

# Risk of delayed bleeding before and after implementation of cold snare polypectomy in a screening colonoscopy setting



## Authors

Li-Chun Chang<sup>1,2,3</sup>, Chia-Tung Shun<sup>4</sup>, Wen-Feng Hsu<sup>1</sup>, Chia-Hong Tu<sup>1,3</sup>, Chieh-Chang Chen<sup>1</sup>, Ming-Shiang Wu<sup>1</sup>, Han-Mo Chiu<sup>1,3</sup>

## Institutions

- 1 Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan.
- 2 Graduate Institute of Clinical Medicine, College of Medicine, National Taiwan University, Taipei, Taiwan.
- 3 Health Management Center, National Taiwan University Hospital, Taipei, Taiwan.
- 4 Department of Pathology, National Taiwan University Hospital, Taipei, Taiwan.

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## Bibliography

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## Corresponding author

Han-Mo Chiu, MD, PhD, Clinical Professor, Department of Internal Medicine, National Taiwan University Hospital, No. 7 Chung-Shan South Road, Taipei, Taiwan  
 Fax: +886-2-2341-2775  
[hanmochiu@ntu.edu.tw](mailto:hanmochiu@ntu.edu.tw)

## ABSTRACT

**Background and study aims** Cold snare polypectomy (CSP) is considered to be effective in reducing risk of delayed bleeding but randomized trials fail to support this ow-

ing to the small sample size. The current study aimed to compare risk of delayed bleeding before and after implementation of CSP in a screening colonoscopy setting.

**Patients and methods** This study retrospectively analyzed a prospectively maintained screening colonoscopy database in a university hospital in Taiwan. We compared the rate of delayed bleeding before and after implementation within similar periods (18 months and 15 months) and the respective number of polypectomies (1,304 and 1,255) performed to remove small and diminutive polyps. The main outcome measurement was delayed bleeding within the two periods. Multivariate analysis was performed to adjust for major confounders.

**Results** A total of 1,304 and 1,225 subjects received hot snare polypectomy (HSP) and CSP in two separate periods, respectively. Compared with the HSP, the CSP had a lower rate of delayed bleeding (0.1% vs. 1.1%,  $P < 0.001$ ), severe bleeding (0% vs. 0.7%,  $P < 0.01$ ), need for second-look colonoscopy (0% vs. 0.8%,  $P < 0.01$ ), and emergency service visits (0.1% vs. 1.0%,  $P < 0.01$ ). Total procedure time ( $12.60 \pm 11.45$  vs.  $16.48 \pm 14.27$  min/person,  $P < 0.01$ ) and duration of hospital stay ( $1.18 \pm 0.50$  vs.  $1.53 \pm 5.78$  hour/person,  $P < 0.03$ ) were also shorter after CSP implementation. Multivariate analysis showed that HSP was an independent risk factor for delayed bleeding after adjusting for age, gender, and number of polyps (adjusted odds ratio 14.4; 95% confidence interval = 1.88–110.6).

**Conclusion** Implementation of CSP significantly reduces risk of delayed bleeding associated with removing small and diminutive polyps in screening colonoscopy.

## Introduction

Nearly 90% of neoplastic polyps usually removed during colonoscopy are small and diminutive [1]. With such a high proportion, it is crucial to find a safe and effective way to resect the lesions to optimize procedural safety, effectiveness, and efficiency. Hot snare polypectomy (HSP) has been applied as the conventional procedure for removing lesions by means of electrocautery. Use of electrocautery, however, may lead to ther-

mal injury of the colonic wall and increase risk of subsequent delayed bleeding, post-polypectomy syndrome and even perforation [2]. Therefore, the authors of prior studies have speculated that these procedure-related risks could be reduced by replacing conventional electrocautery with a more effective polypectomy method [3–4].

