Pneumatic Dilation for the Treatment of Achalasia

34

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Objectives

1. To describe the role of pneumatic dilation in the treatment of achalasia
2. To detail, which patients are appropriate for treatment with pneumatic dilation
3. To instruct, on the proper technique of performing pneumatic dilation in the treatment of achalasia
4. To compare, the efficacy of pneumatic dilation in the treatment of achalasia with other available treatment modalities

Introduction

Achalasia is the quintessential form of esophageal dysmotility characterized by abnormal lower esophageal sphincter (LES) relaxation and aperistalsis. Dilation of the LES has been at the forefront of the treatment of achalasia since 1674 when Sir Thomas Willis described dilation of the LES performed with a whalebone [1].

Modern use of pneumatic dilation for achalasia works by disrupting the LES smooth muscle fibers by forcefully stretching them using air-filled non-compliant balloons. Pneumatic dilation was first described in the early 1960s by Vantrappen et al. Of historical interest, the original technique involved the patient swallowing a weighted bag of mercury tied to a string. A guidewire with an eye was passed over the string. Then, sequential dilating balloons were passed over the guidewire and positioned at the level of the LES using fluoroscopy. Dilations would range from 3–5 cm [2]. Thankfully, the advent of flexible fiber-optic endoscopes has made the practice of swallowing weighted mercury bags obsolete. Modern pneumatic dilation is performed with balloons made from a soft polyethylene polymer mounted on a flexible catheter. Most balloons are 10 cm long and come in three diameters (30, 35, and 40 mm). The balloon is not visible under fluoroscopy but has four radiopaque markers on the shaft that define the upper, lower, and middle borders—the last defined by two markers close together. These balloons are non-compliant and therefore do not inflate maximally beyond the designated diameter [3].

The aim of this chapter is to describe the indications, patient selection, procedure technique, and potential complications of performing pneumatic dilation to treat achalasia.

Definition, Incidence/Prevalence, Epidemiology, Pathophysiology/Mechanism

The term achalasia first appeared in the medical literature in an article by Arthur Hertz in 1915. He credits the name designation to his colleague, Sir Cooper Perry. The term "achalasia" (a, not; χαλάω, I relax) was used to describe the underlying pathophysiology of this esophageal disease where the LES fails to relax [4]. Our understanding of and ability to diagnose, characterize, and treat achalasia has increased greatly since 1915. Achalasia is an esophageal smooth muscle motility disorder that is the result of the LES failure to relax in response to deglutition, resulting in a functional obstruction at the gastroesophageal junction. Complicating matters, there is loss of the esophageal peristaltic function and/or disorganized peristalsis. The combination of a functional obstruction at the LES and aperistalsis results in esophageal bolus stasis, leading to symptoms of dysphagia and voluminous regurgitation.

Achalasia is a rare disease occurring with an annual incidence of approximately one per 100,000 people and a prevalence of 10 per 100,000. Achalasia afflicts humanity as a whole and does not have a preponderance for a particular

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age, race, and/or gender [1]. Achalasia presents with equal frequency in both males and females. Achalasia typically presents between the second to the fifth decade of life with a peak incidence between the ages of 30–60 years. Achalasia occurs in the pediatric population with an estimated annual incidence of 5% in children less than age 16 [5].

The pathogenesis of achalasia is not fully understood. The pathophysiology of achalasia results from the inflammation and degeneration of myenteric plexus ganglion cells that innervate the smooth muscle of the esophagus and LES. Within the myenteric plexus, there are two types of neurons: excitatory cholinergic and inhibitory neurons using nitric oxide (NO) and vasoactive intestinal polypeptide (VIP) as neurotransmitters. This degeneration preferentially involves the NO-producing inhibitory neurons. The cholinergic neurons affecting the tonic contraction of the LES are relatively spared. This loss of inhibitory innervation of the LES results in loss of deglutative reflexive relaxation of the LES. In the smooth muscle portion of the esophagus, the loss of ganglion cells results in disordered peristalsis and subsequent aperistalsis, ultimately resulting in esophagogastric junction outflow obstruction from a poor relaxing LES.

