Effectiveness of Inner Traction Facilitated Endoscopic Submucosal Dissection using Rubber Band and Clips for Colorectal Neoplasms: A Propensity Score-matched Study

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Research Article

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Abstract

Background Colorectal endoscopic submucosal dissection (ESD) is a technically demanding but effective treatment for superficial neoplasms. We conducted a study to compare the effectiveness and safety of inner traction facilitated ESD using rubber band and clip (RAC-ESD) with conventional ESD.

Methods We retrospectively evaluated 622 consecutive patients underwent colorectal ESD between January 2016 and December 2019. To overcome selection bias, we used propensity score matching (1:4) between RAC-ESD and conventional ESD. The frequency of en bloc resections, R0 resections, curative resections, procedure speed and complications were evaluated.

Results After propensity score matching, 35 patients were included in RAC-ESD group and 140 were included in conventional ESD group. RAC-ESD resulted in a significant increase in resection speed (0.14 vs. 0.09 cm^2/min; P=0.003). There were no significant differences in en bloc, R0 and curative resection rates between two groups. In subgroup analysis, the resection speed of RAC-ESD was significantly higher than conventional ESD when the lesions were equal to or larger than 2cm, macroscopically presenting as lateral spreading tumor, and located in transverse colon to ascending colon.

Conclusions RAC-ESD is safe and effective in treating colorectal neoplasms, especially in lesions presenting particular difficulty.

Introduction

Endoscopic submucosal dissection (ESD) has become the standard treatment for low risk of lymph node metastasis superficial neoplasms throughout the gastrointestinal tract[1]. Compared with ESD in esophagus and stomach, ESD in the colon is more technically demanding and risky due to narrow lumen, bowel movements, thinness of the colonic muscularis propria and the poor scope maneuverability. Consequently, the complication rate of colorectal ESD has been reported to be relatively high, especially the perforation rate[2, 3].

Good and constant exposure of the submucosal space is critical for safe and quick ESD. Several traction techniques have been developed worldwide to make ESD a more effective and safer technique[4]. The external grasping forceps facilitated ESD is limited by the lesion location[5]. The dental floss traction cannot be adjusted freely when deep in the colon and is assistant-demanding[6]. Magnetic anchor and balloon-assisted methods require special devices[7, 8].

In this study, a modified ESD named inner traction facilitated ESD using rubber band and clip (RAC-ESD) was designed and evaluated for colorectal neoplasm. This study aimed to evaluate the effectiveness and safety of RAC-ESD in colorectal lesions compared to conventional ESD.

Methods

Patients

This study was a single-center, retrospective, cohort study comparing the effectiveness and safety of RAC-ESD and conventional ESD in patients with colorectal neoplasms. This study was approved by the institutional review board. All patients provided written informed consent before the endoscopic procedure.

Between January 2016 and December 2019, a total of 622 consecutive patients underwent colorectal ESD in Peking University First Hospital, Beijing, China. After excluding patients with missing data including endoscopic or pathological results and patients treated with modified ESD such as ESD with snare, 563 ESD were included in the study. (Fig.1)

Procedure

ESDs were performed under general anesthesia or without accompanying sedation according to the patients' basic condition. Patients taking anticoagulants or antiplatelet drugs consulted cardiologists to decide whether they could change to heparin or discontinue the drugs 5-7 days before ESD.

All ESD were performed using therapeutic endoscope (GIF-Q260J or PCF-Q260JI, Olympus, Tokyo, Japan) and a transparent hood (D-201-11304, Olympus). 1.5mm Dualknife, IT-nano knife (Olympus) and endoclips (HXROCC-D-26-195-C, MICRO-TECH, Nanjing, China) were used. All ESD were performed by Dr. Weidong Nian and Dr. Long Rong, who were both highly experienced in ESD operation.

In the RAC-ESD group, after making a hemicircumferential or circumferential mucosal incision and some submucosal dissection, a rubber band of 2-3mm width and 15-20mm semi-parameter was prepared from the medical latex glove and placed through the operative channel with a clip. The rubber band was fixed at the distal part of the lesion and then affixed with another clip to the contralateral colonic wall to expose the submucosal space (Fig. 2). The strength of traction can be adjusted with the insufflation and deflation of CO_2. If needed, a third or fourth clip could be applied to give further traction.

