Acta Scientific Gastrointestinal Disorders (ISSN: 2582-1091)

Volume 5 Issue 1 January 2022

Review Article

Barrett's Esophagus: The Evolution of Views (Review)

NYU Kohanenko, TSH Morgoshiia, M Ter-Ovanesov, AV Glebova, OG Vavilova and AA Kashintsev*

Federal State Budgetary Educational Institution of Higher Education "Saint Petersburg State Pediatric Medical University" of the Ministry of Health of Russia, Russian Federation

***Corresponding Author:** AA Kashintsev, Federal State Budgetary Educational Institution of Higher Education "Saint Petersburg State Pediatric Medical University" of the Ministry of Health of Russia, Russian Federation.

Received: November 17, 2021

Published: December 31, 2021

Abstract

Barrett's esophagus (BE) is known to be a disease characterized by the replacement of the multilayer flat epithelium with a metaplastic columnar epithelium. Technological advances in endoscopic procedures have radically changed the treatment of dysplastic and early cancers from aggressive to organ-preserving endoscopic treatment. A multi-modal approach to treatment has been shown combining endoscopic resection of visible and/or protruding lesions with ablative methods for early forms of mucosal lesions in Barrett's esophagus, followed by long-term follow-up, which improves the results of treatment of this nosological form. Safe and effective endoscopic treatment can be both tissue acquisition, as in endoscopic mucosal resection with endoscopic submucous dissection, and tissue ablation, as in photodynamic therapy, radiofrequency stimulation and cryotherapy. Joint decision-making between a patient and a doctor is important when considering treatment of Barrett's esophagus and dysplasia.

Keywords: Barrett's Esophagus; Gastroesophageal Reflux Disease; Esophageal Adenocarcinoma; Endoscopy; Dysplasia Treatment; Surgical Treatment

Introduction

Since the first description of Barrett's esophagus (BE), significant advances have been made in understanding the biology and pathology of this disease, its risk factors, and its progression into esophageal cancer. Endoscopic imaging techniques have been improved to identify dysplasia within this nosology. Currently views on the problem of Barrett's esophagus are undergoing an evolution with the emergence of new information in the field of embryology, genetics, biochemistry, clinical medicine and epidemiology. In 2014, the British society of gastroenterology proposed a definition of Barrett's esophagus based only on the description of metaplastic changes in the esophagus without taking into account their precancerous status [1]. According to the authors, this descriptive approach allows us not to focus on the traditional issue of the risk of developing cancer in various types of metaplasia. However, after the diagnosis of Barrett's esophagus, the risk of developing cancer should be determined individually by means of endoscopic, pathologic and molecular data. In accordance with the recommendations of the British Society of Gastroenterology, we consider Barrett's esophagus to be a pathological condition in which normal squamous epithelium of the mucosa of the distal esophagus is replaced by columnar epithelium metaplasticity, which is reliably (validly) determined by endoscopic examination (i.e., larger than 1 cm) above the esophageal-gastric junction and morphologically verified. From this definition, it follows that endoscopic and histological studies are the basis for the correct diagnosis of this pathological condition, and the subsequent endoscopic and histological data allows one to determine the degree of changes in the mucous membrane and the risk of developing esophageal adenocarcinoma

and, as a result, the treatment and management of patients. Despite the high mortality and morbidity associated with surgical resection, esophagectomy was once recognized as the "gold standard" for BE with severe epithelial dysplasia associated with a high risk of developing malignant tumors of gastrointestinal tract - obligate esophageal pre-cancer [2-4]. Undoubtedly, the relevance of timely diagnosis and effective treatment of Barrett's esophagus (BE) is due to its association with an increased risk of esophageal adenocarcinoma. Today, this pathological condition is considered precancerous. This pathology was first described by Norman Rupert Barrett in 1950 [5]. The disease is now known in clinical medicine as" Barrett's Esophagus" (BE). It is the most complex and controversial nosology of the digestive tract, which includes several different subgroups.

