Barrett's Esophagus: Prevalence and Efficacy of Endoscopic Mucosectomy

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Abstract: Background: Barrett's esophagus (BE) is a premalignant condition in which the normal squamous epithelium of the esophagus is replaced by intestinal metaplasia of variable degrees**.** It represents the most serious consequence of gastroesophageal reflux disease (GERD), as it may progress to adenocarcinoma. **Aim of the Work:** The aim of this study is to estimate the prevalence of BE as well as the variable degrees of metaplasia in patients with GERD and to study the efficacy of endoscopic mucosectomy in treatment of BE with high grade dysplasia (HGD) or intramucosal cancer (IMC). **Patients and Methods:** We studied 1268 patients presented to the outpatient clinic and endoscopy unit in Zagazig University hospital complaining of symptoms suggestive of GERD. They were subjected to thorough history taking, full clinical examination, routine laboratory investigations including complete blood count, liver and renal function tests, random blood glucose, coagulation profile in addition to abdominal ultrasonography, electrocardiography, upper gastrointestinal endoscopy for diagnosis of GERD and grading of its severity with biopsy taking and histopathological examination for patients who had BE. All patients with BE had a CT scan of their chest and abdomen. Patients who had BE with HGD or IMC were subjected to endoscopic mucosal resection (EMR). All patients with BE were followed for a median of 20 months with repeated upper endoscopy. **Results :** Out of 1268 patients presented to the outpatient clinic complaining of symptoms suggestive of GERD, 874 had endoscopic finding of various grades of reflux esophagitis and 52 patients had BE. Histopathological examination revealed that 35 patients had HGD, 12 patients had low grade dysplasia (LGD) and 5 patients had IMC. BE was more prevalent among the elderly males, obese patients and smokers. Those with HGD or carcinoma in situ (40 patients) were subjected to EMR and we found that EMR altered the histological grading of BE in 25 % of patients while 12.5 % were downgraded to LGD. EMR was associated with few complications the most significant of which was bleeding (10% of patients). One patient (2.5%) developed esophageal stenosis which was successfully managed by a single bougienage dilatation. Patients with LGD (12 patients) in addition to the 40 patients who had EMR were subjected to follow-up for a median of 20 months. One patient (2.5%) had a metachronous lesion detected after 25 months that was successfully treated with another EMR and histologically was still HGD. LGD patients had no change in grading during the follow up period.**Conclusions:** BE is a substantial medical problem in patients with GERD. EMR is a feasible, effective and low risk procedure that can be used to treat HGD and IMC which may complicate BE. Patients should be evaluated carefully prior to EMR and those with superficial lesions are the ideal candidates for EMR. However, it is strongly recommended to follow those patients by upper gastrointestinal endoscopy at regular intervals to rule out any recurrence.

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1. Introduction

GERD is a very common medical problem that results from reflux of excess acid and digestive secretions into the esophagus resulting in changes in esophageal mucosa **[1]**. Erosive esophagitis can lead to BE, which has been observed in 10% of patients with reflux esophagitis and 44% of those with peptic stricture. BE is defined as replacement of the normal stratified squamous epithelium anywhere within the tubular esophagus with metaplastic columnar epithelium containing goblet cells **[2]**. Most patients with BE are seen initially for symptoms of GERD such as heartburn, regurgitation and dysphagia. The Barrett's segment may be patchy and limited to the distal esophagus, or it may be confluent and involves most of the esophagus. On endoscopy, the presence of Barrett's epithelium is suggested by salmon pink mucosa in place of the paler squamous lining of the esophagus. However, biopsy is usually needed to confirm the diagnosis of BE **[2]**. The management of GERD can be divided into five steps; minimizing exposure of the esophagus to refluxant, alleviating symptoms, healing of esophageal lesions, preventing complications and maintaining remission **[3]**. Dysplasia is a morphological term which etymologically means "mal-formation". It can be a macroscopic or microscopic, congenital or acquired. If acquired, the nature of the dysplastic transformation can be regenerative (due to healing and repair following damage) or neoplastic (degenerative). The global incidence of esophageal adenocarcinoma

