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Underwater endoscopic mucosal resection without submucosal injection (UEMR) for large colorectal polyps: A community-based series

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ABSTRACT

Background: Underwater endoscopic mucosal resection without submucosal injection (UEMR) is an appealing therapy for large colorectal polyps. However, this technique is not practiced widely and there are limited data evaluating UEMR in community settings.
Methods: The study comprised patients undergoing UEMR of large (≥20 mm) sessile colorectal lesions at a community-based center. Residual neoplasia was assessed via follow-up colonoscopy.
Results: Among 264 lesions (diameter 38 ± 18 mm; range 20–110 mm) 99% were successfully resected with UEMR. Two lesions involving the cecum/IC valve required multiple sessions. There were no cases of perforation or post-polypectomy syndrome. Delayed bleeding occurred in 1.6%, all managed conservatively. Residual neoplasia was present in 5.7% and was amenable to UEMR.
Conclusion: This large community-based series demonstrated high efficacy and safety of UEMR for large sessile colorectal lesions. The results support UEMR as first-line therapy for these lesions.
Summary: Underwater endoscopic mucosal resection without submucosal injection (UEMR) is a recently developed method that has advantages over conventional EMR for treatment of large colorectal lesions. However, UEMR is not practiced widely and there are limited data evaluating this technique in everyday practice. This large community-based series demonstrated high efficacy and safety of UEMR for large sessile colorectal lesions.

Introduction

Colorectal cancer is the second leading cause of cancer death in the United States among men and women combined.[1] Colonoscopy with resection of lesions with malignant potential reduces the incidence and mortality of colorectal cancer.[2,3] Large sessile colorectal lesions greater than 2 cm in diameter, though less common than small polyps, demand particular attention due to a greater risk of malignant progression and a prevalence of covert malignancy ranging from 5 to 22%.[4]

Endoscopic mucosal resection (EMR) of large colorectal polyps has established efficacy, and favorable risks and costs compared to surgical resection.[5,6] However, EMR is under-utilized[6] and can be technically challenging. By convention, EMR is commonly performed in a gas-distended colon, using submucosal fluid injection to separate the mucosal lesion from the colon wall. While submucosal injection is purported to enhance the safety of resection, there are no clinical data to support this contention, and EMR for large colorectal lesions can be performed safely and effectively without submucosal injection.[7,8] Apart from added equipment and time, submucosal injection may hinder EMR, through inadvertent disruption of tissue planes, expansion of lesion size, increased tissue tension, and bleeding induced by needle puncture.[9] Further, a high rate of residual/recurrent neoplasia on endoscopic follow-up is common with conventional EMR,[10] raising the question as to whether submucosal injection may deter complete resection of neoplastic tissue.

To address these concerns, Binmoeller and colleagues developed underwater EMR.[11] With this method, the water-filled lumen promotes physiologic separation or lifting of the mucosa, allowing flat lesions to assume an elevated profile more receptive to snare

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capture and resection, obviating submucosal injection. Since the advent of UEMR, small case series of this method have been reported from tertiary centers.[12–18] We report our experience with UEMR for large sessile colorectal lesions in a community-based setting.

Material and methods

Patient population

Procedural and follow-up data were collected among adult patients (age ≥18 years) who had undergone colonoscopy between Jan. 2016 and Oct. 2019 at Victoria General Hospital, Victoria, BC. While ours is a referral center for all of Vancouver Island, the day-to-day activities of endoscopists closely resemble those of a community GI practice. Throughout the study period, we had adopted exclusive use of underwater polypectomy/UEMR for all colorectal polypoid lesions. The study population comprised patients in whom one or more sessile polyps of at least 20 mm diameter were resected via UEMR. Lesions were excluded if there were endoscopic features (e.g. bleeding, ulceration, or irregular/disrupted pit pattern unless en bloc UEMR was deemed appropriate) suspicious for invasive cancer. Given that this was a quality assessment initiative, formal review board approval was not required by our institution.

