

# 学位論文の要旨

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学位論文名 Seasonal Variation in Occurrence of Ischemic Colitis  
: a Retrospective Study

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## 論文内容の要旨

### INTRODUCTION

Ischemic colitis (IC) is the most common form of ischemic injury of the gastrointestinal tract. Many risk factors are reported for IC, including cerebrocardiovascular disease, hypertension, diabetes mellitus, past history of abdominal surgery, irritable bowel syndrome and constipation. Therefore, IC is generally found in elderly individuals with multiple comorbidities; however, it may also occur in young or middle-aged individuals. In routine clinical practice, in our experience, the number of patients admitted for IC seemed to be greater in the spring than in the winter. Therefore, we wanted to investigate the possible presence of seasonal variation in the occurrence of IC. Seasonal variation in disease incidence is a well-known phenomenon. Seasonal variation may also occur with other gastrointestinal diseases, especially during the winter, if their pathogenesis is related to a decreased blood supply. Thus, seasonal variation of IC may occur, but no such findings have been reported to date. We aimed to identify the clinical characteristics of IC and to determine whether there is a seasonal variation in the occurrence of IC.

## **MATERIALS AND METHODS**

This was a retrospective study of the medical charts of patients who were admitted to the gastroenterology wards of Shimane Prefectural Central Hospital from January 2008 to December 2014. A total of 12,804 patients were admitted, and 368 of them had IC. The diagnosis of IC was confirmed by a typical medical history combined with the supporting colonoscopic, histopathological, and radiologic findings. The absence of antibiotic administration prior to the clinical diagnosis and a negative culture of stool specimens were mandatory for the diagnosis of IC. Weather parameters (monthly mean temperature, diurnal temperature difference, mean humidity, mean atmospheric pressure, daylight hours and precipitation) were obtained from the Japan Meteorological Agency. Seasons were defined as follows: winter (December-February); spring (March-May); summer (June-August); and fall (September-November). This study protocol (R14-086) was reviewed and approved by the Shimane Prefectural Central Hospital Ethical Committee and written informed consent was obtained from all subjects.

## **RESULTS AND DISCUSSION**

A total of 368 patients with IC were investigated in the onset evaluation. Four cases that resulted from the administration of laxatives used for colonoscopic preparation were excluded from this study. Therefore, a total of 364 (89 male and 275 female) patients were enrolled in the seasonal onset evaluation. Throughout the year, there was no statistically significant variation in the number of patients hospitalized for the treatment of IC, although small peaks were found in March, June, and September to October ( $P=0.642$ ). The number of patients with IC tended to be lower in November and December, without reaching a statistically significant level. 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%). The lowest number of IC admissions occurred during winter ( $n=84$ , 23.1%). There was no statistically significant difference in frequency of admissions between seasons. No statistically significant differences were found in the seasonal

occurrence of IC, even if male and female patients were analyzed separately. Because of many complex risk factors, the effect of seasonal environmental change on IC might not be clearly demonstrated.

In this study, 315 new-onset cases and 49 recurrent cases were enrolled. There was no significant difference in age, gender, form of disease, comorbidities, and drugs used at the time of IC occurrence between the initial and the recurrent cases. Twenty of 49 recurrent cases developed their initial events before the observation period of this study. The seasonal recurrence of IC was compared in the remaining 18 patients (29 events) who showed initial and recurrent events during the study period. The results showed that half of the recurrent cases developed recurrent IC in the same season as the initial event. The analysis of the recurrent cases with IC, however, suggested a possible role of seasonal environmental changes. In our study, 18 cases hospitalized multiple times for the treatment of IC were used to compare the seasonality of each event. These patients often developed IC in the same season. This suggested that seasonal factors may become clear in individual cases with certain vascular and intestinal factors. Therefore, patients with a history of IC may have a higher chance of developing recurrent IC in the same season in the future, although possible predictive factors suggesting future recurrence in the same season were not identified in this study.

## **CONCLUSION**

Seasonal variation in hospital admissions due to IC were not clearly demonstrated in this study. IC recurs most frequently in the season in which the initial event occurred.

論文審査及び最終試験又は学力の確認の結果の要旨

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論文審査の結果の要旨

虚血性大腸炎は血便を生じる疾病の中で最も頻度の高い消化器疾患である。腸管粘膜の局所循環障害が原因と考えられ、動脈硬化などを背景とする血管側因子と腸管運動異常や便秘などを背景とする腸管側因子が関与するといわれているが、不明な点も多い。一方、心筋梗塞や消化性潰瘍など様々な疾患が気温や気圧などの環境変化の影響を受け、季節性に発症することが知られている。しかし、虚血性大腸炎については明らかでない。そこで申請者は、虚血性大腸炎の季節性の有無に着目し、7年間、364例の虚血性大腸炎患者を対象に後方視的臨床研究を行い、患者背景や季節性の変化の特徴などから、発症機序について検討を行った。その結果、虚血性大腸炎では季節性は認められなかった（月別：p=0.642、四季別：p=0.888）ものの、各年代とも女性が男性よりも多く発症し、男性89例、女性275例と約3倍の男女差を示した。また、高齢者になるほど多く発症していたが、30代女性にも小さなピークを有し、50歳未満の若年女性にも比較的多く発症していることを示した。また、統計学的有意差はないものの、この群は冬から春にかけて発症が減るのに対して、他の群は増加するという異なる季節変化の傾向が見られた（p=0.225）。さらにこの群は他の群と比較して動脈硬化などの血管側因子を持たない群（糖尿病：p=0.037、高血圧：p<0.001、脂質異常症：p=0.005）であり、腸管側因子が発症により重要であることを明らかにした。また、観察期間内に再発した18例（延べ29イベント）の半数が初回発症時と同じ季節に再発していることを示した。つまり、患者個々でみると、ある特定のリスク因子が同じ季節に影響することで、同じ季節に再発しやすいことが示唆された。

本研究結果は、虚血性大腸炎の発症機序を考えるうえで示唆に富むものであり、学位授与に値すると判断した。

最終試験又は学力の確認の結果の要旨

申請者は、虚血性大腸炎患者364例を対象に季節性発症に関する検討を行った。その結果、発症の季節性は見いだせなかつたが、基礎疾患のない若年女性にも比較的多くみられ、その発症に腸管側因子がより重要であることを示した。また再発患者の半数が初回発症時と同じ季節に再発していることを示した。虚血性大腸炎の発症機序を考えるうえで重要な研究成果である。質疑応答も的確で、関連知識も豊富であり、学位授与に値すると判断した。  
(主査：田島義証)

申請者は、364例の虚血性腸大炎患者を対象に、患者背景やその発症の季節性の有無を検討した。その結果、発症の季節性は認めなかつた。発症は女性に多く高齢者に多かつたが、30歳代の女性にも発症があり、腸管側の因子がより重要であることが示された。また質疑応答にも的確に回答された。学位授与に値する研究であると思われた。  
(副査：仁科雅良)

申請者は、虚血性大腸炎の季節性の有無を明らかにするため、実臨床に沿った的確な研究デザイン作成と臨床研究を行っており、倫理的にも問題ない。今まで報告のない新しいエビデンスとなっている。本疾患や研究に関する知識も豊富で、質疑に的確に答えており、学位授与に値すると判断した。  
(副査：駒澤慶憲)

(備考) 要旨は、それぞれ400字程度とする。