Endoscopic resection techniques for squamous premalignant lesions and early carcinoma of the esophagus: ER-Cap, MBM, and ESD, how do we choose? A multicenter experience

Xinying Yu, Jian Chen, Zhiqiang Yuan, Hui Liu, Fugang Liu, Yong Liu, Liyan Xue, Shun He, Yueming Zhang, Lizhou Dou, Xiao Liu, Deli Zhao, Jun Li, Shaofeng Wang, Ping Zhang, Ning Lu and Guiqi Wang

Ther Adv Gastroenterol

2020, Vol. 13: 1–11

DOI: 10.1177/1756284820909172

Correspondence to:
Guiqi Wang
Department of Endoscopy, National Cancer Center/ Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, 17 Panjiayuan, Chaoyang District, Beijing 100021, P.R. China
wangguiq@126.com

Xinying Yu
Yong Liu
Shun He
Yueming Zhang
Lizhou Dou
Xiao Liu
Department of endoscopy, National Cancer Center/ Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China

Jian Chen
Deli Zhao
Department of Early diagnosis and treatment of cancer, Feicheng Peoples Hospital, Shandong, China

Zhiqiang Yuan
Jun Li
Department of Early diagnosis and treatment of cancer, Yanting Cancer Hospital, Sichuan, China

Hui Liu
Shaofeng Wang
Department of Gastroenterology, Changzhi Peoples Hospital, Shanxi, China

Fugang Liu
Ping Zhang
Department of Early diagnosis and treatment of cancer, Dongping Peoples Hospital, Shandong, China

Liyan Xue
Ning Lu
Department of pathology, National Cancer Center/ Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China

Abstract

Background: Endoscopic resection cap technique (ER-Cap), multiband mucosectomy (MBM), and endoscopic submucosal dissection (ESD) have been widely applied in the treatment of esophageal squamous neoplasia and cancer. However, little is known with regards to the comparison of these methods. This study aimed to compare the feasibility, safety, effectiveness, and costs of these three techniques.

Methods: A retrospective analysis of patients with squamous premalignant or early malignant lesions of the esophagus undergoing ER-Cap, MBM, or ESD from January 2009 to December 2015 in one of the centers in China was performed. The procedural data and follow-up data for all patients were recorded.

Results: A total of 672 patients with 733 lesions were included; 148 lesions (133 patients) were treated with ER-Cap, 427 lesions (388 patients) with MBM, and 158 lesions (151 patients) with ESD. The mean age was 61.59 years and the male-to-female ratio was 2.78:1. The operation time was significantly shorter for ER-Cap (29.26 ± 16.73 mins, $p < 0.001$) group, and the hospitalization costs were significantly lower in the MBM group ($20{,}942.03 \pm 8435.56$ ¥, $p = 0.003$). The resection sample size of ESD was significantly larger (4.40 ± 1.20 cm, $p < 0.001$) and the *en bloc* resection rate of ESD was significantly higher ($p < 0.001$) than that of the other two groups. The frequencies of perforation, bleeding, and cicatricial stenosis were significantly lower in the MBM group ($p < 0.001$, $p = 0.011$, $p = 0.009$). Three local recurrences were observed in the ER-Cap group, while no recurrence was observed in MBM and ESD groups. There were three and two metastatic patients observed in the MBM and ESD groups, respectively.

Conclusions: ER-Cap, MBM, and ESD are all minimally invasive, safe, and effective methods for treating early esophageal squamous cell carcinoma. MBM could be considered as a good alternative when performed by a less-experienced endoscopist in high-incidence areas with limited resources.

Keywords: cap-based endoscopic resection, early esophageal neoplasms, endoscopic submucosal dissection, endoscopy, multiband mucosectomy, squamous cell

Received: 1 August 2019; revised manuscript accepted: 4 February 2020.

Introduction

The use of an endoscopic resection (ER) technique is an alternate approach to surgery for treating premalignant lesions or early stage esophageal cancer. For lesions with negligible risk of lymph-node metastasis, ER is associated with fewer complications, lower morbidity rates, and lower procedure-related mortality when compared with surgery, but both these approaches demonstrated similar long-term survival rates.[1–3]

The initially available ER techniques included cap-based endoscopic resection (ER-Cap) and endoscopic submucosal dissection (ESD). ER-Cap technique is easy to perform and is associated with lower risk of complications when compared with ESD. The ER-Cap technique allows *en bloc* resection of mucosal lesions of up to 2 cm, whereas piecemeal resection is required for larger lesions. ESD is regarded as a more difficult procedure and is associated with a high risk of complications such as perforation, but with high *en bloc* resection rates and low risk of local recurrence.[4]

Multiband mucosectomy (MBM) is derived from ER-Cap and uses a modified variceal band ligator for treatment. A prospective study has revealed the feasibility, safety, and effectiveness of MBM by piecemeal resection of early mucosal squamous cell neoplasia.[5] After that, a randomized controlled trial revealed that when compared with ER-Cap, MBM is considered to be a safe, effective, and less-invasive technique with a shorter treatment time and lower cost.[6]

The efficacy and safety of ESD with ER-Cap were compared in several previous studies,[7–9] while there are few studies that compared these three techniques together. This comparison might be practically important for implementation of high-volume screening programs in areas with a high risk of esophageal squamous neoplasia, such as China.

