Endoscopy International Open

Feasibility of progressive polyp contraction with underwater endoscopic mucosal resection of 20mm or larger superficial colorectal lesions


Affiliations below.

DOI: 10.1055/a-1955-3379

Please cite this article as: Okada M, Shinozaki S, Nomura T et al. Feasibility of progressive polyp contraction with underwater endoscopic mucosal resection (PP-CUE) of large superficial colorectal lesions. Endoscopy International Open 2022. doi: 10.1055/a-1955-3379

Conflict of Interest: H.Y. has a consultant relationship with the Fujifilm Corporation and has received honoraria, grants, and royalties from the company. Other authors have no conflicts of interest to disclose.

Abstract:
Background and study aims: Underwater endoscopic mucosal resection (UEMR) does not always result in en bloc resection of large colorectal lesions. The aim of this study is to demonstrate the feasibility of en bloc resection with progressive polyp contraction with underwater endoscopic mucosal resection (PP-CUE) of large superficial colorectal lesions. The advantage of PP-CUE is to enable resection of a superficial non-polypoid lesion that is larger than the snare diameter.

Patients and methods: Eleven consecutive lesions in ten patients who underwent UEMR with PP-CUE of large superficial colorectal lesions (20 mm or greater) were included.

Results: The median lesion diameter was 24 mm (interquartile range [IQR], 20–24 mm). All lesions were larger than the rotatable snare (15 mm) used. Median procedure time and PP-CUE time were 11 min (IQR, 8.5–12.3) and 2.3 min (IQR, 1.9–3.4), respectively. Pathological diagnoses of resected specimens included six adenomas, three sessile serrated lesions and two slightly invasive submucosal carcinomas. En bloc and R0 resection rates were both 91% (10/11). No adverse events occurred.

Conclusions: The PP-CUE is useful to resect superficial non-polypoid colorectal lesions 20–25 mm in diameter in an en bloc fashion.

Corresponding Author:
Yoshikazu Hayashi, Jichi Medical University, Gastroenterology, Yakushiji 3311-1, 329-0498 Shimotsuke-shi, Japan, hayashi@jichi.ac.jp

Affiliations:
Masahiro Okada, Jichi Medical University, Department of Medicine, Division of Gastroenterology, Shimotsuke, Japan
Satoshi Shinozaki, Shinozaki Medical Clinic, Gastroenterology, Utsunomiya, Japan
Tatsuma Nomura, Kinan Hospital, Gastroenterology, Minamimuro-gun, Japan
Hironori Yamamoto, Jichi Medical University, Department of Medicine, Division of Gastroenterology, Tochigi, Japan
Table. Baseline characteristics of patients and outcomes

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of lesions, n</td>
<td>11</td>
</tr>
<tr>
<td>Number of patients, n</td>
<td>10</td>
</tr>
<tr>
<td>Age, years, median (IQR)</td>
<td>77 (62-80)</td>
</tr>
<tr>
<td>Gender, male/female, n</td>
<td>8/2</td>
</tr>
<tr>
<td>Tumor location, n (%)</td>
<td></td>
</tr>
<tr>
<td>Right colon</td>
<td>10 (91%)</td>
</tr>
<tr>
<td>Left colon</td>
<td>1 (9%)</td>
</tr>
<tr>
<td>Macroscopic type, n (%)</td>
<td></td>
</tr>
<tr>
<td>0-IIa</td>
<td>9 (82%)</td>
</tr>
<tr>
<td>0-IIa+IIc</td>
<td>2 (18%)</td>
</tr>
<tr>
<td>Tumor diameter, mm, median (IQR)</td>
<td>24 (20-24)</td>
</tr>
<tr>
<td>Pathological findings, n (%)</td>
<td></td>
</tr>
<tr>
<td>Adenoma</td>
<td>6 (58%)</td>
</tr>
<tr>
<td>Sessile serrated lesion</td>
<td>3 (25%)</td>
</tr>
<tr>
<td>Slightly invasive (&lt;1,000 µm) submucosal carcinoma</td>
<td>2 (17%)</td>
</tr>
<tr>
<td>Lymphovascular invasion, n (%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Cylindrical cap use, n (%)</td>
<td>11 (100%)</td>
</tr>
<tr>
<td>En bloc resection, n (%)</td>
<td>10 (91%)</td>
</tr>
<tr>
<td>R0 resection, n (%)</td>
<td>10 (91%)</td>
</tr>
<tr>
<td>Resected specimen diameter, mm, median (IQR)*</td>
<td>24 (20-24)</td>
</tr>
<tr>
<td>Procedure time, min, median (IQR)</td>
<td>11 (8.5-12.3)</td>
</tr>
<tr>
<td>PP-CUE time, min, median (IQR)</td>
<td>2.3 (1.9-3.4)</td>
</tr>
<tr>
<td>Perforation, n (%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Delayed bleeding, n (%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