Data analysis

Specimen size, procedure time, dissection speed, complications and pathological result were recorded. An en bloc resection was defined as the lesion was resected in a single piece. An R0 resection was defined by pathological confirmed tumor-free vertical and lateral margins. An curative resection was defined as an R0 resection without risk of lymph node metastasis, such as lymphovascular invasion, poorly differentiated components, presence of budding or submucosal infiltration deeper than SM1 (1000μm). The procedure time (minute) was defined as the time between injection and removal of the lesion. Specimen size was calculated by the ellipse formula: large diameter/2×small diameter/2×π (cm^2). Dissection speed was defined by the specimen size divided by procedure time (cm^2/min). Complications

included perforation defined as a hole through the colonic wall during the procedure or clinical evidence of free gas upon postoperative abdominal tomography, and bleeding defined as bleeding after ESD requiring endoscopic, interventional or surgical treatment.

Propensity scoring was used to address the imbalance of potential confounders that may interfere with the results and was calculated using macroscopic type (lateral spreading tumor or not), location and the large diameter of the lesion. We chose 1:4 matching using nearest neighbor matching with a caliper of width 0.1. Only patients matched with propensity scores were included in statistical analysis.

Matched data are presented as frequencies and percentages for categorical data or a median and interquartile range or mean and standard deviation (SD) for continuous data. Fisher's exact test and x^2 test were used for comparisons involving categorical variables and the Wilcoxon rank-sum test and student t test were used for comparisons involving continuous variables. All P values were two-tailed, and $P<0.05$ was considered significant. All statistical analyses were performed using SPSS version 27.0 (IBM Corp., Armonk, New York, USA).

Results

In total, 563 patients were eligible for inclusion. Of these, 35 patients received RAC-ESD, and 528 underwent conventional ESD. The RAC-ESD group and the conventional ESD group differed with respect to the macroscopic type, location and the large diameter of the lesion. In order to mitigate the effects of these confounders, patients were matched at a 1:4 ratio, resulting in 35 in the RAC-ESD group and 140 in the conventional ESD group.

Baseline characteristics

Baseline characteristics of patients in both groups are shown in Table 1. There were no differences in the demographic characteristics, characteristics of the lesion and pathological results.

Table 1
Baseline characteristics of the two groups.

	Conventional ESD group (n = 140)	**RAC-ESD group (n = 35)**	**P value**
Age (years)	63.8 ± 11.0	63.2 ± 10.3	0.791
Gender			0.275
Men (%)	90 (64.3)	19 (54.3)	
Women (%)	50 (35.7)	16 (45.7)	
Localization			0.535
Rectum	24 (17.1)	5 (14.3)	
Sigmoid to descending colon	44 (31.4)	11 (31.4)	
Transverse colon to ascending colon	66 (47.1)	16 (45.7)	
Cecum	6 (4.3)	3 (8.6)	
Macroscopic type			0.935
LST	95 (67.9)	24 (68.6)	
Non-LST	45 (32.1)	11 (31.4)	
Large diameter			0.701
≥2cm	122 (87.1)	29 (82.9)	
<2cm	18 (12.9)	6 (17.1)	

Table 2
Comparison of the RAC-ESD group and conventional ESD group.

	Conventional ESD group (n = 140)	**RAC-ESD group (n = 35)**	**P value**
Resected area (cm^2)	4.1 (2.8–6.9)	6.0 (2.5–9.9)	0.233
Procedure time (min)	30.0 (16.3–55.0)	40.0 (25.0–80.0)	0.031
Resection speed (cm^2/min)	0.09 (0.04–0.16)	0.14 (0.07–0.27)	0.003
En bloc resection (%)	94.3	100.0	0.320
R0 resection (%)	95.0	97.1	0.928
Curative resection (%)	84.3	94.3	0.206
Complications (%)			0.884
Perforation	2 (1.4)	0	
Delayed bleeding	1 (0.7)	0	
Pathological analysis			0.104
Cancer/ HGIN	71 (50.7)	11 (31.4)	
Adenoma	63 (45.0)	21 (60.0)	
Neuroendocrine tumor	6 (4.3)	3 (8.6)	

Table 3
Subgroup analysis of resection speed.

