurrent cases had developed initial events before the start of the study. We compared seasonal recurrence of IC in the remaining 18 patients (29 events), in whom the initial and recurrent events both occurred during the study period. Half of the recurrent cases developed recurrent IC in the same season as the initial event (Table 2). Of the 18 patients, seven (seasonal recurrent group) experienced recurrence in the same season as the initial event, while the other 11 experienced recurrence in a different season (non-seasonal recurrent group). There was no significant difference in age, sex, form of disease, comorbidities, or drug usage between the two groups (Table 3).

Discussion

IC is thought to be caused by changes in the systemic circulation or by anatomic or
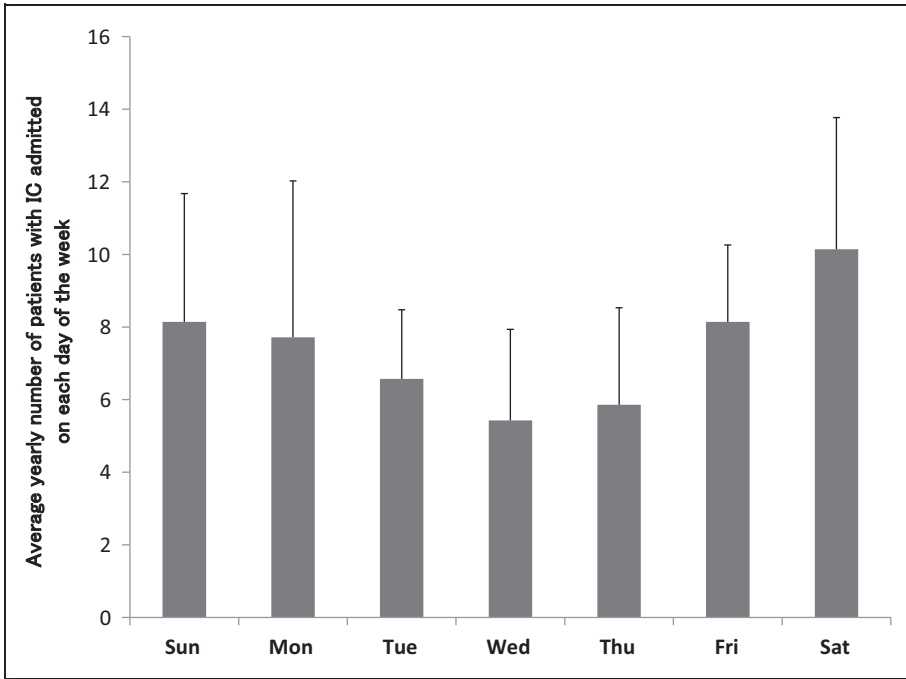
Figure 4. Number of patients with IC admitted on each day of the week. Vertical lines indicate the SD.
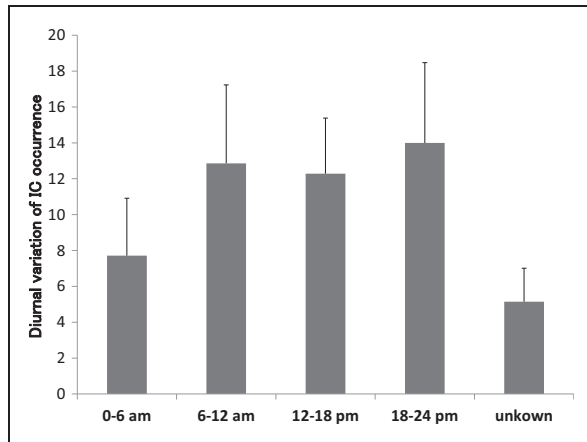

Figure 5. Diurnal variation of IC occurrence. Vertical lines indicate the SD.

functional alterations in the mesenteric vasculature. The specific cause of the ischemia remains unidentified in most cases, and such episodes are attributed to localized non-occlusive ischemia, likely as a result of small-vessel disease.[5] The segmental nature of IC

Table 1. Demographic and clinical characteristics of the study population.