First N. Barrett was certain that they studied the state which was a combination of hernias hiatal (HH) with translocation of the proximal part of the stomach into the mediastinum in the form of a tube ("toborowsky stomach") with the shortened and ulcerated lower third of the esophagus. Only a short time later, Allison and Johnston [6] showed that the tubulated stomach discovered by N. Barrett was actually an esophagus with a cylindrical epithelial metaplasia (CMC) and the formation of peptic ulcers ("Barrett ulcers"). Barrett agreed with this concept only in 1957 [7]. Despite this, since then, cylindrical cell metaplasia of the esophageal mucosa, accompanied by ulceration of the mucosa or stricture, is called "Barrett's Esophagus". Currently, the question remains debatable whether PB is a congenital disease or an acquired pathology, as a result of long-term and severe gastro-esophageal reflux (in gastro-esophageal reflux disease-GERD) [8].

It is no secret that interest in PB has been growing in recent years. This is due to an increase in the frequency of adenocarcinoma of the esophageal-gastric junction in general and the frequency of esophageal cancer in particular. Such changes in epidemiology caused a shift in emphasis on this issue in the direction of determining the risk of developing cancer against the background of Barrett's esophagus, i.e., the study of clinical, morphological and genetic factors of possible malignant transformation. At the same time, the accumulated clinical experience currently shifts the priorities in treatment from conservative therapy, with the long - term use of antacid and antisecretory drugs, to active surgical tactics at all stages of treatment - both in the correction of gastro-esophageal reflux, and later, in the case of epithelial dysplasia. It is well known that when making the diagnosis of "Barrett's Esophagus", a c clinician, as a rule, relies on an endoscopic picture, with the identification of local foci of hyperemia or "flames" against the background of a pale pink esophageal mucosa that extends more than 3 cm above the esophageal-gastric junction zone. However, this interpretation is rather vague, and on the other hand, in our opinion, it is not accurate enough, because it allows us to take for PB and the site of normal inflammation against the background of reflux esophagitis. Also, the location of the transitional squamous-cylindrical cell zone (Linea serrata or Z-line) relative to the intact esophageal mucosa is not absolute, which also introduces additional difficulties, especially given the standardization of the term "Barrett's short esophagus", used in recent years in studies of true cancer of the cardiac stomach [9]. Therefore, today the undisputed and objective criterion for PB is morphological verification of the diagnosis. Note that in clinical practice, for convenience, the classification proposed in 1976 is widely used. Pauli [10]. According to this classification there are three morphological subtypes of PB:

- Cardiac type having a foveolar surface with the presence of mucin-producing cells;
- Fundal type, carrying in addition to mucin-producing also specific to the gastric epithelium main and parietal cells;
- Cylindrical cell type, carrying mucin-producing cylindrical cells that form villous folds, with the inclusion of goblet cells, which are a sign of intestinal epithelial metaplasia.

The first two types can be interpreted as variants of the norm, especially the cardiac type, the presence of which has been proven in newborn patients. The latter type is the most important, because it is the precursor to the development of esophageal dysplasia and cancer. At the same time, the presence of goblet cells is a significant sign of the development of intestinal metaplasia.

It should be emphasized that the length of the PB section is a significant factor. Currently, PB is divided into short - up to 3 cm and long - over 3 cm. This gradation is due to the definition of Hayward, according to which in a healthy person one can also meet the cardiac type of mucosal epithelium, extending 2 cm above the "tooth line". For a long time, the following definition of PB has been generally accepted in clinical practice: it is a pathological condition in which a part of the flat epithelium of the mucous membrane of the distal esophagus is replaced by a metaplastic cylindrical epithelium. The segment of cylindrical metaplasia should be determined

by endoscopic examination, located above the esophageal-gastric junction or junction (Z-line) and confirmed morphologically by detecting intestinal metaplasia (Figure 1). Later it was found that a short segment of PB containing goblet cells is of clinical significance and is the source of carcinoma in the esophageal-gastric junction (true cancer of the cardiac stomach or type II according to the classification of J. R. Siewert) [11]. Based on this, in the modern literature, the presence of a segment of gastric epithelium larger than 3 cm, regardless of the presence or absence of goblet cells, is called PB, while a short section (<3 cm) is divided into a cylindrical cell epithelium without intestinal metaplasia and a cylindrical cell epithelium with intestinal metaplasia (with the presence of goblet cells).