IQR, interquartile range; PP-CUE, progressive polyp contraction with underwater endoscopic mucosal resection
* Only lesions resected in an *en bloc* fashion are included.
Feasibility of progressive polyp contraction with underwater endoscopic mucosal resection of 20mm or larger superficial colorectal lesions

Masahiro Okada¹, Satoshi Shinozaki¹², Tatsuma Nomura¹, Yoshikazu Hayashi¹, Takaaki Morikawa¹, Masafumi Kitamura¹, Hisashi Fukuda¹, Munefumi Arita³, Takahito Takezawa¹, Keijiro Sunada¹, Alan Kawarai Lefor³, Hironori Yamamoto¹

¹Department of Medicine, Division of Gastroenterology, Jichi Medical University, Shimotsuke, Japan
²Shinozaki Medical Clinic, Utsunomiya, Japan
³Department of Surgery, Jichi Medical University, Shimotsuke, Japan

Corresponding author:

Yoshikazu Hayashi, MD, PhD

Department of Medicine, Division of Gastroenterology

Jichi Medical University, Shimotsuke, Japan

3311-1 Yakushiji, Shimotsuke, Tochigi, 329-0498, Japan.

Phone: +81-285-58-7348

Fax: +81-285-44-8297

Email address: hayashi@jichi.ac.jp
Conflicts of Interest: H.Y. has a consultant relationship with the Fujifilm Corporation and has received honoraria, grants, and royalties from the company. Other authors have no conflicts of interest to disclose.
Abstract

Background and study aims: Underwater endoscopic mucosal resection (UEMR) does not always result in en bloc resection of large colorectal lesions. The aim of this study is to demonstrate the feasibility of en bloc resection with progressive polyp contraction with underwater endoscopic mucosal resection (PP-CUE) of large superficial colorectal lesions. The advantage of PP-CUE is to enable resection of a superficial non-polypoid lesion that is larger than the snare diameter.

Patients and methods: Eleven consecutive lesions in ten patients who underwent UEMR with PP-CUE of large superficial colorectal lesions (20 mm or greater) were included.

Results: The median lesion diameter was 24 mm (interquartile range [IQR], 20-24 mm). All lesions were larger than the rotatable snare (15 mm) used. Median procedure time and PP-CUE time were 11 min (IQR, 8.5-12.3) and 2.3 min (IQR, 1.9-3.4), respectively. Pathological diagnoses of resected specimens included six adenomas, three sessile serrated lesions and two slightly invasive submucosal carcinomas. En bloc and R0 resection rates were both 91% (10/11). No adverse events occurred.

Conclusions: The PP-CUE is useful to resect superficial non-polypoid colorectal lesions 20-25 mm in diameter in an en bloc fashion.
Introduction

Endoscopic submucosal dissection (ESD) has become a standard endoscopic treatment modality for large superficial colorectal lesions in east Asian countries and is becoming more commonly performed in western countries. Recently, establishing ESD techniques and developing dedicated devices have made colorectal ESD easier and safer than before. However, ESD is still technically challenging for most endoscopists. Dedicated ESD devices including ESD knives, hemostatic forceps, and traction devices are more expensive than routinely used endoscopic devices such as loop snares. In addition, most colorectal ESDs require more highly skilled support staff to assist the operating endoscopist. ESD procedures occupy the endoscopy suites for a much longer time than conventional endoscopic mucosal resection (EMR). However, conventional EMR does not facilitate en bloc resection of large colorectal lesions. High local recurrence rates were detected at follow-up colonoscopy after piecemeal EMR (12-26%) [1-4].

