

Antireflux surgery is required after endoscopic treatment for Barrett's esophagus

Potrzeba zabiegu antyrefluksowego po endoskopowym leczeniu przełyku Barretta

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ABSTRACT:

Introduction: Barrett's esophagus is an acquired condition that develops as a result of transformation of normal stratified squamous epithelium in the lower part of the esophagus into columnar epithelium. Barrett's esophagus is considered to be a complication of gastroesophageal reflux disease (GERD). Various endoscopic techniques have been shown to be successful in the treatment of this condition. However, long-term success in preventing further esophageal dysplasia is not clear. Biological welding consists in the application of controlled high-frequency current on living tissues and has been used to stop gastrointestinal bleeding, similarly to the APC technique which involves ablation of small intestinal metaplasia of the esophageal mucosa.

Aim: The goal of this study was to evaluate the effectiveness of endoscopic techniques in the treatment of Barrett's esophagus and verify the need for a subsequent surgical intervention in patients with GERD complicated by Barrett's esophagus.

Material and methods: Patients with Barrett's esophagus C1-3M2-4 (Prague classification from 2004) and high dysplasia without nodules, as well as patients with confirmed GERD without hiatal hernia, were included in this study. Endoscopic treatment was performed with the use of argonoplasmic coagulation (APC) and high-frequency welding of living tissues (HFW). After the examination the patients were re-examined. Patients with recurrence of metaplasia and high DeMeester score (>100) underwent antireflux surgery – crurography and Nissen fundoplication with creation of a soft and short cuff.

Results: A total of 89 patients were included in the study, 81 of whom were reexamined after ablation of Barrett's esophagus. In 12 patients, a recurrence of intestinal metaplasia resembling the small intestine was identified. Implementation of two-stage treatment was required for 9 patients – it involved a second procedure of ablation of the esophagus, followed by antireflux surgery. Surgical treatment was refused by 3 patients, who underwent only the second ablation procedure. All patients received drug therapy, consisting of prokinetics and proton pump inhibitors. Esophageal pH monitoring was repeated 3 months after surgery, showing normalization of the DeMeester score. As a result, the patients experienced no complaints such as heartburn, chest pain or dysphagia, which significantly improved their quality of life. Esophagogastroduodenoscopy and biopsy of the mucous membrane of the lower third of the esophagus were performed in accordance with the Seattle Protocol. After examining histological specimens, no regions of metaplasia were identified.

Conclusion: Antireflux surgery is required as a part of the treatment for Barrett's esophagus, which prevents further dysplasia and development of esophageal cancer.

KEYWORDS:

antireflux operation, argonoplasmic coagulation, Barrett's esophagus, gastroesophageal reflux disease, high-frequency welding of living tissues

STRESZCZENIE:

Wprowadzenie: Przełyk Barretta jest nabytym stanem, który rozwija się wskutek zastąpienia prawidłowego nabłonka wielowarstwowego płaskiego w dolnym odcinku przełyku nabłonkiem walcowatym. Uważa się, że przełyk Barretta jest powikłaniem choroby refluksowej przełyku (ang. *gastroesophageal reflux disease*; GERD). W leczeniu tego schorzenia z powodzeniem stosuje się różne techniki endoskopowe. Długotrwały sukces w zapobieganiu kolejnej dysplazji jest jednak niepewny. Spawanie biologiczne, polegające na kontrolowanym działaniu prądu wysokiej częstotliwości na żywe tkanki, wykorzystuje się w hamowaniu krwawienia z przewodu pokarmowego i ablacji błony śluzowej przełyku z metaplazją jelitową.

Cel: Celem niniejszej pracy jest ocena skuteczności technik endoskopowych w leczeniu przełyku Barretta i potrzeby dalszego leczenia operacyjnego u pacjentów z GERD powikłanym przełykiem Barretta.

Materiał i metody: Do badania włączono pacjentów z przełykiem Barretta w stadium C1-3M2-4 (wg klasyfikacji praskiej z 2004 r.), z dysplazją dużego stopnia (bez guzków) oraz potwierdzoną chorobą refluksową przełyku (bez przepukliny rozworu przełykowego). Zastosowano leczenie endoskopowe za pomocą koagulacji plazmą argonową (ang. *argonoplasmic coagulation*; APC) i spawania żywych tkanek prądem wysokiej częstotliwości (ang. *high-frequency welding*; HFW). Po leczeniu pacjenci zostali ponownie zbadani. Osoby z nawrotem metaplazji jelitowej i wysokim wskaźnikiem DeMeestera (>100) poddano operacji antyrefluksowej – wykonano zwężenie rozworu przełykowego i fundoplikację sposobem Nissena przez wytworzenie miękkiego i krótkiego mankietu.

