



## Abstract

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Background: Larger colonic polyps require advanced resection techniques such as endoscopic mucosal resection (EMR) for safe and effective removal. There is a steady accumulation of scientific evidence with regard the technical aspects and long-term outcomes of colonic EMR compared with surgery. *Objective:* This study aimed to identify and analyze different factors predictive of clinical outcomes for patients undergoing EMR of colorectal lesions. Methods: This is a retrospective cohort study on all patients who underwent colorectal EMR from January 2015 to December 2018. The diagnostic yield of Japan NBI Expert Team (JNET) classification and clinical outcomes, namely, R0 resection, complications and recurrence of lesions, were studied. Results: Two hundred eighty-two patients were studied. The R0 resection rate was 96.3% (n=231) for lesions resected en bloc; 15.2% (n=43) presented with a complication, most commonly presenting as intra-procedural bleeding (n=36, 12.8%); and 10.7% (n=11) had recurrence post-EMR on surveillance colonoscopy. Main predictors of recurrence include a non-granular morphology of a resected polyp (cOR 2.621 [95% CI 1.0-6.84]) and piecemeal resection (cOR 2.306 [95% CI 1.06-5.04]). A larger lesion size of >20 mm was associated with both positive resection margin and post-EMR complications. The JNET classification exhibited good sensitivity for Type 1 (71.8%) and Type 2A (91.9%) and good specificity for Type 1 (96.9%) and Type 2B (95.5%). Accuracy was high for JNET Types 1 (91.02%), 2A (80.24%), and 2B (89.22%). Conclusions: EMR is an important advancement in the field of therapeutic endoscopy with good clinical outcomes. The JNET classification has a high diagnostic accuracy rate; hence is a good endoscopic tool for characterization of lesions.

*Keywords:* EMR, endoscopic mucosal resection, colorectal polyp, adenoma, JNET classification

## Introduction

Colorectal cancer is the fourth most common cancer in the Philippines.<sup>1</sup> It is considered the third most deadly and fourth most commonly diagnosed cancer worldwide.<sup>2</sup> Nevertheless, deaths caused by colon cancer have been dropping steadily due to increased efforts in colon cancer screening that allows detection and removal of pre-cancerous and early malignant lesions, including endoscopic mucosal resection (EMR).<sup>3</sup>

EMR is a minimally invasive technique which has become the primary treatment of large (>10mm) laterally spreading lesions (LSLs) and polyps in the colon.<sup>3</sup> It is both diagnostic and therapeutic and enables complete removal and histologic assessment of the lesion. It is cost effective with high success rate, lower morbidity and mortality, and shorter length of hospital stay when compared to surgery. Due to these advantages, it is suggested that EMR should be considered as the first-line treatment for patients with colorectal lesions suspicious for neoplasia.

Different lesion and procedural factors have been reported to predict clinical outcomes and influence choice of resection strategy and endoscopic follow-up.<sup>4</sup> R0 resection, defined as removal of polyp with histologically assessed clear margins, is about 84% for

lesions <20 mm and 50% for lesions >20 mm, if removed via EMR.  $^{5}$ 

While EMR of colorectal neoplasms has been proven feasible and safe, it is associated with a small incidence of procedure-related complications such as bleeding (1-18%) and perforation (0.09-3.1%).<sup>6-7</sup> Literature has shown that certain patient and procedural factors could predict risk of bleeding and perforation.

Adenoma recurrence post-EMR is a major limitation in 10-55% of post-EMR patients.<sup>8</sup> Likewise, the necessity for strict endoscopic surveillance remains a significant challenge. Current guidelines recommend first follow-up colonoscopy at four to six months and a second colonoscopy at a subsequent interval after removal of adenomas through piecemeal EMR.<sup>9</sup> Retrospective studies showed several risk factors contributing to adenoma recurrence after EMR, which includes age >65 years, lesion size >30 mm, localization in the right-sided colon, non-pedunculated morphology, resection in piecemeal technique and tubular-villous histological features.<sup>4</sup> Recognition of these risk factors for tumor recurrence would aid us in predicting recurrence risk which may considerably reduce costs on colon cancer surveillance.

Magnification using narrow band imaging (NBI), which characterizes surface and vascular pattern, is a reliable method for differentiating neoplastic from nonneoplastic colorectal lesions.<sup>10</sup> The Japan NBI Expert Team (JNET) classification developed in 2014 is a proposed system considered to be useful for both expert and non-expert endoscopists in few validation studies.