Hence, in this study, the short-term and long-term outcomes, including operation time, hospitalization costs, *en bloc* resection rate, complications rate, local recurrences, and metastasis rate of ER-Cap, MBM, and ESD in the treatment of squamous premalignant lesions and early carcinoma of the esophagus were compared.

Methods

Patients

A retrospective chart review was performed to identify patients with squamous premalignant or early malignant lesions of the esophagus who underwent treatment with ER-Cap, MBM, and ESD from January 2009 to December 2015 at five large-volume centers in China (Cancer Hospital Chinese Academy of Medical Sciences, Dongping Peoples Hospital, Feicheng Peoples Hospital, Yanting Cancer Hospital, and Changzhi Peoples Hospital). The protocol was approved by the CICAMS Institutional Review Board (Approval Number: 13-043/719) and obtained written informed consent from all patients.

The eligibility criteria of the included patients were as follows: (a) patients with histologically proven high-grade intraepithelial squamous neoplasia (HGIN) or squamous cell carcinoma of the esophagus (SCCE), and (b) patients with more than 1 year follow-up period.

The exclusion criteria were as follows: patients (a) with any clinical evidence of metastasis at baseline, (b) with stricture of the esophagus, (c) who underwent additional treatments including chemotherapy or radiotherapy for less than 6 months after the procedure, and (d) patients with metachronous squamous cancer in other organs such as the hypopharynx or lung.

Endoscopic treatment

All procedures were conducted according to the standardized protocol for endoscopic treatment.

1. Assessment and marking of the lesion: before endoscopic resection, all patients underwent a combination of white light endoscopy, narrow-band imaging, and chromoendoscopy to evaluate the depth and boundary of the lesion. After that, a biopsy of each lesion was performed to histologically confirm the presence of HGIN or SCCE. Endoscopic ultrasonography and computed tomography (CT) scan of the chest were carried out to confirm local disease and excluded metastasis. Informed consent was obtained from all patients before initiating endoscopic treatment. All

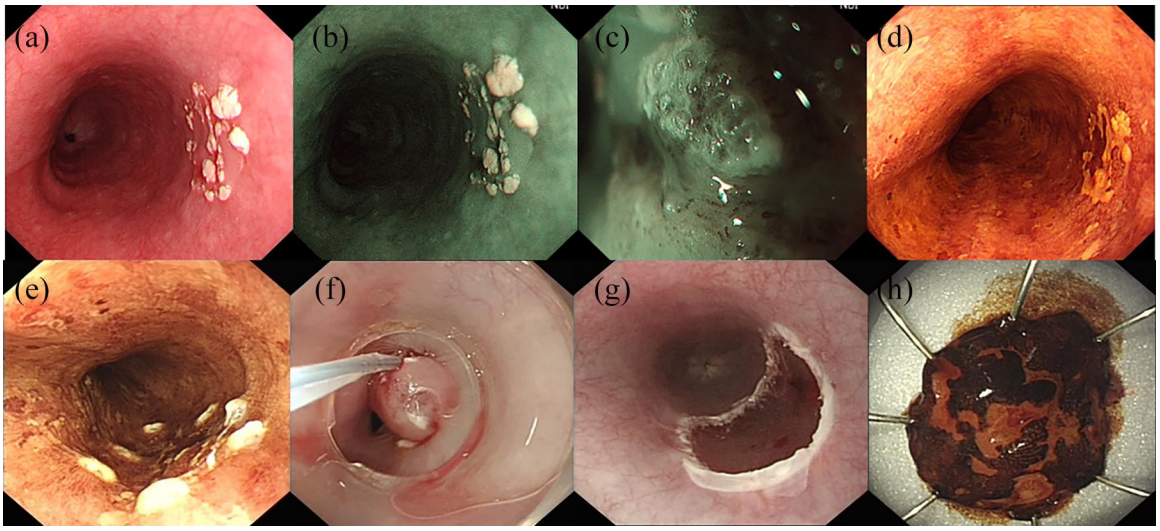

Figure 1. Endoscopic resection cap technique: (a) lesion in white light; (b) lesion in narrow-band imaging; (c) lesion in magnification endoscopy; (d) after spraying Lugol's iodine solution; (e) after making dots; (f) endoscopic resection; (g) ulcer after resection; (h) specimen.

ER treatments were performed by experienced endoscopists on patients under general anesthesia. In the beginning of the ER procedure, the endoscopist performed chromoendoscopy by spraying 20–30 ml of 1.25% Lugol's iodine solution to identify the lesion and include dots with a DualKnife (KD-650Q; Olympus) of 1–2 mm outside the margin of the lesion with a soft coagulation current of 80 W (ICC 350; ERBE).