(EAC) arising from BE is 0.5% per year **[4]**. In the last 3 decades, the incidence of EAC has increased at a faster rate than any other cancer in the US and Western Europe **[5]**. In the Northern Ireland Barrett's esophagus register study, subgroup analysis of 374 patients with LGD followed up for a mean of 7 years, revealed the risk for developing high-grade dysplasia (HGD) or cancer was 1.4% per year **[6]**. In a meta-analysis involving four studies that included patients with HGD but excluded prevalent cancers and those patients with previous endoscopic and/or surgical intervention, the incidence of OA was estimated to be between 5.6% and 6.6% per year **[7]**.

2. Subjects and Methods

This study had been carried out in outpatient clinic and gastroenterology endoscopy unit of Internal Medicine Department in collaboration with Department of Pathology and tropical medicine, Faculty of Medicine, Zagazig University, during the period from April 2010 to October 2012.

Upper gastrointestinal endoscopy was done to all patients presented to the outpatient clinic complaining of symptoms suggestive of GERD. Biopsies were taken if there was endoscopic findings suggestive of BE and those with HGD or IMC within BE were subjected to EMR. The procedure was explained to the patients in details and all patients provided informed written consent.

Patients with decompansated liver disease, renal failure, disseminated malignancy, cardiac diseases such as acute coronary syndromes and heart failure, esophageal diseases such as stenosis, varices and telangectasia as well as pregnant females were excluded from the study.

All patients were subjected to Full history taking, complete clinical examination, routine laboratory investigations including (complete blood picture, liver and kidney function tests, coagulation profile and random blood sugar), abdominal ultrasonography, electrocardiography, upper gastro-intestinal endoscopy for diagnosis of reflux esophagitis and grading its severity were done according to Los Angeles Classification **[8]** as follows :

Grade A*:* One or more mucosal breaks confined to the mucosal folds, each not more than 5 mm in maximum length

Grade B*:* One or more mucosal breaks more than 5 mm in maximum length, but not continuous between the tops of two mucosal folds

Grade C*:* Mucosal breaks those are continuous between the tops of two or more mucosal folds, but which involve less than 75% of the esophageal circumference

Grade D*:* Mucosal breaks, which involve at least 75% of the esophageal circumference.

Biopsy specimens were taken from the esophagus of patients with erosive esophagitis who have criteria suggestive of BE as reported by Ell *et al.* **[9]** with histopathological examination of biopsy specimens.

Esophageal biopsy specimens were obtained by direct endoscopic vision using fenestrated, ellipsoid, spiked 7 mm open span biopsy forceps. Four quadrant biopsies were taken from areas that stained positive with methylene blue and repeated proximally every two cm so long as Barrett epithelium was suspected. The staining by methylene blue included the following steps:

1- Mucolysis by 10-20 ml of 10% acetylcystein solution for 2 minutes.
2- Staining by 10-20 ml of 0.5% methylene blue solution for 2 minutes.
3- Lavage, Rinsing off superficial methylene blue with 100-300ml water **[10].**

Biopsy specimens were fixed in 4% formalin, embedded in paraffin, serially sectioned and then stained with hematoxylin and eosin. Biopsy preparation and step serial sections of biopsy specimens were performed to enhance detection of glandular architecture according to protocols outlined by other investigators **[11].** The presence of distended, barrel, shaped goblet cells, indicated intestinal metaplasia, on routine hematoxylin and eosin stained slides from the esophagus of patients suspected to have SSBE at the time of initial diagnosis was confirmed by further sectioning and staining of the biopsy specimens with Alcian (pH 2.5) and periodic acid-Schiff. Columnar cells that had a barrel shape and intense Alcian blue staining were considered to be diagnostic of Barrett specialized epithelium **[12]**.

