Rezumat

Experiența Clinică de Chirurgie nr. 4 în intervențiile chirurgicale antireflux. Retrospectiva a 20 de ani

Introducere: Patologia non-oncologică a joncțiunii esogastrice (JEG) reprezintă domeniul de interes interdisciplinar pentru mulți specialisti practicieni (endoscopist, gastroenterolog, chirurg, imagist). Fapt determinat de incidența sporită a patologiilor benigne ale joncțiunii esogastrice, în special a bolii de reflux gastro-esofagian, considerată actualmente patologia secolului XXI. Incidența globală a bolii de reflux gastro-esofagian (BRGE) crește anual. Meta-analizele arată prevalența patologiei date în ţările occidentale de aproximativ 10-20%, comparativ cu ţările asiatice unde aceasta este sub 10%, în America de Nord de 27,8% și de 25,9% în Europa (1,2,3).

Material și Metode: Experiența clinicii noastre reprezintă 20 ani (2002-2021) de activitate în chirurgia antireflux, timp în care au fost realizate 768 intervenții antireflux pentru BRGE și hernii hiatale (HH). Pacienții selectați pentru intervențiile chirurgicale au suportat inițial tratament conservativ conform protocoalelor internaționale de specialitate în vigoare. Aproximativ 40% din totalul pacienților erau refractari tratamentului conservativ antireflux și aceste date concordau cu datele de literatură mondială (4). Mai mult, la 24,2% de cazuri simptomele refluxului gastro-esofagian (RGE) a survenit la o lună de la finisarea tratamentului conservativ, iar la 35,8% peste 6 luni.

Rezultate: Tipul intervențiilor chirurgicale antireflux în cadrului studiului nostru a fost diferit și dependent de situație: particularități individuale pentru pacient, abordă diferențe ale tehnicilor chirurgicale în diferite perioade de timp. În ultimii 10 ani predomină operațiile laparoscopice la majoritatea pacienților (96,6%), comparativ...
Introduction
Non-oncological pathology of the esogastric junction (EGJ) is an area of interdisciplinary interest for many practitioners (endoscopist, gastroenterologist, surgeon, radiologist). This is due to the increased incidence of esogastric junction benign pathology, especially gastroesophageal reflux disease (GERD), currently considered the disease of the 21st century. The overall incidence of GERD is increasing annually. Meta-analyses show the prevalence of this pathology in Western countries of about 10-20%, compared to Asian countries where it is below 10%, in North America of 27.8%, and 25.9% in Europe (1,2,3).

Material and Methods: The experience of our department in antireflux surgery represents 20 years (2002-2021) of activity, during this time 768 antireflux interventions were performed for GERD and hiatal hernias (HH). Patients selected for antireflux surgery initially underwent conservative treatment in accordance with applicable international protocols. Approximately 40% of all patients were unwilling to undergo conservative antireflux treatment, and these data are in line with the world literature statistic (4). Moreover, the symptoms of gastroesophageal reflux disease in 24.2% of cases appeared one month after the end of conservative treatment, and in 35.8% after 6 months.

Results: The type of antireflux surgery in this period of activity was different and depended on the situation: the individual characteristics of the patient, different approaches to surgical techniques over different periods of time. Laparoscopic antireflux operations predominate in the majority of patients (96.6%) in the last 10 years, compared to previous years, where the rate of traditional interventions was 15-20. The complete fundoplication Nissen-Rossetti, due to the good control of GERD, has become an intervention of choice mainly for patients with GERD.

Conclusions: 1. Early diagnosis of refractory forms to medical treatment requires referral of patients to laparoscopic antireflux surgery to avoid severe complications of GERD. 2. The minimally invasive approach to antireflux surgery today is a golden standard, and the use of a complete fundoplication ensures the high effectiveness of these interventions.

Key words: gastroesophageal reflux disease, hiatal hernia, metaplasia of esophagus, Barrett’s esophagus
gastroesophageal reflux disease (GERD), currently considered the disease of the 21st century. The overall incidence of GERD is increasing annually. Meta-analyses show the prevalence of this pathology in Western countries of about 10-20%, compared to Asian countries where it is below 10%, in North America of 27.8%, and 25.9% in Europe (1,2,3).

