

Complete biopsy resection of diminutive polyps

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Background and study aims: Cold biopsy forceps polypectomy (CBP) is commonly used for the removal of diminutive polyps; however, evidence for the efficacy of CBP is lacking. The aim of this study was to evaluate the adequacy of resection of diminutive polyps and to identify predictors for complete resection using CBP.

Patients and methods: This was a prospective study from a tertiary referral hospital in Korea. A total of 196 patients were screened, and 65 patients with diminutive polyps were enrolled. CBP was used to resect diminutive polyps until no polyp was visible by chromoendoscopy using indigo carmine spray. Each polyp base was then resected using endoscopic mucosal resection (EMR) with a 1–3-mm free margin. CBP and EMR specimens were sent to the histopathology department for the evaluation of the completeness of the resection. Cross sections of the EMR specimens made at 1-mm intervals were examined by a pathologist.

Results: A total of 86 diminutive polyps were available for assessment. Overall, 90.7% (78/86) of the diminutive polyps were completely resected using CBP (95%CI 84.6–96.8%). The complete resection rate for all diminutive adenomas was 92.3% (60/65; 95%CI 85.8–98.8%) and for 1–3-mm adenomas 100% (95%CI 81.5–100%). Polyp size, histology, and location, and number of biopsies were not different between the complete and incomplete resection groups.

Conclusions: In this small study approximately 90% of all diminutive polyps and 100% of 1–3-mm adenomatous polyps were completely resected using CBP and chromoendoscopy. CBP appears to be adequate for the resection of the majority of diminutive polyps, especially small sized adenomas (≤ 3 mm) if no residual tissue is visible by chromoendoscopy.

Introduction

Diminutive colonic polyps are those of ≤ 5 mm in diameter. The detection rate of diminutive polyps has increased since high definition colonoscopy has become widely available [1]. As a result, interest in diminutive colon polyps has increased. Actually, several recent studies revealed that 75%–82% of polyps found during colonoscopy were diminutive polyps (≤ 5 mm) [2–4]. Diminutive polyps are prone to being neglected because they are usually hyperplastic and pose no immediate threat to patients; however, a significant proportion of diminutive polyps (up to 50%–64%) have been reported to be adenomas [3,5,6]. Furthermore, one recent study reported that 10% of diminutive polyps were advanced adenomas [3]. Considering that approximately 30% of interval colorectal cancer (CRC) cases are caused by incomplete polyp resection [7,8], the complete re-

section of diminutive adenomas should be an issue of concern.

Endoscopic techniques for removing diminutive polyps include cold biopsy, hot biopsy, and cold snaring. There are limited data regarding the completeness of polyp resection with each technique, hence the optimal technique for treating diminutive polyps has not been firmly established. Although cold biopsy forceps polypectomy (CBP) is commonly used for removing diminutive polyps, there is very little evidence regarding the efficacy of CBP for treating diminutive polyps. A previous study found that 29% (23/79) of diminutive polyps removed using CBP had residual polypoid tissue detected by sigmoidoscopy 3 weeks after treatment [9]. However, a more recent study showed that 61% (33/54) of diminutive polyps were incompletely resected using CBP [10]. These results led us to question whether it is reasonable to resect diminutive polyps using CBP. Di-

minutive polyps (≤ 5 mm) are expected to be completely resected with forceps of 7 mm when correct targeting and strict investigation of the residual tissue are performed. Therefore, the present study was conducted to evaluate the adequacy of diminutive polyp resection using CBP and subsequent chromoendoscopy, which was used to detect the presence of residual tissue. The study also sought to identify predictors of complete resection using CBP.

Patients and methods

Patients

This was a prospective study conducted at a tertiary referral center in Seoul, Korea, between March 2012 and December 2012. Adult patients undergoing colonoscopy for CRC screening or non-specific gastrointestinal symptoms and patients who were referred for colon polypectomy were candidates for inclusion in this study. Exclusion criteria were as follows: age under 18 years, treatment with clopidogrel or warfarin with an international normalized ratio of >2 , and thrombocytopenia (platelet count $<100\,000$ cells/ μL). Patients who agreed to participate were enrolled if they were found to have at least one diminutive colonic polyp (≤ 5 mm in diameter).

The study protocol was approved by the institutional review board of Kangbuk Samsung Hospital, Seoul, Korea. All patients who agreed to participate in the study signed a written informed consent form.