This study determined the predictive factors for R0 resection, bleeding, and recurrence of colorectal adenomas after colonic EMR. In addition, this study determined the R0 resection rate, recurrence rate and complication rate (bleeding and perforation) of EMR in the institution where this research was done. The study determined the accuracy of the JNET classification in differentiating neoplastic from non-neoplastic lesions.

## Methods

## Subjects

A retrospective cohort study was conducted on adult patients aged 19 years and above who underwent colonic EMR with Olympus 190, 260 and 290 series highdefinition colonoscopes at the Institute of Digestive and Liver Diseases of the St. Luke's Medical Center Global City, Philippines, within a four-year period from January 2015 to December 2018. Patients without existing medical records and colonoscopy or histopathology reports were excluded. Data on each patient for both their initial and surveillance colonoscopies were obtained and verified using hospital records and review of colonoscopy images and videos. Patient data included age of patient, gender, and admission. Data on lesion characterization included size, localization, morphology, JNET classification, submucosal fibrosis, histopathology, cauterized margins (R0 resection rate), and histopathology size of polyp. Procedural data included colonoscope used, technique of resection, adjunctive therapy used, duration of procedure, intraprocedural bleeding, delayed bleeding, perforation, bowel preparation quality (BPPS score), lifting agent, and antibiotic used. Post-procedural data were also collected from patients included in the study using their follow-up colonoscopy reports; and evidence of any delayed adverse events through their medical records. Patients with lesions suspicious for adenoma and biopsies which were positive for histologic recurrence on surveillance colonoscopies were considered recurrence.

The study was reviewed and approved by the Institutional Review Board (SL-19185) and complied with good clinical practice (ICH-GCP) regulations.

### **Outcome Measures**

The primary outcome was the identification of factors predictive of R0 resection, bleeding, and recurrence of colorectal adenomas in patients who underwent colonic EMR. Secondary outcomes included the R0 resection rate, EMR-related complications, recurrence rate of colorectal adenomas, and the diagnostic accuracy of JNET classification in identifying adenomatous lesions.

### Data Analysis

Descriptive statistics was used to summarize the general and clinical characteristics of the participants. Frequencies and proportions were used for nominal variables; mean and range for ordinal variables; and mean and standard deviation for interval/ratio variables. Independent samples T-test, Mann-Whitney U test and Fisher's Exact/Chi-square test were used to determine the difference of mean, median and frequency between groups, respectively. Odds ratio and the corresponding 95% confidence interval from logistic regression were computed to determine the association between patient profile and rate of complete resection using *en bloc* technique, complication (bleeding or perforation), and resection status. Sensitivity, specificity, predictive values and overall diagnostic accuracy were measured to determine the reliability of the JNET classification in predicting histopathology.

## Results

A total of 282 patients (males: n=161, 57%; mean age 60 ± 12 years) were included. Most underwent conventional EMR (n=266, 94%). Other techniques employed included cap-assisted (n=9, 3%), hybrid EMR (n=6, 2%), and underwater EMR (n=1, 0.4%). Grossly, neoplasms had a mean size of 12 mm (1-490 mm) and were mostly located in the descending part of the colon (n=134, 48%). Majority were sessile (n=211, 75%). Submucosal fibrosis was present in six patients (2%). Majority of lesions were seen on the left side of the colon at 47.5% (n=134) followed by the right side at 24.5% (n=69), rectum at 16.7% (n=47), and lastly in the transverse colon at 11.4% (n=32). Most identified lesions were sessile polyps (n=211, 74.8%). Histopathologic analysis revealed that most lesions were low-grade tubular adenoma (n=146, 51.8%), sessile serrated adenoma (n=40, 14.2%), and low-grade tubulovillous adenoma (n=25, 8.9%). The actual tumor sizes ranged from 3-40 mm, with a mean of 10 mm (Table 1). Of 174 lesions characterized using NBI, most (n=130, 74.7%) were JNET 2A. Most patients had adequate bowel preparation with a BPPS score of 9 (n=206, 73%). Seventy six patients (27%) had poor bowel preparation. Most procedures (n=220, 78%) were performed using Olympus 290. En bloc resection was achieved in 240 lesions (85%). Saline alone was the preferred lifting agent (n=156, 56%), followed by saline plus hyaluronic acid (n=66, 23%). Procedures lasted for a mean duration of 45 (14-263) minutes.