Pathological gastroesophageal reflux is induced by various etiopathogenetic factors: compromised function of the lower esophageal sphincter (LES), as well as esophageal dysmotility (ineffective/fragmented peristalsis).

The importance of specialists’ attention for the benign pathology of gastroesophageal junction (GEJ) is determined by the diversity of complications it can cause (peptic stricture, columnar metaplasia of esophagus, Barrett’s ulcers, adenocarcinoma of gastroesophageal junction), as well as their increased frequency in recent years. Gastroesophageal reflux associated with HH is predominant (54.9%) in our study especially the sliding hiatal hernia, which creates the conditions for the occurrence of GERD through static disorders of GEJ.

Material and Methods

The experience of our department in anti-reflux surgery represents 20 years (2002-2021) of activity, during this time 768 anti-reflux interventions were performed for GERD and HH. Patients selected for antireflux surgery initially underwent conservative treatment in accordance with applicable international protocols. Approximately 40% of all patients were unwilling to undergo conservative antireflux treatment, and these data are in line with the world literature statistics (4). Moreover, the symptoms of gastroesophageal reflux disease in 24.2% of cases appeared one month after the end of conservative treatment, and in 35.8% after 6 months.

The hospitalization of the GERD patients in the clinic over the years is shown in the diagram Fig. 1.

The hospitalization rate of patients in this study group increased during the years 2015-2021, 362 (62.2%) patients, time when it was possible to examine patients multilaterally and, as a result, more frequent diagnoses of uncomplicated (early) forms of the disease.

The number of hospitalizations was on average 2-5 patients per year until the year 2000, and in particular there were patients with complicated forms of GERD (5 our source). With the definite differentiation of GERP and HH notions (>2010 year), the number of hospitalizations for each entity has increased due to the argumentation of antireflux intervention for various forms of GERD refractory to drug treatment, long-term medical treatment with high doses/ in young patients).

Patients with GERD were divided according to two distinct criteria after 2002 year: group I

Figure 1. The dynamics of hospitalization - patients with GERD
referred only to GERD - 269 (35.0%), group II 427 (55.5%) associated with other conditions. The most common of the associated diseases was HH-321 (41.8%). The age of hospitalized patients with GERD and HH in the clinic was with high limits between 22 and 75 years and an average of 41.13±7.72 years. The majority of 57.9% were of working age.

A ratio of 1:1.4 was registered with the predominance of males, according to the gender division of the patients involved in the research project (Fig. 2). The duration of the disease, according to the history of the condition, varied between 1 and 15 years, and averaged 3.03±4.78 years, 40.98% of which were patients who received specific permanent antireflux treatment, and 31.14% patients intermittent treatment.

The clinical manifestation of the disease was largely determined by the form of GERD. Thus, the most common symptom in the uncomplicated form was heartburn, followed by belching and retrosternal discomfort, while in the complicated forms predominated retrosternal or epigastric pain, dysphagia (odynophagia) and less often heartburn or belching. At the same time, extraesophageal symptoms were detected in 94 (22.32%) patients. The most common extraesophageal syndrome was rhino-laryngological caused by high GERD. The most common form of heart attack was caused by giant HH. Persistent dysphagia, progressive weight loss, upper gastrointestinal bleeding, and anemia were the alarming symptoms that usually urged the hospitalization of patients and required complex examination to determine, as soon as possible, the cause of the suffering or evolutionary complication. These clinical signs were found in 39 (12.3%) patients with complicated GERD: peptic stenosis, esophageal ulcer, Barrett’s esophagus (5).

The number of patients hospitalized for uncomplicated GERD, GERD in association with HH has increased over the years, becoming the most significant in the structure of non-oncological pathology of GEJ (Fig. 3).

Patients with refractory forms accounted for 39.7% of all patients hospitalized in the clinic for GERD for the period 2015-2017.

Most patients with GERD were hospitalized after a series of examinations and outpatient treatments. Outpatient examinations were coordinated with the general practitioner or gastrologist and were certainly included in the preoperative examination algorithm for each group of patients with the exception of patients who were often admitted to the emergency department with various advanced complications of GERD.

