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Diagnostics and Treatment of Esophageal Achalasia (Clinical Guidelines of the Russian Gastroenterological Association, Russian Scientific Medical Society of Internal Medicine, Russian Society for the Prevention of Noncommunicable Diseases, REndO Endoscopic Society)

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Aim: to familiarize gastroenterologists, therapists, functional diagnostics and general practitioners (family doctors), radiologists, and endoscopists with modern methods of diagnosis and treatment of achalasia of the cardia.

Key points. Achalasia is an idiopathic neuromuscular disease manifested by a functional disorder of the patency of the cardia due to a lack of coordination between swallowing, reflex opening of the lower esophageal sphincter, and the motor and tonic activity of the smooth muscles of the esophagus. The etiology of achalasia remains unclear. However, it is believed that the key role belongs to the changes in the myenteric (Auerbach's) intermuscular plexus of the enteric nervous system of the esophagus, leading to loss of neuronal function. The following hypotheses have been proposed as the main mechanisms for the development of achalasia: genetic predisposition, exposure to viral infections, and idiopathic autoimmune triggers. Patients with suspected achalasia require a comprehensive instrumental examination, including esophagogastroduodenoscopy, timed barium esophagogram, and esophageal manometry. In recent years, high-resolution esophageal manometry has been recognized as the gold standard for achalasia diagnostics. To analyse the obtained data, the Chicago classification is recommended — it allows to ascertain the type of achalasia, which determines the choice of treatment method and the assessment of the prognosis of the therapy effectiveness. Treatment of achalasia can be pharmacological, endoscopic (pneumatic balloon dilation, peroral endoscopic myotomy, botulinum toxin injection), aimed at regulating the tone and motility of the esophagus and cardia while preserving all anatomical structures, and surgical (laparoscopic esophagocardiomyotomy, esophagectomy), in which the muscle fibers of the esophagus and esophagogastric junction are intersected or the altered esophagus is completely removed with simultaneous formation of an artificial esophagus from the stomach or colon (esophagoplasty).

Conclusion. Implementation of the developed clinical guidelines can help to establish a diagnosis in a timely manner, which will lead to an improvement in the quality of medical care for patients with achalasia.

Keywords: achalasia, cardiospasm, lower esophageal sphincter, esophageal dyskinesia, dysphagia, chest pain, esophagitis, esophageal cancer, pseudoachalasia, diagnostics, high-resolution esophageal manometry, barium sulfate esophageal X-ray, timed barium esophagogram, pneumatic balloon dilation of the cardia, peroral endoscopic myotomy, laparoscopic esophagocardiomyotomy, treatment

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Диагностика и лечение ахалазии кардии (Клинические рекомендации Российской гастроэнтерологической ассоциации, Российского научного медицинского общества терапевтов, Российского общества профилактики неинфекционных заболеваний, Ассоциации эндоскопического общества «РЭндО» (Российского эндоскопического общества))

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Цель: ознакомить врачей-гастроэнтерологов, терапевтов, врачей функциональной диагностики и общей практики (семейных врачей), рентгенологов, эндоскопистов с современными методами диагностики и лечения ахалазии кардии.

Основное содержание. Ахалазия кардии — идиопатическое нервно-мышечное заболевание, проявляющееся функциональным нарушением проходимости кардии вследствие дискоординации между глотком, рефлекторным раскрытием нижнего пищеводного сфинктера, двигательной и тонической активностью гладкой мускулатуры пищевода. В настоящее время этиология ахалазии кардии остается до конца не ясной. Однако считается, что изменения в миэнтеральном (ауэрбаховом) межмышечном сплетении энтеральной нервной системы пищевода, ведущие к потере функции нейронов, играют ключевую роль. В качестве основных механизмов развития ахалазии кардии предложены следующие гипотезы: генетическая предрасположенность, воздействие вирусных инфекций и идиопатические аутоиммунные триггеры. Пациентам с подозрением на ахалазию кардии необходимо проведение комплексного инструментального обследования, включающего в себя эзофагогастродуоденоскопию, рентгенологическое исследование с бариевой взвесью по методике хронометрированной контрастной рентгенографии, манометрию пищевода. В последние годы «золотым стандартом» диагностики ахалазии кардии признана манометрия пищевода высокого разрешения. Для проведения анализа полученных данных рекомендована Чикагская классификация, позволяющая определить развившийся у пациента тип ахалазии кардии, от чего зависит выбор метода лечения заболевания и оценка прогноза эффективности терапии. Лечение ахалазии кардии может быть медикаментозным, эндоскопическим (баллонная пневмодилатация, пероральная эндоскопическая миотомия, инъекция ботулинического токсина), направленным на регулирование тонуса и моторики пищевода и кардии с сохранением всех анатомических структур, и хирургическим (лапароскопическая эзофагокардиомиотомия, эзофагэктомия), при котором пересекаются мышечные волокна пищевода и пищеводно-желудочного перехода или полностью удаляется измененный пищевод с одномоментным формированием искусственного пищевода из желудка или толстой кишки (эзофагопластикой).

Заключение. Выполнение разработанных клинических рекомендаций позволит своевременно установить диагноз, что приведет к улучшению качества оказания медицинской помощи пациентам с ахалазией кардии.

Ключевые слова: ахалазия кардии, кардиоспазм, нижний пищеводный сфинктер, дискинезия пищевода, дисфагия, боль в грудной клетке, эзофагит, рак пищевода, псевдоахалазия, диагностика, манометрия пищевода высокого разрешения, рентген пищевода с сульфатом бария, хронометрированная контрастная рентгенография, баллонная пневмодилатация кардии, пероральная эндоскопическая миотомия, лапароскопическая эзофагокардиомиотомия, лечение

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1. Brief information on the disease or condition (group of diseases or conditions)

1.1. Definition of a disease or condition (group of diseases or conditions)

Achalasia of the cardia (from the Greek *a* — absence, *chalasis* — relaxation) is an idiopathic neuromuscular disease manifested by a functional impairment of the patency of the cardia due to a lack of coordination between swallowing, reflex opening of the lower esophageal sphincter (LES), and the motor and tonic activity of the smooth muscles of the esophagus.

A distinction is made between primary (idiopathic) achalasia and pseudoachalasia, a secondary condition that develops as a consequence of a malignant neoplasm of the esophagogastric junction or adjacent organs (pancreatic cancer, breast cancer, lung cancer, or hepatocellular carcinoma) [1, 2]. In addition, similar complaints are presented by patients with Chagas disease caused by *Trypanosoma cruzi* [3].

Currently, the term "achalasia" is most often used in English-language literature, while in domestic sources there are two names for the disease — "achalasia of the cardia" and "cardiospasm". This is explained by the fact that there are two pathogenetically different forms of functional obstruction of the cardia, identified by H.S. Plummer and P.P. Vinson back in 1921, which differ in clinical symptoms, radiographic picture and esophagomanometry results, especially in the initial stages [4, 5]. These differences are due to different levels of damage to the parasympathetic nervous system. Thus, in patients with cardiospasm, more pronounced changes were found in the preganglionic neurons of the dorsal nuclei of the vagus nerves in the brainstem, and less pronounced ones in the postganglionic neurons of the Auerbach's plexus [6]. In achalasia, the peripheral link is predominantly affected — the postganglionic neurons of the intramural Auerbach's plexus [7, 8], the vagus nerves [9], the sympathetic nerve trunks and ganglia [10], as a result of which the reflex of opening the cardia in response to a swallow is lost. At the same time, the central innervation is preserved.

1.2. Etiology and pathogenesis of a disease or condition (group of diseases or conditions)

The etiology of achalasia remains unclear. However, it is believed that changes in the myenteric (Auerbach's) intermuscular plexus of the enteric nervous system (ENS) of the esophagus, leading to the loss of neuronal function, play a key role [11, 12]. The ENS includes inhibitory neurons, whose neurotransmitters are nitric oxide (NO) and vasoactive intestinal peptide, and excitatory neurons, whose mediator is acetylcholine [13, 14].

In the initial stages of the disease, the inflammatory component predominates, mainly affecting inhibitory neurons, in which NO and vasoactive intestinal peptide are synthesized. As the disease progresses, these cells are completely lost and replaced by connective tissue. The loss of inhibitory NO-ergic neurons leads to incomplete relaxation of the LES and the absence of peristalsis in the thoracic esophagus, which is characteristic of achalasia [11, 15–18].

A number of studies have shown polymorphism of genes encoding all types of NO synthase (neuronal (nNOS), inducible (iNOS) and endothelial (eNOS)). NO synthase is an enzyme that catalyzes the formation of nitric oxide from arginine, oxygen and NADPH. It has been proven that polymorphism of the *iNOS22*A/Ab* and *eNOS*4a4a* genes, which are located in chromosomes 12q24.2, 17q11.2 q12 and 7q36, occurs more frequently [19, 20]. Recent literature data indicate that eosinophils and mast cells may also play a role in the development of achalasia. Aggregation of eosinophils and mast cells in the esophagus causes an increase in the concentration of inflammatory cytokines, which leads to the loss of ganglion cells and fibrous remodeling of the esophageal wall and ultimately causes esophageal dysfunction and extensive clinical symptoms [21, 22]. J. Cools-Lartigue et al. [23] observed 96 patients with achalasia who underwent laparoscopic Heller myotomy. Preoperative biopsy was taken from 50 of them, which revealed eosinophilic infiltration of the esophageal mucosa in 34 % of cases. The median eosinophil count was 3 (1; 21) units per high power field, and in 8 % of cases the cell count met the criteria sufficient to establish a diagnosis

of eosinophilic esophagitis. The authors concluded that the presence of eosinophils in the esophageal mucosa should not stop further diagnostic workup to exclude other diseases, in particular achalasia. However, other studies have not found a relationship between eosinophilic infiltration and the development of achalasia [24].

The following hypotheses have been proposed as the main mechanisms for the development of achalasia: genetic predisposition, exposure to viral infections, and idiopathic autoimmune triggers [25, 26].

In children, the most common cause of achalasia is a mutation in the *AAAS* gene on chromosome 12q13, which encodes the protein ALacrima-Achalasia-aDrenalINsufficiency (ALADIN); the mutation leads to the development of the autosomal recessive disease, Allgrove syndrome, characterized by the development of achalasia, alacrimia, and Addison's disease. Achalasia occurs in approximately 75 % of patients with the syndrome and is often its main clinical manifestation [27, 28].

The risk of developing achalasia in children with Down syndrome is 200 times higher than in the general population. Up to 75 % of these patients have gastrointestinal diseases and 2 % develop achalasia [29].

S. Tanaka et al., having conducted a multicenter study, which included 1115 patients with achalasia (mean age — 42.9 ± 18.6 years), identified the familial form of achalasia, achalasia in combination with other hereditary and autoimmune diseases in 0.63 %, 0.99 % and 2.40 % of cases, respectively. Of the concomitant hereditary diseases, the most frequently diagnosed were Down syndrome (27.2 %) and Allgrove syndrome (18.1 %), Charco — Mari — Tooth neural amyotrophy (18.1 %). Among autoimmune diseases, the most frequently detected were thyroid diseases (hypothyroidism (33.3 %) and hyperthyroidism (14.8 %)), scleroderma (11.1 %), ulcerative colitis (11.1 %), rheumatoid arthritis (11.1 %), Sjögren's syndrome (7.4 %) and Crohn's disease (3.7 %) [30].

The autoimmune hypothesis of disease development is supported by the fact that patients with achalasia have an increased risk of developing autoimmune diseases compared to the general population. In the work of C. Sara et al. [31], a twofold increase in the prevalence of autoimmune diseases was found in patients with achalasia, moreover, it is more often associated with type 1 diabetes (47.80 %) and thyroid diseases (19.60 %). Another work noted a combination of achalasia with such autoimmune diseases as Sjögren's syndrome, psoriasis, autoimmune uveitis, rheumatoid arthritis, etc. [12].

J. Furuzawa-Carballeda et al. conducted a study aimed at analyzing changes in immune components in patients with achalasia: the $CD4^+$ T-lymphocyte pool associated with autoimmune diseases, autoantibodies and their specificity, as well as proteins involved in the exchange of the extracellular matrix, apoptosis, proinflammatory and profibrogenic cytokines, as well as regulatory T- and B-cells. The 26 tissue samples from the lower esophageal sphincter muscles were compared with five biopsies obtained during esophagectomy (control group). The authors identified the following features of the immune response in patients with achalasia compared to the control group ($p < 0.001$): a higher frequency of detection of specific immune response cells in biopsies (among them, an increase in the $CD4^+$ lymphocyte pool) and increased expression of both proinflammatory and anti-inflammatory cytokines (IL-22, IL-17, TNF-α), as well as antibodies to the enteric nervous system, mainly against the PNMA2 antigen (Ma-2/Ta). An increased concentration of extracellular matrix degradation proteinases, namely matrix metalloproteinase (MMP-9) and its tissue inhibitor (TIMP-1), was also detected. In addition, herpes simplex virus type 1 was isolated from all patients with achalasia using polymerase chain reaction. Thus, the researchers concluded that all the supposed etiological factors are involved in the pathogenesis of achalasia, and the mechanism of the immune response is triggered by the persistence of viruses. As a result of histological examination of biopsies of patients with achalasia, capillaritis was detected in 51 % of cases, plexitis in 23 %, and hypertrophy of nerves, venulitis and fibrosis were diagnosed in 16 %, 7 % and 3 %, respectively [32].

In addition, a number of studies have shown that neuronal autoantibodies are present in serum samples of patients with achalasia, especially in carriers of the HLA alleles DQA1*0103 and DQB1*0603 [33, 34].

Herpes simplex virus types 1 and 2, herpes zoster virus, cytomegalovirus, measles virus, and human papillomavirus can disrupt the regulation of esophageal motility in achalasia, but this is not observed in all infected patients [17, 35]. According to a study by R.D. Naik et al., 80 % of patients with achalasia had varicella zoster virus DNA in their saliva [36].

According to the latest literature data, the new coronavirus infection (SARS-CoV-2), which causes a disruption of the immune response and the production of autoantibodies, is considered a possible trigger for gastrointestinal motility disorders, including achalasia. Data on the development of achalasia in patients several months after the infection have been published. In the work of J. Furuzawa-Carballeda et al., it was

demonstrated that the SARS-CoV-2 virus was detected in biopsy material taken from the lower esophageal sphincter of patients with achalasia who had suffered from the new coronavirus infection, which allows us to consider it as a possible etiopathogenetic factor in the development of the disease. However, the likelihood of developing achalasia after SARS-CoV-2 requires additional scientific research [37–40].

1.3. Epidemiology of a disease or condition (group of diseases or conditions)

Achalasia is considered a rare disease: its prevalence, according to various sources, ranges from 10 to 15.7 cases per 100,000 population, and the incidence is 1.07–2.2 per 100,000 per year among adults [41–43] and 0.18 per 100,000 among children and adolescents under 16 years of age [44]. According to the combined data of B.V. Petrovsky and V.V. Utkin, achalasia ranks third as a cause of dysphagia after cancer and burn strictures of the esophagus, the incidence of the disease varies from 5 to 8 % [45, 46]. According to T.A. Suvorova and A.Z. Morgenstern, achalasia accounts for 3.1–20 % of all esophageal diseases [47, 48]. Idiopathic achalasia occurs on all continents, with equal frequency in men and women. However, according to a recent large multicenter study conducted in Japan, male gender and family history may be risk factors for the development of achalasia [30]. In adults, it is most often diagnosed in the age group from 25 to 60 years, and the incidence increases with age [16, 49, 50]. There is no epidemiological data for the Russian Federation.

1.4. Features of coding a disease or condition (groups of diseases or conditions) according to the International Statistical Classification of Diseases and Related Health Problems

K22.0. Achalasia of cardia

1.5. Classification of a disease or condition (group of diseases or conditions)

To determine the stage of the disease, domestic classifications have been proposed and used, for example, the 4-stage classification of cardiospasm by B.V. Petrovsky, the classification by T.A. Suvorova, subsequently supplemented by A.L. Grebenev, in which two types of esophageal achalasia are distinguished; the 3-stage classification of cardiospasm proposed by G.D. Vilyavin (1978) [45, 47, 51–54].

The most widely used classification is that of B.V. Petrovsky [45]:

Stage I — functional intermittent spasm of the cardia without dilation of the esophagus;

Stage II — stable spasm of the cardia with mild dilation of the esophagus (up to 4–5 cm) and increased motility of the walls;

Stage III — cicatricial changes (stenosis) of the muscular layers of the LES with severe dilation of the esophagus (up to 6–8 cm) and disturbances of tone and peristalsis;

Stage IV — severe stenosis of the cardia with significant dilation, elongation, S-shaped deformation of the esophagus, esophagitis and periesophagitis.

