The effect of laparoscopic fundoplication in therapy of Barrett's esophagus

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Abstract

Introduction: *Barrett's esophagus is the most significant precancer of the esophagus. Its malignization gives rise to most adenocarcinomas of the esophagus. Therefore selection of adequate therapy for this precancerous condition is of the utmost importance.*
Aim: *The authors of the work addressed the question of whether effective therapy of reflux disease alone may halt the process of malignization of Barrett's mucosa or even cause its regression.*
Material and methods: *The analyzed set comprised 50 patients with Barrett's esophagus, who in 48 cases underwent laparoscopic fundoplication and in two cases underwent an indirect antireflux procedure in the form of gastric resection with a Roux-en-Y gastrojejunal anastomosis. The effect of the procedure was evaluated by comparing preoperative and postoperative endoscopic examinations, as well as histological analysis by biopsy taken from Barrett's mucosa.*
Results: *In 19 patients (38%), Barrett's mucosa was not detected postoperatively. An improved finding in terms of disappearance of mucosal dysplasia was found in 8 (16%) patients. Findings remained unchanged in 18 (36%) patients. In 5 (10%) patients progression of the disease was discovered.*
Conclusions: *A surgical antireflux procedure, primarily in the form of laparoscopic fundoplication, is considered an effective method for treating Barrett's esophagus up to the stage of mild dysplasia. If this therapy is unsuccessful, the method of choice is local therapy, either an endoscopic mucosectomy or radiofrequency ablation.*

Key words: *Barrett's esophagus, esophageal adenocarcinoma, laparoscopic fundoplication.*

Introduction

Despite all the advances of modern medicine, the prognosis of patients with malignant disease of the esophagus remains very unsatisfactory. Modern suture material, staplers, and introduction of new operation techniques, including minimally invasive procedures, have positively contributed to the decrease in operation lethality and morbidity of patients with esophageal cancer to a level where additional improvement can almost no longer be expected. Nonetheless, this did not, and possibly even could not, also lead to an improvement in the long-term survival of these patients. It has been shown that their survival after a successful operation is determined by other criteria. The most important factor influencing long-term survival of patients with esophageal cancer remains disease staging at the time of diagnosis. The postulate that the sooner the diagnosis of cancer is established, the better the prognosis of the patient, remains valid. Squamous cell cancer in early stages of the disease is asymptomatic, and if diagnosed in this stage, it is usually a chance finding. The situation is different for ade-

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nocarcinoma of the esophagus. This type of cancer is often a result of malignization of Barrett's mucosa and its development therefore is usually preceded by a long history of esophageal reflux disease.

Aim

From this viewpoint we consider the diagnosis of Barrett's esophagus very important, because early diagnosis and suitable therapy may prevent the development of esophageal adenocarcinoma.

Material and methods

Between 2000 and 2010, 70 patients diagnosed with Barrett's esophagus were treated at the 1st Department of Surgery at the University Hospital in Olomouc. Of these, 58 were male and 12 were female. The age range was 25–81 years; the average age was 53 years. Most patients had a long history of reflux disease. Twenty-five (35%) patients had a reflux disease history of 5 years or less, 20 (28%) patients had a reflux disease history of 5–10 years, 9 patients (13%) had a history of over 10 years of reflux disease. In 16 patients (23%) the duration of symptoms was not noted in the documentation. Of the above-mentioned patients, 58 patients underwent a laparoscopic 360-degree fundoplication, 6 patients underwent extirpation of the esophagus, 2 patients underwent a balanced operation consisting of a resection of two-thirds of the stomach with Roux-en-Y gastrojejunal anastomosis, an endoscopic mucosal resection was performed in 2 patients and 2 patients refused invasive treatment and continued to be treated conservatively. To evaluate the effect of treatment, endoscopic examination of the esophagus and stomach was performed along with biopsies of Barrett's esophagus with subsequent histological analysis performed at the Department of Pathology of the University Hospital for all patients. All patients in the study group had one or more esophagogastroscopic examination before the beginning of our treatment and at least one follow-up examination after the completion of surgical therapy. During every gastroscopy, the length of the segment of Barrett's mucosa was measured, biliary reflux was evaluated and biopsies were performed. We considered the length of the segment to be a possible prognostic factor of the effect of therapy. We performed a multi-level biopsy in some patients, and in the others a biopsy was obtained under NBI mode. If the patients underwent several esophagogastroscopic examinations before and after the operation, we evaluated the last examination prior to the operation and the actual postoperative follow-up. In all patients we evaluated only the results of our own examinations and several of the patients remain in our endoscopic follow-up program.