Cold snare polypectomy (CSP) is a method for removing small and diminutive polyps by mechanical transection with polypectomy snare without applying electrocautery. This tech-

nique was first introduced in 1985 by Tappero et al., who removed 288 consecutive small polyps using mechanical stranguation [3]. In their series, no bleeding, perforation or mortality occurred. As such, CSP was considered to have potential to reduce risk of post-polypectomy bleeding attributable to thermal injury. Thus, the European Society of Gastrointestinal Endoscopy clinical guideline recommended CSP for removing diminutive and small polyps [5]. A recent retrospective case-control study also supported that CSP could effectively reduce the risk of post-polypectomy bleeding [6]. The superiority of CSP in reducing bleeding complications was also explored in high-risk subjects. Horiuchi et al. demonstrated in a randomized controlled trial (RCT) that risk of post-polypectomy bleeding of subjects taking anticoagulants could be reduced by CSP [4]. However, one meta-analysis that summarized six RCTs demonstrated that CSP and HSP had a comparable risk of post-polypectomy bleeding [7]. Nevertheless, RCTs investigating the efficacy of CSP in reducing risk of post-polypectomy bleeding in an average-risk screening population are lacking because to show the paucity of bleeding events with sufficient statistical power requires a large sample size [8–12]. Even with the evidence to date of multiple studies, it remains inconclusive whether CSP is able to reduce risk of post-polypectomy bleeding and further investigation is warranted.

We hypothesized that implementation of CSP practice in an endoscopic unit may significantly reduce risk of post-polypectomy bleeding. Therefore, the aim of this study was to compare risk of bleeding in a high-volume screening colonoscopy setting before and after universal implementation of CSP for resecting polyps of less than 10 mm.

## Patients and methods

### Study sample, setting, implementation of CSP, and ethical considerations

Study subjects were selected from a consecutive series of patients who voluntarily submitted to annual health check-ups, including screening colonoscopy, at the Health Management Center of National Taiwan University Hospital. The annual volume of this screening unit is more than 8000 patients. Detected colorectal polyps are routinely removed by forceps biopsy, snare polypectomy, or endoscopic mucosal resection (EMR) as indicated. Patients who receive screening colonoscopy are routinely contacted by telephone after the procedure to monitor and ascertain the occurrence of any adverse events within 48 hours. In addition, a 24-hour hotline is also provided for the convenience of contact by the participants. Any significant post-colonoscopy adverse events, including bleeding, post-polypectomy syndrome, even perforation and emergency department visits, are routinely recorded in the administrative database. Every patient could be reached by this bidirectional telephone contact and this can guarantee the completeness of follow-up and minimize the possibility of response bias.

CSP was implemented in March 2016 and colorectal polyps measuring 4 to 10 mm were removed by CSP thereafter. Prior to implementation of CSP, HSP was the standard way of removing polyps measuring 4 to 10 mm during colonoscopy. Except

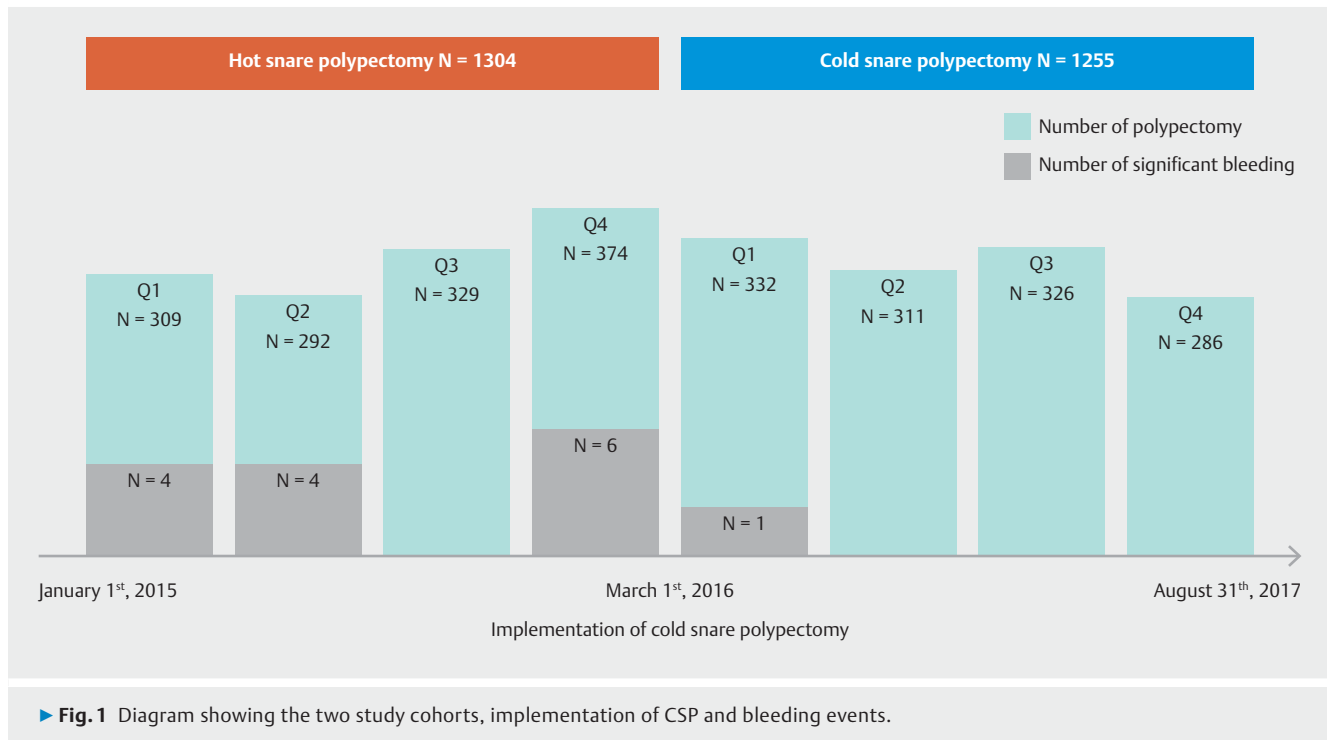
for switching from HSP to CSP, application of forceps biopsy for removing tiny polyps or snare polypectomy/EMR for larger polyps was not changed. Accordingly, the duration of March 2016 to August 2017 was defined as the CSP period and January 2015 to March 2016 as the HSP period as an historical control. Either CSP or HSP was the only modality for removing polyps sized 4 to 10 mm in individual corresponding period.