CT scan of the chest and abdomen were done to all patients with BE and lesions confined to the mucosal layer with no apparent lymph node metastases were considered for EMR.

Statistical analysis:

The Statistical Package for Social Science (SPSS) program version 10 was used for analysis of data. In the statistical analysis, each parameter was expressed as a mean value ± SD. Tests of significant difference were carried out with the *t*-test, and the level of significance was set at $P<0.05$. The t-test was used for analysis of two quantitative data. The Chi square test was used for comparison of qualitative data.

3.Results

Out of 1268 patients presented to the outpatient clinic complaining of symptoms suggestive of GERD, 874 patients had endoscopic finding of various grades of reflux esophagitis and 52 patients had BE (35 patients had HGD, 12 patients had LGD and 5 patients

with IMC). Patients with HGD or IMC were subjected to endoscopic mucosal resection. Patients with LGD were subjected to follow up endoscopy (in addition to those who had endoscopic mucosectomy) after a period of 16.3 to 27 months.

Table (1) Showed that BE was common among elderly patients (≥60 years), male patients, Obese (BMI≥30) and among smokers.

Table (1): Characteristics of Barrett esophagus patients.

Characteristics	No.	%
Age (years)		
Mean ±SD(range)		
62.8±11.4(43-72)		
<60	15	37.5
≥60	25	62.5
SEX ***Male***	35	87.5
Female	5	12.5
Obesity		
Obese(BMI≥ 30)	30	75
Non obese (BMI <30)	10	25
Smoking		
Smoker	28	70
Non smoker	12	30

Table (2) Showed that the mean BE length was 4.3±2.5 cm with a range of (1-11 cm). Long segment BE (LSBE ≥3 cm) was present in 15 patients (37.5%), while short segment BE (SSBE <3 cm) was present in 25 patients (62.5%). The mean size of lesion was 14.8 ± 10.3 mm with a range of (4-35 mm). Hiatus hernia was found in 18 patients (45 %), gastritis was found in 25 patients (62.5%) and duodenitis was found in 12 patients (30%).

Table (2): Characteristics of Barrett esophagus lesions

Characteristics	%	No.
BE length(cm)		
Mean ± SD (range)		
4.3±2.5 (1-11 cm)		
Long segment (≥3 cm)	15	37.5
Short segment (<3 cm)	25	62.5
Size of lesion(mm)		
Mean ± SD (range)		
14.8±10.3 (4-35 mm)		
Endoscopic characteristics (updated Paris classification)		
Slightly elevated (0-IIa)	36	90
Completely flat (0-IIb)	2	5
Slightly depressed (0-IIc)	2	5
Associated endoscopic findings		
Hiatus hernia	18	45
Gastritis	25	62.5
Duodenitis	12	30

According to the updated Paris classification, that is based on the Japanese classification of gastric cancer and among patients with HGD or IMC, thirty sex patients (90%) had type 0-IIa mucosal abnormalities (slightly elevated lesions), two patients (5%) had type 0-IIb mucosal abnormalities (completely flat lesions) and two patients (5%) had type 0-IIc mucosal abnormalities (slightly depressed lesions).

The prevalence of BE in patients with symptoms suggestive of GERD was 4.1% (52/1268, while in those with endoscopic erosive esophagitis was 5.9% (52/874).

Table (3) Among 35 patients who were diagnosed initially (by biopsy) as HGD and after mucosectomy and histopathological examination of the whole excised tissue, five patients were found to have only LGD and two had SMC.

Among five patients who were diagnosed initially as IMC, three patients were reclassified as SMC. There was a significant agreement between histological findings pre-EMR and post-EMR (Kappa Coefficient = 0.5± 0.136, P<0.001).

Table (4) Showed that there was a statistically significant difference in age between different grades of dysplasia with increasing age in patients with submucosal cancer (P<0.001).

