

# 学位論文の要旨

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学位論文名 Prevalence of Irritable Bowel Syndrome-like Symptoms in  
Ulcerative Colitis Patients With Clinical and Endoscopic Evidence  
of Remission: Prospective Multicenter Study

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## 論文内容の要旨

### INTRODUCTION

Irritable bowel syndrome (IBS) is a chronic functional disorder of the intestinal tract in the absence of organic abnormalities and characterized by clinical symptoms such as abdominal pain and discomfort, along with bowel habit alterations. Several studies have investigated the presence of IBS-like symptoms in ulcerative colitis (UC) patients without evidence of ongoing disease activity. In those, remission was mainly defined by clinical symptoms. However, the prevalence of IBS-like symptoms in UC patients with endoscopic evidence of remission shown by mucosal healing remains unknown. We investigated UC patients with clinical as well as endoscopic remission evidence, and evaluated the presence of IBS-like symptoms.

### MATERIAL AND METHODS

This study was prospectively conducted from May 2011 to February 2012 at 1 university hospital and 3 general hospitals in Japan. Diagnoses of UC were based on standard clinical, endoscopic, and histological criteria. All UC patients ( $\geq 18$  years old) with a clinically good appearance as defined by their attending physician were assessed, while patients with hematochezia, history of colectomy, or C-reactive protein  $>0.5$ mg/dl were excluded. IBS diagnosis was evaluated by questionnaire results according to the Rome III criteria. Clinical

remission was defined as clinical activity index (CAI) score  $\leq 4$  for  $\geq 6$  months and endoscopic remission as Matts grade  $\leq 2$  for  $\geq 3$  months. Differences for prevalence of IBS-like symptoms between the UC and control groups were evaluated using a chi-squared test. A *P* value of  $<0.05$  was considered to be significant. The study protocol was approved by the Ethics Committee of Shimane University and written informed consent was obtained from all subjects.

## **RESULTS AND DISCUSSION**

A total of 172 UC patients with clinical evidence of remission (CAI  $\leq 4$ ) were enrolled in the study by their physicians, then carefully screened by 2 inflammatory bowel disease experts prior to analysis. Of those, 43 agreed to undergo a colonoscopy examination, with 39 showing endoscopic evidence of remission (Matts grade  $\leq 2$ ). In addition, 330 healthy subjects were enrolled during the study period as a control group.

The prevalence rate of IBS-like symptoms in UC patients with clinical evidence of remission (CAI  $\leq 4$ ) was 26.7% [46/172, 95% confident interval (CI): 21.0-33.8%], while that in the controls was 4.8% (95% CI: 3.0-7.7%) (26.7% vs 4.8%, OR: 7.17, 95% CI: 3.94-13.0, *p*  $<0.01$ ). Of the 39 UC patients with endoscopic evidence of remission (Matts grade  $\leq 2$ ), 10 met the Rome III criteria (25.6%, 95%CI: 14.6-41.1%), which was similar to that found in UC patients with clinical evidence of remission (26.7%). The prevalence rate of IBS-like symptoms was significantly higher than that in the controls (25.6% vs. 4.8%, OR: 6.77, 95%CI: 2.87-16.0, *p*  $<0.01$ ). When endoscopic remission was strictly defined as Matts grade 1, prevalence decreased to 15.4% (95%CI: 4.3-42.2%) and there was no statistical difference as compared to the controls (15.4% vs. 4.8%, OR 3.57, 95%CI 0.83-15.8, *p* =0.14).

The present results indicate that the prevalence of IBS-like symptoms in UC patients with clinical and endoscopic evidence of remission is significantly higher than that in healthy individuals. In addition, we precisely analyzed endoscopic findings in UC patients and found that the prevalence rate in those with complete endoscopic remission (Matts grade 1) was lower than that in patients with clinical findings of remission (Matts grade  $\leq 2$ ). Since Matts grade 2 is defined as an endoscopic finding with residual mild mucosal damage, our findings suggest that low grade colonic inflammation may partially influence the presence of IBS-like symptoms in UC patients in remission.

