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Underwater versus conventional endoscopic resection of nondiminutive nonpedunculated colorectal lesions: a prospective randomized controlled trial (with video)

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Abstract

Background and Aims: Incomplete resection of colorectal neoplasia decreases colonoscopy efficacy. Conventional resection (CR) of polyps, performed in a gas-distended colon, is the current standard, but incomplete resection rates of approximately 2% to 30% for nondiminutive (>5 mm), nonpedunculated lesions are reported. Underwater resection (UR) is a novel technique. The aim of this study was to determine the incomplete resection rates of colorectal lesions removed by UR versus CR.

Methods: In a randomized controlled trial, patients with small (6-9 mm) and large (≥10 mm) nonpedunculated lesions were assigned to CR (gas-distended lumen) or UR (water-filled, gas-excluded lumen). Small lesions in both arms were removed with a dedicated cold snare. For CR, large lesions were removed with a hot snare after submucosal injection. For UR, large lesions were removed with a hot snare without submucosal injection. Four-quadrant biopsies around resection sites were used to evaluate for incomplete resection.

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Results: Four hundred sixty-two eligible polyps (248 UR vs 214 CR) from 255 patients were removed. Incomplete resection rates for UR and CR were low and did not differ (2% vs 1.9%, p=0.91). UR was performed significantly faster for lesions ≥10 mm in size (10-19 mm, 2.9 minutes vs 5.6 minutes, p<0.0001; ≥20 mm 7.3 minutes vs 9.5 minutes, p=0.015).

Conclusions: Low incomplete resection rates are achievable with UR and CR. UR is effective and safe with the advantage of faster resection and potential cost savings for removal of larger (≥10 mm) lesions through avoidance of submucosal injection. As an added approach, UR has potential to improve colonoscopy cost-effectiveness by increasing efficiency and reducing cost while maintaining quality.

Keywords

underwater; colonoscopy; polypectomy; water exchange

Introduction

Conventional resection (CR) of colorectal neoplasia, performed with the colon fully distended with gas, is the current standard for endoscopic polypectomy. But conventional techniques can result in incomplete resection of polyps—the failure to completely eradicate neoplastic tissue at the site of polyp removal—even for small polyps[1]. Incomplete resection rates of approximately 2% to 30% for nondiminutive (>5 mm) lesions are reported[1–6] and incomplete resection of polyps accounts for an estimated 10 to 30% of postcolonoscopy colorectal cancers (PCCRC)[7,8]. Therefore, alternative methods for safe and effective polypectomy are needed.

Underwater resection (UR) of colorectal polyps is a novel technique. Instead of gas, the colon is filled with water, which decreases colonic wall tension, resulting in potential benefits that may improve the opportunity for safe and complete resection of mucosal lesions[9]. Prior observational studies describing the feasibility of this technique[10–15] come primarily from referral centers and/or have focused on large (≥10 mm) lesions. A series evaluating UR in routine practice across a broader range of polyp sizes was a small retrospective analysis[16] and the only published prospective comparative study evaluated the technique on intermediate-sized lesions (10-20 mm) at referral centers in Japan[17].

In this study, we aimed to assess the incomplete resection rate of nondiminutive (>5 mm), nonpedunculated colorectal lesions removed by UR versus CR. We test the hypothesis that UR decreases the incomplete resection rate compared with CR across a broad range of polyp sizes encountered in routine practice in a U.S. cohort.

Patients and Methods

Study design

This was a prospective randomized controlled trial conducted at a U.S. Veterans Affairs Medical Center. Written informed consent was obtained from all patients. The study was approved by the Institutional Review Board at the Sacramento VA Medical Center, Veterans

Affairs Northern California Health Care System (VANCHCS) July 20, 2016, and registered with clinicaltrials.gov () August 31, 2016.

Study population and polyps

Between October 2016 and September 2018, all consecutive adult (≥18 years old) patients scheduled for outpatient colonoscopy were candidates for inclusion. Because the presence of polyps, their size and characteristics, were largely unknown before colonoscopy, all patients without exclusionary criteria who agreed to participate were enrolled for possible randomization.

Exclusion criteria were patients hospitalized; patients on uninterrupted antithrombotic therapy at the time of colonoscopy (with the exception of low-dose aspirin 81 mg); patients with uncorrected coagulopathy (international normalized ratio >1.5) or thrombocytopenia (platelet count <50,000/microliter); and those with significant comorbidities with an American Society of Anesthesiologists classification[18] ≥4.

Eligible polyps were >5 mm in size. Polyps ineligible for study or control interventions included diminutive (≤5 mm) lesions; pedunculated lesions; and lesions with endoscopic evidence of deep submucosal invasion (NICE[19] type 3; Kudo pit pattern[20] V). All polyps identified during colonoscopy were photographed and their size, morphology and location documented. Polyp sizes were assessed objectively in a gas-distended colon using a fully opened snare of known dimensions for reference. Morphology of polyps was recorded according to the Paris classification[21].

Colonoscopy and instruments

All patients received split-dose bowel preparation of 4 liters polyethylene glycol before colonoscopy. A single, experienced endoscopist (A.W.Y.) performed all procedures using high-definition colonoscopes (Olympus PCF-H190L/I; Olympus America, Center Valley, Pa, USA) with a distal transparent cap attachment (Disposable Distal Attachment D-201-12704; Olympus America, Center Valley, Pa, USA). Patients received moderate or no sedation for their examination. One enrolled patient received anesthesia administered sedation. The technique of combined water exchange and cap-assisted colonoscopy[22] was performed for colonoscope insertion and the colon was fully distended with carbon dioxide for withdrawal inspection. Bowel preparation was scored using the Boston Bowel Preparation Scale[23].

Upon identification of the first study polyp on withdrawal, an opaque, sealed envelope containing a computer-generated randomization code was opened and the polyp was randomized to UR or CR. Only enrolled patients with at least one eligible polyp were randomized 1:1 to the study or control group. If more than 1 eligible polyp was encountered in the same patient, all polypectomies on eligible lesions were performed using the same method (UR vs CR), ie, randomization occurred at the patient level. Patients without study polyps underwent a standard examination without randomization.

Polypectomy techniques

For polyps removed by underwater methods, gas was completely suctioned from the segment of bowel where the lesion was located and sterile water at room temperature was infused with a foot pedal operated water pump for partial distention of the lumen. For polyps removed by conventional methods, the colon was fully distended with carbon dioxide. All polyps were collected and placed in separate jars for histopathologic assessment. Endoscopic ultrasound was not used and the boarders of lesions were not marked with diathermy before resection. Ablation techniques such as snare tip coagulation or argon plasma coagulation were not performed after polyp removal.

Small (6-9 mm) polyps in both groups were removed with a 9 mm dedicated cold snare (Exacto Cold Snare; US Endoscopy, Mentor, Ohio, USA). Large (≥10 mm) polyps in both groups were removed with a 15 mm firm monofilament hot snare (Beamer snare; ConMed, Utica, NY, USA) using the following electrosurgical generator settings (ERBE VIO® 300 D; ERBE USA, Marietta, Ga, USA): Endocut Q, effect 3, cut duration 1, cut interval 3. Choice of snares and electrosurgical settings used in this study were based on endoscopist preference and experience. With underwater methods, no submucosal injection was performed before polyp removal (Video 1). With conventional methods, submucosal injection, using a 25-gauge injection needle (Needlemaster; Olympus America, Center Valley, Pa, USA), of a solution containing hydroxyethyl starch, indigocarmine and epinephrine was performed before polyp removal of all lesions ≥10 mm, eg, traditional endoscopic mucosal resection (EMR)[24,25].