Wyniki: Badanie obejmowało 89 pacjentów, spośród których 81 zbadano ponownie po ablacji przełyku Barretta. U 12 odnotowano nawrót metaplazji jelitowej. U 9 przeprowadzono leczenie dwuetapowe – ponowną ablację zmian

w przełyku, a następnie operację antyrefluksową. Troje pacjentów nie wyraziło zgody na leczenie operacyjne, wykonano u nich jedynie drugi zabieg ablacji. U wszystkich osób stosowano farmakoterapię – leki prokinetyczne i inhibitory pompy protonowej. Po trzech miesiącach od operacji wykonano ponowną pH-metrię przełyku, która wykazała normalizację wskaźnika DeMeestera. W wyniku zabiegu odnotowano ustąpienie zgagi, bólu w klatce piersiowej i dysfagii, co istotnie poprawiło jakość życia pacjentów. Wykonano ezofagogastroduodenoskopię z biopsją błony śluzowej dolnej trzeciej części przełyku zgodnie z protokołem z Seattle. W badaniu histopatologicznym nie stwierdzono ognisk metaplazji jelitowej.

Wnioski: Operacja antyrefluksowa jest koniecznym elementem leczenia przełyku Barretta, zapobiegającym dalszej dysplazji i rozwojowi raka przełyku.

SŁOWA KLUCZOWE: choroba refluksowa przełyku, koagulacja plazmą argonową, operacja antyrefluksowa, przełyk Barretta, spawanie żywych tkanek z zastosowaniem prądu wysokiej częstotliwości

ABBREVIATIONS

APC – argonoplasmic coagulation
GERD – gastroesophageal reflux disease
HFW – high-frequency welding
NBI – Narrow Band Imaging
RFA – radiofrequency ablation

INTRODUCTION

Barrett's esophagus is thought to develop as a complication of acid or bile reflux, which often (but not always) leads to heartburn symptoms [1–3]. In response to these damaging agents, normal squamous epithelium of the esophagus is replaced by cylindrical one, similar to that of the small intestine – this condition is called Barrett's esophagus [4]. These changes are associated with a high risk of malignant transformation over time. Esophageal adenocarcinoma develops in 0.5% of patients with low-grade dysplasia in Barrett's esophagus and in 6% of patients with high-grade epithelial dysplasia every year. The prevalence of Barrett's esophageal metaplasia in Europe ranges from 2 to 5% [5–8].

Barrett's esophagus can only be detected by microscopic examination of the biopsied material and the occurrence rate of adenocarcinomas associated with this condition continues to rise in the Western world. The prognosis for patients with esophageal adenocarcinoma remains poor – less than 15% of them survive more than 5 years [7, 9].

Multiple studies showed that medical acid suppression alone is not effective in Barrett's esophagus treatment. On the other hand, antireflux surgery reduces the degree of dysplasia and protects against its further progression and development of cancer [10, 11]. Generally, treatment for Barrett's esophagus involves removing the regions of cell dysplasia, as well as performing antireflux surgery [12]. In recent years, a number of endoscopic treatment methods have been designed, including photodynamic therapy, APC, HFW, cryodestruction, radiofrequency ablation (RFA) and many other [12–16].

All these methods demonstrate good results in the treatment of Barrett's esophagus, with minor postoperative complications. Although RFA is the most successful of all techniques with a 70–95% success rate, it is extremely expensive, which in turn makes it less accessible around the world [15, 16].

Biological welding is based on controlled exposure of living tissues to high-frequency current [17–19]. As a result, structural changes in the affected tissues occur and a welded seam is formed, that is, a bond characterized by the following properties: high elasticity,

immunity against microbial infections, a stimulating effect on tissue regeneration process, superior speed and quality in comparison to normal, uncomplicated healing.

