Comparison of postpolypectomy bleeding events between cold snare polypectomy and hot snare polypectomy for small colorectal lesions: a large-scale propensity score–matched analysis

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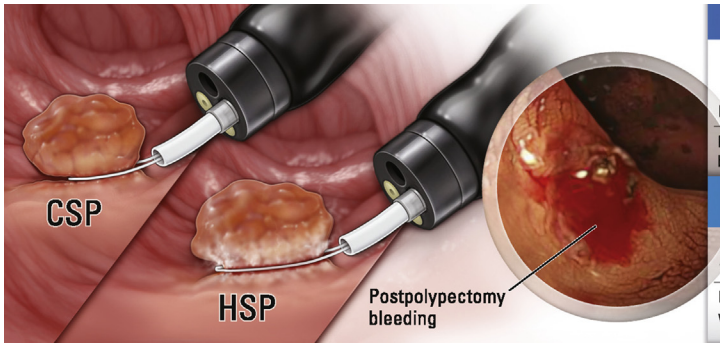
GRAPHICAL ABSTRACT



Postpolypectomy bleeding rate before and after PS matching

	Pre-PS matching			Post-PS matching		
	CSP	HSP	*P* value	CSP	HSP	*P* value
No. of lesions	12,928	2408		2135	2135	
Postpolypectomy bleeding	13 (.1)	13 (.54)	<.001	2 (.10)	12 (.56)	.0075

Risk for postpolypectomy bleeding after HSP compared with CSP for colorectal lesions <10 mm

	Logistic regression model		Propensity score matching	
Variables	Odds ratio	95% CI	Odds ratio	95% CI
HSP compared with CSP	5.39	2.50-11.60	6.0	1.34-26.80

Background and Aims: Cold snare polypectomy (CSP), a safe procedure for removing colon polyps, has a low prevalence of postpolypectomy bleeding (PPB). Previous studies have failed to demonstrate differences in PPB rates between CSP and hot snare polypectomy (HSP), possibly because of their small sample sizes. This study analyzed PPB rates after CSP and HSP.

Methods: This was a retrospective analysis of colorectal lesions (diameter <10 mm) treated using endoscopic resection at our institution between January 2015 and December 2019. Resections were performed using CSP or HSP, depending on the endoscopist's preference. Endoscopic and histologic findings were recorded in the endoscopic database at our institution. Propensity score (PS) matching was performed to match patient age, lesion size, macroscopic features, location of the lesions, clipping after resection, and antithrombotic agent use. The CSP and HSP groups were compared to determine the adverse event (PPB) rates.

Results: The CSP and HSP groups included 12,928 and 2408 lesions (total of 5371 patients), respectively. Univariate analysis revealed that the overall prevalence of PPB after HSP was higher than that after CSP (odds ratio [OR], 5.39; 95% confidence interval [CI], 2.50-11.60). After PS matching (2135 lesions per group), the prevalence of PPB after HSP remained higher than that after CSP (OR, 6.0; 95% CI, 1.34-26.8).

Conclusions: For colorectal lesions <10 mm in diameter, the risk of PPB after CSP is significantly lower than that after HSP, after PS matching. CSP for lesions <10 mm could be safely performed compared with HSP. (Gastrointest Endosc 2022;95:982-9.)

(footnotes appear on last page of article)

Endoscopic resection of colorectal polyps reduces the risk of colorectal cancer mortality.[1] Several guidelines, such as those developed by the American Gastroenterological Association, the American Society for Gastrointestinal Endoscopy, and the European Society of Gastrointestinal Endoscopy, advocate the use of cold snare polypectomy (CSP) for colorectal lesions <10 mm in diameter.[2-4] CSP is reported to be a safe technique with low rates of adverse events, including postpolypectomy bleeding (PPB) and perforations.[2,5,6] However, randomized controlled trials and meta-analyses have failed to reveal significant differences in PPB rates between CSP and hot snare polypectomy (HSP).[7-13] In practice, PPB is occasionally observed after performing HSP for small colorectal lesions but is rarely seen after CSP. The PPB rates after these procedures (an estimate of the risk associated with the procedures) are key clinical management data and are useful for performing procedural comparisons among patients.

Previous studies have only analyzed a small number of patients and/or lesions. For example, Kawamura et al[7] analyzed 796 polyps treated using either CSP or HSP and concluded that the PPB rates for colorectal lesions (diameters, 4-9 mm) were similar for both procedures (CSP 0% vs HSP .5%). A study by Aizawa et al[10] showed a PPB rate of .83% after CSP. Meta-analyses that included these studies found that rates of PPB after HSP were higher than those after CSP, although it did not reach statistical significance.[12,13] The studies included in these meta-analyses only evaluated up to 300 colorectal lesions; therefore, the pooled analyses were performed on a total of approximately 1200 colorectal lesions. The authors stated that larger sample sizes would be required to determine whether CSP results in lower rates of delayed bleeding and other adverse events than HSP.[12] Thus, we conducted a large-scale study to analyze PPB rates after CSP and HSP. To minimize bias and adjust for background factors, we also performed a propensity score (PS)-matching analysis.

METHODS

Patients and lesions

We included patients with colorectal lesions who were treated using endoscopic resection between January 2015 and December 2019 at the National Cancer Center Hospital in Tokyo, Japan. Patients were included if they had a histologically evaluated colorectal lesion <10 mm in diameter and were treated using CSP, polypectomy, or EMR. Patients diagnosed with Lynch syndrome, familial adenomatous polyposis, neuroendocrine tumors, lymphomas, or metastatic tumors were excluded from the study; similarly, lesions without endoscopic size estimates were also excluded (Fig. 1).

This retrospective analysis involved colorectal lesions with endoscopic and histologic findings extracted from an endoscopic database that was maintained prospectively. All factors, findings, and events were calculated for each lesion. The endoscopic findings and images of each patient with PPB were reviewed by 1 endoscopist.