Resection was complete once all macroscopic evidence of the polyp had been resected after careful inspection of the polypectomy margin in a gas-distended colon. If any residual polyp was suspected, additional snare resection was performed by the assigned technique to ensure clearance of the site. To evaluate for incomplete resection, 4-quadrant biopsies around the polypectomy margin were performed with jumbo forceps (Radial Jaw 4; Boston Scientific, Marlborough, Mass, USA) with one cup of the forceps within the resection bed and the other positioned on the normal appearing mucosa to ensure histopathologic assessment at the margin. Biopsy specimens were placed in a separate jar for assessment. Postresection prophylactic clipping was routinely performed for mucosal defects ≥10 mm in size for lesions removed by hot snare after margin biopsy specimens were obtained, when defects were amenable to closure.

Resection times were calculated as follows: Initiation of polyp resection was determined by the appearance of a water jet for luminal filling, injection needle or snare catheter on the video monitor. Resection was deemed complete after inspection of the resection edge and biopsy forceps for 4-quadrant biopsies entered the field of view.

Outcome variables

The primary outcome measure was the incomplete resection rate based on pathologic assessment of biopsies from the resection margin of study polyps. Incomplete resection was the presence of any adenomatous or serrated pathology in the biopsy specimen. Pathologists were blinded to resection techniques.

Secondary outcomes included adverse event rates, resection times, en bloc resection rates and number of snare resections needed to completely remove a lesion. Adverse events were immediate or delayed (within 30 days) and defined as perforation requiring intervention including endoscopic closure or surgery; delayed bleeding requiring blood transfusion and/or need for surgery, an interventional radiology procedure or repeat colonoscopy; or postpolypectomy syndrome or other event requiring unexpected hospitalization. Although not generally considered an adverse event, immediate post-polypectomy bleeding (bleeding that did not stop on its own after 30 seconds requiring intervention) was also recorded.

Randomized patients received postprocedure telephone follow-up at day 1 (the next business day) and day 30 to assess for adverse events and a 30-day research flag was placed in randomized patients' charts to alert providers in the health system that the individual was enrolled in an endoscopic study and to alert the research team of potential adverse events. Departmental notification of postprocedure hospitalizations outside of VANCHCS and within 30 days of an endoscopic procedure was routinely performed as part of standard care. Electronic medical records were assessed at the end of 30 days, at the time of removal of the research flag, to ensure unexpected hospitalizations were not overlooked.

Sample size calculations and statistics

Assuming an incomplete resection rate of 10% for CR for commonly sized lesions[2], and a 4% incomplete resection rate for UR (based on pilot data and published series on underwater resection—an incomplete resection rate of 5% to 6.7%[13] is observed for lesions ≥20 mm, so inclusion of smaller lesions lowers the rate), the number of polyps (n) randomized per group needed to detect a statistically significant difference between techniques at a 5% alpha error level with 80% power was 283. Based on data from the author[22], an average adenoma and clinically significant serrated lesion resection rate of 3 per colonoscopy was anticipated. A clinically significant serrated lesion was defined as a sessile serrated polyp (SSP) with or without dysplasia, a traditional serrated adenoma, a serrated (hyperplastic) lesion found in the proximal colon, or a serrated (hyperplastic) lesion ≥10 mm in size located anywhere in the colon[26–28]. Assuming 30% of lesions were >5 mm[29–32], and based on workload, an estimated 600 patients would need to be enrolled to accrue 566 eligible lesions.

Categorical variables at the patient level were evaluated by chi-square tests and the Fisher exact test as appropriate. For polyp level data, to control for within-patient variability when multiple lesions were removed in a single patient, mixed effects logistic regression models were used to determine incomplete resection rate (primary outcome), adverse event rates, and en bloc resection rates between groups; and mixed effects linear regression models were used to determine resection times and number of snare resections needed for complete polypectomy. Two-sided p-values <0.05 were considered significant. All analyses were performed using SAS for Windows version 9.4 (SAS Institute Inc. Cary, NC, USA).

Results

Patient characteristics

From October 2016 to September 2018, 600 patients were enrolled (Supplementary Table 1). Of those, 255 patients had eligible polyps and underwent randomization (128 UR vs 127 CR) (Figure 1). More patients randomized to UR were whites, and significantly fewer had diabetes, but other demographics, indications, bowel preparation quality, type of sedation and lesion detection rates between groups were comparable (Table 1).

Polyp characteristics

A total of 248 polyps removed by UR and 214 by CR were available for analysis. Ten (6 UR vs 4 CR) resected lesions were excluded from the analysis because pathology revealed nonadenomatous or serrated histology (one leiomyoma), or the specimen was not retrieved. The proportion of nonadenomatous or serrated histology and specimen nonretrieval was low (2%), limited to small lesions, and did not differ between groups. Margin biopsies from all nonretrieved specimens revealed no residual polyp, but these lesions were excluded from the final analysis. Table 2 shows the characteristics of study polyps. The mean polyp size in each group was identical (9.9 ± 5.8 mm vs. 9.9 ± 6.4 mm) and the majority were adenomatous lesions from the proximal colon. There was no crossover of techniques for salvage resection in this series because all polyps were removed by the assigned method.

Incomplete resection rates and secondary outcomes

Table 3 shows primary and secondary outcomes for study polyps. The primary outcome, incomplete resection rate, was low for both UR and CR and did not differ (2.0% vs 1.9%, p=0.91), even in subgroup analysis based on lesion size. Table 4 shows characteristics of the 9 lesions incompletely resected. Because of the low and nearly identical incomplete resection rate between groups at interim analysis at patient 600, when >80% of the total polyp sample size was reached, additional recruitment to reach the initially estimated polyp sample size of 566 was not pursued.

Secondary outcomes (Table 3) of en bloc resection rates were similar (89.9% vs 90.2%, p=0.64), even across size ranges. However, significantly fewer snare resections were needed to resect lesions ≥20 mm using UR (2.4 vs 3.1, p=0.003). UR was also performed significantly faster compared with CR (3.8 minutes vs. 5.4 minutes, p=0.0016), and these results were driven by the resection of larger (≥10 mm) lesions, which required submucosal injection for CR (10-19 mm, 2.9 minutes vs 5.6 minutes, p<0.0001; ≥20 mm, 7.3 minutes vs 9.5 minutes, p=0.015).

Adverse events

Immediate and delayed adverse events, on a per polyp basis, were not observed (0% vs 0%, p>0.99) (Table 3). All randomized patients except one were contacted directly by telephone on 30-day follow-up. The nonresponder had an 8 mm polyp removed by UR and no hospitalizations or emergency department visits were noted in the medical record at the end of follow-up. One patient randomized to UR was hospitalized for postpolypectomy bleeding from a large (25 mm) pedunculated nonstudy polyp despite prophylactic clipping. Procedure reports from an outside facility noted active bleeding from the site of the nonstudy lesion that required endoscopic intervention.

Overall, immediate bleeding was uncommon (2.0% vs 1.9%, p=0.91), although it was observed proportionally more frequently in both groups for giant (≥20 mm) lesions (18.8% vs 12.5%), and all were adequately addressed endoscopically at the time of initial colonoscopy.

There was no difference in the proportion of lesions receiving prophylactic postresection clipping (22.6% vs 21.5%, p=0.98), although there was a trend toward fewer clips for closure of resection defects favoring UR (2.9 vs 3.4, p=0.06), with a significant difference for 10 to 19 mm-sized lesions (2.4 vs 3.0, p=0.04).

Follow-up colonoscopies

For patients with nonpedunculated polyps ≥20 mm, routine short-term colonoscopy (between 3-6 months) was performed to evaluate the scar site for endoscopic and histologic (biopsy of the scar) evidence of residual polyp as part of standard practice. In this series, 32 lesions ≥20 mm were removed from 26 patients. All but 2 patients returned for follow-up. One patient with 2 lesions ≥20 mm did not return after developing recurrent, metastatic head and neck cancer and entered hospice care. Another with a 20 mm lesion did not adhere to surveillance. There was no endoscopic or histologic residual polyp at the 29 scar sites evaluated in surveillance (including a 23 mm tubulovillous adenoma with residual neoplasia on 4-qudrant biopsies). Mean follow-up time for this group was 109.3 ± 42.0 days (range 84-269).