In recent years, high-resolution esophageal manometry has been recognized as the gold standard for diagnosing achalasia. In 2009, the first Chicago classification of esophageal motility disorders was adopted, and to date it has been revised and supplemented three times [55]. In 2018, at a meeting of the Russian Gastroenterological Association and the Russian Group on Neurogastroenterology and Motility, new terminology and classification of esophageal motility disorders diagnosed by high-resolution manometry were approved, and after the recommendation of the Russian Gastroenterological Association on the clinical use of high-resolution manometry in esophageal diseases were approved as well, which allows doctors to adhere to the unity of terminology and diagnostic criteria when describing the results of the studies conducted and establishing a manometric diagnosis [56, 57]. The main indicator characterizing the relaxation of the LES is the integrated relaxation pressure (IRP), the value of which is increased in all types of achalasia, but in some cases normal values can be recorded [58]. The upper limit of the norm varies depending on the type of manometric catheter and recording system. For specialized software Medtronic systems and Medical Measurements Systems (MMS), this value is > 15 mmHg and > 22 mmHg, respectively. Classification by types of achalasia in accordance with the Chicago classification of the 4th revision is based on the peristaltic activity of the thoracic esophagus [55]:

Type I: failed peristalsis of the thoracic esophagus. No swallows with panesophageal pressurization.

Type II: failed peristalsis of the thoracic esophagus, but in ≥ 20 % of swallows, panesophageal pressurization is determined.

Type III: failed peristalsis of the thoracic esophagus, there may be panesophageal pressurization, premature contraction of the esophagus in ≥ 20 % of swallows.

There is a theory that the types of achalasia are not three different forms, but successive stages of the development of this disease. At the initial stage, with the gradual death of inhibitory motor neurons of the intermuscular nerve ganglia,

changes in peristalsis are observed according to the type of spastic achalasia (type III). Then, as excitatory neurons die, the peristalsis of the esophagus is suppressed, which corresponds to the intermediate form of development of achalasia (type II). At the end of the disease, with the complete death of neurons of the intermuscular nerve plexus, changes occur corresponding to achalasia type I (classical achalasia), which is manifested by a significant expansion of the esophagus, its S-shaped deformation [59, 60].

Achalasia type II has the best prognosis for treatment results (in 96 % of cases), while type III has the worst prognosis (66 %) and is associated with a higher relapse rate. Type I may represent a more advanced final stage of achalasia and the prognosis for it varies but is generally worse (81 %) than for type II [58, 61, 62]. The choice of treatment method depends on the type of achalasia, a description of which is given in subsection 2.4 [62–64].

1.6. Clinical picture of a disease or condition (group of diseases or conditions)

The main symptoms of the disease are progressive dysphagia, regurgitation, chest pain, and weight loss.

Dysphagia occurs in 99 % of patients when consuming solid food and in 90–95 % when consuming liquid food. There are two typical variants of dysphagia. Thus, in one of them, dysphagia develops acutely, usually in the midst of complete health, and is associated with a psychotraumatic situation. Young people are more often affected. Patients can accurately indicate when they noticed the onset of symptoms and what it was associated with. Dysphagia is often paradoxical: solid food passes well, but liquid is retained. It should be noted that nervous overexcitement, an unfamiliar environment, talking during meals, and rapid food intake, especially poorly chewed and cold food, contribute to an increase in the severity of dysphagia. Dysphagia may be accompanied by a feeling of food retention in the esophagus for some time with its subsequent "falling" into the stomach. Another form is characterized by gradual development of the disease, often over many years, without paradoxical dysphagia. Middle-aged and elderly people who cannot remember when exactly they fell ill and what caused the disease are more often affected. The patient can independently reduce the severity of dysphagia using various techniques: drinking plenty of liquid with food, swallowing air, repeated swallowing movements, walking. The temperature of the food taken is also of no small importance: most patients note that warm and hot food passes better [65].

A striking symptom of the disease is active and passive regurgitation, which is observed in 84 and 68 % of patients, respectively. Active regurgitation is the regurgitation of freshly eaten food or mucus and is more typical for the initial stages of the disease. It occurs with minor dilation of the esophagus, while significant expansion of the esophagus can lead to delayed regurgitation, the volume of which is much greater. Passive regurgitation occurs outside of meals, usually in a horizontal position of the patient (the "wet pillow" symptom) or when the body is tilted forward. Regurgitation, especially passive, can be accompanied by aspiration of food into the respiratory tract, which can lead to respiratory dysfunction, accompanied by shortness of breath and cough, and mask the underlying disease. It should be noted that nocturnal cough and the "wet pillow" symptom indicate decompensation of the disease [65].

The occurrence of pain in patients with achalasia may be associated with overstretching of the esophagus walls by a food bolus, hypermotor dyskinesia of the thoracic region, and the development of congestive esophagitis. The pain may be localized behind the sternum, radiating to the back, up the esophagus, to the neck, and jaw. The nature of the pain may be intense and spasmodic with type III achalasia, moderate and bursting with type I, and burning with esophagitis. The intensity may range from mild to severe. The pain lasts from several minutes to several hours, and may occur spontaneously, often at night, after and during meals. The pain is relieved by taking $Ca2^{+}$ channel blockers, nitrates, taking a sip of water, adopting a "special" body position, and regurgitating [65–67].

One of the symptoms of achalasia is weight loss, which is observed in 61 % of patients and correlates with the severity of the disease. The average weight loss is 5–10 kg [65].

In some cases, heartburn may be a symptom of the disease, and therefore these patients are diagnosed with gastroesophageal reflux disease (GERD) and prescribed antisecretory therapy. This leads to a long delay in establishing the true diagnosis until the patient develops characteristic symptoms of achalasia [68].

The similarity of clinical symptoms (dysphagia, chest pain, heartburn) requires a thorough differential diagnosis. Following the cancer prevention strategy, first of all, cardioesophageal cancer is excluded, which is characterized by progressive dysphagia, as well as true achalasia. The tumor, growing into the area of the esophagogastric junction and the cardia, leads to impaired relaxation

of the LES, expansion of the esophagus and the absence of peristalsis, which can imitate the clinical, radiological and manometric data of achalasia. This condition is defined as "pseudoachalasia" [49]. More often, malignant lesions are indicated by the patient's advanced age, rapid weight loss, and a short history of the disease. Physical examination may reveal a palpable mass in the abdominal cavity and lymphadenopathy. Barium swallow shows moderate dilation of the esophageal lumen, but the degree of dilation does not correlate with the severity of dysphagia. There is a narrowing in the distal section, but unlike that in achalasia, it does not have the characteristic "bird's beak" or "mouse tail" appearance with gradual symmetrical narrowing of the lumen and smooth walls, but is often eccentrically located, with uneven, bumpy contours. To establish an accurate diagnosis, it is necessary to conduct an esophagogastroduodenoscopy (EGDS). If a malignant process is suspected, it is necessary to obtain material for histological and cytological examination. It is necessary to remember the possibility of cancer developing not only in the area of the esophagogastric junction, but also in the wall of the esophagus [65].

Peptic stricture, which occurs as a complication of long-term GERD, also manifests itself as dysphagia. In the initial stages, only solid food has difficulty passing through the esophagus, while in later stages, patients report difficulty passing mushy and liquid food. Dysphagia is usually preceded by long-term heartburn, which often occurs at night, but by the time the stricture forms, the heartburn may stop. For differential diagnosis, it is important to conduct manometry and radiography of the esophagus with contrast, the results of which indicate the absence of significant expansion of the lumen of the esophagus, the presence of a gas bubble in the stomach, and in the vertical position of the patient, the contrast agent, unlike in achalasia, does not remain in the esophagus for a long time [65].

Achalasia of the cardia with hypermotor dyskinesia of the thoracic esophagus should be differentiated from ischemic heart disease, the main clinical manifestation of which is chest pain. In terms of differential diagnosis, it is impossible to unambiguously assess the effect of taking nitroglycerin, since pain in achalasia, as in ischemic heart disease, is relieved after taking it. ECG also does not always allow for a more precise diagnosis, since myocardial ischemia is very often latent and is detected only during physical exertion [65]. In this regard, in controversial situations it is necessary to conduct a comprehensive cardiological examination, including bicycle ergometry and/or treadmill test, echocardiography, in some cases coronary angiography, as well as esophageal manometry and X-ray examination of the esophagus with barium sulfate contrast. In addition, the presence of esophageal spasm and, especially in young women, neurogenic anorexia are excluded [69, 70].

2. Diagnosis of a disease or condition (group of diseases or conditions), medical indications and contraindications to the use of diagnostic methods

Criteria for establishing a diagnosis of a disease/condition:

The diagnosis of achalasia is established based on:

1. anamnestic data (characteristic complaints);
2. instrumental examination (failed peristalsis, absence of LES relaxation, possible increase in the pressure of the lower esophageal sphincter, premature contractions during high-resolution esophageal manometry, detection of narrowing of the distal esophagus, suprastenotic dilation, slow evacuation of contrast agent from the esophagus, absence of a gas bubble in the stomach during X-ray examination of the esophagus and stomach; during endoscopic examination — dilation of the esophageal cavity, food residues in its lumen, difficulty in passing the endoscope through the cardia and displacement of its center).

2.1. Complaints and anamnesis

Complaints and anamnesis data typical for patients with achalasia are listed in subsection 1.6.

2.2. Physical examination

Physical examination usually does not reveal any findings that are specific to patients with achalasia.

2.3. Laboratory diagnostic tests

Laboratory tests are not important in diagnosing achalasia. They are prescribed when preparing the patient for surgery. The scope of laboratory tests depends on the presence of concomitant diseases in the patient, the proposed type of anesthesia and the method of surgical treatment.

2.4. Instrumental diagnostic studies

• All patients with clinical symptoms that suggest achalasia should undergo esophagogastroduodenoscopy to exclude other diseases [16, 62, 71, 72].

Grade of recommendations — A, level of evidence — 1.

Comment: during endoscopic examination the following parameters should be assessed: degree of esophageal lumen dilation; esophageal tortuosity; presence of fluid, mucus, food debris in the lumen; condition of the mucosa in different parts

of the esophagus; peristalsis — depth, uniformity of the peristaltic wave, presence, severity and level of spastic contractions; position of the cardia relative to the axis of the esophagus; speed of opening of the cardia during insufflation of air or carbon dioxide, elasticity; condition of the mucous membrane of the cardia — presence or absence of scars, infiltration, neoplasms; mandatory examination of the cardia in retroflexion to exclude blastomatous lesions (cardioesophageal cancer, gastric cancer with transition to the cardia).

However, all these changes concern the advanced stages of the disease, whereas in the initial stage there may not be any changes in the esophagus at all, which is why a comprehensive examination is necessary to correctly establish the diagnosis of achalasia [73, 74].

• It is not recommended to formulate a diagnosis of achalasia solely on the basis of endoscopy data. All patients are also recommended to use high-resolution manometry and esophageal radiography data, and, if necessary, computed tomography and ultrasound of the abdominal cavity to verify the diagnosis [75–78].

Grade of recommendations — A, level of evidence — 1.

Comment: for a comprehensive assessment of the clinical situation, it is necessary to use multidirectional classifications that take into account various aspects of the disease: the clinical and radiological classification of B.V. Petrovsky (1962) (cited in [5]*), the endoscopic classification of Yu.I. Gallinger, E.A. Godzhello (1999)* [73]*, the Chicago classification of achalasia types based on high-resolution manometry data* [55, 65].

Endoscopic classification determines the stage of the disease, the main indicator of which is the degree of expansion of the lumen of the esophagus [73].

Stage I — there are no deviations from the normal endoscopic picture, but an increase in the intensity of the peristaltic wave can be noted according to the type of unstable segmental esophageal spasm.

Stage II — the lumen of the esophagus is dilated to 3–4 cm, contains fluid, mucus along the left wall, the cardia is located in the center, tightly closed, the mucous membrane turns white when the distal end of the endoscope is brought forward, the lumen opens with excessive insufflation of air or carbon dioxide.

Stage III: the esophagus is dilated to 5–7 cm, the lumen contains a significant amount of fluid, mucus, and food debris, there is a C- or S-shaped bend in the lower third, the cardia is eccentric, tightly closed, the mucosa turns white when the distal end of the endoscope is brought forward, the lumen opens with excessive insufflation of air or carbon dioxide.

Stage IV — the lumen of the esophagus is expanded to 8–15 cm, contains a lot of fluid, mucus, undigested food, sharply tortuous — there is a pronounced S-shaped bend in the lower third, but there may be a double or triple (from the upper third) bend, there is a "blind sac", the esophagus is elongated, the cardia is sharply eccentric, above the bottom of the "sac", loosely closed, located 45–55 cm from the incisors (with megaesophagus it can be located even 70 cm from the incisors).

Taking into account the manometric types of achalasia, the description of the endoscopic picture should include an assessment of peristaltic activity — the presence, depth, and uniformity of the propulsive peristaltic wave; the presence, severity, and level of spastic contractions. Also, during EGDS, it is possible to presumptively assess the pressure level in the lower esophageal sphincter based on the density of the cardia closure, which is manifested by the whitening of the mucosa when the end of the endoscope is brought to the esophageal-gastric junction area, and an approximate determination of the amount of insufflated gas required to open the cardia, compared with traditional endoscopic examination. This is not related to the stages of the disease, but helps to assume the type of achalasia, which is especially important when high-resolution manometry cannot be performed, since it is important in determining personalized treatment tactics [79].

• All patients with suspected achalasia are recommended to undergo an X-ray examination with timed barium esophagogram for the purpose of differential diagnosis between achalasia and esophageal spasm, as well as to assess the dynamics of treatment [61, 78, 80, 81].

Grade of recommendations — A, level of evidence — 1.

Comment: X-ray examination of the esophagus with barium using the timed barium esophagogram method can be used both for the primary diagnosis of achalasia and for assessing the dynamics during treatment, after balloon dilation or myotomy [78, 82].

The timed barium esophagogram method is similar to the standard X-ray examination, but it uses established time intervals (1, 2, and 5 min) after taking the barium swallow, when the height and width of the barium column are measured, which allows for a more objective assessment of the emptying of the esophagus. Because of this advantage, timed esophagogra barium esophagogram is usually preferable to a standard barium esophagogram [80].

The use of criteria corresponding to a barium sulfate column height of 5 cm after 1 min showed a sensitivity of 94 % and a specificity of 71 %, and the correspondence to a barium sulfate column height of 2 cm after 5 min demonstrated a sensitivity of 85 % and a specificity of 86 % in differentiating achalasia from other obstructions of the esophagogastric junction [80]. *The indicator corresponding to the product of the height and the width of the barium sulfate column in centimeters measured on 1- and 5-minute images can be a quantitative assessment of the percentage of emptying* [83].

The X-ray method is an easily accessible, low-cost technique for examining patients with achalasia. It has virtually no contraindications, with the exception of general contraindications to X-ray examinations (pregnancy, severity of the condition, inability to maintain the patient in an upright position). It is necessary to consider contraindications to taking barium swallow, such as hypersensitivity, perforation of the gastrointestinal mucosa (suspected of it), impaired swallowing, intestinal obstruction, constipation, esophageal stenosis, bleeding from the gastrointestinal tract, atresia, condition after surgery on the gastrointestinal tract, malabsorption syndrome, food allergy, esophagotracheal fistulas [84]. I*n the case of repeated studies to assess the dynamics, it is important to meet the primary conditions, such as the volume and consistency of the contrast agent, the distance from the source, the height of the tube, the position of the patient* [85].

• All patients with dysphagia and suspected achalasia cardia are recommended to undergo esophageal manometry to confirm the diagnosis [62, 86].

Grade of recommendations — A, level of evidence — 1.

Comment: esophageal manometry is recognized as the gold standard for diagnosing achalasia [57, 68, 81, 86–88].

In the work by T. Yamasaki et al., the effectiveness of radiographic examination and high-resolution esophageal manometry was compared, taking the latter as the gold standard for diagnosing achalasia. According to their data, the sensitivity, specificity, and accuracy of the radiographic method were 78.3 %, 88.0 %, and 83.0 %, respectively. Thus, patients with complaints of dysphagia, in whom the diagnosis of achalasia was not confirmed by barium sulfate radiography, should undergo high-resolution esophageal manometry [89].

• High-resolution esophageal manometry is superior to traditional manometry in the diagnosis of achalasia and is recommended as the method of choice for all patients [86, 88].