	All patients (n = 364)	New-onset cases (n = 315)	Recurrent cases (n = 49)	P value
Demographic characteristic				
Age (yr) mean ± SD (IQR)	66.8 ± 16.9 (55.0–80.0)	66.3 ± 17.2 (54.0–80.0)	70.6 ± 14.5 (62.8–80.5)	0.135
Male/female	89/275	79/236	10/39	0.593
Clinical symptoms				
Abdominal pain	341	295	46	1.000
Hematochezia	337	294	43	0.234
Diarrhea	199	172	27	0.984
Form of disease				
Transient type	294	257	37	
Stricture type	17	13	4	
Gangrenous type	2	2	0	
Unknown	51	43	8	
Underlying disease and medications				
Diabetes mellitus	30	27	3	0.781
Hypertension	159	141	18	0.353
Hyperlipidemia	63	53	10	0.551
Smoking history (yes/no/unknown)	60/258/36	55/225/35	5/33/1	
Abdominal surgery history	119	99	20	0.203
Anti-platelet agent use	62	54	8	0.873
Anticoagulant use	11	11	0	0.183
NSAID use	15	14	1	0.427
Laxative use	43	36	7	0.633
Season				
Winter	84	74	10	0.603
Spring	96	86	10	
Summer	93	79	14	
Autumn	91	76	15	
Laboratory data (mean)				
Leukocytes (/μL)	10354.6	10274.6	11084.9	0.332
CRP (mg/dL)	1.492	1.557	1.086	0.070

SD, standard deviation; IQR, interquartile range; NSAID, non-steroidal anti-inflammatory drug; CRP, C-reactive protein

can be explained by the vascular anatomy of the colon and rectum. The boundary of the blood supply from the superior mesenteric artery and the inferior mesenteric artery is located on the descending and sigmoid colons, which are thus vulnerable to ischemic damage. Accordingly, the descending and sigmoid colons were the most commonly involved segments in the current study, as also reported in previous studies.[3,15–17]

Seasonality is a well-known feature of the epidemiology of many diseases. Weather conditions and seasons are associated with the incidence of cardiovascular diseases, such as acute myocardial infarction and acute heart failure,[6–9] and seasonal variation has also been reported in some gastrointestinal diseases. Peptic ulcer diseases frequently occur in colder months,[12] while Crohn's disease peaks in spring and summer.[18–22] Arteriosclerosis is a major

Table 2. Seasonality of initial and recurrent IC in patients with recurrent disease.

Case	Age	Sex	1st	2nd	3rd	4th	5th
1	87	F	Apr (spring)	May (spring)			
2	92	M	Dec (winter)	Aug (summer)			
3	74	F	Feb (winter)	Apr (spring)			
4	72	F	Nov (autumn)	Apr (spring)			
5	75	F	Jan (winter)	Oct (autumn)			
6	71	M	May (spring)	Dec (winter)			
7	80	M	Nov (autumn)	Oct (autumn)			
8	90	F	Mar (spring)	Mar (spring)			
9	74	F	Jul (summer)	Jun (summer)			
10	86	M	Mar (spring)	Sep (autumn)			
11	30	F	Sep (autumn)	Sep (autumn)			
12	54	F	Jun (summer)	Jul (summer)	Jun (summer)		
13	66	F	Sep (autumn)	Sep (autumn)	Jun (summer)	Jan (winter)	Oct (autumn)
14	79	F	Sep (autumn)	Feb (winter)	Oct (autumn)		
15	77	M	Jul (summer)	Sep (autumn)	Feb (winter)	Jun (summer)	
16	81	F	Aug (summer)	Nov (autumn)	Mar (spring)		
17	88	F	Feb (winter)	Mar (spring)	Sep (autumn)		
18	48	F	Nov (autumn)	Feb (winter)	Feb (winter)	Jun (summer)	

risk factor for IC, as well as for many cardiovascular diseases, and we therefore expected to find that IC was most common in the colder seasons. However, the results of this study found no evidence for any significant seasonal variation in the incidence of IC, although there was a tendency for IC to be less frequent during the winter.

Previous studies have indicated that the pathogenesis of IC,[2,5,18,23,24] can be roughly divided into vascular and intestinal factors. Arteriosclerosis, congestive heart disease, atrial fibrillation, and hypotension are considered to be vascular factors that cause a decrease in the blood supply to the colon, while constipation, diarrhea, and irritable bowel syndrome are considered to be intestinal factors that cause intestinal hypercontraction. Both factors may be affected by pharmacologic agents and past history of abdominal surgery, and it is possible that the existence of multiple complex risk factors might mask any effects of seasonal environmental changes on IC. Diarrhea and constipation occurring just before the onset of IC

are considered to be important. Constipation increases colonic intraluminal pressure and can reduce colonic perfusion. Although the possible presence of constipation before the onset of IC could not be evaluated in the current study, laxative use was found in 43 patients (11.8%); however, patients may have constipation without taking a laxative. Longstreth and Yao[3] reported that constipation preceded the symptoms of IC in only 7% of episodes, but another prospective study[15] reported the presence of constipation during the 30 days before the event in 25% of patients with IC.