Underwater EMR without submucosal injection (UEMR) was reported as a revolutionary approach to EMR for the resection of large sessile colon lesions by Binmoeller et al. in 2012 [5]. Although the efficacy and safety of UEMR for large...
superficial colorectal lesions has been fully evaluated and widely disseminated [6],
lesions larger than the snare diameter cannot always be resected in an en bloc fashion
even using UEMR. A snare that is too large cannot be controlled well in the contracted
intestinal lumen filled with water. Further, the endoscopic visual field with water
immersion is narrower than in air due to a difference in the refractive index of light,
which may lead to positive horizontal margins of UEMR specimens. Therefore, even
UEMR can hardly capture a large lesion into the snare allowing visual confirmation of
its margin.

We previously reported the utility of the progressive polyp contraction with
underwater endoscopic mucosal resection (PP-CUE) technique in 2020 as a case report
[7] (Fig 1-2, Video 1). We have performed the PP-CUE technique for superficial
colorectal lesions >20mm diameter for which en bloc resections cannot be performed
without ESD. The main advantage of the PP-CUE is to enable resection of a superficial
lesion that is larger than the snare diameter. The aim of this study is to demonstrate the
feasibility of en bloc resection with PP-CUE for superficial non-polypoid colorectal
lesions larger than 20 mm in diameter.
Patients and Methods

Study population

The inclusion criteria were (1) a superficial non-polypoid colorectal lesion, including sessile serrated lesions resected by UEMR; (2) no visible stigmata of invasive malignancy during magnified observation; (3) 20 mm or greater in size; (4) Endoscope withdrawal was recorded on video and (5) the PP-CUE technique was used. From January 2020 to February 2021, UEMR was performed for 130 superficial colorectal lesions at Jichi Medical University Hospital, and 11 lesions met the inclusion criteria. Medical records and the endoscopic videos which recorded the entire endoscope withdrawal including PP-CUE were retrospectively reviewed. The Institutional Review Board approved this retrospective review (No. 20-103).

Procedure for progressive polyp contraction with underwater endoscopic mucosal resection (PP-CUE) (Fig 1)

A submucosal injection was not used. While the submucosal layer is thickened when under water, the muscularis propria remains circumferential and does not follow the involutions of the folds during UEMR [5]. This allows high quality endoscopic resection without the need for submucosal injection. The PP-CUE was developed to allow resection of a colorectal lesion larger than the diameter of a dedicated
polypectomy snare. The decision to use the PP-CUE technique is made when it is recognized that the target lesion is larger than the snare diameter. In short, the snare is embedded in the portion of a large superficial lesion distal to the endoscope. After that, intentional and incomplete strangulation was performed without resection such that the snare is gently closed until tactile resistance is felt in the handle. The snare is then reopened and the entire lesion ensnared. After confirming that the whole lesion is captured, resection is completed with diathermy. The resulting mucosal defect is closed using endoclips immediately while maintaining water immersion. (Fig 1-2) (Video 1).

A magnifying endoscope (EC-L600ZP or EC-760ZP-V/M, Fujifilm, Tokyo, Japan), a carbon dioxide insufflator (GW-1 or GW-100, Fujifilm), a water irrigator (JW-2, Fujifilm) with distilled water, a transparent distal attachment (D-201-14304, Olympus, Tokyo, Japan) and a diathermy unit (ESG-100, Olympus) were used. For resection, a 15mm Rota snare (Medi-Globe GmbH, Achenmühle, Germany) was used for all PP-CUE. Reopenable endoclips (SureClip, Micro-Tech Co. Ltd., NanJing, China) and ordinary clips (EZ clip, Olympus, Tokyo, Japan) were used to close the mucosal defect.

