Endoscopic therapy of small bowel polyps by single balloon enteroscopy in patients with Peutz-Jeghers syndrome

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Abstract

Background: Little is known about the efficacy and safety of single balloon enteroscopy (SBE) in patients with Peutz-Jeghers syndrome (PJS). The aim of this study was to assess the efficacy and safety of SBE for treatment of small bowel polyps in patients with PJS. Methods: We conducted a single center observational study, which included all patients diagnosed with PJS who underwent SBE for polypectomy between January 2018 and March 2021. Complete treatment was defined as the absence of polyps[?]20mm after SBE resection. The clinical records were retrospectively reviewed. Results: 102 patients (including 40 men and 62 women) with a mean age of 28.7 years (range 13-55y), were enrolled in our study. The intubation depth via oral approach of patients with history of laparotomy was significantly shorter than that of the patients without history of laparotomy ([241.6±64.2] cm vs [280.9±40.2] cm, P = 0.008). The maximum size of the resected polyps via anus during the second hospitalization was significantly smaller than that during the first hospitalization ([2.25±1.29] cm vs [4.26±3.51] cm, P = 0.032). Complications occurred in 10/129 of hospitalizations (4 delayed bleeding, 3 perforation, and 3 acute pancreatitis). Conclusions: SBE is effective and safe for resection of small bowel polyps in patients with PJS.

Introduction

Peutz-Jeghers syndrome (PJS) is a rare autosomal dominant hereditary disorder characterized by mucocutaneous melanin pigmentation and multiple gastrointestinal (GI) hamartomatous polyps[1]. Hamartomatous polyps can be detected in the small bowel, most commonly in the jejunum[2]. These hamartomatous polyps in the small bowel can lead to bleeding, intussusception and obstruction[3,4]. Consequently, patients often undergo multiple laparotomies with intestinal resection, which can ultimately result in short-bowel syndrome and/or severe adhesions[4,5]. It is well acknowledged that large polyps (10-15mm) or symptomatic or rapidly growing polyps should be removed[2,6,7]. In addition, the risks of gastrointestinal and non-gastrointestinal malignancies significantly increase in patients with PJS[8,9].

Double balloon enteroscopy (DBE) was first introduced by *Yamamoto et al* . in 2001. The major advantage of DBE is that a wide variety of therapeutic interventions can be performed during the examination procedure[10-12]. Over the last decade, DBE has been reported to be useful for treatment of small bowel polyps in patients with PJS[13-16]. The data on the usefulness of DBE for treatment of polyps were focus on adult. However, the diagnosis and treatment procedures in children (aged 0-17 years old) with PJS may be difficult. The key reasons are as follows: One is narrow intestinal lumen, another is thinner intestinal wall, and the third is sharper angle of enteroscopy[17]. The evidence in regards to the role of enteroscopy in children with PJS is limited. Single balloon enteroscopy (SBE) was first introduced in 2007. The main advantages of SBE compared with DBE are ease of setup, shorter procedure time and lower operative cost[18,19].

The aim of this study was to evaluate the efficacy and safety of SBE in patients with PJS. In detail, the

aims were: 1) to evaluate the efficacy and safety of SBE in patients with PJS; 2) to evaluate the influence of laparotomy on SBE procedure; 3) to evaluate the efficacy and safety of SBE in children.

Patients and Methods

Patients

We conducted an observational retrospective study which included all patients with PJS from Zhejiang Provincial People's Hospital (People's hospital of Hangzhou medical college, Hangzhou, China), a tertiary-care referral center, who had undergone SBE for polypectomy between January 2018 and March 2021. Medical records of all the included patients were retrospectively reviewed. The following data were collected: age, gender, history of laparotomy, the method of SBE insertion, number of SBE procedures performed, maximum size and number of the resected polys, and complications. A clinical diagnosis of PJS can be made when any one of the following was present: 1) two or more histologically confirmed PJS polyps; 2) any number of PJS polyps detected in one individual who has characteristic mucocutaneous pigmentation or a family history of PJS in close relative(s); and 3) characteristic mucocutaneous pigmentation in an individual who has a family history of PJS in close relative(s)[20]. The study protocol was approved by the Ethics Committee of Zhejiang Provincial People's Hospital (Approval Number 2021QT244). This study was reviewed and approved by the Institutional. All information of patients in these records remained confidential.