Table 1.	Lesion	characteristics	(n=282)	١
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Positive resection margins were present in eleven (3.9%) lesions, of which nine were removed *en bloc* (**Table 2**). Complications were reported in 45 (16.0%) of cases. Intraprocedural bleeding was the most common (n=36, 12.8%). There was one case of perforation.

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Only 103 patients (37%) had follow-up colonoscopy in the institution of study (**Table 3**).

Table 3	. Follow-up (	of endoscopy	patients	(n= 103)
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Follow-up Data	Frequency (%)
Recurrence	11 (10.7)
Histopathology	
Tubular adenoma, LG <sup>a</sup>	8 (66.7)
Hyperplastic polyp	2 (16.7)
Tubulovillous adenoma, HG <sup>b</sup>	1 (8.3)
Others	1 (8.3)
Months since index EMR	
<4	7 (6.8)
4-6	16 (15.5)
6-12	27 (26.2)
>12	53 (51.5)
Endoscopist	
Same	92 (89.3)
Different	11 (10.7)

<sup>a</sup>LG: low-grade dysplasia; <sup>b</sup>HG: high-grade dysplasia

Most had their first surveillance colonoscopies beyond the recommended six-month period (n=80,

77%). Recurrence was noted in 11 patients (11%) with most recurrent lesions being low-grade tubular adenoma (n=8, 67%). Majority (n=92, 89%) of the surveillance colonoscopies were performed by the same endoscopist.

The diagnostic positive predictive value of JNET classification for 167 lesions after excluding nonadenomatous and benign lesions (e.g., leiomyoma, neuroendocrine tumor, and inflammatory polyp) where JNET was not applied, are enumerated in **Table 4**. Majority of JNET Type 1 lesions (n=28, 87.5%) were hyperplastic and sessile serrated polyp on histopathology. For JNET Type 2A lesions, 102 (81%) were low-grade intramucosal neoplasia. The diagnostic yield of JNET classification exhibited moderate to good sensitivity for Type 1 (71.8%) and Type 2A (91.9%), and good specificity for Type 1 (96.9%) and Type 2B (95.5%). Diagnostic accuracy was at 91.0% for Type 1, 80.2% for Type 2A.

#### Table 4. Diagnostic positive predictive value (PPV) of JNET classification

	Hyperplastic and Sessile Serrated Polyp (n = 39)	Low-Grade Intramucosal Neoplasia <sup>a</sup> (n = 111)	High-Grade Intramucosal Neoplasia <sup>a</sup> (n = 12)	Carcinoma (n = 5)
		Frequency (%)		
Type 1 (n = 32)	28 (87.5)	4 (12.5)	0 (0)	0 (0)
Type 2A (n = 126)	22 (8.7)	102 (81.0)	10 (7.9)	3 (2.4)
Type 2B (n = 9)	0 (0)	5 (55.6)	2 (22.2)	2 (22.2)

<sup>a</sup>Comprised of tubular and tubulovillous adenoma variant

Note: There were no Type 3 patients

	Sensitivity	Specificity	PPV	NPV	Accuracy
		% (95% Cl); [Freque	ncy/Total]		
Type 1 (non- neoplastic vs. neoplastic)	71.8 (55.1 to 85) [28/39]	96.9 (92.2 to 99.1) [124/128]	87.5 (71 to 96.5) [28/32]	91.9 (85.9 to 95.9) [124/135]	91.0 (85.62 to 94.89) [152/167]
Type 2A (LGN vs. others)	91.9 (85.2 to 96.2) [102/111]	57.1 (43.2 to 70.3) [32/56]	81 (73 to 87.4) [102/126]	78 (62.4 to 89.4) [32/41]	80.2 (73.4 to 86) [134/167]
Type 2B (HGN and shallow submucosal invasive cancer vs. others)	15.4 (1.9 to 45.4) [2/13]	95.5 (90.9 to 98.2) [147/154]	22.2 (2.8 to 60) [2/9]	93 (87.9 to 96.5) [147/158]	89.2 (83.5 to 93.5) [149/167]

