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CURRENT MANAGEMENT OF ACHALASIA CARDIA

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Introduction

Achalasia cardia (AC) is an esophageal motility disorder characterized by esophageal aperistalsis and incomplete or absent relaxation of the lower esophageal sphincter (LES) in response to swallowing. The functional obstruction at the esophagogastric junction (EGJ) impairs the transit of food [1]. The etiology of the disease has not been fully elucidated, but it is believed that the determining factors may include infectious, autoimmune and genetic components [2]. Achalasia is complex in terms of both etiology and management possibilities.

The most common signs and symptoms of a patient with achalasia are dysphagia (the cardinal symptom), regurgitation, and weight loss [1]. In 1992, the German physician Volker F. Eckardt developed a clinical tool to assess the severity of symptoms, known as the Eckardt score [3]. For the group of patients selected for the doctoral thesis, the Eckardt score was assessed both pre-therapeutically and post-therapeutically, generating statistically significant results, which will be detailed in the special part of the thesis.

According to current European guidelines for achalasia, the diagnosis is primarily established through barium swallow, upper digestive endoscopy, and esophageal manometry, the latter being the "gold standard" investigation with the highest sensitivity [4], [5], [6].

Currently, the first-line therapeutic options are laparoscopic Heller myotomy (HM), pneumatic dilation (PD), and peroral endoscopic myotomy (POEM) [1], [6]. One of the goals of this scientific work is to analyze and compare various aspects related to the therapeutic methods available in our clinic, namely HM and PD.

Due to the growing number and complexity of achalasia cases addressed by the Center of Excellence in Esophageal Surgery over the past 10 years, paraclinical investigations necessary for the management of achalasia, such as endoscopy, esophagogastric barium transit, esophageal pH-metry and high-resolution manometry have been increasingly utilized. These advancements have led me to choose this research topic with the aim of establishing the current optimal management of achalasia cardia, including the possibility of correlating pre-therapeutic clinical status with treatment outcomes and patient satisfaction regarding post-therapeutic quality of life.

The doctoral thesis includes a general part, presenting current concepts regarding the diagnosis and treatment of achalasia, and a special part dedicated to personal contributions.

II. PERSONAL CONTRIBUTIONS

3. Working Hypothesis and General Objectives

The treatment of achalasia is palliative, with the objective of facilitating digestive transit at the level of the esophagus and the LES. Endoscopic techniques play a crucial role in the therapeutic management of achalasia, allowing for the performance of pneumatic dilation (PD), botulinum toxin injection (BTI), peroral endoscopic myotomy (POEM), and stent placement [1], [6]. Surgical intervention (Heller myotomy with partial fundoplication) holds a central role in the therapeutic approach to this pathology and offers long-term results. All therapeutic methods have proven effective, but some patients may relapse or develop symptoms of gastroesophageal reflux disease (GERD) [7].

Esophageal or gastric mucosal perforation is a severe complication of achalasia treatment. Intra-procedural detection allows for the prompt institution of conservative or endoscopic treatment (using clips or temporary esophageal stents) (6). Typically, if repaired intraoperatively, it does not have direct consequences on the patient's outcome. However, if unrecognized, it can lead to complications, increased hospitalization duration, increased treatment costs, and a decrease in the quality of life.

The objectives of the scientific research were to compare various aspects regarding therapeutic methods (PD and HM), assess risk factors for unfavorable therapeutic response and recurrence, evaluate the role of intraoperative endoscopy in preventing acute complications, and optimize treatment to achieve therapeutic success. Additionally, the study evaluated therapeutic response and identified risk factors for the occurrence of esophageal or gastric mucosal perforations during HM or after PD, analyzing their implications on both immediate and long-term outcomes of the performed treatment.

4. General Research Methodology

I conducted a retrospective study analyzing various management approaches for a group of 98 patients with achalasia cardia who were admitted and treated at the General and Esophageal Surgery Clinic of "Saint Mary" Hospital in Bucharest during 2016-2023. We examined general patient identification data, age, sex, risk factors, personal pathological history, symptoms at diagnosis, paraclinical investigations performed, results of these investigations, type of treatment administered, preoperative evaluation, subtype of achalasia, Eckardt score before and after treatment, the length of myotomy in cases where it was performed, intraoperative incidents, intraoperative investigations, early and late postoperative complications, admission to the intensive care unit, length of hospitalization, and the costs of the procedures.

The selection criteria included: achalasia treatment performed through PD or MH via classical or laparoscopic methods, treatment being carried out within the aforementioned clinic, patients treated between 2016 and 2023, age over 18 years, clinical evaluation using the Eckardt score pre- and post-therapeutically, patients with or without other achalasia treatments performed prior to admission, and the patients' consent to be included in the study.

This research includes two studies. Patients were selected from the initial cohort based on the study periods and the specific objectives of each study.

In the first study, a retrospective analysis was conducted on a group of 73 patients with achalasia, treated surgically by Heller myotomy.

Inclusion criteria for the study were laparoscopic surgical treatment of achalasia and age over 18 years.

Exclusion criteria included patients with recurrence after laparoscopic, robotic, or classical esocardiomyotomy. Ultimately, 60 patients treated laparoscopically through esocardiomyotomy with an associated antireflux procedure were included in the study.

Depending on the presence or absence of possible intraoperative perforations of the gastric or esophageal mucosa, they were divided into two subgroups (with or without perforation). Various demographic, preoperative clinical and paraclinical variables, as well as intraoperative data, such as procedures associated with the intervention (intraoperative manometry, intraoperative upper digestive endoscopy, administration of methylene blue on the

Faucher tube) were studied to identify risk factors associated with perforations. Immediate and long-term postoperative follow-up of patients with intraoperative mucosal perforations allowed to collect data regarding the occurrence of postoperative complications and functional outcomes.

In the second study, a retrospective analysis of the observation sheets and operative protocols of 98 patients with achalasia, who were treated either endoscopically (PD) or surgically (laparoscopic HM with Dor or Toupet fundoplication), was conducted.

Inclusion criteria for patients were age between 18 and 86 years, patients with either an initial or recurrent disease, and an Eckardt score of more than 3 at admission.

Exclusion criteria included the inability to evaluate post-therapeutic clinical status using the Eckardt score in 2022.

Clinical evaluation was conducted using the **Eckardt score**, which assesses 4 symptoms: weight loss, dysphagia, retrosternal pain, and regurgitation. Depending on severity, each symptom is assigned between 0 and 3 points, and the total score ranges from 0 to 12 points. Therapeutic success correlates with an Eckardt score ≤ 3 , while a score > 3 indicates therapeutic failure. When the Eckardt score is > 3 , and symptoms have reappeared after a variable remission period, the disease is considered recurrent.

