

Methylene Blue Chromoendoscopy for Detecting Intestinal Metaplasia in Barrett's Esophagus



Medical Science

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ABSTRACT

The presence of intestinal metaplasia (IM) in the columnar lined distal oesophagus defines Barrett's oesophagus with the risk of Malignancy in future. The distribution of both IM and dysplasia (low grade (LGD) and high grade (HGD)) within the columnar lined oesophagus is patchy and mosaic requiring random biopsies. Techniques that could help target areas of high yield within Barrett's mucosa would be helpful.

Methods: patients detected with columnar mucosa in the distal oesophagus were studied. The distal oesophagus was sprayed with Methylene blue and the oesophageal columnar mucosa patterns were noted and targeted for biopsy. All biopsies were read by pathologists blinded to the endoscopic findings.

Results: Eighty patients with suspected Barrett's oesophagus (that is, columnar lined distal oesophagus) were studied: mean age 45 years (range 30–60). Mean length of columnar mucosa was 3.7 cm (range 0.5–17). Three types of mucosal patterns were noted within the columnar mucosa after spraying Methylene Blue - villous pattern, circular pattern, and irregular pattern. The yield of IM on target biopsies according to the patterns was: villous 57/62 (97%) and circular 2/12 (17%). Six patients had an irregular pattern and all had high grade dysplasia (HGD) on biopsy (6/6 (100%)). Eighteen patients had Low grade dysplasia (LGD) on target biopsies; all had the villous pattern. All patients with long segment Barrett's were identified using MCE whereas 23/28 patients (82%) with short segment Barrett's had the villous pattern.

Conclusion : MB helps visually identify areas with IM and HGD having specific patterns but not patients with LGD (appear similar to IM). MB may be a useful clinical tool for the increased detection of patients with IM as well as for surveillance of patients for the detection of HGD. If these preliminary results are validated, MB would help identify high yield areas, potentially eliminating the need for random biopsies.

Barrett's oesophagus is the premalignant lesion for adenocarcinoma. It is a condition in which the squamous mucosa of the distal oesophagus is replaced by columnar mucosa, specifically intestinal metaplasia (IM). The incidence of oesophageal adenocarcinoma is rapidly rising. This has driven efforts to identify patients with the premalignant lesion—that is, Barrett's oesophagus. IM within the columnar lined oesophagus predisposes patients to the development of adenocarcinoma.

As IM is part of the definition and is the epithelial type associated with cancer, obtaining biopsies from the columnar lined distal oesophagus is mandatory. The sensitivity and positive predictive values of standard upper endoscopy for diagnosing Barrett's oesophagus have been reported as 82% and 34%, respectively. This is secondary to the patchy and mosaic presence of IM in the columnar distal oesophagus. Seeing through endoscopy is advocated in patients with gastro-oesophageal reflux (GERD) symptoms for detection of Barrett's oesophagus with random biopsies. Detection of IM from random biopsies of the columnar segment confirms the diagnosis of Barrett's oesophagus.

Methylene Blue is a contrast stain which helps highlight the mucosal surface. Our aim was to use endoscopy in combination with chromoscopy to help identify areas of IM and dysplasia within the columnar lined oesophagus.

METHODS

Patients

Patients undergoing upper gastro intestinal endoscopy for GERD symptoms, suspected Barrett's oesophagus, were enrolled and gave written informed consent. Barrett's oesophagus was defined as the presence of columnar mucosa in the distal oesophagus of any length (< 3cms or >3cms) with IM on biopsy. The length of Barrett's, in patients with circumferential and non-circumferential segments, was measured from the gastro-oesophageal junction, defined as the most proximal portion of the gastric folds, to the proximally displaced squamocolumnar junction. Patient age, sex,

were noted and the length of Barrett's oesophagus was recorded at endoscopy.