Also, contributing to pathogenesis of achalasia is the esophageal response to the esophagogastric outflow obstruction. Feline models show the development of hypertrophy, excitability, and eventually failed peristalsis following placement of pressure cuffs around the distal esophagus, creating esophagogastric outflow obstruction. This occurs in humans as the result of laparoscopic gastric bands, malignancy, and tight fundoplication [6–9].

The clinical presentation of achalasia can be variable but classic symptoms are bland, large volume regurgitation, progressive solid and liquid dysphagia, chest pain/fullness, varying degrees of weight loss, and sometimes retrosternal burning or heartburn. As patients with achalasia may present with regurgitation and/or heartburn, differentiation from gastroesophageal reflux disease (GERD) can be difficult. This leads to many patients being started on pharmacologic therapies such as proton pump inhibitors (PPI) and sometimes even treated with anti-reflux surgery. Undoubtedly, the similarity in symptoms between GERD and achalasia results in a delay in achalasia diagnosis. This has been addressed in recent guidelines from the American College of Gastroenterology, which recommend evaluating patients with refractory GERD for other diseases, including achalasia. They recommend evaluating for achalasia in patients suspected of having GERD but who do not respond to acid suppressive therapy [10].

Despite being a rare disease, achalasia is associated with significant health care costs. A study from 2017 by Wadwha et al. revealed that between 1997 and 2013, the frequency of achalasia-related hospital discharges increased by 108% (from 2493 to 5195) and the national expenditure for achalasia increased by 675.2% from $32,020,083 ± 3,424,012 in 1997 to $248,215,416 ± 19,066,436 in 2013 ($P < 0.001$). These hospitalizations and costs were primarily in patients 65–84 years of age. The authors speculated this rise in discharges and cost may be the result of the introduction and widespread use of high-resolution manometry resulting in better disease recognition [11].

Although, modern treatment of achalasia has advanced significantly from the days of whalebone esophageal dilation, achalasia is still a chronic condition without a cure. All current treatment modalities for achalasia aim to alleviate the functional obstruction created by poor deglutitive relaxation and hypertonicity of the LES. The aims of therapy are to reduce symptoms, improve esophageal emptying, and prevent the development of a megaesophagus. Modern treatment options for achalasia include pharmacologic, endoscopic, and surgical approaches. Pharmacologic therapy has been demonstrated to be the least effective treatment modality for achalasia and should be pursued in patients who are not candidates for endoscopic or surgical therapies. Endoscopic treatments for achalasia include pneumatic dilation, botulinum toxin injection, and per oral endoscopic myotomy (POEM). Surgical options include laparoscopic Heller myotomy, usually performed in conjunction with either a Dor or a Toupet fundoplication. The purpose of this chapter is to discuss the clinical utility of pneumatic dilation in the treatment of achalasia.

Indications

Pneumatic dilation is an important treatment option for any of the diseases of esophagogastric junction outflow obstruction. These disorders include the three subtypes of achalasia and clinically relevant esophagogastric junction outflow obstruction (EGJOO). It is contraindicated in patients with severe coagulopathy and/or poor cardiopulmonary function that would preclude surgery [10].

Patient Selection

The advent of high-resolution impedance manometry has refined the classification of esophageal dysmotility. Disorders with esophagogastric junction outflow obstruction by the Chicago Classification scale v4.0 have a functional esophageal obstruction as the result of a poorly relaxing LES with or without preserved peristalsis. In this category, achalasia is the best-known esophageal disorder but a new manometric

