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学位論文名	クローン病による小腸狭窄に対する内視鏡的バルーン拡張術後の再狭窄に影響する因子の検討
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論文内容の要旨

1 Background

Crohn's disease (CD) is a chronic inflammatory disease of the gastrointestinal tract and characterized by relapsing and remitting courses. The most common complication is an intestinal stricture that frequently locates in small intestine and becomes the independent risk factor for CD related surgical resection. Once the patient underwent initial surgery, a risk of the repeat surgical resections that can lead to short bowel syndrome, increases over the time. Therefore, endoscopic balloon dilation (EBD), a minimally invasive and safe treatment modality performed with assistance of double balloon endoscopy (DBE) for small bowel strictures, became a successful alternative to surgery for the patients with CD related intestinal strictures. But recurrence of obstructive symptoms occurs and requires repetitive EBD or surgical resection in the significant number of the patients because of restenosis, which is an insufficient change on the stricture diameter after EBD. Since measuring a diameter of stricture is difficult, previous studies could not evaluate endoscopic restenosis based on the objective changes on stricture diameter. Therefore, rate of the endoscopic restenosis and factors affecting restenosis after EBD remained unclear.

Aims

The aim of this study is to evaluate efficacy of EBD by identifying endoscopic restenosis and factors for it by considering precise measurement of the diameters of small bowel strictures in patients with CD.

2 Methods

This single-center retrospective study reviewed the patients with CD with small bowel strictures, who underwent two sessions of double-balloon endoscopy (1st: EBD session and 2nd: follow-up session) with EBD performed with longer than 7 months of interval between January 2016 and October 2021 in the Endoscopy center at Jichi medical university hospital. Patients with ileal or ileocolonic CD that complicated with small bowel de novo fibrotic

stricture(s), all whose diameter were evaluated and met the indications for EBD, were included in the study. All clinical and endoscopic data were obtained from the electronic medical records. To measure stricture diameter, a calibrated small-caliber-tip transparent hood, which is a special device attached to the tip of the DBE scope having calibration lines (7, 8, 9 mm) and other landmarks (orifice: 4 mm, edge: 6 mm, outer ring: 10mm), was used. The rate of patients with restenosis was detected based on the comparison of diameters of the narrowest strictures found in all patients during both sessions. Patients were divided into two groups in accordance with the change in diameter of the narrowest stricture, an “improvement”. Univariate and multivariate analysis were performed to identify risk factors for restenosis.

3 Results

Forty-eight patients (37 male and 11 female) with median age of 30 years (range 14-72 years) at the time of diagnosis were analyzed. In 12.8 months of the mean time after the EBD session, decrease of a total number of strictures from 162 to 143 were observed in all patients along with decrease of the mean number of strictures per patient from 3.4 to 3 ($p=0.04$). The mean diameter of all strictures and the narrowest stricture increased significantly from 8.7 mm to 9.7 mm ($p=0.0004$) and from 7.6 mm to 8.7 mm ($p=0.0001$), respectively. Moreover, six patients became stricture free. But 32 (67%) patients developed endoscopic restenosis based on the changes on the diameter of the narrowest stricture. Univariate analysis revealed that a history of previous EBD, the interval between EBD and the follow-up session, and the presence of ulcers at the follow-up session were significantly related to the development of restenosis. Multivariate analysis showed the presence of ulcers at the follow-up session was positively associated with restenosis (odds ratio 9.4; 95% CI 1.51-58.4, $p = 0.01$), and a long interval between EBD and the follow-up session was negatively associated with restenosis (odds ratio 0.7; 95% CI 0.49-0.93, $p = 0.02$). Therefore, patients were categorized into four groups according to the presence of ulcer near stricture during both sessions: ulcer-remaining ($n=16$), ulcer-developed ($n=3$), ulcer-healed ($n=8$) and no-ulcer ($n=21$). Among them, only the no-ulcer group that included patients with complete mucosal healing throughout the study period showed significant improvement in the mean diameter of the narrowest strictures (7.4 to 9.1 mm, +1.7 mm, $p = 0.001$).

4 Conclusions

In summary, EBD is an effective treatment for CD-related small bowel strictures when patients could achieve complete mucosal healing. Therefore, maintaining complete mucosal healing is important factor to improve the long-term efficacy of EBD.

Keywords: calibrated small-caliber-tip transparent hood, Crohn's disease, double-balloon endoscopy, endoscopic balloon dilation, endoscopic restenosis

論文審査の結果の要旨

- ・本学位論文はクローン病における小腸狭窄に対して内視鏡的拡張術を行った際の再狭窄に関する因子を明らかにした。
- ・再狭窄を評価するためにメモリ付きの内視鏡フードを用いて狭窄径を客観的に評価した点に新規性がある。また、再狭窄の因子として、狭窄周囲の潰瘍の存在、特に小さな潰瘍であっても再狭窄の有意な因子であることを発見しており、潰瘍を生じさせないための治療が再狭窄を予防するうえで重要であることを見出した点が評価に値する。
- ・問題点としては、単施設の後向き研究であり、症例数および件数が少ないことが上げられるが、学位論文としてふさわしいと判断した。

最終試験の結果の要旨

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- ・再狭窄を評価するためにメモリ付きの内視鏡フードを用いて狭窄径を客観的に評価した点に新規性がある。また、再狭窄の因子として、狭窄周囲の潰瘍の存在、特に小さな潰瘍であっても再狭窄の有意な因子であることを発見しており、潰瘍を生じさせないための治療が再狭窄を予防するうえで重要であることを見出した点が評価に値する。
- ・問題点としては、単施設の後向き研究であり、症例数および件数が少ないことが上げられた。内視鏡的拡張術後に再狭窄が疑われる症例のフォローアップ期間が短いことに関する考察の追記、およびフォローアップ内視鏡時に観察された潰瘍の意義についての考察の追記を指導した。
- ・本日のプレゼンテーションでは学位論文の発表内容用は明確であり、各委員からの質問にも適切に返答がなされていた。よって全員一致で合格と判断した。