SBE procedure

Before SBE procedures, patients were advised to abdominal ultrasound and CT enterography (CTE) for primary evaluation of small bowel. All the SBE procedures were performed by experienced endoscopists using the SIF-Q260 (Olympus, Japan) with a 200 cm working length and 2.8 mm working channel. In general, both anal and oral SBE procedures were performed. Unless it was clear that no polyps were present in the ileum, the anal approach was performed first because large polyps removed via the oral route may pile up on remaining distal polyps and cause obstruction or intussusception. Patients were advised to fluid diet the day before SBE operation, and poly ethylene glycol-electrolyte powder was used for intestinal cleaning. Because the SBE procedure time was long, all examinations were carried out with patients under general anesthesia with endotracheal intubation.

Polyps were resected during withdrawing endoscope to avoid bleeding and perforation at the wound after polypectomy. A diathermy loop was used to resect a polyp as one block or multi-block according to the size and pattern of base. The polyp size was estimated according to the width of the biopsy forceps or the diameter of the polypectomy snare. The retrieved polyps were measured with a ruler to determine the greatest dimension (Figure 1). Polyp resection was performed for polyps larger than 10 mm. However, if many polyps were found, polyps of over 20 mm in diameter were given priority for resection to prevent intussusception[14] (Figure 2). Complete treatment was defined by the absence of polyps[?]20mm after SBE resections. The absence of residual polyps was considered when all polyps detected at CTE examination were removed. If all of the large polyps could not be removed in one hospitalization, next SBE treatment was repeated within 6 months. Usually, endoclips (ROCC-D-26-230-C, Micro-Tech (Nanjing) Co. Ltd) were used to close the wound to prevent delayed bleeding and perforation. Only large and/or irregularly shaped polyps were retrieved for pathological examination. During the first intubation of SBE, endoclips were used at the deepest position for mark (Figure 3). Insertion depth was measured by accumulation of net advancement of each push-and-pull maneuver as described by *Rondonotti et al* [21]. Complications related to enteroscopy such as bleeding, perforation and acute pancreatitis were noted. Complications were classified as intraprocedural, early (within 24 hours), or delayed (2-30 days)[15]. All complications were obtained from hospitalization records or outpatient assessment.

Statistical analysis

Descriptive statistics were calculated for the patients' characteristics and SBE parameters, and are presented as medians, means, and ranges. Continuous variables were expressed as mean (standard deviation) or median (range). Categorical variables were presented as numbers and percentages or rates. Differences in

numerical variables were analyzed by the Student's t-test, or the Mann-Whitney U test. While differences in categorical variables were analyzed by the χ^2 test, or Fisher's exact test. A two-sided P value of less than 0.05 was considered statistically significant. All the statistical analyses were performed using SPSS 21.0 (IBM, Armonk, USA).

Results

Patient characteristics

As table 1 shows, 102 PJS patients (including 8 children) with a mean age of 28.7 years (range 13-55y), were enrolled in our study. The male/female sex ratio was 40/62. Among them, 43 (42.2%) patients had a family history of PJS. Moreover, 82 (80.4%) patients had a previous history of laparotomy. 23 patients had two or more hospitalizations. Regarding the history of cancer, 18 patients were diagnosed with cancer (breast cancer in three, colorectal cancer in three, and ovarian cancer in two, lung cancer in two, thyroid cancer in two, Cervical cancer in two, duodenal malignancy in two, and gastric cancer in two).

SBE procedure characteristics

All patients underwent CTE examination before SBE procedure, and confirmed the presence of polyps[?]10mm. As table 2 shows, A total of 129 hospitalizations (including 248 SBE procedures, 126 via oral approach and 122 via anal approach) were performed in 102 patients. A total of 5390 polys (diameter[?]10mm) were resected, including 3616 (67.1%) using an oral approach and 1774 (32.9%) using an anal approach. The mean intubation depth was (248.5±62.4) cm and (180.8±32.0) cm for the oral and anal procedures, respectively. The total enteroscopy rate was 42.4% (50/118). Regarding the procedure characteristics of children, A total of 723 polys were resected, including 429 using an oral approach and 294 using an anal approach. The mean intubation depth was (254.5±35.0) cm and (177.3±26.1) cm for the oral and anal procedures, respectively.

