Comparative Outcomes of Cap Assisted Endoscopic Resection and Endoscopic Submucosal Dissection in Dysplastic Barrett's Esophagus

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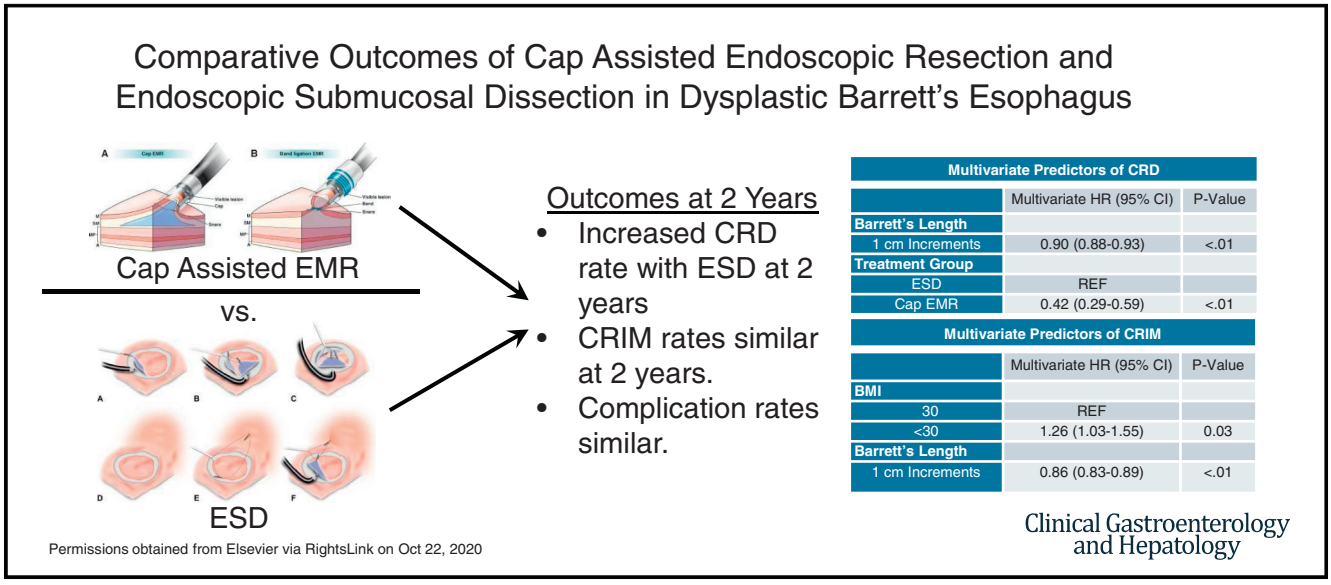
This article has an accompanying continuing medical education activity, also eligible for MOC credit, on page e7. Upon completion of this CME Exam successful learners will be able to demonstrate knowledge of endoscopic management of Barrett's esophagus.



BACKGROUND & AIMS: **Endoscopic resection is an important component of the endoscopic treatment of Barrett's esophagus (BE) with dysplasia and intramucosal adenocarcinoma. Endoscopic resection can be performed by cap-assisted endoscopic mucosal resection (cEMR) or endoscopic submucosal dissection (ESD). We compared the histologic outcomes of ESD vs cEMR, followed by ablation.**

METHODS: **We queried a prospectively maintained database of all patients undergoing cEMR and ESD followed by ablation at our institution from January 2006 to March 2020 and abstracted relevant demographic and clinical data. Our primary outcomes included the rate of complete remission of dysplasia (CRD): absence of dysplasia on surveillance histology, and complete remission of intestinal metaplasia (CRIM): absence of intestinal metaplasia. Our secondary outcome included complication rates.**

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Abbreviations used in this paper: BE, Barrett's esophagus; cEMR, cap-assisted endoscopic mucosal resection; CRD, complete remission of dysplasia; CRIM, complete remission of intestinal metaplasia; EAC, esophageal adenocarcinoma; EET, endoscopic eradication therapy; ER, endoscopic resection; ESD, endoscopic submucosal dissection; HGD, high-grade dysplasia; HR, hazard ratio; IQR, interquartile range; RFA, radiofrequency ablation.

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RESULTS: **We included 537 patients in the study: 456 underwent cEMR and 81 underwent ESD. The cumulative probabilities of CRD at 2 years were 75.8% and 85.6% in the cEMR and ESD groups, respectively ($P < .01$). Independent predictors of CRD were as follows: ESD (hazard ratio [HR], 2.38; $P < .01$) and shorter BE segment length (HR, 1.11; $P < .01$). The cumulative probabilities of CRIM at 2 years were 59.3% and 50.6% in the cEMR and ESD groups, respectively ($P > .05$). The only independent predictor of CRIM was a shorter BE segment (HR, 1.16; $P < .01$).**

CONCLUSIONS: **BE patients with dysplasia or intramucosal adenocarcinoma undergoing ESD reach CRD at higher rates than those treated with cEMR, although CRIM rates at 2 years and complication rates were similar between the 2 groups.**

Keywords: Barrett's Esophagus; Esophageal Adenocarcinoma; Endoscopic Eradication Therapy; Endoscopic Mucosal Resection; Endoscopic Submucosal Dissection.

Barrett's esophagus (BE) is the only known precursor lesion of esophageal adenocarcinoma (EAC), a lethal malignancy.[1] Endoscopic eradication therapies (EETs) have now become the standard of care for the treatment of dysplastic BE and intramucosal EAC, and the prevention of progression to EAC.[2] EET consists of endoscopic resection (ER) of all visible abnormalities followed by endoscopic ablation of flat residual BE mucosa.