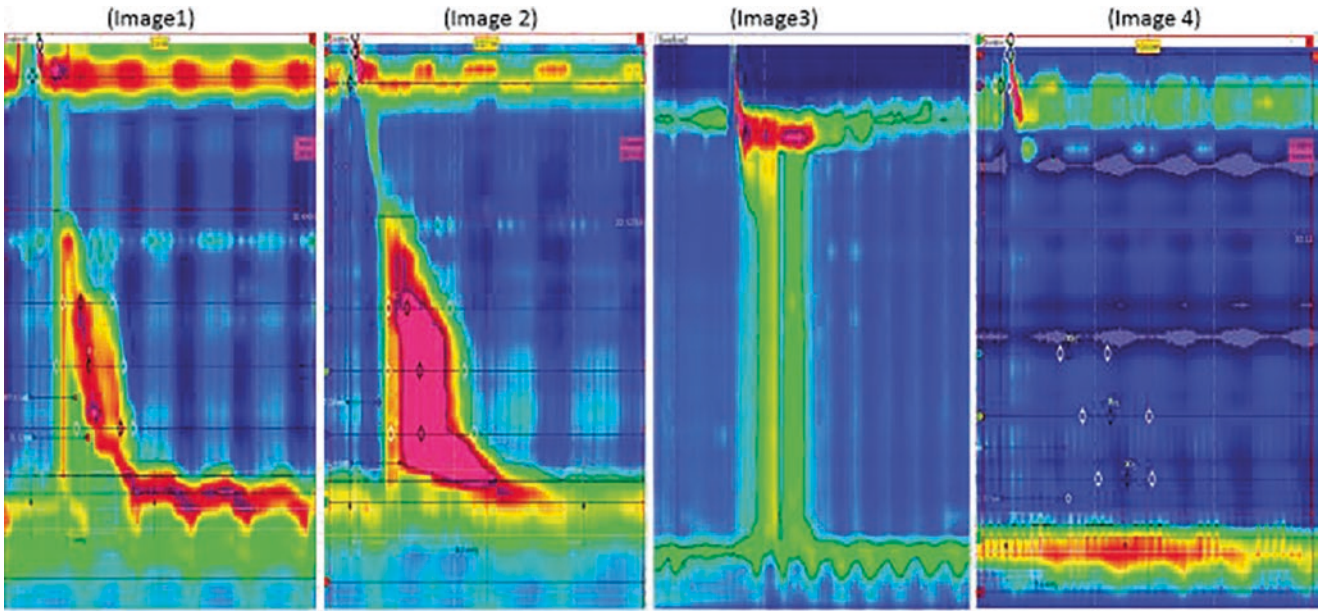

Fig. 34.1 Representative Clause plots representing the four subtypes of disorders of esophagogastric junction outflow obstruction. Image 1—Clinically relevant esophagogastric junction outflow obstruction. Image 2—Type III achalasia. Image 3—Type II achalasia. Image 4—Type I achalasia

diagnosis called esophagogastric junction outflow obstruction (EGJOO) has been defined as having an elevated integrated relaxation pressure (IRP >15 mmHg) with intact esophageal smooth muscle peristalsis [10]. High-resolution manometry allows for achalasia to be differentiated into three subtypes based on manometric patterns: type I (classic) with absent smooth muscle contractility in the esophageal body and an elevated IRP, type II with ≥20% of swallows of panesophageal pressurization and an elevated IRP, and type III (spastic) with shortened distal latency (<4.5 s), DCI >450 mmHg cm s and an elevated IRP. For the diagnosis of achalasia to be made, no identifiable peristalsis should be present. The achalasia subtypes are shown in Fig. 34.1. Subtyping achalasia is of paramount clinical importance as the three achalasia subtypes present very similarly but treatment response varies considerably between the three subtypes [11–13].

Patient selection should be made based upon the patient's cardiopulmonary functional status after high-resolution manometry has confirmed a disorder of esophagogastric junction outflow obstruction, and a balanced discussion about risks and benefits of the different surgical and endoscopic therapies available. In general, male patients less than 40 years of age and type 3 achalasia are better treated with surgical myotomy or POEM. However, this is a general rule of thumb and the authors would like to point out three clinical scenarios where pneumatic dilation may be preferable to surgery or POEM. These scenarios include patients who are morbidly obese (BMI >40), status post laparoscopic sleeve gastrectomy, and clinically relevant EGJOO. Symptomatic GERD is rare after pneumatic dilation (4–37%), compared with laparoscopic Heller myotomy with Dor fundoplication (8.8–26%) and POEM (17–41%) [14]. In a study comparing POEM to pneumatic dilation, 7% of achalasia patients developed post-procedure erosive esophagitis compared to 41% of the patients treated with POEM [15]. Therefore, pneumatic dilation may be a reasonable first procedure in patients with a high risk of post-myotomy GERD such as patients with morbid obesity or with sleeve gastrectomy anatomy. In the setting of EGJOO where peristalsis is routinely preserved, surgical intervention, especially POEM, seems overly aggressive as it creates a scleroderma-like esophagus (absent peristalsis with a hypotensive LES).