Crudely, gross (endoscopic) lesion size >20 mm (cOR 16.375 [95% CI 1.965 to +Inf]), presence of submucosal fibrosis (cOR 15.617 [95% CI 1.22 to 132.98]),

histopathologic size (cOR 1.1 [95/% CI 1.01 to 1.19]), and diagnosis of moderately differentiated adenocarcinoma (cOR 225.106 [95/% CI 17.11 to 14256.58]) were associated with greater odds of having (**Table 6**). a positive resection margin after *en bloc* resection

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Table 6. Factors associated with a positive resection margin after en bloc resection (n=240)

Crude analysis showed the following factors to be associated with occurrence of bleeding or perforation: hybrid EMR technique (cOR 11.816 [95% CI 1.63-134.88]), gross tumor size >20mm (cOR 3.554 [95% CI 1.44-8.79), non-granular morphology (cOR 2.621 [95% CI 1.0-6.84]), histopathologic size (cOR 1.064 [95% CI 1.02-1.11]), piecemeal resection (cOR 2.306 [95% CI 1.06-5.04]), and use of saline and methylene blue as lifting agents (cOR 6.222 [95% CI 1.53-25.32]) (Supplementary Table 1<sup>+</sup>).

In terms of recurrence, the only factors associated as per follow-up visit/s (n=103) were non-granular morphology (cOR 9.683 [95%CI 1.78 to 54.98]) and piecemeal resection (cOR 1.221 [95% CI 2.44 to 60.69]) (*Supplementary Table*  $2^{\varepsilon}$ ).

## Discussion

EMR is considered a safe and effective option for patients with complex colorectal lesions. It was developed for minimally invasive endoscopic removal of benign and early malignant lesions in the GI tract.<sup>11</sup> It is an advanced resection technique that is not routinely part of the general endoscopic training of gastroenterologists hence, requires dedicated training for a high-quality, safe and effective colorectal EMR.<sup>3</sup>

According to the European Society of Gastrointestinal Endoscopy, the goals of EMR are to achieve a completely snare-resected lesion in the safest minimum number of pieces, with adequate margins and without need for adjunctive ablative techniques.<sup>12</sup>

## Patient Characteristics

The study included 282 patients with a mean age of  $60\pm12.36$  years; majority of which were males (57%). This result is consistent and adheres to different screening colonoscopy guidelines, since neoplastic lesions are more commonly found in such age and in males.<sup>9</sup>

### Lesion Characteristics

The study reported a mean endoscopic size of 12 mm (1-490 mm) which appears to be a slight overestimation of histopathologic size. Based on published data, endoscopists tend to overestimate lesions by 3 mm.<sup>13</sup> Such difference could have a significant impact on surveillance colonoscopy where lesions >10 mm in size are recommended to undergo follow-up after six months. A standardized polyp size measurement is recommended.

In terms of morphology, most tumors were sessile (n=211, 74.8%) located on the left side of the colon (n=134, 47.5%) and were low-grade tubular adenoma (n=146, 51.8%) on histopathologic examination. Knowing these characteristics are important since previous reports have shown their association with bleeding, perforation, and adenoma recurrence.<sup>6-7</sup> Lesions proximal to the hepatic flexure have 4.4 times

<sup>\*</sup>Supplementary tables on factors associated with bleeding or perforation (n=282) may be requested from the corresponding author.

<sup>&</sup>lt;sup>6</sup>Supplementary table on factors associated with recurrence (n=103) may be requested from the corresponding author.

higher risk of bleeding than the remainder of the colon.<sup>14</sup> Right-sided colon polyps are associated with increased risk of adenoma recurrence.<sup>4</sup> In addition, lesion characterization is important because it determines the appropriate resection technique, such as EMR for flat lesions like laterally spreading polyps.

### JNET Classification and Histopathologic Results

In the study, the majority of patients (n=130, 74.7%) had a JNET classification of 2A. Diagnostic accuracy tests were used to determine the sensitivity, specificity, predictive value and accuracy of the JNET classification in predicting appropriate histopathology. It should be taken to consideration, however, that the 95% CI are wide for some of the values, or contain 50%, likely due to relatively small sample sizes and different scope models. The study results showed high sensitivity and specificity for Type 1 and Type 2A lesions but as the colorectal lesion becomes endoscopically complex on NBI, the sensitivity of the JNET classification decreases while the specificity remains high. This trend is similar with the published data, hence, supports current knowledge on the variability of diagnosis of JNET Type 2B lesions among endoscopists.<sup>10</sup>

In general, this study shows that the JNET classification is useful in a clinical setting. It can be deduced that endoscopists start to have varied endoscopic diagnosis for lesions that are JNET Type 2A and 2B at least. While adequate examination should be emphasized for lesions regardless of JNET type, this study supports current findings that a more meticulous evaluation is necessary for lesions classified as JNET Type 2B. These lesions are more likely to be high-grade adenoma or intramucosal cancer.<sup>15</sup> Type of resection and management would differ for each lesion and the JNET system aids in its classification.