The comorbid status was measured and quantified with Charlson comorbidity index (CCI), which is a well-documented and comprehensive method for scoring comorbidity [13]. Before implementation of the current study, the study protocol received approval (No.201802040RIND) from the institutional review board and the ethical committee of our institution. The study report manuscript was prepared according to the guidelines provided by the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement [14].

### Endoscopic procedures and perioperative management

Prior to screening colonoscopy, all participants were asked to complete and submit a standard questionnaire to obtain their personal and medical history, including use of antiplatelet or anticoagulant agents, existence of comorbidities, and indications for colonoscopy as described in our previous study [15]. The laxative regimen and timing of bowel preparation in our setting was also addressed as previously described [16]. The regimen for bowel preparation was same-day 2-liter polyethylene glycol electrolyte lavage solution (PEG-ELS) following by 1- to 2-liter water at the timing of 5 to 9 hours prior to colonoscopy. During colonoscopy withdrawal, the detected polyp(s) was documented in terms of anatomical location, size, and methods applied for neoplasm resection. Lesion size was measured using biopsy forceps with a 2-mm outer diameter or snares with an outer diameter of 10 to 20 mm. Polyp morphology was classified according to the Paris classification [17]. Lesions smaller than 4 mm were removed by cold forceps biopsy in both groups. Lesions larger than 10 mm were removed by either endoscopic mucosal resection (EMR) (flat or sessile lesions) or HSP (pedunculated lesions) during both CSP and HSP periods. For lesions measuring 4 to 10 mm, CSP was applied routinely after its March 1 implementation.

The procedures were performed by seven experienced colonoscopists from our institution using a colonoscope with variable-stiffness function (CF-260 or 290 series; Olympus Medical Systems, Tokyo, Japan). All colonoscopists had sufficient expertise and skills for performing polypectomy, together representing at least 5000 previous colonoscopies. Each endoscopist had at least 7 years of experience before the beginning of the study and it ensure the steady performance before and after implementation of CSP. Stiff snares were used for CSP (Captivator-Small Hex 13 mm, Captivator II-Round 10 mm, and Captivator II-Round 15 mm, Boston Scientific, Massachusetts, United States). For each procedure, one of these snares was applied based on the size and morphology of the lesions and preference of the colonoscopists. Either HSP or CSP was performed by the same group of colonoscopists during the two periods. The same types of snares were applied for HSP and CSP.



