Treatment of Barrett’s Esophagus by Endoscopic Laser Ablation and Antireflux Surgery

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Objective
The regeneration of intestinal metaplasia by squamous epithelium in 17 patients with Barrett’s esophagus after endoscopic laser ablation in a reflux-free environment after successful antireflux surgery was prospectively examined.

Methods
All patients had antireflux surgery, and healing of reflux was verified at postoperative endoscopy and 24-hour esophageal pH monitoring. Thereafter, in 11 patients, the whole Barrett’s epithelium was ablated using endoscopic Nd-YAG laser energy in 1 to 8 sessions (mean, 4). The needed energy was 965 to 11,173 joules (mean 4709), or about 1000 joules per centimeter of Barrett’s esophagus. Six patients had no laser ablation but were treated by antireflux surgery and served as a control group.

Results
In all laser-treated patients, the regenerated epithelium was histologically of squamous type in the tubular esophagus, but two patients still had intestinal metaplasia in the gastric cardia. In controls, the length of Barrett’s esophagus and intestinal metaplasia remained unchanged. The length of follow-up was 26 months after the last laser session and 21 months in the control group.

Conclusions
The regenerated esophageal epithelium arising after laser ablation in reflux-free environment surgery is of squamous type. This treatment may have a role in preventing the development of esophageal adenocarcinoma arising in Barrett’s esophagus.

Barrett’s esophagus (BE) is a sequela of longstanding gastroesophageal reflux disease (GERD). Today, BE is defined as a condition in which a variable length of squa-

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with BE already have complications such as ulcerative esophagitis, peptic stricture, ulcer of the esophagus, and even adenocarcinoma, which is diagnosed in about 15% or more of the patients.5-8 Today, BE is considered a major and increasing risk factor for the development of esophageal adenocarcinoma.9,10 Follow-up studies have shown that Barrett patients have a 30- to 125-fold increased risk of developing esophageal adenocarcinoma, which emerges at a rate of about 1 cancer per 125 patient-years.5,6,8

BE is usually considered a nonregressive condition, and there are so far no well-documented reports about its reversal with the use of either medical treatment or antireflux surgery.11-13 However, partial restoration of squamous mucosa after ablation of Barrett's metaplasia with laser ablation or photodynamic therapy in combination with acid suppression has been reliably described.14-18 The patients in these studies have been treated with omeprazole, which reduces esophageal acid exposure but has no or only a modestly inhibitory effect on the reflux of duodenal contents into the esophagus.

The role of duodenal contents in the development of reflux esophagitis, and in particular Barrett's metaplasia and adenocarcinoma arising in BE, has recently been widely emphasized.19-25 At present, antireflux surgery is the only effective treatment that prevents reflux of both duodenal and gastric contents. In this paper, we have studied the restoration of esophageal mucosa in the reflux-free environment generated by antireflux surgery after ablation of the entire intestinal metaplasia with Nd-YAG laser, with the goal of minimizing the risk of esophageal adenocarcinoma. We presented our preliminary results in 1994 in the meeting of the American Gastroenterological Association.26

PATIENTS AND METHODS

A total of 17 patients (15 males, 2 females) with chronic GERD and histologically proven BE (with intestinal metaplasia but without any kind of dysplasia) were prospectively included in the study between 1992 and 1996. Mean age was 56.6 years (range 41-74 years). The duration of reflux symptoms varied between 3 and 15 years. The length of BE (ranging from 1 to 11 cm) was measured at endoscopy from the proximal margin of continuous Barrett's epithelium to the oral end of the gastric mucosal folds, with reference to the distance from the incisors. All patients had been earlier treated with H2 blockers or proton-pump inhibitors.

Before surgical treatment of GERD, all patients underwent esophageal 24-hour pH monitoring, and 8 of the patients also had esophageal manometry. These patients had clinical suspicion of esophageal motility disturbance.27 The mean percentage of time with esophageal pH < 4 was 21.9% (range 2.7%-36.1%). In manometry, the mean lower esophageal sphincter (LES) pressure was 8 mmHg (range 5-10 mmHg). In 16 patients, a floppy fundoplication28,29 (wrap length 2 cm) was performed. Eight fundoplications were open, and eight were performed by laparoscopic technique. Hiatalplasty was performed in all cases. In one patient with two previous unsuccessful fundoplications, a Roux-en-Y duodenal diversion and partial gastrectomy with selective gastric vagotomy was performed.30 There was no operative mortality or complications.

In the follow-up examination 3 months after surgery, all patients were asymptomatic. At endoscopy, the esophagitis was healed, but the length of BE remained unchanged. The healing of GERD was ascertained by postoperative pH monitoring in all patients and the restoration of LES pressure by esophageal manometry in the eight patients who had had preoperative manometry.31 The mean time of pH < 4 was 0.94% in the 24-hour pH monitoring. This was significantly less than the preoperative values (p < 0.01). The mean LES pressure in postoperative manometry was 16.9 mmHg (range 10-22.5 mmHg).