Upper digestive endoscopy (UDE) was performed to exclude pseudoachalasia and to evaluate esophageal stasis after a 12-hour fasting period. This interval is usually insufficient for esophageal emptying, and the present stasis may be mistaken for GERD. The presence of associated esophagitis and gastritis was also assessed.

Barium swallow (BS) was performed for diagnostic purposes, evaluating the following aspects: presence of esophageal stasis, JEG stenosis (defining elements of achalasia), and the degree of esophageal dilation. Radiological diagnostic criteria for achalasia include: *maximum diameter > 2 cm, presence of tertiary contractions, grade III dilation (esophageal diameter greater than 6 cm), barium column height in the esophagus > 5 cm after 1 minute and > 2 cm after 5 minutes.*

Esophageal manometry was performed preoperatively with a conventional manometer. The relaxation of the LES during swallowing was evaluated by measuring its length, basal pressure, resting pressure, LES relaxation, LES relaxation period, and LES

volume vector. Additionally, esophageal motility was evaluated by assessing waves with amplitudes >35 mmHg and the number of propagated waves.

Individually, the type of achalasia was determined based on manometric criteria according to the **Chicago 3.0 Classification**: Type I is characterized by the complete absence of peristalsis and lack of pan-esophageal pressurization; Type II by the complete absence of peristalsis and pan-esophageal pressurization in at least 20% of swallows; and Type III by premature contractions in at least 20% of swallows and absence of peristalsis. All three types have an abnormal median integrated relaxation pressure (IRP).

Patients underwent either endoscopic (PD) or surgical (classical or laparoscopic) treatment. Some of these patients were treated laparoscopically by HM followed by an antireflux procedure, such as anterior 180° hemifundoplication (Dorr procedure) or posterior 270° fundoplication (Toupet procedure). In this case, the esophagus was dissected circumferentially transhiatally for a length of 10-12 cm. The muscle wall was cut with laparoscopic scissors or 5 mm Ligasure-type vascular sealing forceps after dissecting the muscle sheath from the submucosal layer, with identification and preservation of the anterior vagus nerve. The length of the myotomy at the esophagus and cardia was measured intraoperatively.

Intraoperative manometry was performed to verify the reduction of pressure in the lower esophageal sphincter, secondary to an effective esogastric myotomy.

Intraoperative upper digestive endoscopy was performed to evaluate the length of the esocardiomyotomy, the integrity of the mucosa, and to detect possible mucosal perforations.

Esophageal or gastric mucosal perforations were detected by the presence of air bubbles in the lavage fluid (saline) introduced into the hiatal region during endoscopy or by the visualization of methylene blue solution outside the lumen of the digestive tube. They were initially sutured and then covered during hemifundoplication to seal it with the gastric serosa. Millimetric perforations required wound suturing with separate PDO 3-0 or Vicryl 3-0 stitches.

Postoperative or post-dilation treatment outcomes were evaluated by assessing the degree of symptom relief, as evidenced by comparing pre- and post-therapeutic **Eckardt scores**. Treatment was considered optimal if a post-therapeutic Eckardt score of <3 was

achieved. Conversely, patients with a post-treatment Eckardt score of >3 were considered to have recurrent disease or ineffective treatment.

The number of days spent postoperatively in the intensive care unit, in the surgery ward, and the total duration of hospitalization were evaluated.

Statistical Analysis Methods

The data were statistically evaluated using Fisher's test, Independent Samples Test, Mann-Whitney U test, and Likelihood Ratio, as appropriate. The ROC curve was employed to identify threshold values for continuous variables.

After entering the data obtained from the study protocols into the database fields, they were processed using SPSS (Statistical Package for the Social Sciences) version 23.0 and Excel software packages. In the comparison of quantitative data, depending on the normality of the data, the Independent Samples T Test (for groups with normally distributed data) and Mann-Whitney U Test (for groups without normal distribution) were used. Quantitative data were tested for normality and homogeneity of variances using Levene's Test. For categorical data, Pearson Chi-Square and Fisher's Exact Test were utilized. A probability of error less than 5% ($p < 0.05$) was considered the threshold for statistical significance.

5. Laparoscopic Esocardiomyotomy – Risk Factors and Immediate and Long-Term Implications of Intraoperative Mucosal Perforation

5.1. Introduction:

An effective treatment for achalasia is surgical intervention through Heller myotomy [7]. However, the technique is not without risks, one of the serious complications being esophageal perforation, especially if it goes unrecognized [8]. To minimize this risk, it is essential to perform an appropriate surgical technique and to carefully monitor both intra- and post-operatively to promptly identify and manage any perforation.

The aim of the study is to identify the risk factors for the occurrence of esophageal or gastric mucosal perforations during laparoscopic Heller myotomy or after endoscopic dilations, to evaluate the therapeutic response, and to assess the implications of this event on the immediate and long-term outcomes of the treatment performed.

5.2. Patients and methods

A retrospective analysis was performed on a group of 73 patients with achalasia, who were treated surgically through Heller myotomy and divided into two subgroups based on the presence or absence of intraoperative perforations of the gastric or esophageal mucosa.

The distribution of patients by sex and age revealed a predominance of males (60%) over females (40%) within the studied group (the group included 60 patients, 24 females and 36 males) with an average age of **50,42±15,67** years, ranging from 20 to 80 years.

The distribution of patients based on tobacco use showed that, within the studied group, 19 patients were smokers (31,7%).

The distribution of patients based on personal pathological history revealed that, within the studied group, only 3 patients had a history of abdominal surgery (5%).

Distribution of patients based on previous treatment for achalasia cardia. In the studied cohort, pneumatic esophageal balloon dilation of 30 mm was performed on 9 patients (15%), with an average of **1,66±1** session per patient over an average interval of **22,33±22,65** months. The persistence of dysphagia after these dilations served as a criterion for opting for minimally invasive surgical treatment.

Distribution of patients based on symptomatology. The average duration of symptoms in the studied cohort was **39,03 ±54,52** months. The symptoms present included

dysphagia (60/60 patients), retrosternal pain (20/60 patients), regurgitation (42/60 patients), and weight loss over the last 6 months (29/60 patients).

Barium Swallow (BS), using a barium sulfate suspension or iodine-based water-soluble substances, can provide very useful information in diagnosing esophageal stenosis caused by achalasia or pseudoachalasia. The barium swallow assesses the passage of liquids at the level of the esophagogastric junction (EGJ) as well as the height of the esophageal stasis column at 1 minute and 5 minutes after ingestion of the barium suspension.

In the case of the 38 patients who underwent preoperative BS, the following aspects were evaluated: the presence of esophageal stasis and EGJ stenosis (observed in all patients), esophageal dilation (30/38 patients), and the presence of tertiary contractions (9/38 patients). Grade III esophageal dilation was observed in 4 out of 38 patients through BS. The height of the barium column in the esophagus >5 cm after 1 minute was reported in 37 out of 38 patients, and a height > 2 cm after 5 minutes was reported in 36 out of 38 patients.