Polypectomy and EMR protocol

Conventional colonoscopes (CF-Q260AI, CF-H260AI; Olympus Medical Systems, Tokyo, Japan) were used for all procedures. Procedures were performed under conscious sedation by one staff endoscopist who had over 10 years of experience in colonoscopic polypectomy.

On the day before the scheduled colonoscopy (until 20:00 hours), all participants were asked to consume a clear liquid diet for all three meals. All bowel cleansing was performed using 4 L of polyethylene glycol (PEG) solution (Taejoon Pharm. Inc., Seoul, Korea). All participants were instructed to ingest the PEG as a split dose: 2 L between 20:00 and 22:00 on the day before the colonoscopy and the remaining 2 L of the solution between 06:00 and 08:00 on the day of the colonoscopy. All colonoscopy procedures were performed between 2 and 7 hours after the last ingestion of PEG.

As the study was only interested in the complete resection of diminutive adenomas, polyps in the rectosigmoid area that appeared macroscopically hyperplastic were excluded from the study. Polyp size was estimated by open biopsy forceps (oval spoon-shaped mouth without spike; MTW, Düsseldorf, Germany). When these forceps are fully open, the length between the two jaws of the forceps is 7 mm. Using this method, polyps were divided into two groups: ≤ 3 mm and > 3 mm. After polyp size had been documented, the polyp was resected using the biopsy forceps until no residual tissue was seen after spraying with 0.016% indigo carmine solution using a catheter. Before spraying with indigo carmine solution, the CBP site was rinsed with normal saline until oozing stopped. The number of "bites" required for resection was recorded. The specimens were retrieved and stored in formalin, and were labeled "1-1."

The base of the CBP site was lifted by submucosal injection of mixed solution (normal saline+0.016% indigo carmine+0.01%

epinephrine) using a TeleMed disposable sclerotherapy needle (TeleMed Systems, Inc. Hudson, Massachusetts, USA). The base of the CBP site was then resected with a clear margin of 1–3 mm with a ConMed soft loop wire optimizer polypectomy snare (a 15-mm, oval-shaped, and braided snare; ConMed, Utica, New York, USA) and electrocautery. Electrocautery was performed using an ERBE electrosurgical generator on the "Endocut" setting (ERBE Elektromedizin, Tübingen, Germany). Each specimen was retrieved and stored in a separate container labeled "1-2."

CBP and EMR specimens were sent to the histopathology department, and an experienced gastrointestinal pathologist evaluated the completeness of resection. Cross sections of the EMR specimens are usually taken at 2-mm intervals for pathological examination in real practice; however, to examine the residual polyp tissues more meticulously, the pathologist was asked to examine the EMR specimens at 1-mm intervals within the boundary of the CBP margin. Therefore, the pathologist assessing the specimens was not blinded to the study. The process is shown in **Fig. 1**. The participants returned to the hospital within 1 month of their colonoscopy to be assessed for post-procedural complications.

Statistical analysis

The software program SPSS (v. 12, Chicago, Illinois, USA) was used for statistical analyses. The chi-squared test or Fisher's exact test was used to compare categorical variables. *P* values of <0.05 were considered to be statistically significant. A similar study reported that 40% of diminutive polyps were completely resected using CBP [10]. We hypothesized that at least 60% of diminutive polyps would be completely resected using CBP. Assuming a 20% difference in the rate of completely resected polyps between the results of Efthymiou et al. [10] and the current study, the estimated sample size was 48 polyps with an α value of 0.05 and a power of 80%. Considering that the polyp detection rate is 40% and that 70% of polyps found during colonoscopy are diminutive polyps [2–4], we estimated that at least 172 patients would need to be included in the study.

Results

A total of 196 patients were screened, and 65 patients with diminutive polyps were enrolled. A total of 88 diminutive polyps were removed. Of these polyps, two polyps were excluded because they were proven to be normal mucosa. Finally, a total of 86 diminutive polyps were available for assessment (**Fig. 2**). The mean age of the patients was 59.9 ± 11.7 years (range 26–78 years), and 70.8% (46/65) were men. Common indications for colonoscopy were: CRC screening (41.5%), referred for polypectomy (24.6%), and past history of colon polyps (21.5%) (**Table 1**). The mean total procedure time was 18.3 ± 9.6 minutes (range 11–48 minutes), and the mean withdrawal time was 14.1 ± 7.2 minutes (range 7–41 minutes). Complete colonoscopy was performed in all patients.