Discussion

Conventional polypectomy is well established and performed for the removal of noninvasive lesions with the colon distended with gas, and often with the aid of submucosal fluid injection for larger (≥10 m) and/or nonpolypoid lesions[24,25]. Polypectomy is effective, but the risk of incomplete resection remains high at approximately 10% for lesions 5 to 20 mm in one report[2] and increases for larger lesions and those removed piecemeal (>20%) or with serrated histology (30%)[2,3]. Therefore, alternative techniques that safely and effectively decrease the incomplete resection rates are important in optimizing colonoscopy efficacy.

We report the results of the first randomized controlled trial in a U.S. population evaluating outcomes of UR compared with CR for removal of nondiminutive, nonpedunculated colorectal lesions. Previous studies in this field have primarily been observational and limited to large or giant (≥20mm) lesions. The only published randomized trial was conducted at Japanese referral centers and focused on 10 to 20 mm-sized lesions in patients routinely hospitalized for their procedures[17]. We demonstrated the safety, efficacy and potential benefits of UR across a broad range of polyp sizes encountered in routine outpatient clinical practice.

UR is a novel technique that has been well described by experts at a referral center for lesions ≥20 mm[10]. It is easily learned[11,14], does not require additional or new accessories, and has potential advantages compared with CR[9]. An underwater environment can improve polyp visualization from a natural “magnification” effect that occurs when the colonoscope is submerged (because of the higher index of refraction of water compared with air), which helps with evaluation of the boarders of lesions. In a nondistended colon, polyps also often assume more compact and favorable polypoid configurations (Figure 2 and Figure 3) compared with their observed state in a distended colon. Additionally, a larger mucosal surface area can be captured in a snare when the colon is not stretched, which facilitates polypectomy and increases the opportunity of en bloc resection, even for larger (20-40 mm) lesions[13]. Mucosal lesions are also buoyant when submerged because of their fat content and “float” in a water-filled lumen, whereas the underlying muscularis propia retains its circular configuration and native thickness, creating a natural separation between the mucosa and deeper structures of the colonic wall[9]. This obviates the need for submucosal injection while still providing a margin of safety for snare resection. Avoiding submucosal injection avoids the potential disadvantages of traditional EMR, including the theoretical risk of dysplastic seeding into the deep layers of the colon during injection; the risk of local peritonitis if injection is performed too deep; or the potential for submucosal injection to alter lesions into more challenging configurations for resection[9].

In this comparative study, success for UR was high, and low incomplete resection rate was achieved, demonstrating the efficacy of this technique if performed properly. There was no significant difference in the primary endpoint with CR, although the incomplete resection rate for conventional methods in this study was also very low. Incomplete resection rates can vary widely across endoscopists[2], but with an operator achieving high complete resection rates with CR, demonstrating consistent and high complete resection rates with UR supports its feasibility in a nonreferral population, while highlighting its potential benefits.

UR for lesions ≥10 mm was performed significantly faster than CR. This has implications for improving colonoscopy efficiency. Although gas exclusion and water-filling take time, these can be performed simultaneously and are generally performed faster than submucosal injection. Similarities in resection times for small lesions, where submucosal injection was not performed in either group, support this reasoning. Intuitively, avoidance of the additional step of submucosal injection decreases polypectomy time, although this was not demonstrated in a prior study[17]. But calculation of resection times may differ between studies and injection requires the endoscopist to find the correct submucosal plane with the needle, inject solution to form a well-configured fluid cushion, which may require more than one puncture, and exchange of the needle for a snare. Additionally, not factored into resection in this study was the time needed to prepare the injectate solution, including mixing/diluting components and unpacking and priming the needle, so “real world” time savings for UR may be even greater. Submucosal injection also often stretches polyps and increases the size of a lesion. This may adversely impact the success of en bloc resection and/or increase the number of resections needed to completely remove a polyp, which can also prolong polypectomy. Although en bloc resection rates did not differ in this study, for giant polyps (≥20 mm), where expansion of lesions may have the greatest impact, significantly fewer snare resections were needed for UR (2.4 vs 3.1, $p=0.003$).

Avoidance of submucosal injection may also reduce cost. Although a variety of injection practices exist, avoidance of injection needles and injectate solution, which can be costly, may result in meaningful immediate cost savings in a busy endoscopy unit. Furthermore, although the cost effectiveness of post-polypectomy prophylactic clipping remains an area of debate, the observation that significantly fewer clips were needed to close post-resection defects for intermediate sized lesions (10-19 mm) (2.4 vs 3.0, p=0.04), with an overall trend for needing fewer clips across all sizes (2.9 vs 3.4, p=0.06), deserves attention. This finding may be related to the smaller footprint polyps assume in a nondistended colon. Until the colon is fully reinflated with gas, resection bases also remain smaller and if clipping is performed promptly, fewer may be needed after UR.

A recent systematic review and meta-analysis reported on the safety of underwater polypectomy[33], and this prospective study supports these conclusions. To date, only one perforation during underwater polypectomy has been reported[34], and this occurred with the colonoscope retroflexed in the right colon segment. In the current study, adverse events were not observed in either group, likely related to the proportion of cold resection techniques used in the cohort, but the data provide further evidence that underwater interventions are safe.

This study has several limitations. The primary endpoint is a surrogate for PCCRC, and 4-quadrant biopsies were a proxy for completeness of resection. Although pathologic confirmation of complete resection may be preferable, clear histopathologic R0 analysis in routine high-volume practice can be challenging, particularly for small lesions, because of polyp fragmentation during specimen retrieval, variability in histopathologic reporting and the need for specific specimen handling and preparation of resected lesions[35,36]. Because of these concerns, previous investigators have used tissue sampling around polypectomy sites to assess for completeness of resection[2,6,37], similar to the current protocol. For larger lesions, where sampling the margin may be less reliable, follow-up colonoscopy to evaluate for residual neoplasia is often performed. Of the 32 lesions ≥20 mm in this study, 29 were assessed in this manner, and there was no evidence of residual polyp at any of the sites examined. The absence of residual polyp on follow-up for giant polyps lends support to the practice of the sampling protocol and strengthens the findings for the efficacy of the resection techniques used in the cohort. However, in future studies, more methodical collection and processing of polyps to better preserve specimens for pathologic assessment of deep and lateral margins would be instructive.

This study was also performed on a primarily male veteran population by a single endoscopist experienced with UR and CR. Polypectomy outcomes are highly operator dependent, and inclusion of only one endoscopist is a notable limitation affecting generalizability of results. But findings from this comparative trial represent an important step in the evaluation of this new technique, and demonstration of high complete resection rates with CR by a proficient operator validates the comparison and strengthens the findings from this study. Variability in polyp sizing, resection techniques, accessories and electrosurgical generator settings were also reduced with a single operator, but additional studies across a broader range of patients and endoscopists, including assessment of optimal snares and generator settings, in clinical practice remain important.