#### EMR Techniques

There were different EMR techniques employed by the endoscopists in the study. In terms of technique, the conventional EMR technique was the most utilized (n=266, 94.6%). Other resection techniques such as capassisted (3.2%), hybrid EMR (2.1%), underwater EMR (0.4%) were performed in a minority of patients. Capassisted EMR was usually performed in rectal submucosal lesions resembling neuroendocrine tumors. Hybrid EMR, on the other hand, was performed on larger-sized lesions intended for endoscopic submucosal dissection but eventually aborted.

Various lifting agents are utilized in EMR in order to lesion adequately resect the and minimize complications. In our institution, most endoscopists use normal saline (n=158; 56%) because of its availability. However, normal saline is quickly absorbed and could only lift the lesion for a short time. Other agents that may be used are hypertonic saline, hyaluronic acid, and 4% succinylated gelatin. These agents offer an advantage over normal saline as these generally lift the lesions for a prolonged duration. These lifting agents may be mixed with epinephrine at a dilution of 1:10,000 as prophylaxis for post-EMR bleeding. In our center, 26 (9%) of resections utilized addition of epinephrine.

### **Clinical Outcomes**

### 1. R0 Resection

In this study, eleven (3.9%) lesions, nine of which were removed en bloc, had a positive resection margin (Table 6). The R0 resection rate or resected lesions with histologically assessed clear margins is 96.3% for lesions resected en bloc. This is similar to several reports that showed endoscopic resection is successful in 70-100%.<sup>b</sup> Piecemeal resection is generally associated with a positive resection margin. Hence, en bloc snare excision is the principal approach for larger lesions up to 20-25 mm and it is associated with lower rates of recurrence compared with piecemeal resection.<sup>3</sup> However, this study has shown that even en bloc resections could have positive resection margins. Risk factors associated with greater odds of having a positive resection margin include a large lesion (size >20 mm), presence of submucosal fibrosis, and diagnosis of moderately differentiated adenocarcinoma. It is also notable that six patients (2.1%) had submucosal fibrosis characterized as 'positive non-lifting sign' or the inability to adequately lift the lesion after submucosal injection of a lifting agent. Submucosal fibrosis is predictive of incomplete polyp resection which can potentially be a mucosal tumor and thus the unsuitability of performing EMR.<sup>16</sup>

### 2. Bleeding and Perforation

Complications during or after EMR are inevitable but they can be managed readily and safely. In the study, 45 patients (16.0%) experienced complications, most commonly intraprocedural bleeding. Bleeding and perforation are the major complications associated with EMR.<sup>6</sup> The most common complication of EMR is bleeding with a wide-ranging incidence of 1-18%.<sup>7</sup> Generally, factors affecting the risk of post-procedural bleeding include lesion size, flat morphology, location, co-morbidities, coagulation status and lesion histology. However, the reported risk factors are inconsistent across different reports. In this study, the overall bleeding rate was 15.6% with 12.8% (n=36) intra-

co-morbidities, coagulation status and lesion histology. However, the reported risk factors are inconsistent across different reports. In this study, the overall bleeding rate was 15.6% with 12.8% (n=36) intraprocedural and 2.8% (n=8) delayed. Risk factors for bleeding or perforation include using a hybrid EMR technique, gross tumor size of >20 mm, non-granular morphology of a laterally spreading tumor, actual size of histopathology of >20mm, and the use of saline and methylene blue as lifting agents. Based on multivariate analysis, the odds of intra-procedural bleeding were increased with a lesion size of more than 20 mm and piecemeal resection. The larger lesion size and piecemeal resection as risk factors for bleeding and perforation are consistent with published studies.<sup>6-7</sup> The use of saline and methylene blue most likely served as a risk factor in this study because of the lack of adequate lift of the lesions compared to other lifting agents (e.g., hyaluronic acid) which are capable of lifting the lesions longer.