This study was conducted in accordance with the principles outlined in the Declaration of Helsinki and was approved by the Institutional Review Board of the National Cancer Center Hospital (IRB no. 2016-447). For this protocol, our Institutional Review Board did not require individual written informed consent from patients because of the study's retrospective design.

Cold snare polypectomy

A SnareMaster or SnareMasterPlus snare (10 or 20 mm; Olympus Medical Systems, Tokyo, Japan), Profile snare (Boston Scientific, Natick, Mass, USA), Captivator, Captivator II, or Captivator COLD snare (Boston Scientific), Bipolar Snare S DRAGONARE (XEMEX, Tokyo, Japan), or Dualoop double-loop snare (Medico's Hirata, Tokyo, Japan) was used to capture and resect the lesions. We defined snares with wire calibers ≧.40 mm as "regular" snares, whereas those with wire calibers ≦.32 mm were defined as "thin" snares (Supplementary Table 1, available online at www.giejournal.org). When endoscopists found lesions that indicated the need for EMR or polypectomy, a regular snare was used; however, a thin snare was chosen in principle if the endoscopists found lesions indicating the need for CSP exclusively. The specific snare used for each procedure was chosen according to endoscopist preference. Fifty-two endoscopists, including 21 endoscopists who were board-certified fellows of the Japan Gastroenterological Endoscopy Society, performed the interventional procedure. Submucosal injections were not performed during CSP.

Hot snare polypectomy

HSP was defined as a snare resection involving electrocautery, with or without submucosal injection; normal saline solution was used for any submucosal injections that were performed. A SnareMaster or SnareMasterPlus snare (10 or 20 mm), Bipolar Snare S DRAGONARE, Profile snare, Captivator or Captivator II, or Dualoop double-loop snare was used according to endoscopist preference. This procedure involved the use of an electrosurgical unit system (ICC 200; Erbe Elektromedizin, Tübingen, Germany) with settings of "endo cut" (effect 2, interval .8 seconds, and fixed power of 120 W) and "forced coagulation" (fixed power of 50 W) for monopolar snare devices or "forced coagulation" (fixed power of 15 W) for bipolar snare devices, according to the manufacturer's recommendations.

Clipping

Clipping after CSP or HSP was performed using the EZ clip (Olympus Medical Systems), according to the endoscopist's decision.

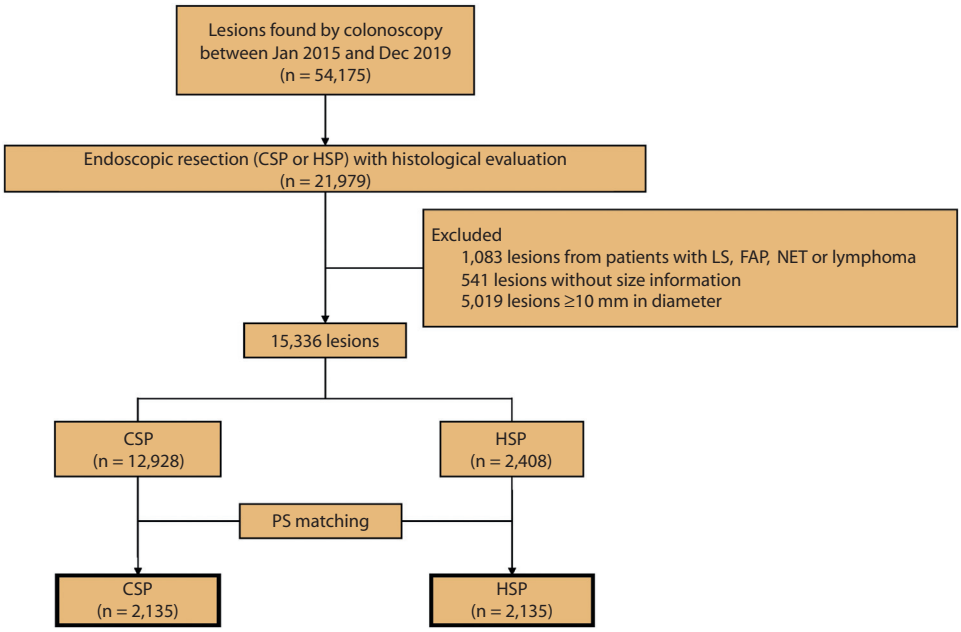


Figure 1. Study flow of 15,336 lesions included in the analysis. PS matching provided 2135 lesions each in the CSP and HSP groups. *CSP*, Cold snare polypectomy; *HSP*, hot snare polypectomy; *LS*, Lynch syndrome; *FAP*, familial adenomatous polyposis; *NET*, neuroendocrine tumor; *PS*, propensity score.

Postpolypectomy bleeding

PPB was defined as the presence of marked bloody stool or the need for some degree of post-treatment hemostasis within 14 days of the procedure, in accordance with the Japan Gastroenterological Endoscopy Society guidelines for colorectal endoscopic submucosal dissection/EMR.[14] Patients in whom bleeding stopped spontaneously and who did not undergo endoscopic examination were not considered to have PPB. Patients were instructed to directly call and visit our hospital if they had bloody stools or experienced changes in their physical condition. All patients visited our hospital 2 weeks after polypectomy to receive a histologic diagnosis of the resected lesions according to the medical law that requires explanation to be conducted in an outpatient department. At the time of this appointment, patients were interviewed regarding adverse events after polypectomy. Follow-up colonoscopy was scheduled for 1 year after polypectomy.