Preoperative Evaluation

All patients being considered for a pneumatic dilation need confirmation of a clinically relevant functional obstruction at the LES. Alternative obstructive etiologies should have been assessed for and ruled out with a prior upper endoscopy. These mechanical alternatives would include but are not limited to esophageal carcinoma involving the GE junction, tight fundoplication, esophageal stricture, and EoE [16].

Other endoscopic findings suggestive of achalasia are a rosette (puckered LES), retained secretions and/or food, and a dilated esophagus.

If feasible, all patients should undergo manometry prior to pneumatic dilation. We have stressed the importance of high-resolution esophageal manometry in subtyping achalasia. In general, type III achalasia patients do better with POEM compared with pneumatic dilation. Complementary tests to manometry are the traditional or timed barium esophagram (TBE) and EndoFlip® impedance planimetry. We would recommend obtaining these tests if they are available to help with the initial diagnosis and patient follow-up after treatment.

The TBE protocol begins with administration of 240 mL (8 oz) of low-density barium in the standing position; two-on-one spot films will be obtained at 1 and 5 min to assess liquid emptying. Barium column height and width will be measured from the GE junction to the top of the column that was recorded from each film. Next, the esophagus will be cleared with water, followed by ingestion of a 13-mm barium tablet. Tablet passage will be evaluated after 5 min with an abnormal test being tablet retention at EGJ. A TBE column height at 1 min of 5 cm and 5 min of 2 cm is used to discriminate between patients with achalasia/clinically relevant EGJOO and patients without disorders of EGJ outflow obstruction [17]. The EndoFlip® impedance planimetry system consists of a 24 cm long, 3 mm outer diameter catheter with a highly compliant balloon. The balloon surrounds 16 paired impedance planimetry sensors mounted on the catheter and a solid-state pressure transducer on the distal end of the catheter. EndoFlip® measures distensibility of the esophageal body and/or EG Junction. Reduced distensibility of the EG-junction is suggestive of LES dysfunction. The benefit of the EndoFlip® is that it can be done before and after an LES intervention to assess for improvement of the EGJ distensibility.

Technique

There are no clear guidelines for performing pneumatic dilation. Most centers in the world utilize an endoscopic approach with fluoroscopy. In Asia predominately, and in small centers without fluoroscopy, a purely endoscopic approach has been described [18]. For this chapter, the authors will describe their endoscopic approach using fluoroscopy, which has been used by the senior author for over 30 years. The most commonly used pneumatic balloon is the Boston Scientific Rigiflex™ balloon system, but other products are available. The Boston Scientific Rigiflex™ balloon system consists of a 10-cm long, non-compliant balloon on a flexible catheter with radiopaque rings defining the balloon location. The balloon system is available in 30, 35, and 40 mm diameters.

Prior to treatment, the authors recommend a complete endoscopic examination of the esophagus. The esophagus should be cleared completely of any retained secretions to minimize the risk of aspiration. Always inspect the cardia as pseudoachalasia from a tumor at the GE-junction is in the differential diagnosis. The initial balloon diameter selection is variable, but the authors tend to start with a 30 mm balloon and subsequently repeat pneumatic dilation with increasing balloon diameter size (35 mm and 40 mm) based on the persistence of symptoms after the initial pneumatic dilation. The pneumatic balloon catheter is advanced into the esophagus over a Savary guidewire. Fluoroscopic guidance is used to ensure appropriate positioning at the level of the LES. Next, the balloon is inflated slightly until a "waist" {a narrowing in the balloon under fluoroscopy representing the non-relaxing LES} (Fig. 34.2) is identified and balloon inflation occurs by increasing the PSI as measured with a sphygmomanometer until the "waist" disappears (Fig. 34.3). Dilation is used and held for 60 s after successful effacement of the "waist". After dilation, the patient is observed for 1–2 h, and we routinely obtain a post-procedure barium esophagram on all patients prior to leaving the endoscopy unit. The authors admit there is considerable variability in clinical practice.