As table 3 shows, the maximum size of the resected polyps via the anal approach during the second hospitalization was significantly smaller than that during the first hospitalization ([2.25±1.29] cm vs [4.26±3.51] cm, P = 0.032). The median number of resected polyps was 38.0(oral approach) and 8.0 (anal approach) during the first hospitalization, and 27.0 (oral approach) and 4.0 (anal approach) during the second hospitalization. The number of resected polyps had a tendency to decrease, although these results were not statistically significant. As table 4 shows, the intubation depth via oral approach of patients with history of laparotomy was significantly shorter than that of the patients without history of laparotomy ([241.6±64.2] cm vs [280.9±40.2] cm, P = 0.008).

The overall complete treatment rate was 95.3%. For patients with total enteroscopy, 1 patient presented many large polyps that could not be resected in one hospitalization. Among the rest patients, all polyps larger than 10 mm were successfully resected. The complete treatment rate in these patients was 98%. For patients without total enteroscopy, 1 patient underwent surgical operation for a giant (>5cm) and wide-base polyp, 1 patient presented a polyp which is a suspect of malignant tumor in duodenum, and was diagnosed as adenocarcinoma after surgical operation, 3 patients presented residual polyps. Among the rest patients, all polyps larger than 10 mm in the examined segment of small bowel were resected successfully. All polyps suspected to be equal or larger than 20 mm by CTE were confirmed by SBE. The complete treatment rate in these patients was 93.7%.

Complications

A total of 10 (7.8%) complications occurred among the 129 hospitalizations. Delayed bleeding occurred in four patients. Two patients underwent conservative therapy, and two were managed with endoscopic hemostasis. Perforation occurred in three patients, among whom one received conservative therapy and two underwent surgical operations. Acute pancreatitis occurred in three patients, and all of them were treated conservatively with a favourable outcome.

Discussion

Our study showed that polyps larger than 10 mm in small bowel can be resected effectively. SBE is effective and safe for resection of small bowel polyps in patients with PJS. Treatment of small bowel polyps in PJS has evolved over the past decades. Before enteroscopy development, patients with PJS often underwent acute or elective operations for elective intestinal resection. *Hinds et al* reported that 68% of PJS patients underwent a laparotomy because of obstruction before the age of 18 years[22]. In our study, 80.4% of patients had undergone at least one laparotomy. In addition, the risks of gastrointestinal and non-gastrointestinal malignancies significantly increase in patients with PJS[8,9]. In our study, 18 (17.6%) patients were diagnosed with cancer (breast cancer in three, colorectal cancer in three, and ovarian cancer in two, lung cancer in two, thyroid cancer in two, Cervical cancer in two, duodenal malignancy in two, and gastric cancer in two). Therefore, except for surveillance of the small bowel, regular check-up on other organs of these patients may be important.

Success rates of total enteroscopy of DBE were reported to be 40% to 80%[23,24]. In our study, the success rate of total enteroscopy was 42.4%, probably because of high rate of previous laparotomies in these patients. Hence, we compared the intubation depth between patients with history of laparotomy and patients without history of laparotomy. We found that intubation depth via oral approach of patients with history of laparotomy was significantly shorter than that of the patients without history of laparotomy ([241.6±64.2] cm vs [280.9±40.2] cm, P = 0.008). Intraabdominal adhesions would influence the motion of small bowel within the abdominal cavity, impacting the intubation depth of SBE. Laparotomies should be avoided if at all possible. The complication rate (7.8%) of this study was slightly higher than that previously reported by *Sakamoto et al* (6.8%)[14] and Mensink et al (4.3%)[25]. The key point may be that most of SBE procedures involved polypectomies of multiple large polyps, which were technically challenging. After conservative therapy or surgical operations, these patients had favorable final outcomes. Regarding the complication of children, only one perforation occurred among the 8 patients. The complication rate was not increased for children as we reported in this study. However, the SBE procedures in children with PJS are difficult. The key reasons are as follows: One is narrow intestinal lumen, another is thinner intestinal wall, and the third is sharper angle of enteroscopy. The sample size of children was small, the safety of SBE in children should be interpreted with caution.

