Removal of small colorectal polyps in anticoagulated patients: a prospective randomized comparison of cold snare and conventional polypectomy

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Background: The bleeding risk after cold snare polypectomy in anticoagulated patients is not known.

Objective: To compare the bleeding risk after cold snare polypectomy or conventional polypectomy for small colorectal polyps in anticoagulated patients.

Design: Prospective randomized controlled study.

Setting: Municipal hospital in Japan.

Interventions: Anticoagulated patients with colorectal polyps up to 10 mm in diameter were enrolled. Patients were randomized to polypectomy with either cold snare technique (Cold group) or conventional polypectomy (Conventional group) without discontinuation of warfarin. The primary outcome measure was delayed bleeding (ie, requiring endoscopic intervention within 2 weeks after polypectomy). Secondary outcome measures were immediate bleeding and retrieval rate of colorectal polyps.

Results: Seventy patients were randomized (159 polyps): Cold group (n = 35, 78 polyps) and Conventional group (n = 35; 81 polyps). The patients’ demographic characteristics including international normalized ratio and the number, size, and shape of polyps removed were similar between the 2 techniques. Immediate bleeding during the procedure was more common with conventional polypectomy (23% [8/35]) compared with cold polypectomy (5.7% [2/35]) (P = .042). No delayed bleeding occurred in the Cold group, whereas 5 patients (14%) required endoscopic hemostasis in the Conventional group (P = .027). Complete polyp retrieval rates were identical (94% [73/78] vs 93% [75/81]). The presence of histologically demonstrated injured arteries in the submucosal layer with cold snare was significantly less than with conventional snare (22% vs 39%, P = .023).

Limitation: Small sample size, single-center study.

Conclusions: Delayed bleeding requiring hemostasis occurred significantly less commonly after cold snare polypectomy than conventional polypectomy despite continuation of anticoagulants. Cold snare polypectomy is preferred for removal of small colorectal polyps in anticoagulated patients. (Clinical trial registration number: NCT 01553565.) (Gastrointest Endosc 2014;79:417-23.)

The success of colonoscopy for prevention of colorectal cancer is predicated on the ability to identify and remove precancerous lesions from the colon and rectum.1,2 However, polypectomy is not without its adverse events (eg, polypectomy is complicated by postpolypectomy bleeding in approximately 1% of patients, irrespective of
the size of polyps removed).\textsuperscript{3,4} Many patients who are candidates for colon cancer screening also take anticoagulants and/or antiplatelet agents for treatment or prevention of cardiovascular or cerebrovascular diseases. Conventional polypectomy without cessation of anticoagulation in anticoagulated patients increases the risk of postpolypectomy bleeding by approximately 10%.\textsuperscript{5} Previous studies have also shown a significant increase in postpolypectomy bleeding rates among anticoagulated patients despite temporary cessation of warfarin therapy.\textsuperscript{6-9} Current practice guidelines for colonoscopy in patients requiring long-term anticoagulation consider polypectomy a high-risk procedure and recommend anticoagulation should be temporarily discontinued, irrespective of whether cold snare polypectomy or conventional polypectomy is used.\textsuperscript{10} Temporary interruption of warfarin for endoscopic procedures is not without its own problems, because interruption is a concern for a thromboembolic risk up to 3%.\textsuperscript{11,12} Our approach has been to perform screening endoscopy without stopping anticoagulation. If large polyps are found, patients are rescheduled and the procedure repeated after interruption of anticoagulation. With this approach and according to the guidelines, even when only small polyps (eg, up to 10 mm) are found in patients receiving anticoagulants, the procedure must be rescheduled.

Because it has been reported that removal of small polyps by cold snaring is associated with a low rate of adverse events,\textsuperscript{13-16} we hypothesized that cold snare removal of small colorectal polyps could be done without stopping warfarin. This hypothesis was based on our belief that rebleeding is frequently related to damage to the submucosal vessels caused by the electrocautery and that the cold snaring technique (ie, without electrocautery) would cause minimal damage to the submucosal layer and thus delayed bleeding would be uncommon despite continuation of anticoagulation. The aim of this study was to compare the risk of post-polypectomy bleeding after removal of small polyps by cold snare transection (ie, without electrocautery) with traditional polypectomy in anticoagulated patients.