Grade of recommendations — B, level of evidence — 2.

Comment: high-resolution manometry has a number of advantages over traditional manometry. For example, a significant number of sensors allows examining the esophagus along its entire length, eliminating the "dropout" of zones from the examination, since the sensors are located at 1 cm from each other. The circular position of several sensors records the change in pressure in the esophagogastric junction zone, allowing for the diagnosis of "pseudorelaxation" of the LES — pulling the sphincter in the proximal direction during shortening of the esophagus at the time of, for example, premature contraction in type III achalasia [57]. *In addition, for better data visualization, a process of automatic interpolation ("completion") of the image between the sensors was introduced in the form of a planar or 3D topographic plot (contour graph)* [88].

A randomized clinical trial (RCT) compared the diagnostic efficacy of traditional manometry and high-resolution esophageal manometry. After 6 months of patient observation and additional examination, the diagnosis of achalasia was more often confirmed in the group that had previously undergone high-resolution manometry. The authors concluded that high-resolution manometry has a higher diagnostic ability, and esophageal motility disorders are detected by this method at earlier stages of the disease [86].

• The Chicago classification is recommended for use in analyzing the obtained data, as it allows one to ascertain the type of achalasia that has developed in the patient, the presence of which determines the choice of treatment method for the disease and the assessment of the prognosis of treatment effectiveness [55–58, 64, 90].

Grade of recommendations — A, level of evidence — 1.

Comment: The diagnosis of achalasia should be excluded in patients with dysphagia in the absence of mechanical obstruction and inflammation in the esophagus. The introduction of high-resolution esophageal manometry into clinical practice and the use of the Chicago classification for analyzing the data obtained have significantly increased the possibilities for diagnosing both the disease itself and the type of achalasia. The type of achalasia in turn determines the choice of treatment method and the prognosis of its effectiveness [55].

C. Andolfi and P.M. Fisichella conducted a meta-analysis of 20 studies, comparing the effects of different treatment methods on disease

outcomes in all types of achalasia. The effectiveness of botulinum toxin therapy, pneumatic balloon dilation, Heller myotomy, and peroral endoscopic myotomy (POEM) was analyzed. The effectiveness rates of Heller myotomy in achalasia types I, II, and III were 81 %, 92 %, and 71 %, respectively. When conducting POEM, the effectiveness was 95 %, 97 %, and 93 %, respectively. POEM demonstrated greater efficacy compared to Heller myotomy in patients with achalasia type I (OR — 2.97; 95 % CI: 1.09–8.03; p = 0.032) and type III (OR — 3.05; 95 % CI: 1.39–8.77; p = 0.007). There was no statistically significant difference in the efficacy of these treatment methods for type II achalasia. Thus, the authors concluded that POEM is the method of choice for achalasia types I and III, and type II is successfully treated with any of the described surgical methods [64].

In a randomized clinical trial comparing the efficacy of treating type II achalasia with pneumatic balloon dilation and Heller myotomy, A. Moonen et al. reported similar results of clinical efficacy of the methods after 5 years of patient follow-up (84 and 82 %, respectively). However, in 25 % of cases, after previously undergoing pneumatic balloon dilation, patients required repeated courses of treatment due to relapse of dysphagia. In addition, the data obtained showed that pneumatic balloon dilation was less effective in type I and III achalasia (treatment success was 61 and 31 %, respectively). The same study assessed the efficacy of botulinum toxin injection, which had the lowest remission rates among all types of achalasia [90].

In a systematic review, J.E. Pandolphino and A.J. Gawron presented data confirming the prognostic value of identifying the type of achalasia when choosing tactics and predicting the effectiveness of the treatment. Patients with type II achalasia have the best prognosis when treated with myotomy or pneumatic balloon dilation (96 % probability of a successful outcome). The clinical response to treatment in patients with type I is less pronounced and amounts to 81 % (and, in addition, decreases with increasing degree of esophageal dilation). Patients with type III have a worse prognosis for treatment effectiveness (66 %) due to the presence of premature contractions in the distal esophagus [62].

Based on the results of a systematic review with meta-analysis, which included 8 randomized clinical trials, 27 prospective cohort studies, and 40 retrospective studies, factors influencing the effectiveness of achalasia treatment were identified. Age and manometric type of the disease were identified by the authors as the most significant predictors of the clinical response to the treatment. The meta-analysis confirmed that older age (mean difference — 7.9 years; 95 % CI: 1.5–14.3) and type III achalasia (OR — 7.1; 95 % CI: 4.1–12.4) are associated with the severity of the clinical response of patients. That is, the authors showed that the best effect of treatment was achieved in elderly patients, and the presence of type III disease was more often associated with a worse prognosis and a higher frequency of relapses [63].

In addition, during esophageal manometry, patients with complaints of dysphagia are recommended to perform an additional provocative test — rapid drink challenge, which allows identifying obstruction of the esophagogastric junction and performing a differential diagnosis with achalasia. The lack of complete opening of the esophagogastric junction during the rapid drink challenge, can be considered as a marker of achalasia and obstruction of the esophagogastric junction. An increase in the total relaxation pressure of the LES above 12 mmHg confirms the diagnosis of achalasia (sensitivity — 85 %, specificity > 95 %) [91].

2.5. Other diagnostic tests

None.

3. Treatment, including drug and non-drug therapy, diet therapy, pain relief, medical indications and contraindications to the use of treatment methods

The objective of treatment of patients with achalasia should be relief of disease symptoms and, consequently, improvement of quality of life. Since evidence for the use of standardized questionnaires in clinical settings is limited, careful clinical assessment of esophageal symptoms before and after therapy should be used to assess treatment success. The most commonly used scale in clinical practice is the scale for severity of achalasia symptoms (Eckardt score; given in Appendix D1—DN) [92]. The use of the Eckardt score is recommended by a number of national clinical guidelines for assessing the effectiveness of treatment [49, 61, 65, 68, 81, 93]. However, despite its widespread use in all large European clinical trials [94–96], the Eckardt score has not been validated and confirmed as a tool for assessing symptom improvement in patients with achalasia [97].

Early treatment can prevent progression to terminal disease and late complications such as aspiration and carcinogenesis. However, there is insufficient natural history data to support this [81, 95, 98, 99].

Treatment of achalasia can be pharmacological, endoscopic, aimed at regulating the tone and motility of the esophagus and cardia while preserving all anatomical structures, and surgical, in which the muscle fibers of the esophagus and esophagogastric junction are intersected or the altered esophagus is completely removed with simultaneous formation of an artificial esophagus from the stomach or colon (esophagoplasty). Access for surgical treatment can be minimally invasive — intraluminal using flexible endoscopes, intracavitary using rigid endoscopic instruments (thoraco- or laparoscopic) or robotics, or traditional — through open surgeries.

3.1. Conservative treatment

• Pharmacological treatment with drugs that have a relaxing effect on smooth muscles is not recommended for patients with achalasia in order to relieve dysphagia [100, 101].

Grade of recommendations — C, level of evidence — 4.

Comment: there is insufficient convincing evidence that calcium channel blockers and nitrates can effectively reduce the tone of the LES and completely relieve the symptoms of achalasia, which calls into question the advisability of their constant use for the symptomatic treatment of achalasia when patients complain of dysphagia [81]. *In this regard, drug therapy is used in the treatment of patients awaiting endoscopic or surgical treatment, and as concomitant therapy in patients with achalasia, accompanied by refractory chest pain* [65].

• Patients with type III achalasia, which manifests as chest pain, are recommended to be prescribed drugs that have a relaxing effect on the smooth muscles of the thoracic esophagus [99].

Grade of recommendations — C, level of evidence — 4.

Comment: in patients with achalasia with complaints of chest pain before surgery or with persistent complaints after treatment, the administration of drugs from the group of calcium channel blockers (nifedipine), nitrates (isosorbide dinitrate) can reduce the intensity of the pain syndrome [102]. *However, when taking these drugs, the possibility of side effects such as arterial hypotension, headache, dizziness should be considered* [65, 103].

In the Russian Federation, achalasia is not mentioned in the instructions for use of these drugs, and therefore therapy with these drugs falls into the category of "off-label". However, "taking into account the global experience of using off-label drugs, when forming the regulatory framework for the implementation of clinical guidelines in the organization of medical care, the Ministry of Health of the Russian Federation provided for the possibility of including off-label drugs with proven effectiveness in clinical guidelines. At the same time, the use of off-label drugs not provided for by medical care standards and clinical guidelines is allowed by decision of the medical commission" (https://minzdrav.gov.ru/news/2022/05/24/18759-primenenie-preparatov-off-label-u-vzroslyh-vozmozhno-na-osnovanii-resheniya-vrachebnoy-komissii). According to national recommendations, nifedipine and isosorbide dinitrate are prescribed in a dose of 5–10 mg 20–30 minutes before meals 3 times a day [65].

The prescription of drug treatment should not exclude the use of endoscopic or surgical treatment [81].

3.2. Endoscopic treatment

3.2.1. Pneumatic balloon dilation

• Stepwise non-forced pneumatic balloon dilation is an effective and fairly safe method for treating achalasia [90, 95, 104, 105].

Grade of recommendations — A, level of evidence — 1.

Comment: pneumatic balloon dilation of the cardia is the gold standard for non-surgical treatment of achalasia [74, 79]. *It is performed under X-ray or endoscopic control to stretch the muscle fibers of the esophagogastric junction until they rupture, which reduces the pressure of the LES and improves the passage of food through the esophagus* [68]. *In Russia, endoscopic dilation of the cardia is performed using a specially designed balloon placed on the distal end of a gastrointestinal endoscope with a diameter of 8.5–9.5 mm* [106]. *The diameter of the balloons for dilation of the cardia is 30–40 mm, the length is 12–15 cm. The "waist" in the middle part of the balloon facilitates its fixation in the cardia. Currently, a two-layer balloon is used (AO MedSil, Mytishchi), which can be filled with either air (pneumatic dilation) or water (hydraulic dilation) to create higher pressure. This is necessary to prevent perforation of a hollow organ — the esophagus and/or stomach, since in the event of a rupture of an air-filled balloon, the risk of barotrauma is significantly greater than with hydraulic dilation. Water, which is practically incompressible, will flow out freely if the balloon ruptures without injuring the organ wall. Thus, in one session it is possible to perform pneumatic and hydraulic dilation without changing the instrument* [107]. *Abroad, Rigiflex or Witzel balloons are used for*

dilation; they are installed in the cardia and have shown similar results in assessing safety, complication rates, and treatment effectiveness in the near and long-term observation periods [108–110]. *The use of a balloon passed through the endoscope channel, as well as bougienage of the cardia, proved ineffective* [68]. *Also, for hydraulic dilation of the cardia, it is possible to use special balloons manufactured by "COOK" or "Boston Scientific" with a diameter of 30 and 35 mm, a length of 8 cm, having two channels: one for passing the guide string, the other for pumping fluid into the balloon.*

The standard mode of endoscopic balloon dilation of the cardia is a course that includes an average of five sessions of pneumatic dilation with a gradual, non-forced increase in pressure from 160 to 300 mmHg to prevent deep tears and the development of cicatricial processes. Initially, the balloon is placed in the cardia with its "waist", and then with its wide part. The exposure is 30–40 seconds. However, the number of sessions is always determined by the endoscopist individually for a specific patient, as well as the substrate filling the balloon (air or water). The decision to perform hydraulic dilation is made if pneumatic dilation is insufficiently effective according to clinical and endoscopic criteria, and sometimes according to the data of a control X-ray examination [106].

When treating patients with achalasia, it should be remembered that this condition is caused by functional, not organic, obstruction. Since the cardia opens as widely in them as in healthy people, and at any stage of the disease it is possible to pass an endoscope into the stomach, there is no need to "bougie" the cardia with an endoscope or Savary bougies, including a bougie with a diameter of 60 Fr (20 mm). In this category of patients, dilation with a balloon with a diameter of 15–20 mm, and especially stenting of the cardia with self-expanding endoprostheses, should not be performed. Forced pneumatic dilation should be avoided, since this leads to deep tears up to perforation or to the development of a cicatricial process with the formation of cicatricial strictures of the esophageal-gastric junction. Technical and tactical errors can discredit the technique [106].

• The choice of treatment method for achalasia depends on the individual characteristics of the patient, their preferences, possible side effects and/or complications, and the experience of the medical institution. In general, stepwise non-forced repeated balloon pneumatic balloon dilations, laparoscopic esophagocardiomyotomy, and peroral endoscopic myotomy are equivalent in effectiveness [63, 90, 95, 105].

Grade of recommendations – A, level of evidence – 1.

Comment: currently, there are several alternative methods of surgical and endoscopic treatment of achalasia aimed at relaxing the LES, the effectiveness of which is comparable. Endoscopic pneumatic balloon dilation (PBD), in contrast to surgical methods, allows preserving the anatomical integrity of the structures that provide the closing function of the cardia, affecting the excessively spasmodic segment of the lower third of the esophagus and the esophagogastric junction, in the absence of radiation exposure [107]. *According to randomized controlled trials, the effectiveness of PBD is 62–90 %* [62, 68]. *A significant number of studies have been devoted to the comparison of laparoscopic esophagocardiomyotomy and endoscopic PBD in the treatment of achalasia. The largest of these is the European multicenter randomized controlled trial. Its conclusion was the comparable effectiveness (about 90 %) of PBD (especially when performing several procedures) and laparoscopic esophagocardiomyotomy, the differences did not reach statistical significance* [90].

In 2019, F. Ponds et al. compared the effectiveness of peroral endoscopic myotomy (POEM) and PBD in a large randomized clinical trial. Observation of 126 patients continued for 2 years. Treatment was considered successful if the Eckardt score decreased to ≤ 3, there were no serious complications, and there was no need for re-treatment. The results of POEM were successful in 92 % of patients, while PBD led to a permanent cure in only 54 % of patients. Postoperative reflux esophagitis after POEM was diagnosed in 41 % of patients, after PBD – in 7 %. Such low efficiency of balloon dilation of the cardia can be explained by the study design: pneumatic dilation was limited to only one or two sessions using 30–35 mm balloons. Therefore, an analysis of the use of additional pneumatic dilation in 14 patients with 40 mm balloons was conducted and success was achieved in 76 % [95].

A retrospective study conducted in 2017 in China included 32 patients who underwent POEM and 40 patients who underwent PBD [111]. A*t short-term follow-up, similar improvements were noted in manometry and esophagography. Patients were followed for 36 months. With PBD, the efficacy at 3 months was 95 %, and at 36 months it was 60 %. For POEM, the efficacy at 3 months was 96 %, and at 36 months it was 93 %. However, when subgroup analysis*

was performed by achalasia types, statistically significant efficacy was higher with POEM compared with PBD only for patients with type III achalasia.

A retrospective review of 200 patients with achalasia found that at 2 months after treatment, there was no significant difference in the effectiveness of 3 procedures (POEM, PBD, and laparoscopic esophagocardiomyotomy) as measured by high-resolution esophagography or esophageal manometry [112].

Recent studies, the results of which are presented in a systematic review with meta-analysis [113], demonstrated that the effectiveness of POEM in the immediate postoperative period is more than 90 % [114–117], *and in the late period after 12, 24 and 36 months — 92.9 %, 90.6 % and 88.4 %, respectively* [118]. *As for side effects, when comparing POEM with traditional methods of treatment, their frequency was 3.6 % after POEM, 4.9 % after laparoscopic esophagocardiomyotomy and 3.1 % when using PBD* [119].

3.2.2. Peroral endoscopic myotomy

Peroral endoscopic myotomy (POEM) has been developed as an endoscopic treatment method that is effective and minimally invasive [120]. The surgical sequence for POEM is as follows: at 12–13 cm from the cardioesophageal junction, an initiating longitudinal mucosal incision of about 2 cm in length is made, sufficient to introduce the distal end of the endoscope with a transparent cap into the submucosa. In the second stage, the submucosa fibers of the esophagus, the esophagogastric junction, and then the stomach are dissected for about 3 cm. The next stage is a myotomy of 7–13 cm or more in length (in type III achalasia, the length of the muscle incision depends on the proximal level of spastic lesion of the esophagus). The last stage is hermetically sealing the mucosal incision with hemostatic clips.

• All patients with achalasia during POEM are recommended to undergo a dissection of the muscular layer of the stomach of at least 2–3 cm in length, which is optimal for achieving the target parameters of the operation [95].

Grade of recommendations — A,
level of evidence — 1.