The primary author routinely performs a pre-pneumatic dilation Endoflip®, endoscopic evaluation for perforation after every pneumatic dilation, and then performs a post-pneumatic dilation Endoflip; however, this is not practiced at all centers. The primary author also marks the rosette and the diaphragmatic hiatus with radio-opaque markers (Fig. 34.4). There is

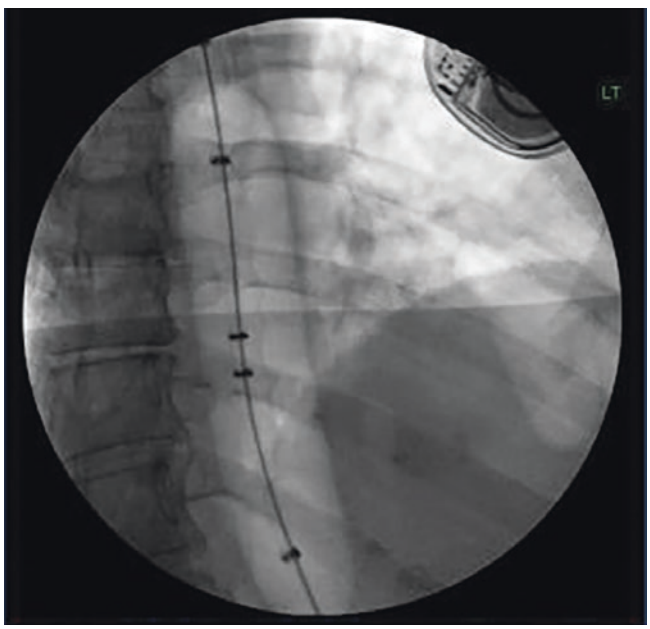

Fig. 34.2 Flattening of the "waist" following inflation of a 30 mm Rigiflex balloon

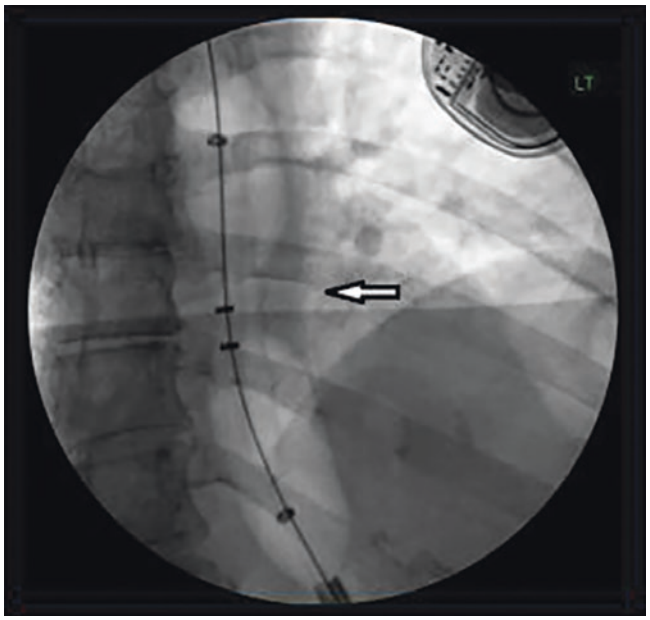

Fig. 34.3 Inflation of a 30 mm Rigiflex balloon revealing a "waist" at the EGJ. The waist is always on the left side of the balloon

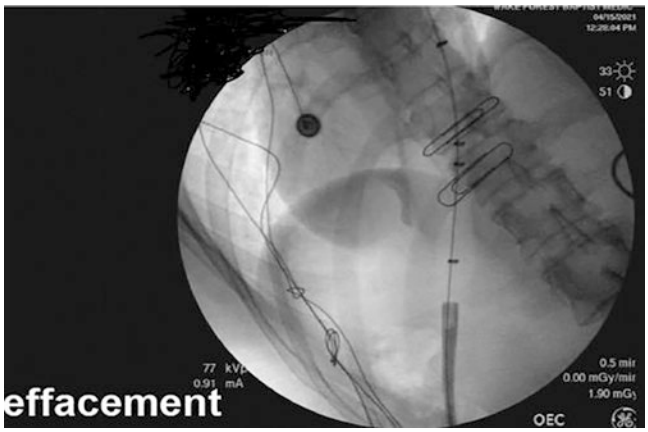

Fig. 34.4 Radiographic markers identifying the lower esophageal sphincter and the diaphragmatic hiatus

some controversy about the necessity of post-pneumatic dilation radiographic testing with gastrografin/barium esophagram to evaluate for perforation prior to discharge. The authors still routinely obtain an esophagram post-pneumatic dilation because esophageal perforation carries a high morbidity and mortality rate if not treated quickly and appropriately.