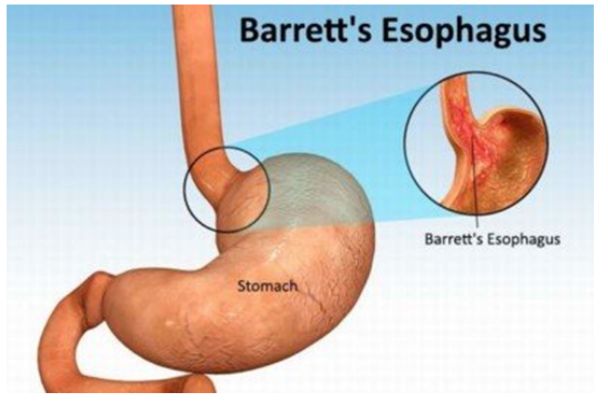

Figure 1: The mucosa of the gastroesophageal junction in the Barrett's esophagus.

It should be particularly noted that the pathognomonic sign of BE is the detection of goblet cells with acidic mucin, stained with Alcian blue dye at pH 2.5. the presence of such cells in the esophageal mucosa, regardless of the length of the metaplasia zone (whether it is short or long) is an important sign of the possible development of dysplasia and subsequent malignization [12-14]. In this aspect, the presence of goblet-shaped cells in the mucosa, rather than the fundal or cardiac type of epithelium, has been suggested to consider a true Barrett's esophagus by many researchers. The length of the cylindrical-rockethotdog metaplasia is also quite highly correlated with the presence of goblet cells. The most significant factor in the development of metaplasia in the esophagus is reflux esophagitis. In 6-12% of patients suffering from gastroesophageal reflux, BE is formed with time, and this pathology is considered the final stage of the evolution of GERD [15]. According to a nationwide population-based controlled study conducted in Sweden, the relationship between the frequency, duration, and severity of gastro-esophageal reflux, with the frequency of esophageal BE and adenocarcinoma was shown. This ratio was insignificant in cardia adenocarcinoma and absent in esophageal squamous cell carcinoma.

It is believed that the risk of developing adenocarcinoma with BE on the background is 30-125 times higher than in the population [16]. As noted above, one of the key points in the development of metaplasia in BE is the appearance of goblet cells. The mechanism of goblet cells formation among the cylindrical epithelium has long been unclear and debatable. It is known that casting from the stomach induces cylindrical cell metaplasia of the epithelium without the appearance of goblet cells. In the experimental model, Bremner C.G., *et al*. (1997) [17] showed that in the structure of metaplasticized epithelium, goblet cells appear only when duodenal juice is added to the reflux contents. These data formed the basis of the assumption, confirmed later, according to which CMC is a compensatory mechanism aimed at protecting the mucosa from acidic stomach contents, whereas meta - and dysplasia appears only against the background of duodenoastro-esophageal reflux, which determines the subsequent development of a malignant tumor. According to Gillen P. (1988) [18], in the acidic juice reaction, metaplasia of the distal third of the esophagus is usually characterized by the presence of epithelium of the cardiac or fundal type, whereas when the duodenal contents are thrown into the esophagus, changes in the type of intestinal metaplasia with the appearance of foci of dysplasia predominate. It should be noted that these data are indirectly confirmed by the development of BE with the appearance of goblet cells in patients after gastrectomy with the formation of esophago-eunoanastomosis in the presence of casting of duodenal secretions into the esophagus [19], or even after that Subtotal resections of the esophagus with the formation of esophago-gastroanastomosis on the neck [20].

In the last decade, epidemiological studies have noted a regular increase in the incidence of cancer of the proximal stomach with the transition to the esophagus [21,22]. In Western Europe and the United States, adenocarcinoma is increasingly detected in esophageal cancer. Note that in the United States over the past 35 years, the incidence of esophageal adenocarcinoma has increased by almost 300% [23].

In our country, the growth of esophageal adenocarcinoma is not so pronounced: in 7-20% of cases of esophageal cancer, there are morphological signs of adenocarcinoma [24]. The prognosis of the disease after the diagnosis of adenocarcinoma is unfavorable: the 5-year survival rate does not exceed 10-20%, and the improvement of treatment methods has little effect on improving these indicators [25].

It should be noted that today Barrett's esophagus is the most acute problem in the Western hemisphere, while in the East this pathology is rare.

