

## One-step chromoendoscopy and structure enhancement using balsamic vinegar for screening of Barrett's esophagus

Oliver Pech<sup>1</sup>, Maria C. Petrone<sup>2</sup>, Hendrik Manner<sup>1</sup>, Thomas Rabenstein<sup>1</sup>, Andrea May<sup>1</sup>, Jürgen Pohl<sup>1</sup>, Christian Ell<sup>1</sup>

(1) Department of Medicine II, HSK Wiesbaden, Teaching Hospital of the University of Mainz, Germany ; (2) Division of Gastroenterology, IRCCS San Raffaele Hospital, Milan, Italy.

### Abstract

**Background and study aims :** Screening for specialized columnar epithelium (SCE) within columnar lined esophagus (CLE) with standard video endoscopes is not reliable enough. Several methods to improve accuracy of predicting presence of SCE like chromoendoscopy with vital stains or structure enhancement with acetic acid have been introduced but data up to now remains controversial. The present prospective study was conducted to evaluate a combination of chromoendoscopy and acetic acid structure enhancement using the naturally brownish coloured balsamic vinegar during routine upper endoscopy.

**Patients and methods :** Between March and July 2006 20 patients with macroscopic suspicion for SCE during routine endoscopy were included prospectively. Saline diluted balsamic vinegar (3%) was administered with a spraying catheter at the distal esophagus. After 1 minute the distal esophagus was evaluated for the presence of SCE according to the mucosal surface pattern (pattern I-II : round pits/circular pattern predicting gastric epithelium ; pattern III-IV : ridged/villous pattern predicting Barrett's epithelium). Only HR-videoendoscopes without magnification were used. After presence or absence of SCE was defined by the endoscopist targeted biopsies of the CLE were performed. Histological results were compared with endoscopic findings.

**Results :** In 9 of 20 patients (13 male, 7 female ; mean age 60.0 ± 12.8 years) biopsy specimen revealed SCE within CLE on histology. Prediction of BM after balsamic vinegar staining was possible in all cases. Surface pattern I-II was found in 9 patients and pattern III-IV in 11 patients. Accuracy, sensitivity and specificity for BV staining predicting SCE were 90%, 100% and 82%, respectively.

**Conclusion :** Chromoendoscopy with balsamic vinegar combines the advantages of chromoendoscopy and structure enhancement by acetic acid for detection of SCE. The reliability in predicting the presence of SCE was high in this prospective feasibility study. (*Acta gastroenterol. belg.*, 2008, 71, 243-245).

**Key words :** Barrett's esophagus ; endoscopy ; chromoendoscopy ; esophagus ; reflux disease.

### Introduction

During the last 30 years the incidence of adenocarcinoma in Barrett's esophagus has raised six fold and mortality of esophageal adenocarcinoma even more than seven fold (1). Barrett's esophagus is a known premalignant condition for adenocarcinoma and therefore several gastroenterological associations developed guidelines for surveillance of patients with Barrett's metaplasia (2,3).

Detection of Barrett's esophagus, especially small areas of specialized columnar epithelium (SCE) within columnar lined esophagus, is a well known problem and therefore several methods to improve endoscopic diagnosis have been introduced. Especially chromo-

endoscopy with vital stains like methylene blue and structure enhancement with acetic acid are promising techniques to visualize Barrett's epithelium during endoscopy (4-9).

Guelrud *et al.* (7) was able to demonstrate that structure enhancement with acetic acid in combination with magnification endoscopy could discriminate different mucosal structure patterns (I-IV). Villous and cerebriform pit surface structure were present in 87% and 100% of SCE. Round and straight pits predicted gastric epithelium in 89%.

We evaluated a new method combining the advantages of chromoendoscopy and acetic acid structure enhancement by using balsamic vinegar in patients with suspected SSBE. The objective of this prospective feasibility study was to investigate the diagnostic yield of HR-endoscopy without magnification after application of balsamic vinegar (histological diagnosis of SCE per patient).

### Methods

Consecutive patients with columnar lined distal esophagus (columnar mucosa < 3 cm) were prospectively included in this study. Patients with known Barrett's esophagus were excluded. Reasons for upper endoscopy were chronic reflux symptoms in 6, former ablation of Barrett's esophagus in 6, referral with suspected Barrett's esophagus without histological confirmation in 4 and other in 4 patients.