Resection speed (cm^2/min)	No. (ESD/RAC-ESD)	Conventional ESD group (n = 140)	RAC-ESD group (n = 35)	P value
Localization				
Rectum	24/5	0.10 (0.07–0.16)	0.10 (0.06–0.19)	0.978
Sigmoid to descending colon	44/11	0.09 (0.03–0.16)	0.13 (0.10–0.27)	0.121
Transverse colon to ascending colon	66/16	0.08 (0-0.13)	0.14 (0.09–0.27)	0.001
Cecum	6/3	0.13 (0.04–0.20)	0.06 (0.01–0.27) *	1.000
Macroscopic type				
LST	95/24	0.08 (0-0.14)	0.14 (0.07–0.27)	0.001
Non-LST	45/11	0.11 (0.07–0.16)	0.11 (0.06–0.17)	0.741
Large diameter				
≥2cm	122/29	0.10 (0.04–0.17)	0.14 (0.10–0.27)	0.454
<2cm	18/6	0.05 (0-0.08)	0.05 (0.03–0.11)	0.002

*Data presented with median and range due to the limited sample size

Outcomes

There were no significant differences in the resected area (cm^2), with 6.0 (2.5–9.9) versus 4.1(2.8–6.9) for the RAC-ESD and the conventional ESD group (P = 0.233). However, there were significant differences in procedure time and resection speed, with 40.0 (25.0–80.0) versus 30.0 (16.3–55.0) min for the procedure time of the RAC-ESD and the conventional ESD group (P = 0.031), and 0.14 (0.07–0.27) versus 0.09 (0.04–0.16) cm^2/min for the resection speed of RAC-ESD and conventional ESD group (P = 0.003).

En bloc resection was achieved in 100.0% (35/35) of cases in RAC-ESD group and 94.3% (132/140) of cases in conventional ESD group. R0 resection was achieved in 97.1% (34/35) of cases in RAC-ESD group and 95.0% (133/140) of cases in conventional ESD group. Curative resection was achieved in

94.3% (33/35) of cases in RAC-ESD group and 84.3% (118/140) of cases in conventional ESD group. There were no significant differences in all these resection rates between two groups.

Among the 24 patients without curative resection, 8 had non-assessable horizonal margins due to piecemeal resection, 5 had positive horizonal margins and 11 had submucosal deep-invasive cancer > 1000 μm. Patients with non-assessable or positive horizonal margins were intimately followed up endoscopically. 7 of the 11 patients with submucosal deep-invasive cancers underwent additional surgery and 4 decided to receive endoscopic and radiological follow-up.

In the subgroup analyses, the differences of resection speed were significantly associated with tumor location, macroscopic type and tumor size (whether diameter ≥ 2cm or not). For lesions located in transverse colon to ascending colon, the resection speed was significantly higher in RAC-ESD group than conventional ESD group (0.08 versus 0.14, P = 0.001). Compared with non-LST lesions, the resection speed for LST lesions was higher in RAC-ESD group than conventional ESD group (0.08 versus 0.14, P = 0.001). For lesions with diameter equal to or larger than 2cm, the resection speed was also significantly higher in RAC-ESD group than conventional ESD group (0.10 versus 0.14, P = 0.002).

Perforation occurred in 2 cases (1.4%) in the conventional ESD group, 1 managed by endoscopic closure and the other required surgery for his elder age and the development of peritonitis. No perforation occurred in RAC-ESD group. 1 patient (0.7%) in the conventional ESD group experienced delayed bleeding 1 day after procedure and was managed by electric coagulation hemostasis and clips. No other adverse events related to traction procedure occurred in the study.

After 24(6–60) months follow-up, 2 patients (1.4%) of the conventional ESD group developed local recurrence at 1-year follow-up and were both managed by repeated ESD, 1 of which was with positive horizonal margin. No occurrence was found in the RAC-ESD group. 1 patient died of ruptured abdominal aortic aneurysm 46 months after ESD.

Discussion

Oyama T. published the first study about counter traction in ESD in 2002, using the clip with line method[9]. After that, endoscopists around the world working on different traction strategies to facilitate ESD procedure. Xia. et al reported in a meta-analysis that traction ESD was superior to standard ESD in terms of perforation rate and resection speed, confirming the importance of traction method[10].

In our study, the procedure time of the RAC-ESD group was longer than that of the conventional ESD group. We believe that this can be explained by the fact that the resected area of RAC-ESD group was slightly larger than that of the conventional ESD group, although the difference was not significant. Overall, the resection speed of the RAC-ESD group was significantly faster than that of the conventional ESD group. The en bloc resection rate, R0 resection rate and the curative resection rate of both groups are quite satisfied, similar to the other studies in Asia[10, 11]. There was no significant difference in oncological and safety data between the two group may be owing to the operators involved in this study

were experienced in ESD technique. The learning curve in previous study confirmed that ESD with traction could also be used in the training progress of inexperienced ESD operators[12, 13], as it continuously optimizes exposure of the submucosal space, making the process of submucosal dissection much easier.

