

that *Helicobacter pylori* CagA seropositivity is strongly associated with findings of duodenal ulcer.

Contemporary concepts of management of peptic ulcer disease have radically changed, *Helicobacter pylori* eradication being the mainstay of therapy (NIH Consensus Statement 1994; 12:14-5, Gut 1997;41:8-13). Endoscopy is needed to diagnose and appropriately manage peptic ulcer disease. The extent to which dyspepsia should be investigated is controversial, especially in younger patients (Lancet 1987;2:779-82, Lancet 1988;2:1349-51). Only a few patients have peptic ulcer disease and even fewer have cancer; nonetheless, in most centers demand for endoscopy exceeds the resources available. The fact that eradication of *Helicobacter pylori* may lead to longstanding remission of duodenal ulcer disease strengthens the case of accurate endoscopic diagnosis of dyspepsia. Limited endoscopy resources must therefore be allocated effectively. Various screening policies for endoscopy have been proposed-*ie*, use of simple age restrictions (Br Med J 1990; 301:515-15), strategies that attempt to identify patients at high risk of ulcer and cancer on the basis of their symptoms (Gut 1995;36:330-33).

Recently several studies have shown that younger dyspeptic patients with negative serology for *Helicobacter pylori* infection are extremely unlikely to have peptic ulcer disease unless there is a history of exposure to ulcerogenic non-steroidal anti-inflammatory drugs (NSAIDs) (Lancet 1995; 346:1315-18). In the study above, the option of consuming NSAIDs did not occur. No cancers were reported in those less than 45 years old in these studies but some included data on older dyspeptic patients in whom cases of adenocarcinoma were also detected by positive *Helicobacter pylori* serology (Lancet 1994; 344:511-12). In this issue the authors selected a cut-off of 45 years, below which gastric cancer is rare and virtually always presents with established alarm symptoms. On the basis of evidence from these studies, a policy of restricting endoscopy in younger patients to those with positive serology for *Helicobacter pylori*, unless there are alarm symptoms or a history of NSAID use, has been advocated recently in the UK (London:BCG;1996).

A systemic antibody response to CagA is almost invariable in patients infected with CagA positive strains (J Clin Microb 1995; 33:1496-500). Several studies have shown that, whereas more than 80% of peptic ulcer patients harbor CagA + strains, the prevalence is only around 60% in non-ulcer subjects, coming into agreement with the study above. Serologic screening of younger dyspeptics by serology for *H. Pylori* enables iden-

tification of those patients who are at risk of having serious gastroduodenal lesions. It was previously shown that a policy of restricting endoscopy to patients with serologic evidence of CagA+ *H Pylori* infection by Western blotting would have improved the results obtained with an optimized *H. Pylori* ELISA (Scand J Gastroenterol 1999;9:856-63). So, Rokkas et al proposed that dyspeptic individuals infected with *H. Pylori* could be further screened on the basis of serum recognition of CagA, using an immunoblotting assay, thereby identifying those at highest risk of serious lesions requiring prompt endoscopy.

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## Regression of Barrett's esophagus with heat probe thermocoagulation: mid term results

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The aim of this study was to assess whether ablation of Barrett's mucosa with heat probe combined with acid suppression therapy could regenerate the normal esophageal squamous epithelium and what was the outcome after the ablation of Barrett's esophagus (BE).

Thirteen patients (8 men and 5 women [mean age 54.6 years]), with BE (endoscopically and histologically confirmed and without dysplasia), were enrolled in the study. At the beginning endoscopy was performed in order to assess the presence, length, place and histology of BE and the presence of *Helicobacter pylori*, which whenever was found it was eradicated. Then, BE was ablated with heat probe (pulses of 5 to 10 joules, mean number of sessions until complete ablation  $2.77 \pm 1.69$ ), together with continuous use of omeprazole, 40 mg/day. Four - quadrant biopsies were taken from 1 to 2 cm intervals, 1 to 3 months after the last heat probe session to assess results.

Ablation of Barrett's esophagus was achieved mac-

roscopically in all patients confirmed with methylene blue. Residual specialized columnar epithelium beneath the restored mucosa was found histologically in three patients, without over expression of p53 and c-erbB-2. Ablation was once more applied with the same method. Finally only one patient had islands of BE with low-grade dysplasia. During follow up (every 6 months, up to 36 months) BE relapsed in two patients, 3 and 9 months respectively after discontinuation of omeprazole. Both had long BE at the beginning of the study (6 and 5 cm respectively).