Symptoms of BE in General resemble signs of gastro-esophageal reflux disease - GERD) - abandonment with the development of heartburn, discomfort behind the sternum after eating and on an empty stomach, as well as the possible development of dysphagia. However, there are some differences. This is mainly due to the fact that the reconstruction of the esophageal epithelium is a protective function. Therefore, in most patients with BE, heartburn is not expressed, and sometimes it is absent. This is due to the low sensitivity metaproterenol epithelium to the action of acid content. However, when collecting anamnesis, patients may note that heartburn and discomfort behind the sternum were pronounced, but over time almost disappeared. This development of "imaginary well-being" is a strong argument in favor of immediate examination.

The frequency of combination of BE and esophageal strictures is from 30 to 80%. It should be emphasized that the combination of radiological signs of esophageal reflux with the presence of stricture in the middle third of the esophagus is almost always interpreted in favor of the development of BE. Out of every hundred patients with BE and a lesion length of more than 3 cm, 60% will have stricture, and 40% will have ulceration, and 10-12% will later have glandular cancer [26]. At the same time, the presence of stricture in the BE region is a fairly important sign of possible development of adenocarcinoma. It should be borne in mind that at present, the increase in the frequency of adenocarcinoma of the proximal stomach and distal esophagus exceeds the incidence of any other malignant tumor.

According to Camerona A. J., *et al*. (1997) [26] the clinical detection rate of BE is 22.6 per 100 thousand population, while the autopsy rate is much higher - 376 per 100 thousand. This fact allows us to emphasize that most patients do not notice symptoms of reflux, and, consequently, do not seek medical help from doctors. On the other hand, minor manifestations of reflux esophagitis in the form of belching and heartburn in modern conditions with a wide availability of antacids, lead to uncontrolled and unsystematic self-treatment. As a result, when the diagnosis is made, the disease is often at a far advanced stage, with the development of severe dysplasia and even pre-or invasive adenocarcinoma.

At the initial stage of examination of patients with suspected BE, a polypositional x-ray examination is performed (Figure 2). The main signs of BE development are a picture of severe reflux esophagitis in combination with a hernia UNDER, high and extended strictures of the esophagus, as well as the presence of its ulceration. Often, to increase the resolution of this method, double contrast of the esophagus is performed with a detailed study of the structure of the mucous membrane in the distal third (reticular character with the possible appearance of foveolar structures) in combination with the skills and experience of the radiologist.

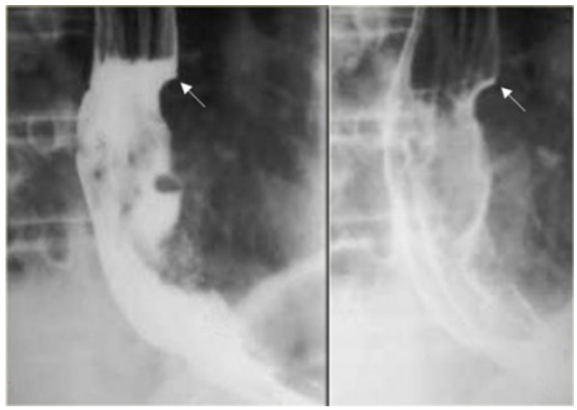

Figure 2: Radiograph when Barrett's esophagus (filling defect of the esophagus, or ectopic arrow).

The endoscopic method is the main and most informative when making a diagnosis of BE. Such instrumental methods as radiography and scintigraphy can only assume this diagnosis, endoscopic method allows you to establish it with a high degree of probability (it should be noted that the final diagnosis of Barrett's esophagus is established by morphological verification). It is well known that endoscopy determines the extent of changes in the mucous membrane, its relation to the esophageal-gastric transition. At the same time, the spread of the metaplasia site is adequately defined as

foci of hyperemia ("flames") against the background of the "pearl - white" epithelium of the esophageal mucosa (Figure 3).