Initially, ER used cap-assisted endoscopic mucosal resection (cEMR) using either a cap and snare technique or the band ligation technique.[3] This allowed for accurate histologic staging of disease, in addition to upstaging of pathology in 30% to 40% of cases and higher interobserver agreement among pathologists.[4] However, en bloc resection generally is possible only for lesions smaller than 1.5 cm. Larger lesions had to be resected piecemeal, preventing assessment of lateral margins and potentially increasing the rates of recurrence.[5]

More recent developments in ER include endoscopic submucosal dissection (ESD), which allows for en bloc resection of larger lesions, enabling more accurate histopathologic staging, with less diagnostic uncertainty.[6] Challenges with ESD include limited training opportunities in the West owing to a lack of large volumes of suitable pathology (such as early gastric cancer), increased time, and a higher complication rate.[7] A meta-analysis of 501 patients with BE neoplasia from 11 cohort studies showed that ESD has high rates of en bloc resection, an acceptable safety profile, and low rates of recurrent disease.[8] Data show that resection of esophageal squamous neoplasia in a piecemeal fashion is associated with higher recurrence rates than en bloc resection with ESD.[9]

A pertinent difference between the endoscopic management of gastric/colonic neoplasia and BE neoplasia is that endoscopic resection typically is followed by ablation of residual BE unlike in the stomach/colon, which likely influences histologic outcomes favorably. There are very limited comparative data on the longer-term (histologic) outcomes of BE-related neoplasia treated by cEMR followed by ablation and those treated by ESD followed by ablation. A small randomized trial of 40 patients comparing cEMR with ESD found no difference in rates of esophagectomy or complete remission of neoplasia between the treatment groups at 3 months.[10]

Hence, we aimed to assess histologic outcomes in patients with BE-related dysplasia/neoplasia undergoing initial resection with either cEMR or ESD followed by ablative therapy. Our primary outcome of interest was the rate of complete remission of dysplasia (CRD) and complete remission of intestinal metaplasia (CRIM) at 2 years. Our secondary outcome assessed the safety of these 2 approaches by comparing complication rates.

Methods

This study was approved by the Mayo Clinic Institutional Review Board.

Patient Selection

We queried a prospectively maintained database of all patients undergoing EET for the management of BE or EAC from January 2006 to March 2020 at our institution, a quaternary referral center.

Patients were included if they underwent either cEMR or ESD, followed by endoscopic ablation for management of dysplastic BE or EAC. Patients who underwent both cEMR and ESD or received surgery or chemoradiation before endoscopic therapy were excluded from the analysis.

Abstracted information included demographics, treatment details, histology, complications (perforation, clinically significant intraprocedure or postprocedure bleeding, or stricture formation requiring dilation within 120 days of the initial procedure), and date of last follow-up evaluation. For patients undergoing cEMR, we also abstracted whether the cap and snare or band ligation method was used.

Methods of Endoscopic Eradication Therapies

More than 98% of the procedures during the study period were performed by 2 endoscopists (P.G.I. and K.K.W.) with considerable expertise in endoscopic resection

and ablation of esophageal neoplasia. Patients received general anesthesia, sedation with propofol, or conscious sedation. Patients typically were discharged after the procedure, although in certain instances (after large piecemeal resections or ESD) patients were admitted overnight for observation and discharged the next morning.

Standard diagnostic and therapeutic (if needed) endoscopes were used (Olympus, Center Valley, PA; or Fujinon-Fujifilm Medical Systems USA, Lexington, MA). Lesions were assessed carefully with narrow-band imaging (including near focus) and marked circumferentially with cautery before resection. In general, cEMR was used for lesions less than 1 to 1.5 cm in diameter, and ESD was used for larger lesions. ESD has been used at our institution since 2015.

What You Need to Know

Background

Cap-assisted endoscopic mucosal resection (cEMR) and endoscopic submucosal dissection (ESD) are used in the treatment of Barrett's neoplasia. Long-term comparative outcomes are uncertain.

Findings

A review of patients at our institution undergoing cEMR vs ESD for management of Barrett's neoplasia showed higher rates of clinical remission of dysplasia for ESD patients, but no difference in clinical remission of intestinal metaplasia at 2 years, even after adjustment for confounding variables in a multivariate model. Complication rates were similar between the 2 treatment groups.

Implications for patient care

cEMR and ESD followed by ablation appear to be equally effective in the management of Barrett's neoplasia, although ESD leads to clinical remission of dysplasia faster and may be preferable in larger lesions given the ability to assess lateral margins. Long-term recurrence outcomes in the 2 strategies need to be studied.

Cap-Assisted Endoscopic Mucosal Resection Procedure

We previously described the cEMR technique.[3] A hard cap (EMR001; Olympus USA) was fitted onto the end of the endoscope. A saline and epinephrine solution was injected submucosally under the lesion of interest. A crescent-shaped snare (SnareMaster Crescent; Olympus USA) was seated on the inner aspect of the cap, followed by suction of the lesion into the cap, closure of the snare, and resection using a combination of cutting and coagulation current from an electrosurgical generator using 16 W blended current (Conmed Beamer; Conmed USA, Utica, NY). For band-ligator EMR, either the Duette Multi-Band Mucosectomy System (Cook Medical, Bloomington, IN) or the Captivator EMR System (Boston Scientific, Marlborough, MA) was used. In both kits, a preloaded band ligator was attached to the endoscope to allow for sequential banding of mucosa. Afterward, a hexagonal snare was used to resect the banded tissue with electrocautery.