Upper digestive endoscopy (UDE). All included patients were examined through UDE. In addition to the standard evaluation (applicable to any patient undergoing UDE), this investigation revealed the following findings: the presence of stasis fluid in the esophagus in 19 out of 60 patients, esophagitis in 5 patients (5/60), and gastritis in 9 patients (9/60).

Preoperative manometry was performed on 48 patients, during which the following parameters were monitored: the average length LES (**4,67±1,63cm**), basal pressure of the LES (**20,54±8,24mmHg**), resting pressure of the LES (**49,47±25,64mmHg**), LES relaxation (**68.78±29.86%**), relaxation period (**1.78±1,85**), wave amplitude >35 mmHg (**56,32±26.72**), and the volume vector of the LES. For the **number of propagated contraction waves**, a threshold value of ≤ 6 was obtained using the ROC curve with AUC = 0,780, with a specificity of **81.8%** and a sensitivity of **75%** (Fig. 5.1).

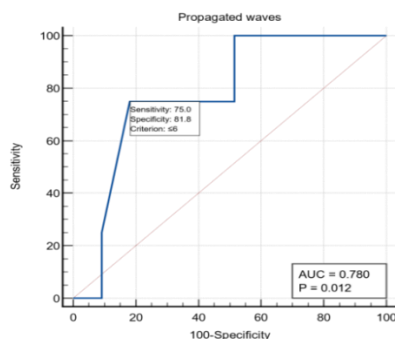


Fig. 5.1. ROC curve for the manometric variable, represented by the number of propagated waves.

In the studied group, it was possible to evaluate the type of achalasia using manometric criteria. For 11 patients, the type of achalasia was determined using high-resolution manometry (HRM) in other clinics, while for the remaining patients, conventional manometry was used. Type I achalasia was found in 16 patients, and 32 patients had Type II achalasia. No cases of Type III achalasia were identified within the group.

Using the volume vector in conventional manometry, it was possible to create a 3D representation of the lower esophageal sphincter (LES), where a hypertonic sphincter, often found in achalasia, was suggested.

The chosen surgical technique for treating achalasia was **anterior Heller esocardiomyotomy via laparoscopy, followed by an antireflux mechanism**, most commonly an anterior 180° Dor fundoplication.

Operative Setup:

Patient Positioning: The patient is placed in a dorsal decubitus position with the arms abducted at 90°, in a 20° antitrendelenburg position with the legs abducted, and the operating table rotated to the right (French position).

Surgical Team Positioning: The primary surgeon stands between the patient's lower limbs, with the cameraman to the left and the assistant surgeon to the right of the primary surgeon.

Surgical Instruments:

- Standard 3D HD laparoscopic surgery kit.
- 5 mm Ligasure Endoscopic vascular sealing forceps.
- "Snake" endoscopic retractor, intestinal forceps, needle holder.
- Faucher 40 Fr. oro-gastric tube.

A minimal incision is made 3 cm above the umbilicus, with insufflation of the peritoneal cavity using a Verres needle. The incision and insufflation can also be performed immediately above the umbilicus. The optical trocar and laparoscope are introduced, and the peritoneal cavity is inspected for any visible pathological aspects or macroscopic formations. Recently,

the optical trocar has been positioned higher, nearly halfway between the xiphoid process and the umbilicus, to allow better visualization of the thoracic esophagus. The working trocars are inserted in the standard positions for esogastric operations: a 10 mm working trocar on the midclavicular line under the left costal margin (for the surgeon's right hand), a 5 mm trocar on the midclavicular line under the right costal margin (for the surgeon's left hand), a 5 mm trocar in the epigastrium for the liver retractor (either snake-type or sometimes just a forceps), and a 5 mm trocar on the left anterior axillary line under the costal margin for assistance.

The lesser omentum is incised, and the pre-esophageal peritoneum is dissected, revealing the right and left diaphragmatic pillars. The surgeon enters the inferior mediastinum and dissects the anterior esophagus for approximately 6 cm transdiaphragmatically, identifying, isolating, and preserving the vagus nerve. The myotomy begins approximately 1 cm above the EGJ, followed by an anterior myotomy extending over the last 6 cm of the esophagus (approximately), cardia, and 1.5-2 cm of the stomach (anteriorly), by cutting the circular muscle fibers down to the mucosa, with the esophagus intubated with the Faucher tube. Next, an intraoperative endoscopic control of the myotomy is performed to detect any lesions of the esophageal and gastric mucosa, both through direct observation and by air insufflation under the liquid level. An antireflux mechanism is created, with the division of the short gastric vessels as needed. Subsequently, a contact drain tube is placed and removed through the existing 5 mm incision in the right flank. The peritoneal cavity is deflated, the working trocars are removed under direct visualization to identify any bleeding from the trocar sites. Finally, the skin is sutured, and a sterile dressing is applied to the surgical wounds.

5.3. Results

Length of Esophageal Myotomy. The median length of the esophageal myotomy was 6.0 cm, with an interquartile range [5.0-7.0] for those without perforation, and 7.0 cm [6.5-10.0] for those with perforation (**p=0.039614**).

Length of Gastric Myotomy. The median length of the gastric myotomy was 2.0 cm, with an interquartile range of [2.0-3.0] for both analyzed groups (p=0.635863).

Total Length of Myotomy. The median total length of the myotomy was 8.0 cm [8.0-9.0] for those without perforation, and 9.0 cm [8.5-13.0] for those with perforation (**p=0.044228**).

The average length of the esophageal myotomy was **6,25±1,58** cm, the average length of the gastric myotomy was **2,32±0,68** cm, and the total average length of the myotomy was **8,57±1,52** cm.

Intraoperative UDE. The accuracy of the esocardiomyotomy was checked through intraoperative endoscopy in 48 patients (**p=0.003256**).

Intraoperative manometry was performed in 2 patients (p=0.161017).

Methylene blue. The integrity of the esophageal mucosa was verified by administering a methylene blue solution through the Faucher tube in 7 patients (**p=0.000343**).

We detected **5 intraoperative perforations** (8,33%)- 4 patients had 2-3 mm perforations of the esophageal mucosa, and 1 patient had a perforation of the gastric mucosa.

Intraoperative mucosal perforation was associated with the presence of tertiary contractions detected during the barium swallow (BS) (**p=0.034708**, Fisher's Exact Test), which typically indicated a more spastic character, potentially extending muscle involvement toward the proximal esophagus. Additionally, perforation was associated with a propagated wave count of ≤ 6 —a manometric variable (**p=0.037520**, Fisher's Exact Test)—and with certain intraoperative variables: the length of the esophageal myotomy (**p=0.039614**, Mann-Whitney U test), the total length of the myotomy (**p=0.044228**, Mann-Whitney U test), administration of methylene blue (**p=0.000343**, Fisher's Exact Test), performance of intraoperative endoscopy (**p=0.003256**, Fisher's Exact Test), and other variables such as the number of days spent in the surgical ward (**p=0.001369**, Mann-Whitney U test) and the total number of hospitalization days (**p=0.034373**, Mann-Whitney U test).