Although we accepted Savary-Miller’s endoscopic classification as a guide in assessing medical-surgical tactics in GERD, the experience gained over the years suggested that there are other features that should be considered in the complete evaluation of the morphopathological substrate, seen through
the prism of modern technologies for diagnosis and minimally invasive (endoluminal) treatment. Thus, we consider it necessary to take into account the spread of the process in the surface of the esophageal mucosa on both the circumferential and the longitudinal segment, and this has led to the completion of the existing classifications (Prague C&M classification). Thus, based on the clinical and paraclinical examination (fibrogastroendoscopy, barium X-ray, pH-metry, esophagomanometry, scintigraphy) we managed to divide the patients with GERD into three clinical-evolutionary forms, which required a different surgical conduct:

- I group - 269 (35.0%) patients with GERD refractory to medical treatment;
- II group - 427(55.5%) patients with associated GERD;
- III group – 72 (9.5%) patients with complicated GERD.

The most common complication in III group was columnar metaplasia of the esophageal mucosa (72% intestinal metaplasia, 28% gastric metaplasia). The detection of complicated forms by metaplastic columnar esophagus in recent years is due to the implementation of advanced digestive endoscopy techniques that allow a better visualization of cellular and microvascular pitpatterns.

An important place in the assessment of the medical-surgical conduct was the changes of the esophageal mucosa visualized in the upper digestive endoscopy, in association with magnification and NBI +, technologies usually used when we intended to decide further medical-surgical tactics.

Non-erosive refractory form or reflux esophagitis (RE GR.0) was found in 57 (12.4%) patients who were included in this study. This was the most difficult category to argue for surgery. It should be noted that the number of patients with such esophagitis, especially in the presence of insignificant axial HH, sent by internists for antireflux surgery was at least 5-6 times higher (5 our source).

Reflux esophagitis 1-2 gr. were the most common motivations for surgery. A total of 189 patients were operated on whose morphopathological substrate was the esophagitis mentioned above (Fig. 4).

The medical-surgical tactics towards patients with complicated GERD was different. Some of these patients were hospitalized in emergency with signs of upper gastrointestinal hemorrhage, posthemorrhagic anemia or severe pain syndrome due to esophageal ulcer and/or GEJ stenosis (Fig. 5).

Changes in the esophageal mucosa evidenced by upper digestive endoscopy in complicated GERD required biopsy of the mucosa for histopathological examination to rule out GEJ neoplasia.

At the same time, changes in the esophageal mucosa were not the only or decisive factor in the selection of the method.
and volume of surgery. Thus, a special place had the character of reflux seen through the prism of pH-metry, but also the functional state of LES appreciated by high-resolution esophagomanometry (6). Acid or mixed pathological reflux (De Meester score) refractory to medical treatment, also confirmed radio-logically as high and aggressive reflux, LES incompetence detected by esophageal high resolution manometry (HRM), delayed esophageal clearance - were the criteria that directed the treatment to antireflux surgery and facilitated the choice of surgical technique (Fig. 6). The diagnostic-curative algorithm for patients with associated GERD has been implemented in the department of surgery no. 4 (Fig. 7).

Thus, according to the conceptual treatment scheme in different evolutionary phases of GERD and also according to the standard diagnostic-curative algorithm, we selected patients for antireflux surgery, varied both in form and volume of intervention.

![Figure 4. The distribution of refractory GERD patients according to the degree of reflux esophagitis](image)

![Figure 5. (A,B) The complicated forms of GERD RE gr. III-IV, Barrett's esophagus](image)

![Figure 6. HRM esophagomanometry and esophageal scintigraphy](image)
Indications for Surgical Treatment of Patients with GERD:

1. GERD complicated (stenosis, Barrett’s esophagus, ulcer or hemorrhage, esophageal cancer);
2. GERD refractory to antireflux medical treatment for 3 months or those with recurrent reflux symptoms 8-12 weeks after completion of antireflux drug treatment;
3. Progression of peptic esophagitis by the appearance of ulcerations or the appearance of histopathologically confirmed dysplasia sectors on the basis of drug treatment;
4. Presence of associated conditions requiring surgical treatment (HH, especially paraesophageal, gallstones or gastroduodenal ulcer);
5. Long-term treatment with high-dose drugs or those who, for socio-economic reasons, cannot follow drug treatment;
6. Young people who insist on a surgical treatment instead of a conservative one for life;
7. Recurrent GERD/ HH.