Endoscopic Submucosal Dissection Procedure

The Olympus water jet endoscope (180J) was used with a soft plastic cap attached to the end of the endoscope. A methylene blue, epinephrine, and hydroxyl methyl propyl cellulose solution was injected submucosally under the lesion of interest. Incision and dissection were performed with endoscopic knives, including the DualKnife (Olympus USA), HookKnife (Olympus USA), IT Knife (Olympus USA), or Clutch Cutter (Fujifilm Medical USA) at the discretion of the proceduralist.[11] A standard electrosurgical generator (VIO 300D, ENDO CUT Q; Erbe USA, Inc, Marietta, GA) was used with appropriate current settings as previously described.[12] Resected specimens were pinned to a Styrofoam (Dow Chemical Company, Midland, MI) piece, and submitted to pathology for interpretation (Figure 1).

All pathology was read by pathologists with expertise in gastrointestinal pathology. R0 resections were defined as EAC/high-grade dysplasia (HGD) with both deep and lateral margins negative for dysplasia.

Follow-up Evaluation

After initial resection, patients were followed up at 3-month intervals to assess for the presence of and treat residual neoplasia and BE.[13,14] Careful inspection of the esophageal mucosa was performed with both high-definition white-light endoscopy and narrow-band imaging, surveillance biopsy specimens were obtained,[15] and ablation was accomplished using radiofrequency ablation (RFA) (BarrX device; Medtronic, Minneapolis, MN), liquid nitrogen cryoablation (TruFreeze spray cryotherapy system; Steris, Mentor, OH), or balloon cryoablation (CryoBalloon Focal Ablation System; Pentax Medical, Montvale, NJ). This was applied using standard manufacturer-recommended methodology.

Primary and Secondary Outcomes

Our primary end points were the rate and time to CRD (defined as the absence of dysplasia on biopsy specimens from the tubular esophagus and gastroesophageal junction, during at least 1 surveillance endoscopy), and the rate and time to CRIM (defined as the absence of intestinal metaplasia on biopsy specimens from the tubular esophagus and gastroesophageal junction, during at least 1 surveillance endoscopy). Our secondary outcome was the

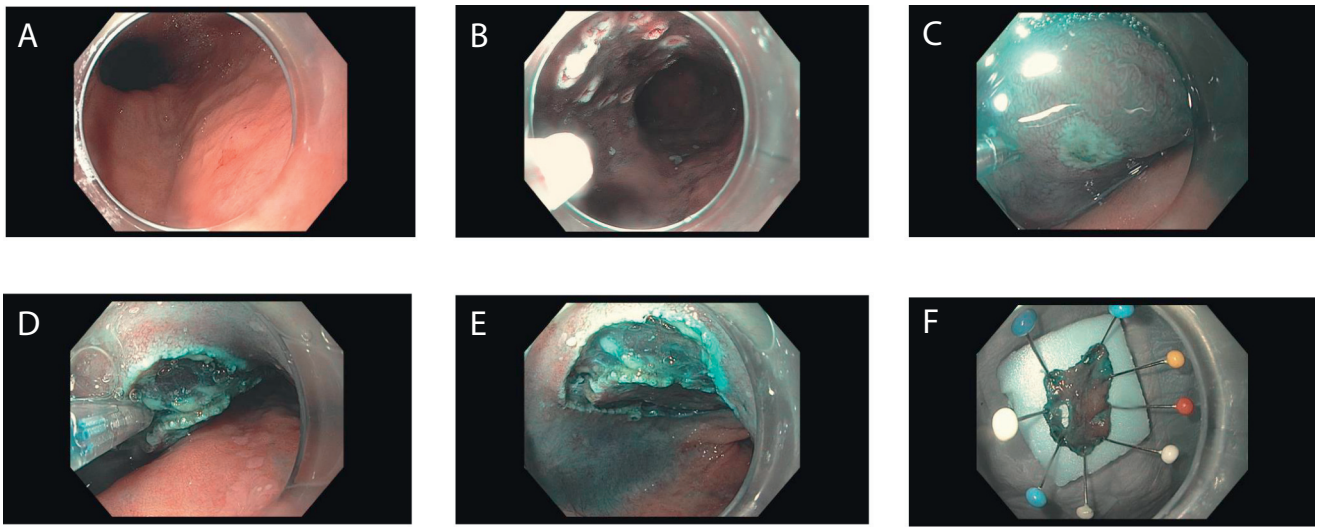

Figure 1. (*A*) A nodular area is noted in Barrett's esophagus mucosa. (*B*) The margins of the lesion are marked with cautery. (*C*) Methylene blue saline injection is used to lift the lesion. (*D*) Dissection proceeds using the Hook Knife (Olympus USA). (*E*) The dissection bed after removal of the lesion. (*F*) Pinning of the resected lesion to Styrofoam (Dow Chemical Company, Midland, MI).

rate of complications (including perforation, clinically significant intraprocedure or postprocedure bleeding requiring hospitalization, endoscopic assessment/therapy or receipt of red blood cells within 30 days, or stricture formation requiring dilation within 120 days of the initial procedure). An a priori subgroup analysis also was planned to assess outcomes between patients who underwent piecemeal cEMR (those with >1 resection piece per lesion) vs those who underwent ESD because piecemeal cEMR is performed in larger lesions that may be comparable in size with those that received ESD.