Conclusions

Low incomplete resection rates are achievable with UR and CR. UR is effective and safe with the advantage of faster resection and possible cost savings for removal of larger (≥10 mm) lesions through avoidance of submucosal injection. UR has potential to improve colonoscopy cost-effectiveness by increasing efficiency and reducing cost, while maintaining quality. Based on the current data, UR is a valuable new addition in the armamentarium for the removal on nondiminutive, nonpedunculated colorectal lesions.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations/acronyms

AADR	advanced adenoma detection rate
ADR	adenoma detection rate
ASA	American Society of Anesthesiologists
ASGE	American Society for Gastrointestinal Endoscopy
CSSLDR	clinically significant serrated lesion detection rate
CR	conventional resection
CRC	colorectal cancer
CS	cold snare
EMR	endoscopic mucosal resection
HP	hyperplastic polyp
IQR	interquartile range
NIH	National Institutes of Health
pADR	proximal colon adenoma detection rate
PCCRC	post-colonoscopy colorectal cancer
pSLDR	proximal colon serrated lesion detection rate
SD	standard deviation

SE	standard error
SSP	sessile serrated polyp
SSPDR	sessile serrated polyp detection rate
TA	tubular adenoma
TVA	tubulovillous adenoma
UCS	underwater cold snare
UEMR	underwater hot snare/endoscopic mucosal resection
UR	underwater resection
VANCHCS	Veterans Affairs Northern California Health Care System