Comment: the length of the gastric portion of the myotomy is similar in most RCTs and is essentially the same as that of open or laparoscopic esophagocardiomyotomy. However, increasing the incision by more than 2–3 cm does not improve the target parameters of the operation [121]. *In this case, the muscular layer in the stomach is transected to its full depth (keeping the mucous membrane above it intact), whereas in the esophagus, the inner, circular layer is most often dissected* [122].

• All patients with AC are recommended to undergo POEM with carbon dioxide insufflation, but not air, in order to minimize complications [123].

Grade of recommendations — B,
level of evidence — 2.

Comment: a large retrospective cohort study analyzed the incidence of complications after POEM. The authors reported a very high incidence of serious gas-related complications (27.8 %), especially during the first year when room air insufflation was used during POEM [123]. *The incidence of complications decreased to 1.9 % after the introduction of CO_2 insufflation and stabilized at about 1 % after 3.5 years. Carbon dioxide is sterile, does not support combustion, and is rapidly absorbed from closed cavities due to its high affinity for blood hemoglobin.*

• All patients with achalasia undergoing POEM are recommended to receive antibiotic prophylaxis in order to exclude infectious complications, and the timing, volume and duration should be regulated by the protocols adopted in the clinic for "clean" surgical interventions [124].

Grade of recommendations — B,
level of evidence — 2.

Comment: there are numerous studies indicating the need for perioperative antibiotic prophylaxis in patients with achalasia when POEM is prescribed. Various regimens are used, for example, a single dose of antibiotics administered 1 hour before anesthesia [125]. *A randomized clinical trial conducted in China found a reduced need for postoperative antibiotics in the group of patients receiving preoperative antibiotic prophylaxis, while no difference in the number of documented infectious complications was found between the two groups* [124]. *The study by Y. Zhai et al.* [126] *did not reveal any additional clinical benefit from preoperative antibiotic administration compared to a group of patients who were prescribed antibiotics only postoperatively to prevent infectious complications after POEM. All researchers agree that antibiotic prophylaxis is necessary, since patients who have undergone POEM may have significant inflammatory reactions and are likely to have microbial translocation, which has been confirmed by a corresponding study* [127].

• POEM is more effective in the short and long term compared to pneumatic balloon dilation [95, 118].

Grade of recommendations — A,
level of evidence — 1.

Comment: according to a meta-analysis including 66 scientific papers, the clinical success of treatment with POEM was higher than with PBD after 12, 24 and 36 months of observation (92.9 % vs. 76.9 %, p = 0.001; 90.6 % vs. 74.8 %, p = 0.004; 88.4 % vs. 72.2 %, p = 0.006, respectively). Moreover, the results of POEM statistically significantly exceeded the results of PBD in achalasia types I, II and III (92.7 % vs. 61 %, p = 0.01; 92.3 % vs. 80.3 %, p = 0.01; 92.3 % vs. 41.9 %, p = 0.01, respectively). The total indicators of clinical success after 12 and 24 months were also significantly higher when using POEM (8.97; p = 0.001 and 5.64; p = 0.006). Thus, based on the results of the meta-analysis, it was concluded that POEM is more effective than PBD in the treatment of patients with achalasia in both short-term and long-term observations [118].

The efficacy of POEM and PBD in the treatment of different types of achalasia was also studied in another comparative study. The authors found that there was a significant difference in the time to symptom recurrence between the POEM and PBD groups (p = 0.002). At 24-month follow-up, the clinical success rates of POEM and PBD were 91.8 and 68.0 %, respectively. The hazard ratio for symptom recurrence was 6.54 for PBD compared with POEM (95 % CI: 2.12–20.22; p = 0.001). Moreover, the clinical success rates of POEM were significantly higher than in patients after PBD for all types of achalasia (type I: 92.0 % vs. 51.1 %, p = 0.004; type II: 92.3 % vs. 59.8 %, p = 0.007; type III: 91.7 % vs. 55.6 %, p = 0.051) [129].

It should be noted that when using PBD, the recurrence rate of clinical symptoms is higher than with POEM, which leads to a higher frequency of re-treatment. Significantly higher rates of re-interventions were noted in a multicenter RCT (PBD — 46 %, POEM — 8 %) [95] and the work of researchers from Korea (PBD — 45.2 %, POEM — 7.8 %) [129].

• Gastroesophageal reflux as an adverse event occurs more frequently after POEM than after PBD [118].

Grade of recommendations — A, level of evidence — 1.

Comment: a group of researchers conducted a meta-analysis comparing the effectiveness of treating achalasia using POEM and PBD methods. In the analysis of cohort studies, no significant difference was observed in the severity of gastroesophageal reflux manifestations in large groups of patients who underwent these interventions, either in terms of the clinical picture (19 (13.7–25.8)% with POEM vs. 17.8 (12.7–24.4) % with PBD, p = 0.78) or in terms of endoscopy data (27.5 (17.5–40.3) % with POEM vs. 14.1 (5.7–30.8) % with PBD, p = 0.15) and pH monitoring (48.6 (31.6–66) % with POEM vs. 41.3 (22.8–62.6) % with PBD, p = 0.61). However, an analysis of controlled studies demonstrated a significantly higher overall risk of developing reflux esophagitis with POEM compared to PBD, both in terms of the presence of symptoms 2.95 (95 % CI: 1.46–5.95; p = 0.02) and in terms of endoscopy results 6.98 (95 % CI: 2.41–20.22; p = 0.001) [118].

In a retrospective analysis of the medical records of patients who underwent POEM, erosive reflux esophagitis grade A–B according to the Los Angeles classification was observed in 37.5 % of patients during a 2-year follow-up. It is worth noting that the symptoms were easily controlled by the administration of proton pump inhibitors in all patients [130].

According to Russian authors, among 100 patients with reflux esophagitis after POEM, erosive reflux esophagitis was diagnosed in 24.24 % of patients during the observation period of 1 to 5 years. Among them, grade A according to the Los Angeles classification was diagnosed in 15.2 % of patients, B — in 7.1 %, and C — in 2.02 %. In their work, the authors noted the peculiarity of the clinical course of the postoperative period in some patients. Among 24 patients with reflux esophagitis, 12 persons did not complain of heartburn or other characteristic complaints. After the appointment of antisecretory therapy, endoscopic remission occurred. The asymptomatic course of postoperative reflux esophagitis once again emphasizes the need for dynamic monitoring of patients after POEM [131].

3.2.3. Botulinum toxin injection

Intrasphincteric injection of botulinum toxin (BT) for achalasia was first proposed and performed by P.J. Pasricha et al. in 1994 [132]. The principle of the method is based on the fact that botulinum toxin A, used to treat achalasia, blocks the release of acetylcholine from nerve endings into the synaptic cleft, which leads to temporary relaxation of the muscle fibers of the LES.

• Endoscopic intrasphincteric injection of botulinum toxin is recommended for patients with achalasia as an effective and safe therapy only for temporary relief of disease symptoms [133, 134].

Grade of recommendations — B, level of evidence — 2.

Comment: indications for the use of BT injection as an effective and safe means for temporary relief of achalasia symptoms are reflected in a number of clinical guidelines [49, 81, 93].

Possible complications of BT injection include esophageal perforation or inflammatory mediastinitis [135], *chest pain (4.3 %) or heartburn (0.7 %)* [136], *but despite this, BT injection is considered a relatively safe treatment due to the low probability of complications* [49].

A number of clinical studies have shown that, compared with placebo, BT injection into the LES area reduces achalasia symptoms (dysphagia, regurgitation, and chest pain), reduces LES pressure, and improves esophageal emptying compared with placebo injection [137, 138].

In a systematic review with meta-analysis based on the results of data from 9 studies including 315 patients with achalasia, symptom relief or improvement after BT injection was noted in 78.7 % of patients at their re-examination 1 month after the procedure. However, in the following months, the effectiveness of therapy decreased and was 70 % after 3 months of observation, 53.3 % — after 6 months, and 40.6 % — after 12 months or more. In this regard, some patients required various additional treatment methods. Repeated BT injection was required in 46.6 % of patients, 3.8 % were referred for PBD and 3.2 % — for surgical myotomy [139].

Randomized clinical trials compared the efficacy of endoscopic intrasphincteric injection of BT and PBD [133, 134]. *Data from a meta-analysis including 5 RCTs indicate that BT injections significantly reduce LES pressure, relieve clinical symptoms and esophageal congestion in the short term. No significant difference was found between PBD and BT injection in achieving remission within 4 weeks after the initial intervention (the risk ratio for remission was 1.11; 95% CI: 0.97–1.27). There was also no significant difference in the mean LES pressure between the treatment groups: the weighted mean difference for the group with PBD was –0.77 (95% CI: –2.44–0.91; p = 0.37). During dynamic observation, relapse of symptoms was noted, and to a greater extent in the group of patients with BT injection. After 6 months, 46 of 57 patients in the PBD group were in remission, while in the group with BT injection only 29 of 56, which gives a remission risk ratio of 1.57 (95% CI: 1.19–2.08; p = 0.0015). Over time, the gap between the groups increases: after 12 months, 55 of 75 participants in the PBD group were in remission, while in the participants with BT injection only 27 of 72 people (remission risk ratio 1.88; 95% CI: 1.35–2.61; p = 0.0002)). In addition, it is worth mentioning that no serious adverse outcomes were observed in the participants who received BT injections, while in the PBD group, a severe complication in the form of wall perforation was noted in three cases. Thus, as a result of the comparative analysis, the authors concluded that both these methods are equally effective in the short term, while the use of pneumatic balloon dilation is more reliable in the long term (more than 6 months)* [133].

The impact of repeated BT injections on the efficacy and safety of subsequent myotomy treatment remains controversial. There is an opinion that multiple injections may cause a chronic inflammatory fibrotic reaction in the esophageal wall, leading to obliteration of the muscular-submucosal layer, which may increase the risk of perforation during subsequent surgical treatment [64]. *Data on the potential harm of BT administration before surgical and endoscopic myotomies are contradictory, and it is possible that the uncertainty regarding the negative effects of previous use of the drug is related to the fact that the data have been obtained from observational studies that included small numbers of patients and limited follow-up periods* [68].

• Endoscopic intrasphincteric injection of BT is recommended for patients with achalasia who, due to the severity of the concomitant pathology, cannot undergo more invasive and effective treatment for the purpose of temporary relief of symptoms [49, 65, 81].

Grade of recommendations — B, level of evidence — 2.

Comment: according to the Seoul Consensus and the American College of Gastroenterology guidelines for the treatment of achalasia, BT injections are recommended for patients with achalasia whose general condition does not allow for endoscopic or surgical treatment [49, 68]. *The guidelines of the Russian Gastroenterological Association emphasize that this most often applies to older individuals with severe concomitant cardiovascular and bronchopulmonary pathology, as well as in the presence of an S-shaped esophagus* [65]. *Considering the significant technical simplicity of performing BT injections, the short time spent on this procedure, and the minimal number of complications (usually associated with individual intolerance to BT drugs), this procedure can be recommended for patients in decompensation due to concomitant (therapeutic or surgical) pathology* [81]. *It should also be noted that to date in the Russian Federation the botulinum toxin A drug Dysport has not been registered as a means for use in gastroenterology, it is only permitted to be used in neurology and cosmetology, in connection with which therapy with this drug falls into the category of "off-label" use. Nevertheless, "considering the global experience of using off-label drugs, when*

forming the regulatory framework for the implementation of clinical guidelines in the organization of medical care, the Ministry of Health of the Russian Federation has provided for the possibility of including off-label drugs with proven effectiveness in clinical guidelines. At the same time, the use of off-label drugs that are not provided for by medical care standards and clinical guidelines is permitted by decision of the medical commission" (https://minzdrav.gov.ru/news/2022/05/24/18759-primenenie-preparatov-off-label-u-vzroslyh-vozmozhno-na-osnovanii-resheniya-vrachebnoy-komissii).

3.3. Surgical treatment

• The indication for surgical treatment of patients with achalasia is, mainly, the ineffectiveness of pneumatic balloon dilation [98, 141].

Grade of recommendations — B, level of evidence — 2.

Comment: absolute indications for surgical intervention are the impossibility or ineffectiveness of pneumatic balloon dilation (the "rubber cardia" symptom), rapid relapse of symptoms after dilation, ineffectiveness of drug treatment or the administration of botulinum toxin type A, relapse after previously performed esophagocardiomyotomy [141], *as well as the severity of the manifestations of the disease and the impairment of quality of life, the risk of complications and (or) their consequences at stage IV of the disease (megaesophagus)* [98].

• The laparoscopic version of esophagocardiomyotomy is recognized as the gold standard for this intervention [142].

Grade of recommendations — B, level of evidence — 2.

Comment: the standard surgical treatment for achalasia is laparoscopic esophagocardiomyotomy, which is based on the dissection of the muscular layer of the esophagus along the anterior wall of the organ with the transition to the anterior wall of the stomach in the cardia zone [143]. *The consequence of the intervention is a decrease in the tone of the cardia and the elimination of dysphagia with an efficiency of 80–90%* [144].

• The advisability of performing laparoscopic esophagocardiomyotomy for achalasia as a first-line treatment method is controversial [145].

Grade of recommendations — C, level of evidence — 3.

Comment: the reserved attitude towards the use of laparoscopic esophagocardiomyotomy as an initial method of treating achalasia is due to the high efficiency of more gentle treatment methods, primarily balloon dilation.

• The demonstrated effectiveness of robot-assisted technology in performing myotomy should, however, be confirmed by additional randomized clinical trials [140, 141].

Grade of recommendations — C, level of evidence — 1.

Comment: the use of a robotic surgical system in the treatment of patients with achalasia is safe and convenient for the surgeon due to improved tissue visualization and increased dissection accuracy. The method is an effective alternative to other minimally invasive approaches and may become the procedure of choice, especially with reduced costs. Randomized clinical trials are needed to evaluate long-term functional outcomes [148].

• The impact of non-surgical methods of treating achalasia on the safety and efficacy of laparoscopic esophagocardiomyotomy is controversial [149, 150].

Grade of recommendations — C, level of evidence — 3.

Comment: the increased risk of intra- and postoperative complications, as well as the insufficient effectiveness of laparoscopic esophagocardiomyotomy after previously performed balloon dilation or the introduction of botulinum toxin type A is controversial. A number of studies indicate an increased frequency of esophageal perforations in these groups of patients.

• The main results of POEM and laparoscopic esophagocardiomyotomy are comparable. POEM demonstrates a lower rate of serious complications, but a higher incidence of gastroesophageal reflux disease [142–144].

Grade of recommendations — A, level of evidence — 1.

Comment: most of the current studies have found no significant difference between POEM and laparoscopic esophagocardiomyotomy in terms of intervention time, postoperative pain scores and analgesic requirements, and complication rates, with a significant reduction in hospital stay. Symptomatic gastroesophageal reflux outcomes after these surgical procedures have shown a trend toward a significant reduction in favor of laparoscopic esophagocardiomyotomy compared to POEM. However, future studies are needed to examine the long-term effects of POEM on acid reflux [147].

• POEM in patients with achalasia, compared with laparoscopic esophagocardiomyotomy, reduces the duration of hospitalization and reduces the need for analgesics [145].

Grade of recommendations — C, level of evidence — 3.

Comment: despite the active implementation of the POEM method, which has demonstrated good results in resolving dysphagia in patients with achalasia, there remains a need for further research to compare this treatment method and the current standard of surgical care — laparoscopic esophagocardiomyotomy.

• In patients with uncomplicated achalasia, transabdominal esophagomyotomy combined with fundoplication effectively restores swallowing function and relieves dysphagia without causing gastroesophageal reflux [146].

Grade of recommendations — A, level of evidence — 2.

Comment: most surgeons prefer to supplement the dissection of the esophageal muscles with an antireflux intervention, although the role of fundoplication in esophagocardiomyotomy, as well as the technology for its implementation, continues to be discussed.

• The incidence of gastroesophageal reflux symptoms with esophagomyotomy without fundoplication is 31.5 %, and with the addition of antireflux surgery to esophagomyotomy, it is 8.8 % [139].

Grade of recommendations — A, level of evidence — 1.

Comment: the role of fundoplication in myotomy remains controversial, although most surgeons prefer to supplement the dissection of the esophageal muscles with an antireflux procedure. The antireflux procedure reduces the incidence of heartburn, esophagitis, and peptic stricture in the postoperative period. One of the arguments of opponents of fundoplication is the presence of concomitant aperistalsis of the esophagus, in which case the fundoplication itself can cause the development of dysphagia. Various variants of "incomplete" fundoplication (such as Toupet or Dor) are used to prevent this complication [148].

