Safety and efficacy of a new cold snare technique with clipping for colorectal angioectasia


Abstract:
Colorectal angioectasia is a major cause of lower gastrointestinal bleeding. The use of antithrombotic agents is expected to increase with the aging of the population, and bleeding from angioectasia is an important issue. Although the effectiveness of endoscopic mucosal resection for colorectal angioectasia has been reported, there are no reports of cold snare technique for angioectasia (CSA). From February 2018 to February 2022, the safety of CSA was evaluated at Omori Red Cross Hospital. We investigated the incidence of bleeding (delayed post-polypectomy bleeding (DPPB) and immediate bleeding) after CSA and the incidence of rebleeding requiring repeated endoscopic treatment. During the study period, 106 angioectasias were identified during colonoscopy. We only targeted patients with bloody stools and/or anemia requiring treatment for bleeding from angioectasia. Finally, we included 11 angioectasias in this study. The rates of DPPB and rebleeding after CSA were 0%. The rate of immediate bleeding during CSA was 27.3% (3/11). Dilated capillaries could be observed pathologically in 9 of the 11 lesions (81.8%). CSA was safe and can be a new treatment option in the future. To confirm our results and verify the long-term safety and efficacy of CSA, further studies are desirable.
Safety and efficacy of a new cold snare technique with clipping for colorectal angioectasia

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Conflicts of interest: The authors have no conflicts of interests to disclose.

Key Words
Colorectal angioectasia, Cold snare technique

ABSTRACT
Colorectal angioectasia is a major cause of lower gastrointestinal bleeding. The use of antithrombotic agents is expected to increase with the aging of the population, and bleeding from angioectasia is an important issue. Although the effectiveness of endoscopic mucosal resection for colorectal angioectasia has been reported, there are no reports of cold snare technique for angioectasia (CSA). From February 2018 to February 2022, the safety of CSA was evaluated at Omori Red Cross Hospital. We investigated the incidence of bleeding (delayed post-polypectomy bleeding (DPPB) and immediate bleeding) after CSA and the incidence of rebleeding requiring repeated endoscopic treatment. During the study period, 106 angioectasias were identified during colonoscopy. We only targeted patients with bloody stools and/or anemia requiring treatment for bleeding from angioectasia. Finally, we included 11 angioectasias in this study. The rates of DPPB and rebleeding after CSA were 0%. The rate of immediate bleeding during CSA was 27.3% (3/11). Dilated capillaries could be observed pathologically in 9 of the 11 lesions (81.8%). CSA was safe and can be a new treatment option in the future. To confirm our results and verify the long-term safety and efficacy of CSA, further studies are desirable.

INTRODUCTION
Colorectal angioectasia has been increasingly recognized as a major cause of lower gastrointestinal bleeding in the elderly [1]. Argon plasma coagulation (APC) and clipping are often performed for bleeding from angioectasia. However, there are some reports of colonic gas explosion leading to perforation in some cases during APC [2], and endoscopists also often experience patient suffering due to gas explosion. Furthermore, regarding clipping for colorectal angioectasia, the problem of rebleeding commonly occurs.

Four cases of colorectal angioectasia treated by hot snare polypectomy (HSP) or endoscopic mucosal resection (EMR) have been reported [1,3]. In EMR/HSP, the dilated capillaries are resected; therefore, the possibility of rebleeding from angioectasia is low. This is the most different technique from APC or traditional clipping. However, patients with clinically severe anemia due to bleeding from angioectasia often take antithrombotic agents, and delayed post-polypectomy bleeding (DPPB) after EMR/HSP is major concern in these patients. Several studies have shown that DPPB is less common after cold snare polypectomy (CSP) than after conventional EMR/HSP [4,5].

The use of antithrombotic agents is expected to increase with the aging of the population [6]; therefore, the safety of the procedure itself is increasingly important. We have previously reported that the use of antithrombotic agents, even multiple antithrombotic agents, does not increase the risk of DPPB after CSP [7]. Therefore, we hypothesized that cold snare technique for angioectasia (CSA) is safer than EMR/HSP.

We examined cases of CSA for bleeding from angioectasia at our hospital.

METHODS

Patients
This study is a retrospective case series evaluating the safety and efficacy of a new treatment for colorectal angioectasia using cold snare technique with clipping. From February 2018 to February 2022, the safety of CSA with clipping was evaluated at Omori Red Cross Hospital. During the study period, 106 angioectasias were identified during colonoscopy. We excluded patients who did not need treatment, such as those with angioectasia that was diagnosed incidentally during colonoscopy, and we only targeted patients with bloody stools and/or anemia requiring treatment for bleeding from angioectasia. Finally, we included 11 angioectasias (5 patients) in this study. We investigated the incidence of bleeding (DPPB and immediate bleeding) after CSA with clipping and the incidence of rebleeding requiring repeated endoscopic treatment. Although CSP for polyps has been shown to be safe, CSA has not been reported, and its safety is unknown. We also examined whether DPPB after CSA is extremely rare similar to that after CSP for polyps.