Statistical Analysis

For continuous variables, descriptive statistics were presented as means (with SD) and for discrete variables as numbers (percentage). The Kaplan–Meier method was used to estimate the cumulative probability of CRD and CRIM, and cumulative probability curves were generated that examined the time to outcomes of interest based on treatment modality. Cox proportional hazards models were used to assess the association of baseline covariates with the outcomes of CRD and CRIM. Variables of interest in the models included age (in 10-year increments), sex, body mass index (as <30 vs ≥ 30), history of ever smoking, length of BE at initial procedure, presence of a hiatal hernia, treatment group (cEMR vs ESD), and histology at baseline procedure (low-grade dysplasia vs HGD/EAC). The α level was set at .05 for statistical significance.

Results

From January 2006 to June 2020, we identified 537 patients who underwent either cEMR or ESD followed by ablation, of whom 456 underwent cEMR and 81 underwent ESD.

Basic demographics between the 2 groups appeared similar (Table 1). The mean length of resected specimens was larger in the ESD group (23.9 vs 10.9 mm), and the rates of en bloc and R0 resection also were higher in the ESD group. On final histology there were 88 cases (19.3%) of EAC in the EMR group, and, of these, 70 (79.5%) were stage T1a and 18 (20.5%) were stage T1b. In the ESD group, 40 cases (49.4%) of EAC were diagnosed, with 27 (67.5%) stage T1a and 13 (32.5%) stage T1b. Most patients within the EMR group received RFA, while 25 (5.5%) received cryotherapy. In the ESD group, 52 (64.2%) patients received RFA and 11 (13.1%) received cryotherapy.

Primary Outcomes: Complete Remission of Dysplasia and Complete Remission of Intestinal Metaplasia

In total, 420 patients in the cEMR group achieved CRD over a median follow-up period of 11.2 years (interquartile range [IQR], 6.5–15.7 y), while 48 patients in the ESD group achieved CRD over a median follow-up period of 1.4 years (IQR, 0.8–2.0 y).

The Kaplan–Meier curve (Figure 2) shows that the 2-year cumulative probability of CRD was lower in cEMR patients compared with ESD patients (75.8% vs 85.6%). Furthermore, univariate analysis showed significantly lower odds of achieving CRD in cEMR patients (hazard ratio [HR], 0.41; 95% CI, 0.31–0.54; $P < .01$).

To assess whether improvements in cEMR technique over time may have contributed to the results, an analysis comparing cEMR (N = 48) with ESD (N = 80) in patients undergoing procedures from 2015 to 2019 showed that the odds of CRD remained lower than that of ESD (HR, 0.67; 95% CI, 0.45–0.99) (Supplementary

Table 1. Baseline Demographics and Procedural Outcomes

	Cap EMR (N = 456)	ESD (N = 81)	*P* value
Demographics			
Age, *y*			**<.01**
Mean (SD)	65.2 (9.8)	68.6 (10.3)	
Sex, N (%)			.83
Male	382 (83.8)	67 (82.7)	
Female	74 (16.2)	14 (17.3)	
Body mass index			**.02**
Mean (SD)	31.1 (5.5)	29.4 (5.1)	
Smoking status			.35
Current	52 (11.4%)	9 (11.1%)	
Past	262 (57.5%)	44 (54.3%)	
None	121 (26.5%)	27 (33.3%)	
Unknown	21 (4.6%)	1 (1.2%)	
Maximal Barrett's length			.26
Mean (SD)	5.8 (3.7)	6.3 (4.0)	
Hiatal hernia			.43
Present, N (%)	380 (83.3)	55 (87.3)	
Mean follow-up period, *y* (IQR)	11.2 (6.5–15.7)	1.4 (0.8–2.0)	**<.01**
Procedural details and outcomes			
Mean (SD) length of resected specimen, *mm*	10.9 (3.4)	23.9 (9.6)	**<.01**
In patients undergoing piecemeal EMR, mean (SD) length of lesion, *mm*[a]	21.8 (10.3)		
In patients undergoing piecemeal EMR, mean (SD) number of resected pieces	3.4 (1.8)		
Preresection worst histology			.89
LGD	90 (19.6%)	15 (20.3%)	
HGD + EAC	369 (80.4%)	59 (79.7%)	
Postresection worst histology			.31
LGD	76 (19.1%)	19 (24.1%)	
HGD + EAC	322 (80.9%)	60 (75.9%)	
EAC histology	88	40	**<.01**
T1a	70 (79.5%)	27 (67.5%)	
T1b	18 (20.5%)	13 (32.5%)	
Ablation methods, n (%)			**<.01**
Radiofrequency	456 (100)	52 (64.2)	
Spray cryotherapy	23 (5.0)	5 (6.2)	
Balloon cryotherapy	2 (0.4)	6 (7.4)	
EMR method (%)			
Cap and snare	274 (60.1)		
Band ligator	175 (38.4)		
ESD knives (%)			
Clutch-Cutter		42 (51.9)	
Hook Knife		37 (45.7)	
En bloc resection (%)	191 (41.9)	79 (97.5)	**<.01**
R0 resection (%)	92 (20.2)	47 (58.0)	**<.01**

NOTE. Boldface indicates significance.
EAC, esophageal adenocarcinoma; EMR, endoscopic mucosal resection; ESD, endoscopic submucosal dissection; HGD, high-grade dysplasia; IQR, interquartile range; LGD, low-grade dysplasia; SD, standard deviation.
[a]Of 117 who had lesion size described in a procedure note before resection.