When PPB was documented to have occurred, the associated medical records and endoscopic findings were reviewed. The resected lesion that caused PPB was determined to be the lesion (if only 1 lesion was resected in the previous colonoscopy) that was resected during the most recent endoscopy, and its location was noted. If multiple polyps were resected during the most recent endoscopy or if the patient with PPB had a history of multiple endoscopic resections, all endoscopic images of the resected lesions were reviewed, and the lesion most likely to have caused the bleeding, as well as its location, was determined by the endoscopist.

Evaluation

We compared patient demographics, medication use, clinicopathologic findings, endoscopic procedures, endoscopic observation methods, antithrombotic agent use, histologic diagnoses, and adverse events (including PPB) between the CSP and HSP groups. All analyses and events were calculated for each lesion.

Statistical analysis

Continuous variables, between the 2 groups, were compared using the Student *t* test, whereas categorical variables were compared using the χ^2 test, using Yates' correction for continuity where appropriate. Missing values regarding the use of antithrombotic agents (n = 6178 [40.3%]), location of the lesion (n = 119 [.78%]), and macroscopic features (n = 92 [.60%]) were replaced using multiple imputations with the Markov chain Monte Carlo method.[15]

To compensate for selection bias and potential confounding factors between the CSP and HSP groups, a PS model was derived using binary logistic regression to express the probability of the assigned treatment conditioned on patient characteristics.[16] We assessed factors previously reported to have influenced PPB, including patient age, lesion size, macroscopic features (0-Ip/0-Is/0-IIa), location of the lesions involved (proximal, distal, and rectum), endoscopic clipping after resection, and antithrombotic agent use, to calculate the PS.[17,18] Greedy matching was performed to create a matched sample using a caliper width equal to .2 of the standard deviation of the logit of the PS.

Model discrimination was assessed with c statistics (c = .810), and model calibration was assessed using Hosmer-Lemeshow statistics (χ^2 = 9.91, P = .272). Standardized mean differences were used to diagnose the baseline balance, and all values were <.1 after matching. After matching, we used paired t tests for continuous variables and Wilcoxon signed-rank and McNemar tests for categorical variables.

To prevent any influence of submucosal injection and multiple imputation on the PPB rates, sensitivity analyses of lesions that did not undergo submucosal injection and lesions without missing data were additionally performed; PS matching was performed, as described above. After PS matching, 902 matched lesions without injection and 1402 matched lesions without missing data in each of the CSP and HSP groups were included in the subanalysis. We also performed stratified analysis to investigate the influence of the type of snare (regular or thin) on the PPB rate. PPB rates for the CSP and HSP groups were compared and evaluated using the odds ratio (OR). A binary logistic regression model was used to calculate the OR and confidence interval (CI) for the total study population, and a conditional logistic regression model was used for matched analysis. Although some patients contributed more than 1 polyp to the data set used, quantities observed in different polyps were assumed to be independent observations for the purposes of data analysis.

All statistical tests were evaluated at the α = .05 significance level. It is recognized that some lesions were the subject of multiple tests for the outcome data. The uncorrected P values are presented, and it should be noted that there were no instances of statistical testing where correction by Bonferroni's method would have removed the significance of a main finding at the P < .05 level. Statistical analyses were performed using SPSS statistics version 26.0 for Windows (IBM, New York, NY, USA) and R software (version 3.6.2; R Foundation for Statistical Computing, Vienna, Austria) with "MatchIt" packages.

RESULTS

Patients

Based on the database contents, 54,175 colorectal lesions were detected between January 2015 and December 2019. Among these, 21,979 lesions were resected using either the CSP or HSP techniques. The following lesions were excluded from the study: 977 lesions caused by Lynch syndrome or familial adenomatous polyposis; 106 lesions diagnosed histologically as neuroendocrine tumors, lymphomas, or metastatic tumors; 541 lesions entered without lesion size descriptions; and 5019 lesions ≥10 mm in diameter. Thus, 15,336 lesions (5371 patients) with diameters <10 mm were resected using CSP or HSP and analyzed (Fig. 1). After PS matching, 2135 lesions (1531 patients in the CSP group and 1343 patients in the HSP) were included in each of the matched CSP and HSP groups.

Lesion characteristics and overall outcomes

The overall analysis revealed that the CSP and HSP groups differed with respect to age, mean lesion size, macroscopic features, location of the lesions, use of magnified endoscopic observations, endoscopic clipping, and histologic diagnoses (Tables 1 and 2). The per-lesion analysis showed that the OR of the PPB after HSP and CSP was 5.39 (95% CI, 2.50-11.60) (Table 3). There were no differences in the use of antithrombotic agents or in the details of the antithrombotic agents used between the 2 groups (Supplementary Table 2, available online at www.giejournal.org). Invasive cancer was revealed by histologic diagnosis in 1 (.01%) CSP-resected lesion and in 9 (.37%) HSP-resected lesions. Intraprocedural and delayed perforations were not observed in either group. All patients with PPB were treated endoscopically without blood transfusion. The characteristics of the 13 patients with PPB after CSP are shown in Supplementary Table 3 (available online at www.giejournal.org).

PS-matched study

A PS was calculated for each lesion using the 6 previously described confounders (patient age, lesion size, macroscopic features, location of the lesions, clipping after resection, and antithrombotic agent use). After PS matching, 2135 matched pairs were selected; the matching percentage was 88.7%. Standardized mean differences were used to diagnose the baseline balance, and all values were <.1 after matching (Table 1). The PPB rate in the CSP group (.10%) remained lower than that in the HSP group (.56%, P = .0075) (Table 2). The OR after matching was 6.0 (95% CI, 1.34-26.80) (Table 3).

A representative case of PPB after CSP is shown in Figure 2. The risk (OR) of PPB before and after PS matching using a regular-caliber wire snare was 6.99 (95% CI, 2.98-16.4) and 4.0 (95% CI, 1.13-14.2), respectively (Supplementary Table 4, available online at www.giejournal.org) in the analysis stratified by snare type. In contrast, it was difficult to calculate the risk (OR) of PPB using a thin-caliber wire snare before and after PS matching because of the small sample size (Supplementary Table 4).