Several studies have demonstrated the effectiveness of inner traction method in colorectal ESDs using clips with either rubber band or looped thread[12, 14, 15]. In their study, the rubber band was already a commercial product but has not been approved for medical use in many other countries. The production of looped thread was comparatively complicated for the need of measuring the length of thread and the knot-tying process. In our study, we use a kind of rubber band made of latex examination gloves, which are extremely easy to get among medical centers, suitable to be cut into circles and above all, inexpensive. Unlike several other previously reported traction systems, the rubber band and clip can pass through the working channel of the scope without scope removal. The elasticity of the rubber band makes it more adaptable in the ESD practice. Operators can increase or decrease the countertraction by control the air volume in the colorectal space. Moreover, when dealing with the giant lesions which cannot be handled by a single traction, a third or a fourth clip can be applied for traction, attaching the rubber band to the opposite site of the remnant lesion to obtain continuous countertraction as we have previously reported[16].

Although many previous studies have confirmed the superiority of traction ESD compared with conventional ESD, few studies discussed that in which kinds of lesions traction method could show the greatest effect. The subgroup analysis of our study showed that RAC-ESD improved the resection speed in lesions located in transverse colon to ascending colon, lesions macroscopically presenting as lateral spreading tumor (LST) and lesions with large diameter equal to or greater than 2cm. ESD is not easy to perform in transverse colon to ascending colon owing to the poor scope maneuverability and limited use of gravitation. Iacopini et al reported that positional changes did not harness the power of gravity in 22% of colonic ESD cases, compared with only 3% of rectal ESD cases[17]. Moreover, lesions presenting as LST and larger lesions are also thought to be more challenged for endoscopist, especially inexperienced endoscopist to perform ESD, as the technical difficulty of procedure increases with the size of the lesion. Thus, the advantage and efficiency of RAC-ESD for these lesions were shown more obviously, counting for the differences displayed in the subgroup analysis, even for skillful endoscopists, as the operators included in our study are both highly experienced in ESD (performing more than 500 colorectal ESD).

The propensity score-matched method was used to reduced bias in this study. Propensity scoring was calculated by using the above-mentioned confounders including localization, macroscopic type and the large diameter equal to or larger than 2cm or not, as these confounders should possibly influence the difficulty of ESD process and thus interfere with the clinical outcomes between groups. These basic characteristics were balanced between groups after propensity score-matched, making the technical data between the RAC-ESD group and the conventional ESD group more comparable.

There are a few limitations to this study. First, it was a single center, retrospective study susceptible to selection bias. Although the use of propensity score matching allowed us to balance the two groups, some confounders that were not incorporated into the propensity score, may still influence the results. However, we consider it difficult to conduct randomized trials between RAC-ESD and traditional ESD as the former has shown to be much superior in challenging cases. Second, the two operators included in our study are both experienced endoscopists in ESD. We did not discuss the effectiveness of RAC-ESD strategy in the learning process for trainees in ESD. Finally, as the rubber band we used in this study was made out of latex gloves, although we did not encounter any allergy complications during the traction process, we are unaware that whether patients being allergic to latex would develop an allergic reaction when the latex come into contact with the colonic wall. Therefore, for patients with definite medical history of severe latex allergy, RAC-ESD might shall be avoided in the process of endoscopic treatment.

In conclusion, RAC-ESD is a safe, effective and cheap method to treat colorectal neoplasms, especially in lesions presenting particular difficulty: larger lesions, lesions macroscopically presenting as lateral spreading tumor and lesions located in right-sided colon. A multicenter study including inexperienced endoscopist is needed to confirm the reproducibility and its effect in the training process of ESD.

Abbreviations

ESD endoscopic submucosal dissection

RAC-ESD inner traction facilitated endoscopic submucosal dissection using rubber band and clip

LST lateral spreading tumor

Declarations

Acknowledgement

Not applicable.

Author contributions:

GY: study concept and design, drafting of the manuscript; GXY: drafting of the manuscript, picture formatting; CYL: critical revision of the manuscript; RL and NWD: operating all the endoscopic resection, critical revision of the manuscript; ZJX: pathological analysis of all the resected specimen.