2. Procedure of ER techniques. (a) ER-Cap. Initially, a forward-viewing endoscope (GIF-Q260J; Olympus) with a plastic cap (MAJ-1990, Olympus) on the tip was introduced into the lesion site. Saline solution mixed with methylene blue (0.04 mg/ml) and epinephrine (0.002 mg/ml) was injected into the submucosa using an injection needle (Optiflo, 25G; Boston). The endoscopist opened the snare (SD-7P-1; Olympus) within the cap, aspirated the lesion into the cap and then closed the snare. The lesion was then resected using a forced coagulation current of 28 W (ICC 350; ERBE; Figure 1). (b) MBM. A multiband mucosectomy set (Duette-kit, DT-6-5F; Cook Ireland Medical) was assembled at the tip of a forward-viewing endoscope (GIF-Q260J or GIF-1T240; Olympus). The endoscope was then introduced, and the lesion was sucked into the barrel of the set. A soft hexagonal snare (DT-MH-5F; Cook Ireland Medical) was used to resect the pseudopolyp with a forced coagulation current of 28 W (ICC 350; ERBE; Figure 2). (c) ESD. A forward-viewing endoscope (GIF-Q260J; Olympus) was introduced with a transparent cap attachment (D-201-11804; Olympus) on its tip. The procedure of injection was the same as that of ER-Cap. Then a mucosal incision at the periphery of the lesion and dissection of submucosal connective tissue was performed with a DualKnife (KD-650Q; Olympus) in the end-cut mode (300D, ERBE; Figure 3).
3. Treatment after procedure. If there are no complications, the patients are fasted for about 3 days, and then advanced to a liquid diet. After discharge, patients were placed on proton pump inhibitors (PPIs) for 4–8 weeks.

Follow-up

All patients underwent follow-up endoscopy examination with Lugol's iodine staining at 3, 6, and 12 months and thereafter annually, and also received a CT scan annually. The duration of follow-up was defined as the time between the operation and the last follow-up visit for undergoing endoscopy.

Histologic evaluation

All specimens were stretched out and pinned on a foam board to avoid shrinkage and curling, and the proximal and distal ends were identified on the board. The specimens were then promptly fixed

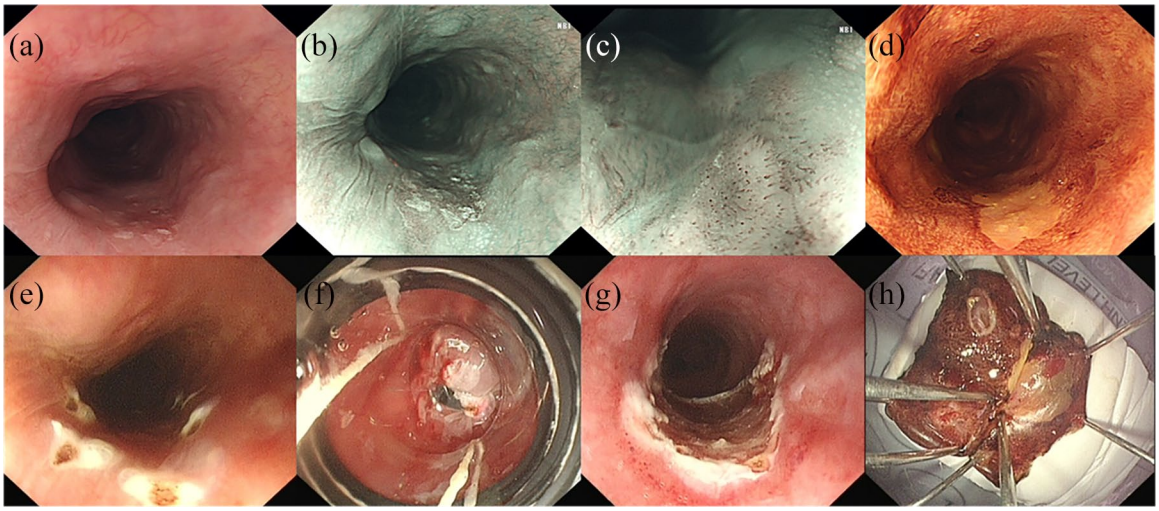

Figure 2. Multi-band mucosectomy: (a) lesion in white light; (b) lesion in narrow-band imaging; (c) lesion in magnification endoscopy; (d) after spraying Lugol's iodine solution; (e) after making dots; (f) endoscopic resection; (g) ulcer after resection; (h) specimen.