Diminutive polyps were most often resected in the descending colon (23.3%) and sigmoid colon (33.7%) (**Table 2**). Of all polyps, 75.6% (65/86) were adenomas and 24.4% (21/86) were hyperplastic. All adenomas displayed low grade dysplasia. Overall, the median number of bites of the forceps was 2 (range 1–5). The median number of bites for adenomas and hyperplastic polyps were 2 (range 1–4) and 2 (range 1–5), respectively. The complete resection rate using CBP was 90.7% (78/86). The size, histology, and location of polyps and the number of bites

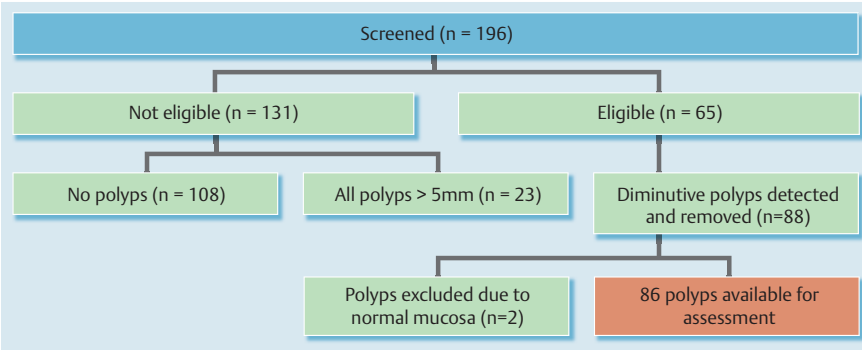
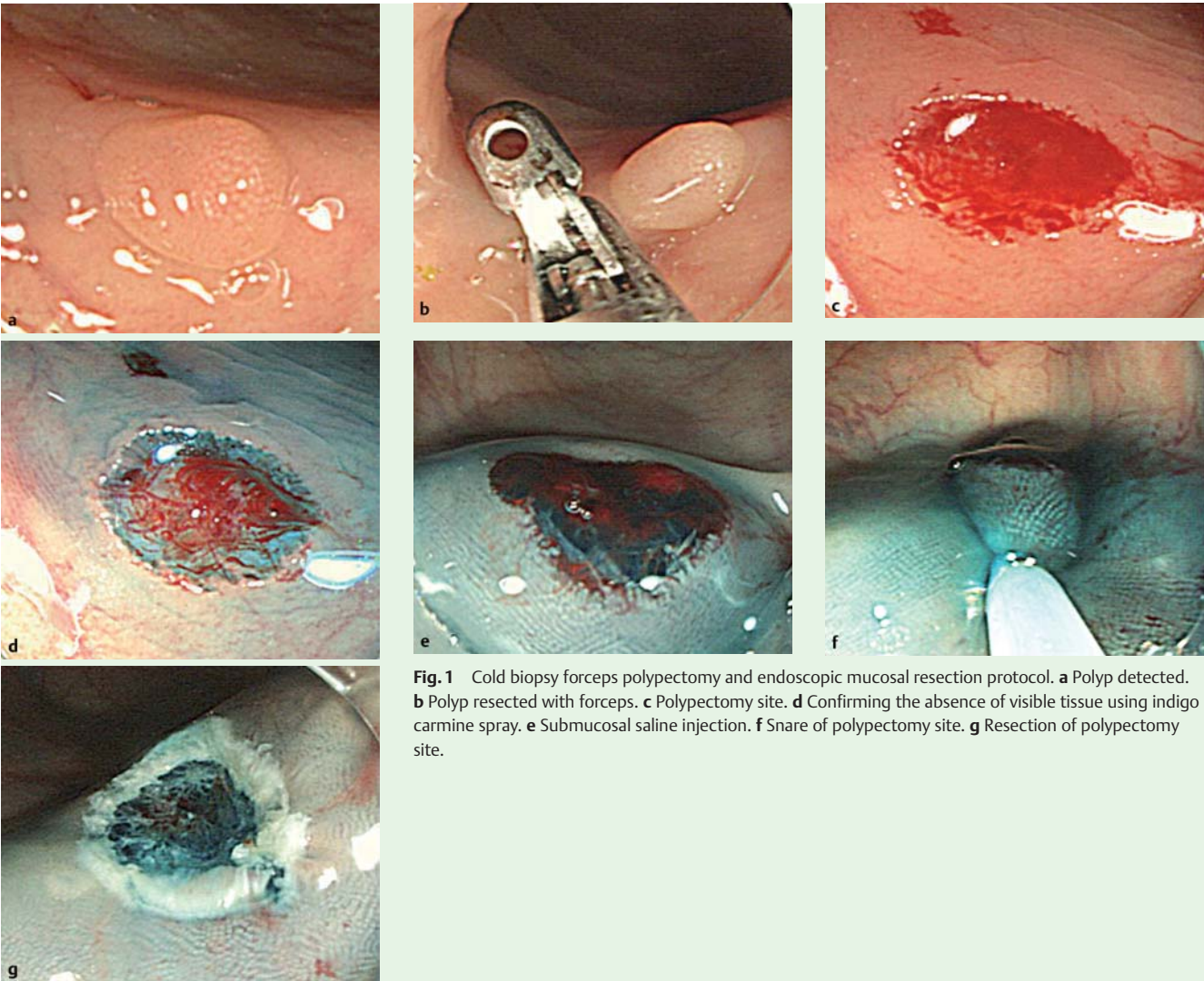