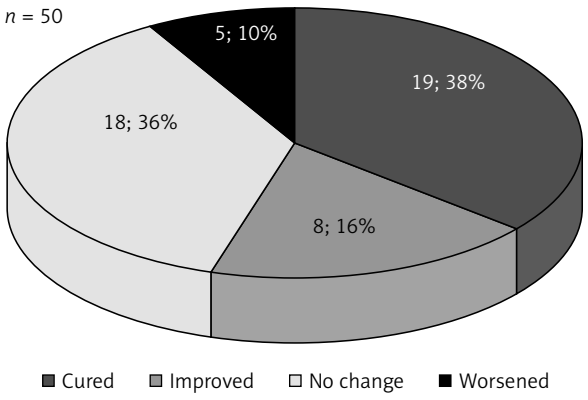

Figure 1. Effect of fundoplication

Results

We evaluated the effect of the antireflux procedure on Barrett's mucosa in 50 patients. In these patients an indirect antireflux procedure consisting of resection of two-thirds of the stomach with a Roux-en-Y gastrojejunal anastomosis was performed in 2 patients and in the remaining 48 patients a 360-degree laparoscopic fundoplication was performed. Ten patients who underwent laparoscopic fundoplication did not attend the post-operative follow-up and thus the effect of the procedure could not be evaluated.

We consider 19 (38%) of the patients as cured; post-operative histological examinations in these patients did not reveal Barrett's mucosa. An improved finding was seen in 8 patients (16%). Post-operative findings remained unchanged, meaning they did not progress or significantly worsen, in 18 patients (36%). Worsened findings post-operatively were observed in 5 patients (10%) (Figure 1).

In the group of cured patients (19), all underwent laparoscopic fundoplication. Follow-up examination at various intervals post-operatively ruled out the presence of Barrett's mucosa, even though pre-operative examinations described severe dysplasia in