Figure 1). Furthermore, within the cEMR group, higher odds of achieving CRD were found in later years (2013–2019; N = 129) compared with earlier years (2006–2012; N = 112) of study (HR, 2.09; 95% CI, 1.59–2.75; $P < .01$).

Cox proportional hazard models were developed incorporating variables in Table 2. Longer BE segment length was associated with decreased odds of CRD (HR, 0.90; $P < .01$), as was treatment with cEMR (HR, 0.42; $P < .01$) compared with ESD.

In total, 358 patients (78.5%) in the cEMR group and 33 (40.7%) in the ESD group achieved CRIM. The median follow-up period was 7.8 years (IQR, 3.1–10.5 y) in the cEMR group and was 1.1 years (IQR, 0.6–1.8 y) in the ESD group.

The Kaplan–Meier curve in Figure 3 illustrates that although patients in the ESD group tended to achieve CRIM sooner than in the cEMR group, by 2 years the cumulative probabilities for CRIM in the cEMR and ESD groups were comparable at 59.3% (95% CI, 54.3–63.7)

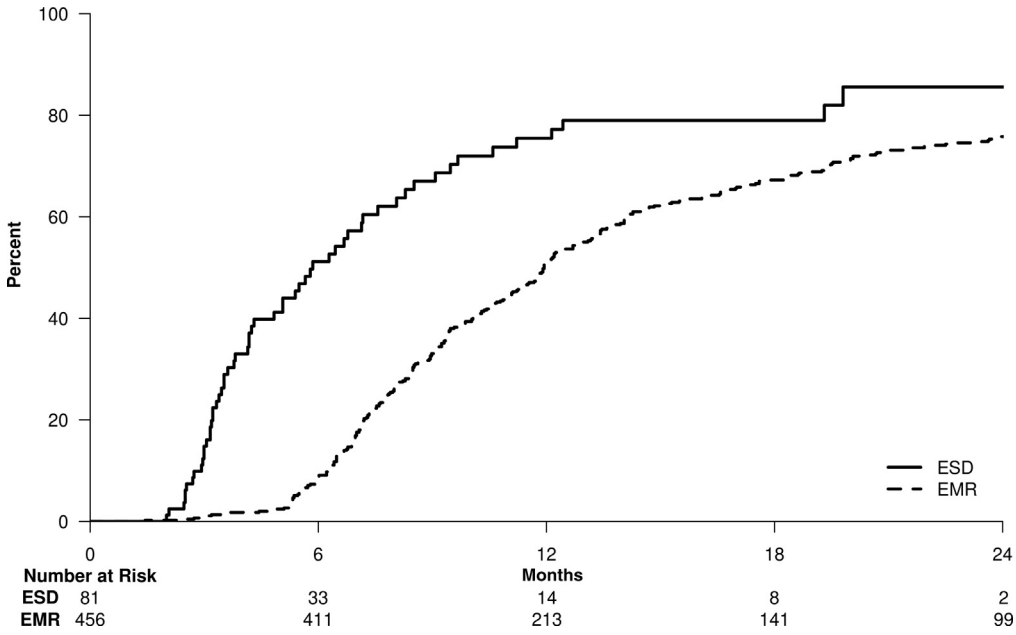

Figure 2. Kaplan–Meier curve for achieving complete remission of dysplasia. At 2 years, the rates of achieving complete remission of dysplasia were higher ($P <$ .01) in the endoscopic submucosal dissection (ESD) group (85.6%; 95% CI, 70.5%–94.3%) compared with the cap-assisted endoscopic mucosal resection (cEMR) group (75.8%; 95% CI, 71.4%–79.5%).

and 50.6% (95% CI, 34.9–69.0), respectively. Overall, there was no statistically significant difference between the 2 groups in achieving CRIM (cEMR relative to ESD: HR, 0.74; 95% CI, 0.52–1.07; $P = .11$).

An analysis comparing cEMR (n = 48) with ESD (n = 81) in patients undergoing procedures from 2015 to 2019 showed that the odds of CRIM achievement were not statistically significant between the treatment modalities (HR, 0.88; 95% CI, 0.54–1.43; $P = .6$) (Supplementary Figure 2). However, within the cEMR group, higher odds of achieving CRIM also were found in later years (2013–2019) compared with the earlier years (2006–2012) of study (HR, 2.01; 95% CI, 1.50–2.69; $P < .01$).

Table 2. Predictors of Complete Remission of Dysplasia in Barrett's Esophagus Patients Undergoing Endoscopic Therapy

	Univariate HR (95% CI)	*P* value	Multivariate HR (95% CI)	*P* value
Age				
10-year increments	1.04 (0.95–1.15)	.36	1.03 (0.93–1.40)	.55
Sex				
Female	Ref		Ref	
Male	1.12 (0.88–1.44)	.35	1.25 (0.97–1.61)	.09
BMI				
≥30	Ref		Ref	
<30	0.94 (0.78–1.12)	.47	1.19 (0.99–1.44)	.07
Smoking				
Never	Ref		Ref	
Ever	1.20 (0.99–1.46)	.06	1.15 (0.93–1.41)	.20
Barrett's length				
1-cm increments	0.91 (0.89–0.94)	<.01	0.90 (0.88–0.93)	**<.01**
Hiatal hernia				
Absent	Ref		Ref	
Present	0.90 (0.71–1.16)	.42	0.96 (0.74–1.25)	.76
Treatment group				
ESD	Ref		Ref	
Cap EMR	0.41 (0.31–0.54)	**<.01**	0.42 (0.29–0.59)	**<.01**
Worst histology				
HGD/EAC	Ref		Ref	
LGD	1.02 (0.82–1.27)	.89	0.99 (0.78–1.25)	.93

NOTE. Boldface indicates significance.
BMI, body mass index; EAC, esophageal adenocarcinoma; EMR, endoscopic mucosal resection; ESD, endoscopic submucosal dissection; HGD, high-grade dysplasia; HR, hazard ratio; LGD, low-grade dysplasia.