Sensitivity analysis of lesions without submucosal injection and without missing data

To investigate the effect of submucosal injection and multiple imputation to PPB after the procedure, we performed 2 sensitivity analyses using the lesions without submucosal injections and the lesions without missing data. After performing a subanalysis of 13,847 lesions that did not receive submucosal injections, PS matching identified 902 matched lesions in the CSP and HSP groups; 98.2% of the cases matched (Supplementary Table 5, available online at www.giejournal.org). The OR of the PPB after HSP was 7.0 (95% CI, .086-59.9) (Supplementary Table 6,

TABLE 1. Patient demographics and clinicopathologic characteristics before and after PS matching

		Pre-PS matching			Post-PS matching		
	Total	CSP	HSP	Standardized mean difference	CSP	HSP	Matched standardized mean difference
No. of lesions*	15,336	12,928	2408		2135	2135	
Age at colonoscopy, y		67.5 ± 10.0	66.0 ± 11.6	–.1320	60.4 ± 10.3	66.1 ± 11.7	–.0250
Lesion size, mm		4.8 ± 1.5	6.4 ± 1.5	.9919	6.25 ± 1.55	6.20 ± 1.53	.0328
Macroscopic feature†				–.3574			–.0478
Ip, Ip + IIc	137	45 (.4)	92 (3.8)		24 (1.0)	75 (3.5)	
Is, Is + IIa, Is + IIc	4422	3406 (26.4)	1016 (42.2)		865 (40.5)	859 (40.2)	
IIa, IIb, IIc, IIa + IIc	10,727	9464 (73.2)	1263 (52.5)		1245 (58.3)	1165 (54.6)	
Others (recurrence, submucosal tumor)	50	13 (.1)	37 (1.5)		1 (.1)	36 (1.7)	
Lesion location†				.2150			.0030
Proximal colon (cecum to transverse)	8913	7718 (59.7)	1195 (49.6)		1076 (50.4)	1076 (50.4)	
Distal colon (descending to rectosigmoid)	5704	4674 (36.2)	1030 (42.8)		900 (42.2)	896 (42.0)	
Rectum	719	536 (4.1)	183 (7.6)		159 (7.5)	163 (7.6)	
Antithrombotic agent use†				–.0142			.0124
Used	1616	1371 (10.6)	245 (10.2)		224 (10.50)	232 (10.9)	
Not used	13,720	11,557 (89.4)	2163 (89.8)		1911 (89.5)	1903 (89.1)	
Endoscopic clipping after resection				.5190			.0477
With endoclips	1361	671 (5.2)	690 (28.7)		379 (17.8)	425 (19.9)	
Without endoclips	13,975	12,257 (94.8)	1718 (71.4)		1756 (82.3)	1710 (80.1)	
Resection procedure							
CSP	12,928	12,928 (100)			2135 (100)		
Polypectomy	919		919 (38.2)			871 (40.8)	
EMR	1489		1489 (61.8)			1264 (59.2)	

Values are n (%) or mean ± standard deviation.
PS, Propensity score; *CSP*, cold snare polypectomy; *HSP*, hot snare polypectomy.
*Cumulative number of patients.
†After multiple imputation for missing data.

available online at www.giejournal.org). Similarly, PS matching of 9043 lesions without missing data identified 1402 matched lesions in the CSP and HSP groups; the percentage of matching was 89.7% (Supplementary Table 7, available online at www.giejournal.org). Standardized mean differences were also used to diagnose the baseline balance, and all values were <.1 after matching (Supplementary Tables 5 and 7). The OR of PPB for lesions where there was no missing data after matching was 2.67 (95% CI, .709-10.0) (Supplementary Table 8, available online at www.giejournal.org). The PPB rates observed in the 2 groups were similar to those reported for the main analysis, with a trend toward fewer PPB cases in the CSP group than in the HSP group (.2% vs .6%, respectively; $P = .13$) (Supplementary Table 7).

DISCUSSION

This large-scale study is the first to demonstrate the statistical differences in the PPB rate between CSP and HSP; the large number of patients also enabled a PS-matched analysis. CSP was observed to have a significantly lower rate of PPB than HSP for colorectal lesions <10 mm, after adjusting for other variables. The overall PPB rate in the CSP cohort was .1%. One of the strengths of this study was that we clarified the PPB rate between CSP and HSP in a clinical setting with a large sample size.

Shinozaki et al[13] reported the PPB rates after CSP and HSP as 0% (0/893) and .78% (7/898), respectively. The PPB rates after HSP tended to be higher, although no statistical difference was seen between CSP and HSP ($P = .06$). These authors indicated that a larger sample size was needed to clarify whether there are differences in the PPB rates for these procedures.[13] Qu et al[12] reported that the PPB rates after CSP and HSP were .34% (4/1157) and .52% (6/1156), respectively. Their analysis was based on a per-lesion analysis of 9 studies, including conference abstracts, and showed a higher tendency of PPB after HSP, although no statistically significant difference was seen between the 2 groups ($P = .65$). Our findings support these previous studies.