Only HR-videoendoscopes without magnification (Fujinon EG-450HR ; Fujinon Europe, Inc., Willich, Germany) were used. All patients with known BM were excluded. Endoscopic procedures were performed by experienced endoscopists in the field of Barrett's esophagus (O.P., T.R., H.M.). 5-10 ml of diluted BV (50% BV and 50% saline resulting in 3% acetic acid) were sprayed over columnar mucosa in the distal esophagus with a

Correspondence to : Oliver Pech, M.D., Department of Internal Medicine II, HSK Wiesbaden, Ludwig-Erhard-Strasse 100, 65199 Wiesbaden, Germany. E-mail : oliver.pech@t-online.de

Submission date : 17.10.2007  
Revised version : 08.01.2008  
Acceptance date : 07.03.2008

special spraying catheter (PW-5L, Olympus, Germany). After staining presence or absence of SCE was defined by the endoscopist according to the surface structure within CLE according to Guelrud's classification (round pits/circular pattern predicting gastric epithelium (type I-II) and ridged/villous pattern predicting Barrett's epithelium (type III-IV) (7). Pictures of the distal esophagus were acquired and digitally stored. After the staining procedure four quadrant biopsies every 1 cm within the columnar lined esophagus were performed according to the guidelines of the German Gastroenterological Society (2). Biopsies were routinely fixed in formalin and paraffin embedded. Serial sections (5  $\mu$ m) were cut and stained with haematoxylin and eosin. Diagnoses were made according to the WHO classification (10). Barrett's esophagus was diagnosed if intestinal metaplasia with columnar and goblet cells were present. The histological specimens were assessed by an experienced pathologist in the field of Barrett's esophagus blinded to patterns.

Pathology was considered as the "gold standard" for detection of BM. The histological results were compared with the results of the BV staining and sensitivity, specificity, positive predictive value, negative predictive value were calculated for the diagnosis of BM with HR-videoendoscopy and BV staining.

All patients were informed before endoscopy with a standardized information brochure and by the endoscopist about the procedure and the performance of chromoendoscopy with acetic acid (BV). Research was carried out in accordance with the Helsinki Declaration.

## Results

20 patients (13 male, 7 female; mean age  $60.0 \pm 12.8$  years) were included prospectively between March and July 2006 in this feasibility study.

In 9 of 20 included patients (45%) Barrett's esophagus could be confirmed histologically and in 11 patients only gastric mucosa without the presence of goblet cells was found on histology.

In total, 98 biopsy specimens were obtained (4.9 biopsies/patient) and in 38 specimens (38.8%) intestinal metaplasia with goblet cells were found on histology. The mean length of those patients with proven Barrett's esophagus was  $13 \pm 8$  mm.

In all patients SCE could be predicted by BV staining according to the observed mucosal pattern (III-IV) (Fig. 1a, b). Two patients were considered as positive for Barrett's epithelium but histology revealed only gastric epithelium. Gastric epithelium could be predicted correctly in 9 of 11 patients (Table 1).

Accuracy, sensitivity and specificity for BV staining predicting SCE within CLE were 90%, 100% and 82%, respectively.

Accuracy, sensitivity and specificity for BV staining predicting gastric epithelium within CLE were 82%, 82% and 100% respectively.