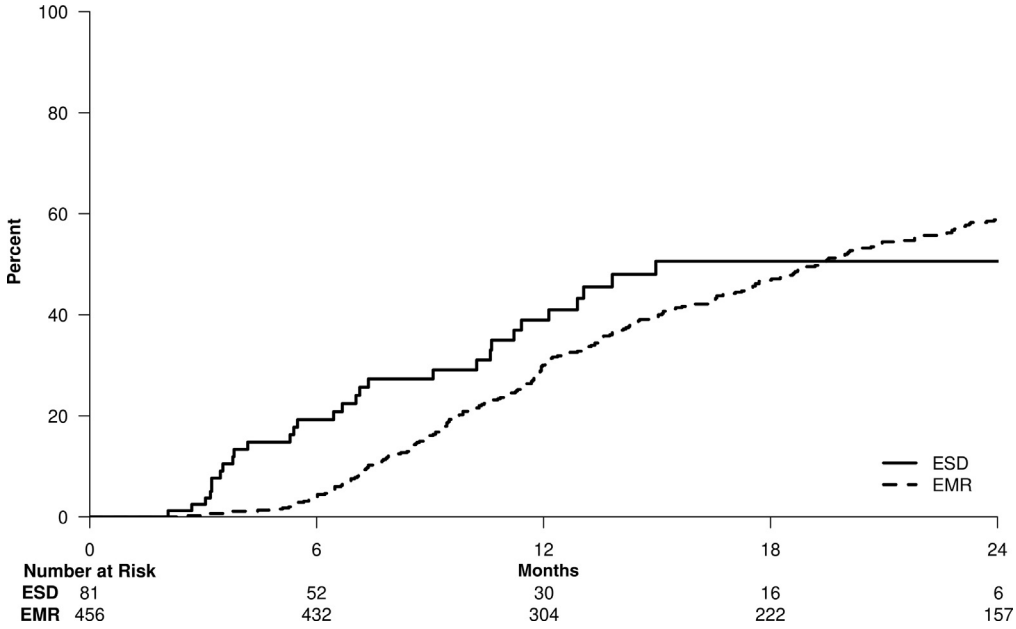

Figure 3. Kaplan–Meier curve for achieving complete remission of intestinal metaplasia. At 2 years, rates of achieving complete remission of intestinal metaplasia in the endoscopic submucosal dissection (ESD) group (50.6%; 95% CI, 34.9%–69.0%) and the cap-assisted endoscopic mucosal resection (cEMR) group (59.3%; 95% CI, 54.3%–63.7%) were comparable ($P = .11$).

On multivariate analysis, the 2 variables associated significantly with achievement of CRIM were longer BE length, associated with a lower probability of achieving CRIM (HR, 0.86; $P < .01$), and body mass index less than 30, which was associated with a higher probability of CRIM (HR, 1.26; $P = .03$) (Table 3).

Secondary Outcome: Complications

Complication rates did not differ significantly between the treatment groups. Clinically relevant bleeding occurred in 2 cases each in both treatment groups (cEMR, 0.4%; ESD, 2.5%; $P = .11$). There were no

Table 3. Predictors of Complete Remission of Intestinal Metaplasia in Barrett's Esophagus Patients Undergoing Endoscopic Therapy

	Univariate HR (95% CI)	*P* value	Multivariate HR (95% CI)	*P* value
Age				
10-year increments	0.93 (0.84–1.03)	.15	0.96 (0.86–1.06)	.40
Sex				
Female	Ref		Ref	
Male	1.01 (0.78–1.32)	.93	1.14 (0.86–1.50)	.36
BMI				
≥30	Ref		Ref	
<30	0.93 (0.77–1.14)	.51	1.26 (1.03–1.55)	**.03**
Smoking				
Never	Ref		Ref	
Ever	1.12 (0.91–1.39)	.28	1.02 (0.82–1.28)	.84
Barrett's length				
1-cm increments	0.86 (0.83–0.89)	**<.01**	0.86 (0.83–0.89)	**<.01**
Hiatal hernia				
Absent	Ref		Ref	
Present	0.78 (0.60–1.02)	.07	0.83 (0.63–1.10)	.19
Treatment group				
ESD	Ref		Ref	
Cap EMR	0.74 (0.52–1.07)	.11	0.78 (0.48–1.27)	.32
Worst histology				
HGD/EAC	Ref		Ref	
LGD	0.9 (0.71–1.16)	.42	1.10 (0.85–1.42)	.47

NOTE. Boldface indicates significance.
BMI, body mass index; EAC, esophageal adenocarcinoma; EMR, endoscopic mucosal resection; ESD, endoscopic submucosal dissection; HGD, high-grade dysplasia; HR, hazard ratio; LGD, low-grade dysplasia.

perforations in either group. Strictures occurred in 17 cEMR patients (3.8%) and in 4 ESD patients (5.9%), but this difference also was not statistically significant ($P = .50$).

