P. Marco Fisichella
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Editors

Achalasia

Diagnosis and Treatment

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To Dr. Melina R. Kibbe, inspiration and role model for those who have committed their lives to academic surgery.

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Introduction

Esophageal achalasia is motility disorder characterized by the absence of esophageal peristalsis and failure of the lower esophageal sphincter to relax in response to swallowing. These abnormalities lead to impaired emptying of food from the esophagus into the stomach with resulting food stasis. Most patients experience severe dysphagia, and regurgitation can lead to aspiration and respiratory problems. As a consequence, the quality of life of patients affected by this disease is severely affected.

The last 25 years have witnessed a significant improvement in the understanding of the pathophysiology of achalasia, and our ability to diagnose it and treat it. Today the results of treatment are significantly better than they were in the past.

This book represents a joint effort of experts who have focused their career on the treatment of this disease. The reader will find an excellent presentation of the pathophysiology of the disease and its diagnostic approach. In addition, the treatment is carefully described, from dilatation to per oral endoscopic myotomy (POEM), from a laparoscopic Heller myotomy to esophageal resection. Special emphasis is given to new techniques such as POEM, and to special situations such as the treatment of pediatric patients, patients with achalasia and epiphrenic diverticulum, patients with achalasia and obesity, and those with recurrent dysphagia after prior treatment.

This is an important contribution for residents, fellows, and practicing gastroenterologists and surgeons who have an interest in helping patients with esophageal achalasia.

A One Hundred Year Journey: The History of Surgery for Esophageal Achalasia

1

P. Marco Fisichella and Marco G. Patti

Introduction

> There is probably no disease that responds more satisfactorily to proper treatment than cardiospasm. Herman J. Moersch, Mayo Clinic, 1933 [1]

Dr. Moersch could not have been more accurate. Today, like in 1933, operations for achalasia are very gratifying for the patients, as their quality of life is often dramatically improved. How did we get here today, from 1933? The history of treatment of achalasia is mesmerizing, and is deeply intertwined with the thought processes involved in trying to identify its etiology and determine its pathophysiology. What is striking today is the evolution of the concept of this disease which takes place at the beginning of the twentieth century, a time when only post mortem examinations could shed light on indirect evidence of actual pathophysiologic theories. Giants of surgery, like Maingot, Wangesteen, Ochsner, and Plummer and Vinson, clearly understood the importance of recognizing the pathophysiology of this obscure disease and used this knowledge as a guide for the best form of treatment. Therefore, by reading the original accounts of those days early in 1900 the modern surgeon is definitely fascinated by the great wisdom and surgical acumen of the fathers of modern surgery. Our goal is to revisit those early accounts faithfully to understand the lessons learned over a journey that has lasted 100 years since the first report of Dr. Heller. We also aim to continue our journey to modern days to describe the development of fundoplications and other endoscopic treatments to finally illustrate the modern surgical approach of patients with achalasia.

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Early Accounts and First Attempts to Propose a Pathophysiologic Mechanism of an Elusive Disease. The Term: "Achalasia" Is Coined

Early accounts of dysphagia relieved by mechanical anterograde dilatation with a whalebone date back to 1674 [2]. In more modern times, Purton in 1821 reported the first case of cardiospasm treated by dilatation, while Zenker and Von Ziemssen in 1878 reported 17 cases [3].

The origin of the disease remained elusive and many theories were proposed. Crossan Clark from Hamilton, Canada, enumerated in detail

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those theories most in vogue at the beginning of the century. Clark illustrated how Flainer, Zenker, and Sievers theorized that esophageal dilatation resulted from congenital muscular irritability; how Martin considered primary esophagitis the most important factor; how Kraus claimed that there was paralysis of the circular musculature of the esophagus; and how Golden and Mosher thought that "*the upper border of the liver*" exerted outflow obstruction at the distal esophagus [3]. During the same time, Jackson also proposed that the diaphragmatic pinchcock action could provoke an outflow obstruction to the food bolus by incoordination or spasm of the diaphragm during the act of swallowing [4].