• There is no statistically significant difference in long-term outcomes between the groups of patients who underwent isolated myotomy and myotomy combined with fundoplication [149].

Grade of recommendations — C, level of evidence — 1.

Comment: the literature on this topic lacks high-quality studies, and further research using large-scale randomized clinical trials comparing different treatments is needed to confirm this finding.

• Terminal stage (stage IV) of the disease (megaesophagus) develops in 10–15 % of patients suffering from achalasia. Subtotal resection of the esophagus (esophagectomy) in this case is usually the method of choice, although it is accompanied by a higher incidence of complications [68, 99].

Grade of recommendations — A, level of evidence — 1.

Comment: the basic indications for subtotal removal of the esophagus with subsequent esophagoplasty in patients with achalasia include significant expansion of the esophageal lumen with its elongation and S-shaped deformation, as well as ineffective (or completely absent) motility, leading to persistent disruption of food evacuation into the stomach. These circumstances call into question the effectiveness of both balloon dilations and isolated surgical intervention in the lower esophageal sphincter area. In addition, the basis for removal of the esophagus is concomitant congestive erosive-ulcerative esophagitis with the risk of bleeding, aspiration complications, as well as an increasing risk of developing squamous cell carcinoma of the esophagus against the background of mucosal dysplasia. Nevertheless, some authors believe that esophagectomy is indicated only if organ-preserving interventions are unsuccessful [151, 152].

• Complications during esophagectomy in patients with terminal stage of achalasia develop in 19–50 % of cases, with fatal outcomes occurring in 0–3.8 % of cases [150].

Grade of recommendations — A, level of evidence — 1.

Comment: the use of minimally invasive (primarily thoracoscopic) approaches in surgical treatment of terminal achalasia, in combination with other elements of the fast-track surgery program, is accompanied by a lower surgical stress response and a decrease in the severity of pain syndrome [139], *although it has a number of technical limitations* [128]. *The use of this program helps to reduce the duration of postoperative observation in the intensive care unit, as well as the duration of inpatient treatment due to a significant reduction in the incidence of postoperative complications and mortality.*

• In most patients with end-stage of achalasia, myotomy allows avoiding esophagectomy, with re-intervention required in 16 % of cases [151].

Grade of recommendations — B, level of evidence — 1.

Comment: According to the ISDE (International Society for Diseases of the Esophagus) guidelines published in 2018, high preoperative LES pressure has a beneficial effect on the outcome of myotomy, while stage IV (sigmoid esophagus) is a factor for an unfavorable prognosis [61]. *The patient's belonging to an older age group and the duration of symptoms also worsen the results of organ-preserving intervention in case of S-shaped deformation of the esophagus.*

4. Medical rehabilitation, medical indications and contraindications for the use of rehabilitation methods

The issues of medical rehabilitation, as well as health resort treatment for patients with achalasia, have not been developed. When resolving these issues, one should be guided by Order of the Ministry of Health of the Russian Federation No. 1029н of September 28, 2020 "On approval of the lists of indications and contraindications for health resort treatment".

5. Prevention and regular medical checkup, medical indications and contraindications for the use of prevention methods

Issues of prevention and regular medical checkup of patients with achalasia have not been developed.

6. Organization of medical care

If there is a suspicion that a patient has achalasia, general practitioners, district general practitioners, family doctors, medical specialists, and paramedical workers refer the patient in the prescribed manner for consultation to a medical organization that has a gastroenterologist's office or an outpatient gastroenterology center (department) to provide them with primary specialized health care. A gastroenterologist at a medical organization that has a gastroenterologist's office or an outpatient gastroenterology center (department) organizes the diagnostic tests necessary to establish a diagnosis (mandatory EGDS, barium X-ray examination of the esophagus using the method of timed contrast radiography, esophageal manometry (high resolution, if possible)). After confirming the diagnosis of achalasia, the patient is recommended to be referred to a specialized surgical hospital to determine further treatment tactics.

Examination and treatment of patients with achalasia is carried out on an outpatient basis or in a day hospital setting.

7. Additional information (including factors that influence the outcome of the disease or condition)

Achalasia is associated with an increased risk of esophageal cancer. A systematic review and meta-analysis of 11,978 patients with achalasia found that the incidence of esophageal squamous cell carcinoma and adenocarcinoma was 26 (95 % CI: 18–39) and 4 (95 % CI: 3–6) per 1000 patients with achalasia, respectively. The absolute increase in the risk of squamous cell carcinoma was 308.1 and adenocarcinoma was 18.03 cases per 100,000 patients per year. In addition, the increased risk of adenocarcinoma in patients with achalasia suggests fundoplication after myotomy to minimize the likelihood of developing gastroesophageal reflux and Barrett's esophagus, a known risk factor for adenocarcinoma. The need for routine endoscopic surveillance of patients with achalasia remains controversial [68, 153].

8. Criteria for assessing the quality of medical care

Quality criteria	Level of evidence	Grade of recommendations
Esophagogastroduodenoscopy is performed	A	1
X-ray examination with barium swallow is performed using the method of timed contrast radiography	A	1
Esophageal manometry is performed	A	1
Endoscopic or surgical treatment is performed	A	1
Drug treatment is performed	C	4

Appendix A2.
Methodology for developing clinical guidelines

The proposed recommendations are intended to convey to practicing physicians modern ideas about the etiology and pathogenesis of achalasia, to acquaint them with the currently used algorithm for its diagnosis and treatment.

The target audience of these clinical recommendations:
1) gastroenterologists;
2) general practitioners (family doctors);
3) therapists;
4) functional diagnostics doctors;
5) radiologists;
6) endoscopists.

In these clinical recommendations, all information is ranked by the level of reliability (evidence) depending on the number and quality of studies on this problem.

Table 1. Grading of Levels of Evidence (GLE for diagnostic methods (diagnostic interventions)

GLE	Explanation
1	Systematic reviews of studies with reference method control or systematic review of randomized clinical trials using meta-analysis
2	Individual studies with reference method control or individual randomized clinical trials and systematic reviews of studies of any design, excluding randomized clinical trials, using meta-analysis
3	Studies without sequential control with a reference method or studies with a reference method that is not independent of the study method or non-randomized comparative studies, including cohort studies
4	Non-comparative studies, case reports
5	There is only a rationale for the mechanism of action or expert opinion

Table 2. Grading of Levels of Evidence (GLE) for prevention, treatment and rehabilitation methods (preventive, curative, rehabilitative interventions)

GLE	Explanation
1	Systematic review of RCTs using meta-analysis
2	Individual RCTs and systematic reviews of studies of any design, excluding RCTs, using meta-analysis
3	Non-randomized comparative studies, including cohort studies
4	Non-comparative studies, case reports or case series, case-control studies
5	There is only a rationale for the mechanism of action of the intervention (preclinical studies) or expert opinion

Table 3. Grading of Recommendations (GoR) for methods of prevention, diagnosis, treatment and rehabilitation (preventive, diagnostic, therapeutic, rehabilitation interventions)

GoR	Explanation
A	Strong recommendation (all efficacy measures (outcomes) considered are important, all studies are of high or satisfactory methodological quality, their conclusions on the outcomes of interest are consistent)
B	Conditional recommendation (not all efficacy measures (outcomes) considered are important, not all studies are of high or satisfactory methodological quality, and/or their findings are inconsistent for the outcomes of interest)
C	Weak recommendation (lack of good quality evidence (all efficacy measures (outcomes) considered are unimportant, all studies are of low methodological quality and their conclusions are inconsistent for the outcomes of interest)

Procedure for updating clinical guidelines

The mechanism for updating clinical guidelines provides for their systematic updating — at least once every 3 years, as well as when new data appears from the standpoint of evidence-based medicine on issues of diagnosis, treatment, prevention and rehabilitation of specific diseases, the presence of justified additions/comments to previously approved clinical guidelines, but not more often than once every 6 months.

Limitation of application of the guidelines

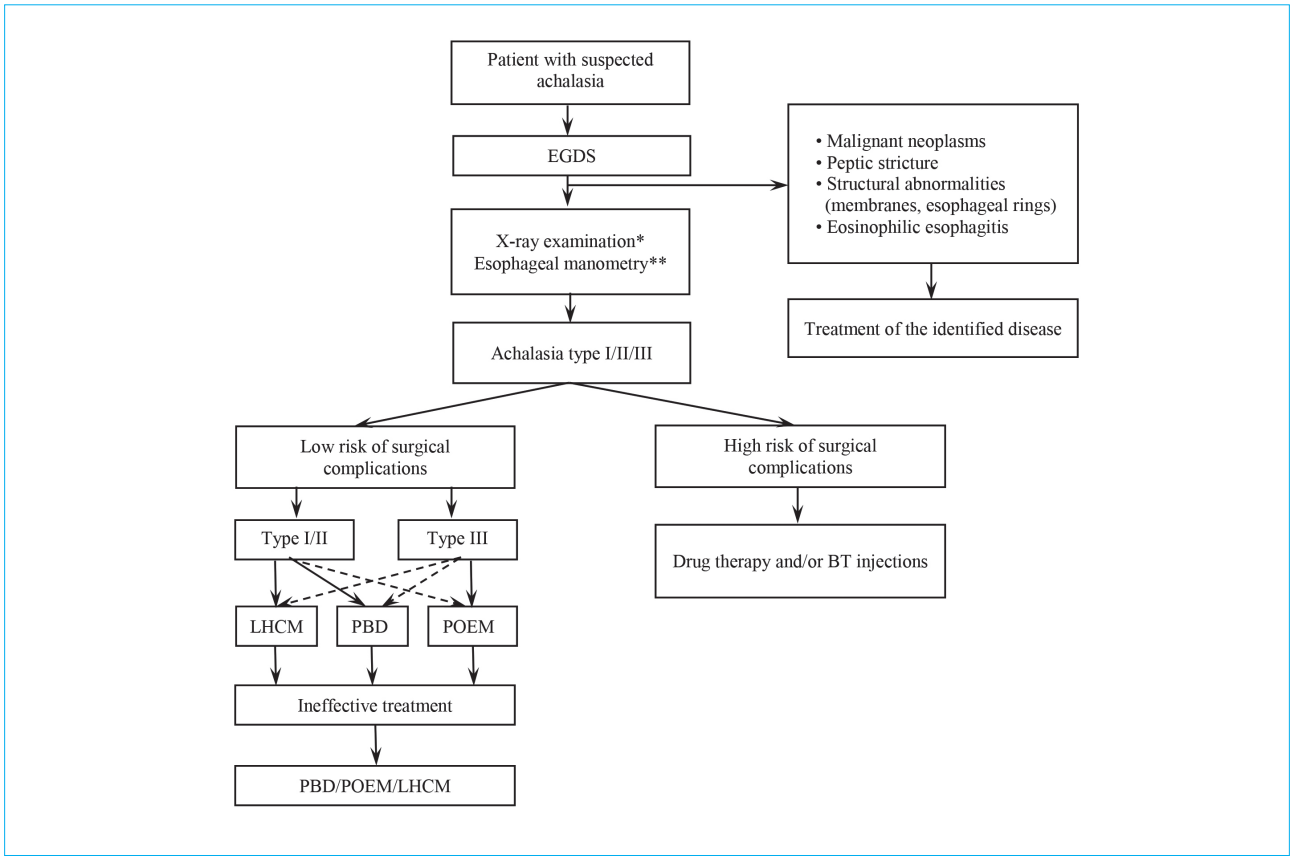
Clinical guidelines reflect the opinion of experts on the most controversial issues. In clinical practice, situations may arise that go beyond the guidelines presented, so the final decision on the tactics of managing each patient should be made by the attending physician, who is responsible for his treatment.

Appendix A3. Reference materials, including the correspondence of indications for use and contraindications, methods of administration and dosages of medicinal products to the instructions for use of the medicinal product

These clinical guidelines have been developed with consideration of the following regulatory documents:

1. Order of the Ministry of Health of the Russian Federation No. 906н of November 12, 2012 “On approval of the Procedure for providing medical care to the population in the profile of ”gastroenterology””.
2. Order of the Ministry of Health of the Russian Federation No. 203н of May 10, 2017 “On approval of criteria for assessing the quality of medical care”.
3. Order of the Ministry of Health of the Russian Federation No. 1029н of September 28, 2020 “On approval of the lists of indications and contraindications for health resort treatment”.
4. Federal Law of the Russian Federation No. 326-FZ of November 29, 2010 (as amended on December 19, 2022, No. 519-FZ) “On compulsory medical insurance in the Russian Federation”.

Appendix B. Algorithms of physician actions



Note: EGDS — esophagogastroduodenoscopy; LHCM — laparoscopic Heller’s cardiomyotomy; PBD — pneumatic balloon dilation; POEM — peroral endoscopic myotomy; BT — botulinum toxin; * — according to the method of timed barium esophagogram; ** — high-resolution esophageal manometry, the gold standard for achalasia diagnostics with classification by achalasia types.

Appendix C. Information for patients

Achalasia of the cardia is a chronic progressive disease, manifested by complaints of progressive difficulty in the passage of solid and liquid food through the esophagus, regurgitation (regurgitation of eaten food, the "wet pillow" symptom in the morning), chest pain. Achalasia is diagnosed with equal frequency in men and women, the age group of those affected is from 25 to 60 years, and the incidence increases with age.

The etiology and pathogenesis of achalasia have not been fully studied. The following hypotheses have been proposed as the main mechanisms of disease development: genetic predisposition, exposure to viral infections, and idiopathic autoimmune triggers.

If achalasia is suspected, the patient undergoes a comprehensive examination aimed at excluding the oncological process, diseases with a similar clinical picture — gastroesophageal reflux disease, ischemic heart disease, esophageal spasm. The patient is required to undergo esophagogastroduodenoscopy, X-ray examination of the esophagus with barium swallow using the method of timed barium esophagogram, manometry of the esophagus (preferably with high resolution).

When the diagnosis is confirmed and the type of achalasia is determined, it is recommended to refer the patient to a specialized surgical hospital to determine further treatment tactics. Due to the fact that achalasia is a chronic progressive disease, the patient should be explained the need for mandatory treatment in order to exclude the development of severe forms of the disease and complications.

In cases where the general condition of the patient does not allow endoscopic or surgical treatment, the issue of prescribing drug therapy to alleviate symptoms should be considered.

Appendix D1–DN. Rating scales, questionnaires and other patient assessment instruments provided in clinical guidelines

Table 4. Severity of achalasia clinical symptoms scale (Eckardt score)

	Symptom			
Points	**Weight loss**	**Dysphagia**	**Chest pain**	**Regurgitation**
0	no	no	no	no
1	< 5 kg	occasionally	occasionally	occasionally
2	5–10 kg	daily	daily	daily
3	> 10 kg	at every meal	at every meal	at every meal

The Eckardt score is based on the assessment of the main clinical manifestations of achalasia — weight loss, dysphagia, chest pain, regurgitation. The patient can score a maximum of 12 points, which is considered a negative result. Points from 0 to 3 are awarded if the symptoms never bother the patient, occur episodically, daily or at each meal, respectively. Points from 0 to 3 are also awarded in accordance with the degree of weight loss in the patient (Table 4).

Next, the following correspondence between the symptom score (points scored) and the clinical stage of achalasia is determined:

0–1 point — stage 0;
2–3 points — stage I;
4–6 points — stage II;
> 6 points — stage III.

After the patient's treatment, a repeated assessment of the clinical symptoms is performed. Correspondence between stage 0–I of the disease indicates achievement of clinical remission. Treatment is considered ineffective if, according to the assessment of the clinical symptoms, achalasia corresponds to stages II and III of the disease [92].