In the univariate logistic regression analysis, the following risk factors were identified for the occurrence of esophageal or gastric mucosal perforations during laparoscopic esocardiomyotomy: the presence of tertiary contractions during BS (OR=14,00, 95% CI=[1,23, 158,84] **p=0.033206**), propagated waves ≤ 6 (OR=14,50, 95% CI=[1,18, 153,33], **p=0.035788**), the length of the esophageal myotomy (OR=1,74, 95% CI=[1,04, 2,89], **p=0.031957**), the total length of the myotomy (OR=1,74, 95% CI=[1,04, 2,89], **p=0.031957**), and the administration of methylene blue (OR=69,33, 95% CI=[5,79, 828,89], **p=0.000813**). Intraoperative endoscopy was identified as a protective factor, with OR<1 (OR=0,037, 95% CI=[0,003, 0,382], **p=0.005656**).

The implications of intraoperative perforations were as follows: 4 out of 5 patients had a good outcome, with only one patient developing a digestive fistula and a subphrenic abscess that required a laparoscopic reintervention and the placement of an esophageal stent.

Days of hospitalization in the intensive care unit. The median was 1.0 day, with an interquartile range of [1.0-1.0 days] for both groups analyzed ($p=0.318258$).

Days of hospitalization in the surgery ward. The median was 3.5 days, with an interquartile range of [2.25-4.75 days] for the group without perforation, and 8.0 days [5.5-9.0 days] for the group with perforation ($p=0.001369$). This difference was found to be statistically significant.

Total hospitalization days. The median was 6.0 days, with an interquartile range of [4.0-9.0 days] for the group without perforation, and 10.0 days [7.0-12.5 days] for the group with perforation ($p=0.034373$). This difference was found to be statistically significant.

5.4. Discussions

The treatment of cardiac achalasia can be performed either surgically (via Heller myotomy) or endoscopically (via pneumatic dilation or POEM). Post-procedural follow-up is essential, both clinically and endoscopically, to detect potential complications that may arise from the treatment. These include esophageal perforation, persistent dysphagia, and gastroesophageal reflux.

The risk factors for perforation during laparoscopic esocardiomyotomy, identified in this study through statistical analysis, included: *the presence of tertiary contractions detected via barium swallow (TB), a propagated wave count of ≤ 6 , longer esophageal myotomy, and greater total myotomy length.*

Tertiary contractions observed during TB are non-propulsive contractions found in various esophageal motility disorders, such as achalasia and gastroesophageal reflux disease [9]. In achalasia patients, these contractions can be repetitive, primarily causing retrosternal pain and are particularly characteristic of vigorous achalasia [10].

The number of propagated waves <6 , determined preoperatively using conventional manometry, is a functional rather than a morphological variable that characterizes esophageal motor function, indicating a profound disturbance in peristaltic function. In the studied cohort,

impaired esophageal motility was shown to be a predictive factor for intraoperative perforation complications.

Intraoperative manometry did not prove to be a risk factor for mucosal perforation. This procedure, necessary for evaluating the degree of LES relaxation, was shown to be safe in the studied cohort. Newer equipment (high-resolution manometry), due to the associated impedance, does not recommend the use of the catheter in the presence of electrocautery, making intraoperative investigation more challenging.

Moreover, statistical analysis of the data suggested that **intraoperative UDE** serves as a **protective factor** against mucosal perforation during esocardiomyotomy (OR <1). The study confirms the role of administering methylene blue via the Faucher tube in detecting perforations that were not immediately apparent and, more importantly, in verifying the integrity of the mucosal suture after identifying a perforation.

Prompt intraoperative recognition and early treatment of perforation are crucial for preventing postoperative complications such as digestive fistulas. These can prolong hospitalization, sometimes necessitate reintervention, or require treatment through endoscopic procedures, such as esophageal stent placement. In our cohort, among patients who had intraoperative mucosal perforation, *1 out of 5 developed a digestive fistula, but no postoperative deaths were recorded.*

Preoperative Paraclinical Investigations

In line with current trends, in this study, clinical symptomatology was assessed using the pre- and postoperative Eckardt score, without being able to establish a correlation between the preoperative score and the risk of perforation.

Although the value of endoscopy in diagnosing achalasia is relatively low, it is recommended for all patients with suggestive symptoms, primarily to exclude malignant tumors. Endoscopy can reveal the presence of salivary stasis or ingested food, stasis esophagitis, and esophageal dilation [11], findings also observed in patients in this study. Although esophagitis was present in five patients in the studied cohort, it was not statistically associated with intraoperative mucosal perforations.

Based on manometric data, we identified *Type I achalasia in 16 patients and Type II in 32 patients*. No patients had Type III achalasia. **The type of achalasia was not a risk factor** for procedural complications.

Heller esocardiomyotomy

In the studied cohort, **the length of the myotomy** was 6 cm in patients without mucosal perforations and 7 cm in those with mucosal perforations, with this variable being a **risk factor for perforation** (OR=1.74, 95%CI [1.04, 2.89]). The greater cranial extension of the myotomy in patients with mucosal perforations was performed with the aim of achieving optimal functional results. It is presumed that this could favor perforation at the proximal extremity of the myotomy; however, in our cohort, *perforation always occurred at the esophagogastric junction*, either above it (on the esophageal mucosa) in four patients or below the junction (on the gastric mucosa) in one patient. The average length of extramucosal gastromyotomy in our study was 2.32 cm and was not shown to be a risk factor for intraoperative mucosal perforations. The traditional 2 cm extension of the myotomy on the anterior wall of the stomach has been contested by a prospective study by Oelschlager [12], which showed better results with a 3 cm extension. **The average total length of esocardiomyotomy** was 8 cm in patients without mucosal perforations and 9 cm in those with perforations, with this variable proving to be a **risk factor for perforations** (OR=1.74, 95%CI [1.04, 2.94]).

Antireflux Procedure

All patients in the cohort underwent an antireflux procedure after HM (anterior Dor fundoplication in 59/60 patients and Toupet procedure in one patient). Among the arguments in favor of the Dor procedure is that it requires less hiatal dissection and covers the exposed mucosa at the myotomy site, which can offer protection in cases of microscopic mucosal perforation or lesions with potential for further complications.

Intraoperative Control Methods

In some patients in the cohort, intraoperative endoscopy was performed to verify the complete sectioning of the circular fibers of the LES and the integrity of the esogastric mucosa after myotomy, or conventional intraoperative manometry was used to check the decrease in LES pressure following myotomy. Another intraoperative control method, also used in other studies in the literature, was the administration of methylene blue via the Faucher tube to detect perforation and evaluate the integrity of the mucosal suture [13].