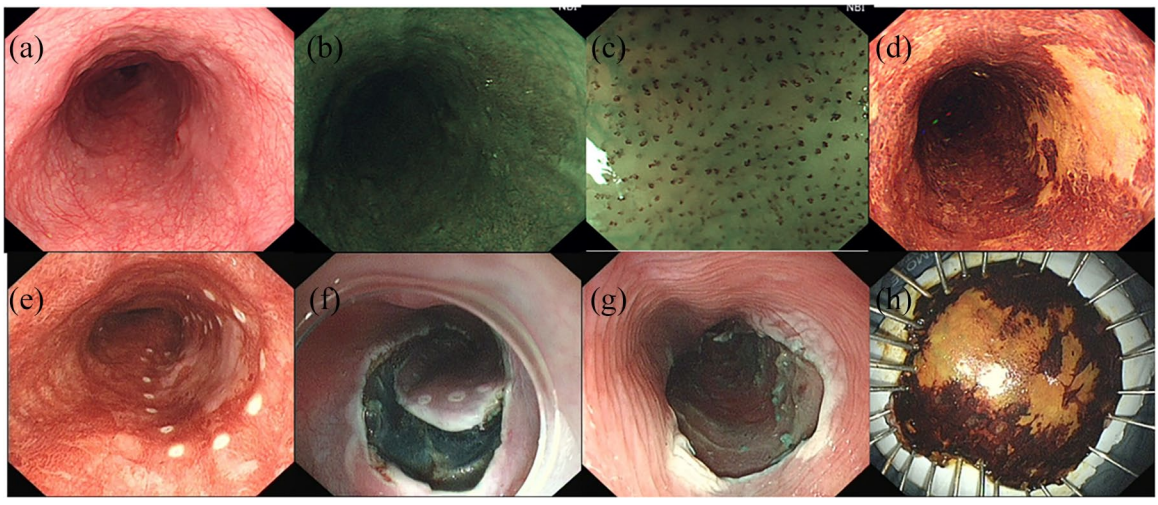

Figure 3. Endoscopic submucosal dissection: (a) lesion in white light; (b) lesion in narrow-band imaging; (c) lesion in magnification endoscopy; (d) after spraying Lugol's iodine solution; (e) after making dots; (f) endoscopic resection; (g) ulcer after resection; (h) specimen.

in formalin solution (10%) for 24 h. If the lesion was resected by piecemeal during the procedure of ER-Cap or MBM, the specimens were recombined into one piece on a foam board to simulate the original morphology. The entire specimen was continuously sectioned at 2 mm intervals. The resected specimens were examined according to the Japanese Classification of Esophageal Carcinoma[10] by experienced pathologists. The status of margin, depth of invasion, lymphovascular invasion, and differentiation were then analyzed. The depth of invasion was specified in m1 (epithelium), m2 (lamina propriamucosa), m3 (muscularis mucosa) and superficial sm (depth of submucosal invasion of $<200\,\mu m$) or deep sm (depth of submucosal invasion of $>200\,\mu m$).

Evaluation of the three methods

The operation time was measured from the time of marking dots until the total removal of the lesion.

Hospitalization costs were defined as the overall cost of the expenses during the hospital stay.

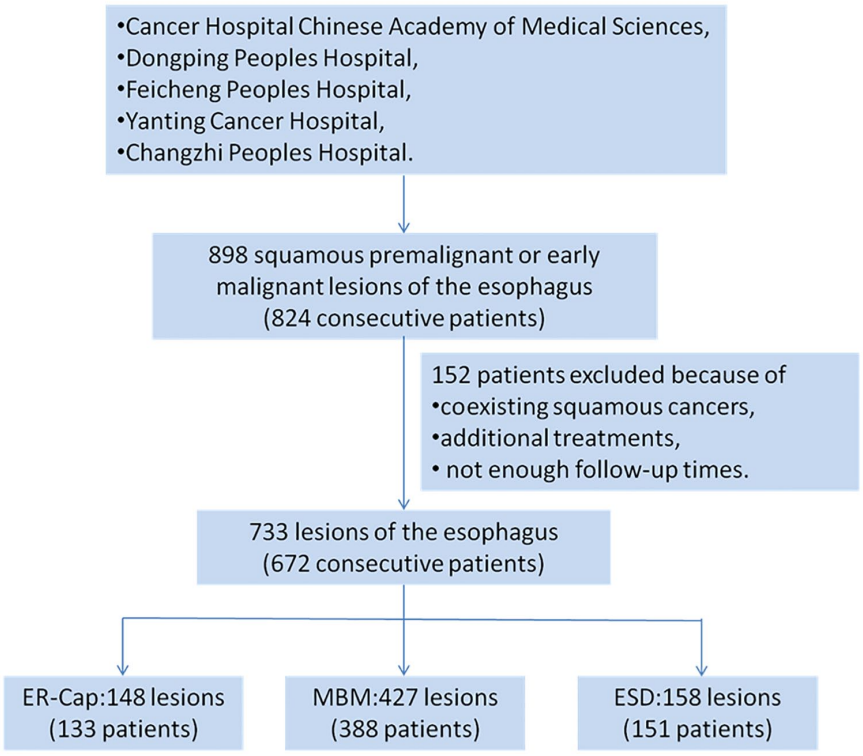

Figure 4. Study population distribution.
ER-Cap, endoscopic resection cap technique; ESD, endoscopic submucosal dissection; MBM, multiband mucosectomy.

R0 resection was defined as *en bloc* resection of the tumor with tumor-free margins, including vertical margin and horizontal margin.

Bleeding related to the procedure was defined as bleeding that required postoperative hemostatic treatment, such as endoscopic clipping, thermocoagulation, or surgical intervention. Immediate perforation was diagnosed when the mediastinal connective tissue was observed during the procedure and used the closure methods. Delayed perforations were detected when there were pneumoperitoneum or pneumomediastinum. Postoperative cicatricial stenosis was defined when a standard endoscope with a diameter of 9.9 mm could not pass through it.

Tumor recurrence was defined as the presence of local recurrence, excluding the metachronous multiple primary carcinoma. Metastasis included nodal or distant metastasis detected by endoscopy or CT scan and confirmed histologically.

Statistics

Demographics, endoscopic, and histology variables were compared using chi-squared test, analysis of variance, and Kruskal–Wallis rank sum test. The level of significance was set at 0.05. All analyses were performed with SAS 9.2.