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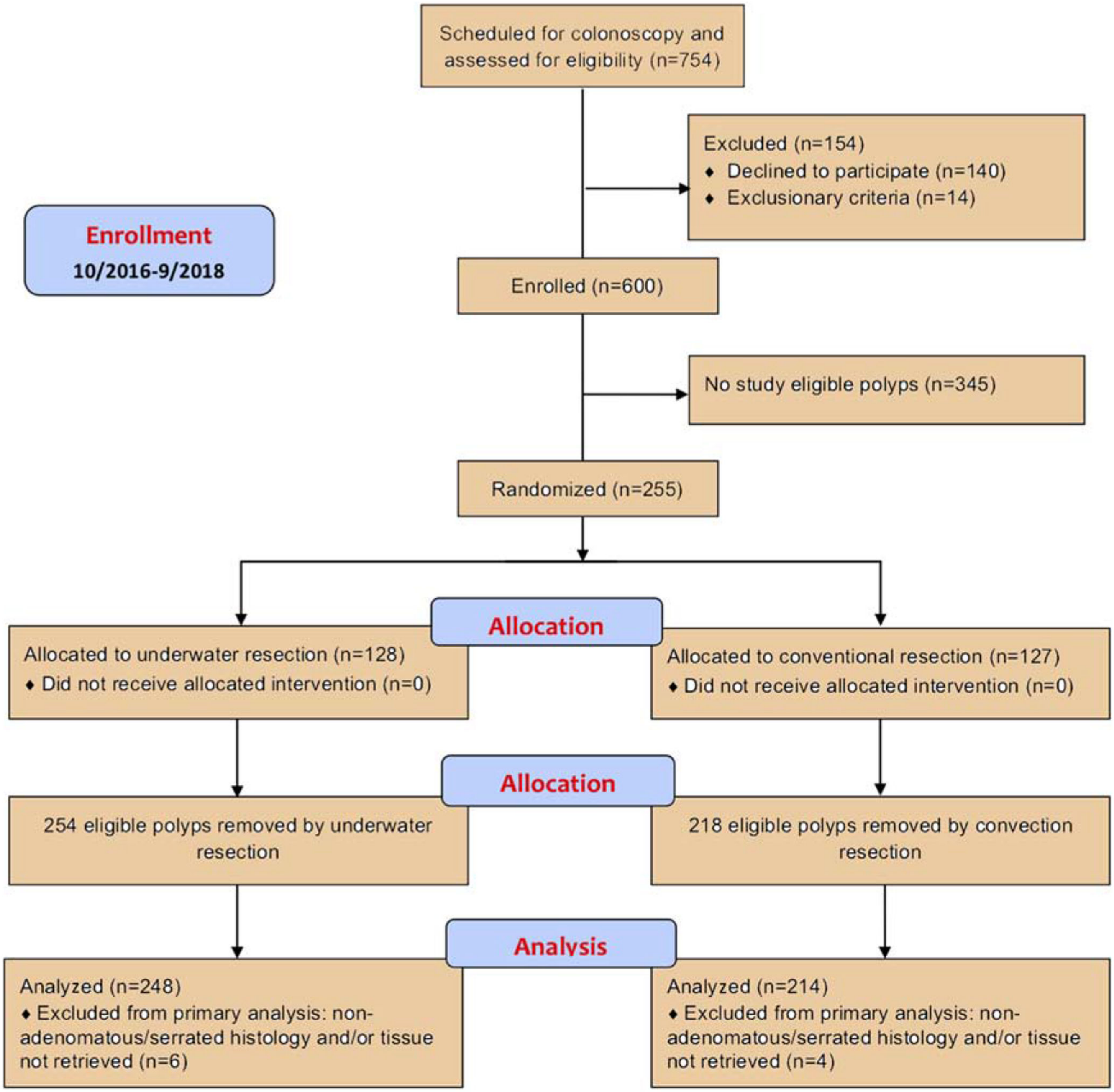
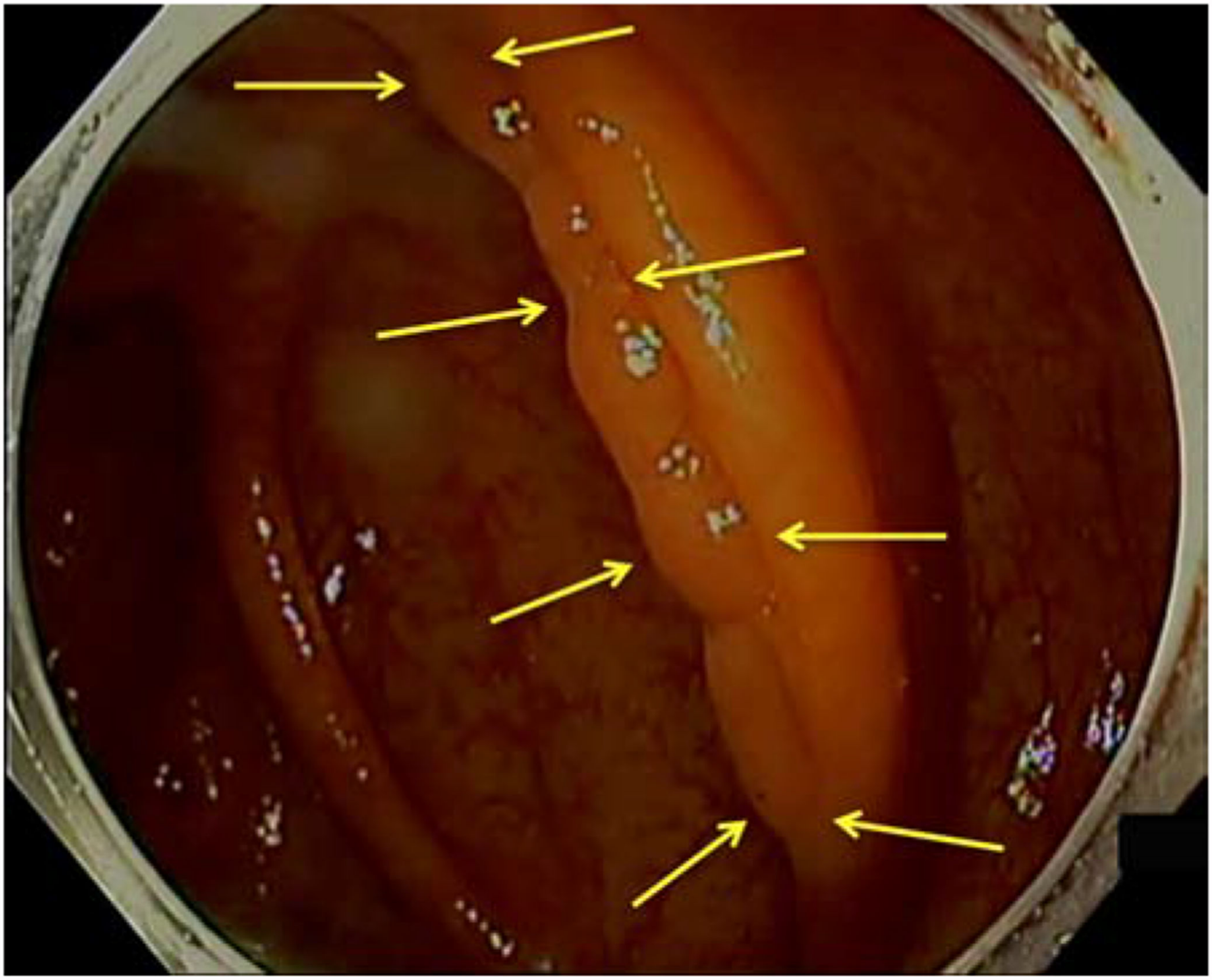
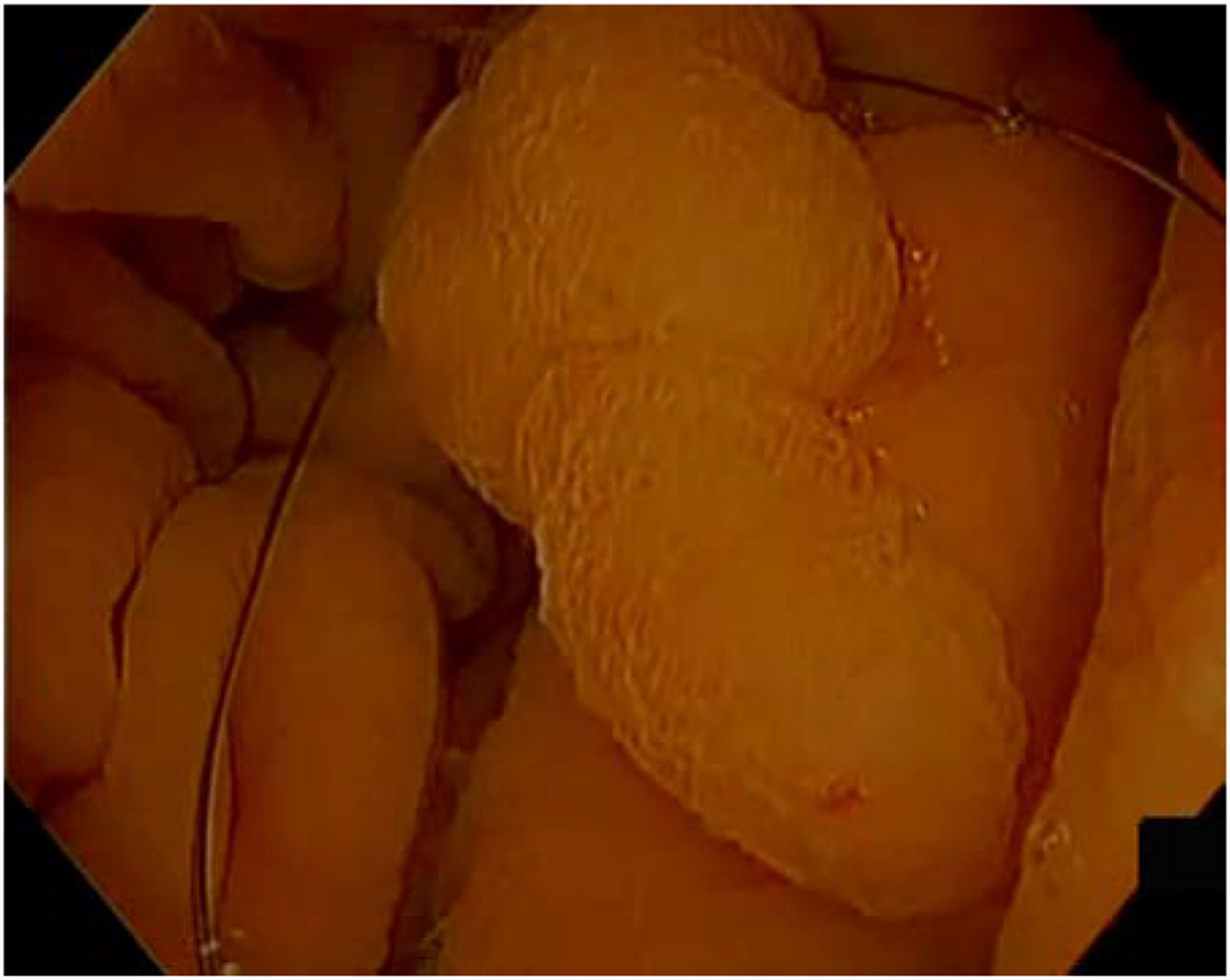
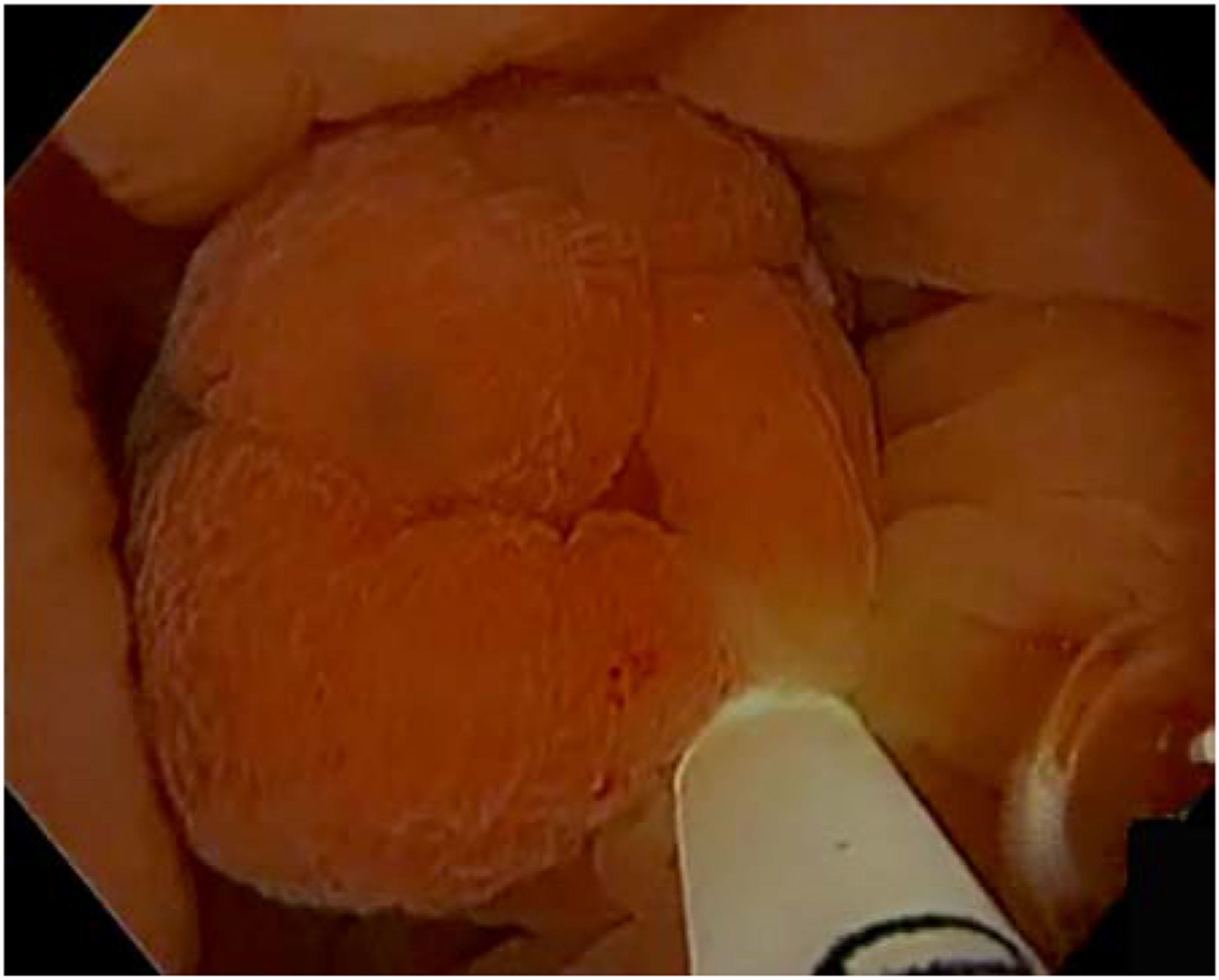


Figure 1:
CONSORT flow diagram.