TABLE 2. Patient demographics and clinicopathologic characteristics before and after PS matching

		Pre-PS matching			Post-PS matching		
	Total	CSP	HSP	*P* value	CSP	HSP	*P* value
No. of lesions*	15,336	12,928	2408		2135	2135	
Kinds of snare used				<.001			<.001
Regular-caliber wire		11,131 (86.1)	2311 (96.0)		1894 (88.7)	2053 (96.2)	
Thin-caliber wire		1309 (10.1)	46 (1.9)		136 (6.4)	35 (1.6)	
Not reported		488 (3.8)	51 (2.1)		105 (4.9)	47 (2.2)	
Histology				<.001			<.001
Cancer (submucosal invasive cancer)	10	1 (.01)	9 (.37)		0 (0)	6 (.28)	
Intramucosal neoplasia/high-grade dysplasia	103	32 (.25)	71 (3.0)		10 (.47)	51 (2.4)	
Adenoma/low-grade dysplasia	12,004	10,039 (77.7)	1965 (81.6)		1647 (77.1)	1741 (81.6)	
Hyperplastic/sessile serrated lesion	1713	1550 (12.0)	163 (6.8)		337 (15.8)	148 (6.9)	
Other tumors†	32	13 (.1)	19 (.8)		5 (.2)	18 (.8)	
Non-neoplastic polyp‡	1474	1293 (10.0)	181 (7.5)		136 (6.4)	171 (8.0)	
Postpolypectomy bleeding¶	30	13 (.1)	13 (.54)	<.001	2 (.10)	12 (.56)	.0075
Intraprocedural perforation¶	0	0 (0)	0 (0)	N/A	0 (0)	0 (0)	N/A
Delayed perforation¶	0	0 (0)	0 (0)	N/A	0 (0)	0 (0)	N/A

Values are n (%).
PS, Propensity score; *CSP*, cold snare polypectomy; *HSP*, hot snare polypectomy; N/A, not available.
*Cumulative number of patients.
†Lipoma or hamartomatous polyp.
‡Inflammatory polyp or colon mucosa.
¶No patients overlapped.

TABLE 3. Risk for postpolypectomy bleeding after HSP compared with CSP for colorectal lesions <10 mm

	Logistic regression model		Propensity score matching*	
Variables	Odds ratio	95% Confidence interval	Odds ratio	95% Confidence interval
HSP compared with CSP	5.39	2.50-11.60	6.0	1.34-26.80

HSP, Hot snare polypectomy; *CSP*, cold snare polypectomy.
*Conditional logistic regression model.

Previous studies reported PPB rates after CSP and HSP of 0% to .35% and .45% to .52%, respectively, in the per-lesion analyses.[5,7,10,12,13] Our data showed that the overall PPB rates for CSP and HSP were in line with these reported ranges.

The use of antithrombotic agents may affect PPB after CSP and HSP. Horiuchi et al[19] conducted a randomized controlled trial to analyze post-CSP adverse events in patients who also received anticoagulation; they observed a significant increase in the PPB rate after HSP, but not after CSP (14% vs 0%, $P = .027$). In our study, the use of antithrombotic agents by patients in the HSP and CSP groups was PS-matched; therefore, the differences between the 2 groups were minimized (Table 1, Supplementary Table 2). However, only a small number of patients received antithrombotic agents. There was substantial missing data regarding the use of antithrombotic agents, which was a limitation of this study. Because of the wider 95% CI, the clinical impact is unclear. Further studies with greater sample sizes are needed to improve results.

Our study findings support the safety of CSP for colorectal lesions <10 mm in diameter. However, T1 (invasive) cancer was detected in 1 CSP-resected lesion with a diameter <10 mm. This case was surgically managed because the patient had another invasive colorectal cancer near the lesions removed using CSP. Furthermore, en-bloc resection of high-grade dysplasia decreases the frequency of recurrence and enables more precise histologic evaluation.[20] For such lesions, several guidelines recommend HSP to achieve en-bloc resection.[2,3,21] Magnifying endoscopy, including narrow-band imaging magnification or pit pattern diagnosis by magnifying chromoendoscopy, can aid in determining the appropriate resection method.[22-26] For example, narrow-band imaging magnification and pit pattern diagnosis can predict the histology of colorectal lesions.[2,3,25,27-30] Hence, after detailed observations using magnifying endoscopy, we can make an appropriate decision regarding the resection method.

The PS-matching method can include several covariates or confounding factors; however, in logistic regression analysis, the number of covariates is limited by the number