Results

Patient characteristics

A total of 898 squamous premalignant or early malignant lesions of the esophagus in 824 consecutive patients treated by ER-Cap, MBM, and ESD from January 2009 to December 2015 in multiple centers of China (including Cancer Hospital Chinese Academy of Medical Sciences, Dongping Peoples Hospital, Feicheng Peoples Hospital, Yanting Cancer Hospital, and Changzhi Peoples Hospital) were included. Of these patients, 152 were excluded because of the coexistence of squamous cancers, had undergone additional treatments, or did not have enough follow-up time. Finally, 672 patients with a total of 733 lesions who met the eligibility criteria were included in our study (Figure 4).

The clinicopathologic features of these patients are presented in Table 1. ER-Cap, MBM, and

Table 1. Clinicopathologic features of the study population.

	ER-Cap group	MBM group	ESD group	*p* value
Number of lesions	148	427	158	–
Number of patients	133	388	151	
Age, years, mean ± SD (range)	60.42 ± 8.34 (41–81)	62.66 ± 7.62 (41–80)	60.70 ± 7.88 (35–79)	0.035
Sex, *n* (%)				
Male	92 (69.2)	246 (63.4)	108 (71.5)	0.150
Female	41 (30.8)	142 (36.6)	43 (28.5)	
Tumor location, *n* (%)				
Neck	2 (1.4)	9 (2.1)	1 (0.6)	0.363
Upper	14 (9.4)	42 (9.8)	11 (7.0)	
Middle	58 (39.2)	198 (46.4)	68 (43.0)	
Lower	74 (50.0)	178 (41.7)	78 (49.4)	

ER-Cap, endoscopic resection cap technique; ESD, endoscopic submucosal dissection; MBM, multiband mucosectomy; SD, standard deviation.

ESD were carried out in 148 lesions (133 patients), 427 lesions (388 patients), and 158 lesions (151 patients), respectively. The mean age of the patients was 61.59 years (range: 35–81) and the male-to-female ratio was 2.78:1. The mean follow-up time was 44.37 months.

Endoscopic procedural characteristics

The resection procedure outcomes of the three groups are given in Table 2. The resection sample size was significantly larger in the ESD group (4.40 ± 1.20 cm, $p < 0.001$) when compared with the other two groups. The operation time was significantly shorter for ER-Cap (29.26 ± 16.73 min, $p < 0.001$) group, and the hospitalization costs were significantly lower in the MBM group (20,942.03 ± 8435.56¥, $p = 0.003$). A mean number of 5.64 ± 3.56 resections per session were performed in the MBM group and were significantly higher than the ER-Cap group ($p < 0.001$). The mean operation time was significantly longer for the ESD procedure (58.39 ± 26.70 min) than for the ER-Cap and MBM procedures (29.26 and 35.64 min respectively, $p < 0.001$).

Clinical outcomes

As shown in Table 3, the average follow-up period was significantly longer for the ER-Cap group. The average invasive depth of the submucosa remained the highest for ESD group (611.207 for ESD) but was not significantly higher than the other two groups ($p = 0.493$). The procedure-related bleeding was significantly higher in ER-Cap group ($p = 0.011$). In addition, the frequencies of perforation and cicatricial stenosis were significantly higher in the ESD group ($p < 0.001$, $p = 0.390$) (Table 3).

R0 resection rate in en bloc *resection lesions*

The number of *en bloc* resection lesions included in ER-Cap group was 43/148, in MBM group was 29/427, and in ESD group was 158/158. As listed in Table 4, there was no significant difference among the three groups in R0 resection rate. The mean size of R0 resection lesions in the three groups are shown in Table 4.

Follow-up results

Three patients with local recurrences were observed in ER-Cap group and received another endoscopic treatment after confirmation of recurrences histologically; all have achieved complete response. No recurrence was detected in MBM and ESD groups. There were three and two metastatic patients observed in the MBM and ESD groups, respectively. The metastatic rate

Table 2. Comparison of features of resection procedure between the three groups.

	ER-Cap group	MBM group	ESD group	*p* value
Mean size of lesion, cm ± SD (range)	3.15 ± 1.24 (1.4–8.8)	3.38 ± 1.30 (0.8–10.8)	4.40 ± 1.20 (1.5–7.5)	<0.001
Pieces of specimen, mean ± SD	2.83 ± 2.28	5.64 ± 3.56	1.00 ± 0.00	<0.001
Operation time, Minutes ± SD	29.26 ± 16.73	35.64 ± 19.77	58.39 ± 26.70	<0.001
Operation time/size of lesion, Minutes ± SD	9.50 ± 4.73	11.00 ± 6.27	13.71 ± 5.88	<0.001
Hospitalization cost ¥ ± SD	23,958.11 ± 10,923.57	20,942.03 ± 8435.56	24,716.82 ± 8347.15	0.003

ER-Cap, endoscopic resection cap technique; ESD, endoscopic submucosal dissection; MBM, multiband mucosectomy; SD, standard deviation.

Table 3. Comparison of clinical outcomes between the three groups.