**Evaluation of PP-CUE**
Procedure time was defined as the time between the start of water irrigation and closure of the mucosal defect by endoclip application. PP-CUE time was defined as the time between the snare exiting the working channel under endoscopic vision and confirming the mucosal defect. The size of the lesion was measured by comparison with the 15mm width of the fully opened Rota snare. En bloc resection was defined as a lesion resected as a single piece. R0 resection was defined as en bloc resection with negative pathological margins. Delayed bleeding was defined as hematochezia with a decrease of hemoglobin level >2 g/dL, requiring transfusion or endoscopic hemostasis within 14 days after the procedure. Intraprocedural perforation was defined as visualization of the peritoneal cavity through damaged muscularis during PP-CUE, and delayed perforation was defined as presence of free air on computed tomography scan with abdominal symptoms after the PP-CUE procedure even though there was no intraprocedural perforation seen.
Results

The Table 1 shows the characteristics of lesions in patients who underwent PP-CUE. Ten lesions were in the right colon and one lesion was in the left colon. Tumor morphologies included nine 0-IIa and two 0-IIa+IIc. The median diameter of the lesions was 24 mm (IQR 20-24 mm, range 20-26 mm). All lesions were larger than the rotatable snare diameter (15 mm) used. Median procedure time and PP-CUE time were 11 min (IQR, 8.5-12.3) and 2.3 min (1.9-3.4), respectively. Pathological diagnoses of the resected specimens included six adenomas, three sessile serrated lesions and two slightly invasive submucosal carcinomas. Magnifying endoscopy of the two slightly invasive submucosal carcinomas before PP-QUE was classified as JNET type 2A and 2B indicating intramucosal cancer, but there were no visible stigmata of invasive cancer during magnified endoscopy [8]. The three sessile serrated lesions were JNET type 1. Both en bloc and R0 resection rates were 91% (10/11). The lesion with a failed en bloc resection was on the haustra. The lesion was resected in a two-piece fashion unintentionally because the tip of the Rota snare failed to capture the edge of the lesion distal to the endoscope. However, no residual lesion was observed around the mucosal defect even with magnified observation, and the pathological diagnosis was adenoma. No adverse events occurred.
**Discussion**

In 11 consecutive lesions >20mm in diameter resected with PP-CUE, both *en bloc* and R0 resection rates were 91% with short procedure times and without adverse events. The major advantage is that PP-CUE enables resection of a superficial lesion larger than the snare diameter. PP-CUE can be an alternative resection technique to performing piecemeal EMR or ESD for non-polypoid colorectal lesions (20mm or greater).

The “underwater revolution” is breaking the mold for endoscopic resections recently. It is reported that UEMR is safe and reliable to resect not only superficial colorectal lesions but also superficial non-ampullary duodenal epithelial tumors [9]. The underwater technique is also useful to facilitate ESD [10,11]. However, the more UEMR is performed, the more its limitations are revealed. Although the *en bloc* resection rate using UEMR for colorectal non-polypoid lesions is as good as that of conventional EMR, both *en bloc* resection rates are lower when evaluating resections of >20mm lesions [12]. The risk of piecemeal resection is still considerable when performing UEMR for >20mm lesions. However, piecemeal resections have a high risk of local recurrence and require that patients are followed with short-interval surveillance.
colonoscopy [3]. If one performs endoscopic en bloc resection even for >20mm lesions with low malignant potential such as serrated lesions without obvious dysplasia, ESD is an ideal choice, which makes the procedure more expensive and less cost-effective than piecemeal EMR. The present study shows that PP-CUE potentially achieves a high-rate of en bloc resections for superficial colorectal lesions (20 mm or greater). A recent prospective randomized control trial revealed that en bloc and R0 resection rates of UEMR are not significantly different from conventional EMR [13]. The R0 resection rates of conventional EMR and UEMR for 20-30mm lesions were 20.0% and 37.7%, respectively [13], which means that PP-CUE achieved a much higher R0 resection rate (91%) for >20mm lesions compared with both conventional EMR and UEMR. The present study also includes an unexpected R0 resection of a T1a carcinoma using PP-CUE although PP-CUE would not have been performed if the lesion had been correctly diagnosed as a T1a carcinoma.