Pathophysiologic theories in the early 1900 were based on anecdotal evidence at its best. However, in 1914 Dr. Arthur Hertz, while commenting a paper form F. Parker Weber proposed that the disease was not due to a spasm of the cardia, like most at that time believed [5]. As a proof of his thesis Hertz brought the results of his studies done in 1909 at the Guy's Hospital on extensive post mortem examination of cases thought to be caused by cardiospasm. Hertz argued against a cardiospasm because "*the symptoms were often present for many years before death and it was quite unconceivable that a spasm of such long duration should not lead to any hypertrophy of the cardiac sphincter… The condition was really due to the absence of the normal relaxation, which should occur when each peristaltic wave, travelling down the oesophagus, reached the cardiac sphincter. It had been experimentally shown that section of the vagi … prevented this relaxation, and led to accumulation of food in the oesophagus, which consequently became dilated*" [5]. Intrigued by Hertz's logic, F. Parker Weber replied that "*such state of affairs might almost be compared to what occurred in cases of "heart-block"*" [5]. It was the first time that an unknown abnormality of peripheral nervous system was implicated in the pathophysiology of the disease. Later studies from Rake would confirm this simple intuition.

In 1915, Dr. Hertz reiterated formally his theory to which he gave the name of "*achalasia of the cardia*". In fact, in his paper "Case of Achalasia of the Cardia (so-called cardiospasm)" Hertz writes that "*the term "achalasia" (a, not; χαλαω, I relax) was coined for me by Sir Cooper Perry to replace the term "spasm", which is incorrect*" [6]. The arguments of Hertz were subsequently substantiated by Rake who is credited to have been the first to show a degeneration of the Auerbach plexus in patients with non-organic dysphagia [7]. Rake, in fact, in post-mortem examinations of specimens demonstrated that the Auerbach plexus in those with cardiospasm was twice its normal size and infiltrated with small round cells, which Hertz attributed to "*primary*" inflammation of the esophageal epithelium [7].

Hertz's theory was later accepted by Plummer and Mikulicz who believed (based on the experiments done by Rake and the observation by Hertz that symptoms could be alleviated by atropine and worsened by transection of both vagi) that there was some sort of "*neuromuscular disturbance*" responsible for the esophageal dilatation [3]. Clark also added to the argument that: "*No other lesion in the oesophagus causes such marked dilatation above the point of constriction, and therefore the factor of loss of tone is as much as considered as stenosis"* [3].

From Ineffective Esophageal Plications and Retrograde Dilatations to the Successful Cardiomyotomy: The Golden Era of Heller and Zaaijer

Hertz's theory was not widely accepted right away. To summarize the sentiment at that time, Greenwood recites in the British Medical Journal in 1928: "*The term "achalasia" is a premature attempt at generalization, facile and tempting, but quite unjustified by the present state of our knowledge*" [8]. Those who disagreed with Hertz hypothesized that the esophageal dilatation was responsible for the cardiospasm and that an operation should aim to treat the former rather than the latter. The logic was proven fault. The operation of plication consisted in invaginating the upper segment of the dilated and sigmoid esophagus into the lower one, without opening its lumen,

"*thus restoring the proper length and longitudinal tension*" (Dr. Leonard Freeman, 1923) [9]. Also, by Freeman's accounts: "*A number of similar operations also have been done, with more or less success, by various other surgeons (Sencert, Oettinger, Caballero, Sauerbruck, Exner, Tuffier, etc.) having the common objective of straightening out the oesophaus by pulling its redundant portion down into the abdominal cavity and perhaps anastomosing it to the stomach or to the duodenum*" [9]. These operations soon fell out of favor because of their dismal results. Similar fate attended the operation devised by Mikulicz in 1904. Mikulicz devised the technique of retrograde dilatation in which after a gastrotomy was done, he introduced a clamp with rubber covers and used it to stretch the cardia [10].

It was 1910 when Wendel reported the first cardioplasty performed through a vertical incision onto the anterior wall of the cardia and sutured it transversally [11]. Then, in 1914 Heller first described a transabdominal extramucosal cardioplasty performed onto the anterior and posterior walls of the cardia [12]. Heller presented his excellent results at the German Surgical Congress in 1921 [13]. Heller's operation (a modified Ramsted procedure used to treat pyloric stenosis in infants) was a real revolution at that time. As Watts put it in 1923: *"…it would seem that the simplest operative measure is stretching the cardia… but this may be followed by a recurrence. The extramucous cardioplasty of Heller is probably the simplest and best radical operation, if it is as easy and efficient as the reports would lead us to believe"* [14].