Chromoendoscopy procedure

At the time of upper endoscopy, the columnar mucosa in the distal oesophagus was sprayed with Methylene Blue using a spray probe. Once the mucosa was exposed to the stain, the different mucosal patterns were carefully observed. After a mucosal pattern was observed, a biopsy forceps was then passed through the channel to the endoscope tip and to the specific targeted area, and was then biopsied (captura serrated max forceps – spike from Wilson-Cook Medical Inc).

Histology

All biopsy specimens were fixed in 10% buffered formalin and submitted for histopathological examination. The tissues were then embedded in paraffin and stained with haematoxylin-eosin and alcian blue at pH 2.5. All biopsy specimens were then reviewed by pathologists who were blinded to the endoscopy results and patterns. Dysplasia in the biopsies was classified as no dysplasia, low grade dysplasia (LGD), high grade dysplasia (HGD), and adenocarcinoma.

Statistical analysis

The investigators examined the initial chromoendoscopy images to decide on the various patterns visualised. Biopsy confirmed IM and dysplasia were used as the outcome measures. The sensitivity, specificity, and positive predictive value of chromoendoscopy patterns for the detection of IM and dysplasia were then calculated.

RESULTS

Eighty patients with suspected Barrett's oesophagus were studied. Mean age 45 years (range 30–60). Mean length of columnar mucosa was 3.7 cm (range 0.5–17). Long segment Barrett's oesophagus (LSBO) was documented as ≥ 3 cm of columnar mucosa whereas short segment Barrett's oesophagus (SSBO) was <3 cm of columnar mucosa. No linear ero-

sions or plaques were seen on standard upper endoscopy, except in one patient, as described below. No adverse reaction to Methylene blue was identified in the group.

CE patterns

Three types of mucosal patterns were noted within the columnar mucosa after spraying Methylene blue and using endoscopy: villous pattern, circular pattern, and irregular pattern

Three distinct mucosal patterns observed after spraying methylene blue: villous, circular and irregular.

villous pattern : presence of a clear villiform pattern including tortuous and thick villi, appearance but regular.

Circular pattern : presence of circular areas arranged in a regular fashion.

Irregular: significant distortion and irregularity pattern.

The yield of IM on target biopsies according to the patterns was as follows: villous 57/62 (97%) and circular 2/12 (17%). Thirty four of 80 patients had LSBO and all were identified using CE whereas 23/28 patients (82%) with SSBO had the villous pattern. Sensitivity, specificity, and positive predictive values of the villous pattern for detecting IM were 97%, 76%, and 92%, respectively. All patients with LSBO were detected with the villous pattern (sensitivity and specificity 100%), and in the 41 patients with SSBO the sensitivity and specificity of the villous pattern for detecting IM were 92% and 69%, respectively.

Detection of dysplasia

LGD was detected in 18 patients; all had the villous pattern. Six patients had an irregular pattern and all had HGD on biopsy (6/6 (100%)) Mean length of Barrett's in patients with HGD was 5 cm (range 1-10 cms).

DISCUSSION

Currently, endoscopy with biopsy is the gold standard in making a diagnosis of Barrett's oesophagus. In a study of 570 patients undergoing upper endoscopy, Barrett's oesophagus was suspected in 146 patients; however, only 60 patients had a diagnosis confirmed by biopsy. SSBO was more frequently suspected than LSBO but was correctly diagnosed only 25% of the time compared with 55% for LSBO. The positive predictive value of endoscopy for making a diagnosis of Barrett's oesophagus was only 34%. Thus improvements are clearly needed in improving our diagnostic techniques for this premalignant lesion.

The presence of the villous pattern had a high sensitivity, specificity, and positive predictive value—97%, 76%, and 92% respectively. CE helps visually identify areas with IM and HGD that have specific patterns.

chromoendoscopy offers good imaging. Our results show that CE can be a significant standard endoscopy for diagnosing Barrett's. future applications of this technique may include the recognition of IM in patients with suspected SSBO, and screening patients with chronic GORD for the documentation of Barrett's oesophagus as well as for the detection of HGD during surveillance endoscopy. The sensitivity and specificity results for detecting HGD were high but are based on a small number of patients and a larger number of such patients should be evaluated to confirm these results.

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