	ER-Cap group	MBM group	ESD group	*p* value
Average follow-up period, months ± SD, range	66.63 ± 20.15 (21.57–94.03)	41.36 ± 15.46 (6.27*–74.57)	31.86 ± 7.22 (22.03–42.73)	<0.001
Average submucosal invasion depth, μm ± SD, range	581.25 ± 423.36 (50–1250)	453.261 ± 320.98 (75–1150)	611.207 ± 587.01 (50–2400)	0.493
Complication, no. (%)				
Perforation	1 (0.7)	0 (0.0)	15 (9.5)	<0.001
Bleeding	6 (4.1)	3 (0.7)	4 (2.5)	0.011
Cicatricial stenosis	12 (8.1)	38 (8.9)	27 (17.1)	0.009
Progression of disease, no. (%)				
Negative	145 (98.0)	424 (99.3)	156 (98.7)	–
Local recurrence	3 (2.0)	0 (0.0)	0 (0.0)	0.008
Metastasis	0 (0.0)	3 (0.7)	2 (1.3)	0.491

ER-Cap, endoscopic resection cap technique; ESD, endoscopic submucosal dissection; MBM, multiband mucosectomy; SD, standard deviation.
*Two patients whose follow-up periods were just 6.27 months and 10.57 months died because of other diseases.

showed no significant difference in the three groups ($p = 0.491$). The features of the eight patients with local recurrence or metastasis were described in detailed in Table 5.

Discussion

In the recent years, ER-Cap, MBM, and ESD have been widely accepted as standard treatments for treating early esophageal squamous cell carcinoma in China.[11–13] According to the previous studies, ESD has been reported to be the best treatment option to perform *en bloc* resection,[9,14] but the procedure highly depends on the operator's skills and experience and involves a longer learning curve.[15] In contrast, ER-Cap and MBM are easy to perform,[16,17] and ER-Cap has been reported to be a safe and effective procedure after the experience of 40 cases.[18] Therefore, it is imperative to choose an easily available and cost effective treatment for early SCCE. Our study, to the best of our knowledge, is the first large-scale,

Table 4. Comparison of the mean size of R0 and curative resection lesions.

	ER-Cap group	MBM group	ESD group	*p* value
En bloc resection rate	29.1% (43/148)	6.8% (29/427)	100% (158/158)	<0.001
R0 resection rate of en bloc resection lesions	100% (43/43)	100% (29/29)	97.5% (154/158)	0.756
Mean size of R0 resection lesions, cm ± SD (range)	2.41 ± 0.60 (1.4–4.0)	1.73 ± 0.59 (0.8–2.4)	4.37 ± 1.19 (1.5–7.5)	<0.001

ER-Cap, endoscopic resection cap technique; ESD, endoscopic submucosal dissection; MBM, multiband mucosectomy; SD, standard deviation.

long-term study that has compared three different methods with regard to operation time and cost, R0 resection rate, complication rate, local recurrence, and metastasis.

In the three groups, the ESD technique obtained the largest size of the sample, whereas ER-Cap had the shortest operation time, and the MBM technique had the lowest hospitalization cost. The results obtained from our study might help clinicians decide the future of treating early esophageal cancer. It has been reported that the *en bloc* resection rate and the completeness of the resection were significantly greater in lesions larger than 2 cm in diameter with the ESD technique, but the technique is associated with an increased operation time, high cost, and an experienced operator in large medical centers.[19] The MBM technique is an easier and safer technique for removing the lesion, and can be used by an unskilled operator with simple training. Most importantly, the advantage of the low cost makes it particularly suitable for high-volume screening programs such as in China,[20] wherein the incidence of SCCE is high but the number of skilled endoscopists is small.

Our study showed that the *en bloc* resection rate of ESD was significantly higher than the other two groups, which was in accordance with the previous studies.[14,21] However, Ishihara and colleagues[19] have reported in lesions of <1.5 cm, ER-Cap and ESD had similar *en bloc* and curative resection rates. Our data also showed that ER-Cap and MBM achieved high R0 resection rate by *en bloc* resection of lesions with an average sample size of 2.41 ± 0.60 cm and 1.73 ± 0.59 cm. The size of the lesions is limited when ER-Cap or MBM are used to achieve an *en bloc* resection. We hypothesized that when *en bloc* resection can be achieved for a lesion size of <2.0 cm, then an ER-Cap technique would be the preferred approach due to the shorter operating time and high R0 resection rate.

Perforation is the most serious complication of ER. In this study, the perforation rate was 9.5% in ESD group, which was higher than that of the previous studies.[9,22,23] The perforation rates of ER-Cap and MBM were significantly lower than that of ESD, which is similar to that of previous reports.[9] All perforations were handled by endoscopic clipping immediately after the procedure and recovered by conservative management.

A higher bleeding rate after the operation was observed in the ER-Cap group (4.1%) than in the MBM group (0.7%) and ESD group (2.5%). According to the previous studies, preventive coagulation of treatment-induced ulcers is a well-established and effective method for preventing bleeding. In our study, patients in the ER-Cap underwent treatment in the early period and might not receive sufficient preventive coagulation, which might be the main reason for a high rate of bleeding.

The frequency of cicatricial stenosis was significantly higher in the ESD group ($p = 0.009$), which could be explained by the larger resection sample size of ESD ($p < 0.001$). It has been reported that cicatricial stenosis is observed along with the endoscopic removal of circumferential lesions,[24] and has shown no significant association with the choice of endoscopic methods.

During the follow-up period, all patients survived, except two patients who died due to other diseases. All 427 lesions in the MBM group showed no signs of local recurrence after an average follow-up period of 41.36 months, and similar results were observed in the ESD group. Wang and colleagues[13] have reported that the local recurrence rate of MBM after a median follow-up

Table 5. Features of the eight patients with local recurrence or metastasis.