METHODS

Study design

This was a prospective randomized comparison of cold snare polypectomy and conventional polypectomy in anticoagulated patients with small colorectal polyps. The study was done at the Showa Inan General Hospital in Japan. The Institutional Review Board of Showa Inan General Hospital approved the study protocol, and all subjects gave written informed consent when the procedure was scheduled. The study was registered at ClinicalTrials.gov (NCT 01553565).

Study population

Subjects referred and scheduled for screening or surveillance colonoscopy were prospectively enrolled between March 2012 and December 2012; during this time, 3056 patients underwent colonoscopy. Inclusion criteria were patients with colorectal polyps up to 10 mm in diameter who were anticoagulated and in whom warfarin had not been discontinued. Exclusion criteria were age less than 20 years old, pregnancy, history of previous colorectal surgical resection, American Society of Anesthesiologists class III and IV, overweight (body weight > 100 kg), or allergic to propofol or its components (soybeans or eggs). Those in whom < 90% of mucosa was seen because of mixture of semisolid and solid colonic contents were also excluded because of poor bowel preparation. In patients whose warfarin was discontinued or in patients who were not selected for this study, heparin was used per the decision of the gastroenterologist. Recorded patient parameters were demographics, indication of colonoscopy, indication for anticoagulation, international normalized ratio (INR), aspirin use, and history of prior abdominal surgery.

Endoscopists and equipment

All procedures were performed by 1 of 2 experienced endoscopists (having performed > 10,000 colonoscopies each). A pediatric variable-stiffness colonoscope (model PCF-Q260AZI; Olympus Medical Systems, Tokyo, Japan) was used in all subjects. The instrument has a distal tip diameter of 11.7 mm and insertion tube diameter of 11.8 mm (working length, 1330 cm; accessory channel diameter, 3.2 mm). As is our standard practice, a transparent short cap (Olympus D-201-12704) with an outer diameter of 13.4 mm and an inner diameter of 12 mm was attached to the tip of the colonoscope in an attempt to improve adenoma detection rate.\textsuperscript{17} The edge of the cap protrudes for approximately 4 mm beyond the tip of the colonoscope. Retrotroflexion in the rectum was routinely performed. The standard bowel preparation was performed using split dosing of a polyethylene glycol-electrolyte solution (Ajinomoto Pharmaceutical Co, Tokyo, Japan) in all patients. All procedures were conducted with the patient under nurse-administered propofol sedation (AstraZeneca, Osaka, Japan).\textsuperscript{18}

Randomization

Randomization was done using a table of random numbers using block sizes of 4. Subjects receiving warfarin
were allocated by a reception nurse to be eligible to enter the cold snare polypectomy (Cold group) versus conventional polypectomy (Conventional group) study if they qualified by having a polyp of the appropriate size. For subjects who qualified, the sealed opaque envelopes were opened shortly before the start of the polypectomy procedure.

**Procedure**

Cecal intubation was verified by identification of the appendiceal orifice and ileocecal valve. The time taken to reach the cecum, intubation rate of the terminal ileum, procedure time, location of polyps, and size (estimated using the open-forceps technique, forceps span = 8 mm) and shape of each polyp were recorded. All colorectal polyps up to 10 mm found, except for tiny hyperplastic polyps in the rectum and distal sigmoid colon, were removed. The snare for both cold and conventional polypectomy was a dual-loop wire snare with a loop size of 33/16 mm (SN-3316LX; Medico’s Hirata Inc, Osaka, Japan). The technique used was cold resection of the polyp without tenting and then suction of the transected polyp into a trap followed by submission for histopathologic evaluation. An ERBE ICC200 (Amco, Tokyo, Japan) was used in the Endocut mode with the effect 3 current set at output limit 120 W and forced coagulation current set at output limit 35 W for conventional polypectomy. Submucosal injection of saline solution before removal was not performed, regardless of the type of polypectomy. Prophylactic clipping after polyp removal was not routinely performed; however, hemostatic clipping was carried out during the procedure for immediate bleeding, irrespective of the type of polypectomy.

