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Depth of resection using two different endoscopic mucosal resection techniques

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Abstract

Background and study aims—Endoscopic mucosal resection (EMR) has been carried out for high-grade dysplasia (HGD) and intramucosal carcinoma (IMCA) in Barrett’s esophagus using two different cap-assisted techniques, the “inject, suck, and cut” and the “band and snare.” Previous work has demonstrated comparable specimen diameters. However, the two techniques have not been previously compared with respect to depth of resection.

Patients and methods—From a database of patients with Barrett’s esophagus, we identified 40 consecutive specimens removed using EMR from patients with HGD or IMCA, 20 each from the “inject, suck, and cut” and the “band and snare” techniques. Specimens were evaluated and measured separately by two pathologists for greatest diameter and depth, and for the presence of submucosa and muscularis propria at the deepest margin of resection. Follow-up data were collected regarding clinical outcome and stricture formation.

Results—The mean depth of the specimens from the two techniques was not significantly different (0.51 cm vs. 0.50 cm, $P = 0.76$). All specimens contained substantial submucosa, allowing accurate staging of the neoplastic lesions resected. Muscularis propria was identified at the base of 65% of the “band and snare” and 50% of the “inject, suck, and cut” specimens ($P = 0.52$).

Conclusions—The “inject, suck, and cut” and “band and snare” techniques both yield equivalent adequate depth of histological specimens from Barrett’s esophagus with HGD or IMCA, and both provide accurate pathological staging.

Introduction

Endoscopic therapies have been explored as alternative treatments to esophagectomy in patients with Barrett’s esophagus and high-grade dysplasia (HGD) or intramucosal carcinoma (IMCA) [1–8], where the risk of nodal metastasis is very low [9–11]. Endoscopic mucosal resection (EMR) is one such treatment option, which is increasingly being used to cure HGD and IMCA [2,5,8,12–14].

Various techniques have been utilized to perform EMR in the esophagus. One of the most commonly used methods, perfected by Inoue in Japan, involves the injection of fluid, usually saline or dilute epinephrine, into the submucosa to “lift” the area to be resected away from the muscularis propria [15]. The lifted area of mucosa and sub-mucosa is then suctioned into a cap attached to the end of the endoscope, and a cautery snare placed inside the cap is used to remove the targeted tissue. This technique allows removal of tissue into the submucosa with complete resection of areas of HGD or IMCA. EMR using this “inject, suck, and cut” technique has also been shown to be safe and associated with minimal complications [16].

A newer technique using a multiband ligator, improved by Soehendra in Germany, has been called the “band and snare” method [17]. The area in question is suctioned, usually without prior injection, into a cap attached to the end of the endoscope, and a multiband ligator is used to deploy a rubber band around the tissue. A cautery snare is then used through the ligation device to resect the mucosa and submucosa that is “trapped” in the rubber band. This technique has gained favor among many advanced endoscopists due to its efficiency and relative ease of use [16]. May and colleagues performed a prospective randomized trial of these two EMR techniques to assess size of resection and complication rates [18]. They found no difference in the mean diameters of the specimens from the two techniques. Depth of resection was not reported. The most important aspect of EMR for the treatment of HGD and IMCA is to ensure adequate depth of resection and to stage the depth of tumor invasion. The risk of lymph node metastasis is less than 1% when the tumor is confined to the mucosa and lamina propria, but rises to 35–50% once the tumor crosses the muscularis mucosa and invades the deep submucosa [9,10].

We therefore decided to compare our resection specimens with respect to depth from these two EMR techniques: the Inoue “inject, suck, and cut” method and the Soehendra “band and snare” method without injection.

Methods

Patient selection

Cases in which EMR had been performed were identified from a database of procedures performed by a single endoscopist (CJL). Consecutive cases of patients who underwent upper endoscopy with EMR for previously biopsy-proven Barrett’s esophagus with HGD or IMCA were selected. Endoscopic ultrasound with 20-MHz miniprobe and ultrasound endoscopes had been performed first (either on the same day as the EMR or during the prior endoscopy) in order to avoid carrying out EMR in patients with evident submucosal invasion or lymph node metastases. EMR was performed for one of the following reasons: (1) resection of endoscopically apparent nodular HGD or IMCA; (2) removal of multifocal flat HGD or IMCA; or (3) removal of residual nondysplastic Barrett’s esophagus after prior resection of focal HGD or IMCA.

Twenty consecutive specimens obtained using each technique (total of 40) were selected from the database for comparison. For patients in whom multiple resections were performed as part of an attempt to remove the entire Barrett’s esophagus segment, a single random specimen was selected for measurement and analysis. The changeover in use from the “inject, suck, and cut” technique to the “band and snare” technique was relatively abrupt, so for each technique the specimens were consecutive in time. All follow-up upper endoscopies, pathology, and complications were recorded.