The operation devised by Heller had such a success that it was readily adopted and simplified by surgeons in Holland. Dr. J.H Zaaijer from Leiden, in 1923 reported that the Heller operation was a great operative intervention in those cases in which antegrade dilatation was not possible (he cited data from by Plummer and Porter that reported a 25 % failure rate in treating dysphagia with a hydrostatic dilator) [15]. Zaaijer in fact treated eight cases without mortality and with excellent outcomes. As to the details of the operation Zaaijer highlighted that: "*It does not appear to make any difference relative to the subsequent findings whether the incision is made on the anterior side and one on the posterior side as Heller did, or one incision only on the anterior side as has been employed by de Bruine, Groeneveldt and myself*" [16]. Zaaijer continues: "*Heller points out that he considers it necessary to lengthen the incision particularly downwards, whereas it needs only to be carried upwards as far as the beginning of the dilatation"* [16].

Early Attempts to Approach Megaesophagus: The Rise and Fall of Esophagogastrostomy

At the beginning of the 1940s the operations of esophagogastrostomy (side-to-side, Finney type, or Heyrovsky-Grondahl – 1912–1916) still performed by Ochsner and DeBakey fell out of favor mainly because their major side effects. Dr. Rodney Maingot in 1944 recite that "*Although the technical beauty (ndr. esophagogastostomy) has nevertheless one flaw – regurgitation"* [17]. In fact, in those who had an esophagogastrostomy the regurgitation of gastric contents was particularly severe, especially in the supine position, and caused severe esophagitis. Conversely, Maingot noted, "*Oesophagocardiomyotomy is, in my opinion, worthy of a more general adoption, as it is a simple and safe operation, the technique is readily mastered, and the immediate and late results are most gratifying"…"It is associated with negligible mortality and a stay in the hospital which does not in the average case exceed eight days, there is no regurgitation of gastric contents into the oesophagus or mouth and there are no teasing complications such as peptic ulceration. The patient can furthermore enjoy hearty meals without the slightest restraint or discomfort* [17]. Curiously, Maingot's myotomy was "*10 to 15 cm in length… curving slightly upwards towards the fundus, until the oesophageal mucosa and the gastric mucosa bulge boldly outwards without restraint*" [17]. Finally, Maingot claimed that Gottstein in 1901 first suggested the operation later popularized by Heller. Maingot further explained: "*We name certain operations after certain well-known surgeons*

merely because it is customary and more convenient; but it is often the best known sponsor rather than the originator of a particular operation who receives all the praise and credit" [17].

Importantly, it was evident in the 1940s and 1950s that a transabdominal approach was considered the best approach, even though many still preferred a transthoracic approach. Earle B. Kay from Cleveland noted in 1948: "*Most opinions have favored the transabdominal approach, in that this was felt to be associated with less risk*" [18]. Indeed, in 1951 Owen Wangesteen preferred a transabdominal cardiomyotomy, even though this was performed under digital control through a finger inserted into esophagus through a gastrotomy [19].

The Advent of the Partial Fundoplication to Prevent Gastroesophageal Reflux

Up until the late 1960s there is no mention in the literature about the necessity to control or prevent gastroesophageal reflux that arises after the cardiomyotomy. Rudolph Nissen popularized a fundoplication the bears his name in 1956, but it was in 1962 that J. Dor from Marseille, France, proposed an operation that he called "*technique de Heller-Nissen modifiee*" for the treatment of reflux with esophagitis associated with cardiospasm [20]. This operation was performed though a transabdominal approach and involved the performance of a single longitudinal anterior extramucosal cardiomyotomy 10 cm long, extending 5 cm onto the anterior wall of the stomach, below the level of the angle of His. Then, the left side of the myotomy was sutured to the anterior wall of the stomach, which was then folded anteriorly and secured to the right edge of the myotomy with another row of sutures. This is the technique used today in most centers. Of note, Dor never transected the short gastric vessels to facilitate the anterior rotation of the fundus of the stomach to cover the myotomy. In 1967, Dor published a modification of the technique best suited for those who had their gastroesophageal region shaped like a "*hotte de cheminee*", or "the flue of a chimney" (with a very wide angle of His, which Dor aimed at reconstructing to avoid reflux) [21]. This modification still involved a 10 cm extramucosal cardiomyotomy which was then encircled with a sling and pulled down to allow the greater curvature to be folded upwards thus recreating a new angle of His. The edges of the myotomy were then suturing together to form a modified, side-to-side, Finney type, cardioplasty [21].