Table (5) Showed that there was statistically significant difference in BE length between different grades of dysplasia toward LGD (P =0.04) while there was no statistically significant difference in lesion size between different grades of dysplasia (P =0.25).

Table (6) Showed that five patients with SMC had a mean age of 73.6 ± 8.3 years. The mean BE length was 5.8 ± 3.1 cm, and the mean lesion size was 17.6±11.9 mm with a range from 5 to 30 mm. The lesions were type IIa (superficial elevated). Histologic assessment detected tiny areas of low-grade differentiation moreover; lymphatic permeation was detected in two patients of them. Three patients of them (7.5% of all patients) underwent esophagectomy and the histopathologic assessment showed one T0N0 and two T1N0 while the other two patients were considered unfit for surgery due to advanced age (81 and 84 years) and/or comorbidity (cardiovascular disease) and they were included in the follow-up program .

Table (7) Showed that intra-procedural bleeding occurred in four patients (10%) which was controlled with epinephrine injections in two patients and with epinephrine injections plus clipping in the other two patients. Neither delayed bleeding nor perforations occurred and blood transfusion was not required but retrosternal pain was present in one patient (2.5%).

Table (8) Showed that endoscopic follow-up was performed to 46 patients (3 SMC patients did surgery and 3 HGD patients refused repeated examination). The follow up ranged from 6-27 months. In patients with HGD (33 patients), one patient with an original lesion of 20 mm, a metachronous lesion was

detected after 25 months. It was easily removed by EMR and the histologically was still HGD. BE patients with LGD had no change in grading during follow up period. One of the two patients with SMC enrolled in the follow up program and did not undergo surgery died from cardiovascular event 26 month later and the other was alive and cancer free at a 27 month follow-up.

An esophageal stenosis developed 8 months later in one patient (2.5%) with LSBE (7 cm). He had a 30 mm HGD lesion that was successfully treated by a single bougienage dilatation.

CT scan of the chest and upper abdomen were also performed after 6 months and then after 1 year to evaluate the lymph node status and the presence of metastases and were revealed no abnormality.

Table (3): Histology pre and post EMR.

	High-grade dysplasia	**Intramucosal cancer**	**Total number**	**Kappa Coefficient**	*P*
Histology (pre-EMR)	**No = 35**	**No = 5**	**40**		
Histology (post-EMR)				0.5 ± 0.136	< 0.001
Low-grade dysplasia	5	0	5		
High-grade dysplasia	28	0	28		
Intramucosal cancer	0	2	2		
Submucosal cancer	2	3	5		

(Strength of Agreement; < 0 Poor, 0 - 0.2 Slight, 0.21- 0.4 Fair, 0.41–0.6 Moderate, 0.61–0.8 Substantial, 0.81–1 Almost perfect).

Table (4): Grades of dysplasia in relation to age of patients.

Grade of dysplasia	**Number**	**%**	**Mean age of patients ± SD**	*P*
LGD	5	12.5	60.6±8.8	<0.001
HGD	28	70	61.76±11.8	
IMC	2	5	56±4.2	
SMC	5	12.5	*73.6±8.3	

Table (5): Grades of dysplasia in relation to BE length and size of resected lesions.

Grade of dysplasia	**Number**	**%**	**Mean length of BE ±SD(cm)**	**Mean size of BE ± SD (mm)**
LGD	5	12.5	6.6±4.1	22.5±8.7
HGD	28	70	3.6±1.8	13±10.2
IMC	2	5	3.7±1.8	16±5.7
SMC	5	12.5	5.8±3.1	17.6±11.9

P=0.04 P=0.25

Table (6): Characteristics of patients and lesions in patients with submucosal cancer (SMC).