References / Литература

1. *Ates M.F., Vaezi F.* The pathogenesis and management of achalasia: Current status and future directions. *Gut Liver*. 2015;9(4):449–63. DOI: 10.5009/gnl14446
2. *Campo S.M., Zullo A., Scandavini C.M., Frezza B., Cerro P., Balducci G.* Pseudoachalasia: A peculiar case report and review of the literature. *World J Gastrointest Endosc*. 2013;5(9):450–4. DOI: 10.4253/wjge.v5.i9.450
3. *de Oliveira R.B., Rezende Filho J., Dantas R.O., Iazigi N.* The spectrum of esophageal motor disorders in Chagas' disease. *Am J Gastroenterol*. 1995;90(7):1119–24.
4. *Ванцян Э.Н., Черноусов А.Ф.* Хирургия пищевода. Современные достижения реконструктивной хирургии: Сб. научных трудов. М., 1988:34–7. [*Vantsyan E.N., Chernousov A.F.* Esophageal surgery. Modern advances in reconstructive surgery: Abstracts. Moscow, 1988:34–7. (In Russ.)].
5. *Черноусов А.Ф., Богопольский П.М., Курбанов Ф.С.* Хирургия пищевода. Руководство для врачей. М.: Медицина, 2000. [*Chernousov A.F., Bogopolsky P.M., Kurbanov F.S.* Esophageal surgery. Manual for physicians. Moscow: Meditsina Publ., 2000. (In Russ.)].
6. *Сакс Ф.Ф.* Функциональная морфология пищевода. М., 1987:121–64. [*Saks F.F.* Functional esophageal morphology. Moscow: Meditsina Publ., 1987:121–64. (In Russ.)].
7. *Иорданская Н.И.* Изменения экстра- и интрамуральной нервной системы при кардиоспазме. *Казанский медицинский журнал*. 1961;1:49–51. [*Iordanskaya N.I.* Changes of extra- and intramural nervous system at cardiospasm. *Kazan Medical Journal*. 1961;1:49–51. (In Russ.)].
8. *Adams C.W., Marples E.A., Trounce J.R.* Achalasia of the cardia and Hirschsprung's disease. The amount and distribution of cholinesterases. *Clin Sci*. 1960;19:473–81.

9. *Зиверт К.Н.* Спазм и стеноз кардии. *Труды 26-го Всесоюзного съезда хирургов.* М., 1962:182–6. [*Zievert K.N.* Spasm and stenosis of cardia. *Abstracts of the 26th All-Union Congress of Surgeons.* Moscow, 1962:182–6. (In Russ.)].
10. *Воронцова Н.И.* Изменения вегетативной нервной системы при функциональных заболеваниях пищевода. *Клиническая медицина.* 1966;2:33–4. [*Vorontsova N.I.* Changes of autonomous nervous system at functional esophageal diseases. *Clinical Medicine* (*Russian Journal*). 1966;2:33–4. (In Russ.)].
11. *Savarino E., Bhatia S., Roman S., Sifrim D., Tack J., Thompson S.K., et al.* Achalasia. *Nat Rev Dis Primers.* 2022;8(1):28. DOI: 10.1038/s41572-022-00356-8
12. *Romero-Hernández F., Furuzawa-Carballeda J., Hernández-Molina G., Alejandro-Medrano E., Núñez-Álvarez C.A., Hernández-Ramírez D.F., et al.* Autoimmune comorbidity in achalasia patients. *J Gastroenterol Hepatol.* 2018;33(1):203–8. DOI: 10.1111/jgh.13839
13. *Lee J.Y., Kim N., Kim S.E., Choi Y.J., Kang K.K., Oh D.H., et al.* Clinical characteristics and treatment outcomes of 3 subtypes of achalasia according to the Chicago classification in a tertiary institute in Korea. *J Neurogastroenterol Motil.* 2013;19(4):485–94. DOI: 10.5056/jnm.2013.19.4.485
14. *Furuzawa-Carballeda J., Torres-Landa S., Valdovinos M.Á., Coss-Adame E., Martín Del Campo L.A., Torres-Villalobos G.* New insights into the pathophysiology of achalasia and implications for future treatment. *World J Gastroenterol.* 2016;22(35):7892–907. DOI: 10.3748/wjg.v22.i35.7892
15. *Schlottmann F., Neto R.M.L., Herbella F.A.M., Patti M.G.* Esophageal achalasia: Pathophysiology, clinical presentation, and diagnostic evaluation. *Am Surg. 2018;84(4):467–72.*
16. *Boeckxstaens G.E., Zaninotto G., Richter J.E.* Achalasia. *Lancet.* 2014;383(9911):83–93. DOI: 10.1016/S0140-6736(13)60651-0
17. *Ghoshal U.C., Daschakraborty S.B., Singh R.* Pathogenesis of achalasia cardia. *World J Gastroenterol.* 2012;18(24):3050–7. DOI: 10.3748/wjg.v18.i24.3050
18. *Patel D.A., Kim H.P., Zifodya J.S., Vaezi M.F.* Idiopathic (primary) achalasia: A review. *Orphanet J Rare Dis.* 2015;10(1):89. DOI: 10.1186/s13023-015-0302-1
19. *Mearin F., García-González M.A., Strunk M., Zárate N., Malagelada J.R., Lanas A.* Association between achalasia and nitric oxide synthase gene polymorphisms. *Am J Gastroenterol.* 2006;101(9):1979–84. DOI: 10.1111/j.1572-0241.2006.00762.x
20. *Vigo A.G., Martínez A., de la Concha E.G., Urcelay E., de León A.R.* Suggested association of NOS2A polymorphism in idiopathic achalasia: No evidence in a large case-control study. *Am J Gastroenterol.* 2009;104(5):1326–7. DOI: 10.1038/ajg.2009.72
21. *Ghisa M., Laserra G., Marabotto E., Ziola S., Tolone S., de Bortoli N., et al.* Achalasia and obstructive motor disorders are not uncommon in patients with eosinophilic esophagitis. *Clin Gastroenterol Hepatol.* 2021;19(8):1554–63. DOI: 10.1016/j.cgh.2020.07.056
22. *Nelson M., Zhang X., Genta R.M., Turner K., Podgaetz E., Paris S., et al.* Lower esophageal sphincter muscle of patients with achalasia exhibits profound mast cell degranulation. *Neurogastroenterol Motil.* 2021;33(5):e14055. DOI: 10.1111/nmo.14055
23. *Cools-Lartigue J., Chang S.-Y., Mckendy K., Mayrand S., Marcus V., Fried G.M., et al.* Pattern of esophageal eosinophilic infiltration in patients with achalasia and response to Heller myotomy and Dor fundoplication. *Dis Esophagus.* 2013;26(8):766–75. DOI: 10.1111/j.1442-2050.2012.01385.x
24. *Schizas D., Syllaios A., Vailas M., Sotiropoulou M., Triantafyllou T., Tsapralis D., et al.* Eosinophilic esophagitis and achalasia: Two distinct nosologic entities or a possible etiopathogenic association? *Dig Dis.* 2021;39(6):553–60. DOI: 10.1159/000515520
25. *de Moura E.T.H., Jukemura J., Ribeiro I.B., Farias G.F.A., de Almeida Delgado A.A., Coutinho L.M.A., et al.* Peroral endoscopic myotomy vs laparoscopic myotomy and partial fundoplication for esophageal achalasia: A single-center randomized controlled trial. *World J Gastroenterol.* 2022;28(33):4875–89. DOI: 10.3748/wjg.v28.i33.4875
26. *Mota R.C.L., de Mouro E.G.H., de Mouro D.T.H., Bernardo W.M., de Moura E.T.H., Brunaldi V.O., et al.* Risk factors for gastroesophageal reflux after POEM for achalasia: A systematic review and meta-analysis. *Surg Endosc.* 2021;35(1):383–97. DOI: 10.1007/s00464-020-07412-y
27. *Allgrove J., Clayden G.S., Grant D.B., Macaulay J.C.* Familial glucocorticoid deficiency with achalasia of the cardia and deficient tear production. *Lancet.* 1978;311(8077):1284–6. DOI: 10.1016/S0140-6736(78)91268-0
28. *Prpic I., Huebner A., Persic M., Handschug K., Pavletic M.* Triple A syndrome: Genotype-phenotype assessment. *Clin Genet.* 2003;63(5):415–7. DOI: 10.1034/j.1399-0004.2003.00070.x
29. *Moore S.W.* Down syndrome and the enteric nervous system. *Pediatr Surg Int.* 2008;24(8):873–83. DOI: 10.1007/s00383-008-2188-7
30. *Tanaka S., Abe H., Sato H., Shiwaku H., Minami H., Sato C., et al.* Frequency and clinical characteristics of special types of achalasia in Japan: A large-scale, multicenter database study. *J Gastroenterol Hepatol.* 2021;36(10):2828–33. DOI: 10.1111/jgh.15557
31. *Sara C., Marcella P., Martina C., Marta A., Eleonora E., Giovanni A., et al.* Clinical correlation and disease phenotype in patients with esophageal achalasia and comorbid autoimmune diseases. *Dis Esophagus.* 2021;34(1):doaa072. DOI: 10.1093/dote/doaa072
32. *Furuzawa-Carballeda J., Aguilar-León D., Gamboa-Domínguez A., Valdovinos M.A., Nuñez-Álvarez C., Martín-del-Campo L.A., et al.* Achalasia — an autoimmune inflammatory disease: A cross-sectional study. *J Immunol Res.* 2015:2015:729217. DOI: 10.1155/2015/729217
33. *Storch W.B., Eckardt V.F., Wienbeck M., Eberl T., Auer P.G., Hecker A., et al.* Autoantibodies to Auerbach's plexus in achalasia. *Cell Mol Biol* (*Noisy-le-grand*). 1995;41(8):1033–8.
34. *Moses P.L., Ellis M.L., Anees M.R., Ho W., Rothstein R.I., Meddings J.B., et al.* Antineuronal antibodies in idiopathic achalasia and gastro-oesophageal reflux disease. *Gut.* 2003;52(5):629–36. DOI: 10.1136/gut.52.5.629
35. *Hernández-Ramírez D.F., Olivares-Martínez E., Nuñez-Álvarez C.A., Coss-Adame E., Valdovinos M.A., López-Verdugo F., et al.* Triosephosphate isomerase, carbonic anhydrase, and creatinine kinase-brain isoform are possible antigen targets in patients with achalasia. *Neurogastroenterol Motil.* 2020;32(5):e13804. DOI: 10.1111/nmo.13804
36. *Naik R.D., Vaezi M.F., Gershon A.A., Higginbotham T., Chen J.J., Flores E., et al.* Association of achalasia with active varicella zoster virus infection of the esophagus. *Gastroenterology.* 2021;161(2):719–21.e2. DOI: 10.1053/j.gastro.2021.04.057
37. *Mobasheri L., Nasirpour M.H., Masoumi E., Azarnaminy A.F., Jafari M., Esmaeili S.A.* SARS-CoV-2 triggering autoimmune diseases. *Cytokine.* 2022;154:155873. DOI: 10.1016/j.cyto.2022.155873
38. *Ruz Zafra P., García Sánchez C.J., Pérez Ramírez A., Guil Soto A., Leo Carnerero E.* Infection with SARS-CoV-2 as potential achalasia trigger. *Rev Esp Enferm Dig.* 2023;115(4):203–4. DOI: 10.17235/reed.2022.8975/2022
39. *Furuzawa-Carballeda J., Icaza-Chávez M.E., Aguilar-León D., Uribe-Uribe N., Nuñez-Pompa M.C., Trigos-Díaz A., et al.* Is the SARS-CoV-2 virus a possible trigger agent for the development of achalasia? *Neurogastroenterol Motil.* 2023;35(3):e14502. DOI: 10.1111/nmo.14502
40. *Ивашкин В.Т., Шептулин А.А., Зольникова О.Ю., Охлобыстин А.В., Полуэктова Е.А., Трухманов А.С. и др.* Новая коронавирусная инфекция (COVID-19) и система органов пищеварения. *Российский журнал*

гастроэнтерологии, гепатологии, колопроктологии. 2020;30(3):7–13. [*Ivashkin V.T., Sheptulin A.A., Zolnikova O.Yu., Okhlobystin A.V., Poluektova E.A., Trukhmanov A.S., et al.* New coronavirus infection (COVID-19) and digestive system. *Russian Journal of Gastroenterology, Hepatology, Coloproctology.* 2020;30(3):7–13. (In Russ.)]. DOI: 10.22416/1382-4376-2020-30-3-7
41. *Van Hoeij F.B., Ponds F.A., Smout A.J., Bredenoord A.J.* Incidence and costs of achalasia in the Netherlands. *Neurogastroenterol Motil.* 2018;30(2). DOI: 10.1111/nmo.13195
42. *Samo S., Carlson D.A., Gregory D.L., Gawel S.H., Pandolfino J.E., Kahrilas P.J.* Incidence and prevalence of achalasia in central Chicago, 2004–2014, since the widespread use of high-resolution manometry. *Clin Gastroenterol Hepatol.* 2017;15(3):366–73. DOI: 10.1016/j.cgh.2016.08.030
43. *Sadowski D.C., Ackah F., Jiang B., Svenson L.W.* Achalasia: Incidence, prevalence and survival. A population-based study. *Neurogastroenterol Motil.* 2010;22(9):e256–61. DOI: 10.1111/j.1365-2982.2010.01511.x
44. *Marlais M., Fishman J.R., Fell J.M.E., Haddad M.J., Rawat D.J.* UK incidence of achalasia: An 11-year national epidemiological study. *Arch Dis Child.* 2011;96(2):192–4. DOI: 10.1136/adc.2009.171975
45. *Петровский Б.В.* Кардиоспазм и его хирургическое значение. *Труды 27-го Всесоюзного съезда хирургов.* М., 1962:162–73. [*Petrovsky B.V.* Cardiospasm and surgical significance. *Abstracts of the 27th All-Union congress of surgeons.* Moscow, 1962:162–73. (In Russ.)].
46. *Уткин В.В.* Кардиоспазм. Рига: Зинатне, 1966. [*Utkin V.V.* Cardiospasm. Riga: Zinatne, 1966. (In Russ.)].
47. *Суворова Т.А.* Функциональные заболевания пищевода. В кн.: *Многотомное руководство по хирургии.* М., 1966: Т. 6, кн. 2:317–55. [*Suvorova T.A.* Functional esophageal diseases. In: *Multi-volume manual of surgery.* Moscow, 1966; Vol. 6, book 2:317–55. (In Russ.)].
48. *Моргенштерн А.З.* Ахалазия пищевода. М.: Медицина, 1968. [*Morgenstern A.Z.* Esophageal achalasia. Moscow: Meditsina Publ., 1968. (In Russ.)].
49. *Jung H.-K., Hong S.J., Lee O.Y., Pandolfino J., Park H., Miwa H., et al.* 2019 Seoul Consensus on esophageal achalasia guidelines. *J Neurogastroenterol Motil.* 2020;26(2):180–203. DOI: 10.5056/jnm20014
50. *Swanstr m L.L.* Achalasia: Treatment, current status and future advances. *Korean J Intern Med.* 2019;34(6):1173–80. DOI: 10.3904/kjim.2018.439
51. *Гребенев А.Л.* Ахалазия кардии (клиника, диагностика, лечение): дисс. ... *д-ра мед. наук.* М., 1969. [*Grebenev A.L.* Cardiac achalasia (clinical presentation, diagnosis, treatment): *Dr. Sci.* (*Med.*) *thesis.* Moscow, 1969. (In Russ.)].
52. *Василенко В.Х., Суворова Т.А., Гребенев А.Л.* Ахалазия кардии. М.: Медицина, 1976. [*Vasilenko V.Kh., Suvorova T.A., Grebenev A.L.* Cardiac achalasia. Moscow: Meditsina Publ., 1976. (In Russ.)].
53. *Гребенев А.Л.* Влияние лекарственных препаратов (ацетилхолин, адреналин, папаверин, нитроглицерин и морфин) на двигательную функцию пищевода. *Советская медицина.* 1987;7:17–21. [*Grebenev A.L.* Effect of drugs (acetylcholine, epinephrine, papaverine, nitroglycerin and morphine) on motor function of the esophagus. *Sovetskaya meditsina.* 1987;7:17–21. (In Russ.)].
54. *Вилявин Г.Д., Соловьева В.И., Тимофеева Т.А.* Кардиоспазм. *Патогенез, клиника и лечение.* М.: Медицина, 1971. [*Vilyavin G.D., Solovyov V.I., Timofeyeva T.A.* Cardiospasm. *Pathogenesis, clinical presentation and treatment.* Moscow: Meditsina Publ., 1971. (In Russ.)].
55. *Yadlapati R., Kahrilas P.J., Fox M.R., Bredenoord A.J., Prakash Gyawali C., Roman S., et al.* Esophageal motility disorders on high-resolution manometry: Chicago classification version 4.0. *Neurogastroenterol Motil.* 2021;33(1):e14058. DOI: 10.1111/nmo.14058
56. *Ивашкин В.Т., Маев И.В., Трухманов А.С., Сторонова О.А., Кучерявый Ю.А., Баркалова Е.В. и др.* Манометрия высокого разрешения и новая классификация нарушений моторики пищевода. *Терапевтический архив.* 2018;90(5):93–100. [*Ivashkin V.T., Maev I.V., Trukhmanov A.S., Storonova O.A., Kucheryavyi Yu.A., Barkalova E.V., et al.* High resolution manometry and new classification of esophageal motility disorders. *Terapevticheskii arkhiv.* 2018;90(5):93–100. (In Russ.)]. DOI: 10.26442/terarkh201890593-100
57. *Ивашкин В.Т., Маев И.В., Трухманов А.С., Сторонова О.А., Абдулхаков С.А., Андреев Д.Н. и др.* Рекомендации Российской гастроэнтерологической ассоциации по клиническому применению манометрии высокого разрешения при заболеваниях пищевода. *Российский журнал гастроэнтерологии, гепатологии, колопроктологии.* 2020;30(3):61–88. [*Ivashkin V.T., Mayev I.V., Trukhmanov A.S., Storonova O.A., Abdulkhakov S.A., Andreev D.N., et al.* Recommendations of the Russian Gastroenterological Association on clinical use of high-resolution manometry in diagnosis of esophageal disorders. *Russian Journal of Gastroenterology, Hepatology, Coloproctology.* 2020;30(3):61–88. (In Russ.)]. DOI: 10.22416/1382-4376-2020-30-3-61-88
58. *Kahrilas P.J., Bredenoord A.J., Fox M., Gyawali C.P., Roman S., Smout A.J.P.M., et al.* Expert consensus document: Advances in the management of oesophageal motility disorders in the era of high-resolution manometry: A focus on achalasia syndromes. *Nat Rev Gastroenterol Hepatol.* 2017;14(11):677–88. DOI: 10.1038/nrgastro.2017.132
59. *Sodikoff J.B., Lo A.A., Shetuni B.B., Kahrilas P.J., Yang G.Y., Pandolfino J.E.* Histopathologic patterns among achalasia subtypes. *Neurogastroenterol Motil.* 2016;28(1):139–45. DOI: 10.1111/nmo.12711
60. *Salvador R., Voltarel G., Savarino E., Capovilla G., Pesenti E., Perazzolo A., et al.* The natural history of achalasia: Evidence of a continuum — "The evolutive pattern theory". *Dig Liver Dis.* 2018;50(4):342–7. DOI: 10.1016/j.dld.2017.11.012
61. *Zaninotto G., Bennett C., Boeckxstaens G., Costantini M., et al.* The 2018 ISDE achalasia guidelines. *Dis Esophagus.* 2018;31(9). DOI: 10.1093/dote/doy071
62. *Pandolfino J.E., Gawron A.J.* Achalasia: A systematic review. *JAMA.* 2015;313(18):1841–52. DOI: 10.1001/jama.2015.2996
63. *Oude Nijhuis R.A.B., Prins L.I., Mostafavi N., van Etten-Jamaludin F.S., Smout A.J.P.M., Bredenoord A.J.* Factors associated with achalasia treatment outcomes: Systematic review and meta-analysis. *Clin Gastroenterol Hepatol.* 2020;18(7):1442–53. DOI: 10.1016/j.cgh.2019.10.008
64. *Andolfi C., Fisichella P.M.* Meta-analysis of clinical outcome after treatment for achalasia based on manometric subtypes. *Br J Surg.* 2019;106(4):332–41. DOI: 10.1002/bjs.11049
65. *Ивашкин В.Т., Трухманов А.С., Годжелло Э.А., Маев И.В., Евсютина Ю.В., Лапина Т.Л. и др.* Рекомендации Российской гастроэнтерологической ассоциации по диагностике и лечению ахалазии кардии и кардиоспазма. *Российский журнал гастроэнтерологии, гепатологии, колопроктологии.* 2016;26(4):36–54. [*Ivashkin V.T., Trukhmanov A.S., Godzhello E.A., Mayev I.V., Evsyutina Yu.V., Lapina T.L., et al.* Diagnostics and treatment of cardiac achalasia and cardiospasm: Guidelines of the Russian gastroenterological association. *Russian Journal of Gastroenterology, Hepatology, Coloproctology.* 2016;26(4):36–54. (In Russ.)]. DOI: 10.22416/1382-4376-2016-4-36-54
66. *Трухманов А.С.* Тактика комплексного лечения ахалазии кардии: *дисс. ... канд. мед. наук.* М., 1995. [*Trukhmanov A.S.* Comprehensive treatment approach in cardiac achalasia: *Cand. Sci.* (*Med.*) *thesis.* Moscow, 1995. (In Russ.)].
67. *Евсютина Ю.В., Сторонова О.А., Трухманов А.С., Ивашкин В.Т.* Ахалазия кардии: современные представления об этиологии, патогенезе, клинической картине и диагностике. *Российский журнал гастроэнтерологии, гепатологии, колопроктологии.* 2014;24(6):4–12.