The INR was checked on the day of the procedure. When the INR was supratherapeutic (up to a maximum of 2 times), the procedure was performed as scheduled and the dose of warfarin was stopped or adjusted shortly after the procedure. The size, shape, and location of all polyps were recorded. All patients who underwent polypectomy visited our hospital 2 weeks after polypectomy to be informed of the pathologic results of polyps removed. Adverse events and all GI symptoms within 2 weeks after each polypectomy were recorded. When delayed bleeding was suspected without a decrease in hemoglobin, the bleeding was judged to be “slight” postpolypectomy bleeding, which was designated as hematochezia.

Secondary outcome measures included immediate bleeding during the procedure and the complete retrieval rate of colorectal polyps based on the pathologic examination. Immediate bleeding that required hemostatic clipping was defined as spurting or oozing that continued for more than 30 seconds. Because the endoscopist was not blinded to whether electrocautery was used or not, this definition was used to avoid the potential for a biased assessment of immediate bleeding.

**Sample size calculation and statistical analysis**

One previous study reported that postpolypectomy bleeding occurred in at least 10% of patients who underwent conventional polypectomy without stopping warfarin, and this value was used as the basis for sample size estimation.\(^5\) We hypothesized that if the postpolypectomy bleeding in anticoagulated patients was aggravated by the electrocautery, the proportion of patients with postpolypectomy bleeding in the Cold group would be no more than 1%. The sample size was estimated based on the complicated rates of delayed bleeding within 2 weeks after polypectomy and was based on the detecting a difference in proportions at the 5% level of significance with a power of 80% for the rate of delayed bleeding; at least 53 patients were required to be enrolled in each group. During this study, a planned interim analysis confirmed whether the rate of postpolypectomy bleeding was not more than 10%. However, after 35 patients for each arm were enrolled, the study was halted to avoid exposing patients to unnecessary postpolypectomy bleeding because the overall proportion of patients with postpolypectomy bleeding was 40% in those receiving conventional polypectomy versus 10% in the Cold group and delayed bleeding occurred in 14% of those in the Conventional group.

Polyps were measured in increments of 1 mm. Statistical differences were analyzed by \(\chi^2\) tests of independence and the Fisher exact test or Student \(t\) test. \(P < .05\) were considered significant. Statistical analysis was performed by using JMP 9.0.2 version software (SAS Institute Japan Inc, Tokyo, Japan).

**RESULTS**

**Patients**

Seventy-seven patients were recruited for the study; however, 7 patients found to have a larger polyp (>10 mm) during the procedure were dropped from the study. Therefore, 70 patients were actually enrolled in the study and received polypectomy: 35 in the Cold group and 35 in the Conventional group. The patients’
demographic characteristics, indications for colonoscopy, indications for warfarin, INR, aspirin use, intubation time, and intubation rate of the terminal ileum were similar between the 2 techniques. No significant difference was found in patients with the supratherapeutic INR on the day of the procedure between both groups (4 in the Cold group or 3 in the Conventional group, $P = .69$).

Mean procedure time was significantly shorter in the Cold group (16/7 minutes) compared with the Conventional group (26/9 minutes; $P < .001$) (Table 1).

### Polypectomy

The characteristics of number, size, and shape of polyps removed are shown in Table 2 and were similar between the 2 techniques: Cold group, 78 polyps, average size 6.5 mm, median size 6.5 mm; Conventional group, 81 polyps, average size 6.8 mm, median size 6 mm) (Table 2).

There was a significant increase in delayed bleeding after polypectomy with conventional snaring compared with cold snaring (14% [5/35] vs 0% [0/35]; $P = .027$) (Table 3). Delayed bleeding occurred within 5 days after conventional polypectomy, and all 5 patients experienced more than a 2-g/dL decrease in hemoglobin. Active bleeding was successfully stopped by 1 session of endoscopic intervention. However, no blood transfusions were required in any patients. Four of 5 patients with hematochezia (mild uninvestigated bleeding) in both groups were also aspirin users (Table 1). There was also a significant increase in immediate bleeding after polypectomy with