A Priori Sensitivity Analyses

We assessed histologic outcomes between patients receiving piecemeal cEMR (>1 resection specimen per procedure) and those receiving en bloc ESD. Of the cEMR patients, 266 underwent piecemeal cEMR. The average size of cEMR lesions undergoing piecemeal resection was 21.8 (SD, ±10.3) mm, compared with 23.9 (SD, ±9.6) mm in the ESD treatment group. The mean number of specimens resected in the piecemeal EMR group was 3.4 (SD, ±1.8). ESD was associated with a significantly higher probability of achieving CRD compared with piecemeal cEMR on univariate and multivariate analysis (multivariate HR, 2.23; 95% CI, 1.55–3.21; $P < .01$). However, there was no significant difference in achieving CRIM between ESD and piecemeal cEMR (HR, 1.37; 95% CI, 0.66–1.79; $P = .30$). Within the cEMR group, piecemeal resection was associated with a higher probability of CRIM (HR, 1.34; 95% CI, 1.08–1.66; $P < .01$) and CRD (HR, 1.24; 95% CI, 1.02–1.51; $P = .04$).

Discussion

We analyzed a comprehensive, prospectively maintained database of all patients at our institution receiving endoscopic treatment of dysplastic BE or early stage EAC with cEMR vs ESD followed by endoscopic ablation. The vast majority of procedures were performed by 2 endoscopists experienced in BE endotherapy. We show that CRD was achieved in a higher proportion of patients receiving ESD compared with cEMR at 2 years. However, the odds of patients achieving CRIM were similar at 2 years after initial resection. Although we did observe that histologic outcomes improved over time in the cEMR group, potentially owing to improvements in cEMR or ablation techniques, the difference in histologic outcomes between the 2 groups persisted in patients treated after 2015.

The solitary study to date that evaluated comparative histologic outcomes of ESD with cEMR was a small randomized trial of 40 patients. The primary outcome was R0 resection, with a secondary outcome of complete remission of neoplasia (defined as an absence of HGD or EAC on at least 1 follow-up endoscopy) at 3 months.[10] Rates of neoplasia remission were similar between the groups. CRD and CRIM rates were not reported. Our results substantially extend these findings. In addition to longer follow-up periods, our more stringent criteria for CRD may explain why our CRD and CRIM rates are lower than the neoplasia remission rates reported by Terheggen et al.[10]

Another observation from our study was the higher rate of CRD in the ESD group, with a comparable rate of CRIM between the 2 groups after ablation after resection. Lower rates of CRIM compared with CRD have been observed in many endoscopic eradication therapy trials and likely reflect the persistence of nondysplastic BE epithelium after the eradication of dysplasia and the longer time taken to achieve CRIM.[16,17] Faster progression to CRD in the ESD group may reflect that larger resected specimens leave less residual flat BE mucosa to be treated. On multivariate analysis, as the length of BE increased, the likelihood of CRD decreased, which is consistent with this line of reasoning. Supporting this theory, our study showed that rates of CRD were higher in the ESD group compared with the piecemeal EMR group as well because the latter group may not remove as much residual BE as the ESD group. In a recent study we showed that the goal of endoscopic therapy for dysplastic BE should be CRIM given the higher risk of recurrence after achieving only CRD.[18]

Our other outcomes (CRIM rates and complication rates) were consistent with findings reported in the literature.[8] A recent meta-analysis incorporating 5 studies suggested that outcomes for management of early esophageal cancer between multiband mucosectomy and cEMR were similar in regard to resection and complication rates, mirroring our results.[19]

Compared with cEMR, ESD is a newer technique, and hence follow-up time after ESD is relatively short to robustly assess recurrence outcomes. Approximately 10% of patients in the ESD group and 7% in the cEMR group received cryotherapy, which may indicate more resistant disease because cryotherapy typically was used in our practice in situations in which RFA was unable to induce CRIM. As such, our results likely include patients with more severe disease than may be found in the general population. Another limitation of our study was the lack of randomization. Propensity score matching was considered, but given the clear confounding because of the time (because ESD was performed only after 2015) in choosing which resection technique was used, this was not performed. However, our results are unlikely to be the result of time period differences because the 2 groups otherwise appeared similar in regard to patient demographics and procedures were performed in both groups by the same endoscopists with extensive experience in endoscopic therapy. In addition, our institution's database of EET procedures is maintained prospectively and updated consistently, and our ability to examine patient charts allowed us to abstract in granular detail a variety of important variables that affect clinical management of these patients.

Although cEMR has a current procedural terminology code for reimbursement, no specific code exists as of yet for ESD. There are greater capital expenses associated with ESD including specialized equipment and dedicated training, as well as longer procedural times and duration of anesthesia.[20] As such, ESD has not been as widely

adopted as cEMR. However, economic analyses have shown that ESD is still more cost effective compared with surgery, which may be the alternative if ESD is not available at an institution.[21]

In conclusion, we report that in the management of dysplastic BE with cEMR and ESD followed by endoscopic ablation, although CRD is achieved earlier and in a higher proportion of patients with ESD, CRIM rates appear to be similar between the 2 groups. In expert hands both sets of procedures appear to be safe and well tolerated. Continued monitoring for additional outcomes such as recurrence are required for further elucidation of the optimal role of these procedures in the management of BE neoplasia.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Clinical Gastroenterology and Hepatology* at www.cghjournal.org, and at https://doi.org/10.1016/j.cgh.2020.11.017.