The major limitation of this study was its retrospective and single center design. However, due to its large number of patients and polypectomies, it allows us to draw some conclusions regarding efficacy and safety.

Conclusion

In summary, SBE is effective and safe for resection of small bowel polyps in patients with PJS. More well-designed studies, particularly those focusing on the safety and operation technique of SBE in children, are required.

Authors' Contributions: (I) study concept and design: All authors; (II) acquisition of data: Cao ZS and Wu XP; (III) drafting of the manuscript: Cao ZS and Jin WL; (IV) statistical analysis: Cao ZS and Jin WL; (V) study supervision: All authors; (VI) obtained funding: Pan WS; (VII) critical revision of the manuscript: Pan WS; (VI) Final approval of manuscript: All authors.

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Statement of Ethics: The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the Ethics Committee of Zhejiang Provincial People's Hospital (Approval Number 2021QT244). The exception to the requirement of informed consent was obtained from the Ethics Committee of Zhejiang Provincial People's Hospital.

Data Availability Statement: All information of patients in these records remained confidential. Further enquiries can be directed to the corresponding author.

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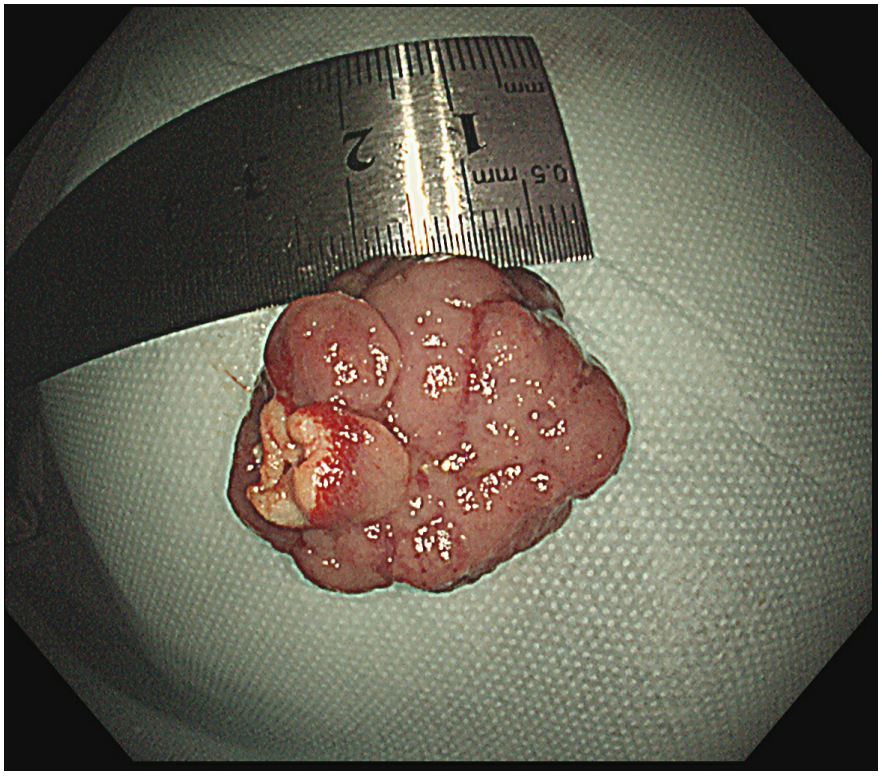
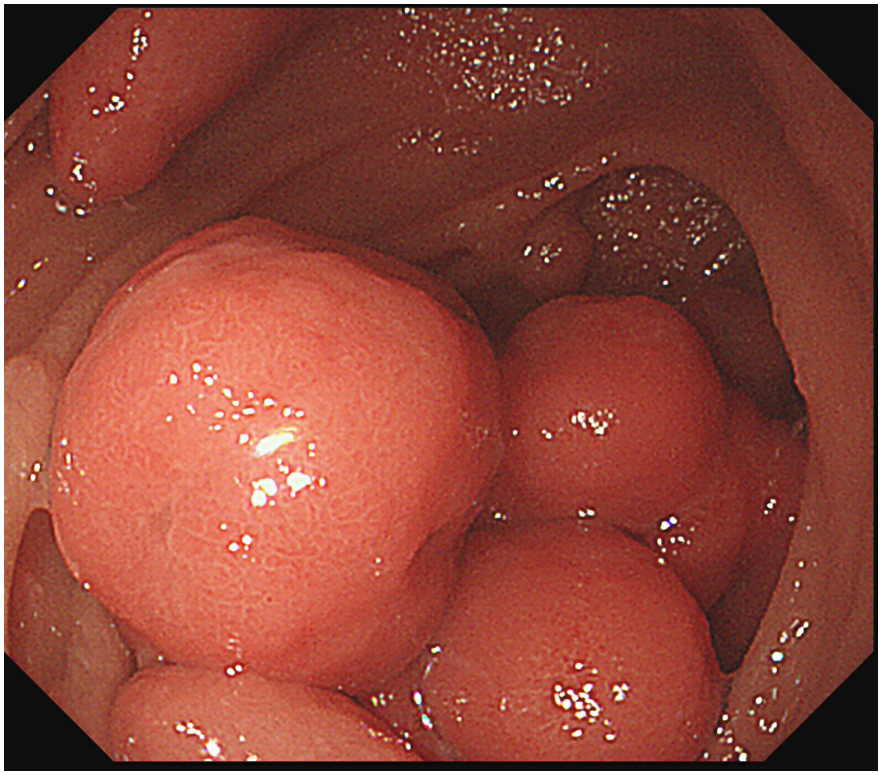
Figure legends