Patient		Case1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8
ER type		EMR-Cap	EMR-Cap	EMR-Cap	MBM	MBM	MBM	ESD	ESD
Resection		Piecemeal	Piecemeal	Piecemeal	Piecemeal	Piecemeal	Piecemeal	En bloc	En bloc
Histologic Evaluation	Resection margin	Negative	Negative	Negative	Negative	Negative	Negative	Positive lateral margin	Negative
	Differentiation	Well	Well	Well	Poorly	Poorly	Poorly	Poorly	Poorly
	Invasion depth	m1	m1	m1	m3	Deep sm	Deep sm	Deep sm	Deep sm
	lymphovascular invasion	Negative	Negative	Negative	Negative	Negative	Negative	Negative	Positive
Progression		Local recurrence	Local recurrence	Local recurrence	Right trache-oesophageal groove nodal metastasis	Lung metastasis	Right tracheo-esophageal groove nodal metastasis	Mediastinal nodal metastasis	Mediastinal nodal metastasis
Duration (month)		76	50	50	62	47	17	37	18
Additional treatment*		RFA	ESD	ESD	Radiotherapy	Chemotherapy	Lymph node dissection	Radiotherapy	Radiotherapy

ER-Cap, endoscopic resection cap technique; ESD, endoscopic submucosal dissection; MBM, multiband mucosectomy; SD, standard deviation; RFA, Radiofrequency Ablation.
*Additional treatment was performed after the confirmation of recurrence or metastasis.

of 27.75 months was 2.4% (3/125). However, the local recurrence rate of ER-Cap has been reported to be 9.1–15.4%,[7,9,25] but the recurrence rate in this study was noticeably inferior to other series in the field, which could be explained by the absence of metachronous recurrences, the rate of which was 3.2% (22/733). All three patients with recurrence in ER-Cap in our study underwent treatment in 2009, but the technique was not very skilled and canonical. Our study, along with other reports showed that MBM could achieve a lower local recurrence rate than that of ER-Cap, and a similar local recurrence was observed when compared with ESD. Three and two metastatic patients were observed in MBM and ESD groups, respectively, but the metastatic rate was similar in the three groups ($p = 0.491$). All the three treatment techniques showed no significant differences with regard to metastasis. According to the previous studies, the metastatic rate is associated with submucosal invasion, differentiation of pathology, and lymphatic permeation,[1] which have been decided before treatment and cannot be changed by the methods of treatment. More importantly, prognostic evaluation of the pathology of resected specimens and follow-up project are necessary for additional treatment. However, regarding the five metastasis patients, research discussions regarding the pathological features should be conducted in the future.

However, there are some limitations in our study. First, this was a retrospective study, and is subjected to bias. Second, all procedures were performed by highly experienced endoscopists who underwent systemic training, which might possibly contribute to the favorable outcomes. In addition, the three endoscopic techniques were performed in different time periods during the study. ER-Cap was used in an earlier period, MBM was used in the later period, and ESD was used in the most recent years. The average follow-up period of ESD group was comparatively short, which was approximately half the time of the ER-Cap group. Finally, the proportion of patients who underwent endoscopy follow-up at 1, 2, and 3 years was 99.7%, 92.9%, and 67.1% respectively. There are still some patients who were lost to endoscopic follow-up, influencing the long-term outcomes.

In conclusion, our study has demonstrated that ER-Cap, MBM, and ESD are minimally invasive, safe, and effective methods for the treatment of early esophageal squamous cell carcinoma. ESD is suitable for large-area lesions and provided an *en bloc* resection but is a time-consuming procedure that requires highly skilled endoscopists in large medical centers. MBM is a safe, simple, and effective procedure that requires low technical skill, has low local recurrence, and has similar metastatic rate to that of ESD. This therapeutic approach is considered as a good alternative and an extremely common technique for high-risk areas of esophageal squamous cell carcinoma, but the resources are limited in places such as rural China.

Funding

The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: CAMS Innovation Fund for Medical Sciences (CIFMS) [grant number: 2016-12M-001, 2017-I2M-1-001, 2019-12M-2-004]; Sanming Project of Medicine in Shenzhen [grand number: SZSM201911008]; The National Key Research and Development Program of China [grant number: 2016YFC1302800, 2018YFC 1313103]; The PUMC Youth Fund and the Fundamental Research Funds for the Central Universities [grant number: 2017320012].

Conflict of interest statement

The authors declare that there is no conflict of interest.

ORCID iD

Xinying Yu https://orcid.org/0000-0002-5160-4344

References

1. Oyama T, Inoue H, Arima M, *et al*. Prediction of the invasion depth of superficial squamous cell carcinoma based on microvessel morphology: magnifying endoscopic classification of the Japan esophageal society. *Esophagus* 2017; 14: 105–112.
2. Lee CT, Chang CY, Tai CM, *et al*. Endoscopic submucosal dissection for early esophageal neoplasia: a single center experience in South Taiwan. *J Formos Med Assoc* 2012; 111: 132–139.
3. Pioche M, Mais L, Guillaud O, *et al*. Endoscopic submucosal tunnel dissection for large esophageal neoplastic lesions. *Endoscopy* 2013; 45: 1032–1034.
4. Pech O, May A, Rabenstein T, *et al*. Endoscopic resection of early oesophageal cancer. *Gut* 2007; 56: 1625–1634.