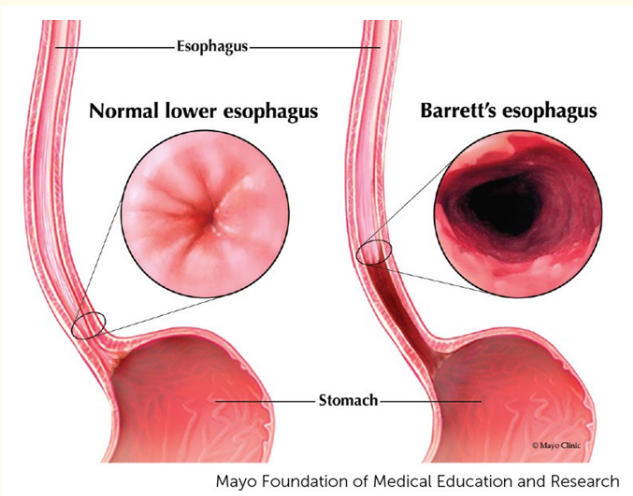

Figure 3: Endoscopic picture of Barrett's esophagus.

It is important to nmention that metalizowany mucosa upon closer inspection looks like in atrophic gastritis, the blood vessels have a longitudinal direction. In such cases, the technique of chromoendoscopy with 2% Lugol mucosal color is used. The accuracy of the method in the diagnosis of metaplasia foci is about 80%. Also today, other technologies for painting the mucosa with chromoendoscopy are widely used - methylene blue, indigocarmine, and 1% acetic acid solution. The main purpose of endoscopic examination is to obtain biopsy material for morphological research, which is aimed not only at confirming metaplasia of the esophageal mucosa, but also at detecting dysplasia and (or) foci of adenocarcinoma. It is noted that adenocarcinoma developing against the background of Barrett's esophagus is most often characterized by endophytic more aggressive growth, which makes it difficult to visually diagnose, and it often requires the use of a specific technique for taking a biopsy. According to the method proposed by G. N. J. Tytgat (1994) [27], biopsy is performed from four quadrants along the circumference of the esophagus every 2 cm, starting from the border of the metaplasia zone. Some authors [28] indicate that a biopsy above the visually determined border of metaplasia is mandatory since it is there that the foci of dysplasia and foci of malignant cells are most often localized.

In recent years, modern endoscopic techniques have been frequently used in the diagnosis and screening of Barrett's esophagus: endoscopic ultrasound, optical coherence tomography (OCT), and magnetic endoscopy [29]. Of the above methods, the most interesting one is OCT which allows performing a real-time intravital "optical" biopsy of the esophageal wall with visualization of layers and targeted biopsy of suspicious areas of the mucosa. Correlation analysis of OCT data and morphological studies indicate a high resolution of the method in the differential diagnosis of BE and esophageal adenocarcinoma, as well as in monitoring the recovery of esophageal mucosa after thermal ablation of BE foci.

To date, the risk of developing adenocarcinoma with BE at the background is considered to be significant, with this condition being an obligate precancer. However, the appearance of cancer is preceded by a gradual progressive development of dysplastic changes, with the cells losing signs of differentiation, i.e. the development of dysplasia. Progression from mild dysplasia (low-grade dysplasia) to severe one (high - grade dysplasia) takes on average 29 months, while the subsequent development of adenocarcinoma takes half the time-14 months [30].

In clinical practice, it is quite difficult to determine the interval between control endoscopic examinations in such patients. Based on computer analysis of the survival results of patients with BE based on the calculated life expectancy, as well as the cost-effectiveness of endoscopic screening, it is shown that in mild and moderate dysplasia, control studies should be repeated every 2-3 years, and in the group of patients with severe dysplasia, the method of choice is esophagectomy [31]. At the same time, in patients at a low risk of cancer - women, non - smoking and non-alcohol abusing patients-endoscopic screening once every three years is sufficient. At the same time, in the group at a high risk of developing cancer - male smokers-annual endoscopic screening with multiple biopsies is justified.

The 5-year survival rate of patients with adequate surgical treatment for esophageal adenocarcinoma against the background of Barrett's esophagus (with screening and active detection) is about 96% and is statistically significantly higher than in the surgical treatment of patients operated for symptomatic esophageal adenocarcinoma (26%) [32].

Treatment

The purpose of treatment of this pathology is to relieve symptoms of gastro-esophageal reflux disease (GERD) and reduce the risk of malignancy. The accumulated experience changes the concept of treatment: from conservative treatment to active surgical tactics. To eliminate reflux as an etiological factor antireflux surgery is performed. Eradication metaproterenol is carried out by endoscopic mucosal destruction. As for the indications for ablation of metaplasticized mucosa, there is currently no single approach. However, the radiofrequency ablation (RFA) method used in recent years is fundamentally different from other ablation techniques in terms of safety [33]. In this regard, radical treatment becomes appropriate for a larger group of patients, and the results of the method require additional analysis and study.