The new technique was able to provide relief of dysphagia while limiting gastroesophageal reflux. Also at the same time, Andre' Toupet in 1963 devised the posterior fundoplication that bears his name; however, this technique was not implemented until 1976 and only in children [22, 23]. These techniques of fundoplication were not readily incorporated into the surgical treatment as a few still considered a fundoplication unnecessary. Results from the Mayo Clinic confirmed the tendency of not adding a fundoplication during a myotomy. Ellis and Olsen in fact favored a transthoracic short esophagomyotomy, ("*a 3 cm anterior extramucosal esophagomyotomy which extended only a few millimiters onto the stomach*") over a long one "*extending 3 cm onto the anterior wall of the esophagogastric region* [24]". Backed up by manometric data and a review of the outcomes of their 269 patients, Ellis and Olsen argued that a short esophagomyotomy relieved dysphagia and controlled reflux better than the "classic" Heller and "long" Heller. Ellis attributed the good results of the short myotomy in preventing significant gastroesophageal reflux to the preservation of the gastric sling fibers (Willis' loop or collar of Helvitius, or "*sphincteric remnant*"), which contributed to the continent mechanism of the cardial region [24].

Nevertheless, the Heller myotomy and Dor fundoplication become widely implemented, probably because many were not able to reproduce the results of the Mayo Clinic. In 1988, the first long term results of the Heller myotomy and Dor fundoplication on a large case series started to appear in the literature. Csendes et al. performed on 100 patients "*an anterior esophagomyotomy 6 cm long, not extending into the stomach more than 5–10 mm, with the*

addition of an anterior hemi-Nissen or Dor procedure, similar to the Thal serosal patch" and reported, at a mean follow-up of 6.8 years, excellent and good outcomes in 92 of the 94 patients followed-up and objective reflux in 19 % of patients [25]. Subsequently, Bonavina et al. published in 1992, the long-term outcome (median follow-up 64.5 months) on 206 patients operated on from 1976 to 1989 with a cardiomyotomy "*10 cm long (8 cm on the esophagus and 2 cm on the stomach)*" and Dor fundoplication, and reported clinical results excellent or good in 93.8 % and fair in 2.6 % of patients. Similarly, 24-four-hour esophageal pH monitoring showed an abnormal acid exposure in seven (8.6 %) of 81 patients tested [26].

From Thoracoscopic to Laparoscopic Cardiomyotomy

At the beginning of the 1990s minimally invasive techniques were introduced in the clinical treatments of foregut diseases. Because of their advantages in minimizing pain and shortening length of stay, these approaches gained widespread popularity. Therefore, it seemed natural at that time to reproduce the well-known operations with the new minimally invasive approaches. Dr. Cuschieri first performed a laparoscopic cardiomyotomy in 1991 [27]. In 1992, Dr. Pellegrini, aiming to reproduce the technique of Ellis, described the results of 17 patients who underwent a thoracoscopic short myotomy onto the left side of the esophagus extending only 5 mm onto the gastric wall, with the goal to balance the relief of dysphagia with the prevention of reflux [28]. Dr. Pellegrini is also credited to be the first to perform the first two cases of laparoscopic myotomies in United States. These were patients in whom a thoracoscopic myotomy proved to be too short and a second myotomy was then performed laparoscopically [28]. Although the short and long term outcomes proved to be excellent in about 90 % cases, it soon become evident that the thoracoscopic approach had some drawbacks: it required lung exclusion intraoperatively and a chest tube postoperatively, and when reflux was objectively measured by pH-monitoring 60 % of patients had abnormal acid exposure [29]. In 1995, Bonavina et al. first adopted the new minimally invasive techniques to the treatment of patients with achalasia, when they reported a laparoscopic esophageal myotomy combined with a Dor fundoplication that was performed uneventfully in 33 patients [30]. In another study on the same year, the group of Padua concluded that outcome of the laparoscopic approach was as good as that of the open approach, and concluded that because of lesser surgical trauma with consequent reduced postoperative pain and fast return to work the laparoscopic approach was preferable [31]. The laparoscopic approach therefore became at the end of the 1990s the standard of care and relegated the thoracoscopic approach in patients with a hostile abdomen and previous complex abdominal surgery. A few questions remained open, though: (1) How long the myotomy should be? (2) Which fundoplication should be done?