MATERIALS AND METHODS

This is a retrospective review of patients undergoing treatment for Barrett's esophagus at a single tertiary medical center in Kiev, Ukraine between January 2015 and October 2020. All patients were diagnosed based on histological evaluation preceded by endoscopic examination and biopsy. Only patients with severe dysplasia were included in the study. All patients underwent esophageal impedance pH monitoring, as well as upper GI contrast examination in order to evaluate esophageal reflux and verify the presence of hiatal hernia [20]. Patients with adenocarcinoma at the time of presentation, pregnant, younger than 18 years of age or with exacerbations of chronic diseases which would not allow them to undergo surgery, as well as patients suffering from hiatal hernia were all excluded from this research. Patients were offered APC and HFW procedures available at our center as possible treatment options for this condition. Every patient was informed about each procedure in detail. Informed consent for treatment was obtained from every patient. After that, patients were assigned to groups that suited them best, considering the area of the esophageal lesion. In these groups, all patients underwent appropriate procedures of ablation of the affected mucosa: the first group received APC treatment, while the second group underwent HFW, according to standard methods [12, 13, 18, 19, 21].

Patients who needed further surgical intervention for GERD underwent laparoscopic cruraphy and Nissen fundoplication. The procedure was performed in the standard fashion – five laparoscopic ports were used and the lower third of the esophagus was mobilized with adhesiolysis, posterior cruraphy was performed if necessary and a short (2–3 cm) and soft circular cuff of the stomach was formed without crossing the short arteries.

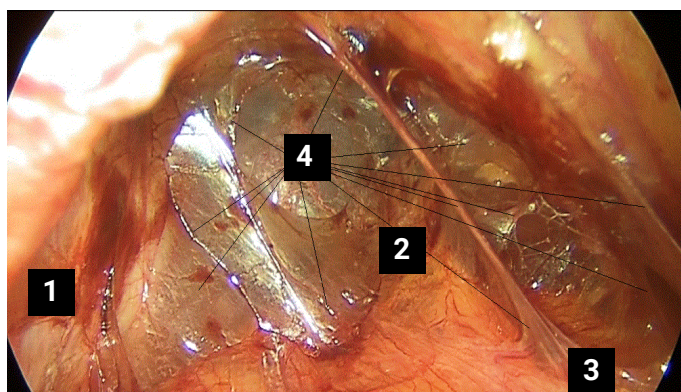
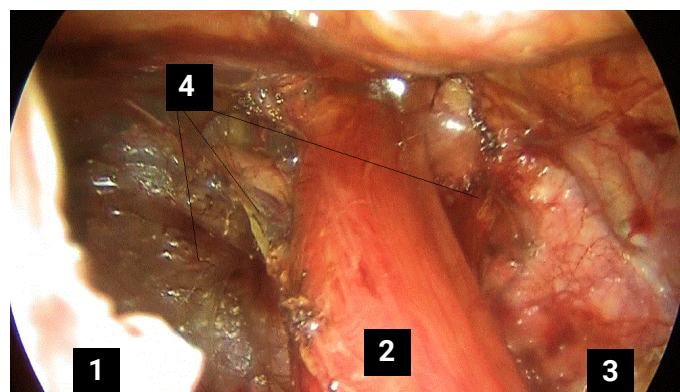
Statistical analysis of the examined indicators was performed using the system "STATISTICA 10 for Windows". The χ^2 test was used to compare qualitative indicators (percentages in the two groups). To compare the parameters that had a small number of observations in the study groups (5 or fewer cases), Fisher's exact test was used. The obtained value of Fisher's exact test $P > 0.05$ indicated the absence of statistically significant differences, while the value of $P < 0.05$ was interpreted as the presence of statistically significant differences. For all statistical estimates, their statistical significance was verified at the level of not less than 95.0% ($P < 0.05$).

Tab. I. Results of esophageal pH monitoring in patients with recurrent Barrett's esophagus at the preoperative stage.

		GROUP APC, 9 (22.5%)	GROUP HFW, 3 (7.3%)	P
De Meester	< 40	1 (11.1%)	0	>0.05
	41–100	1 (11.1%)	1 (33.3%)	>0.05
	101 and >	7 (77.8%)	2 (66.7%)	>0.05

Tab. II. Results of esophageal pH monitoring 3 months after surgery.