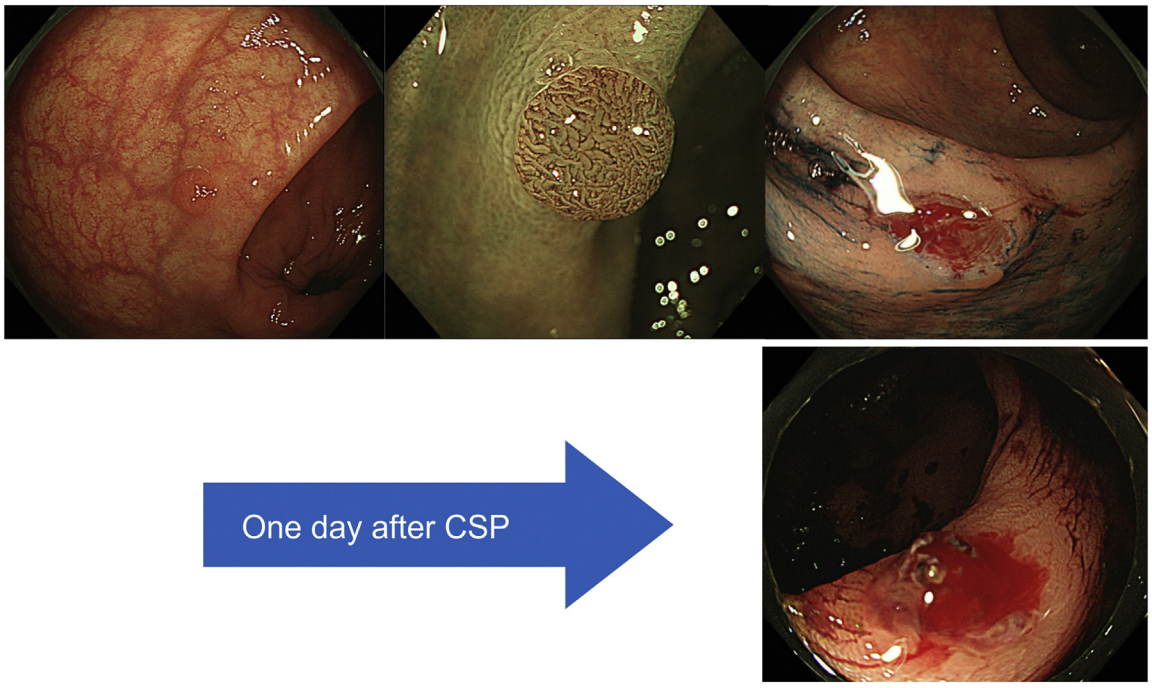


Figure 2. Representative case of postpolypectomy bleeding requiring endoscopic hemostasis after cold snare polypectomy (CSP). A 0-IIa lesion (4 mm in diameter) was treated using CSP. Hematochezia was observed at 1 day after the procedure, and an emergency colonoscopy was performed. Active bleeding was detected in the mucosal defect.

of events (10 events per variable required for each covariate). We believe PS matching was a more suitable analysis for this study because of the small number of PPB events.

Because we used the multiple imputation method, we also reported a sensitivity analysis that only included lesions without missed baseline data. The OR of the PPB in this analysis was similar to that reported in the main analysis, with a trend toward a lower OR in HSP than in the CSP (2.67; 95% CI, .71-10.0). The relatively small sample size may have contributed to this trend not achieving statistical significance.

The ratio of clipping after HSP may be higher than that of the usual North American practice for small polyps. One reason for this difference may be that endoclips are less expensive in Japan than in Western countries. This finding suggests that careful consideration should be given when applying our conclusions in endoscopy units of primary clinics and hospitals in Western countries.

This study has several limitations. First, it was a single-center retrospective analysis; therefore, there is a potential for bias. However, because the analyzed data were obtained from a single center, the CSP and HSP procedural techniques are more standardized than they would be if the procedures were performed at different institutions. Additionally, PPB was evaluated using the same criteria for all participants. Second, the influence of submucosal injections was unclear because the HSP group included patients treated using both EMR and polypectomy. Taking into account the result of the sensitivity analysis of lesions without submucosal injection (Supplementary Tables 5 and 6), the CSP procedure showed a trend of lower PPB risk than the HSP procedure when submucosal injections were not performed. Third, the type of snare used was determined as indicated by the resection method. Because only a few cases used a thin snare, the data were insufficient to elucidate a risk difference between CSP and HSP. Further studies with larger sample sizes for CSP and HSP using thin snares are needed. Finally, this study was based on an endoscopic database; therefore, several values were missing. Specifically, we could not determine the effect of antithrombotic agents on PPB, because relatively large data about antithrombotic agents were missing. Nevertheless, our study findings may represent real-world practice.

In conclusion, our study demonstrated that the PPB rate after CSP was significantly lower than that after HSP for lesions <10 mm in diameter. Therefore, CSP for lesions <10 mm could be safely performed compared with HSP. It may be possible to expand the indications for CSP based on the results of studies.

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Abbreviations: CSP, cold snare polypectomy; HSP, hot snare polypectomy; PPB, postpolypectomy bleeding; PS, propensity score.

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SUPPLEMENTARY TABLE 1. List of snares used for cold snare polypectomy and hot snare polypectomy

Name of snare	Wire type	Caliber of the wire (mm)	Snare classification
SnareMaster	Braided	.47	Regular snare
SnareMasterPlus	Braided	.30	Thin snare
Captivator	Braided	.40	Regular snare
Captivator II	Braided	.40	Regular snare
Captivator COLD	Braided	.32	Thin snare
Profile	Braided	.40	Regular snare
DRAGONARE	Braided	.40	Regular snare
Dualoop	Braided	.43	Regular snare

SUPPLEMENTARY TABLE 2. Details of antithrombotic agent use by patients

	Cold snare polypectomy	Hot snare polypectomy	*P* value
Cumulative no. of patients using an antithrombotic agent	796	167	.31
Single use of antithrombotic agent	557 (70.0)	125 (74.9)	
Double use of antithrombotic agents	1 (.13)	1 (.60)	
Anticoagulated agent with or without anticoagulants	208 (26.1)	37 (22.2)	
Antiplatelet therapy combined with aspirin use	30 (3.77)	4 (2.40)	

Values are n (%).

SUPPLEMENTARY TABLE 3. Patients with postpolypectomy bleeding after cold snare polypectomy

Gender	Age (y)	Location	Size (mm)	Macroscopic feature	Snare used	Filament of snare	Clipping after procedure	Histology	Antithrombotic agent
M	74	Descending colon	3	IIa	SnareMaster	Regular/ braided	No	Adenoma/LGD	No
M	48	T/C	8	IIa	SnareMaster	Regular/ braided	No	HP	No
M	67	T/C	4	Is	Profile	Regular/ braided	No	Adenoma/LGD	Aspirin
M	67	T/C	6	Is	Profile	Regular/ braided	No	Adenoma/LGD	Aspirin
M	75	T/C	2	Is	DRAGONARE	Regular/ braided	Yes	Adenoma/LGD	No
M	62	Lower rectum	6	Is	Profile	Regular/ braided	No	Intramucosal neoplasia/high-grade dysplasia	No
M	63	S/C	5	IIa	Profile	Regular/ braided	No	Adenoma/LGD	Clopidogrel
F	81	A/C	7	Is	SnareMasterPlus	Thin/braided	No	Adenoma/LGD	Aspirin and prasugrel
M	74	S/C	4	IIa	Profile	Regular/ braided	Yes	Adenoma/LGD	No
M	73	A/C	8	IIa	SnareMaster	Regular/ braided	No	Adenoma/LGD	No
M	78	Cecum	8	IIa	SnareMasterPlus	Thin/braided	No	Adenoma/LGD	No
M	78	A/C	8	IIa	SnareMasterPlus	Thin/braided	No	Adenoma/LGD	No
M	76	T/C	6	IIa	SnareMasterPlus	Thin/braided	No	Adenoma/LGD	Dabigatran

T/C, Transverse colon; *S/C*, sigmoid colon; *A/C*, ascending colon; *LGD*, low-grade dysplasia.