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<thead>
<tr>
<th>TABLE 1. Baseline characteristics, indications, and outcomes in patients with cold snare polypectomy and conventional polypectomy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cold group</strong></td>
</tr>
<tr>
<td>Number of patients</td>
</tr>
<tr>
<td>Mean age, y (SD)</td>
</tr>
<tr>
<td>Gender (female)</td>
</tr>
<tr>
<td>Indications for warfarin</td>
</tr>
<tr>
<td>Hemo-positive stool</td>
</tr>
<tr>
<td>Screening</td>
</tr>
<tr>
<td>Other</td>
</tr>
</tbody>
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| mean INR* (SD) | 2.4 (4) | 2.3 (4) | .13 |
| Aspirin use | 2 | 2 |  |
| Cecum intubation rate, % | 100 | 100 |  |
| Mean cecal intubation time, min (SD) | 5.5 (5) | 5.4 (7) | .57 |
| Intubation rate of terminal ileum, % | 89 | 86 | .72 |
| Mean procedure time, min (SD) | 16 (7) | 26 (9) | <.001 |

$SD$, Standard deviation; *INR, international normalized ratio.
*Differences between cold snare polypectomy (Cold) and conventional polypectomy (Conventional) compared using the Student $t$ test for continuous variables.
<table>
<thead>
<tr>
<th>TABLE 2. Comparison of polyps in patients undergoing cold snare polypectomy (Cold group) and conventional polypectomy (Conventional group)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cold group</strong></td>
</tr>
<tr>
<td>Total number of polyps removed</td>
</tr>
<tr>
<td>Mean number of polyps per patient* (SD)</td>
</tr>
<tr>
<td>Mean polyp size, mm (SD)</td>
</tr>
<tr>
<td>Median polyp size, mm</td>
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<tr>
<td>Complete retrieval rate, %</td>
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</tbody>
</table>

| Characteristics of polyps removed |  |  |  |
| Pathology |  |  |  |
| High-grade adenoma | 2 | 2 | .99 |
| Adenoma | 70 | 72 |  |
| Hyperplastic polyp | 6 | 7 |  |
| Size |  |  |  |
| ≤ 5 mm | 44 | 45 | .91 |
| 6 mm ≤ size ≤ 10 mm | 34 | 36 |  |
| Shape |  |  |  |
| Flat | 23 | 19 | .71 |
| Sessile | 50 | 56 |  |
| Pedunculated | 5 | 6 |  |

$SD$, Standard deviation.
*Differences between cold snare polypectomy (Cold group) and conventional polypectomy (Conventional group) compared using the Student $t$ test for continuous variables.
| Differences between the Cold group and the Conventional group compared using the $\chi^2$ test for categorical data.
conventional snaring compared with cold snaring (23% [8/35] vs 5.7% [2/35]; \( P \) = .042) (Table 3). Irrespective of group, immediate bleeding that required hemostatic clipping was in the form of vigorous oozing. The odds ratio of total postpolypectomy bleeding was 6.5 (95% confidence interval, 1.9-22.5). Neither perforation nor thromboembolic events was observed in either group during this study.

Pathologic examination

Histopathologic evaluation showed no significant difference in the complete retrieval rate of colorectal polyps between the Cold group and the Conventional group (94% [75/78] vs 93% [75/81]) (Table 2). We reexamined the polypectomy site for 2 patients with high-grade adenomas 3 to 6 months after polypectomy and found no endoscopic evidence of incomplete resection. Except for 2 high-grade adenomas in each group, the polyps resected were adenomas or hyperplastic polyps. We were able to examine the tissue for arteries in the submucosal layer in 92% (72/78) of resected polyps in the Cold group and 93% (75/81) of resected polyps in the Conventional group (Table 4). Submucosal arteries were detected in the submucosal layer more often in the Conventional group than in the Cold group (47% vs 32%, \( P = .049 \)). The presence of injured arteries in the submucosa layer was significantly less in the Cold group than in the Conventional group (22% vs 39%, \( P = .023 \)) (odds ratio, 2.2; 95% confidence interval, 1.1-4.6).