Fig. 2 Enrollment flow chart.

Table 1 Indication for colonoscopy.

Indication	No. of patients (%) n = 65
Screening	27 (41.5)
Referred for polypectomy	16 (24.6)
Past history of colon polyps	14 (21.5)
Abdominal pain	2 (3.1)
Hematochezia/melena	3 (4.6)
Altered bowel habits	1 (1.5)
Other	2 (3.1)

Table 2 Distribution of diminutive polyps.

Location	No. of polyps (%) n = 86
Cecum	2 (2.3)
Ascending colon	15 (17.4)
Hepatic flexure	4 (4.7)
Transverse colon	8 (9.3)
Descending colon	20 (23.3)
Sigmoid colon	29 (33.7)
Rectum	8 (9.3)

Table 3 Diminutive polyp complete resection rate using cold biopsy forceps polypectomy according to size, histology, number of bites, and location.

	Complete resection rate, n/N (%)	95%CI	P value
Overall complete resection	78/86 (90.7)	84.6–96.8	
Size			
≤3 mm	21/22 (95.5)	86.8–104.6	0.674
>3 mm	57/64 (89.1)	81.5–96.7	
Histology			
Adenoma	60/65 (92.3)	85.8–98.8	0.398
Hyperplastic polyp	18/21 (85.7)	70.7–100.7	
Number of forceps bites			
≤2 bites	61/66 (92.4)	86.0–98.8	0.381
>2 bites	17/20 (85.0)	69.4–100.6	
Location			
Right colon	17/21 (81.0)	64.8–97.8	0.095
Left colon and rectum	61/65 (93.8)	87.9–99.7	

taken with the forceps were not different between the complete resection group and the incomplete resection group. The complete resection rates were as follows: 95.5% (21/22) for polyps ≤3 mm vs. 89.1% (57/64) for polyps >3 mm ($P=0.674$); 92.3% (60/65) for adenomas vs. 85.7% (18/21) for hyperplastic polyps ($P=0.398$); and 92.4% (61/66) for polyps with ≤2 bites vs. 85.0% (17/20) for polyps with >2 bites ($P=0.381$). The complete resection rate of polyps in the right colon was lower than that of polyps in the left colon and rectum, but this trend did not reach statistical significance (81.0% vs. 93.8%; $P=0.095$) (Table 3). The complete resection rate of adenomatous polyps ≤3 mm was higher than that of adenomatous polyps >3 mm, although this trend did not reach statistical significance (18/18, 100% [95%CI 81.5–100%] vs. 42/47, 89.4% [76.9–96.5%]; $P=0.311$).

There were no complications such as delayed bleeding or perforation due to colonoscopy or polypectomy.