The authors suggested that heat probe is an inexpensive and effective method for BE ablation, safe and very easy to use. Residual specialized columnar epithelium was found only in 23% of the patients. This was ablated with the same method. Also the length of BE determined relapse after omeprazole discontinuation.

## COMMENT

Barrett's esophagus is a condition in which the squamous mucosa that lines the distal esophagus is replaced by specialized columnar epithelium, containing goblet cells (Gastrointest Endosc 1996; 44:91-5). It is associated not only with GERD, strictures and ulcers but also with esophageal adenocarcinoma (Ann Intern Med 1982; 97:103-7), whose incidence is increasing rapidly through the last years worldwide (J Gastroenterol Hepatol 1998; 13:356-62 - JAMA 1993; 270:1320). The usual procedure in a BE, is to perform endoscopic surveillance with multiple biopsies from the four quadrants and the whole length of the abnormal mucosa (J Clin Gastroenterol 1989; 11:369-372). Whenever intramucosal carcinoma is found, esophagectomy is performed. The operative mortality is up to 30% (Gut 1992; 33:1454-1458), complications are around 78% (Am J Gastroenterol 1993; 88:1832-6) and quality of life after surgery is about 0,8 in a scale 0-1 (Am J Gastroenterol 1994; 89:670-80). The lifelong endoscopic and histological surveillance program for the early detection of dysplasia and cancer in a BE, is very expensive (Am J Gastroenterol 1998; 83:291-294). Also, its cost effectiveness has been questioned (Gut 1996; 39:574-579). Thus acid suppression (medical therapy or surgery) combined or not with various ablative methods (thermal, chemical, mechanical) have been used in order to induce regression of Barrett's epithelium and re-epithelization with squamous epithelium. Always the aim is to eliminate the risk of adenocarcinoma developing in BE.

Medical therapy rarely, if ever, causes consistent regression of BE. H2 receptors antagonists (J Clin

Gastroenterol 1987; 9:139-141 - Arch Intern Med 1980; 140:475-477) and prokinetic agents (Dig Dis Sci 1990; 35:93-96) have not proved helpful at all. The results of the use of PPIs are controversial, with some showing partial regression (Aliment Pharmacol Ther 1993; 7:623-628 - Gut 1999; 45:489-494) and only one full (Gastrointest Endosc 1996; 44:700-5), but most not showing any change at all (Am J Gastroenterol 1997; 92:582-585 - Aliment Pharmacol Ther 1998; 12:893-897).

Antireflux surgery that has been used in addition with H2 receptors antagonists has been proved better in controlling the symptoms of GERD compared with the use of medical therapy alone (Br J Surg 1992; 79:1050-1053 - Br J Surg 1996; 83:274-278), but no consistent regression of BE was demonstrated. The same results are obtained with its combination with PPIs (Aliment Pharmacol Ther 1993; 7:623-628 - Ann Intern Med 1994; 121:161-167).

All the ablative methods try to achieve a sufficient depth of injury in the metaplastic mucosa, so that BE could be replaced by squamous epithelium. This requires an adequate acid suppression either with medical or surgical methods (Gastrointest Endosc 1995; 3:267).

Argon plasma coagulation causes a limited depth of tissue destruction minimizing the risk of side effects, such as perforation or stricture (Endosc Surg Allied Tech 1994; 2:71-77). It is relatively inexpensive compared with laser therapy, easy to use but multiple sessions are required (mean sessions= 6) and in 22-29% of the patients persistent residual foci of BE under the neosquamous epithelial lining can be found (Gut 1998; 43:747-751 - Gastrointest Endosc 1999; 50:18-22), thus complete regression is estimated in different studies to be in 50-90% of the patients (Gastroenterology 1993; 104:1686-1689 - Am J Gastroenterol 1998; 93:1810-1815).

When KTP (potassium - titanyl - phosphate) laser was used glandular elements in the surface or buried beneath the squamous mucosa were found in 20% of the treated patients and several sessions (3) were performed (Gastrointest Endosc 1999; 49:8-12). Complete regression differs from 10 to 80%. Also, its use is difficult (Gastrointest Endosc 1999; 49:8-12 - Am J Surg Pathol 1998; 22:239-245). It is safer than Nd:YAG laser in causing perforation and it has enhanced focusing accuracy (Gastrointest Endosc 1999; 49:8-12).