Surgical Treatment of Patients with GERD

One of the major goals for our patients over the years has been to minimize the number of resection interventions in non-oncological pathology of GEJ. The implementation of the clinical protocol and the treatment algorithm, the early detection of GERD forms refractory to medical treatment, the widespread introduction of minimally invasive surgical techniques (laparoscopic and endoscopic) were the most important steps that changed the surgical attitude towards patients with this condition.

Carrying out an anti-reflux installation aims to improve the performance of the physiological barrier, which has become inefficient. The main steps of an anti-reflux surgery (Fig. 8 A,B,C,D).

The type of antireflux surgery in our study was different and dependent on the situation. Laparoscopic surgery has predominated in the majority of patients (96.6%) in the last 10 years, compared to previous years, where the rate of traditional interventions was 15-20%. The complete fundoplication Nissen-Rossetti, due to the good control of GERD, has become an intervention of choice mainly for patients with GERD.
Also, the form of fundoplication was the basis for dividing the patients into four distinct groups (Table 1).

Of the total number of patients undergoing antireflux surgery, 14 patients formed the group for esophagoplasties, due to the pre-operative diagnosis confirmed by: peptic strictures (10 cases), 4 patients with GEJ adenocarcinoma.

Thus, according to the data in the Table 1, the surgical interventions addressed to patients with GERD were diverse and practically included the whole range of antireflux operations described in the specialized literature. However, the Nissen-Rossetti procedure predominated in the structure of the complete fundoplications, and among the partial ones we pleaded for the Lortat-Jacob fundoplication in the modified version (270°). The effectiveness of

---

**Table 1.** Types of antireflux interventions performed on GERD patients in our ward

| Fundoplication            | Traditional interventions | Laparoscopic interventions | Total (%) |
|---------------------------|---------------------------|----------------------------|-----------|
| Nissen-Rossetti 360°      | 6 (0.8%)                  | 298 (38.8%)                | 304 (39.6%)|
| Nissen 360°               | 49 (6.4%)                 | 65 (8.4%)                  | 114 (14.8%)|
| Belsey-Mark IV 360°       | 7 (0.9%)                  | -                          | 7 (0.9%)  |
| Toupet 270°               | 28 (3.6%)                 | 66 (8.5%)                  | 94 (12.2%)|
| Lortat-Jacob (modified)   | 59 (7.6%)                 | 190 (24.7%)                | 249 (32.4%)|
| Total                     | 149 (19.4%)               | 619 (80.6%)                | 768 (100%)|
different forms of fundoplication is analyzed in terms of intraoperative complications, immediate and distant postoperative results. The examination of patients in the postoperative period was performed by clinical-paraclinical examination (fibrogastroendoscopy, barium X-ray), as well as by the questionnaire of evaluation of quality of life “GERD-Health Related Quality of Life Questionnaire” at 1 month, 3 months, and one year after reflux interventions (7).

The following complications were reported from the total group:
- Transient postoperative dysphagia (78 (10.42%) patients), the majority of patients being after Nissen-Rossetti fundoplication;
- Gass-bloat syndrome [65 (8.68%) patients];
- Postoperative diarrhea [7 (0.93%) patients];
- Recurrence reflux symptoms [17 (3.2%) patients], 2 (0.26%) cases resolved by surgical reoperation, the other cases being controlled by diet and light supportive drug treatment;
- Intraoperative hemorrhage (5 (0.66%) cases): 1 case of upper epigastric artery injury, 2 (0.26%) cases of aa breves injury, and 2 (0.26%) cases of marginal rupture of the upper pole of the spleen;
- Conversion to traditional surgery (5 (0.66%) cases, 3 (0.4%) cases due to intraoperative hemorrhage, 2 (0.26%) cases of voluminous HH);
- Recurrence of HH (7 (0.93%) cases), 4 (0.53%) cases resolved by laparoscopic reoperations;
- TEAP [2 (0.26%) cases];
- Postoperative stasis pneumonia, basal discoidal atelectasis (11 (1.47%) case).