Complications

We identified 5 *intraoperative mucosal perforations*, 4 of them on the esophageal mucosa and one on the gastric mucosa. The intraoperative identification of these events played an important role in the healing process and allowed for immediate resolution through mucosal suturing and covering the suture with gastric serosa during hemifundoplication. Two patients experienced postoperative complications, one of them developing a digestive fistula (in a patient where the intraoperatively detected perforation was sutured, later requiring reintervention for drainage and esophageal stent placement) and the other developing postoperative hemoperitoneum (due to an epigastric injury caused by trocar insertion in the right flank, later requiring reintervention for hemostasis).

The average duration of postoperative hospitalization was longer in patients with mucosal perforations (8.0 days) compared to those without perforations (3.5 days). The extended hospitalization was due to the need to maintain the nasogastric tube for a longer period and the gradual resumption of oral feeding. *No statistically significant difference was observed between the two groups (with or without perforations) regarding postoperative complications, the need for surgical reintervention, or the duration of stay in the intensive care unit.*

Additionally, *no difference was found between the functional outcomes* (assessed by the pre- and postoperative Eckardt score) of patients with mucosal perforations and those without perforations, suggesting that **mucosal injury itself did not affect postoperative outcomes.**

Eckardt Score

In our study, over 80% of patients reported an improvement in symptoms postoperatively, results comparable to those in the literature.

Symptom Persistence and Recurrence

In cases of treatment failure, the possibility of an initial misdiagnosis may be suggested, often necessitating the repetition of basic investigations with increased attention. A stepwise comprehensive evaluation is preferred, involving barium swallow, endo-FLIP (endoluminal functional lumen imaging probe), high-resolution manometry, and sometimes esophageal pH-metry, in an attempt to identify a specific etiology for symptoms. Ultimately, when the specific mechanism behind symptoms after achalasia therapy is identified, targeted therapy can be administered [14].

5.5. Conclusions

1. Intraoperative and early postoperative management during Heller myotomy is crucial for effectively managing the condition and minimizing the risk of complications.
2. In recent years, our clinic has introduced intraoperative endoscopy as a standard for evaluating the effectiveness of the therapeutic method, the length of the myotomy, and ensuring the integrity of the esophageal and gastric mucosa. This approach has enabled the early diagnosis of potential complications, such as perforations, and allowed for adjustments to the surgical procedure to achieve the best possible outcomes.
3. Postoperative evaluation within the first 24 hours using a water-soluble contrast medium barium swallow (Iopamiro) for patients who have undergone Heller myotomy or pneumatic dilation is essential. This assessment can establish mucosal integrity or detect lesions, thereby simplifying postoperative care. The use of these two investigations has resulted in reduced hospitalization costs, quicker social reintegration, and improved quality of life for patients.
4. Laparoscopic Heller esocardiomyotomy combined with an antireflux procedure is a safe and effective treatment for achalasia.
5. Intraoperative mucosal perforation is a severe, life-threatening complication, and its intraoperative detection is crucial. Most often, this complication is observed at the time of occurrence and treated immediately.
6. Identifying risk factors for the occurrence of perforations can reduce the incidence of this undesirable intraoperative event and increase the safety of the surgical intervention. The factors influencing the occurrence of perforations, identified in the study, include: the presence or absence of tertiary contractions during barium swallow (BS) examination, the number of propagated waves (≤ 6 as a risk factor), the length of the esophageal myotomy, the total length of the myotomy, and the intraoperative administration of methylene blue.
7. Performing endoscopy during surgical procedures has proven to be a protective factor against the occurrence of perforations. The benefit of intraoperative endoscopy can be explained by the fact that esophageal distension due to endoluminal insufflation provides better exposure of the mucosa, thereby avoiding perforation. Based on these findings, endoscopy associated with Heller esocardiomyotomy can be used both as a method for

verifying the accuracy of the myotomy and the integrity of the esogastric mucosa, as well as a tool for preventing intraprocedural complications.

8. Although one patient with an intraoperative mucosal perforation developed a digestive fistula on the second postoperative day, we did not find statistically significant differences regarding the immediate outcomes (postoperative complications, reinterventions) and functional results between patients with mucosal perforations and those without perforations.
9. The duration of hospitalization was longer for patients with mucosal perforations compared to those without. This was due to the need to maintain the nasogastric tube for a certain period and the delay in resuming oral feeding.

6. Comparative Study of Long-Term Outcomes Between Pneumatic Dilation and Laparoscopic Heller Myotomy in the Treatment of Achalasia

6.1. Introduction:

Regarding the treatment of achalasia, the main methods used are endoscopic (such as balloon dilation and peroral endoscopic myotomy) or surgical (Heller esocardiomyotomy). Both Heller myotomy (HM) and pneumatic dilation (PD) can lead to symptom improvement, patient satisfaction, and a similar enhancement in quality of life.

PD is a relatively safe and easy-to-perform method, with advantages including being less invasive compared to HM and not requiring general anesthesia [15]. The main disadvantage of this method is the rapid reformation of the circular muscle fibers at the level of the lower esophageal sphincter (LES) [15]. Therefore, multiple dilation sessions may be necessary to achieve an adequate therapeutic response.

In comparison, myotomy provides more sustained long-term results [16]. Surgical treatment through Heller myotomy (HM) can be performed either laparoscopically or robotically and allows for the simultaneous creation of an antireflux mechanism (with partial fundoplication, either anterior or posterior, being recommended) [17], [18].

Another effective therapeutic method for patients with achalasia is peroral endoscopic myotomy (POEM). However, in Romania, this type of treatment is less available compared to the previously mentioned therapeutic methods.

The aim of the study is to evaluate the therapeutic response following Heller esocardiomyotomy or pneumatic dilation and to compare the results, including the impact on quality of life, obtained from these two treatment methods.

6.2. Patients and methods

A retrospective study was conducted, with the study population consisting of a cohort of 98 patients with cardiac achalasia who were treated in our clinic, divided into two subgroups based on the chosen therapeutic method. Of these, 73 patients (74,49%) were treated surgically through HM, while 25 patients (25,51%) were treated endoscopically using PD.

Preoperative manometry was performed on only 59 patients (out of 98), as the remaining patients either could not tolerate the investigation or the manometer could not pass

through the cardia due to a severely dilated and tortuous esophagus. According to the Chicago Classification 3.0[19], 20 patients had Type I achalasia, while 39 patients had Type II achalasia.

Pneumatic balloon dilation was performed on 25 patients after the insertion of a guidewire, under endoscopic control, using a 30 mm balloon (Fig. 6.1).



Fig. 6.1. The endoscopic appearance of the pneumatic dilation balloon shows the presence of the dilated balloon at the level of the esophagogastric junction (EGJ).