Outcomes

Pneumatic dilation is a safe and effective treatment for achalasia and should be part of any tertiary referral center's achalasia treatment armamentarium. Pneumatic dilation has proven clinical efficacy, resulting in good to excellent symptom relief with 3.0-, 3.5-, and 4.0-cm in 74%, 86%, and 90% of patients with an average follow-up of 1.6 years (range 0.1–6 years) [19]. As previously mentioned, the authors generally start with a 30 mm balloon for most patients, Pneumatic dilation can be repeated every 2–4 weeks in a sequential fashion with incremental increasing (30 mm–35 mm–40 mm) balloon size if persistence of symptoms necessitates. Serial pneumatic dilation has similar efficacy to laparoscopic Heller myotomy at two (85% vs 90%, respectively) and 5 years (82% vs 84%, respectively) [20], based on a large randomized control trial from Europe.

Patients that have the most optimal treatment response after treatment with pneumatic dilation include the following: older age (>45 years), female sex, narrow (non-dilated) esophagus, and LES pressure after pneumatic dilation of <10 mmHg [21]. Esophageal perforation is the most serious complication, with an overall rate, by experienced endoscopists, of 1–2.0%. The senior author has performed 680 pneumatic dilations over the last 25 years with 15 perforations (overall rate of 2.2%) The vast majority occurred with the 30 cm balloon and three with 35 cm balloons. Every patient undergoing pneumatic must be aware of the perforation risk and understand that surgical intervention is possible in the event of perforation [22]. In the last 10 years, we have successfully treated all perforations with an esophageal stent rather than surgery. In a large high-volume single-center study comparing complications and deaths after achalasia treatment, the authors reported significantly fewer complications in patients treated with pneumatic dilation compared to patients treated with laparoscopic Heller myotomy ($p = 0.02$) [23].

Healthcare Costs

Pneumatic dilation is highly cost-effective compared with both laparoscopic Heller myotomy and POEM. Patients undergoing Laparoscopic Heller myotomies are charged on average $44,839 and patients undergoing POEM are charged $41,730. Comparatively, an EGD with pneumatic dilation is $9190 per procedure. Therefore, pneumatic dilation remains the most cost-effective treatment, as long as the patient requires less than four dilations to achieve symptom relief [24].

In conclusion, pneumatic dilation remains a safe, effective, cost-efficient procedure to treat achalasia and should remain at the forefront for treating disorders of esophagogastric outflow obstruction, especially achalasia.

Questions

1. Which patient listed below would have the most favorable outcome after treatment with pneumatic dilation?
   A. 35-year-old male with type I achalasia
   B. 65-year-old female with type III achalasia
   C. 85-year-old male with severe COPD requiring high levels of supplemental oxygen and type II achalasia
   D. 50 year female with type II achalasia

Answer: D. Older patients, female gender, and narrow caliber esophagus tend to have more favorable outcomes when treated with pneumatic dilation. Pneumatic dilation should be avoided in patients who are poor surgical candidates. Type I and II achalasia patients can be treated effectively with pneumatic dilation. Type III achalasia patients should be considered for per oral endoscopic myotomy.

2. A 45-year-old female with type II achalasia presents for consultation to discuss treatment options for her achalasia. She is concerned about post-lower esophageal sphincter intervention risk of gastroesophageal reflux. Which of the following procedures is appropriate for the treatment of achalasia and has the lowest risk of post-treatment GERD?
   A. Nissen fundoplication
   B. Pneumatic dilation
   C. Laparoscopic Heller myotomy with Dor Fundoplication
   D. Per Oral Endoscopic Myotomy

Answer: B. Only 7% of achalasia patients develop post-pneumatic dilation erosive esophagitis, compared with 16% and 41% for laparoscopic Heller myotomy with Dor fundoplication and POEM, respectively. Therefore, pneumatic dilation may be a reasonable first procedure in patients with a high risk of either post-myotomy GERD, such as patients with morbid obesity or with sleeve gastrectomy anatomy. Nissen Fundoplication is an anti-reflux surgery and is not appropriate for the treatment of achalasia.

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