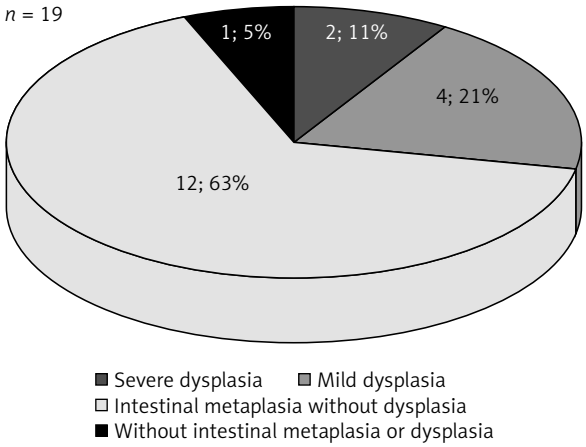

Figure 2. Cured patients – preoperative findings

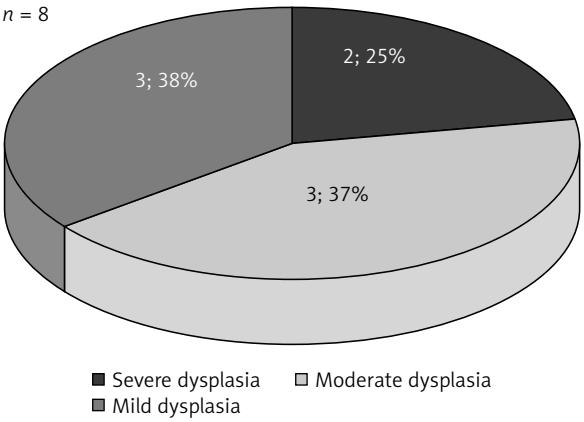

Figure 3. Improved findings – preoperative status

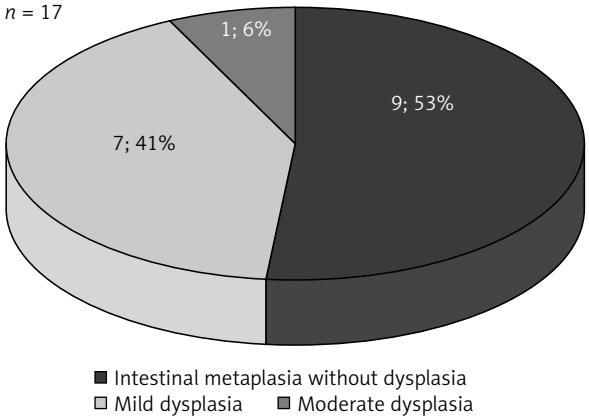

Figure 4. Unchanged findings

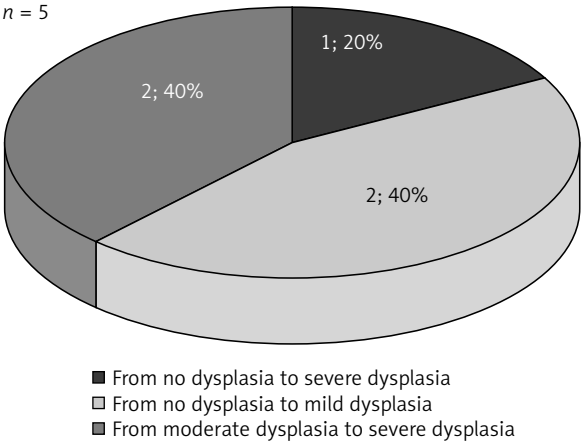

Figure 5. Worsened findings

2 patients, mild dysplasia in 4 patients, 12 patients showed only intestinal metaplasia without dysplastic changes and 1 patient had Barrett's esophagus without intestinal metaplasia (Figure 2).

Of the 8 patients where post-operative findings improved, 7 underwent laparoscopic fundoplication and 1 patient underwent a balanced operation for brachyesophagus accompanying bile reflux. In 2 patients findings regressed from severe dysplasia to intestinal metaplasia without dysplastic changes; in 3 patients with pre-operatively determined moderate dysplasia post-operative findings after laparoscopic fundoplication showed an absence of dysplasia, and 1 patient had post-operative findings of mild dysplasia. In the remaining 3 patients of this group, who pre-operatively had findings of mild dysplasia, post-operative results revealed only intestinal metaplasia without dysplastic changes (Figure 3).

In 17 patients the histological findings remained unchanged after the operation. This group comprised 16 patients who underwent laparoscopic fundoplication and 1 patient who underwent an indirect antireflux procedure for massive bile reflux into the esophagus. In 9 cases pre- and post-operative findings revealed intestinal metaplasia without dysplastic changes, 7 patients continue to have findings of mild dysplasia and in 1 patient findings of moderate dysplasia persist (Figure 4).

Of the 5 patients who contrarily showed worse findings post-operatively, severe dysplasia was determined post-operatively in 3 cases, whereas preoperative findings showed an absence of dysplastic changes in 1 patient and moderate dysplasia in the other 2 patients. In the remaining 2 patients from this group, findings worsened from intestinal metaplasia to mild dysplasia (Figure 5). At endoscopic

follow-up after the operation, 3 patients presented with lower esophageal sphincter incompetence (1 case of overly loose cuff, 2 cases of cuff dislocation into the mediastinum). In the remaining 2 patients the endoscopic findings were very favorable, the cuff was properly configured and positioned, and Barrett's mucosa was macroscopically regressing. The only pathological finding was a larger amount of concentrated bile in the stomach.

Discussion

Although it has been over 60 years since Norman Barrett first attempted to describe findings of cylindrical epithelium in the esophagus, not all questions regarding Barrett's esophagus have been answered yet [1]. The pathophysiological basis of Barrett's esophagus is straightforward. The condition for establishing the diagnosis is the presence of cylindrical epithelium, containing intestinal metaplasia with goblet cells, stained with Alcian blue [2]. Furthermore, it has been established that the cause of Barrett's esophagus is acid and bile reflux into the esophagus. However, it remains unclear why in one group of patients with severe and long-lasting reflux to Barrett's mucosa the disease develops, and in another group of patients with the same quality and intensity of reflux it does not. A possible explanation may be differences in the aggressiveness of the reflux, as well as the duration of action on the esophageal mucosa [3]. Numerous pH-metric studies and analyses of gastric juice refluxed into the esophagus indicate that the quality of the reflux is different in patients with Barrett's esophagus and patients with sole esophagitis. Patients with Barrett's esophagus have a higher acidity as well as a higher bile content in the reflux [4, 5]. A different reaction of the mucosa to exposure to stomach acid may also play a significant role. It has been determined that the level of extracellular-regulated kinase enzyme, which is part of the system ensuring cellular proliferation after exposure to acid, is significantly lower in patients with esophagitis compared to patients with Barrett's mucosa [6]. It is known that Barrett's esophagus is a progressive precancerous condition, where malignization gradually develops through stages of mild and severe dysplasia, but it is unknown whether esophageal adenocarcinoma develops predominantly or exclusively in the terrain of Barrett's esophagus [7]. Discrepancies remain in the treatment of Barrett's esophagus, which consists of local therapy of Barrett's mucosa and treatment of the cause of Barrett's esophagus – gastroesophageal reflux. Conservative treatment of Barrett's esophagus is identical to the treatment of simple reflux disease. It consists of acid suppression by proton pump inhibitors (PPI). This does not directly inhibit reflux but decreases its aggressiveness. However, this is only valid for acid reflux. If the reflux contains a significant concentration of bile, this therapy is substantially less effective [8]. Nonetheless, according to some studies, the acid suppressing effect of PPI may on the contrary enhance the development of intestinal metaplasia and cellular proliferation in duodenogastroesophageal reflux leading to malignization of Barrett's mucosa [9]. Prokinetic drugs may to a certain extent aid stomach evacuation; however, an absolute effect cannot be expected. Of the many types of local treatments, endoscopic mucosal resection and radiofrequency ablation are currently most effective. Both are currently considered an effective and relatively safe method; however, each has its negative aspects. Radiofrequency ablation thermally destroys the mucosa, but unlike in the case of mucosectomy, the mucosa cannot be sent for histological analysis. Nonetheless it is a very promising procedure which destroys Barrett's mucosa without leading to submucous scarring and esophageal functional impairment [10]. However, it is still a novel method and long-term results are not yet available [11]. Endoscopic mucosectomy enables histological analysis of the resected mucosa and thus can determine the exact depth and extent of impairment by dysplastic changes or early adenocarcinoma [12]. Its disadvantage is a significantly greater number of sessions in cases of large lesions or multifocal localization of areas of severe dysplasia or early adenocarcinoma in Barrett's mucosa [13]. Prior to mucosectomy or radiofrequency ablation, precise endosonographic examination must be performed to rule out tumorous infiltration to the submucosa [14]. However, a local procedure on the mucosa without parallel anti-reflux therapy to treat the cause of Barrett's mucosa is senseless. Conversely, it cannot be ruled out that effective reflux therapy may lead to cessation of growth and malignization of Barrett's mucosa and in some cases may even lead to complete regression. In such cases a local mucosal procedure would be futile. Surgical treatment of Barrett's esophagus includes an antireflux operation, or, in cases of ad-