As a routine procedure, a final endoscopic check is performed to evaluate the effect of the treatment and any potential mucosal lesions. In case of esophageal wall perforation, the affected area is closed using Large endoscopic clips.

The surgical interventions were performed using an open approach in 2 patients and a laparoscopic approach in 71 patients (using a 3D HD kit with 5 trocars and standard instruments). An anterior Heller esocardiomyotomy was performed (Fig. 6.2), with the restoration of the His angle and anterior Dor hemifundoplication at 180 degrees. Intraoperative endoscopic control was routinely performed to assess the integrity of the mucosa and evaluate the effectiveness of the myotomy.

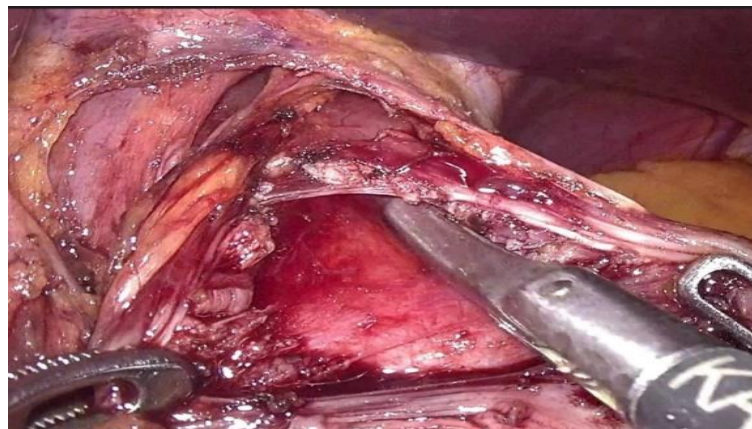


Fig. 6.2. Myotomy performed on the lower esophagus and extended onto the EGJ.

Barium Swallow. Preoperative radiological control is considered very useful and cost-effective compared to other methods, both for diagnosing and for post-therapeutic reevaluation.

Pre- and post-therapeutically, we used **the Eckardt score** [20] for patients evaluation.

To monitor the postoperative evolution of patients, we developed a questionnaire with 4 questions at the clinic (Annex 1):

1. *What symptoms did you experience postoperatively (when, what type, how long after)?*
2. *Have you undergone any additional treatment since then?*
3. *Have you experienced any other symptoms?*
4. *How much has your quality of life improved after the procedure?*

6.3. Results

Within the two subgroups, demographic data (such as gender and age) as well as lifestyle and habits, like smoking status, were analyzed. We found that for all these patient characteristics, there were statistically significant differences ($p < 0.05$).

Distribution of patients by gender. The analysis shows that, in the PD group, out of a total of 25 participants, 16 are women (64%), while 9 are men (36%). In the HM group, out of a total of 73 participants, 28 are women (38.4%), and 45 are men (61.6%) ($p=0.026090$). Thus, pneumatic dilation is more frequently recommended and used as a therapeutic method for female patients, whereas myotomy is more commonly performed on male patients (Fig.6.3).

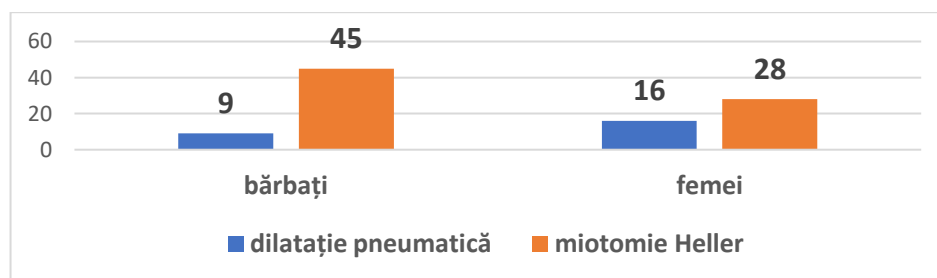


Fig. 6.3. Distribution of patients by gender and type of treatment performed

Age of patients. In the case of age, we discovered a statistically significant difference. The average age in the PD group was higher, at **64,36** years, with a standard deviation of 14, while in the HM group, the average age was **50,12** years, with a standard deviation of **15,625** ($p=0.000115$).

Distribution of patients by tobacco use. Smoking is not a risk factor for the development of achalasia, but it may increase the risk of pulmonary infection. In our study, none of the 25 patients in the PD group were smokers, whereas, in the HM group, 16 out of 73 were smokers (21.9%) (**p=0.009738**).

As part of the diagnosis and to establish the definitive therapeutic strategy, patients were evaluated clinically, through imaging, endoscopy, and manometry. Upon admission, the following were recorded: the history of the condition (whether it was the first presentation or a recurrence), duration of symptoms, type of symptoms (weight loss, dysphagia, retrosternal pain, regurgitation, other symptoms), and the Eckardt score in the two groups. For the therapeutic intervention, the risk associated with anesthesia and surgical procedures (ASA risk) was assessed. Among all these factors, only the type of disease at admission (initial or recurrent) was statistically significant ($p < 0.05$).

Distribution of patients by type of disease at admission. The types of disease at admission (initial or recurrent) were analyzed in both groups. In the PD group, 15 out of 25 patients (60%) had initial disease at admission, while 10 patients (40%) had recurrent disease. On the other hand, in the HM group, the majority (61 out of 73) of the patients had initial disease at admission, and 12 (16.4%) had recurrent disease (**p=0.014815**). PD is the most frequently used therapeutic method in cases of recurrence, being less invasive and carrying lower risks.

UDE. Endoscopically, the presence of esophageal stasis, difficult passage at the EGJ, esophageal dilation, presence of stasis esophagitis, and gastritis were assessed. Among these, esophageal stasis, EGJ stenosis, and esophageal dilation were statistically significant.

Esophageal stasis. In the PD group, 20 out of 25 patients (80%) were found to have esophageal stasis. In the HM group, 41 out of 73 participants (56.2%) had esophageal stasis on endoscopy (**p=0.033854**). The difference in the proportions of esophageal stasis between the PD and HM groups is statistically significant. These results may correlate with a longer duration of symptoms, indicating an older disease.

EGJ stenosis. In the PD group, 23 out of 25 participants (92%) had EGJ stenosis. In the HM group, this was observed in only 46 out of 73 patients (63%) (**p=0.006136**). The difference was statistically significant and may correlate with the presence of stasis.

Esophageal dilation. During endoscopy, evaluating the diameter of the esophageal lumen is more challenging compared to imaging methods such as barium swallow or computed tomography. However, in the PD group, esophageal dilation was reported in 23 out of 25 patients (92%). In the HM group, esophageal dilation was quantified endoscopically in 48 out of 73 participants (65.8%) ($p=0.011239$).