All procedures were performed at Columbia University Medical Center. The study was approved by the Columbia University Institutional Review Board.

Procedure

The two EMR techniques were as follows. The “inject, suck, and cut” technique was performed using the Olympus EMR K-001 kit [internal cap volume 0.049 in^3 (0.80 cm^3)]. Dilute 1:200 000 epinephrine, 10–20 mL, was injected into the submucosa of the targeted area in order to lift the tissue. The raised area was then sucked into a cap and subsequently removed using a crescent-shaped cautery snare provided as part of the kit. The “band and snare” technique was performed using the Duette system [internal cap volume 0.042 in^3 (0.69 cm^3)] by Cook Endoscopy. The targeted area was sucked into a cap at the end of the endoscope, and a rubber band was then deployed around the suctioned tissue. A hexagonal cautery snare was passed around the newly formed “polyp” to perform the resection, with the goal of resecting below the band.

Histological analysis

Specimens were sectioned at 2- to 3-mm intervals, and three 5-3m-thick levels were cut from each formalin-fixed, paraffin-embedded tissue block and stained with hematoxylin and eosin (H&E). The greatest depth was measured under the microscope with an ocular micrometer. Mean and standard deviation of the depth of the specimens were calculated for each technique.

Power and statistical analysis

Assuming a mean resection depth of 0.5 cm for the “inject, suck, and cut” technique, we calculated that 16 specimens of each technique (32 total) would be needed to demonstrate with 80% power a difference in depth of 0.1 cm between the two techniques, assuming a common standard deviation of 0.1 cm. Fisher’s exact test was used for all categorical variables, and a two-sided Student’s *t*-test was used for comparison of continuous variables. Statistical significance was defined as $P < 0.05$. Inter-cooled Stata 9.2 (StataCorp., College Station, Texas, USA) was used for all statistical analyses.

Results

A total of 40 EMR specimens were reviewed from 31 different patients. The patient characteristics are shown in Table 1. There were no significant differences with respect to sex, race, or age between the two groups. Twelve of the specimens (30%) were resected from mucosa that appeared nodular on endoscopy. In all but one of the cases, the nodular area was removed in piecemeal fashion.

There was no significant difference in the mean depth of the resection specimens using the two techniques (Fig. 1). The specimens from the “inject, suck, and cut” technique had a mean depth of 0.50 cm as compared to 0.51 cm for the “band and snare” resection specimens ($P = 0.76$). There was no significant difference in the depth of resection between endoscopically nodular and flat mucosa (0.53 cm vs. 0.49 cm, respectively; $P = 0.32$).

There was no significant difference between the two techniques in the endoscopic appearances or in the degrees of neoplasia found in the EMR specimens (Table 2). All of the nodular specimens contained at least low-grade dysplasia. None of the 20-MHz miniprobe ultrasound examinations revealed submucosal invasion, although in two specimens histological evaluation showed invasive adenocarcinoma extending through the muscularis mucosa.

The median follow-up time for the 31 patients was 18 months (range 0–39 months). One patient was lost to follow-up. A mean of 3.5 (range 0–9) subsequent upper endoscopies was performed. Nearly half of the patients (15/31, 48.4%) underwent additional ablative

techniques, such as argon plasma coagulation and radiofrequency ablation. The histology results of the last follow-up endoscopies are shown in Table 3. A total of 65% (20/31) of patients had either no Barrett's esophagus or residual non-dysplastic Barrett's esophagus only. Three patients (9.7%) elected to undergo esophagectomy: one for invasive adenocarcinoma, one for IMCA, and one for HGD.

There were no perforations as a result of EMR. Eight patients (25.8%) developed strictures requiring dilation. A higher but nonsignificant proportion of patients who underwent the "band and snare" technique developed strictures compared to those in whom the "inject, suck, and cut" technique was used (33.3% vs. 15.4%, respectively; $P = 0.24$). No circumferential mucosal resections were performed. All but one of the patients who developed a stricture did so after large but noncircumferential resections (50–90%); the remaining one had a 50% circumferential resection, but only developed a stricture after circumferential radio-frequency ablation was performed on a subsequent endoscopy. Ten other patients had circumferential ablation performed (7 argon plasma coagulation, 3 radiofrequency ablation) after EMR, none of whom developed strictures.

Many of the specimens from both techniques were noted to include small amounts of muscle from the muscularis propria at the deep cautery margin. This finding was present in the specimens from both techniques (Fig. 2). There was no statistically significant difference between the two techniques in the proportion of specimens containing muscularis propria [50% (10/20) for "suck and cut" vs. 65% (13/20) for "band and snare", $P = 0.52$].