## Main outcome measures

The major outcome measure in this study was delayed post-polypectomy bleeding before and after implementation of CSP. Bleeding severity was graded as spontaneous stop, need for second-look colonoscopy, and severe bleeding. Bleeding with spontaneous stop was defined as bloody stool stopped spontaneously without the need for any medical or surgical intervention. Need for second-look colonoscopy was defined as bleeding needing second-look colonoscopy but did not require hemostasis procedure. Severe bleeding was defined as active bleeding that required colonoscopic hemostasis, involved a hemoglobin drop of 2 g/dL or more as compared with baseline, or required blood transfusion. Emergency services (ES) visits and hospitalization were also recorded. Both CSP and HSP were performed during colonoscope withdrawal and total procedure time was recorded and compared. The hospital stay for each study subject was defined as the average summation of the procedure time, ES stay time, and hospitalization time.

## Histological diagnosis

Colorectal polyps, including conventional adenomas and serrated lesions, were classified according to World Health Organization (WHO) criteria [18]. Lesion location was defined by anatomic distribution. Proximal location was defined as the colon above the splenic flexure and the remaining part of the colon, from the descending colon to the rectum, was defined as the distal colon.

## Statistical analysis

Student *t*-test was used for comparison of continuous variables including age, gender, body mass index (BMI), CCI, tumor size, polyp number, procedure time and hospital stay. Pearson  $\chi^2$

test was used for comparison of categorical variables, such as bleeding risk, ES visit, hospitalization, tissue retrieval rate and use of medications.

Logistic regression analysis was used to estimate risk of post-polypectomy bleeding and odds ratios (ORs) with 95% confidence intervals (CI) were calculated. Univariate analysis was used to evaluate variables such as age, gender, tumor size, number of polyps, polypectomy method, anatomical location, bowel cleansing level, BMI and CCI. Those variables with a *P* value < 0.1 in univariate analysis were entered into multivariate analysis. In multivariate analysis, *P* values < 0.05 were considered statistically significant. Statistical analysis was performed using SPSS statistical package, version 17.0 (IBM Corp, Armonk, New York, United States).

## Results

### Patient demographic and clinical characteristics

A total of 16,873 subjects received screening colonoscopy during the whole study period (January 2015 to August 2017). Of these, 9,804 colonoscopies were performed and 1,304 subjects received polypectomy prior to implementation of CSP. After implementation of CSP, 7,069 colonoscopies were performed and 1,255 subjects received polypectomy (► **Fig. 1**).

Study subjects' demographic and clinical characteristics population are shown in ► **Table 1**. No significant differences were found between the two cohorts in proportion of subjects using antiplatelet or anticoagulant agents and comorbidity status. Clinical information on the colorectal polyps resected during both time periods is shown in ► **Table 2**. A total of 1,822 and 1,850 colorectal polyps were removed in CSP and HSP periods, respectively. Anatomical distribution (proximally

► **Table 1** Demographic and clinical characteristics of the study cohorts.

	CSP cohort N = 1,255	HSP cohort N = 1,304	P value
Age, years ± SD	58.84 ± 11.63	57.86 ± 11.73	0.04
Male, n (%)	780 (62.1)	811 (62.2)	0.98
Subject with more than 3 polyps, n (%)	117 (9.3)	125 (9.6)	0.82
Use of antiplatelet or anticoagulant agents, n (%)	75 (6.0)	84 (6.4)	0.63
BMI, kg/m <sup>2</sup> ± SD	24.48 ± 3.39	24.43 ± 3.56	0.74
Charlson comorbidity index	0.11 ± 0.48	0.13 ± 0.45	0.37

CSP, cold snare polypectomy; HSP, hot snare polypectomy; BMI, body mass index; SD, standard deviation

► **Table 2** Clinical data on colorectal polyps.

	CSP N = 1,822	HSP N = 1,850	P value
Proximal location, n (%)	1126 (61.8)	1115 (60.3)	0.34
Resected lesion, n (%)			
HP	202 (11.0)	259 (14.0)	
SSA/P	207 (11.3)	237 (12.8)	
TA	1128 (61.6)	1047 (56.5)	
TVA	242 (13.2)	278 (15.0)	
HGD	6 (0.3)	4 (0.2)	
Unknown	37 (2.0)	25 (1.4)	
Tissue retrieval rate, n (%)	1785 (98.0)	1825 (98.7)	0.11
Tumor size, mm ± SD	7.42 ± 5.72	7.65 ± 5.23	0.19