Depending on the attending physician, an intra-procedural method for evaluating the outcome of the intervention is chosen. During the interventions, intraoperative methylene blue was used to assess potential perforations, and manometry and UDE were performed on selected patients. These methods, along with intra-procedural incidents and post-procedural complications, did not show statistical significance.

An analysis of the post-procedural Eckardt score in 2022 and 2024 in the two groups revealed a superior improvement in symptoms in the HM group.

Post-procedural Eckardt Score. A statistically significant difference was found between the postoperative Eckardt scores from 2022 ($p=0.044498$) and 2024 ($p=0.006281$) of the PD and HM groups, suggesting that patients in the HM group had lower postoperative scores compared to those in the PD group. This indicates a superior improvement in postoperative symptoms in the HM group.

Next, to evaluate the treatment, we analyzed aspects such as the duration of hospitalization, treatment costs, and the prevalence of recurrence in the two groups. All variables showed statistically significant differences.

Duration of hospitalization: A statistically significant difference was observed in the median duration of hospitalization. In the PD group, the median duration was 3 days, with an interquartile range between 2 and 6 days, while in the HM group, the median duration was 6 days, with an interquartile range between 4 and 9 days ($p=0.000764$). These figures are important, being justified by the invasiveness of the procedure, the anesthesia administered, and the post-procedural recovery.

Treatment costs. Regarding costs, in the PD group, the median cost was **1597 RON**, with an interquartile range between **857,7** and **3.881,5 RON**. In the HM group, the median cost was **4124 RON**, with an interquartile range between **2893** and **5.285 RON**, with the difference being statistically significant ($p=0.000250$).

Recurrence: In terms of recurrence, in the PD group, 5 out of 25 patients (20%) were diagnosed with recurrence, compared to the HM group, where 3 out of 73 patients (4.1%) experienced recurrence ($p=0.024186$) (Fig. 6.4).

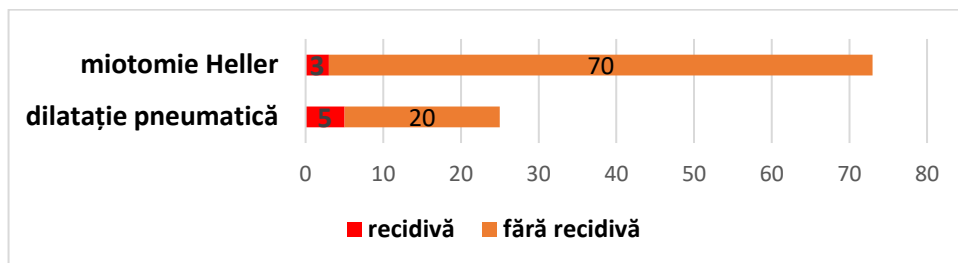


Fig. 6.4. Distribution of patients based on the recurrence of symptoms.

The improvement in quality of life was assessed using a questionnaire consisting of 4 questions. In the PD group, 13 out of 25 patients (52%) reported a significant improvement in quality of life after treatment. Similarly, in the HM group, a larger number, 53 out of 73 patients (72.6%), reported a significant improvement in quality of life post-treatment, with the difference being close to statistical significance ($p=0.057969$).

6.4. Discussions

A study conducted in 2013 showed that the therapeutic response and success rates of PD and HM are similar in Type I achalasia ($p = 0.84$). The highest success rate is observed with PD in Type II achalasia ($p = 0.03$), although both treatments are highly effective. In patients with Type II achalasia, a difference between the two methods was observed, but it was not statistically significant ($p = 0.12$) [21]. It seems that PD is the least effective treatment method for Type III achalasia. In our cohort, we did not encounter cases of this type.

Regarding treatment, **dilation was more frequently performed in female patients, while males predominantly underwent HM.** The literature also recommends surgical intervention as the first therapeutic option in men under 45 years old, and dilation in female patients or those over 45 years old [22]. Of course, these are just recommendations, and the final decision is made by the attending physician together with the patient after discussing the benefits and risks of each method.

As patients age, comorbidities become more common, making surgical treatment riskier than dilation. **In our case, the age was higher in the PD group compared to the HM group.**

Clinically, patients in both groups had the same average pre-therapeutic Eckardt score, but **post-therapeutic evaluation showed a lower Eckardt score in the HM group compared to the PD group**, with the difference being statistically significant ($p < 0.05$). However, **in both cases, the Eckardt score was within the normal range**. Thus, we can conclude that *both procedures are effective* and can be performed depending on patient preference, medical history, and the expertise of medical centers [16].

There is an ongoing debate in the literature regarding the assessment of treatment response, specifically whether it is sufficient for the patient to be symptom-free (Eckardt score of 3 or less) or if confirmation of complete esophageal emptying through barium swallow or normalization of LES relaxation through manometry is also necessary to consider the therapeutic response satisfactory.

Some authors have demonstrated, on a limited number of achalasia cases, a correlation between clinical score and serial barium swallow (at 1 and 5 minutes) [23]. Other authors recommend a more comprehensive evaluation using multiple questionnaires (including reflux questionnaires) and investigation results.

It is certain that clinical results are often better than those obtained from investigations [24]. Achalasia is a condition for which treatment is palliative and symptomatic. Therefore, *specialists debate whether recurrence should be considered based on clinical evaluation or investigations*. Additionally, in the case of symptom recurrence, it is worth discussing the decision for another therapeutic session, determining its indications, and the expected outcomes.

In our cohort, **symptom recurrence was more frequent in the PD group**, necessitating another therapeutic intervention, most often endoscopic.

Some authors believe that PD and HM are equally effective, even after 10 years of follow-up, with a limited risk of developing gastroesophageal reflux. Based on these data, we conclude that both procedures can be proposed as initial treatments for achalasia [25]. **The cost of treatment and the number of hospitalization days were lower in the PD group due to the nature of the method.**

The advantage of our study was the long-term follow-up of results, with a reevaluation using the Eckardt score after an average interval of 4.5 years. Both therapeutic methods had their advantages and disadvantages, with results remaining stable over time. We found that the

quality of life assessment was better in surgically treated patients, but without a statistically significant difference.

6.5. Conclusions

1. Both surgical treatment and pneumatic dilation lead to symptom improvement in patients with achalasia.
2. In the case of dilations, it was often necessary to repeat the procedure.
3. The post-procedural Eckardt score was lower in the case of laparoscopic myotomy compared to PD, which might suggest recommending surgical treatment as the first option.