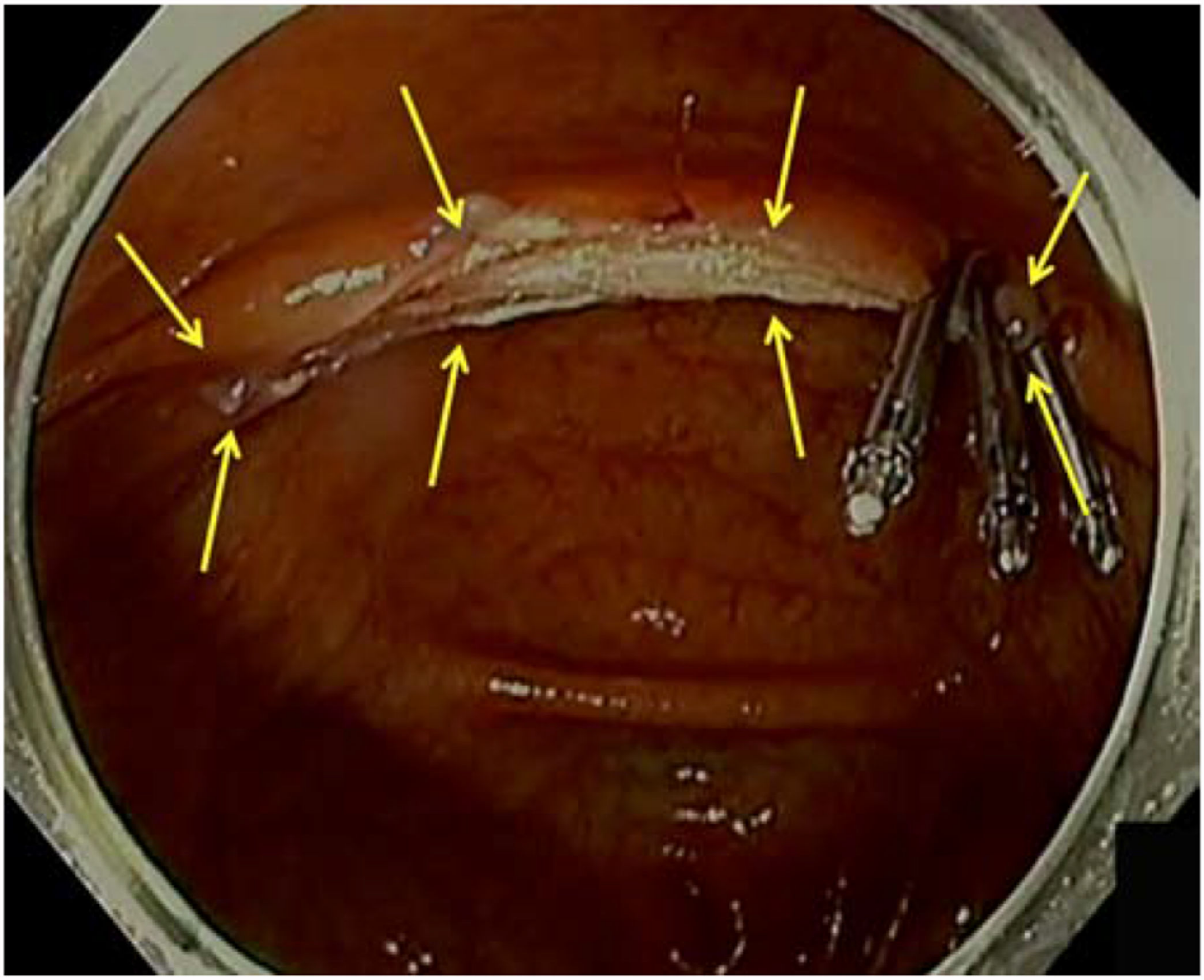
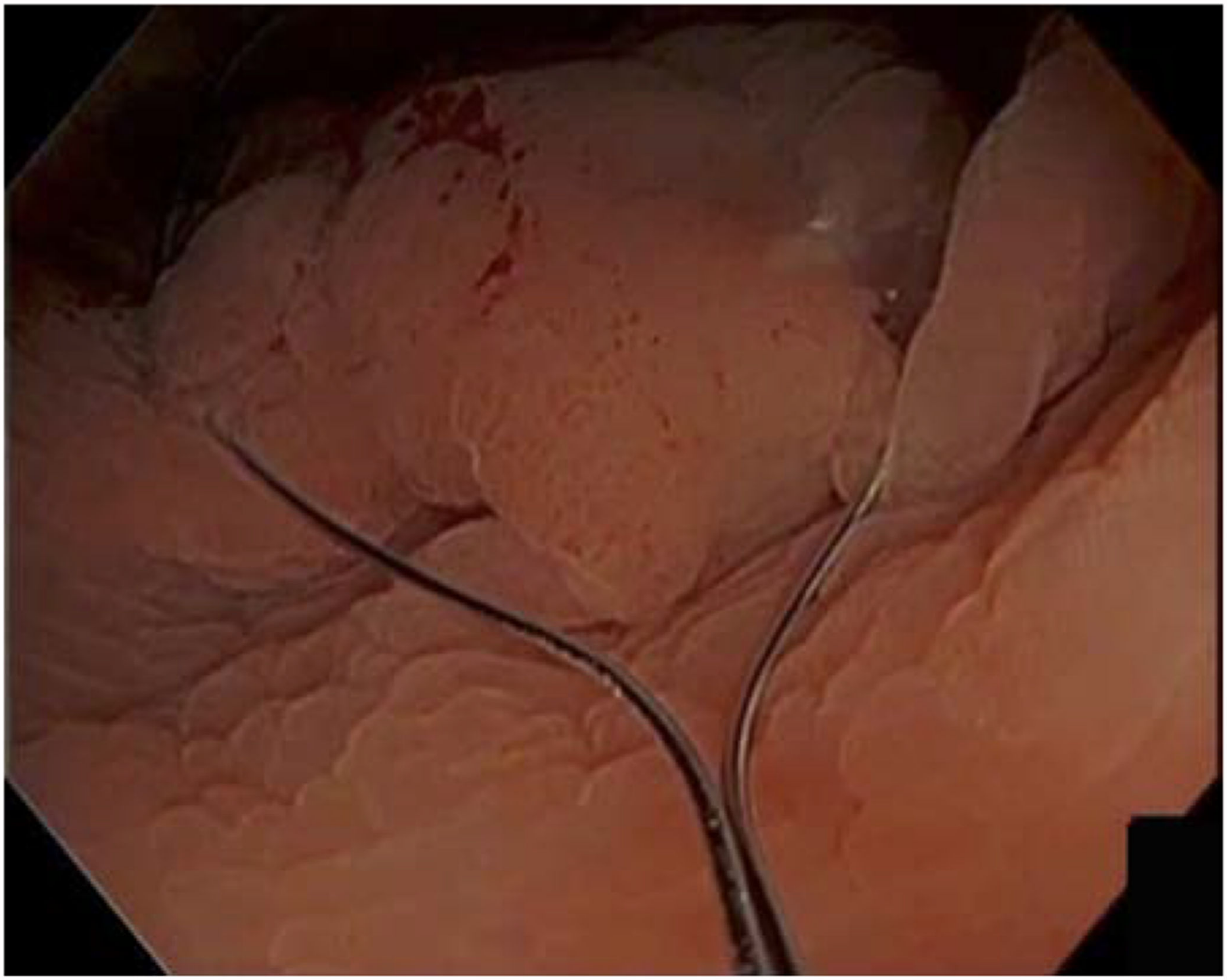


Figure 2.