Discussion

The results of this study demonstrate that the "inject, suck, and cut" and the newer "band and snare" techniques for EMR produce resection specimens that are comparable in depth. The goal of EMR is to remove the entire mucosa and most of the sub-mucosa to provide precise pathological staging of depth of tumor invasion and to ensure complete resection of IMCA. Analysis of our resection specimens shows that this can be successfully achieved using either of the two EMR techniques.

Upon examining the pathology specimens, we noted that there was a marked amount of tissue edema within the submucosa of the specimens from the "inject, suck, and cut" technique, related to the fluid (dilute epinephrine) injected into the submucosa prior to resection. However, there was no difference in the depth of the resections between the two techniques, and the presence of muscularis propria near the cautery margins in the specimens was not significantly different between the techniques. The "band and snare" technique was associated with a nonsignificantly increased proportion of patients who developed strictures by comparison to the "inject, suck, and cut" technique. All but one of the strictures occurred immediately after the mucosal resection. However, we were unable in all cases to account for the percentage of circumference resected, an important confounder in assessing stricture rates. Further investigation is warranted to determine whether there is a true difference in risk of stricture between the two techniques.

Over a median follow-up time of 18 months, 65% of the subjects in this study had a complete response, defined as having either nondysplastic Barrett's esophagus or no residual Barrett's esophagus, and many patients are still undergoing treatment. No patients died of esophageal adenocarcinoma. Our study was not designed to specifically evaluate clinical response to EMR, and we included a heterogeneous group of patients. All but one of the patients (96.7%) in our study had either flat HGD or IMCA or had nodularity removed in a piecemeal fashion, in which lateral margins could not be assessed.

While techniques continue to evolve, EMR has become an established method for the treatment of HGD and IMCA in Barrett's esophagus. This study demonstrates that two of the most popular cap-assisted techniques currently used to perform EMR provide equivalent tissue specimens for accurate staging and the possibility of complete cure. Sequential radical resection of all Barrett's mucosa (Fig. 3) in patients with HGD and IMCA has been reported to be a very promising means to replace surgical esophagectomy [5,8,17,18]. A persistent problem with circumferential piecemeal resection of Barrett's mucosa using various EMR techniques has been a high incidence of esophageal stricture [8,17,18]. Since the "inject, suck, and cut" and "band and snare" techniques have been shown to result in equivalent depths of resection, prospective studies would seem warranted to compare the two methods for efficacy and safety in the complete resection of Barrett's mucosa in patients with early neoplasia.

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Fig. 1. Comparison of mean depth of resection from the "band and snare" and "inject, suck, and cut" EMR techniques.

Fig. 2. EMR specimens of Barrett's esophagus. **a** Specimen with low-grade dysplasia using the "band and snare" technique (magnification $\times 2$, H&E). **b** Specimen with high-grade dysplasia using the "inject, suck, and cut" technique (magnification $\times 2$, H&E).

Fig. 3. Endoscopic view of patient with Barrett's esophagus with high-grade dysplasia **a** before and **b** after endoscopic mucosal resection using the "band and snare" technique (endoscope was slightly rotated for image **b**).

Table 1

Characteristics of patients who underwent endoscopic mucosal resection

	Technique		<i>P</i> value
	“Inject, suck, and cut”	“Band and snare”	
No. of specimens	20	20	
No. of patients	13	18	
Sex			0.62
Male	12 (92 %)	15 (83 %)	
Female	1 (8 %)	3 (17 %)	
Race/ethnicity			
White	13 (100 %)	18 (100 %)	1.00
Mean age, years (SD)	58.7 (9.6)	59.9 (12.9)	0.74

Table 2

Comparison of the specimens from the two techniques with respect to the highest degree of neoplasia found in each specimen

	Technique		<i>P</i> value
	“Inject, suck, and cut”	“Band and snare”	
Number of specimens	20	20	
Endoscopic appearance			0.30
Flat	16	12	
Nodular	4	8	
Histology *			0.17
Normal	5	0	
Barrett’s without dysplasia	1	2	
Low-grade dysplasia	1	2	
High-grade dysplasia	9	10	
Intramucosal carcinoma	4	4	
Invasive adenocarcinoma	0	2	

* Highest degree of neoplasia detected in each specimen.

Table 3

Results of final follow-up endoscopies in patients who underwent endoscopic mucosal resection

	No.	%
Histology [*]		
Normal	14	45.2
Barrett's esophagus	6	19.4
Low-grade dysplasia	3	9.7
High-grade dysplasia	5	16.1
Intramucosal carcinoma	1	3.2
Invasive adenocarcinoma [†]	1	3.2
Lost to follow-up	1	3.2

^{*} Highest degree of neoplasia detected.

[†] Pathology from esophagectomy specimen.