7. CONCLUSIONS AND PERSONAL CONTRIBUTIONS

Conclusions

1. Achalasia is the most studied esophageal motility disorder with an unknown etiology to date, which benefits from a palliative yet effective treatment.
2. Achalasia is not a commonly encountered condition, and the analysis of a study group with a large number of patients reflects the accessibility of the General and Esophageal Surgery Clinic at “Saint Mary” Clinical Hospital in Bucharest, as well as the clinic's focus on the diagnosis and treatment of esophageal motility disorders.
3. According to the current European guidelines for the management of achalasia (*United European Gastroenterology (UEG), European Society of Neurogastroenterology and Motility (ESNM), European Society of Gastrointestinal and Abdominal Radiology (ESGAR), The European Association of Endoscopic Surgery (EAES)*) the diagnosis is primarily established through barium esophagram, upper digestive endoscopy, and esophageal manometry, the latter being the "gold standard" investigation with the highest sensitivity.
4. In the studied cohort, a higher proportion of esophageal dilation was observed in the PD group compared to the HM group, with this difference being statistically significant.
5. Currently, the following treatment options are used: medication, botulinum toxin injections into the LES, endoscopic pneumatic dilation (PD), POEM, and Heller myotomy (HM) via laparoscopic or open approach.
6. Laparoscopic HM, combined with an antireflux procedure (anterior Dor fundoplication [180°], posterior Toupet fundoplication [270°]), is a safe and effective procedure for treating achalasia.
7. In Romania, the most common methods are PD and laparoscopic HM, which were analyzed in my doctoral thesis.
8. In recent years, our clinic has introduced intraoperative endoscopy as the standard for evaluating the effectiveness of the therapeutic method and the length of the myotomy, as well as ensuring the integrity of the esophageal and gastric mucosa. This approach has allowed for the early diagnosis of potential complications, such as perforations, and has facilitated adjustments to the surgical procedure to achieve the best possible outcomes.

9. Postoperative evaluation within the first 24 hours using a barium swallow with water-soluble contrast agents (Iopamiro, Omnipaque, Gastrografin) for patients who underwent Heller myotomy or PD is essential. This evaluation can establish mucosal integrity or the presence of lesions, allowing for simplified postoperative care. The use of these two investigations resulted in reduced hospitalization costs, faster social reintegration, and improved patient quality of life.
10. The majority of patients were treated surgically, while 25.51% were treated endoscopically.
11. In the PD group, more patients presented with recurrent disease at admission. On the other hand, in the HM group, the majority of patients had initial disease at admission.
12. Regarding treatment, female patients more frequently underwent dilation treatment, while male patients predominantly underwent Heller myotomy.
13. As age advances, comorbidities become more common, making surgical treatment riskier than dilation. In our study, the age was higher in the PD group compared to the HM group.
14. In the studied cohort, a higher proportion of esophageal stasis was observed in the PD group compared to the HM group, with this difference being statistically significant. These results may correlate with a longer duration of symptoms, indicating an older disease.
15. The main complication of both treatment methods for achalasia is *perforation of the esophageal or gastric mucosa*. We analyzed factors that may be related to the risk of perforation in the treatment of achalasia to identify possible prevention methods.
16. Intraoperative and early postoperative management in the case of Heller myotomy is essential for managing the condition and minimizing the risk of complications.
17. Risk factors associated with mucosal perforation include: *the presence or absence of tertiary contractions during BS, the number of propagated waves (≤ 6 being a risk factor), the length of the esophageal myotomy, the total length of the myotomy, and the intraoperative administration of methylene blue*.
18. The benefit of intraoperative endoscopy can be explained by the fact that esophageal distension, due to endoluminal insufflation, allows better exposure of the mucosa, thus avoiding perforation.
19. In patients with achalasia and a risk of perforation, the physician must inform the patient about this risk.

20. To evaluate treatment outcomes from a clinical perspective, the Eckardt score remains the most commonly used tool.
21. The results of treatment for achalasia cardia are reflected in the post-procedural quality of life of the patients.
22. In the studied group, patients who underwent pneumatic dilation for achalasia had shorter hospitalization and faster social reintegration.
23. Regarding recurrence, it was more frequent in patients treated with dilation, who more often required repeat treatment compared to those who underwent surgery.
24. The recurrence of symptoms requires a thorough analysis of risk factors.
25. Using a questionnaire created at our clinic to evaluate patients after treatment, we found that, clinically, patients treated by both methods had an improved Eckardt score.
26. In the case of dilations, the procedure cost was lower compared to laparoscopic surgery, which is an important advantage.
27. Both endoscopic dilation and Heller esocardiomyotomy resulted in significant long-term clinical improvement for patients, making them similar in terms of effectiveness.
28. We found that surgically treated patients had a statistically significantly lower post-therapeutic Eckardt score, suggesting that laparoscopic intervention could be recommended as the first therapeutic option.

Personal contributions

During my residency and training at the General Surgery Clinic, Center of Excellence in Esophageal Surgery at “Sfânta Maria” Clinical Hospital in Bucharest, I had the opportunity to be part of a dedicated team focused on diagnosing patients with esophageal motility disorders. This experience allowed me to directly participate in essential investigations such as esophageal manometry, barium swallow, upper digestive endoscopy, and esophageal pH-metry.

I was actively involved in evaluating patients from the onset of symptoms through to the monitoring of post-procedural outcomes. By performing esophageal manometries, participating in surgical interventions, and following up with patients during the post-therapeutic period, I was able to create a solid database that enabled me to accurately reassess the therapeutic response.

Throughout this time, I maintained a constant focus on establishing optimal management for patients with cardiac achalasia, which led me to delve deeper into this subject during my doctoral studies. In an effort to scientifically validate and support the results obtained, I focused on identifying and preventing post-therapeutic complications, thereby contributing to the improvement of patients' quality of life.

Decisions regarding the appropriate treatment for patients with achalasia were made based on thorough investigations, supported by extensive surgical experience in laparoscopic techniques. This allowed me to develop solid expertise in managing cases, with the ultimate goal of achieving optimal post-therapeutic outcomes.

The management of achalasia is continuously evolving, and technological advancements have a significant impact on diagnostic and treatment methods. My ongoing focus on managing esophageal conditions has also been supported by the recent implementation of advanced technologies within the clinic, such as HRM and 3D HD laparoscopic surgery.

In my doctoral thesis, I found that the effectiveness of dilation treatment in symptom relief was comparable to surgical intervention. A rigorous multidisciplinary analysis and adherence to updated guidelines for esophageal motility disorders were essential in interpreting the results. The biological status of patients, their surgical history, comorbidities, and patient preferences allowed for individualized treatment.

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1. **Alkadour Abdullah**, Hoară P, Constantinoiu S, Predescu D, Bîrlă R, Gîndea C, Gheorghe M, Mitrea-Tocitu M, Panaitescu E, Velicu RG, Achim F. The Clinical Efficacy, and Long-Term Outcomes Between Pneumatic Dilatation and Laparoscopic Heller Myotomy în Achalasia. *Chirurgia (Bucur)*. 2024 Jun;119(3):311-317. doi: 10.21614/chirurgia.2024.v.119.i.3.p.311. PMID: 38982909.
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