One study assessed the combination of Nd:YAG laser and antireflux surgery. Multiple sessions (4) and continuous life long acid suppression are needed. With this treatment, ablation can be achieved in 65 to 100% (Dig

Dis Sci 1993; 38:365-368 - Ann Surg 1998; 227:40-44). It is a very difficult and quite expensive technique.

Photodynamic therapy uses substances that are localized especially in neoplastic mucosa and with exposure to light, high energy singlet oxygen is produced destroying the tissue. Large areas can be treated in a single session, with total regression of BE in 30 to 87% of the patients (Gastrointest Endosc 1995; 42:64-70 - Am J Gastroenterol 1996; 91:1719-1723) but photosensitivity is a problem. Homogenous application throughout the esophagus is very difficult (Gastrointestinal Endosc 1999; 49:1-7). The cost of using this method is very high (Endoscopy 1998; 30:408-11).

Multipolar electrocoagulation (MPEC) is successful in the 66 to 100% of patients, depending on the length of Barrett's epithelium (Gastrointest Endosc 1999; 50:173-177 - Gastrointest Endosc 1999; 49:547-553). Many sessions are needed (mean sessions= 3,5), it is easy to use but serious side effects have been reported (Gastrointest Endosc 1996; 44:532-535). In only one study the investigators showed that the adequate acid suppression was not mandatory for therapy with MPEC (Gastrointest Endosc 1999; 49: 547-553).

Cavitron US surgical aspirator for ultrasonic dissection of the superficial squamous mucosa has been used in a porcine model. Complete ablation of the squamous epithelium was achieved in a single session. Whether this method would be useful for humans and Barrett's epithelium, it is still unknown (Surg Endosc 1998; 12:342-347).

The ideal ablative therapy must be inexpensive, easy to use, to not require more than one or two sessions, to provide uniform results over the entire surface area, to destroy the tissue in sufficient depth and to have no serious side effects. The ideal result must be the complete re-epithelization by squamous epithelium without any residual underlying intestinal metaplasia. The above mentioned data show that we are still looking for it.

Heat probe has been used in only the above study (Gastrointest Endosc 1999; 50:165-172). BE was meticulously searched, measured, histologically proved and followed up for up to 36 months after ablation with heat probe. All patients were instructed to be on continuous PPIs. Ablation of BE was achieved in all patients macroscopically. Histologically, in three out of thirteen patients residual columnar epithelium was found under

the squamous epithelium, seen in deep biopsies and only one of them had dysplasia. Another important issue in the study was the fact that cessation of PPIs led to re-emergence of BE in 50% of patients within one year. This shows the importance of the lifelong antireflux measures that are needed, as in all the others used methods. But it was also shown that, the longer the BE is, the greater necessity of acid inhibition is. BE relapsed after the omeprazole discontinuation in two patients that had BE greater than 2.5cm, whereas this did not happen in another two patients with length less than 2.5cm. The method is thought to be by the authors effective and inexpensive. Although the number of patients is small, the results are comparable with those of the other ablative techniques. It does not need very sophisticated equipment or special drugs.

But yet, it has not been answered, either by this nor by all the other ablative methods, whether BE regression through ablation increase or decrease the incidence and mortality of adenocarcinoma of the esophagus. It has not yet been proved that with the ablation of BE, we can stop the chronic endoscopic surveillance of these patients. The course and malignancy potential of the areas with the new squamous mucosa have not been determined (published literature is lacking but anecdotal reports from investigators have noted the presence of squamous cell cancers - Gastrointest Endosc 1999; 49:S20-23). Thus, assessment might be helpful with the use of other methods, such as molecular markers or aneuploidism. Also, the cancer risk of the residual intestinal metaplasia needs to be defined. Larger number of patients should be evaluated for longer periods of time. The combination of various ablative methods might be more effective than one by itself. Though the early results of this method are very promising, since it is quite effective, inexpensive and is not associated with serious side effects, it is too early to use it in daily practice. Follow up of the patients undergoing ablation by any mean should continue. If the results of this study will be confirmed by others, surveillance could be avoided for those patients, who have had BE shorter than 2.5(?)cm. Prospective randomized population based studies are needed, in order to elucidate the effect of endoscopic ablation on the prevention of esophageal cancer associated with BE. In conclusion, we should continue the research in ablation of BE, hoping that we will be able to find the "magic bullet" that is still lacking.

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