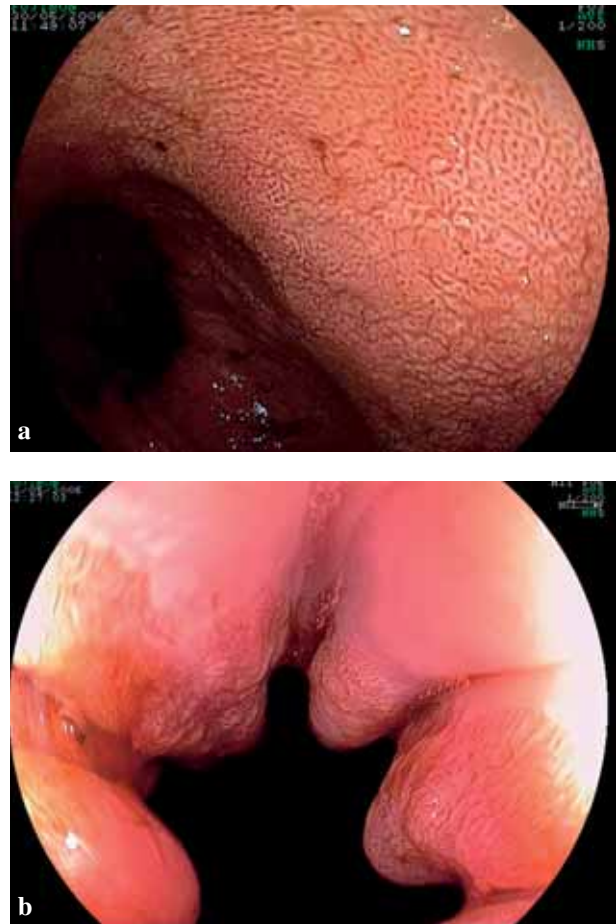


Fig. 1. — Ridged (1a) and cerebriform (1b) mucosal surface pattern after staining with balsamic vinegar predicting Barrett's esophagus.

## Discussion

Endoscopic detection of BM and the discrimination of cardiac mucosa, particularly in short segments of CLE, remains a well known problem. In a study of 570 patients SSBE was only correctly diagnosed 25% and LSBE 55% of the time (11). Several efforts have been made to improve diagnosis of BE and its discrimination from cardiac epithelium but up to now data are controversial.

Especially chromoendoscopy with methylene blue was considered to be a promising method to improve detection of BM and Barrett's neoplasia (5,6,12). The vital stain MB is taken up preferably by goblet cells in specialized intestinal metaplasia in BM. Canto *et al.* (6) evaluated a high accuracy of 95 % of MB staining for the detection of SIM in both short and long-segment Barrett's esophagus. However, other investigators have not been able to confirm these results (13-15).

Further approaches to improve detection of BM were magnification endoscopy with or without prior staining. Sharma *et al.* studied 80 patients with suspected Barrett's esophagus (4). He performed magnification endoscopy after staining with indigo carmine and three types of mucosal patterns were discriminated. 97% of patients

Table 1. — Surface pattern analysis predicting Barrett's and gastric epithelium

	Barrett's epithelium	Gastric epithelium	N
Pattern I-II	0	9	9
Pattern III	5	1	6
Pattern IV	4	1	5

with a ridged/villous pattern had BM on target biopsy. In contrast only 17% mucosal areas with circular pattern had proven BM on histology. Sensitivity and specificity and positive predictive value of the ridged/villous pattern for detection of BM were 92%, 69% and 92% respectively.

Guelrud *et al.* (7,8) also performed enhanced magnification endoscopy but after application of acetic acid and detected four different mucosal surface patterns: I, round pits; II, reticular; III, villous; and IV, ridged. The yields for detecting SCE according to endoscopic patterns were 87% for pattern III and 100% for pattern IV. Recent reports confirmed the promising results of Guelrud *et al.* that acetic acid staining facilitates the detection of SCE within CLE (11,16). One major disadvantage of magnification endoscopy is the time consuming procedure especially at the gastro-esophageal junction with peristalsis and respiratory movements. Therefore, it would be desirable to achieve similar results by using regular HR-videoendoscopes combined with chromoendoscopy.

In our series we combined the advantages of chromoendoscopy and the structure enhancement effect of acetic acid by using balsamic vinegar. In this preliminary study we were able to demonstrate that the effect of acetic acid could be enhanced by the dark brownish color of the vinegar and the pattern could be recognized easily even with regular HR-videoendoscopes without the time consuming procedure of magnification. Even though the number of patients is limited accuracy, sensitivity and specificity were very promising. One disadvantage of staining with BV is the impaired assessment of the gastric epithelium after staining because of the dark color of BV, similar to the use of methylene blue or other dyes. Therefore, staining with BV should be performed at the end of the procedure.

Chromoendoscopy with balsamic vinegar seems to be a promising new staining method to facilitate detection of BM during routine endoscopy. Further prospective

studies, especially comparing BV with regular acetic acid in a prospective fashion are needed to confirm the results of this preliminary report.