To date, the treatment of patients with Barrett's esophagus consists of two main points: 1. Elimination of signs and manifestations of GERD; 2. Treatment of high-grade dysplasia and reduction of the risk of esophageal adenocarcinoma.

In the world medical literature, generally accepted approaches to the treatment of BE are: lifestyle changes and specific anti-reflux measures-stopping smoking, abuse of strong alcohol, excluding snacks before bed, overeating, excluding food that can irritate the esophageal mucosa (fats, chocolate, coffee, beverages such as Coca-Cola, onion, garlic, alcohol, etc.), and in patients with severe obesity - weight loss. The head end of the bed should be raised 15-20 cm.

The main tasks in the treatment of Barrett's esophagus:

- Treatment of erosive esophagitis;
- Correction of esophageal strictures if present;
- Prevention of complications;
- Early detection and treatment of esophageal dysplasia.

The latter implies dividing patients into subgroups without signs and with signs of dysplasia, which determines the tactics of diagnosis, screening and possible treatment, the spectrum of which is wide and consists of drug-induced antisecretory correction, performing minimally invasive laparoscopic anti-reflux surgery, subtotal esophageal resections.

It is important to emphasize that in recent years, the treatment of gastroesophageal reflux disease has been dominated by two main competing trends:

- Performing maximum suppression of stomach acid function by employing proton pump inhibitors (omeprazole, pantoprazole, losek, lansoprazole, etc.) in combination with H2 blockers;
- Performing anti-reflux surgery. The rapid development of minimally invasive endovideosurgical techniques for performing various types of fundoplications contributed to the wide implementation of the latter.

Medication

It is known that after the introduction of proton pump inhibitor (PPI) drugs, the possibilities of conservative therapy significantly increased, which allowed reducing some restrictions in the diet and lifestyle of patients with GERD. Studies have shown that when combined with the use of PPIS and simple physiological techniques (lifting the head end of the bed by 40-45°, reducing fat consumption, reducing smoking and vertical position during the day, at least 3 hours after eating) significantly reduce the frequency and volume of reflux esophagitis. The use of proton pump inhibitors is recommended because H2-receptor blockers do not achieve a positive effect in GERD stages II-IV. Treatment of patients with BE, which is one of the most pronounced forms of GERD, requires the use of high doses of H2-receptor blockers (cimetidine, ranitidine, famotidine), but even so, success was extremely rare. Patients who are resistant to high doses of H2 blockers can be successfully treated with proton pump inhibitors (omeprazole, lansoprazole, pantoprazole, rabeprazole). Treatment with proton pump inhibitors should be long and continuous. Interruption of treatment leads to a rapid relapse of the disease and the development of complications.

Today PPIS are considered the first-line therapy for a long segment of BE without signs of dysplasia [34]. However, with a short BE, it is possible to conduct therapy only with H2 blockers, since in these cases, reflux esophagitis is not so pronounced.

One of the key points is the combination of H. Pylori infection and reflux esophagitis. To date, the concept of an increased risk of developing atrophic gastritis and stomach cancer in the presence of H. Pylori infection is considered to be rather justified [35]. At the same time, the presence of this pathogen proves not to be associated with damage to the normal esophageal mucosa or the development of atrophy, metaplasia or cancer. According to Kuipers, E. J., *et al*. (1996) [36] in patients with both factors, omeprazole therapy significantly increases the risk of developing atrophic gastritis and

stomach cancer. At the same time, without suppressing acid production, however, with fundoplication performed, there is a positive dynamics in the esophagus causing no concomitant disorders in the gastric mucosa. The author concludes that in conservative treatment with the application of proton pump inhibitors (PPIS), effective H. Pylori eradication should be carried out.

If the drug therapy is ineffective, as well as the detection of dysplastic changes in the mucous membrane, it is possible to use surgical and endoscopic methods of treatment successfully.