Endoscopic procedure

Procedures were performed by a single experienced operator (RLB) with over 15 years of experience in therapeutic endoscopy. We used high-definition colonoscopes (Pentax Medical, Mississauga, ON, Canada) mounted with a soft cap (Olympus Medical, Tokyo, Japan). Patients received a standard split-dose bowel prep with either Pico Salax (Ferring Pharmaceuticals, North York, ON) or Golytely (Braintree Laboratories, Braintree, MA) and procedural sedation with midazolam and fentanyl.

Water exchange[19] was used during insertion to the cecum. During our initial experience, the colon was inspected via air insufflation during withdrawal, instilling water and aspirating air for UEMR as needed. With more experience with underwater methods, we transitioned to complete underwater colonoscopy,[20] with no gas insufflation during the entire procedure unless selectively needed for visualization. Sterile water was instilled into the lumen via a foot-activated pump (EndoGator, Byrne Medical, Conroe TX).

UEMR was performed as described previously.[11] Briefly, diathermic markings were placed around the periphery of the lesion with brief electrosurgical pulses applied to the mucosa with snare-tip coagulation or with APC. Lesions were sized and resected with large stiff snares, (25–33 mm diameter, Captivator II, Boston Scientific, Marlborough, MA), laying the open snare flat against the colon wall and allowing the lesion to "float" into the snare either spontaneously or with bowel contractions before closing the snare while torquing the endoscope slightly for optimal tissue capture. Tissue was resected with Endocut Q (Effect 2, Cut duration 1, Cut interval 4) electrosurgical setting (Erbe Vio 300 unit, Tuebingen, Germany). Any visible islands or bridges of polyp tissue were resected with a smaller snare or hot or cold biopsy forceps, with specific avoidance of ablation techniques. Normal mucosa along the resection margin was not treated separately. Unless to address bleeding, post-polypectomy defects were not closed with clips. When feasible, en bloc resection was attempted, generally for lesions ≤30 mm in diameter. Intra-procedural bleeding, defined as any use of instrumentation to treat bleeding, was treated with one or more of soft coagulation via snare tip or biopsy forceps, adrenalin injection, APC or clips (Resolution 360 clip, Boston Scientific, Marlborough, MA).

Follow up

Follow up colonoscopy was generally advised six months from the index procedure, consistent with current guidelines.[21] Selected patients with en bloc resection of smaller lesions with favorable histology were advised to undergo surveillance colonoscopy in one year. At the surveillance endoscopy, the post-UEMR scar site was identified and inspected for residual neoplasia using an established enhanced imaging protocol.[22] Visible neoplastic tissue was resected via UEMR snare or biopsy resection. Bland scar tissue with normal pit and vascular pattern was not biopsied routinely.

Results

Patients

264 lesions among 242 patients (mean age 67; 59% males) were treated with UEMR (Table 1). The most frequent indications for colonoscopy were referral for large polyps (71%) and positive FOBT (25%). 17% of patients were referred for lesions which had failed a resection attempt with conventional EMR. Continuous data are reported as means ± SD.

Lesion characteristics

Table 2 shows details of lesion location, size and histology. More than half were located in the cecum and ascending colon. The mean polyp diameter was 38 ± 18 mm. Most lesions had Paris IIa or Is Paris morphology; 3% had central depression. One-third of lesions were tubular adenomas; one-third tubulovillous adenomas; 26% sessile serrated lesions; and 5% contained adenocarcinoma.

Resection details

99% of lesions were able to be completely resected with UEMR. Two extensive lesions involving the cecum and IC valve required three separate endoscopies for complete resection; all others were resected during a single session. The three lesions not able to be resected via UEMR included one benign tubulovillous adenoma with deep extension into the appendix lumen and two cases of deeply invasive cancer; these patients all underwent surgery. Lesion resection time was 13.7 ± 10.6 min. En bloc resection was performed for 74 lesions (28%; mean diameter 24.4 ± 6.3 mm).

Complications

Intra-procedural bleeding occurred in 39 subjects (16%), controlled in all via endoscopic maneuvers (snare-tip soft coagulation (74%) and/or clips (38%), adrenalin injection (18%), APC (10%), hot biopsy coagulation (5%)). Four patients (1.6%) experienced delayed (>48 h) bleeding, which resolved in all without intervention. One patient had persistent pain following UEMR of an 8-cm

Table 1
Patient baseline data.