		GROUP APC, 7 (77.8%)	GROUP HFW, 2 (22.2%)	P
De Meester	< 14.7	5 (71.4%)	1 (50%)	>0.05
	14.7–20	0	1 (50%)	>0.05
	20.1–25	2 (28.6%)	0	>0.05

**Fig. 1.** Periesophagitis in patients undergoing APC (well pronounced): (1) Right crus of the diaphragm; (2) Esophagus; (3) Left crus of the diaphragm; (4) Adhesions.**Fig. 2.** Periesophagitis in patients undergoing HFW (minimally expressed): (1) Right crus of the diaphragm; (2) Esophagus; (3) Left crus of the diaphragm; (4) Adhesions.

RESULTS

A total number of 89 patients with Barrett's esophagus and GERD were treated at our institution in years 2015–2020. The APC method was used to treat 45 patients, while the remaining 44 patients received HFW treatment.

Repeated examination was required for 81 patients (91%) – 40 patients (49.4%) from the APC group and 41 patients (50.6%) from the HFW group. The average follow-up period per patient was 9 months.

In 56 patients (69.2%) no endoscopic or histological signs of dysplasia were observed.

A total of 24 patients were noted to have abnormal endoscopy results: 12 patients (14.8%) with signs of reflux esophagitis (type A) and without signs of metaplasia and 12 patients (14.8%) with Barrett's esophagus recurrence with a high-grade dysplasia without nodules resembling the small intestine: 9 patients (75%) from the APC group, 3 patients (25%) from the HFW group, respectively. These patients underwent 24-hour esophageal pH monitoring (Tab. I.).

One patient (1.2%) from the APC group was diagnosed with anodocarcinoma during a follow-up visit and was therefore excluded from further analysis.

There was no significant difference in DeMeester scores measured before and after ablation.

Most patients with metaplasia were found to have DeMeester score > 41; 11 patients (91.7%) were found to have DeMeester score > 41 and were offered a surgery. Of all patients included in the study, 3 (25%) with DeMeester score < 100 refused surgery and insisted only on repeated ablation and antireflux drug therapy, which was performed in accordance with their will. Overall, 9 (75%) patients underwent Nissen fundoplication. Of note, patients who underwent HFW were observed to have much less inflammation on endoscopic ultrasound when compared to the APC group and were able to proceed with surgical treatment much sooner: 53 +/- 7 days for HFW versus 115 +/- 4 days for APC.

No significant intra- and postoperative complications were recorded. During surgery, significant manifestations of periesophagitis were observed in patients who underwent APC (Fig. 1.). These manifestations were minimally expressed in the group of patients who underwent the HFW procedure [19] (Fig. 2.).

Three months after surgery, 9 patients underwent esophageal pH monitoring, the results of which showed better DeMeester score in the HFW group when compared to the APC group, though numbers were generally small (Tab. II.).

Six months after the operation all patients underwent repeated esophagogastroduodenoscopy in the NBI mode, along with biopsy of the mucosa according to the Seattle protocol. The following conclusion was drawn after these examinations – no areas of metaplasia were detected [22, 23].

Tab. III. Complaints after surgery.

COMPLAINTS	GROUP APC, 7 (77.8%)	GROUP HFW, 2 (22.2%)	P
Dysphagia	0	0	>0.05
Heartburn and taking proton pump inhibitors	1 (11.1%)	0	>0.05
Chest pain	0	0	>0.05

Follow-up examinations of patients were carried out 12 months after the operation – during these 12 months, we observed a complete absence of complaints such as dysphagia, heartburn, chest pain or complete refusal to take antacids in patients from the welding group. One patient (11.1%) from the APC group suffered from recurrent episodes of mild heartburn, which forced him to occasionally take proton pump inhibitors (Tab. III.).

DISCUSSION

Although endoscopic approach offers adequate treatment for Barrett's esophagus, this procedure alone may not be sufficient in preventing further development of metaplasia and should be followed by surgery.

Despite the fact that less invasive approaches allowed for achieving initial success and were preferred by patients, a significant number of individuals treated with these methods progressed to more severe disease, being at continuous risk of cancer development. In our study, 14.8% of patients met the inclusion criteria for surgery after endoscopic treatment. It is consistent with other studies, which report that 11.8% of patients require surgical procedure [24, 25]. Progression to esophageal cancer remains a significant problem in these patients [26, 27]. Although the overall success rate for endoscopic techniques was high, a large number of patients were still at risk for developing this difficult-to-treat disease.

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