Delayed bleeding occurring after the procedure requiring hospital re-admission or intervention is considered a significant post-endoscopic resection bleeding.<sup>12</sup> Studies showed that it can occur in up to 7% of patients after EMR and that is mainly observed between 2-7 days after the EMR.<sup>14</sup> Endoscopic intervention is required for ongoing or recurrent bleeding. In this study, 2.8% had delayed bleeding, most of which occurred within the first 48 hours after resection. Hemoclipping was done on the post-EMR defects to control the bleeding.

Perforation is the most serious complication of EMR. Peritonitis can occur if perforation is not managed accordingly. According to a meta-analysis by De Ceglie, EMR-related perforation rate was reported at 0.09% to 3.1%.<sup>7</sup> It can be readily managed by endoscopic clip closure when recognized intraprocedurally. In this study, only one patient (0.35%) had a perforation after resection of a descending colon polyp measuring 2.5 cm through a hybrid EMR technique. The perforation was managed with 12 hemoclips and one resolution clip deployed the post-polypectomy on site and administration of intravenous piperacillin-tazobactam.

Recurrence after colorectal EMR is considered the greatest drawback of EMR and it occurs in 10-30% of patients.<sup>17</sup> In this study, 10.7% (n=11) had lesions suspicious of recurrence post-EMR on their surveillance colonoscopy. It should however be noted that only 36.5% (n=103) had follow-up colonoscopies in the study; hence, the recurrence rate may be underreported. Risk factors associated with recurrence on follow-up visits include non-granular morphology (cOR 9.683 [95%Cl 1.78 to 54.98]) and piecemeal resection (cOR 1.221 [95% CI 2.44 to 60.69]). A study by Uraoka, et al. (2006) showed that laterally spreading tumors of non-granular morphology had higher potential for malignancy with greater submucosal depth compared with the granular type.<sup>17</sup> These LSTs should hence be removed en bloc. Piecemeal resections as earlier discussed have higher rates of recurrence compared to en bloc snare excision especially for larger lesions. In general, given the possibility of recurrence of lesions post-EMR, it is recommended to have structured surveillance protocol with at least one done 6-12 months post-EMR.<sup>3</sup> Time interval could change depending on the characteristic of the resected lesion.

# Follow-Up

The aim of follow-up after colorectal EMR is the early detection of local recurrence and metachronous lesions.<sup>18</sup> In the study, there is a poor follow-up rate for all patients who underwent EMR. Only 36.5% or 103 patients returned for follow-up, most of which were >12 months post-procedure, or 53% of the study population, followed by 27% at 6-12 months after the index EMR. The most plausible reason for a low follow-up rate is that bulk of the patients was only referrals to the institute for EMR; and their surveillance colonoscopies performed in referring hospitals. Furthermore, a fraction of the patients are of terminal age; hence, follow-up was no longer recommended, unless the lesion on the index EMR warrants surveillance. Some of the patients also expired for unrelated reasons along the window period before their next surveillance.

## Limitations and Recommendations

This study was limited by its single-center, retrospective study design. A multicenter collaboration of that do large-volume EMRs would validate and yield

more conclusive results. A prospective study design could control confounding variables and would have fewer potential sources of bias. Given the study's retrospective design, there are also several important factors not analyzed such as co-morbidities or use of anticoagulants in relation to post-polypectomy bleeding. Inclusion of these in further studies is recommended. The study is also limited in its sampling as it used a total enumeration scheme. This may affect the results yielding outcomes of statistical insignificance.

## Conclusion

In conclusion, EMR remains a technically challenging procedure that requires considerable skill and experience. It is an important advancement in the field of therapeutic endoscopy with good clinical outcomes sparing patients from surgery with an R0 resection rate at 96.3%, low complication rate at 15.2%, and low recurrence rate at 10.7%. A larger lesion size of >20 mm is associated with both positive resection margin and post-EMR complications. Recurrence rates were noted to be higher in lesions with a non-granular morphology of a resected LST and piecemeal necrosis. In these cases, we recommend a greater resection margin or a more specialized resection technique such as endoscopic submucosal dissection to possibly reduce the risk of recurrence.

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## **Conflict of Interest**

The authors declare no conflicts of interest.

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