No.	**Age (years) Mean ± SD**	**Sex**		**BE length(cm) Mean ± SD**	**Size of lesion(mm) Mean ± SD**	**Endoscopic characteristics**	**Pathological characteristics**	
		F	**M**				**Low grade of differentiation**	**Lymphatic permeation**
5	73.6±8.3	2	3	5.8±3.1	17.6±11.9	Superficial elevated (type IIa)	5	2

Table (7): Early complications after EMR

	No.	**%**	Management
Bleeding intraprocedural	4	10	Epinephrine and clipping
Delayed bleeding	0	0	
Blood transfusion	0	0	
Perforation	0	0	
Retrosternal pain	1	2.5	

Table (8) Endoscopic and histopathologic follow up of Barrett's esophagus patients (6-27 months).

	Grade of dysplasia	**Histopathologic change**		**Late complications**		
		- ve	**+ ve**	**Stenosis**	**Metachronous lesion**	**Death**
Without mucosectomy	low-grade dysplasia no=(12)	12	0	0	0	0
Post-endoscopic mucosectomy	low-grade dysplasia no=(5)	5	0	0	0	0
	high-grade dysplasia no=25/28	24	1	1	1	0
	Intramucosal cancer no=2	2	0	0	0	0
	submucosal cancer (no surgery) no= 2	2	0	0	0	1

4.Discussion

BE is a premalignant condition in which the normal squamous epithelium of the esophagus is replaced by intestinal metaplasia of variable length**.** It represents the most serious consequence of GERD, as it is associated with an increased incidence of esophageal adenocarcinoma **[13]**. The risk of esophageal adenocarcinoma with BE is 30 to 40 times higher than in patients without this condition. The progression of BE may involve the development of LGD and HGD before the eventual development of cancer **[14]**. The current therapeutic standard of care for Barrett's HGD or esophageal adeno-carcinoma is esophagectomy **[15]**. However esophagectomy is associated with very high rates of procedure related mortality and long term morbidity. Mortality rates ranging from 2.5–20.3% have been reported, and 30–50% of patients may develop serious postoperative complications such as pneumonia, anastomotic leaks and myocardial infarction. In addition, there have been reports of patients whose preoperative biopsy specimens showed IMC that was not seen in the surgical specimens **[16]**. Endoscopic ablative therapies such as Argon plasma coagulation (APC) and photodynamic therapy (PDT) have been proposed as less invasive alternatives to esophagectomy, but are clearly not optimal. These therapies are limited by the lack of tissue for histological assessment, which is crucial for determining treatment adequacy, and the possibility that the ablation may be incomplete, with remnant Barrett's mucosa after treatment; this persistent BE will remain at risk for progression to adenocarcinoma **[17]**.

EMR is increasingly being utilized as an alternative to surgery in the management of HGD and IMC of the gastrointestinal tract. Performing EMR is similar to surgical resection of the diseased mucosa. It is less invasive than surgery and, unlike ablative therapies; it provides tissue for histological assessment. The role of EMR in the treatment of early esophageal squamous cell carcinoma, early gastric cancer and early colonic cancer is established. More data concerning the efficacy of EMR in the context of BE with HGD and IMC are available **[18]**.

In the present study, we recruited 1268 patients referred to endoscopy units for evaluation of chronic GERD symptoms and we found that 52 patients had BE during the study period. In a study done in Germany**,** as much as 115 patients were found to have BE **(19)**. This difference may be attributed to the limited number of patients with early neoplastic lesions in BE detected in our endoscopy units. Furthermore, as surgery is still the gold standard treatment for HGD and IMC, the majority of those patients are referred for esophagectomy.

The prevalence of BE was 5.9% in patients with GERD symptoms. Taking into considerations the type of subjects included, the prevalence could have been much lower in the general population because of the known association of BE and GERD. In Northern Egypt, **Hak *et al.*** have found a prevalence rate of 9.9% of BE in patients with GERD, which agrees with the results of our study. They recruited symptomatic patients with GERD, but with an emphasis on the effect of acid and bile reflux on the esophageal mucosa **[20]**. Also **Fouad *et al.*** found a prevalence rate of 7.3% in patients with GERD in the Southern part of Egypt **[1]** which agrees with the results of our study.