[*Yevsyutina Yu.V., Storonova O.A., Trukhmanov A.S., Ivashkin V.T.* Cardiac achalasia: Modern concepts on etiology, pathogenesis, clinical presentation and diagnostics. *Russian Journal of Gastroenterology, Hepatology, Coloproctology.* 2014;24(6):4–12. (In Russ.)].
68. *Vaezi M.F., Pandolfino J.E., Yadlapati R.H., Greer K.B., Kavitt R.T.* ACG clinical guidelines: Diagnosis and management of achalasia. *Am J Gastroenterol.* 2020;115(9):1393–411. DOI: 10.14309/ajg.0000000000000731
69. *Бектаева Р.Р.* Недостаточность кардии в клинике внутренних болезней (Патогенез. Особенности клинического течения. Дифференцированная терапия): *дисс. … д-ра мед. наук.* М., 1991. [*Bektaeva R.R.* Insufficiency of cardia in the clinic of internal diseases (Pathogenesis. Features of the clinical course. Differentiated therapy): *Dr. Sci.* (*Med.*) *thesis.* Moscow, 1991. (In Russ.)].
70. *Сторонова О.А.* Структурные и метаболические характеристики загрудинной боли эзофагогенного происхождения: *дис. … канд. мед. наук.* М., 2011. [*Storonova O.A.* Structural and metabolic characteristics of sternal pain of esophagogenic origin: *Cand. Sci.* (*Med.*) *thesis*. Moscow, 2011. (In Russ.)].
71. *Boeckxstaens G.E.E.* Achalasia. *Best Pract Res Clin Gastroenterol.* 2007;21(4):595–608. DOI: 10.1016/j.bpg.2007.03.004
72. *Triadafilopoulos G., Boeckxstaens G.E., Gullo R., Patti M.G., Pandolfino J.E., Kahrilas P.J., et al.* The Kagoshima consensus on esophageal achalasia. *Dis Esophagus.* 2012;25(4):337–48. DOI: 10.1111/j.1442-2050.2011.01207.x
73. *Галлингер Ю.И., Годжелло Э.А.* Оперативная эндоскопия пищевода. М.: РНЦХ РАМН, 1999. [*Gallinger Yu.L, Godzhello E.A.* Operational endoscopy of the esophagus. Moscow: RNTsH RAMN Publ., 1999. (In Russ.)].
74. *Годжелло Э.А., Хрусталева М.В., Шатверян Д.Г., Булганина Н.А.* Диагностика и лечение ахалазии кардии – обзор зарубежной литературы. *Экспериментальная и клиническая гастроэнтерология.* 2020;177(5):21–35. [*Godzhello E.A., Khrustaleva M.V., Shatveryan D.G., Bulganina N.A.* Diagnosis and treatment of achalasia – a review of foreign literature. *Experimental and Clinical Gastroenterology.* 2020;177(5):21–35. (In Russ.)]. DOI: 10.31146/1682-8658-ecg-177-5-21-35
75. *Howard P.J, Maher L., Pryde A., Cameron E.W., Heading R.C.* Five year prospective study of the incidence, clinical features, and diagnosis of achalasia in Edinburgh. *Gut.* 1992;33(8):1011–5. DOI: 10.1136/gut.33.8.1011
76. *Reynolds J.C., Parkman H.P.* Achalasia. *Gastroenterol Clin North Am.* 1989;18(2):223–55.
77. *Fisichella P.M., Raz D., Palazzo F., Niponmick I., Patti M.G.* Clinical, radiological, and manometric profile in 145 patients with untreated achalasia. *World J Surg.* 2008;32(9):1974–79. DOI: 10.1007/s00268-008-9656-z
78. *Andersson M., Lundell L., Kostic S., Ruth M., Lönroth H., Kjellin A., et al.* Evaluation of the response to treatment in patients with idiopathic achalasia by the timed barium esophagogram: Results from a randomized clinical trial. *Dis Esophagus.* 2009;22(3):264–73. DOI: 10.1111/j.1442-2050.2008.00914.x
79. *Булганина Н.А., Годжелло Э.А., Хрусталева М.В.* Многолетние результаты лечения ахалазии кардии методом комбинированной баллонной дилатации. Роль манометрии высокого разрешения в диагностике ахалазии. Эндоскопические и манометрические параллели. *Экспериментальная и клиническая гастроэнтерология.* 2023;5:34–44. [*Bulganina N.A., Godzhello E.A., Khrustaleva M.V.* Long-term results of treatment of achalasia cardia by combined balloon dilation. The role of high-resolution manometry in the diagnosis of achalasia. Endoscopic and manometric parallels. *Experimental and Clinical Gastroenterology.* 2023;5:34–44. (In Russ.)]. DOI: 10.31146/1682-8658-ecg-213-5-34-44
80. *Blonski W., Kumar A., Feldman J., Richter J.E.* Timed barium swallow: Diagnostic role and predictive value in untreated achalasia, esophagogastric junction outflow obstruction, and non-achalasia dysphagia. *Am J Gastroenterol.* 2018;113(2):196–203. DOI: 10.1038/ajg.2017.370
81. *Oude Nijhuis R., Zaninotto G., Roman S., Boeckxstaens G., Fockens P., Langendam M.W., et al.* European guideline on achalasia – UEG and ESNM recommendations. *United European Gastroenterol J.* 2020;8(1):13–33. DOI: 10.1177/2050640620903213
82. *Blonski W., Kumar A., Feldman J., Richter J.E.* Timed barium swallow for assessing long-term treatment response in patients with achalasia: Absolute cutoff versus percent change – A cross-sectional analytic study. *Neurogastroenterol Motil.* 2021;33(3):e14005. DOI: 10.1111/nmo.14005
83. *De Oliveira J.M., Birgisson S., Doinoff C., Einstein D., Herts B., Davros W., et al.* Timed barium swallow: A simple technique for evaluating esophageal emptying in patients with achalasia. *AJR Am J Roentgenol.* 1997;169(2):473–9. DOI: 10.2214/ajr.169.2.9242756
84. *Barium sulfate.* In: *Meyler's Side Effects of Drugs.* (*Sixteenth Edition*). *The International Encyclopedia of Adverse Drug Reactions and Interactions.* Elsevier: 2016:827–829. DOI: 10.1016/B978-0-444-53717-1.00350-4
85. *Hajhosseini P., Forootan M., Shadbakht B., Bakhtavar K., Zali M.R., Sedighi N.* Novel description on esophageal timed barium swallow: A correlation between advanced parametrization and esophageal X-ray images. *Gastroenterol Hepatol Bed Bench.* 2022;15(4):366–76. DOI: 10.22037/ghfbb.v15i4.2467
86. *Roman S., Huot L., Zerbib F., Bruley des Varannes S., Gourcerol G., Coffin B., et al.* High-resolution manometry improves the diagnosis of esophageal motility disorders in patients with dysphagia: A randomized multicenter study. *Am J Gastroenterol.* 2016;111(3):372–80. DOI: 10.1038/ajg.2016.1
87. *Tack J., Pauwels A., Roman S., Savarino E., Smout A.; ESNM HRM consensus group.* European Society for Neurogastroenterology and Motility (ESNM) recommendations for the use of high-resolution manometry of the esophagus. *Neurogastroenterol Motil.* 2021;33(5):e14043. DOI: 10.1111/nmo.14043
88. *Savarino E., de Bortoli N., Bellini M., Galeazzi F., Ribolsi M., Salvador R., et al.* Practice guidelines on the use of esophageal manometry – A GISMAD-SIGE-AIGO medical position statement. *Dig Liver Dis.* 2016;48(10):1124–35. DOI: 10.1016/j.dld.2016.06.021
89. *Yamasaki T., Tomita T., Mori S., Takimoto M., Tamura A., Hara K., et al.* Esophagography in patients with esophageal achalasia diagnosed with high-resolution esophageal manometry. *J Neurogastroenterol Motil.* 2018;24(3):403–9. DOI: 10.5056/jnm17147
90. *Moonen A., Annese V., Belmans A., Bredenoord A.J., Bruley des Varannes S., Costantini M., et al.* Long-term results of the European achalasia trial: A multicentre randomised controlled trial comparing pneumatic dilation versus laparoscopic Heller myotomy. *Gut.* 2016;65(5):732–9. DOI: 10.1136/gutjnl-2015-310602
91. *Ang D., Hollenstein M., Misselwitz B., Knowles K., Wright J., Tucker E., et al.* Rapid Drink Challenge in high-resolution manometry: An adjunctive test for detection of esophageal motility disorders. *Neurogastroenterol Motil.* 2017;29(1):e12902. DOI: 10.1111/nmo.12902
92. *Eckardt V.F., Aignherr C., Bernhard G.* Predictors of outcome in patients with achalasia treated by pneumatic dilation. *Gastroenterology.* 1992;103(6):1732–8. DOI: 10.1016/0016-5085(92)91428-7
93. *Khashab M.A., Vela M.F., Thosani N., Agrawal D., Buxbaum J.L., Abbas Fehmi S.M., et al.* ASGE guideline on the management of achalasia. *Gastrointest Endosc.* 2020;91(2):213–27.e6. DOI: 10.1016/j.gie.2019.04.231
94. *Boeckxstaens G.E., Annese V., des Varannes S.B., Chaussade S., Costantini M., Cuttitta A., et al.* Pneumatic dilation versus laparoscopic heller's myotomy for idiopathic achalasia. *N Engl J Med.* 2011;364(19):1807–16. DOI: 10.1056/NEJMoa1010502
95. *Ponds F.A., Fockens P., Lei A., Neuhaus H., Beyna T., Kandler J., et al.* Effect of peroral endoscopic myotomy