vanced tumor in Barrett's esophagus, esophageal resection. Currently, practically the only used anti-reflux procedure is fundoplication, which is almost always performed laparoscopically. It is most effective in its complete, or 360-degree version. This reliably prevents acidic as well as alkali reflux [15]. Not only does it completely restore the function of the lower esophageal sphincter, but in patients with impaired esophageal motility it restores it to physiological parameters [16]. Nonetheless, in cases of massive bile reflux, the stomach is often also impaired, presenting with significant symptoms and endangering the patient with severe complications, including possible malignization. In such cases a direct anti-reflux procedure is insufficient. We consider an indirect antireflux procedure consisting of an aboral gastric resection with Roux-en-Y gastrojejunal anastomosis to be the method of choice. This procedure does not prevent reflux completely, but it significantly reduces the aggressiveness of the reflux by deriving via the Roux loop and decreases the secretion of acidic gastric juices by reducing the secretory surfaces of the stomach [17]. A disadvantage of this operation is that if a subsequent resection of the esophagus is necessary, the stomach can no longer be used as replacement. We focused on evaluating the effect of a direct antireflux procedure on Barrett's mucosa in the form of a laparoscopic fundoplication. We asked ourselves which patients have a chance of achieving regression of Barrett's mucosa with solely an anti-reflux procedure and in which patients a local treatment is also necessary. The effect of the antireflux procedure on Barrett's mucosa was seen to be significantly positive in 54% of patients; in these patients post-operative follow-up findings did not show Barrett's mucosa or at least the dysplastic changes disappeared. The operation may also be considered successful in 36% of patients where the findings of Barrett's mucosa did not change after the operation. In these cases the anti-reflux procedure prevented further progression of Barrett's mucosa and the findings may remain permanently stationary. Therefore it is not necessary to expect the disappearance of Barrett's mucosa, although we do have such a group in our patient set. Similar experiences are described by other authors [18]. Suppression of the gastroesophageal reflux may lead to, and not only in our experience leads to, a halt in the progression of intestinal metaplasia to carcinoma [19].

Progression of Barrett's mucosa after the antireflux procedure was observed in only 10% of the patients; in 3 of the 5 patients this may be attributed to a late complication of fundoplication, which caused an alteration of its antireflux function. It is questionable in the remaining two patients with a functional cuff to what extent duodenogastric bile reflux contributes to the progression of Barrett's disease. If this is the case, there was an error in indicating the patients for laparoscopic fundoplication instead of an indirect antireflux procedure.

Conclusions

We consider the surgical antireflux procedure in the form of a 360-degree fundoplication, presently standardly performed laparoscopically, as effective treatment for patients with Barrett's esophagus up to the stage of mild dysplasia. In patients with severe dysplasia of Barrett's mucosa or early carcinoma in Barrett's esophagus, we first indicate a local procedure on the mucosa, such as an endoscopic mucosal resection, with subsequent endoscopic follow-up. Then after a period of at least 12 months following this procedure, in the absence of disease recurrence, a laparoscopic fundoplication is performed.

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