CSP, cold snare polypectomy; HSP, hot snare polypectomy, HP: hyperplastic polyp; SSA/P, sessile serrated polyp/adenoma; TA, tubular adenoma; TVA, tubulovillous adenoma; HGD, high-grade dysplasia; SD, standard deviation

located: 61.8% vs. 60.3%,  $P=0.34$ ) and mean lesion size ( $7.42 \pm 5.72$  vs.  $7.65 \pm 5.23$ ,  $P=0.19$ ) were similar between the two cohorts. The tissue retrieval rate was also similar (CSP vs. HSP = 98.0% vs. 98.7%,  $P=0.11$ )

### Adverse events and procedure times for CSP and HSP

Only one delayed post-polypectomy bleeding event occurred during the CSP period, which subsided spontaneously and required neither intervention nor blood transfusion. During the HSP period, a total of 14 subjects experienced delayed post-colonoscopy bleeding. All delayed bleeding events occurred between the first and eighth day after polypectomy, with a mean of  $2.79 \pm 2.01$  days. Among those patients, 11 subjects required second-look colonoscopy, nine had severe bleeding, and two were hospitalized. The CSP cohort had significantly lower rates of bleeding ( $P<0.001$ ), need for second-look colonoscopy ( $P<0.01$ ), severe bleeding ( $P<0.01$ ), and ES visits ( $P<0.01$ ) com-

pared with the HSP cohort. Mean procedure time,  $12.60 \pm 11.45$  vs.  $16.48 \pm 14.27$  min/person, and mean hospital stay,  $1.18 \pm 0.50$  vs.  $1.53 \pm 5.78$  hour/person, were both significantly shorter in the CSP period than in the HSP period ( $P$  values  $<0.01$  and  $0.03$ , respectively) (► **Table 3**).

### Analyses of the risk factors associated with delayed post-polypectomy bleeding

Univariate analysis revealed that HSP was associated with significantly higher delayed post-polypectomy bleeding (OR = 13.6, 95% CI = 1.79–103.65). Number of polyps per patient was marginally associated with risk of bleeding (OR = 1.22, 95% CI = 0.98–1.52). Tumor size (OR = 2.20, 95% CI = 0.78–6.22), anatomical location (proximal vs. distal, OR = 1.32, 95% CI = 0.44–3.93), bowel cleansing level (adequate vs. inadequate, OR = 0.84, 95% CI = 0.30–2.37), BMI (low vs. high, OR = 0.90, 95% CI = 0.75–1.10) and CCI (low vs. high, OR = 0.70, 95% CI = 0.15–3.31) were not associated with risk of bleeding. In multivariate analysis, HSP remained an independent significant risk factor for delayed post-polypectomy bleeding after adjustment for age (aOR = 0.99, 95% CI = 0.95–1.04), male gender (aOR = 0.58, 95% CI = 0.18–1.83) and number of polyps (aOR = 1.26, 95% CI = 0.99–1.59) (► **Table 4**).

## Discussion

Results of the current study demonstrated that risk of delayed post-polypectomy bleeding, need for second-look colonoscopy, frequency of ES visits and total procedure times could be significantly reduced via implementation of CSP. The safety and efficiency of polypectomy was significantly improved by implementation of CSP in the screening colonoscopy setting.

Clinicians performing CSP speculated that it would be able to reduce risk of delayed post-colonoscopy bleeding by avoiding thermal injury. Most of the direct evidence to support this hypothesis has come from descriptive studies in which the adverse events were investigated after CSP for consecutively enrolled subjects [3,19]. However, even though those studies demonstrated the superiority of CSP in reducing delayed post-colonoscopy bleeding, most studies did not compare results with those of HSP as a control. To the best of our knowledge,

► **Table 3** Comparison of adverse events and procedure times for CSP vs. HSP.

	CSP N = 1,255	HSP N = 1,304	P value
Bleeding, n (%)	1 (0.1)	14 (1.1)	<.001
▪ Spontaneous stop	1 (0.1)	3 (0.2)	0.34
▪ Second-look colonoscopy	0 (0.0)	11 (0.8)	<.01
▪ Severe <sup>1</sup>	0 (0.0)	9 (0.7)	<.01
ES visit, n (%)	1 (0.1)	13 (1.0)	<.01
Hospitalization, n (%)	0 (0.0)	2 (0.2)	0.17
Total procedure time, min/person ± SD	12.60 ± 11.45	16.48 ± 14.27	<.01
Hospital stay, hour/person ± SD <sup>2</sup>	1.18 ± 0.50	1.53 ± 5.78	0.03

CSP, cold snare polypectomy; HSP, hot snare polypectomy; ES, emergency services; SD, standard deviation

<sup>1</sup> Severe bleeding: hemostasis by colonoscopy; hemoglobin dropped by 2 gm/dL in comparison with baseline; or require blood transfusion.