Surgical treatment

It should be emphasized that surgical treatment of BE is generally consistent with that of GERD until severe dysplasia or cancer is detected. Performing anti-reflux surgery restores the function of the lower esophageal sphincter and reduces or completely eliminates the throwing of gastric and duodenal contents into the esophagus. The choice of fundoplication method depends on the nature of the changes, the state of the lower esophageal sphincter, the esophageal reflux index, and the technical preferences of various surgeons, but the most commonly performed fundoplication is the Nissen procedure. When shortening of the esophagus it is possible to perform the esophago-gastroplasty for Kallis with the Nissen-Rosetti and Toupet: stages of intervention: surgical access; mobilization of the left lobe of the liver; exposure of the distal esophagus; skeletonization of the proximal part of the large curvature of the stomach; displacement of the bottom of the stomach; stitching the cuff from the bottom and confirming the width of the cuff with the index and thumb of the surgeon. According to some researchers, performing the Collis-Nissen operation is pathogenetically more justified and purposeful, since it has better results in all cases. Currently, the most actively developed is minimally invasive surgical approach to performing anti-reflux manipulations. The main advantage of performing such interventions is a relatively low rate of complications and mortality (0.1 - 0.2%), combined with early activation of patients, shortened stay in the clinic (2-3 days) and early recovery of working capacity (10-14 days). According to various authors, the results of surgical treatment of PB are somewhat superior to conservative therapy [37]. Moreover, surgical correction better controls not only the number and frequency of reflux episodes, but also reduces the severity of esophagitis and even affects metaplasia. We emphasize that active surgical tactics is especially effective in the presence of BE complications such as strictures and ulcers of the esophagus, when a conservative therapy is little or not effective. A safe and effective endoscopic treatment may consist in mucous membrane resection and submucous dissection. Tissue ablation is performed both in the photodynamic therapy and in the radiofrequency stimulation and cryotherapy.

A similar conclusion was drawn by A. Ortiz., *et al.* 10 years later (1996) [38] when comparing the use of omeprazole and the laparoscopic fundoplication. Another large prospective study including Swedish population register [39] (32,274 patients), covering a period of up to 32 years, reported the risk of adenocarcinoma development equal to 6.3 (95% the validity interval 4.5 - 8.7) in the group with the conservative treatment, whereas in the surgical group (n=6406) it was higher - 14.1 (95% the validity interval 8.0 - 22.8). It should be mentioned that, according to the findings of McDonald., *et al.* (1996) [40] (Mayo Clinic), adenocarcinoma developed after fundoplication in BE patients within 39 months. However no such complication was noticed after this period. The author concludes that the surgical treatment has a protective quality and it is effective only in a long term perspective, especially in patients without any signs of dysplasia, though in the presence of dysplasia the patients may already have insidious cancer.

Today dysplasia is generally recognized not to be a marker of esophagus adenocarcinoma presence presence. Nevertheless, it may transform into that with time. Unfortunately, about 30-40% of patients with severe dysplasia already have pre-invasive or invasive carcinoma at the time of diagnosis [41]. Therefore, some researchers insist on conducting a wide multi-locus biopsy not only with morphological, but also with cytometric and genetic research of the biomaterial. The data from these studies have an extremely high prognostic value in identifying cases at the highest risk of subsequent development of adenocarcinoma. The modern concept of malignant neoplasm therapy makes serious demands not only on the oncological effectiveness of the treatment, but also on improving the functional results that determine the quality of life of patients [42]. Despite the data of additional studies, most clinicians consider severe dysplasia an indication for radical surgical treatment in the volume of subtotal esophageal resection. When performing esophageal resection, it should be taken into account that even in cases of a hidden tumor that is not detected in fegds, a locally spread adenocarcinoma can be detected morphologically, sprouting the esophageal wall with metastases to the lymph nodes. These factors should determine that interventions performed for

severe dysplasia should take into account the oncological principles of surgery:

- Interventions are performed transthoracically,
- Subtotal resection of the esophagus is performed,
- An adequate volume of lymphodissection is performed (taking into account the localization in n/3 of the esophagus, an extended two-zone lymphodissection 2F en blok is sufficient).