Discussions

GERD must be diagnosed early and treated according to the standard protocols in force, given that the non-ecological pathology of GEJ has a growing incidence, in order to avoid the occurrence of complicated forms. Laparoscopic surgery is an indispensable indication for the refractory forms of GERD to drug treatment, knowing that minimally invasive procedures have fewer complications compared to traditional surgery. Antireflux surgery is more of a functional surgery, unlike resection surgery, all dissected anatomical structures during the operation must be kept intact, because they will later form an anti-reflux installation that will ensure the antireflux barrier. The choice of the type of antireflux fundoplication is a basic component for a good postoperative result and the evaluation of the functionality of the esophageal muscle, its degree of purification, as well as the type of GERD by contemporary functional methods (pH-metry, scintigraphy, manometry) are indispensable diagnostic stages. Therefore, anti-reflux surgery is a surgery of choice in the uncomplicated forms of GERD, and the surgeon must choose the method of fundoplication based on the degree of competence of LES and the degree of dysmotility of the esophagus to obtain a satisfactory postoperative result.

The criteria for selecting the total fundoplication are:
- Severe esophagitis (2-3 grade);
- Preserved esophageal motility, dysmotility gr.1;
- Decreased competence of LES;
- High, severe, aggressive, mixed or alkaline reflux;
- Changes caused by the previous operation.

The criteria for selecting the partial fundoplication are:
- Decreased esophageal motility, dysmotility gr. 2-3;
- Incompetence of the LES;
- Esophagitis 0-1-2 gr.;
- Medium, moderate, acid reflux;
- Moderate periesophageal changes.

Moreover, the specialist who claims to approach the antireflux surgery must possess good knowledge of the pathophysiology of GER, as well as a thorough understanding of the biomechanical principles underlying these interventions. Although we have always opted for a Nissen fundoplication, which ensures a high efficacy as an anti-reflux barrier, the experience of our department shows that the
application of a certain type of valve must be absolutely individualized, based on the results of preoperative functional diagnosis and selection criteria for antireflux fundoplication.

The occurrence of serious postoperative complications is a phenomenon determined by several factors: insufficient preoperative assessment of the patient, the surgeon’s skills, and, last but not least, the individual characteristics of the body. Postoperative dysphagia, gas-bloat syndrome especially after Nissen fundoplication is a relatively common complication, but in most cases functional, transient, sensitive to drug treatment and vice versa organic dysphagia caused by incorrect surgical technique requires surgical reoperation. In our practice, all cases of dysphagia and gas-bloat syndrome were resolved without surgery, postoperative endoscopic dilatation was necessary in only 7 patients. Recurrent reflux symptoms that cannot be controlled with diet and light supportive medications should be resolved by reconstructing the previously applied fundoplication. Intraoperative hemorrhage is more commonly caused by decapsulation of the spleen by traction of the gastric fornix. We can avoid it by increasing the accuracy of the surgical technique, as well as the use of endoscopic hemostasis (ligature) methods.

The implementation of laparoscopic technique has significantly increased the possibilities of esogastric junction surgery, these are currently high-performance interventions which significantly reduce the trauma of surgical manipulations. Minimally invasive anti-reflux interventions are the surgery of choice, the “gold standard” in the treatment of GERD and hiatal hernias. Nowadays, given the good learning curve of specialists in the minimally invasive surgery, even the giant HH, recurrent HH can be solved laparoscopically. According to the Anglo-American classification (Shackelford 1978) there are four types of hiatal hernias. More recent literature oftentimes mentions type IV of HH – giant hernias. The presence of 1/3 stomach in the thorax is considered giant HH. Policy of surgical treatment depends on the size of this hernia. In the period of 20 years in our department were operated 44 (10%) patients with giant HH, 39 (88.63%) of them laparoscopically. Surgical intervention included the following steps: gastro-esophageal junction dissection with/without resection of the hernia sac, combined cruroraphy and fundoplication. Resection of the hernia sac was necessary in the case of a big hernia sac (23 cases, 52.27%), with fibrous walls, sometimes it was even necessary to fragment it to be later extracted from the abdominal cavity. Synthetic mesh was used in 14 (31.81%) cases, 9 cases of which were solved by laparoscopic way, and 5 case by laparotomy. In all operated cases giant HH were confirmed with a diameter of esophageal hiatus > 5 cm and presence of 1/3 stomach in the thorax.