SUPPLEMENTARY TABLE 4. Risk for postpolypectomy bleeding after HSP compared with CSP for colorectal lesions <10 mm stratified by the type of snare used

	Logistic regression model			Propensity score matching*		
Variables	No. of lesions	Odds ratio	95% Confidence interval	No. of lesions	Odds ratio	95% Confidence interval
HSP compared with CSP using a regular-caliber wire snare	13,442	6.99	2.98-16.4	4062†	4.0	1.13-14.2
HSP compared with CSP using a thin-caliber wire snare	1355	0	N/A	36‡	N/A	N/A

HSP, Hot snare polypectomy; *CSP*, cold snare polypectomy; *N/A*, not available .
*Conditional logistic regression model.
†Matching percentage was 87.9%.
‡Matching percentage was 78.3%.

SUPPLEMENTARY TABLE 5. Sensitivity analysis of patients and lesions without injection (CSP vs polypectomy only)

		Pre-PS matching				Post-PS matching			
	Total	CSP	HSP	Standardized mean difference	*P* value	CSP	HSP	Standardized mean difference	*P* value
No. of lesions*	13,847	12,928	919			902	902		
Age at each colonoscopy, y		67.5 ± 10.0	64.7 ± 13.6	–.2076	<.001	65.5 ± 10.9	64.9 ± 13.4	–.0383	.21
Lesion size, mm		4.8 ± 1.5	5.9 ± 1.6	.6363	<.001	5.9 ± 1.6	5.8 ± 1.6	–.0538	.006
Macroscopic feature				–.3664	<.001			–.0218	.36
Ip, Ip+IIc	91	45 (.4)	46 (5.0)			17 (1.9)	36 (4.0)		
Is, Is+IIa, Is+IIc	3777	3406 (26.4)	371 (40.4)			380 (42.1)	364 (40.4)		
IIa, IIb, IIc, IIa+IIc	9956	9464 (73.2)	492 (53.3)			505 (56.0)	492 (54.6)		
Other (recurrence, s ubmucosal tumor)	23	13 (.1)	10 (1.1)			0 (.0)	10 (1.1)		
Location of the lesion				.2117	<.001			.0177	.48
Proximal colon (cecum to transverse)	8174	7718 (59.7)	456 (49.6)			454 (50.3)	450 (49.9)		
Distal colon (descending to rectosigmoid)	5070	4674 (36.2)	396 (43.1)			387 (42.9)	385 (42.7)		
Rectum	603	536 (4.2)	67 (7.3)			61 (6.8)	67 (7.4)		
Resection procedure									
CSP	12,928	12,928 (100)				902 (100)			
Polypectomy	919		919 (100)				902 (100)		
EMR	0		0 (0)				0 (.0)		
Antithrombotic agent usage				–.0590	.12			.0039	1.00
Used	1453	1371 (10.6)	82 (8.9)			78 (8.7)	79 (8.8)		
Not used	12,394	11,557 (89.4)	837 (91.1)			824 (91.4)	823 (91.2)		
Endoscopic clip after resection				.2524	<.001				<.001
With endoclips	799	671 (5.2)	128 (13.9)			107 (11.9)	116 (12.9)		
Without endoclips	13,048	12257 (94.8)	791 (86.1)			795 (88.1)	786 (87.1)		
Kind of snare used					<.001				<.001
Regular	12,017	11,131 (86.1)	886 (96.4)			46 (5.1)	19 (2.1)		
Thin	1323	1309 (10.1)	14 (1.5)			813 (90.1)	869 (96.3)		
Not reported	507	488 (3.8)	19 (2.1)			43 (4.8)	14 (1.6)		
Histology					<.001				.10
Cancer (submucosal invasive cancer)	1	1 (.01)	0 (0)			0 (.0)	0 (.0)		
Intramucosal neoplasia/high-grade dysplasia	44	32 (.25)	12 (1.3)			5 (.6)	10 (1.1)		
Adenoma/low-grade dysplasia	10,766	10,039 (77.7)	727 (79.1)			717 (79.5)	714 (79.2)		
Hyperplastic/sessile serrated lesion	1641	1550 (12.0)	91 (9.9)			128 (14.2)	90 (10.0)		
Other tumors†	22	13 (.1)	9 (1.0)			1 (.1)	9 (1.0)		

(*continued on the next page*)

SUPPLEMENTARY TABLE 5. Continued

		Pre-PS matching				Post-PS matching			
	Total	CSP	HSP	Standardized mean difference	*P* value	CSP	HSP	Standardized mean difference	*P* value
Non-neoplastic polyp	1373	1293 (10.0)	80 (8.7)			51 (5.7)	79 (8.8)		
Postpolypectomy bleeding‡	20	13 (.1)	7 (.8)		<.001	1 (.1)	7 (.8)		.077
Intraprocedural perforation‡	0	0 (0)	0 (0)		N/A	0 (.0)	0 (.0)		N/A
Delayed perforation‡	0	0 (0)	0 (0)		N/A	0 (.0)	0 (.0)		N/A

Values are n (%) or mean ± standard deviation.
PS, Propensity score; *CSP*, cold snare polypectomy; *HSP*, hot snare polypectomy; N/A, not available.
*Cumulative number of patients.
†Neuroendocrine tumor, lymphoma, etc.
‡No patient was overlapped.

