# EMR for Barrett's esophagus–related superficial neoplasms offers better diagnostic reproducibility than mucosal biopsy CME

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**Background:** EMR of Barrett's esophagus (BE)–related superficial neoplasms represents an efficacious staging modality. It also allows for better pathologic grading compared with mucosal biopsy specimens. However, the interobserver variation in the interpretation of EMR specimens has not been tested.

**Objective:** To evaluate consistency in the diagnosis of BE–related neoplasia on EMR specimens.

**Design:** Nine pathologists reviewed 25 esophageal EMR specimens and corresponding biopsy specimens independently. Each pathologist classified the cases as either non-neoplastic BE, low-grade dysplasia, high-grade dysplasia, intramucosal adenocarcinoma, or invasive adenocarcinoma. Interobserver concordance for both specimens from EMRs and biopsies was measured by intraclass correlation and Kendall's coefficient of concordance. The proportion of agreement was also calculated for each specimen and compared for EMR and biopsy by using the Wilcoxon signed rank test.

**Setting:** Teaching hospitals.

**Patients:** Twenty-five patients who underwent EMR for BE–related neoplasia.

**Results:** The intraclass correlation and the Kendall's coefficient for the 25 biopsy specimens was 0.938 (95% CI 0.880-0.965) and 0.677, respectively; for the 25 EMRs, these were significantly improved, at 0.977 (95% CI 0.957-0.987) and 0.831, respectively. In addition, the proportion of agreement for EMR specimens was significantly better compared with biopsy specimens ($P = .015$).

**Conclusions:** Interobserver agreement of BE-related neoplasia on EMR specimens is significantly higher compared with biopsy specimens. The results may relate to the larger tissue sampling compared with biopsy specimens and the ability to evaluate mucosal landmarks, such as double muscularis mucosae. Thus, we suggest that EMRs, in addition to being a staging and therapeutic procedure, improve diagnostic consistency. (Gastrointest Endosc 2007;66:660-6.)

The incidence of adenocarcinoma arising in Barrett's esophagus (BE) has risen over the last few decades. Detection of superficially invasive tumors is critical, because these tumors have a relatively good 5-year prognosis compared with advanced cases.[1] To this day, and despite continued controversy, esophagectomy is the standard therapy for not only invasive esophageal adenocarcinoma but also superficial adenocarcinoma. Furthermore, some authorities advocate esophagectomy for high-grade dysplasia (HGD),[2-5] whereas other investigators recommend monitoring patients until intramucosal adenocarcinoma develops.[6,7] Finally, surgeons gradually rely more heavily on preoperative tumor grading, staging, and estimation of the risk of lymph-node metastasis to introduce techniques with less morbidity, eg, vagal-sparing esophagectomy, for presumed node-negative cases.[8]

Despite recent advances in endoscopic imaging techniques, such as optical coherence tomography[9,10] and confocal endomicroscopy,[11,12] histopathologic evaluation of mucosal biopsy specimens remains the foundation of

*Abbreviations: BE, Barrett's esophagus; CA, adenocarcinoma; HGD, high-grade dysplasia; IMC, intramucosal adenocarcinoma; IND, epithelial atypia, indefinite for dysplasia; LGD, low-grade dysplasia.*

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clinical decision making of patients with BE. However, the limited reproducibility of diagnoses of BE-related neoplasms, particularly dysplasia on biopsy specimens,[13,14] has raised concern in clinical circles about the ability of pathologists to provide consistent and accurate diagnoses upon which management decisions are based.