Thus, various methods of endoscopic ablation are currently widely used for the complete removal, i.e. eradication, of the entire metaplasticized epithelium of Barrett's esophagus. Eradication of all metaproterenol epithelium is necessary in cases of high risk of development of adenocarcinoma of the esophagus. These are cases with high-grade dysplasia or intra-mucosal cancer without endoscopically visible pathological areas verified by randomized four-quadrant biopsy. The choice of ablation technique for endoscopic treatment is possible only after a thorough study of the metaplasia zone in a specialized expert center using modern endoscopic techniques, such as magnifying and narrow-spectrum endoscopy, and confirmation of the absence of visible pathological areas. In addition, after endoscopic resection of the mucosa (ERS) with a pathological site, 20% of patients develop metachronous formations in the segment of metaplasia in the next 2 years. And as studies show, with ERS for early cancer in 80% of cases, these patients already have moderate or high-grade dysplasia in other areas of the metaplasticized epithelium [43]. Therefore, endoscopic ablation of the metaplasia segment is indicated in patients after endoscopic resection of early Barrett's esophageal cancer, since this can significantly reduce the risk of metachronous cancer in other areas of the metaplastic epithelium.

If severe mucosal dysplasia is detected and there is a genetically determined risk of developing adenocarcinoma the method of choice in treatment is subtotal resection of the esophagus. The exception is elderly patients with severe comorbidities and contraindications to surgical treatment [44]. In such cases, it is optimal to perform conservative ablation of the affected areas, primarily through photodynamic therapy (PDT). This tactic should standardize therapeutic approaches, improve the quality of life, and most importantly, the long-term results of treatment of this pathology.

Currently, cryotherapy looks promising, with a good efficiency and safety profile. However, larger studies and long-term data on treatment tolerance are needed.

To date, the tactics of surgical treatment of early forms of esophageal cancer are undergoing a radical change in approach, which is determined by the widespread introduction of minimally invasive options for surgical interventions in surgical practice. Strategically this approach is determined, on the one hand, by the rather pessimistic results of surgical treatment of esophageal cancer, with the exception of early forms, some of which are shown in figures L. V.-level 15-25% [45], and on the other hand, by the high rates of postoperative complications and mortality. Currently, the rates of postoperative complications after open operations are at the level of 45-65% with a high frequency of esophageal anastomosis failure (at the level of 6.5-11.5%) and high rates of postoperative mortality (from 8 - 23%) [46]. These data, in turn, are actively used by supporters of conservative RP therapy who insist on the possibility of using local methods - radiofrequency ablation or photodynamic therapy in the treatment of early forms of RP.

Among minimally invasive treatment methods, both hybrid and fully minimally invasive interventions can be used with both intra-thoracic anastomoses (Ivor Lewis type) and three-zone interventions with neck anastomosis (McKeown-Nakayama). For early, non-invasive forms of esophageal cancer with a low potential for lymphogenic metastasis, such operations are justified in terms of low trauma, early activation of patients with the ERAS (Enhanced Recovery after Surgery) program, and comparability of long-term results [47]. However, starting from the level of invasion of the submucosal layer, the question of the oncological adequacy of minimally invasive interventions remains open, since in the conditions of extremely high metastatic potential of esophageal cancer (with pT1sm, the frequency of lymphogenic metastases can be 30-40%) and the variability of metastasis, their oncological radicality has not been proven by the data of prospective randomized studies, which is mandatory at present! [48].

Conclusion

Thus, endoscopic therapy appears to be safe and effective for the treatment of BE with dysplasia. Eradication is recommended for the treatment and prevention of metachronous and synchronous lesions. Further research is needed to assess the long-term persistence of endoscopic therapy, identify and treat Barrett's esophagus, and determine the strategy for surgical treatment in patients with non-dysplastic BE [49]. Treatment of this pathology is a dynamic process and will continue to evolve as we move forward in our understanding of the development of dysplasia and cancer in BE, the

genetics of this process, the identification of molecular markers or less expensive methods of screening and monitoring for esophageal cancer, dysplasia, and develop safer treatments that effectively eliminate the pathology and the need for long-term treatment [50]. Treatment of such patients requires an interdisciplinary approach in collaboration with experts-endoscopists, surgeons, oncologists and pathologists. In our opinion, a clear understanding of the biology of BE - risk of tumor progression, appropriate screening and follow-up is necessary. Selection of patients, availability of various modern endoscopic ablation methods, determination of their advantages, risk profile for patients - will help in the future successful endoscopic and/or surgical treatment of Barrett's esophagus.

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