**CSA with clipping**

A standard or magnifying colonoscope with carbon dioxide insufflation was used in all cases (CF-HQ290ZI, PCF-Q260AZI, PCF-Q260AI, and PCF-H290ZI; Olympus Co., Tokyo, Japan). After the CSA, we performed clipping in all cases. CSA is a challenging treatment that has not been reported so far, therefore, we performed clipping in all cases for patient safety. DPPB was defined as a reduction in hemoglobin level by at least 2 g/dl below the most recent preoperative level or the necessity for endoscopic hemostasis and/or blood transfusion and/or massive melena within 2 weeks of procedure [8,9]. Immediate bleeding that necessitated hemostatic clipping was defined as spurting or oozing that continued for more than 30 seconds [9]. This definition was used to avoid
the potential for a biased assessment of immediate bleeding. Figure 1 shows a case of CSA with clipping. A 78-year-old man taking edoxaban visited the outpatient department of our hospital with a chief complaint of bloody stools. We performed hemostasis with endoscopic clipping. However, bleeding from the same site was observed after 2 days, and hemostasis was performed again by clipping for bleeding. Five months later, the patient returned to our hospital with a complaint of bloody stool. Bleeding from angioectasia at another site was observed. We performed CSA with clipping. The histopathologic findings of the resected specimen showed some obvious dilated capillaries in the mucosa. At the one-year follow-up visit, the patient experienced no rebleeding or DPPB after CSA, and we confirmed scarring at same site after 1 year. Video 1 shows another case of CSA with clipping in the cecum. Although immediate bleeding occurred, the feeding vessel was clearly observed in the defect. The exposed bleeding vessel was clipped, adequately controlling the bleeding through endoscopic hemostasis. At the one-year follow-up visit, this patient also did not experience complications.

In this study, we counted each angioectasia lesion that was resected, even if two or more angioectasias were resected during the CSA procedure; two or more angioectasias resected during the same CSA procedure were counted as two or more angioectasias. The study protocol complied with the Declaration of Helsinki and the Ethics Guidelines for Clinical Research published by the Ministry of Health, Labour and Welfare, Japan. Approval for this study was obtained from the Ethics Committee of Omori Red Cross Hospital on October 1, 2021. This is a retrospective study, and patients were enrolled according to an opt-out policy of our hospital.
RESULTS

Characteristics of patients

Five patients (11 angioectasias) were included in this study. The clinical characteristics of the patients are presented in Table 1. Five patients were enrolled in this analysis, and the mean age (± SD) was 83.4 ± 3.6 years. All patients were receiving antithrombotic therapy, and antithrombotic therapy was continued even on the day of colonoscopy in all cases. All patients had comorbidities and anemia due to hematochezia.

Characteristics of the angioectasias

The characteristics of the angioectasias are presented in Table 2. There were 11 total angioectasias. Six (54.5%) angioectasias were located in the cecum. The rate of immediate bleeding during CSA was 27.3% (3/11), and we performed prophylactic clipping in all cases even without immediate bleeding. The rates of DPPB after CSA and rebleeding from angioectasia were 0%. Regarding the histopathology, dilated capillaries could be confirmed in nine of the 11 lesions (81.8%).

DISCUSSION

Angioectasia is defined as abnormal, dilated, tortuous, and usually small (<10 mm) blood vessels visualized within the mucosal and submucosal layers of the gut, and the colon is the most frequent site of angioectasia in the gut [2]. Bleeding from colorectal angioectasia can be mild and chronic and can stop spontaneously in up to 90% of patients [2]. However, the use of antithrombotic agents is expected to increase with the aging of the population [6]; therefore, bleeding from angioectasia is increasingly important. Bleeding from angioectasia can be recurrent and life-threatening.
The effectiveness of EMR/HSP for colorectal angioectasia has been reported in some cases [1,3]. In EMR/HSP the dilated capillaries are resected; therefore, the possibility of rebleeding from angioectasia is low. This is the most different technique from APC or traditional clipping. However, patients with clinically severe anemia due to bleeding from angioectasia often take antithrombotic agents, and DPPB after EMR/HSP is a major concern for these patients. On the other hand, DPPB after CSP is very rare [4,5], and the use of antithrombotic agents does not increase the risk of DPPB after CSP even if patients are taking multiple antithrombotic agents [7]. Both EMR/HSP and CSA are treatments that involve resection of the dilated capillaries in the same manner. If the therapeutic effects are same, the rate of complications from an endoscopic procedure is important in clinical practice. The rate of DPPB after CSP is very rare and less than that after EMR/HSP. In addition, with this procedure, it is unnecessary to prepare a high-frequency device, apply a counter electrode, and evaluate for the absence of metal in the body and clothes. CSP is convenience and safe. Therefore, we think that cold snare technique with clipping is superior to EMR/HSP as a treatment for colorectal angioectasia.