**DISCUSSION**

ASGE guidelines for colonoscopy in patients requiring long-term anticoagulation consider cold snare and conventional polypectomy to be high-risk procedures and recommend the temporary discontinuation of anticoagulation therapy.\(^\text{10}\) Cold snare polypectomy was previously reported to be associated with a low rate of postpolypectomy bleeding.\(^\text{14,15}\) We compared the bleeding risk after cold snare polypectomy with that of conventional polypectomy for small colorectal polyps in anticoagulated patients and found no delayed bleeding requiring hemostasis after cold snare polypectomy despite continuation of anticoagulants. Our study does not provide data for colorectal polyps greater than 10 mm encountered in anticoagulated patients, and until new data are obtained, we recommend that the procedure should be rescheduled and polypectomy delayed until after anticoagulation is suspended. However, in clinical practice, most colorectal polyps we...
encountered were less than 10 mm in size, and our data suggest that cold snare polypectomy can be done immediately without discontinuation of anticoagulation. Although hemostatic clipping is effective for control of immediate bleeding after polypectomy, the prophylactic use of hemostatic clips has not been proven to prevent delayed bleeding after conventional polypectomy even in patients not receiving anticoagulants or antiplatelet agents.19

We speculated that the cause of delayed bleeding would be related to injury of blood vessels in the submucosal layer caused by electrocautery. Arteries were detected more often in the submucosal layer in the Conventional group than in the Cold group (47% vs 32%, \( P = .049 \)). However, the difference was of borderline significance, possibly related to the small sample size. Importantly, injured submucosal arteries were seen significantly less frequently in the Cold group than after conventional polypectomy (22% vs 39%, \( P = .023 \)) (Table 4). This difference is consistent with the increase in delayed bleeding associated with conventional compared with cold snare polypectomy and with our previous study showing that conventional polypectomy was associated with more abdominal symptoms after polypectomy than after cold snare polypectomy. Together, these data support the notion that symptoms and delayed bleeding are likely related to the tranmural burn syndrome caused by conventional polypectomy.20

One concern associated with cold snaring is whether there is an increased difficulty in resection and retrieval of specimens for pathologic examination.15,21-23 As shown in Table 2, complete retrieval rate was possible in 94% in the Cold group, which is within the recommendations of the U.S. Multi-Society Task Force (ie, more than 95% success in polyp retrieval is recommended as a quality indicator in continuous quality improvement programs).24 Another advantage of the cold snaring technique is histologically the margins of transected polyps are undamaged because of the lack of burn artifact. The success of resection and polyp retrieval with the cold snare technique may depend in part on the selection of snare. An exclusive snare for cold polypectomy is not available in Japan, and we used a dual-loop snare because its sheath is firmer than that of a regular cold polypectomy snare. Studies of different snare types and composition of the sheath will be required to test whether snare characteristics are important in terms of the outcomes measured here.

This study also showed that cold snare polypectomy had the advantages of shorter total procedure time without a difference in adverse events or polyp retrieval rates. The shorter total time likely relates to the lack of the need to prepare the electrocautery equipment required for conventional polypectomy because preprocedure preparation of electrocautery equipment is not done in anticoagulated patients. The mean procedure time in the Cold group was also shorter than that of the Conventional group because hemostatic clipping for immediate bleeding was less in the Cold group (2 patients) than in the Conventional group (8 patients).

A retrospective study demonstrated that only 1 of 12 patients (8%, 95% confidence interval, 1%–4.5%) who were maintained on warfarin developed major postpolypectomy bleeding that required transfusion.25 If confirmed, prophylactic clipping for conventional polypectomy using prophylactic clipping in anticoagulated patients with polyps up to 1 cm in size may be an alternative option to the interruption of warfarin.

We used the Endocut mode for the electrocautery setting for conventional polypectomy. Although it is thought that the choice of electrocautery setting would influence the rate of immediate and/or delayed bleeding, it is unknown how the Endocut mode would influence postpolypectomy bleeding. In addition, the immediate bleeding rate (25%) in the conventional group was higher than we expected. We suspect that the high rate may depend in part on the definition of immediate bleeding used and suggest that studies are needed to define the most clinical definition of immediate bleeding.

This study has some limitations. In addition to the small sample size, the study was conducted in a single hospital in Japan. The results in this study will need to be confirmed in multicenter studies and in different populations and ethnic groups.

In conclusion, neither delayed bleeding nor difficulty in polyp retrieval occurred after cold snare polypectomy in anticoagulated patients. The cold snare technique is preferred for removal of small polyps in anticoagulated patients because it was associated with less bleeding risk than conventional polypectomy.

REFERENCES


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