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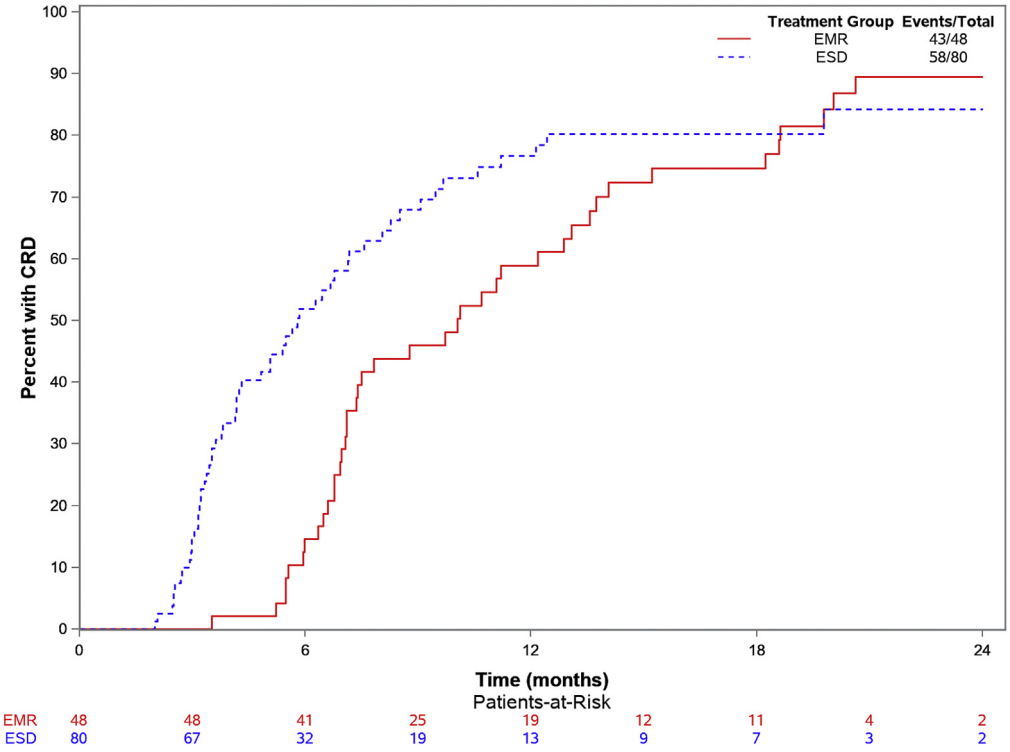
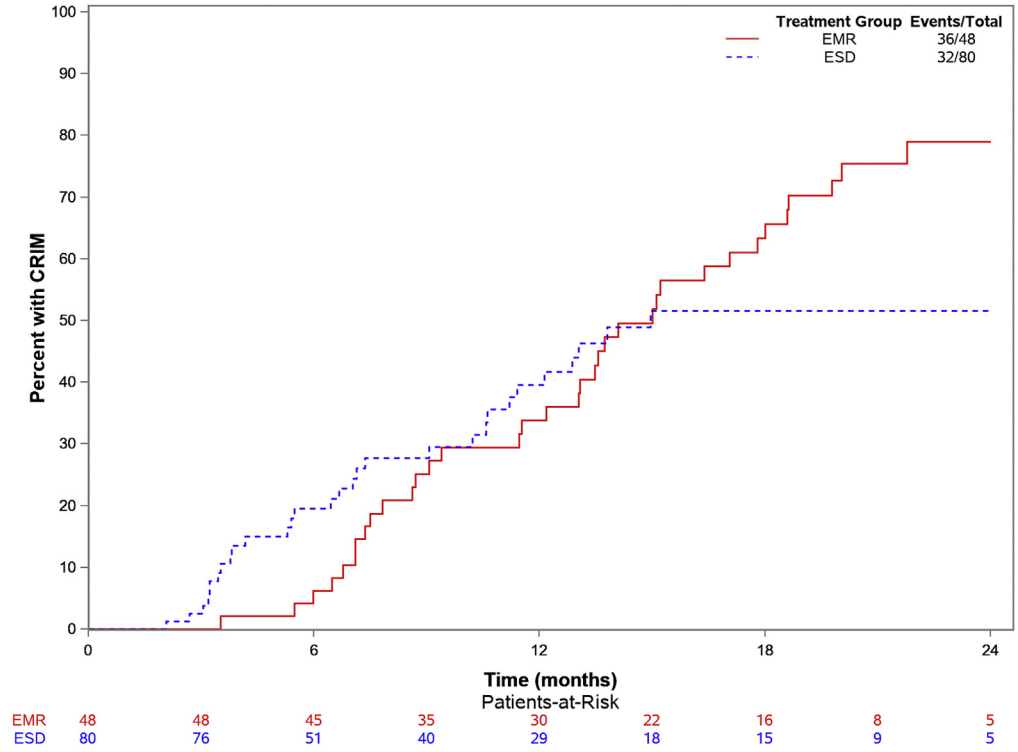


Supplementary Figure 1. Kaplan–Meier curve for achieving complete remission of dysplasia in a subset of patients treated from 2015 to 2020. The odds of complete remission of dysplasia (CRD) remained lower for cap-assisted endoscopic mucosal resection (EMR) than for endoscopic submucosal dissection (ESD) (hazard ratio, 0.67; 95% CI, 0.45–0.99).



Supplementary Figure 2. Kaplan–Meier curve for achieving complete remission of intestinal metaplasia in a subset of patients treated from 2015 to 2020. The odds of complete remission of intestinal metaplasia (CRIM) were not statistically significant between the treatment modalities (hazard ratio, 0.88; 95% CI, 0.54–1.43). EMR, endoscopic mucosal resection; ESD, endoscopic submucosal dissection.