vs pneumatic dilation on symptom severity and treatment outcomes among treatment-naive patients with achalasia: A randomized clinical trial. *JAMA*. 2019;322(2):134–44. DOI: 10.1001/jama.2019.8859
96. *Werner Y.B., Hakanson B., Martinek J., Repici A., von Rahden B.H.A., Bredenoord A.J., et al.* Endoscopic or surgical myotomy in patients with idiopathic achalasia. *N Engl J Med*. 2019;381(23):2219–29. DOI: 10.1056/NEJMoa1905380
97. *Slone S., Kumar A., Jacobs J., Velanovich V., Richter J.E.* Accuracy of Achalasia Quality of Life and Eckardt scores for assessment of clinical improvement post treatment for achalasia. *Dis Esophagus*. 2021;34(2):doaa080. DOI: 10.1093/dote/doaa080
98. *Müller M., Keck C., Eckardt A.J., Werling S., Wehrmann T., König J., et al.* Outcomes of pneumatic dilation in achalasia: Extended follow-up of more than 25 years with a focus on manometric subtypes. *J Gastroenterol Hepatol*. 2018;33(5):1067–74. DOI: 10.1111/jgh.14044
99. *Eckardt V.F., Hoischen T., Bernhard G.* Life expectancy, complications, and causes of death in patients with achalasia: Results of a 33-year follow-up investigation. *Eur J Gastroenterol Hepatol*. 2008;20(10):956–60. DOI: 10.1097/MEG.0b013e3282fbf5e5
100. *Gelfond M., Rozen P., Gilat T.* Isosorbide dinitrate and nifedipine treatment of achalasia: A clinical, manometric and radionuclide evaluation. *Gastroenterology*.1982;83(5):963–69.
101. *Bortolotti M., Labò G.* Clinical and manometric effects of nifedipine in patients with esophageal achalasia. *Gastroenterology*. 1981;80(1):39–44.
102. *George N., Abdallah J., Maradey-Romero C., Gerson L., Fass R.* Review article: The current treatment of non-cardiac chest pain. *Aliment Pharmacol Ther*. 2016;43(2):213–39. DOI: 10.1111/apt.13458
103. *Bassotti G., Annese V.* Review article: Pharmacological options in achalasia. *Aliment Pharmacol Ther*. 1999;13(11):1391–6. DOI: 10.1046/j.1365-2036.1999.00645.x
104. *Chrystoja C.C., Darling G.E., Diamant N.E., Kortan P.P., Tomlinson G.A., Deitel W., et al.* Achalasia-specific quality of life after pneumatic dilation or laparoscopic heller myotomy with partial fundoplication: A multicenter, randomized clinical trial. *Am J Gastroenterol*. 2016;111(11):1536–45. DOI: 10.1038/ajg.2016.402
105. *van Hoeij F.B., Prins L.I., Smout A.J.P.M., Bredenoord A.J.* Efficacy and safety of pneumatic dilation in achalasia: A systematic review and meta-analysis. *Neurogastroenterol Motil*. 2019;31(7):e13548. DOI: 10.1111/nmo.13548
106. *Годжелло Э.А., Хрусталева М.В., Булганина Н.А., Шатверян Д.Г., Дехтяр М.А.* Место и роль эндоскопической баллонной дилатации при ахалазии кардии в эпоху пероральной эндоскопической миотомии (POEM). Тридцатилетний опыт. *Экспериментальная и клиническая гастроэнтерология*. 2019;4:105–10. [*Godzhello E.A., Khrustaleva M.V., Bulganina N.A., Shatveryan D.G., Dekhtyar M.A.* Endoscopic balloon dilation for achalasia in the era of peroral endoscopic myotomy (POEM). Thirty years' experience. *Experimental and Clinical Gastroenterology*. 2019;4:105–10. (In Russ.)]]. DOI: 10.31146/1682-8658-ecg-164-4-105-110
107. *Булганина Н.А., Годжелло Э.А., Хрусталева М.В.* Эндоскопическая баллонная гидродилатация в лечении ахалазии кардии. *Клиническая и экспериментальная хирургия. Журнал имени академика Б.В. Петровского*. 2022;10(1):41–52. [*Bulganina N.A., Godzhello E.A., Khrustaleva M.V.* Endoscopic balloon hydrodilation in the treatment of achalasia of the cardia. *Clinical and Experimental Surgery. Petrovsky Journal*. 2022;10(1):41–52. (In Russ.)]. DOI: 10.33029/2308-1198-2022-10-1-41-52
108. *Ponce J., Garrigues V., Pertejo V., Sala T., Berenguer J.* Individual prediction of response to pneumatic dilation in patients with achalasia. *Dig Dis Sci*. 1996;41(11):2135–41. DOI: 10.1007/BF02071392
109. *Alonso-Aguirre P., Aba-Garrote C., Estévez-Prieto E., González-Conde B., Vázquez-Iglesias J.L.* Treatment of achalasia with the Witzel dilator: A prospective randomized study of two methods. *Endoscopy*. 2003;35(5):379–82. DOI: 10.1055/s-2003-38777
110. *Tuset J.A., Luján M., Huguet J.M., Canelles P., Medina E.* Endoscopic pneumatic balloon dilation in primary achalasia: Predictive factors, complications, and long-term follow-up. *Dis Esophagus*. 2009;22(1):74–9. DOI: 10.1111/j.1442-2050.2008.00874.x
111. *Meng F., Li P., Wang Y., Ji M., Wu Y., Yu L., et al.* Peroral endoscopic myotomy compared with pneumatic dilation for newly diagnosed achalasia. *Surg Endosc*. 2017;31(11):4665–72. DOI: 10.1007/s00464-017-5530-0
112. *Sanaka M.R., Hayat U., Thota P.N., Jegadeesan R., Ray M., Gabbard S.L., et al.* Efficacy of peroral endoscopic myotomy vs other achalasia treatments in improving esophageal function. *World J Gastroenterol*. 2016;22(20):4918–25. DOI: 10.3748/wjg.v22.i20.4918
113. *Dahiya D.S., Nivedita F., Perisetti A., Goyal H., Inamdar S., Gangwani M.K., et al.* Clinical outcomes and complications for achalasia patients admitted after per-oral endoscopic myotomy. *Gastroenterology Res*. 2023;16(3):141–8. DOI: 10.14740/gr1617
114. *Kim J.Y., Min Y.W.* Peroral endoscopic myotomy for esophageal motility disorders. *Clin Endosc*. 2020;53(6):638–45. DOI: 10.5946/ce.2020.223
115. *Li H., Peng W., Huang S., Ren Y., Peng Y., Li Q., et al.* The 2 years' long-term efficacy and safety of peroral endoscopic myotomy for the treatment of achalasia: A systematic review. *J Cardiothorac Surg*. 2019;14(1):1. DOI: 10.1186/s13019-018-0811-9
116. *Khashab M.A., Benias P.C., Swanstrom L.L.* Endoscopic myotomy for foregut motility disorders. *Gastroenterology*. 2018;154(7):1901–10. DOI: 10.1053/j.gastro.2017.11.294
117. *Stavropoulos S.N., Modayil R.J., Friedel D., Savides T.* The International Per Oral Endoscopic Myotomy Survey (IPOEMS): A snapshot of the global POEM experience. *Surg Endosc*. 2013;27(9):3322–38. DOI: 10.1007/s00464-013-2913-8
118. *Ofosu A., Mohan B.P., Ichkhanian Y., Masadeh M., Febin J., Barakat M., et al.* Peroral endoscopic myotomy (POEM) vs pneumatic dilation (PD) in treatment of achalasia: A meta-analysis of studies with ≥ 12-month follow-up. *Endosc Int Open*. 2021;9(7):E1097–107. DOI: 10.1055/a-1483-9406
119. *Niño-Ramírez S., Ardila O., Rodrigues F.H., Londono J., Pérez S., Sánchez S., et al.* Major adverse events related to endoscopic or laparoscopic procedures in achalasia. A systematic review and meta-analysis. *Rev Gastroenterol Mex (Engl Ed)*. 2023;88(1):36–43. DOI: 10.1016/j.rgmxen.2021.11.012
120. *Inoue H., Minami H., Kobayashi Y., Sato Y., Kaga M., Suzuki M., et al.* Peroral endoscopic myotomy (POEM) for esophageal achalasia. *Endoscopy*. 2010;42(4):265–71. DOI: 10.1055/s-0029-1244080
121. *Teitelbaum E.N., Sternbach J.M., El Khoury R., Soper N.J., Pandolfino J.E., Kahrilas P.J., et al.* The effect of incremental distal gastric myotomy lengths on EGJ distensibility during POEM for achalasia. *Surg Endosc*. 2016;30(2):745–50. DOI: 10.1007/s00464-015-4269-8
122. *Crespin O.M., Liu L.W.C., Parmar A., Jackson T.D., Hamid J., Shlomovitz E., et al.* Safety and efficacy of POEM for treatment of achalasia: A systematic review of the literature. *Surg Endosc*. 2017;31(5):2187–201. DOI: 10.1007/s00464-016-5217-y
123. *Zhang X.-C., Li Q.-L., Xu M.-D., Chen S.-Y., Zhong Y.S., Zhang Y.Q., et al.* Major perioperative adverse events of peroral endoscopic myotomy: A systematic 5-year analysis. *Endoscopy*. 2016;48(11):967–78. DOI: 10.1055/s-0042-110397
124. *Zhu B.-Q., Cai M.-Y., Zhang X.-C., Yu Y.-F., Chen S.-Y., Zhou P.-H.* Benefit of preoperative antibiotic prophylaxis for peroral endoscopic myotomy (POEM):

A randomized controlled trial. *Gastrointest Endosc*. 2017;85(5):AB184–5. DOI: 10.1016/j.gie.2017.03.403
125. *Appendix E.* Algorithms for diagnosing infections. *Am J Epidemiol.* 1980;111(5):635–43. DOI: 10.1093/oxfordjournals.aje.a112941
126. *Zhai Y., Linghu E., Li H., Qin Z., Shi X., Peng L., et al.* Is preoperative antibiotics necessary for infection prevention before peroral endoscopic myotomy. *Am J Gastroenterol.* 2013;108:S587.
127. *Maselli R., Oliva A., Attardo S., Nicoletti R., Finati E., Vetrano S., et al.* Risk of microbial translocation in patients undergoing per-oral endoscopic myotomy for achalasia. Preliminary results. *Dig Liver Dis.* 2018;50(2 Suppl.): e183–4. DOI: 10.1016/S1590-8658(18)30532-2
128. *Bonavina L., Asti E., Sironi A., Bernardi D., Aiolfi A.* Hybrid and total minimally invasive esophagectomy: how I do it. *Journal of Thoracic Disease.* 2017;9(Suppl 8): S761-S772. DOI: 10.21037/jtd.2017.06.55
129. *Kim G.H., Jung K.W., Jung H.-Y., Kim M.-J., Na H.K., Ahn J.Y., et al.* Superior clinical outcomes of peroral endoscopic myotomy compared with balloon dilation in all achalasia subtypes. *J Gastroenterol Hepatol*. 2019;34(4):659–65. DOI: 10.1111/jgh.14616
130. *Werner Y.B., Costamagna G., Swanström L.L., von Renteln D., Familiari P., Sharata A.M., et al.* Clinical response to peroral endoscopic myotomy in patients with idiopathic achalasia at a minimum follow-up of 2 years. *Gut.* 2016;65(6):899–906. DOI: 10.1136/gutjnl-2014-308649
131. *Дробязгин Е.А., Чикинев Ю.В., Митько Н.И.* Применение пероральной эндоскопической миотомии при лечении пациентов с ахалазией пищевода (опыт 100 операций). *Доказательная гастроэнтерология*. 2023;12(2):25–33. [*Drobayzgin E.A., Chikinev Yu.V., Mitko N.I.* Peroral endoscopic myotomy for the treatment of achalasia: Single-center experience from 100 operations. *Russian Journal of Evidence-Based Gastroenterology*. 2023;12(2):25–33. (In Russ.)]. DOI: 10.17116/dokgastro20231202125
132. *Pasricha P.J., Ravich W.J., Hendrix T.R., Sostre S., Jones B., Kalloo A.N.* Treatment of achalasia with intrasphincteric injection of botulinum toxin: A pilot trial. *Ann Intern Med.* 1994;121(8):590–1. DOI: 10.7326/0003-4819-121-8-199410150-00006
133. *Leyden J.E., Moss A.C., MacMathuna P.* Endoscopic pneumatic dilation versus botulinum toxin injection in the management of primary achalasia. *Cochrane Database Syst Rev.* 2014;2014(12):CD005046. DOI: 10.1002/14651858.CD005046.pub3
134. *Pasricha P.J., Ravich W.J., Hendrix T.R., Sostre S., Jones B., Kalloo A.N.* Intrasphincteric botulinum toxin for the treatment of achalasia. *N Engl J Med*. 1995;332(12):774–8. DOI: 10.1056/NEJM199503233321203
135. *van Hoeij F.B., Tack J.F., Pandolfino J.E., Sternbach J.M., Roman S., Smout A.J., et al.* Complications of botulinum toxin injections for treatment of esophageal motility disorders. *Dis Esophagus.* 2017;30(3):1–5. DOI: 10.1111/dote.12491
136. *Zaninotto G., Annese V., Costantini M., Del Genio A., Costantino M., Epifani M., et al.* Randomized controlled trial of botulinum toxin versus laparoscopic Heller myotomy for esophageal achalasia. *Ann Surg.* 2004;239(3):364–70. DOI: 10.1097/01.sla.0000114217.52941.c5
137. *Annese V., Basciani M., Perri F., Lombardi G., Frusciante V., Simone P., et al.* Controlled trial of botulinum toxin injection versus placebo and pneumatic dilation in achalasia. *Gastroenterology.* 1996;111(6):1418–24. DOI: 10.1016/s0016-5085(96)70002-1
138. *Annese V., Bassotti G., Coccia G., Dinelli M., D'Onofrio V., Gatto G., et al.* A multicentre randomised study of intrasphincteric botulinum toxin in patients with oesophageal achalasia. GISMAD Achalasia Study Group. *Gut*. 2000;46(5):597–600. DOI: 10.1136/gut.46.5.597
139. *Campos G.M., Vittinghoff E., Rabl C., Takata M., Gadenst tter M., Lin F., et al.* Endoscopic and surgical treatments for achalasia: A systematic review and meta-analysis. *Ann Surg.* 2009;249(1):45–57. DOI: 10.1097/SLA.0b013e31818e43ab
140. *Maeso S., Reza M., Mayol J.A., Blasco J.A., Guerra M., Andradas E., et al.* Efficacy of the Da Vinci surgical system in abdominal surgery compared with that of laparoscopy. *Ann Surg.* 2010;252(2):254–62. DOI: 10.1097/SLA.0b013e3181e6239e
141. *Ataya K., Bsat A., Aljaafreh A., Bourji H., Al Ayoubi A.R., Hassan N.* Robot-assisted Heller myotomy versus laparoscopic Heller myotomy: A systematic review and meta-analysis. *Cureus.* 2023;15(11):e48495. DOI: 10.7759/cureus.48495
142. *Facciorusso A., Singh S., Abbas Fehmi S.M., Annese V., Lipham J., Yadlapati R.* Comparative efficacy of first-line therapeutic interventions for achalasia: A systematic review and network meta-analysis. *Surg Endosc*. 2021;35(8):4305–14. DOI: 10.1007/s00464-020-07920-x
143. *Mundre P., Black C.J., Mohammed N., Ford A.C.* Efficacy of surgical or endoscopic treatment of idiopathic achalasia: A systematic review and network meta-analysis. *Lancet Gastroenterol Hepatol*. 2021;6(1):30–8. DOI: 10.1016/S2468-1253(20)30296-X
144. *Talukdar R., Inoue H., Reddy D.N.* Efficacy of peroral endoscopic myotomy (POEM) in the treatment of achalasia: A systematic review and meta-analysis. *Surg Endosc*. 2015;29(11):3030–46. DOI: 10.1007/s00464-014-4040-6
145. *Docimo S. Jr., Mathew A., Shope A.J., Winder J.S., Haluck R.S., Pauli E.M.* Reduced postoperative pain scores and narcotic use favor per-oral endoscopic myotomy over laparoscopic Heller myotomy. *Surg Endosc*. 2017;31(2):795–800. DOI: 10.1007/s00464-016-5034-3
146. *Falkenback D., Johansson J., Öberg S., Kjellin A., Wenner J., Zilling T., et al.* Heller's esophagomyotomy with or without a 360° floppy Nissen fundoplication for achalasia. Long-term results from a prospective randomized study. *Dis Esophagus*. 2003;16(4):284–90. DOI: 10.1111/j.1442-2050.2003.00348.x
147. *Marano L., Pallabazzer G., Solito B., Santi S., Pigazzi A., De Luca R., et al.* Surgery or peroral esophageal myotomy for achalasia: A systematic review and meta-analysis. *Medicine (Baltimore)*. 2016;95(10):e3001. DOI: 10.1097/MD.0000000000003001
148. *Wright A.S., Williams C.W., Pellegrini C.A., Oelschlager B.K.* Long-term outcomes confirm the superior efficacy of extended Heller myotomy with Toupet fundoplication for achalasia. *Surg Endosc.* 2007;21(5):713–8. DOI: 10.1007/s00464-006-9165-9
149. *Santoro G., Sheriff N., Noronha J., Nunes Q., Tandon A.* Heller myotomy versus Heller myotomy with fundoplication in patients with achalasia: A systematic review and meta-analysis. *Ann R Coll Surg Engl*. 2022;104(3):158–64. DOI: 10.1308/rcsann.2020.7123
150. *Aiolfi A., Asti E., Bonitta G., Bonavina L.* Esophagectomy for end-stage achalasia: Systematic review and meta-analysis. *World J Surg.* 2018;42(5):1469–76. DOI: 10.1007/s00268-017-4298-7
151. *Orlandini M.F., Serafim M.C.A., Datrino L.N., Tavares G., Tristão L.S., Dos Santos C.L., et al.* Myotomy in sigmoid megaesophagus: is it applicable? A systematic review and meta-analysis. *Dis Esophagus*. 2021;34(10):doab053. DOI: 10.1093/dote/doab053
152. *Stefanidis D., Richardson W., Farrell T.M., Kohn G.P., Augenstein V., Fanelli R.D.; Society of American Gastrointestinal and Endoscopic Surgeons.* SAGES guidelines for the surgical treatment of esophageal achalasia. *Surg Endosc*. 2012;26(2):296–311. DOI: 10.1007/s00464-011-2017-2
153. *Tustumi F., Bernardo W.M., da Rocha J.R.M., Szachnowicz S., Seguro F.C., Bianchi E.T., et al.* Esophageal achalasia: A risk factor for carcinoma. A systematic review and meta-analysis. *Dis Esophagus*. 2017;30(10):1–8. DOI: 10.1093/dote/dox072

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