A, Elongated cecal lesion overlying a fold in a gas-distended lumen. B, Underwater view of the lesion in a nondistended colon. The lesion is smaller and assumes a polypoid configuration more amenable to en bloc resection. C, Ensnaring the lesion with a rim of normal mucosa without submucosal injection. D, Postresection site in a gas-distended lumen. E, Continued expansion of the resection site to the original size of the lesion during clip closure.



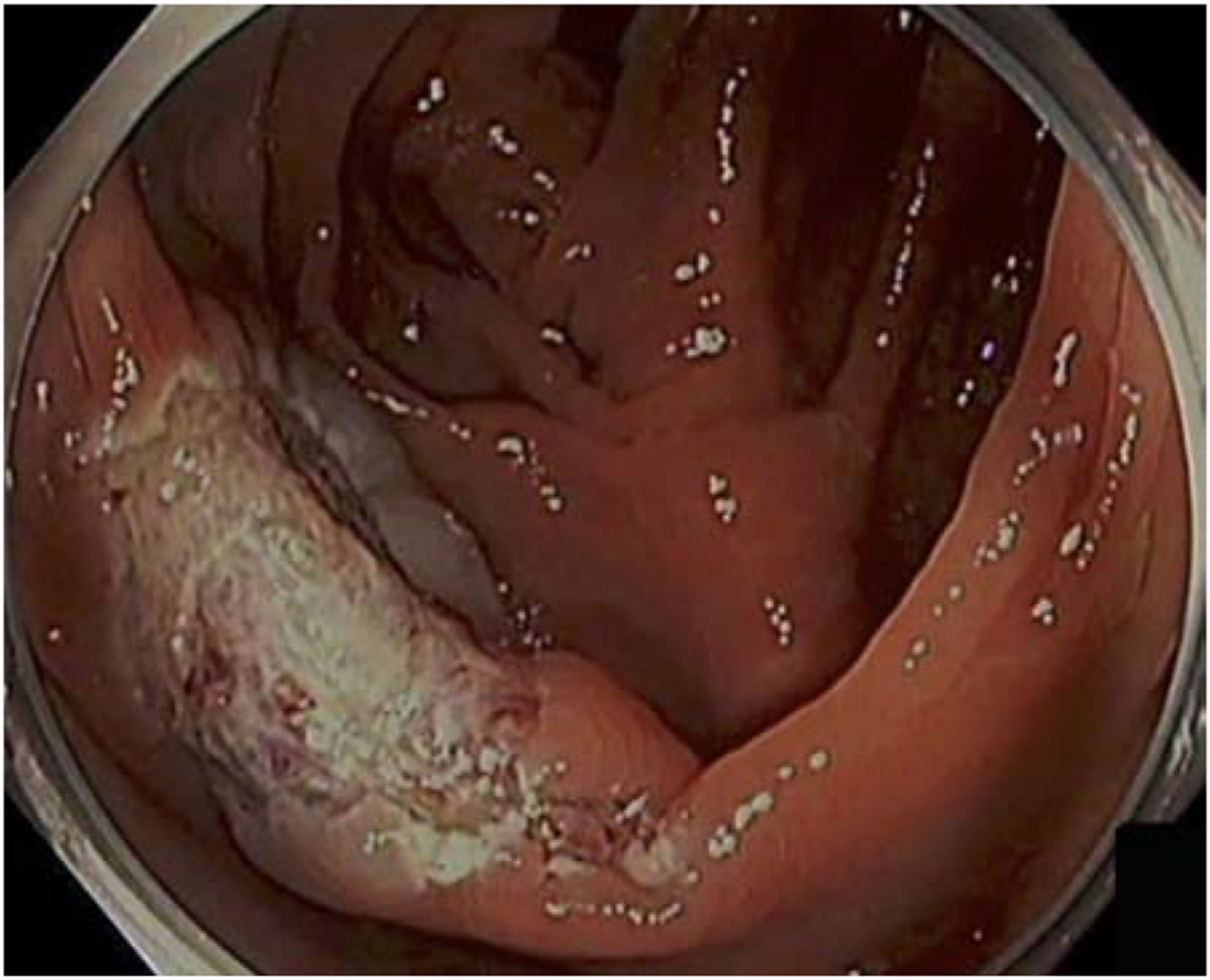


Figure 3.

A, Large nonpolypoid (IIa) transverse colon lesion in a clamshell configuration straddling a haustral fold. B, Underwater view of the lesion in a nondistended colon. Less wall tension flattens colonic folds and the lesion is in a more favorable polypoid configuration for ensnarement and en bloc resection without submucosal injection. C, Postresection site in a clamshell configuration in a gas-distended lumen.

Table 1:

Randomized patient characteristics (n=255)

	Underwater (n=128)	Conventional (n=127)	*P* value
Mean Age: years (SD) [range]	64.4 (8.3) [35-81]	64.6 (8.3) [26-78]	0.81 *
Gender			
Male (%)	123 (96.1%)	125 (98.4%)	0.45 **
Female (%)	5 (3.9%)	2 (1.6%)	--
Race/Ethnicity			0.009 ** (white vs. nonwhite)
White (%)	116 (90.6%)	100 (78.7%)	
Nonwhite (%)	12 (9.3%)	27 (21.3%)	
Black (%)	9 (7.0%)	12 (9.5%)	
Hispanic (%)	0 (0%)	7 (5.5%)	
Asian (%)	0 (0%)	3 (2.4%)	
Other (%)	3 (2.3%)	5 (3.9%)	
Mean body mass index (SD) [range]	30.7 (6.3) [20.2-59.8]	30.6 (6.4) [16.9-58.6]	0.92 *
ASA classification			0.78 †
I (%)	2 (1.6%)	2 (1.6%)	
II (%)	83 (64.8%)	77 (60.6%)	
III (%)	43 (33.6%)	48 (37.8%)	
Indications for procedure			0.89 ‡
Screening (%)	34 (26.6%)	32 (25.2%)	
Surveillance (%)	65 (52.3%)	65 (51.2%)	
Diagnostic (%)	16 (12.5%)	16 (12.6%)	
Therapeutic (%)	9 (7.0%)	13 (10.2%)	
Follow-up of EMR (%)	2 (1.6%)	1 (0.8%)	
High-risk family history of CRC (%)	8 (6.3%)	14 (11.0%)	0.19 **
Diabetes (%)	32 (25.0%)	50 (39.4%)	0.02 **
Smoker (%)	37 (28.9%)	24 (18.9%)	0.08 **
Antithrombotic use			

	Underwater (n=128)	Conventional (n=127)	*P* value
Aspirin (%)	58 (45.3%)	71 (55.9%)	0.10 **
Other (%)	9 (7.0%)	10 (7.9%)	0.82 **
Moderate sedation (%)	119 (93.0%)	116 (91.3%)	0.65 **
Cecal/ileal intubation (%)	128 (100%)	127 (100%)	>0.99 **
Median Boston Bowel Preparation Scale (IQR)	9 (1)	9 (1)	0.47 ‡
Right colon segment	3 (0)	3 (0)	0.39 ‡
Mid-colon	3 (0)	3 (0)	0.79 ‡
Left colon segment	3 (0)	3 (0)	0.27 ‡
Adenoma detected (ADR)	116 (90.6%)	120 (94.5%)	0.34 **
Median adenomas per colonoscopy (IQR)	3 (4)	3 (3)	0.42 ‡
Proximal colon adenoma detected (pADR)	111 (86.7%)	117 (92.1%)	0.22 **
Advanced adenoma detected (AADR)	34 (26.6%)	34 (26.8%)	>0.99 **
Sessile serrated polyp detected (SSPDR)	32 (25.0%)	28 (22.0%)	0.65 **
Proximal colon serrated lesion detected (pSLDR)	50 (39.6%)	54 (42.5%)	0.61 **
Clinically significant serrated lesion detected (CSSLDR)	51 (39.8%)	56 (44.1%)	0.52 **
Cancer (%)	2 (1.6%)	1 (0.8%)	>0.99 **