Discussion

Diminutive polyps can be removed using biopsy forceps or snaring, with or without electrocautery. CBP is commonly used for removing diminutive polyps because of its convenience and speed; however, the completeness of diminutive polyp resection using CBP is not well known. To the best of our knowledge, there have been only two studies that have investigated the efficacy of CBP. Woods et al. [9] reported that the rate of complete resection using CBP was 71%. In their study, sigmoidoscopy was performed 3 weeks after CBP, and biopsies were performed at the CBP site. Moreover, biopsies of residual polypoid material could not be uniformly obtained. Therefore, their study was limited in that the completeness of diminutive polyp resection by CBP could not be assessed accurately. More recently, Efthymiou et al. [10] used EMR to evaluate the efficacy of CBP for the resection of diminutive polyps. They reported that only 39% of diminutive polyps were completely resected using CBP, and concluded that biopsy forceps were inadequate for the resection of diminutive polyps. It is surprising that the complete resection rate of CBP for diminutive polyps was so low, because diminutive polyps are expected to be resected completely by forceps 7 mm in size. Their results led us to question whether CBP is adequate for the resection of diminutive polyps.

Although Efthymiou et al. stated that no remaining tissue was visible following washing we postulated that a more detailed assessment of the polypectomy site may help to identify residual tissue and thus allow for complete resection with subsequent “bites.” In the current study, therefore, chromoendoscopy with indigo carmine spray was used to assess CBP resection. This is the first prospective study to investigate the outcomes of CBP for the resection of diminutive polyps using EMR and chromoendoscopy. In contrast to the results of Efthymiou et al., the current results showed that the complete resection rate of CBP for diminutive polyps was high (90.7%). Based on these results, CBP seems to be adequate for the resection of the majority of diminutive polyps if no evidence of residual tissue is confirmed after CBP.

Another reason for the discrepancy between the current results and those of Efthymiou et al. may be the difference in polyp volume. More polyps with large volume (high height) may have been included in the Efthymiou study than in the current study, even though the polyp sizes (diameter) in the two studies were similar. Furthermore, the types of forceps and colonoscopies used in the current study were different from those used in the Efthymiou study, which might have been the reason for the differences in the outcomes between the two studies.

There are three main objectives to consider when removing diminutive polyps: (1) complete removal of the polyps, (2) avoidance of complications such as bleeding or perforation, and (3) maintenance of the histological quality of the polyps. Approximately 30% of interval CRC occurs in the same segment as the previous polypectomy, suggesting incomplete resection [7,8]. Several studies have reported that 50%–64% of diminutive polyps are adenomas and that 10% have advanced histology [3, 5,6]. Although the size of diminutive polyps is small, it is important to remove diminutive polyps completely. Unfortunately, only a few studies have assessed the completeness of diminutive polyp resection with each polypectomy technique. A previous study reported that the residual rate after the removal of diminutive polyps was not different between the cold biopsy group (29%) and the hot biopsy group (21%) [9]. In several studies of hot biopsy forceps treatment of diminutive polyps, the failure rate of polyp eradication was 17%–22% [11–13]. Although the current study was an indirect comparison, it does show that cold biopsy is not inferior to hot biopsy in terms of the efficacy of diminutive polyp removal. Furthermore, the residual rate in previous studies may have been underestimated because the presence of residual tissue was only confirmed by sigmoidoscopic biopsy for macroscopically identifiable polyp remnants 1–4 weeks after hot biopsy forceps polypectomy. In the current study, EMR was performed immediately after CBP to confirm the existence of residual tissue.

Some endoscopists recommend cold snaring for diminutive polyp resection [14]. Deenadayalu et al. [15] and Ichise et al. [16] reported a polyp retrieval rate approaching 100% with cold snaring. Furthermore, several studies have demonstrated that there were no complications from cold snaring [15,17]. The polyp retrieval rates and complication rates between cold snare and cold forceps are unlikely to vary significantly. Therefore, the choice of technique should be based on the efficacy of polypectomy. To our knowledge, there have been no published studies evaluating the completeness of cold snaring for diminutive polyp resection. Only two unpublished studies (abstracts) have reported on cold snare polypectomy, with incomplete resection rates of 11%–14% [13,18]. Although these results may be unreliable, cold snaring does not seem to be superior to CBP. However, there are no pub-