Generally, a large snare is used to resect a large lesion. It is not easy to manipulate an entire snare larger than 20mm even with gas insufflation because the tip of a large snare on the proximal side often goes beyond the visual field. Therefore, appropriate anchoring of the tip and subsequent capturing of the lesion while closing the snare may sometimes fail by slipping, which results in a piecemeal resection. The large
snare is more difficult to manipulate in the narrowed space due to intestinal contraction under water immersion. In addition, being under water changes the reflective index of light with a further narrowed visual field. An intermediate-size rotatable snare such as a 15mm Rota snare may be appropriate to perform UEMR because it represents a balance between maximal width and controllability. The tip of the intermediate-size snare can be placed at the normal mucosa beyond the lesion because the entire snare can be identified even in the narrowed endoscopic view under water immersion. Even if a targeted non-polypoid lesion is >20mm, PP-CUE can completely resect it using an easily controllable intermediate-size rotatable snare by multiple snaring maneuvers that transiently make it smaller. Above all, PP-CUE is a useful technique when performed underwater without injection. In case of the presence of submucosal injection, the first application of the snare makes a groove and subsequent applications of the snare tend to go back into the same groove. In the case of an air-filled lumen, the compressed polypoid shape after the first application of the snare does not remain and returns to its original flat shape easily due to intraluminal pressure. However, if it is performed underwater without injection, the compressed polypoid shape after the first application of the snare remains even after reopening the snare and an even larger area can be grasped by the next application of the snare because the mucosa floats in the water.
without tension. If a weak point of PP-CUE has to be described, it would be that the anchored tip of the snare cannot be observed during re-snaring. The failed en bloc resection of a lesion in this study was caused by failure to continuously capture the proximal edge of the lesion. Sure fixation of the snare tip to normal mucosa beyond the lesion may resolve this weakness [14].

In conclusion, PP-CUE is useful to resect superficial non-polypoid colorectal lesions 20-25 mm in diameter in an en bloc fashion.
References


Figure legends

Fig 1  Schema for progressive polyp contraction underwater endoscopic mucosal resection (PP-CUE). a) A large flat superficial colorectal lesion is extended with insufflation. b) Although the lesion contracts with water immersion, a medium-size snare which has a controllable size, even in the contracted narrow intestinal lumen after water immersion, cannot capture the entire lesion if it is too large. c) The far side of the lesion is surely captured by the snare under direct visualization identifying the lesion margin and involving as much area of the lesion as possible. Then, the lesion is captured to a certain extent without damaging it. d) The snare is carefully opened again while hooking the far side of the strangulated protrusion. e) The snare is pulled back to include the remaining part of the lesion before the previously snared area may extend again. f) The entire lesion is completely captured within the snare.

Fig 2  Sequential endoscopic pictures of the PP-CUE procedure. A) A 24mm laterally spreading lesion, granular type with Kudo’s type IV pit pattern, Type 2A of the Japan narrow band imaging expert team (JNET) classification in the transverse colon. B) The tumor morphology was transformed from flat to protruded after
water immersion. Most of the lesion was captured in the snare with direct visual confirmation of the margin. C) The snare was carefully closed until resistance is felt through the snare handle. D) Opening the snare again while fixing the snare tip at the normal mucosa. E) Ensnaring the uncaptured part of the lesion and more surrounding mucosa with direct visual confirmation. The lesion is progressively contracted by repeated snaring to assure complete resection. There are first and second snaring marks (arrows). F) The specimen is cut with pure-cut mode diathermy. There were no residual fragments of lesion nor sites of perforation. G) The mucosal defect was completely closed with endoclips. H) Pathology was a tubulovillous adenoma with negative margins.
**Video legend**

PP-CUE of a laterally spreading tumor, granular type (LST-G) in the transvers colon.

**Video text**

1) A 24mm laterally spreading tumor, granular type (LST-G) with JNET Type 2A in the transverse colon

2) Placing the snare tip at normal mucosa beyond the lesion while securing an adequate proximal margin

3) Opening the snare while keeping the snare tip at normal mucosa to stretch the proximal mucosa to capture it without skipped areas

4) Capturing most of the lesion while confirming the margin

5) Opening the snare again while fixing the snare tip at normal mucosa

6) Ensnaring uncaptured lesion and more surrounding mucosa with direct visual confirmation

7) The lesion is progressively contracted by repeated snaring to assure complete resection

8) Cutting with pure-cut mode diathermy

9) Confirming there are no residual lesion fragments

10) Closing with endoclips while maintaining water immersion

11) Tubulovillous adenoma with a negative margin