EMR, originally developed as a diagnostic procedure (''strip-off biopsy'') in the early 1980s, has gained considerate attention recently as a potential curative form of therapy for patients with HGD and superficial cancers of the esophagus and the stomach.[15] Although most centers report EMR to be effective as a therapeutic modality,[16-18] some studies showed worrisome high rates of positive lateral and/or deep resection margins.[19-21] More recently, EMR has also been advocated as a staging modality,[22-24] because the procedure allows to remove intact mucosa and submucosa, thus enabling complete and thorough microscopic evaluation for the presence or the absence of mucosal and submucosal invasion. For instance, we previously demonstrated that EMR, as a diagnostic tool, is superior to mucosal biopsy. In our experience, up to 34% of mucosal biopsy specimens of esophagogastric neoplasms were upgraded on EMR specimens.[25] However, unlike mucosal biopsy specimen analysis, the reproducibility of the histopathologic evaluation of BE and its neoplasms in EMR specimens has not been previously tested. Therefore, in this study, we evaluated the reproducibility of grading dysplasia and cancer in EMR specimens by comparing the interobserver concordance of 9 pathologists, all of whom independently reviewed EMR specimens and mucosal biopsy specimens from a cohort of 25 patients with BE and with neoplasia.

**Capsule Summary**

**What is already known on this topic**

- EMR of Barrett's esophagus (BE)–related superficial neoplasms allows for better pathologic grading than mucosal biopsy specimens, but interobserver variation in the histologic interpretation of EMRs has not been studied.

**What this study adds to our knowledge**

- Interobserver agreement of BE-related neoplasia on EMRs was significantly higher compared with biopsy specimens, possibly because of the larger size of tissue samples.

## MATERIALS AND METHODS

Twenty-five EMR specimens from 25 patients with BE, all of whom had corresponding perioperative (either before or after EMR) biopsy specimens from the same area performed within 3 months of the EMR procedure form the basis of this study. All specimens were obtained from the surgical pathology files of the Massachusetts General Hospital (n = 21) or Sullivan Nicolaides Laboratory (n = 4). All mucosal biopsy specimens were obtained by using a large-particle biopsy forceps (''jumbo forceps''). EMR was performed according to a standardized protocol after informed consent was obtained from the patients. Briefly, upon visual inspection of the size and confines of the neoplastic lesion, the mucosal target was lifted from the underlying muscularis propria by injecting saline solution, either with or without epinephrine, into the submucosa to form a sublesional bulla. The cap or snare technique[26] was then used to resect the lesion. In accordance with a previously published protocol,[21] all EMR specimens were marked with India ink along their lateral and deep margins, then were stretched and pinned to a wax block, photographed, fixed in 10% formaldehyde for 24 hours, and then serially sectioned at 2-mm intervals before routine histologic processing of all tissue. Sections were stained with H&E for microscopic analysis.

Before this study, the 25 EMR specimens at the time of resection had been diagnosed as BE, 3; low-grade dysplasia (LGD), 2; HGD, 7; intramucosal adenocarcinoma (IMC), 10; superficially invasive adenocarcinoma (CA), 3. The 25 corresponding biopsy specimens that had for original diagnoses: BE, 2; LGD, 3; HGD, 7; IMC, 10; and invasive CA, 3 were independently and blindly reviewed by 9 pathologists with expertise in GI pathology. All reviewers, with the exception of a senior resident with a particular interest in the field, are GI pathologists with years of experience. At the time of the review, the pathologists were blinded as to the original biopsy specimens (albeit it was not considered for this analysis) and to the relationship between biopsy and EMR specimens.

Lesions upon review were classified based on previously published criteria[14,27] For the purpose of this study, the lesions had to be classified in 1 of 5 categories, ie, no dysplasia, LGD, HGD, IMC, and invasive CA. ''Epithelial atypia, indefinite for dysplasia'' (IND) was not an option, and it was recommended to the reviewers to choose LGD instead. The rationale was the similar combination of IND and LGD for statistical purposes, by previous investigators,[7,14] and reinforced by the clinical practice that dictates the same surveillance protocol for both lesions when they are diagnosed.[28]

Briefly, LGD was characterized by mild architectural complexity, with glands lined by crowded, elongated cells with hyperchromatic and basilar pseudostratified nuclei. HGD displayed more pronounced architectural abnormalities, with gland branching and budding. Vesicular nuclei with prominent nucleoli, partial or total loss of nuclear polarity, and a high nuclear-to-cytoplasmic ratio were also commonly observed. Mitoses were usually numerous. IMC required high nuclear grade and a back-to-back or syncytial growth pattern, abortive microglands, or small