Conclusions

1. Early diagnosis of refractory forms to medical treatment requires referral of patients to laparoscopic antireflux surgery to avoid severe complications of GERD.
2. The minimally invasive approach to antireflux surgery today is a golden standard, and the use of a complete fundoplication ensures high effectiveness of these interventions.
3. The application of a certain type of anti-reflux installation must be absolutely individualized based on the results of the preoperative functional diagnosis.
4. The implementation of minimally invasive treatment techniques (laparoscopic, endoscopic) offers a wider range of surgical approaches to GERD, with better immediate and distant results compared to open surgery.

Conflict of Interests

The authors declare no conflicts of interests.

Ethical Statement

All procedures performed were in accordance
References

1. Zheng Z, Shang Y, Wang N, Liu X, Xin C, Yan X, et al. Current Advancement on the Dynamic Mechanism of Gastroesophageal Reflux Disease. Int J BioSci 2021;17(15):4154-4164.

2. Moreas-Filho JPP, Domingues G, Chinzon D, Roveda F, Lobao Neto AA, Zateka S. Impact of Heartburn and Regurgitation on Individuals’ Well-Being in the General Population: A Brazilian National Survey. Arq Gastroenterol. 2021;58:5-9.

3. Eusebi LH, Ratnakumarar R, Yuan Y, Solaymani-Dodaran M, Bazzoli F, Ford AC. Global prevalence of, and risk factors for, gastro-oesophageal reflux symptoms: a meta-analysis. Gut. 2018;67:430-40.

4. Rettura F, Bronzini F, Campigotto M, Lambiase C, Pancetti A, Berti G, et al. Refractory Gastroesophageal Reflux Disease: A Management Update. Front Med (Lausanne). 2021;8:756061.

5. Ungureanu S. Tratamentul pacientilor cu patologia neoncologica a jonctiunii esogastrice autoref. tezei de doctor hab. in st. med. Chisinau. 2017.

6. HRQL, Velanovich V. The development of the GERD-HRQL symptom severity instrument. Dis Esophagus. 2007;20:130-4.

7. Naini BV, Souza RF, Obre RD. Barrett's esophagus: a comprehensive and contemporary review for pathologists. In J Surg Pathol. 2016(40):45-66.

8. American Gastroenterological Association; Spechler SJ, Sharma P, Souza RF, Inadomi JM, Shaheen NJ. American Gastroenterological Association medical position statement on the management of Barrett’s esophagus. Gastroenterology, 2011;140(3):1084-91.

9. Specchier Sj, Sharma P, Souza RF, John M Leadami, Nicholas J Shaheen, American Gastroenterological Association. American Gastroenterological Association technical review on the management of Barrett's esophagus. Gastroenterology, 2011;140(3):s19-52; quiz e13.

10. Sikkema M, de Jonge PJ, Stuyverberg EW, Kuipers EJ. Risk of esophageal adenocarcinoma and mortality in patients with Barrett’s esophagus: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2010; 8(3):235-44; quiz e32.

11. Pavlov K, Meijer C, van den Berg A, Peters FT, Kruijt FA, Kleibuerke JH. Embryological signaling pathways in Barrett's metaplasia development and malignant transformation: mechanisms and therapeutic opportunities. Crit Rev Oncol Hematol. 2014;92(1):25-37.

12. Karagiannis-Voultsis DA, Biedermann P, Epo UF, et al. Global, regional, and national age–sex specific all-cause and cause-specific mortality for 240 causes of death, 1990–2013: a systematic analysis for the global burden of disease study 2013. Lancet. 2015;385(9963):117-71.