SUPPLEMENTARY TABLE 6. Risk for postpolypectomy bleeding after HSP compared with CSP without submucosal injection for colorectal lesions <10 mm

	Logistic regression model		Propensity score matching*	
Variables	**Odds ratio**	**95% Confidence interval**	**Odds ratio**	**95% Confidence interval**
Comparison between HSP and CSP of lesions, performed without submucosal injections	7.63	3.03-19.2	7.0	.086-59.9

HSP, Hot snare polypectomy; *CSP*, cold snare polypectomy.
*Conditional logistic regression model.

SUPPLEMENTARY TABLE 7. Sensitivity analysis of patients and lesions without missing data

		Pre-PS matching				Post-PS matching			
	Total	CSP	HSP	Standardized mean difference	*P* value	CSP	HSP	Standardized mean difference	*P* value
No. of lesions*	9043	7480	1563			1402	1402		
Age at each colonoscopy, y		67.3 ± 10.0	66.1 ± 10.8	−.1061	<.001	66.6 ± 10.0	66.0 ± 10.9	−.0582	.035
Lesion size, mm		4.9 ± 1.5	6.4 ± 1.5	1.0193	<.001	6.3 ± 1.5	6.2 ± 1.5	−.0282	.17
Macroscopic feature				−.3329	<.001			−.0483	.20
Ip, Ip+IIc	81	27 (.4)	54 (3.5)			15 (1.1)	41 (2.9)		
Is, Is+IIa, Is+IIc	2690	2032 (27.2)	658 (42.1)			549 (39.2)	561 (40.0)		
IIa, IIb, IIc, IIa+IIc	6241	5414 (72.4)	827 (52.9)			838 (59.8)	776 (55.3)		
Other (recurrence, submucosal tumor)	31	7 (.1)	24 (1.5)			0 (0)	24 (1.7)		
Location of the lesion				.2165	<.001			−.0138	.57
Proximal colon (cecum to transverse)	5213	4446 (59.4)	767 (49.1)			686 (48.9)	708 (50.5)		
Distal colon (descending to rectosigmoid)	3414	2730 (36.5)	684 (43.8)			629 (44.9)	597 (42.6)		
Rectum	416	304 (4.1)	112 (7.2)			87 (6.2)	97 (6.9)		
Procedure of resection									
CSP	7480	7480 (100)				1402 (100)			
Polypectomy	571		571 (36.5)				535 (38.2)		
EMR	992		992 (63.5)				867 (61.8)		
Antithrombotic agent usage				−.0072	.83			−.0184	.63
Used	961	792 (10.6)	169 (10.8)			155 (11.1)	147 (10.5)		
Not used	8082	6688 (89.4)	1394 (89.2)			1247 (88.9)	1255 (89.5)		
Endoscopic clip after resection				.4908	<.001			.0484	.14
With endoclips	789	372 (5.0)	417 (26.7)			229 (16.3)	259 (18.5)		
Without endoclips	8254	7108 (95.0)	1146 (73.3)			1173 (83.7)	1143 (81.5)		
Kind of snare used					<.001				<.001
Regular	8075	6556 (87.7)	1519 (97.2)			1253 (89.4)	1366 (97.4)		
Thin	644	627 (8.4)	17 (1.1)			88 (6.3)	12 (.9)		
Not reported	324	297 (4.0)	27 (1.7)			61 (4.4)	24 (1.7)		
Histology					<.001				<.001
Cancer (submucosal invasive cancer)	5	0 (0)	5 (.3)			0 (0)	5 (.4)		
Intramucosal neoplasia/high-grade dysplasia	69	23 (.3)	46 (2.9)			9 (.6)	34 (2.4)		
Adenoma/low-grade dysplasia	7189	5906 (79.0)	1283 (82.1)			1072 (76.5)	1148 (81.9)		
Hyperplastic/sessile serrated lesion	939	832 (11.1)	107 (6.9)			229 (16.3)	100 (7.1)		
Other tumors†	18	4 (.1)	14 (.9)			1 (.1)	13 (.9)		
Non-neoplastic polyp‡	823	715 (9.6)	108 (6.9)			91 (6.5)	102 (7.3)		
Postpolypectomy bleeding¶	19	10 (.1)	9 (.6)		.002	3 (.2)	8 (.6)		.13

(*continued on the next page*)

SUPPLEMENTARY TABLE 7. Continued

		Pre-PS matching				Post-PS matching			
	Total	CSP	HSP	Standardized mean difference	*P* value	CSP	HSP	Standardized mean difference	*P* value
Intraprocedural perforation¶	0	0 (0)	0 (0)	N/A	N/A	0 (0)	0 (0)	N/A	N/A
Delayed perforation¶	0	0 (0)	0 (0)	N/A	N/A	0 (0)	0 (0)	N/A	N/A

Values are n (%) or mean ± standard deviation.
PS, Propensity score; *CSP*, cold snare polypectomy; *HSP*, hot snare polypectomy; N/A, not available.
*Cumulative number of patients.
†Lipoma or hamartomatous polyp.
‡Inflammatory polyp or colon mucosa.
¶No patients overlapped.

SUPPLEMENTARY TABLE 8. Comparison of risks for postpolypectomy bleeding after HSP and CSP of colorectal lesions <10 mm that have no missing data

	Logistic regression model		Propensity score matching*	
Variables	**Odds ratio**	**95% Confidence interval**	**Odds ratio**	**95% Confidence interval**
Comparison of postpolypectomy bleeding risk after HSP and CSP of lesions without missing data	4.33	1.76-10.7	2.67	.709-10.0

CSP, Cold snare polypectomy; *HSP*, hot snare polypectomy.
*Conditional logistic regression model.