Modern Era: Standardization of the Surgical Technique

Today, it is generally believed that a laparoscopic short myotomy, usually associated with an inadequate extension onto the gastric wall, is often associated with persistent or recurrent dysphagia. Wright et al. compared 52 consecutive patients with achalasia who underwent a Heller myotomy extending for 1–2 cm onto the gastric wall and Dor fundoplication to 63 patients who underwent an extended myotomy (3 cm onto the gastric wall) with a Toupet fundoplication, and found that an extended myotomy gave better relief of dysphagia [32]. Therefore, today most surgeons perform a long myotomy which extends for 2–3 cm onto the gastric wall, as originally described by Heller. A fundoplication is also today routinely performed to prevent postoperative reflux. In fact, a randomized trial by Richards et al. showed that when a fundoplication is not performed, the incidence of abnormal postoperative reflux was 48 %, whereas it was 9.5 % only when a Dor fundoplication was added

to the myotomy [33]. As far as the type of fundoplication, Rawlings et al. in 2012 compared a Dor fundoplication to a Toupet fundoplication after myotomy for achalasia, and found no significant difference in terms of relief of dysphagia and reflux control [34]. On the other hand, a Nissen, 360° fundoplication, is contraindicated as it causes too much of an outflow obstruction in patients without peristalsis. In 2008, Rebecchi et al. in a prospective randomized trial comparing the outcome of a Heller/Dor and floppy Heller/Nissen demonstrated that while reflux was controlled in all cases, the incidences of dysphagia were 2.8 and 15 %, respectively [35]. Therefore, the current recommendation from the Society of American Gastrointestinal and Endoscopic Surgeons is that only a partial fundoplication to prevent reflux should be always done together with a cardiomyotomy [36].

Robotic Surgery, Single Site Surgery, and POEM: The Future?

A few groups have tried to apply the robotic techniques to perform the Heller myotomy arguing that the absence of tremor and magnified 3-D view can reduce the incidence of esophageal perforation. Horgan et al. in 2005 showed that the incidence of perforation was 0 % in the robotic group vs. 16 % in the laparoscopic group [37]. Later, in 2007, Huffman et al. showed similar findings (perforation rate: 0 % in the robotic group vs. 8 % in the laparoscopic group) [38]. Non-superiority of robotic surgery in terms of clinical outcomes when compared to laparoscopic surgery and significant cost and operating room times might raise concerns about the cost-benefit of this approach.

Notably, in the last few years there has been an impetus towards a more minimal approach to achalasia. Single-site surgery has been used to mimic the laparoscopic operation using only one port and short-term results have been promising. Barry et al. compared the short-term outcomes of 66 patients who underwent conventional multi-port Heller myotomy and Dor fundoplication with 66 patients who underwent single site Heller myotomy and Dor fundoplication [39]. They found that the single site operation took longer, but was as safe and effective in relieving dysphagia when compared to conventional surgery. However, their follow-up was short and no data were provided on the postoperative incidence of reflux [39].

In 2010, Inoue developed the Per-Oral Esophageal Myotomy (POEM) with overall initial good patient satisfaction and relief of dysphagia [40]. However, subsequent larger studies showed that this endoscopic surgical technique was frown by a high incidence of pneumothorax, pleural effusions, and heartburn [41]. Since 2010, then, many centers started performing POEM to evaluate objectively the efficacy and safety of this innovative technique. In 2013, Dr. Swanstrom reported his initial results on 18 patients. Although the clinical outcomes were good, 28 % of patients had esophagitis, the residual esophageal sphincter pressure after the procedure was still high (16.8 mmHg), and 46 % of patients had pathologic gastroesophageal reflux on pH- monitoring [42]. At the same time, 70 patients with Type II achalasia were recruited for POEM in five centers in Europe and North America. Again, the clinical outcomes were good but intraoperative complications were substantial (full thickness dissection in the mediastinum was 69 % and perforation into the peritoneal cavity was, 57 %). Also 42 % of patients in this series had esophagitis on follow-up endoscopy and no data on pH monitoring were available [43]. Finally, the most recent comparative study published in 2013 comparing objective outcomes of laparoscopic Heller myotomy with POEM for achalasia showed at a follow up 6 months a disturbing high persistent dysphagia in 76 % of patients who laparoscopic Heller myotomy compared to none in the POEM group [44].

In summary, time will test the outcomes of POEM against the long-term results benchmarked by those of laparoscopic myotomy with partial fundoplication and will assign POEM a defined and very specific role in the treatment of patient with achalasia.

Conclusions

The 100-year journey through the history of surgery for achalasia has identified through its successes and failures what constitutes today the "*proper treatment*" imagined by Moersch

in 1933 and Maingot in 1944. The cardiomyotomy, as envisioned by Heller exactly a century ago, performed laparoscopically together with a partial fundoplication is today the surgical treatment of choice. Longer follow-up and objective assessments of newer endoscopic techniques will characterize their role in the management of patients with achalasia.

Conflicts of Interest The authors have no conflicts of interest to declare.

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