CSA with clipping also has other advantages. As shown in the Video 1, the feeding vessel was clearly observed in the defect. Therefore, we were able to perform clipping directly on the exposed blood vessel. We think this is likely to be effective for bleeding from angioectasia. On the other hand, CSA with clipping is not without potential disadvantages. Angioectasia is present in the mucosal and submucosal layers of the colon [2]. The incidence of incomplete mucosal layer resection after CSP was 57% in a previous study [10], and the submucosal layer cannot be removed with CSP. Therefore, how effective CSA remains unclear. However, feeding vessels can be visually
recognized by performing CSA, and clipping of the exposed blood vessel can be performed directly as shown in Video 1. In addition, considering the pathophysiologic mechanisms of colorectal angioectasia, we believe that CSA with clipping could be clinically useful for treating bleeding from colorectal angioectasia. Sami et al. reported on the pathophysiologic mechanisms contributing to angioectasia and subsequent bleeding [2]. Histologic evaluation of resected colon specimens from patients with angioectasia revealed dilated and tortuous veins in the submucosa, even without obvious mucosal lesions. Therefore, it was suggested that lesions develop with ageing because of chronic, low-grade, and intermittent obstruction of submucosal veins, resulting from increased contractility of the muscularis propria, which leads to venous dilation in the submucosal layer. Eventually, an arteriovenous collateral circulation is formed in the mucosal layer. When this circulation spreads superficially, and can be seen endoscopically, it is diagnosed as angioectasia, and bleeding from dilated veins can occur. Considering the pathophysiologic mechanisms of angioectasia, we thought it would be advantageous if blood vessels exposed on the superficial mucosal surface were removed. Numerous blood vessels exist within the walls of the gastrointestinal tract; however, only blood vessels exposed on the surface layer of the gastrointestinal wall cause bleeding. Therefore, we think it is unnecessary to completely resect all blood vessels from the submucosal layer. Resection of superficial blood vessels with CSA means that the tissue returns to a normal state, with veins only present in the submucosa. From this state, contraction of the muscularis propria causes venous congestion, and vasodilation of the submucosal layer is expected to result in a considerable time before blood vessels become re-exposed as angioectasias on the surface layer. This theory is supported, in part, by the fact that angioectasias are more
common in older individuals. Additionally, clipping the wound may prevent the future exposure of blood vessels in superficial layers. Therefore, we believe that CSA with clipping, which involves resecting superficial blood vessels and suturing the wound, is an effective treatment for angioectasia.

Although this is a retrospective case series performed at single center, the rates of DPPB and rebleeding after CSA were 0% in this study. In conclusion, CSA with clipping was safe and can be a new treatment option in the future. To confirm our results and verify the long-term safety and efficacy of CSA, further studies are desirable.

ACKNOWLEDGMENTS
The authors would like to thank the staff of the participating institutions for their support in recruiting eligible patients and the patients who participated in this study.

AUTHOR CONTRIBUTIONS
JA, HC and KO conceived of the study. JA, HC, KY, NO, MK, HK and MN performed the CSP. JA, HC, KY, NO, MK, HK and MN recruited the study participants. Analysis and interpretation of the data was conducted by JA and HC. All the authors have read the final manuscript and approve of its submission for publication.

ABBREVIATIONS
APC: argon plasma coagulation
HSP: hot snare polypectomy
EMR: endoscopic mucosal resection
DPPB: delayed post-polypectomy bleeding
CSP: cold snare polypectomy
CSA: cold snare technique for angioectasia

COMPETING INTEREST STATEMENT (COI)
No support from any organization was received for the submitted work; there were no financial relationships with any organizations that might have had an interest in the submitted work in the previous three years, and there are no other relationships or activities to declare that could have potentially influenced the outcomes of the submitted work.

FUNDING
This study received no external funding. There was no sponsor for this study.

Figure Legends
Figure 1. (a) Bleeding from angioectasia in the transverse colon. (b) Hemostasis was performed by clipping for bleeding. (c) Two days later, bleeding from the same site was observed. (d) Hemostasis was performed again by clipping for bleeding. (e) Five months later, the patient returned to our hospital with a complaint of bloody stool. Bleeding from angioectasia at another site was observed. (f) We performed CSP for the resection of angioectasia. (g) Some dilated capillaries were found in the mucosa of the resected specimen. (h) We confirmed scarring after one year.

Video Legends
Angioectasias in the cecum.
Snaring of the angioectasias.
Resection.
Feeding vessel in the defect.

Clipping of the exposed bleeding vessel.

Additional clipping.

Confirmation of hemostasis.

REFERENCES


Table 1. Characteristics of the enrolled patients.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>Antithrombotic agents</th>
<th>Comorbidity</th>
<th>Hematochezia</th>
<th>Hb</th>
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<td>1</td>
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<td>2</td>
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<tr>
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<tr>
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<td>8.2</td>
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CKD, chronic kidney failure; Af, atrial fibrillation; AMI, acute myocardial infarction; Hb, hemoglobin
Table 2. Characteristics of the angioectasias.

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Location</th>
<th>IB</th>
<th>Clipping</th>
<th>DPPB</th>
<th>Rebleeding</th>
<th>Pathological dilated capillaries</th>
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IB, immediate bleeding; DPPB, delayed post-polypectomy bleeding.