5. Zhang YM, Boerwinkel DF, He S, *et al.* Prospective feasibility study on the use of multiband mucosectomy for endoscopic resection of early squamous neoplasia in the esophagus. *Endoscopy* 2013; 45: 167–173.
6. Zhang YM, Boerwinkel DF, Qin X, *et al.* A randomized trial comparing multiband mucosectomy and cap-assisted endoscopic resection for endoscopic piecemeal resection of early squamous neoplasia of the esophagus. *Endoscopy* 2016; 48: 330–338.
7. Ishihara R, Iishi H, Takeuchi Y, *et al.* Local recurrence of large squamous-cell carcinoma of the esophagus after endoscopic resection. *Gastrointest Endosc* 2008; 67: 799–804.
8. Yamashita T, Zeniya A, Ishii H, *et al.* Endoscopic mucosal resection using a cap-fitted panendoscope and endoscopic submucosal dissection as optimal endoscopic procedures for superficial esophageal carcinoma. *Surg Endosc* 2011; 25: 2541–2546.
9. Takahashi H, Arimura Y, Masao H, *et al.* Endoscopic submucosal dissection is superior to conventional endoscopic resection as a curative treatment for early squamous cell carcinoma of the esophagus (with video). *Gastrointest Endosc* 2010; 72: 255–264, 264.e1–e2.
10. Japan Esophageal Society. Japanese classification of esophageal cancer, 11th edition: part I. *Esophagus* 2017; 14: 1–36.
11. Chen Y, Zhao Y, Zhao X, *et al.* Clinical outcomes of endoscopic submucosal dissection for early esophageal squamous cell neoplasms: a retrospective single-center study in China. *Gastroenterol Res Pract* 2016; 2016: 3741456.
12. Jiang D, Li X, Wang H, *et al.* A retrospective study of endoscopic resection for 368 patients with early esophageal squamous cell carcinoma or precancerous lesions. *Surg Endosc*. Epub ahead of print 11 November 2016. DOI: 10.1007/s00464-016-5208-z.
13. Wang Z, Lu H, Wu L, *et al.* Long-term outcomes of endoscopic multiband mucosectomy for early esophageal squamous cell neoplasia: a retrospective, single-center study. *Gastrointest Endosc* 2016; 84: 893–899.
14. Teoh AY, Chiu PW, Yu Ngo DK, *et al.* Outcomes of endoscopic submucosal dissection versus endoscopic mucosal resection in management of superficial squamous esophageal neoplasms outside Japan. *J Clin Gastroenterol* 2010; 44: e190–e194.
15. Kakushima N, Fujishiro M, Kodashima S, *et al.* A learning curve for endoscopic submucosal dissection of gastric epithelial neoplasms. *Endoscopy* 2006; 38: 991–995.
16. Zhang YM, He S, Xue LY, *et al.* Comparative study of endoscopic mucous resection with transparent cap and endoscopic multi-band mucosectomy for early esophageal cancer and precancerous lesion. *Zhonghua wei chang wai ke za zhi* 2012; 15: 913–917.
17. Chen ZY, Yang YC, Liu LM, *et al.* Comparison of the clinical value of multi-band mucosectomy versus endoscopic mucosal resection for the treatment of patients with early-stage esophageal cancer. *Oncol Lett* 2015; 9: 2716–2720.
18. Choi IJ, Kim CG, Chang HJ, *et al.* The learning curve for EMR with circumferential mucosal incision in treating intramucosal gastric neoplasm. *Gastrointest Endosc* 2005; 62: 860–865.
19. Ishihara R, Iishi H, Uedo N, *et al.* Comparison of EMR and endoscopic submucosal dissection for en bloc resection of early esophageal cancers in Japan. *Gastrointest Endosc* 2008; 68: 1066–1072.
20. Wei WQ, Chen ZF, He YT, *et al.* Long-term follow-up of a community assignment, one-time endoscopic screening study of esophageal cancer in China. *J Clin Oncol* 2015; 33: 1951–1957.
21. Cao Y, Liao C, Tan A, *et al.* Meta-analysis of endoscopic submucosal dissection versus endoscopic mucosal resection for tumors of the gastrointestinal tract. *Endoscopy* 2009; 41: 751–757.
22. Ono S, Fujishiro M, Niimi K, *et al.* Long-term outcomes of endoscopic submucosal dissection for superficial esophageal squamous cell neoplasms. *Gastrointest Endosc* 2009; 70: 860–866.
23. Repici A, Hassan C, Carlino A, *et al.* Endoscopic submucosal dissection in patients with early esophageal squamous cell carcinoma: results from a prospective Western series. *Gastrointest Endosc* 2010; 71: 715–721.
24. Ono S, Fujishiro M, Niimi K, *et al.* Predictors of postoperative stricture after esophageal endoscopic submucosal dissection for superficial squamous cell neoplasms. *Endoscopy* 2009; 41: 661–665.
25. Urabe Y, Hiyama T, Tanaka S, *et al.* Advantages of endoscopic submucosal dissection versus endoscopic oblique aspiration mucosectomy for superficial esophageal tumors. *J Gastroenterol Hepatol* 2011; 26: 275–280.