lished studies comparing the complete resection rate of cold snaring and cold forceps. Further studies are required to directly compare the efficacy of these two techniques. Very recently, Pohl et al. [19] revealed that of 346 neoplastic polyps between 5 and 20 mm, 10.1% were incompletely resected. In their study, all polyps were removed using hot snare polypectomy. Although there were differences in polyp size and techniques for removing polyps in this study compared with the current study, the rate of incompletely resected polyps was similar. The current study may have less clinical relevance to the practice of colonoscopy because it only included diminutive polyps and investigated a much smaller number of polyps. Both studies suggest that a non-negligible portion of polyps may be incompletely resected in clinical practice. Considering that incomplete resection might contribute to the development of interval cancers, colonoscopy quality measures need to focus on polyp resection as well as polyp detection. Several studies have investigated complication rates after the removal of diminutive polyps. In a study of 907 polyps removed by hot biopsy [20] and a study of 208 polyps removed by cold snaring [17], there were no complications. Conversely, one study reported that 53 (0.41%) bleeding events and 7 (0.05%) perforations occurred in the removal of 13 081 polyps by hot biopsy [21]. Most of the complications of polypectomy are related to electrocautery [14]. The electrocautery burn can be uncontrolled, deep, and cause transmural injury or perforation [14]. Considering these potential risks together with the evidence of ineffective resection, hot biopsy polypectomy seems to be inadequate for the resection of diminutive polyps. Moreover, in a study comparing the diagnostic quality of polyps obtained using hot biopsy and cold biopsy techniques, histological evaluation was more difficult in polyps resected with hot biopsy compared with cold biopsy [22].

There was a trend toward a higher complete resection rate in polyps ≤ 3 mm compared with polyps > 3 mm (95.5% vs. 89.1%), although this trend did not reach statistical significance. Adenomatous polyps also showed a similar trend (100% vs. 89.4%). These results suggest that CBP can be considered as the first-line treatment for polyps ≤ 3 mm. However, a 10% incomplete resection rate of diminutive polyps > 3 mm is not low. When a diminutive polyp > 3 mm is resected using CBP, a more detailed inspection of the resection site is essential for the complete resection. Further large scale studies are needed to confirm the efficacy of CBP as a technique for removing diminutive polyps, especially polyps > 3 mm.

CBP is a simple and quick technique allowing complete resection of most diminutive polyps provided that the polypectomy site is assessed using chromoendoscopy. Under these circumstances, CBP may be a suitable alternative to cold snare polypectomy. However, the efficacy of CBP in the absence of assessment of the polypectomy site with chromoendoscopy may be significantly lower than that demonstrated in this study and therefore cannot be recommended for routine polypectomy at this point in time. Moreover, it should be noted that a non-negligible proportion of diminutive polyps (9.3%) were incompletely resected using CBP. The optimal CBP technique is as follows. Following the detection of the diminutive polyp, the polyp is resected using biopsy forceps, ensuring accurate targeting and using multiple "bites" if necessary. After resection, the resection site is rinsed with normal saline until oozing stops. Then, the resection site is thoroughly inspected using a method such as chromoendoscopy. If residual tissue is seen, this process is repeated.

The current study had several limitations. First, the sample size was small; however, the study included the largest number of polyps compared with other studies of the residual rate of diminutive polyps after CBP. Second, CBP was not compared with other techniques such as cold snaring and hot biopsy. Therefore, further investigations are needed to evaluate whether CBP is the best treatment modality for diminutive polyps. Third, as diminutive polyps are commonly encountered during colonoscopies, spraying of indigo carmine onto all CBP sites may be time consuming and cumbersome. Finally, only one experienced endoscopist performed CBP for diminutive polyps in this study. Therefore, it is possible that operator-related factors influenced the results and that the efficacy of CBP for the resection of diminutive polyps might be lower in average practice. The efficacies of CBP performed by many endoscopists should be investigated to generalize the results.

In conclusion, approximately 90% of diminutive polyps and 100% of adenomatous polyps ≤ 3 mm were completely resected using CBP and chromoendoscopy. Based on the results of this study, CBP seems to be adequate for the resection of the majority of diminutive polyps, especially small sized polyps (≤ 3 mm) when performed by a very experienced and meticulous endoscopist with a thorough inspection of the resection site using a chromoendoscopy technique such as indigo carmine spray. Further studies comparing the efficacy of CBP with cold snare polypectomy are warranted to confirm the reliability of CBP as a technique for removing diminutive polyps.

Competing interests: None

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