## References

1. POHL H., WELCH H.G. The role of overdiagnosis and reclassification in the marked increase of esophageal adenocarcinoma incidence. *J. Natl. Cancer Inst.*, 2005 Jan 19, **97** (2): 142-6.
2. KOOP H., SCHEPP W., MULLER-LISSNER S., MADISCH A., MICKLEFIELD G., MESSMANN H., FUCHS K.H., HOTZ J. Consensus conference of the DGVS on gastroesophageal reflux. *Z. Gastroenterol.*, 2005 Feb, **43** (2): 163-4.
3. SAMPLINER R.E., PRACTICE PARAMETERS COMMITTEE OF THE AMERICAN COLLEGE OF GASTROENTEROLOGY. Updated guidelines for the diagnosis, surveillance, and therapy of Barrett's esophagus. *Am. J. Gastroenterol.*, 2002 Aug, **97** (8): 1888-95.
4. SHARMA P., MAYO M., TOPALOVSKI M., WESTON A.P. Methylene blue chromoendoscopy for the detection of patients with short segment's Barrett's esophagus. *Gastrointest. Endosc.*, 2001, **54**: 289-93.
5. CANTO M.F., SETRAKIAN S., WILLIS J., CHAK A., PETRAS R., POWE N.R. *et al.* Methylene blue-directed biopsies improve detection of intestinal metaplasia and dysplasia in Barrett's esophagus. *Gastrointest. Endosc.*, 2000, **51**: 560-8.
6. GOSSNER L., PECH O., MAY A., VIETH M., STOLTE M., ELL C. Comparison of methylene blue-directed biopsies and four-quadrant biopsies in the detection of high-grade intraepithelial neoplasia and early cancer in Barrett's oesophagus. *Digest. Liver Dis.*, 2006, **38**: 724-29.
7. GUELTRUD M., HERRERA I. Acetic acid improves identification of remnant islands of Barrett's epithelium after endoscopic therapy. *Gastrointest. Endosc.*, 1998 Jun, **47** (6): 512-5.
8. GUELTRUD M., HERRERA I., ESSENFELD H., CASTRO J. Enhanced magnification endoscopy: a new technique to identify specialized intestinal metaplasia in Barrett's esophagus. *Gastrointest. Endosc.*, 2001 May, **53** (6): 559-65.
9. HOFFMAN A., KIESSLICH R., BENDER A., NEURATH MF., NAFE B., HERRMANN G., JUNG M. Acetic acid-guided biopsies after magnifying endoscopy compared with random biopsies in the detection of Barrett's esophagus: a prospective randomized trial with crossover design. *Gastrointest. Endosc.*, 2006, **64** (1): 1-8.
10. WERNER M., FLEJOU J.F., HAUNAUT P. *et al.* Adenocarcinoma of the esophagus. In: AALTONEN L.A., HAMILTON S., KLEIHUES P. *et al.* (eds). WHO classification of tumors: pathology and genetics of tumors of the digestive system. Berlin: Springer, 2000, 16-22.
11. ELOUBEIDI M.A., PROVENZALE D. Does this patient have Barrett's esophagus? The utility of predicting Barrett's esophagus at the index endoscopy. *Am. J. Gastroenterol.*, 1999 Apr., **94** (4): 937-43.
12. KIESSLICH R., HAHN M., HERRMANN G., JUNG M. Screening for specialized columnar epithelium with methylene blue: chromoendoscopy for patients with Barrett's esophagus and a normal control group. *Gastrointest. Endosc.*, 2001, **53**: 47-52.
13. DAVE U., SHOUSA S., WESTABY D. Methylene blue staining: is it really useful in Barrett's esophagus? *Gastrointest. Endosc.*, 2001, **53**: 333-335.
14. WESTON A.P., KRMPOTICH P.T., CHERIAN R., DIXON A., TOPALOSVKI M. Prospective long-term endoscopic and histological follow-up of short segment Barrett's esophagus: comparison with traditional long segment Barrett's esophagus. *Am. J. Gastroenterol.*, 1997, **92**: 407-13.
15. EGGER K., WERNER M., MEINING A., OTT R., ALLESCHER H.D., HOFLER H. *et al.* Biopsy surveillance is still necessary in patients with Barrett's esophagus despite new endoscopic imaging techniques. *Gut*, 2003, **52**: 18-23.
16. MAYINGER B., OEZTURK Y., STOLTE M., FALLER G., BENNINGER J., SCHWAB D., MAISS J., HAHN E.G., MUEHLDOERFER S. Evaluation of sensitivity and inter- and intra-observer variability in the detection of intestinal metaplasia and dysplasia in Barrett's esophagus with enhanced magnification endoscopy. *Scand. J. Gastroenterol.*, 2006, **41** (3): 349-56.