	N (%)
Patients	242
Sex (F/M)	99/143 (41/59)
Age (mean ±SD)	67 ± 9
Prior endoscopic therapy	41 (17)
Indication	
Positive FOBT	60 (25)
Large polyp referral	172 (71)
Surveillance	20 (8)

Table 2
Lesion characteristics.

Size (mean ± SD)		38 ± 18 mm					
Location		Cecum	Ascending 64 (24)	Transverse 41 (16)	Descending	Sigmoid	Rectum	Total
N (%)		87 (33)			16 (6)	31 (12)	24 (9)	264 (100)
F								
Paris Class	IIa	Is	Isp	IIa-c				
N (%)	162 (61)	85 (32)	16 (6)	7 (3)				
Histology	TA	TVA	VA	SSP	HGD	adenoCa		
N (%)	86 (33)	90 (34)	11 (4)	69 (26)	18 (7)	13 (5)		

TA Tubular Adenoma, TVA Tubulovillous Adenoma, VA Villous Adenoma, SSP Sessile Serrated Polyp.
HGD High Grade Dysplasia, adenoCa adenocarcinoma.

sigmoid lesion. She was observed in hospital over 24 h, with negative CT findings and resolution of pain. There were no cases of perforation or post-polypectomy syndrome.

Follow up and recurrence rate

Follow up data over 8 ± 4 months were available for 174 patients (72%), including 170 patients who underwent repeat colonoscopy and 4 patients who underwent surgery. Among these patients there were 10 cases of residual/recurrent neoplasia (5.7%): 9 cases of benign adenomatous tissue (8 ± 3 mm diameter) successfully resected via UEMR; and one patient whose piecemeal UEMR contained adenocarcinoma whose subsequent surgical resection showed T1N0 cancer. Among subjects who had undergone en bloc UEMR, 31 (42%) underwent follow up colonoscopy, with no cases of residual/recurrent neoplasia.

Cancer cases

Thirteen patients (5.3%) had adenocarcinoma identified (Table 3). In two patients, the lesion could not be resected via UEMR; they both underwent surgery, with T2N0 and T4N0 cancer in the operative specimen. One patient who underwent piecemeal UEMR at index colonoscopy had high-risk pathology which prompted subsequent surgery, with operative pathology showing T1N0 cancer. Three patients who underwent follow up surgery had surgical specimens with no residual cancer or neoplasia. Five patients who did not undergo surgery underwent close surveillance, with negative clinical, endoscopic and CT follow up over a mean of 14 months. Two patients are awaiting follow up.

Discussion

Despite consensus that EMR is preferable to surgery for non-malignant colorectal polyps, surgery is performed for a substantial and growing volume of these lesions in both tertiary and non-academic centers in the United States.[23] While there are likely several contributors to this practice pattern, one factor may be the inherent limitations of conventional EMR. As outlined above, UEMR was developed to address the shortcomings of conventional EMR.

Our study is the largest published series of colorectal UEMR cases and has several important features. While the patient population reflected a typical community-based practice, the study included a significant number of “difficult” lesions, such as previously treated lesions, giant polyps, and those involving the ileocecal valve. Considering a mean lesion diameter approaching 4 cm, the en bloc resection rate of 28% is noteworthy. Although the study was not designed to confirm en bloc or R0 resection in the pathologic specimens, the zero residual/recurrence rate on follow up endoscopy for all lesions resected en bloc is consistent with complete resection at the index procedure. Similar to other published UEMR series,[8] the low (5.7%) rate of residual/recurrent neoplasia in our study is significantly lower compared to studies of conventional EMR.[10] Residual lesions were generally diminutive, benign and easily treated via UEMR. We believe precise characterization of lesion margins aided by underwater inspection, superior snare capture of tissue with UEMR, and avoidance of ablative techniques contributed to our low rate of residual pathology. Thermal ablation of polyp tissue resistant to snare resection at the time of index resection is associated with an increased risk of recurrence.[24,25]

We found colorectal UEMR to be extremely safe, with no cases of perforation or post-polypectomy syndrome. As in other series of

Table 3
UEMR cases containing adenocarcinoma.