SD=standard deviation; ASA=American Society of Anesthesiologists; EMR=endoscopic mucosal resection; IQR=interquartile range; CRC=colorectal cancer; ADR=adenoma detection rate; pADR=proximal colon adenoma detection rate; AADR=advanced adenoma detection rate; SSPDR=sessile serrated polyp detection rate; pSLDR=proximal colon serrated lesion detection rate; CSSLDR=clinically significant serrated lesion detection rate

* Satterthwaite;

** Fisher Exact Test;

† Chi-square;

‡ Kruskal-Wallis Test

Table 2:

Colorectal study polyps (n=462)

	Underwater Resection (n=248)	Conventional Resection(n=214)
Polyp counts		
Total	248	214
6-9 mm (%)	180 (72.6%)	164 (76.6%)
10-19 mm (%)	52 (21.0%)	34 (15.9%)
≥20 mm (%)	16 (6.5%)	16 (7.5%)
Mean size (mm) (SD) [range]	9.9 (5.8) [6-40]	9.9 (6.4) [6-45]
Pathology		
Adenomatous lesions (%)	183 (73.8%)	171 (79.9%)
Tubular adenoma (%)	169 (68.2%)	162 (75.7%)
Tubular adenoma with high grade dysplasia (%)	4 (1.6%)	6 (2.8%)
Tubulovillous adenoma (%)	6 (2.4%)	1 (0.5%)
Tubulovillious adenoma with high grade dysplasia (%)	1 (0.4%)	0 (0%)
Villous adenoma (%)	3 (1.2%)	2 (0.9%)
Serrated class lesions (%)	65 (26.2%)	43 (20.1%)
Sessile serrated polyp without dysplasia (%)	40 (16.1%)	26 (12.2%)
Sessile serrated polyp with dysplasia (%)	3 (1.2%)	0 (0%)
Traditional serrated adenoma (%)	0 (0%)	1 (0.5%)
Hyperplastic polyp–proximal or distal colon (%)	22 (8.9%)	16 (8.5%)
Location		
Proximal colon (%)	202 (81.5%)	172 (80.4%)
Cecum (%)	25 (10.1%)	22 (10.3%)
Ascending (%)	67 (27.0%)	56 (26.2%)
Transverse (%)	110 (44.4%)	94 (43.9%)
Left colon (%)	46 (18.5%)	42 (19.6%)
Descending (%)	15 (6.1%)	14 (6.5%)
Sigmoid (%)	21 (8.5%)	22 (10.3%)
Rectum (%)	10 (4.0%)	6 (2.8%)
Morphology		
Is (%)	126 (50.8%)	115 (53.7%)

	Underwater Resection (n=248)	Conventional Resection(n=214)
IIa (%)	107 (43.2%)	88 (41.1%)
IIb (%)	11 (4.4%)	4 (1.9%)
IIc (%)	0 (0%)	1 (0.5%)
Mixed (%)	0 (0%)	1 (0.5%)

SD=standard deviation

Table 3:

Resection outcomes for colorectal study polyps (n=462)

	Underwater (n=248)	Conventional (n=214)	*P* value*
Incomplete resection			
Overall (%)	5/248 (2.0%)	4/214 (1.9%)	0.91
6-9mm (%)	3/180 (1.7%)	4/164 (2.4%)	0.11
10-19mm (%)	1/52 (1.9%)	0/34 (0%)	0.07
≥20mm (%)	1/16 (6.3%)	0/16 (0%)	0.66
En bloc resection			
Overall (%)	223/248 (89.9%)	193/214 (90.2%)	0.64
6-9mm (%)	175/180 (97.2%)	163/164 (99.4%)	--†
10-19mm (%)	44/52 (84.6%)	25/34 (73.5%)	--†
≥20mm (%)	4/16 (25.0%)	7/16 (43.8%)	--†
Number of snare resections			
Overall (SE)	1.17 (0.07)	1.22 (0.07)	0.62
6-9 mm (SE)	1.04 (0.05)	1.01 (0.05)	0.68
10-19 mm (SE)	1.20 (0.09)	1.33 (0.11)	0.39
≥20 mm (SE)	2.36 (0.16)	3.06 (0.16)	0.003
Resection time [minutes]			
Overall (SE)	3.8 (0.34)	5.4 (0.35)	0.0016
6-9 mm (SE)	1.3 (0.30)	1.1 (0.30)	0.51
10-19 mm (SE)	2.9 (0.40)	5.6 (0.47)	<0.0001
≥20 mm (SE)	7.3 (0.62)	9.5 (0.66)	0.015
Immediate bleeding			
Overall (%)	5/248 (2.0%)	4/214 (1.9%)	0.91
6-9 mm (%)	0/180 (0%)	1/164 (0.6%)	--†
10-19 mm (%)	2/52 (3.9%)	1/34 (2.9%)	--†
≥20 mm (%)	3/16 (18.8%)	2/16 (12.5%)	--†
Perforation, post-polypectomy syndrome or delayed (30 day) adverse events			

	Underwater (n=248)	Conventional (n=214)	*P* value[*]
Overall (%)	0/248 (0%)	0/214 (0%)	--[†]
6-9 mm (%)	0/180 (0%)	0/164 (0%)	--[†]
10-19 mm (%)	0/52 (0%)	0/34 (0%)	--[†]
≥20 mm (%)	0/16 (0%)	0/16 (0%)	--[†]
Clipping (prophylactic)			
Overall (%)	56/248 (22.6%)	46/214 (21.5%)	0.98
6-9 mm (%)	0/180 (0%)	0/164 (0%)	--[†]
10-19 mm (%)	41/52 (78.6%)	30/34 (88.2%)	--[†]
≥20 mm (%)	15/16 (93.8%)	15/16 (93.8%)	--[†]
Number of clips (for clipped lesions)			
Overall (SE)	2.86 (0.17)	3.38 (0.20)	0.06
6-9 mm (SE)	--	--	--[†]
10-19 mm (SE)	2.41 (0.18)	3.00 (0.21)	0.04
≥20 mm (SE)	4.07 (0.30)	4.13 (0.30)	0.87

SE=standard error

[*] From mixed effects logistic (incomplete resection, en bloc resection, immediate bleeding, delayed adverse events, clipping) and linear (resection times, number of snare resections, number of clips) regression models.

[†] Dash (--) indicates that the treatment by size effect was not estimable (model did not converge).

Table 4:

Characteristics of incompletely resected lesions

	Size (mm)	Technique	Location	Morphology	Pathology	Snare resections
Underwater						
Polyp 1	7	UCS	transverse	IIa	serrated (SSP)	1
Polyp 2	23	UEMR	ascending	IIa	adenoma (TVA)	3
Polyp 3	9	UCS	cecum	IIa	adenoma (TA)	1
Polyp 4	15	UEMR	ascending	IIb	serrated (SSP)	1
Polyp 5	9	UCS	ascending	IIa	serrated (SSP)	1
Conventional						
Polyp 1	6	CS	ascending	Is	serrated (HP)	1
Polyp 2	6	CS	cecum	Is	adenoma (TA)	1
Polyp 3	9	CS	sigmoid	Is	adenoma (TA)	1
Polyp 4	7	CS	transverse	Is	adenoma (TA)	1

UCS=underwater cold snare; UEMR=underwater hot snare/endoscopic mucosal resection; CS=cold snare; SSP=sessile serrated polyp; TVA=tubulovillous adenoma; TA=tubular adenoma; HP=hyperplastic polyp