The prevalence of BE varies around the world and it seems to be higher in western than eastern countries. Focusing on patients who presented for their initial endoscopy in the setting of suspected GERD, **Westhoff *et al.*** studied 378 consecutive patients who had biopsies taken from areas suspicious for BE. The overall prevalence of BE was found to be 13.2% **[22]**. **Ronkainen *et al.*** have used a population based study to estimate the prevalence of BE in Sweden. Of 19 000 subjects within a target age range of 20-80 years, a random sample of 3000 was surveyed by questionnaire. A random sub-sample of 1000 subjects then underwent upper digestive system endoscopy, in which an overall BE prevalence of 1.6% was observed. However, when reflux symptoms were present, the prevalence rose to 2.3% **[23]**. In another study in Korea, **Kim *et al.*** have found that, in the general population, the prevalence of BE was < 1%, and remained less common in Korea than in western countries **[24]**.

In our study, the mean age of patients with BE was 62.8 years. This is in agreement with **Cameron *et al.*** who found a mean age of 63 years at diagnosis of BE **[25]** and **Romero *et al.*** who found that the prevalence of BE increases with age from 20 to over 70 years **[26],** but this was against the results of **Fouad *et al.*** who found a mean age of 48.3 years at the diagnosis of BE **[21]**. It was suggested that, on average, a newly diagnosed BE had actually been present but undetected for over 20 years.

In the present study, BE was prevalent in males than females (male to female ratio was 7:1). This goes in the same way of the results of **Eisen *et al.*** yet with a lesser degree of male preponderance. They detected a male to female ratio of 2:1 **[27]**. On the other hand **Fouad *et al.*** found a greater degree of male preponderance. They detected a male to female ratio of 13.6:1 [**21**]. However, **Ritenbaugh *et al.*** have shown that there was an equal prevalence of BE in

men and women diagnosed with severe reflux by 24-hrs pH monitoring **[28]**. Considering the fact that sex distribution among Egyptians is homogenous with minimal female preponderance as reported in Demographic Health Survey in 1999, together with our finding of male to female ratio of 7:1 in patients with BE reflect a more propensity for males to be subjects for BE. Probably, men have more reflux symptoms or seek medical advice and endoscopic evaluation more than women do.

In the present work, Obesity was found in 75% of BE patients. In agreement with our findings, **Conio *et al.*,** found that obesity was associated with a 2.5 fold increase in the risk of BE, specifically that for each 10 pound increase in weight, or 5 point increase in BMI, there was a 10% and 35% increase in the risk of BE, respectively **[29]**. It has long been postulated that obesity increases GERD and could thus predispose individuals to BE.

We found also that BE was common in smokers (70% of BE patients) than non-smokers (30% of BE patients). Similar findings were reported by **Fouad *et al.,*** who found a statistically significant difference between smokers (61.6%) and nonsmokers (38.4%) in patients with BE **[21]**. On the other hand, **Moss *et al.*** showed no significant difference of smoking in patients with BE **[30]**.

In our study, the mean BE length was 4.3 cm, SSBE was found in 62.5% of patients and LSBE was found in 37.5% of patients. In agreement with our findings is the findings of **Fouad *et al.*** who reported that SSBE was present in 61 patients (84%), while LSBE was present in 12 patients (16%) **[21]**, and that of **Hak *et al.*** **,** who found the prevalence of endoscopically recognizable SSBE at 5-7% versus 1-3.4% for LSBE **[20]**.

Regarding associated endoscopic findings, hiatus hernia was found in 45% of BE patients, gastritis was found in 62.5% of BE patients and duodenitis was found in 30% of BE patients. In agreement with our findings is that of **Peters *et al.,*** who found that hiatus hernia was found in 39.7% of BE patients , gastritis was found in 72.7% of BE patients and duodenitis was found in 28.7% of BE patients **[31]**.