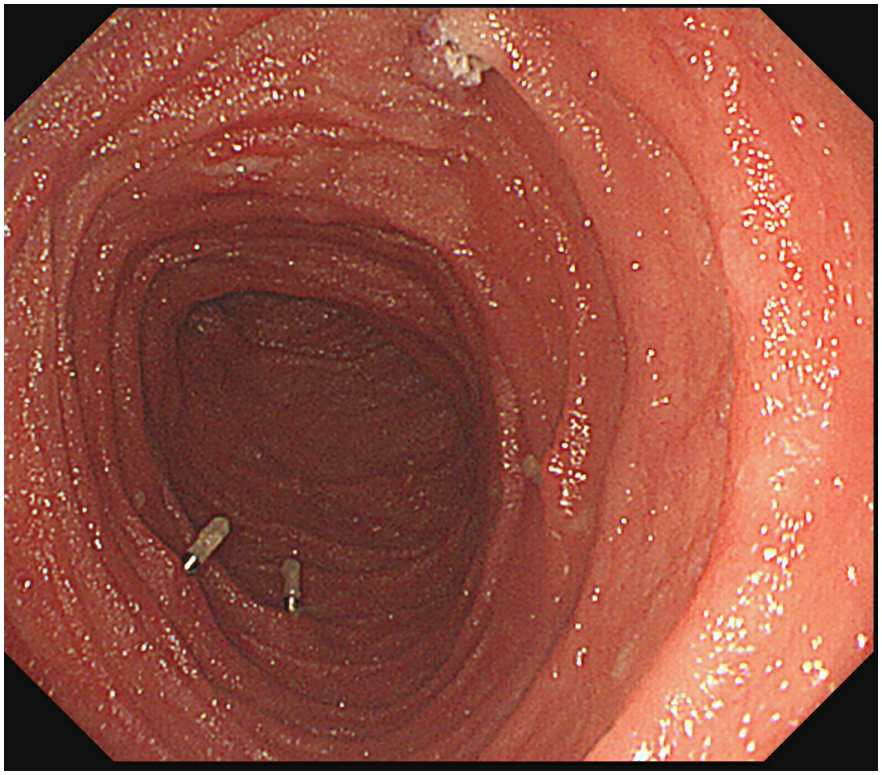
Figure 1. A retrieved polyp was measured with a ruler to determine the greatest dimension.

Figure 2 . Multiple polyps observed under SBE.

Figure 3 . Endoclips were used at the deepest position for mark.







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