Laser Ablation of Barrett's Metaplasia

All patients were informed about the possibility of laser coagulation to ablate BE. Eleven patients (10 males and 1 female, mean age 56 years) chose this form of treatment (the laser group). Informed consent was obtained from all patients participating in the study. The remaining 6 patients (5 males and 1 female, mean age 57 years) did not want to have laser treatment; they served as a control group. There were statistically no significant differences between the two groups in regard to length of BE (4 cm in the laser group and 8 cm in the control group), age, sex or pre-and postoperative results in pH monitoring and esophageal manometry.

The endoscopic laser ablation (Fig. 1) was performed using Nd-YAG laser energy via sapphire contact tip with 13 watts (W) of power in periods of 3 seconds or in continuous applications. BE was coagulated until the color of the mucosa appeared brown. Before using the above-mentioned power in patients with BE, the depth of mucosal lesion caused by 13 W power had been tested on pigs and on patients undergoing laser ablation of esophageal cancer.

For endoscopic laser ablation, all patients received local hypopharyngeal anesthesia with Xylocaine. Intravenous propofol, midazolam, or fentanyl was used for sedation. All patients had continued monitoring of blood pressure, electrocardiography, and pulse oximetry. The esophageal peristaltic movements were paralyzed with intravenous glucagon. The ablation of BE was performed.
starting mostly from the proximal end of the squamocolumnar border. The amount of energy in one session ranged from 300 to 4000 joules (J), and the longest laser session lasted 40 minutes. After the first laser ablation, all patients had esophagograms performed with water-soluble contrast medium on the first postoperative day to exclude esophageal perforation. Subsequently, esophagograms were not routinely performed postoperatively in asymptomatic patients who had had only small amounts of laser energy. The patients were treated with repeated laser sessions at intervals of about 3 months. Before starting the next ablation, four-quadrant biopsies at a distance of 1 cm from each other (forceps: Olympus FB-24 K(R); length of the biopsy, 3.5 mm) were taken from the lasertreated area of BE.

RESULTS

One to eight sessions (mean four) were required for all the intestinal metaplasia to be ablated and for squamous epithelium but no intestinal metaplasia to appear in biopsies. At endoscopy, reepithelialization of squamous epithelium advanced from the oral squamocolumnar border and also occurred inside the laser-treated area within BE (Fig. 2). The total amount of energy needed to ablate the entire Barrett’s mucosa ranged from 965 to 11173 J (mean 4709 J), totalling 942 J per centimeter of tubular BE. In all laser-treated patients, intestinal metaplasia of the entire tubular esophagus was replaced by histologic squamous epithelium. However, two patients had intestinal metaplasia in the mucosa of the gastric cardia distally to the oral end of the gastric mucosal folds. The mean endoscopic follow-up with no intestinal metaplasia in biopsies after the last session was 26 months (range 6–52 months). In 10 patients, the follow-up was more than 1 year, in 5 more than 2 years, and in 2 more than 3.5 years. In the control group, the length of BE with intestinal metaplasia in biopsies at endoscopy remained unchanged during the whole follow-up period (mean 21 months, range 12.5–38 months).

DISCUSSION

This study clearly shows that in a reflux-free environment created by successful antireflux surgery, the regenerated esophageal epithelium arising after ablation of Barrett’s intestinal metaplasia with endoscopic laser energy is of squamous type. Further, the entire tubular esophagus with intestinal metaplasia was restored by squamous epithelium.

Chronic GERD is the cause of BE, but the exact cellular origin of the intestinal metaplasia is still unknown. It has been proposed that BE grows upward from the adjacent gastric cardiac epithelium,31 but recently evidence has been accumulating to indicate a true metaplastic nature of BE.15,32–36

Up to now, several reports on laser ablation of Barrett’s epithelium with successful medical treatment of GERD with omeprazole have been published. Berentson et al.15 performed laser photoablation in 10 patients with long-standing BE. During multiple endoscopic sessions, 1 to 8 segments of BE with areas ranging from 0.25 cm² to 4 cm² were treated using argon laser until the treated segment turned white. The acid reflux was treated with 40 mg omeprazole daily, beginning 2 weeks before the first

Figure 1. Nd-YAG laser ablation of Barrett’s esophagus using a power of 13 watts. The mucosa was coagulated until it appeared brown.

Figure 2. Squamous reepithelialization of the laser-treated area within Barrett’s esophagus. (a) Barrett’s metaplastic epithelium. (b) Regenerated squamous epithelium.
laser session and continuing until the end of the study (6–38 weeks). Laser ablation was given to each segment in one to six sessions. Eighty-five percent of the laser-treated area was re-covered with squamous tissue, occurring in 38 of the 40 laser-treated segments. Sampliner et al.\textsuperscript{16} reported regression of Barrett’s epithelium after ablation with Nd-YAG laser and acid suppression in a 76-year-old man.