<sup>2</sup> Hospital stay was defined as the average summation of the procedure time, ES stay time, and hospitalization time for each person.

► **Table 4** Risk of post-polypectomy bleeding associated with polypectomy method and other factors.

	Univariate analysis		Multivariate analysis	
	OR (95%CI)	P value	aOR (95%CI)	P value
Age	0.99 (0.95 – 1.03)	0.64	0.99 (0.95 – 1.04)	0.73
Gender	0.60 (0.19 – 1.88)	0.38	0.58 (0.18 – 1.83)	0.35
Tumor size, ≥ 10 mm vs. < 10 mm	2.20 (0.78 – 6.22)	0.13	–	–
Number of polyps per patient	1.22 (0.98 – 1.52)	0.07	1.26 (0.99 – 1.59)	0.06
HSP vs. CSP	13.6 (1.79 – 103.7)	0.01	14.4 (1.88 – 110.6)	0.01
Anatomical location, Proximal vs. distal	1.32 (0.44 – 3.93)	0.62	–	–
Bowel cleansing level, adequate vs. inadequate	0.84 (0.30 – 2.37)	0.74	–	–
BMI (high vs. low)	0.90 (0.75 – 1.10)	0.26	–	–
Charlson comorbidity index (high vs. low)	0.70 (0.15 – 3.31)	0.65	–	–

aOR, adjusted odds ratio; HSP, hot snare polypectomy; CSP, cold snare polypectomy; BMI, body mass index

only one retrospective case-control study compared these two methods. Yamashina et al. explored whether CSP could reduce post-colonoscopy bleeding by comparing 330 and 209 subjects who received CSP and HSP, respectively [6]. In the current study, a total of 2,559 of 16,873 subjects who received screening colonoscopy and polypectomy in a large-volume screening colonoscopy setting were enrolled. The sample size is larger than previous studies and it provides a more accurate demonstration of the superiority of CSP over HSP in reducing risk of post-polypectomy bleeding. Recent RCTs comparing CSP and HSP have failed to demonstrate the superiority of CSP to reduce risk of post-colonoscopy bleeding except for the study by Horiuchi et al. He explored the superiority of CSP in a high-risk population taking anticoagulant agents, demonstrating that CSP could significantly lower risk of bleeding [4]. The actual risk of bleeding after removing small and diminutive polyps was very low, ranging from 0% to 1.3%. Both the low risk and small sam-

ple may explain why the pooled risk of bleeding in the meta-analysis was also non-significant. Designing a large-scale RCT using the bleeding event as a primary outcome would be most ideal, but long-term study is required. An alternative approach would be to explore such risk in a screening setting involving a large patient population. The current study enrolled 2,559 of 16,873 subjects participating in screening colonoscopy and such a large sample size provides sufficient statistical power to demonstrate the superiority of CSP. Not only colonoscopy experts but also general endoscopists performed the procedures in our institute hence the results are more likely to reflect the real-world practice setting rather than an experimental study involving only expert colonoscopists.

In several previous studies, bleeding was the most common adverse event after polypectomy, occurring either immediately or days after the procedure, and the overall bleeding rate after HSP was reported to range from 0.65% to 0.87% [20–22]. Be-

cause bleeding events increase medical costs and decrease patient satisfaction, several screening programs have proposed a benchmark threshold for the rate of significant bleeding events. Immediate bleeding was more common when electrocautery with cutting or blended current was used, whereas delayed bleeding was more common when coagulation current was used. Therefore, risk of delayed bleeding could be theoretically reduced by avoiding electrocautery use [23–24]. A study by Repici et al. demonstrated that risk of delayed bleeding after CSP was zero based on the observation of 823 patients. Although that study was only a single-arm descriptive study without a control group, the advantage of CSP in the real-world practice setting was well demonstrated [19]. In summary, a growing body of evidence supports the efficacy of CSP in reducing post-polypectomy bleeding, including observational cohort studies and retrospective case-control studies. Most of the RCTs to date have been either underpowered to evaluate bleeding events owing either to a small sample size or a high-risk population, which are not totally representative of the general screening population. Large-scale RCTs with sufficient sample size enrolling a general screening population are still warranted.