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Availability of data and materials

The datasets generated and/or analyzed in the present study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The study was conducted in compliance with the International Conference on Harmonization guidelines for Good Clinical Practice (E6) and the 2013 Declaration of Helsinki. The study was approved by the institutional review board of Peking University First Hospital and all patients provided written informed consent.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Figures

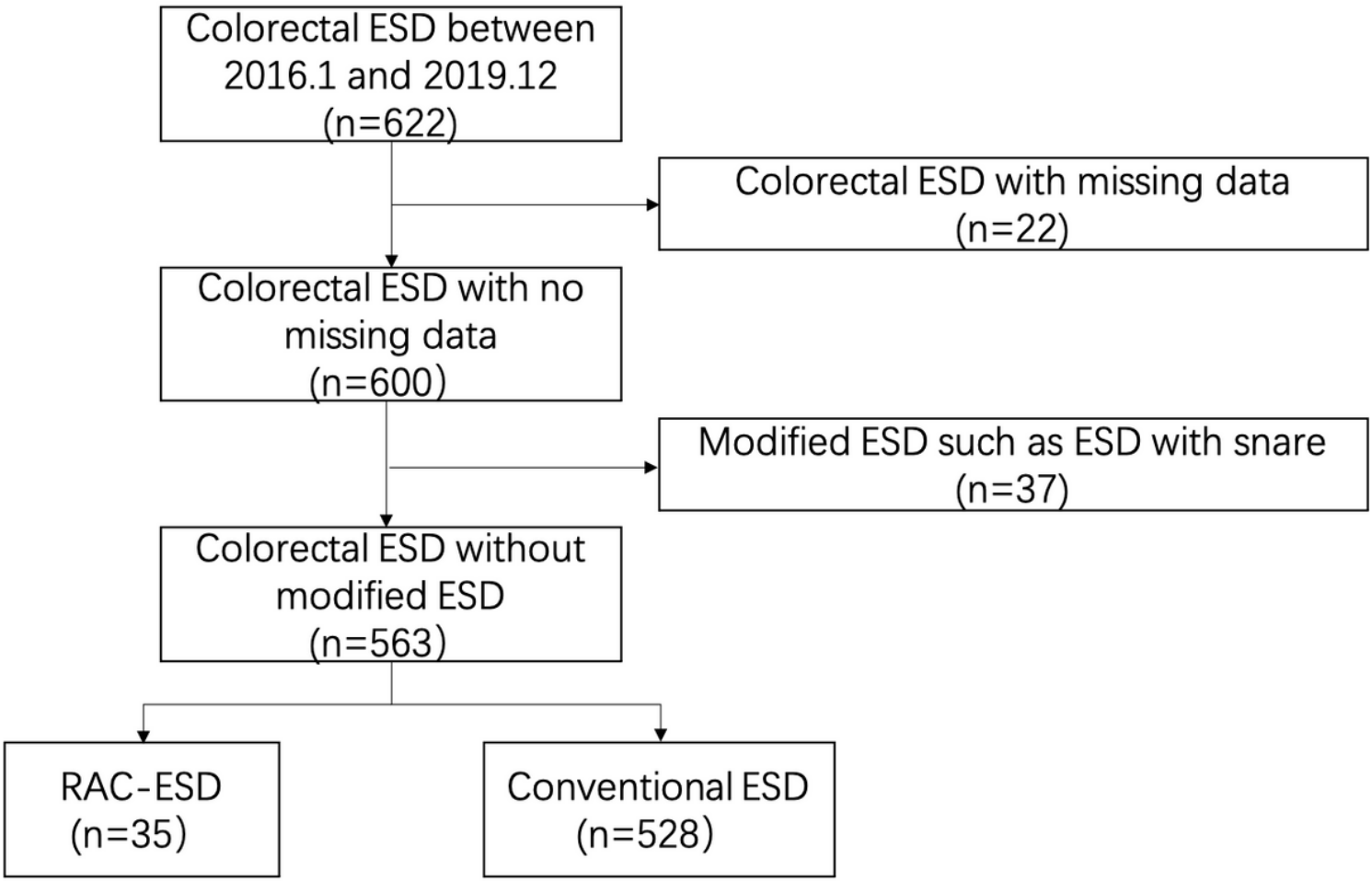

Figure 1

Study flow diagram. ESD, endoscopic submucosal dissection; RAC-ESD, inner traction facilitated ESD using rubber band and clip.