Photodynamic therapy has also been reported to reduce the extent of BE. Laukka and Wang\textsuperscript{17} successfully used hematoporphyrin derivate and photoradiation in combination with acid suppression. Overholt and Panjehpour\textsuperscript{18} treated BE with the intravenous administration of porfimer sodium and argon laser with a wavelength of 630 nm, followed by omeprazole treatment.

Unsuccessful results of laser photoablation of Barrett’s epithelium have also been described. Brand and Kauvar\textsuperscript{37} reported that an initial endoscopic examination performed 6 weeks after treatment with Nd-YAG laser revealed no endoscopic or histologic signs of Barrett’s epithelium, but follow-up endoscopic examination 14 weeks later showed that Barrett’s epithelium had reappeared despite acid suppression with 20 mg omeprazole daily. Also, squamous islands have been found overgrowing BE, although the squamocolumnar junction after therapy has demonstrated only squamous epithelium.\textsuperscript{38} On the other hand, Sampliner and Jaffe\textsuperscript{39} described an adenocarcinoma in BE despite regression of almost all the Barrett’s mucosa after laser photocoagulation.

The reasons for these failures are unclear, but one very important reason may be that medical acid suppression therapy does not prevent the reflux of duodenal contents into the esophagus. Reflux of pancreatic and biliary secretions may contribute to the development of complications and even to carcinogenesis in BE.\textsuperscript{22–24} Another reason for failure may be that not all of the intestinal metaplasia in the esophagus was ablated. In addition, there are no statements of esophageal pH monitoring, which would ascertain that acid reflux had really been abolished by acid-suppression therapy with omeprazole. The adequate reduction of esophageal acid exposure can be verified by 24-hour pH monitoring. Sometimes very high doses of proton-pump inhibitors are needed to reduce esophageal acid exposure to normal.\textsuperscript{40} In contrast, successful antireflux surgery brings the esophageal acid exposure to normal.\textsuperscript{38}

There may also be differences in the ablation techniques. Berentson et al.\textsuperscript{15} used 4.5 to 5 W power, which caused the mucosa to turn white. We used 13 W and burned the mucosa until it became brown, reflecting deeper coagulation.

BE is a major recognized risk factor for the development of esophageal adenocarcinoma, whose incidence is increasing rapidly.\textsuperscript{9,10} Theoretically, the regression of the entire BE with intestinal metaplasia might prevent dysplasia and subsequent adenocarcinoma. The role of dysplasia is, however, debatable. Usually dysplastic epithelial changes precede Barrett’s adenocarcinoma. Some authors consider the diagnosis of high-grade dysplasia of Barrett’s epithelium equivalent to the diagnosis of esophageal cancer,\textsuperscript{41} but it has been shown that an effective endoscopic biopsy protocol can differentiate high-grade dysplasia from early adenocarcinoma in BE.\textsuperscript{42} Dysplasia is not an ideal indicator in the early diagnosis of adenocarcinoma arising in BE because of problems in the follow-up and number of biopsies. Even in high-grade dysplastic histologic specimens, the observer variability among experienced pathologists is 85% to 87%.\textsuperscript{43} In addition, as yet there are no reliable markers that can predict the development of cancer.

The ideal method used for ablation of BE should be effective, safe, easy, and inexpensive. Our Nd-YAG laser ablation has been effective and safe when using the 13 W power. Recently we have used energy of up to 4000 J in 1 session. We have had no complications either in laser ablation of BE or in the surgical treatment of GERD. Hence, the amount of energy necessary to ablate the 5-cm-long tubular BE segment is about 5000 J.

Patients with intestinal metaplasia in the gastric cardia may present problems because the distal endpoint of the laser ablation is difficult to estimate, and histologic biopsies may still show intestinal metaplasia. We had this finding in two patients. The mucosal folds of the gastric cardia present a fixed point, and the cardiac mucosa should be biopsied below this area. The clinical importance of intestinal metaplasia in the cardia is unclear. However, at present, we recommend lifelong endoscopic follow-up in these patients.

All our 11 patients showed that the regenerated epithelium after endoscopic laser ablation of the entire BE in a reflux-free environment is of squamous type; in control patients treated only with antireflux surgery, the esophageal mucosa still had intestinal metaplasia. Theoretically, restoration of squamous epithelium in BE might prevent the development of esophageal adenocarcinoma. However, only long-term follow-up studies lasting more than 10 years can prove the possible cancer-preventing results of laser treatment in a reflux-free environment.\textsuperscript{44}

**Acknowledgement**

The authors thank Ms. Yvonne Sundström for her skillful technical and secretarial assistance.

**References**