The main limitation of this study is the low number of patients who underwent colonoscopy examinations, as those were only conducted after receiving consent. Since patients

in clinical remission were in relatively good health as compared to those in an active stage, it is understandable that they might not agree to a colonoscopic examination after achieving remission. However, the low number analyzed might have affected the results. To confirm the influence of endoscopic findings on the presence of IBS-like symptoms in UC patients, it is important to analyze a large number of subjects who underwent a colonoscopy.

### **CONCLUSIONS**

The prevalence of IBS-like symptoms in UC patients with clinical and endoscopic remission findings was significantly higher than that in control subjects. Furthermore, the prevalence in patients with complete endoscopic remission was decreased. Our findings suggest that residual low-grade inflammation influences IBS-like symptoms in UC patients in remission.

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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<p>論文審査の結果の要旨</p> <p>過敏性腸症候群 (irritable bowel syndrome:IBS) は、器質的異常を示さない機能的消化管疾患とされるがその機序は定まらない。近年、潰瘍性大腸炎 (ulcerative colitis:UC) の臨床症候的寛解症例でのIBS様症状の存在からIBSの炎症性機序が注目されているが、内視鏡的寛解を確認した症例での研究は少ない。本研究では、臨床症候的および内視鏡的寛解を確認したUC症例におけるIBS様症状の罹患率を検討した。外来通院中のUC患者208例を対象としclinical activity index4以下を臨床症候的寛解群、内MATTSgrade2以下を内視鏡的寛解群、健診受診者330例をコントロール群としてRome III質問票を用いてIBS様症状の有無を調査した。その結果、臨床症候的寛解群で26.7%(46/172)、内視鏡的寛解群で25.6%(10/39)にIBS様症状を認めいずれもコントロール群の4.8%(16/330)に比して有意(p&lt;0.01)に高かった。また内視鏡的寛解群においてMATTSgrade1に限ると15.4%とやや頻度は低下したがコントロール群より高い傾向を示した。これらの結果は、臨床症候的および内視鏡的寛解症例においてもIBS様症状の罹患率が高く、内視鏡的な更なる寛解とともに罹患率が減少することを示している。すなわち、UC寛解症例におけるIBS様症状には、軽度ながら残存する炎症が影響していることが示唆された。本研究は、IBSの発生機序の一つとして炎症機転を示唆しており、今後の新たな治療戦略を期待させるものである。</p> <p>最終試験又は学力の確認の結果の要旨</p> <p>申請者は、UC寛解症例においてIBS様症状を来す機序に注目し、症候的かつ内視鏡的寛解を示すUC症例におけるIBS様症状の罹患率がコントロール群に比して有意に高いことを示し、UC寛解症例でのIBS様症状発症には潜在的な炎症機転が関与することを提唱した。本研究は、UCの新たな治療を想起させ得るものであり、関連知識も豊富で学位授与に値すると判断できる。 (主査：石橋 豊)</p> <p>申請者は臨床症候的と内視鏡的に寛解を確認したUC症例におけるIBS様症状の罹患率を検討した研究により、寛解例においても対照例より罹患率が有意に高いことを示した。本結果はUC寛解例のIBS様症状に残存する炎症機転の関与、そしてIBS患者の治療に新たなアプローチを提起する。関連領域の知識も豊富であり、学位授与に値すると判断した。 (副査：杉本利嗣)</p> <p>申請者らは、Post-infectious IBSに着目、炎症性腸疾患の一つであるUCの臨床的および内視鏡的寛解症例を対照群、健診受診者をコントロール群として、UCにおけるIBS様症状の頻度および臨床像の特徴について比較検討、IBS様症状の発生機序に関する新しい知見を得た。関連知識も豊富であり、学位授与に値すると判断した。 (副査：津本周作)</p>		

(備考) 要旨は、それぞれ400字程度とする。