Another advantage of CSP was saving procedural time, which may impact the efficiency and cost-effectiveness of colonoscopy. Previous RCTs have demonstrated that CSP could significantly save procedural time even though risk of bleeding was similar to HSP [7, 25]. The current study demonstrated that CSP could significantly save total procedure time compared with HSP and could save as much as 23.5% procedure time per colonoscopy that polypectomy was performed. Another significance of CSP is the completeness of neoplasm eradication. Several RCTs have demonstrated that the complete eradication rate using CSP was not only better than by cold forceps polypectomy [26–27], but also was not inferior to or even better than by HSP [25]. Another study reported a low rate of 0.98% for pathologically verified residual adenoma using CSP, which is an important indicator of efficacy [28]. Though not evaluated in the current study, the issue of histological eradication had been well addressed in previous RCTs. Technical aspect was another issue worthwhile to be discussed for CSP. Din et al. reported that the thickness and shape of the different snares may have affected histological eradication rate of CSP [29]. Horiuchi et al. also noticed that a dedicated snare for CSP was able to achieve more complete removal of the polyps [8]. Based on the results of that study, a shield-shaped and thin snare was considered to be more suitable for complete removal of polyps. A thin snare provides more precise cutting and the shield shape may facilitate proper positioning of the snare, both contributing to better maneuverability in the CSP procedure. Further standardization of the procedure is still necessary, including the technical details and optimal device selection.

There were several strengths in the current study. First, the study was strengthened by its large sample size. To the best of our knowledge, this was by far the largest study population in which these two methods are compared. As such, it provides a sufficient statistical power to test our hypothesis and allows comprehensive multivariate analysis adjusting for potential

confounders. Second, the short study period minimized the influence of other factors, such as operator and endoscopic instrumental factors, including the colonoscope, snare or electrocautery unit. Operator members were completely the same across two operative periods and so were the instruments used for colonoscopy. Third, subjects who had concurrent polyp(s) larger than 10 mm were enrolled. For such cases, small polyps were removed with either HSP or CSP as per the study period and conventional methods, either HSP or EMR, were applied for resection of larger polyps as indicated at the same endoscopic session. Such an approach is more likely to reflect the real-world practice of screening colonoscopy. Finally, we also took into account the comorbidity status of the study subjects, which may influence risk of post-polypectomy bleeding. CCI, a comprehensive scoring system, was used to quantify comorbidity and was taken into consideration in the regression analysis. This may provide a more precise estimate of the effect of different polypectomy methods on bleeding risk.

Nevertheless, the current study was not without limitations. First, the retrospective and non-randomized design, and therefore, the results, may be confounded by hidden factors even though comprehensive multivariate analysis was conducted to adjust for various confounders. Second, histological eradication rate was not re-assessed in this study. Owing to the retrospective design, information on histologic eradication was totally dependent on the initial pathology report thus interobserver variation may exist. Nevertheless, such a histological issue has been well addressed in previous RCTs for which histological eradication rate was primary endpoint. In this study, bleeding event, rather than the histological eradication rate, was the main study outcome. Third, one may argue that endoscopist experience might have changed over time and affected the results. In this study, only experienced endoscopists were enrolled and all of them performed colonoscopy for at least 7 years (ranged from 7 to 15 years), hence significant differences in polypectomy performance before and after implementation of CSP are less likely. Finally, although we observed significantly lower overall procedural time using CSP, retrospective analysis did not allow us to specify and compare the time spent on polypectomy itself. However, this is not likely to be an issue, as the main difference in procedural time is more likely to be associated with the different polypectomy methods rather than with scope insertion, withdrawal or lesion observation, which were the same across the HSP and CSP periods.

## Conclusion

In conclusion, CSP significantly reduces the risk of post-polypectomy bleeding and overall procedural time compared with HSP for removing small and diminutive polyps in a large screening colonoscopy setting. Further large-scale RCTs with a sufficient sample from a screening population are still warranted to confirm results of the current study and demonstrate the safety, efficacy and efficiency of CSP.

## Competing interests

None

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