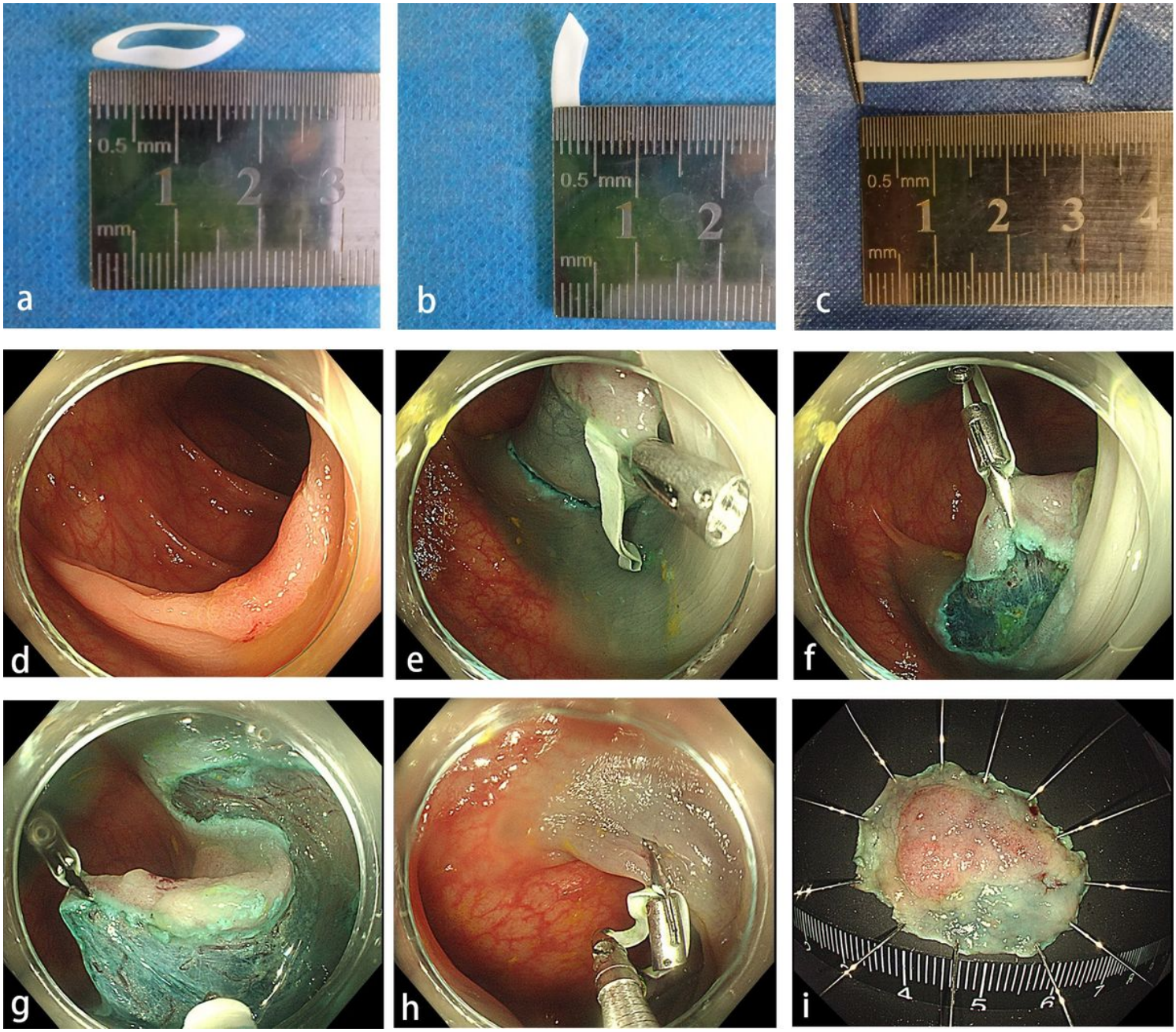

Figure 2

A case of inner traction facilitated ESD using rubber band and clip (RAC-ESD). a-b. Rubber bands made of latex glove was prepared before ESD, usually with semi-parameter of 15-20mm and width of 2-3mm. c. The elasticity of the rubber band makes it more adaptable in the ESD practice. d. A lesion of LST-NG-F type was found located in the transverse colon. e. After making a circumferential dissection, the first clip holding the rubber band was fixed at the distal part of the lesion. f. The second clip fixed the rubber band to the contralateral colonic wall, fully exposing the submucosal layer. g. Dissection could be safely and effectively performed. h. The specimen was removed with cutting forceps. i. The specimen was clear and intact.