Patient	Sex	Age	Location	Size (mm)	Histology	UEMR details	Surgical Pathology	Non-operative follow-up
1	M	71	cecum	25	TVA	piecemeal	Neg	—
2	M	55	rectum	55	TVA	Unable to resect	T2N0	—
3	M	77	ascend	60	TVA	piecemeal	Neg	—
4	F	55	sigmoid	20	TA	en bloc	—	Neg colon, CT 6 mos
5	F	72	rectum	20	TA	en bloc	—	Neg colon, CT 6 mos
6	F	82	sigmoid	60	TVA	piecemeal	—	Neg colon, CT 4, 18 mos
7	F	78	sigmoid	110	TVA	piecemeal	—	Neg colon, CT 5, 12 mos
8	M	60	descend	50	TVA	piecemeal	T1N0	—
9	F	66	rectum	60	TVA	piecemeal	Neg	—
10	F	52	descend	40	VA	Unable to resect	T4N0	—
11	F	61	sigmoid	20	TA	en bloc	NA	NA
12	M	52	rectum	20	TA	en bloc	NA	NA
13	M	68	descend	40	TVA	piecemeal	—	Neg colon, CT 3, 10 mos

TA Tubular Adenoma, TVA Tubulovillous Adenoma, VA Villous Adenoma, NA Not Available, CT Computed Tomography.

UEMR, the absence of post-polypectomy syndrome supports the hypothesis that this phenomenon may relate more to submucosal injection than thermal injury from polypectomy. Alternatively, the UEMR technique may confer better protection than submucosal injection against deep thermal injury.[26] Given that much of the rationale for EMR being preferable to surgery for large colorectal lesions rests on its superior safety profile, this advantage may be even more compelling with UEMR.

Among the eleven subjects with cancerous lesions that were able to be resected with UEMR, surgical or close endoscopic follow up was negative in all but 1 patient in whom T1NO adenocarcinoma was present in the surgically resected specimen. EMR of early stage (T1) colorectal cancer may confer similar long-term outcomes to surgery, particularly in the absence of high-risk histology.[27] While further study is needed to determine if UEMR provides advantages over conventional EMR for colorectal lesions with superficially invasive cancer, it is reasonable to speculate that the superior en bloc resection rate afforded by UEMR could expand the number of lesions with superficially invasive cancer suitable for endoscopic therapy. A recent study comparing conventional EMR to UEMR for intermediate (10–20 mm diameter) sessile colon polyps showed a significantly greater rate of en bloc resection with UEMR.[18]

Our study is limited by the lack of direct comparison of UEMR to conventional EMR or surgery. Additional prospective comparisons are anticipated. This was a single center study of procedures performed by one operator. However, conventional EMR is widely practised and UEMR can be easily adopted by those with experience with conventional EMR.[12] It is possible the residual/recurrence rate was under-estimated by lack of dedicated biopsies of the EMR scar site. However, we used an established protocol for scar site inspection which closely mirrors routine biopsies for detection of residual neoplasia.[22] Therefore, it is doubtful that routine follow-up biopsies would have substantially affected the observed recurrence rate in our study.

Conclusions

In this large community-based series we found UEMR for large sessile colorectal polyps to be highly efficacious and safe, with a low rate of residual/recurrent neoplasia on endoscopic follow-up. Based on available literature consistent with these findings, we believe UEMR is a favorable first-line approach to large colorectal lesions.

Declaration of competing interest

Manuscript title: Underwater endoscopic mucosal resection without submucosal injection (UEMR) for large polyps: A community-based series.

The authors whose names are listed below certify that they have no affiliations with or involvement in any organization or entity with any financial interest in the subject matter or materials discussed in this manuscript. There are no conflicts of interest to disclose.

We confirm that this work has not been published elsewhere, nor is it currently under consideration for publication elsewhere.

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