This study demonstrated an obvious female predominance in IC occurrence, as previously reported.[3,5,15,16,18,25–27] Although oral contraceptives may cause hypercoagulability and ischemia,[28,29] these are rarely used in Japan and were not used in this study population. In addition, this would not explain the female predominance among elderly women who do not use oral contraceptives. However, constipation and laxative use are more common in women than in

Table 3. Characteristics of seasonal recurrent and non-seasonal recurrent cases.

	Seasonal recurrent cases (n = 7)	Non-seasonal recurrent cases (n = 11)	P value
Demographic characteristic			
Age (yr) mean ± SD	68.71 ± 21.08	76.64 ± 11.66	0.263
Male/female	1/6	3/8	0.485
Clinical symptoms			
Abdominal pain	7	11	1.000
Hematochezia	7	9	0.560
Diarrhea	5	5	0.278
Form of disease (initial event)			
Transient type	4	8	
Stricture type	1	0	
Gangrenous type	0	0	
Unknown	2	3	
Underlying disease and medications			
Diabetes mellitus	1	0	0.389
Hypertension	4	5	0.500
Hyperlipidemia	3	1	0.137
Smoking history	0	2	0.231
Abdominal surgery history	3	5	0.648
Anti-platelet agent use	1	2	0.674
Anticoagulant use	0	0	1.000
NSAID use	0	1	0.611
Laxative use	0	2	0.359
Season			
Winter	0	4	0.351
Spring	2	2	
Summer	2	2	
Autumn	3	3	

SD, standard deviation; NSAID, non-steroidal anti-inflammatory drug

men, among both young and elderly individuals,[30–33] and this may contribute to the female predominance of IC.

Chang et al.[23] reported that the odds of developing IC were six times greater in patients with IBS than in those without IBS, while the risk was only about two-fold among elderly patients with IBS. This suggests that IBS was more strongly associated with IC risk among young patients.

The present analysis of patients with recurrent IC suggested a possible role of seasonal environmental changes. We compared the seasonality of each event in 18 patients hospitalized for treatment of IC multiple times, and found that IC often recurred in the same season. This suggested that seasonal factors may play a role in in individuals with certain vascular and intestinal factors. Patients with a history of IC may thus have a higher chance of developing recurrent IC in the same season in the future, though we were unable to identify possible predictive factors for future recurrence in the same season.

There were no deaths, including deaths from comorbidities, during the observation period in this study. Cosme et al.[34] reported mortalities due to IC in Spain of 5.9% at first admission and 7.4% 5 years later,

and overall mortalities, including deaths from comorbidities, of 8.8% and 31.1%, respectively. These rates were high compared with those observed in the current study. In contrast, Nagata et al.[35] reported that only one of 57 patients (1.8%) with IC died from a comorbidity during a mean follow-up period of 29 months in a study in Japan, with cumulative 12- and 60-month mortalities, including deaths from comorbidities, of 0% and 6.7%, respectively. The apparent differences in mortalities between Japan and Western countries are interesting. Some authors[16,26] reported that IC has a worse prognosis when isolated in the right side of the colon, and about 25% of patients in the United States were classified as having right-colon ischemia. This was higher than in the current study, and in sharp contrast with the previous Japanese reports. Differences in lifestyle and genetic factors may influence the prognosis of patients with IC, and further studies are needed to investigate the predictive factors for IC.

This study had several strengths, including being the first report of seasonal variation in IC onset. Furthermore, although no clear seasonality was observed, we determined that IC was more likely to recur during the same season as the initial event. This study also had some limitations. First, it was a single-center, retrospective study. Second, the overall temperature of a specified geographic area may not accurately represent the actual temperature that an individual is exposed to, which is also influenced by personal behavior. Third, daily variations in weather conditions were not evaluated.

Conclusions

This study found no evidence for seasonal variations in hospital admissions due to IC, though IC may recur more frequently in the same season as the initial event.

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