13. Old O, Mcaiayedi P, Love S, Roberts C, Hapesji J, Foy C, et al. Barrett’s Oesophagus Surveillance versus endoscopy at need Study (BOSS): protocol and analysis plan for a multicentre randomised controlled trial. J Med Screen. 2015;22(3):158-64.

14. Naini BV, Chak A, Ali MA, Ozde RD. Barrett’s oesophagus diagnostic criteria: endoscopy and histology. Best Pract Res Clin Gastroenterol. 2015;29(1):77-96.

15. Grin A, Streutker CJ. Histopathology in Barrett esophagus and Barrett esophagus-related dysplasia. Clin Endosc. 2014;47(1):31-9.

16. Wallace MB, Sharma P, Lightdale C, Wolfson H, Coron E, Buchner A, et al. Preliminary accuracy and interobserver agreement for the detection of intraepithelial neoplasia in Barrett’s esophagus with probe-based confocal laser endomicroscopy. Gastrointest Endosc. 2010;72(1):19-24.

17. Pech O. Endoscopic therapy of high-grade dysplasia and intramucosal adenocarcinoma: 2 small steps for the endoscopists but a fine step forward for the patient. J Gastrointest Endosc. 2015;81(5):1167-9.

18. Constantinou S, Birla R, Copca N, Iosi C. Adenocarcinomul de jonctiune esogastrica. Bucuresti: Editura Medicai Amaliaa; 2008. p. 35-37.

19. Copaescu C. Tratamentul laparoscopic al bolii de reflux gastroesofagian. Bucuresti: Ed. Celsius; 2012.

20. Constantinou S, Cordos I, Ciucu G, Scipirciu V. Tratat de patologie si chirurgie esofagiana. Bucuresti: Editura Academiei Romane; 2017. p. 189-317.

21. El-Serag HB, Sweet S, Winchester CC, Dent J. Update on the epidemiology of gastro-oesophageal reflux disease: a systematic review. Gut. 2014;63(6):871-80.

22. Fock KM, Talley N, Goh KL, Sugano K, Katelaris P, Holtmann G, et al. Asia–Pacific consensus on the management of gastro-oesophageal reflux disease: an update focusing on refractory reflux disease and Barrett’s oesophagus. Gut. 2016;65(9):1402-15.

23. Abraham JJ Jr, Lemme EM, Carvalho BB, Alvariz A, Calcena Aquero GC, Bihari Schechter R. Relationship between the size of hiatal hernia and esophageal acid exposure time in erosive and non-erosive reflux disease. Arq Gastroenterol. 2006;43(1):37-40. Portuguese

24. Siegel SR, Dolan JP, Hunter JG. Modern diagnosis and treatment of hiatal hernias. Langenbecks Arch Surg. 2017;402(8):1145-1151.

25. Yu HX, Han CS, Xue JR, Han ZF, Xin H. Esophageal hiatal hernia: risk, diagnosis and management. Expert Rev Gastroenterol Hepatol. 2018;12(4):319-329.

26. Old O, Mcaiayedi P, Love S, Roberts C, Hapesji J, Foy C, et al. Barrett’s Oesophagus Surveillance versus endoscopy at need Study (BOSS): protocol and analysis plan for a multicentre randomised controlled trial. J Med Screen. 2015;22(3):158-64.

27. Seif Amir Hosseinia A, Uhlig U, Streit U, Uhlig A, Sprenger T, Wedi E, et al. Hiatal hernias in patients with GERD-like symptoms: evaluation of dynamic real-time MRI vs endoscopy. Eur Radiol. 2019;29(12):6653-6661.

28. Eusebi LH, Ratnakumarar R, Yuan Y, Solaymani-Dodaran M, Bazzoli F, Ford AC. Global prevalence of, and risk factors for, gastro-oesophageal reflux symptoms: a meta-analysis. Gut. 2018;67(3):430-440.

29. Gastro-oesophageal reflux disease. Nat Rev Dis Primers. 2021;7(1):56.

30. Capello M, Karup AL, Rask P, Pahle E, Nielsen MF. Overweight and gastro-oesophageal reflux disease. Ugeskr Laeger. 2018;180(21):v06170444. Danish.