With respect to endoscopic characteristics, thirty six patients with a percentage of 90% had type 0-IIa mucosal abnormalities (slightly elevated lesions), two with a percentage of 5% had type 0-IIb mucosal abnormalities (completely flat) and two had type 0-IIc mucosal abnormalities (slightly depressed) with a percentage of 5%. Supporting our results, the findings of **Conio *et al.,*** who found that thirty six patients had type 0-IIa mucosal abnormalities and three, had HGD detected by random biopsies in a normal appearing BE [**29**]. In contrast **Moss *et al.,*** found that the endoscopic appearance of the area for EMR was flat and inconspicuous in 26 patients (35%), mucosal irregularity in 28 patients (37 %), nodule in 20 (27 %), and ulcerated in 1 patient (1 %) **[30]**.

Interestingly, in the present work, accurate dysplasia grading are essential, and this series demonstrates the limitations of a biopsy-alone strategy, with EMR resulting in change in grade of dysplasia in 25%. Of the patients, 5 (12.5%) were downgraded (LGD). Therefore, without EMR, nearly one in eight patients would have undergone unnecessary esophagectomy if surgery based on biopsy alone was the first-line therapy for Barrett's HGD or IMC. The results of **Moss *et al.,*** are supportive to our findings. They found a change in the grade of dysplasia in 48% of BE patients [**30]**. In the same context, **Peters *et al.,*** found that there was a change in diagnosis in 49% and a relevant change in treatment policy in 30% [**31**]. Our results confirm that this phenomenon is likely to be a pervasive problem with biopsy-directed treatment, as, in contrast to biopsies, EMR provides information on breadth, depth, and potentially focal areas of more advanced pathology.

We found that there was statistical significant difference in BE length (p=0.04) between different grades of dysplasia toward LGD while there was no statistically significant difference in lesion size (P=0.25) between different grades of dysplasia. In agreement with our results is that of **Conio *et al.,*** who found no statistically significant difference between the grades of dysplasia regarding size of lesion resected [**29]**. But we found a statistical significant difference between the grades of dysplasia regarding age. In agreement with our results is that of **Conio *et al.,*** who found statistically significant difference between the grades of dysplasia regarding age [**29**].

Regarding submucosal cancer, there were no deaths due to progression of Barrett's adenocarcinoma (the death of patients due to unrelated causes), closely similar findings were reported by **Moss *et al.*,(30)** and **Pech *et al.,* [32]**.

EMR was associated with few complications, corroborating the findings of others; **[9**, **19, 32]**. Intra-procedural bleeding occurred in 10% of our patients and was managed endoscopically without blood transfusion. Esophageal stenosis is a late complication of EMR. In our study, one patient (2.5%) developed stenosis. Larger EMR resections may increase the risk; in a study of 137 patients, stenosis was seen only when EMR involved more than two-thirds of the esophageal circumference **[33]**. However, **Seewald *et al.,*** had found that only two of 12 patients developed stenosis after circumferential EMR [**34**].

The perforation risk is generally 0-2.6%. No perforations occurred in our series. There is limited

information on the long-term effectiveness of EMR. In our study, follow-up for a median 20 months was available in 94.2% of patients. One of the 40 patients (2.5%) had a metachronous lesion after 25 months, successfully treated with another EMR. According to **Sampliner *et al.*,** malignant transformation of HGD is about 34% in 6-54 months [**35**], While according to **Ell *et al.*,** the incidence of metachronous HGD or esophageal adenocarcinoma during follow up was 11% **[9]**.

We can conclude that BE is considerable medical problem in GERD patients and EMR is a feasible, low risk procedure for the treatment of HGD and IMC within BE. It has the advantage of leaving the esophagus in situ and tissue confirmation of the disease. Patients need careful evaluation prior to EMR, and only those with superficial lesions and no lymph node involvement should undergo the procedure. Disadvantages include the need for frequent and meticulous surveillance as well as leaving at-risk mucosa remaining behind.

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