

Perspective on Peroral Endoscopic Myotomy for Achalasia: Zhongshan Experience

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Worldwide, peroral endoscopic myotomy (POEM) has achieved remarkable initial outcomes in the treatment of achalasia. In China, POEM has developed very quickly since the first case was performed in our center in August 2010. With experience, we have successfully performed POEM for special cases (such as pediatric patients, patients with sigmoid-type esophagus, and patients with recurrent symptoms after previous surgery) and have altered our technique to achieve long-term symptom remission and simplify the POEM procedure. These changes include posterior wall incision, full-thickness myotomy, a “push-and-pull” technique for myotomy, and water-jet assisted POEM. In this article, our experiences in POEM are summarized, including changes in technique, applications of the procedure, and the management of possible complications. (*Gut Liver*, 2015;9:152-158)

Key Words: Peroral endoscopic myotomy; Achalasia

INTRODUCTION

Peroral endoscopic myotomy (POEM) has been developed as a nonincision, minimally invasive endoscopic treatment becoming the most effective option for achalasia, maybe the primary and permanent one.¹ This procedure incorporates concepts of natural orifice transluminal endoscopic surgery (NOTES) and achieves endoscopic myotomy by using the submucosal tunnel as an operating space. In 2007, Pasricha *et al.*² used this technique successfully to perform endoscopic myotomy in a porcine model. Later, Inoue *et al.*³ made it successful in human patients and got a satisfactory outcome. Then, POEM has been developed very quickly and initial published experience in humans is more than encouraging despite a relatively short follow-up.¹

In China, the first case of POEM was performed in our center in August 2010.⁴ To date POEM procedures have been per-

formed in over 1,300 patients in our center, which may be over half the total cases of the world. Initial experiences from our center about complication managements and POEM for special cases (such as pediatric patients, patients with sigmoid-type esophagus, and recurrent symptoms after Heller myotomy [HM] or previous POEM) have been reported in several international conferences many times. As becoming more experienced, we also make some technique changes for achieving long-term symptom remission and simplifying the procedure of POEM.

In this article, our experiences in the technique changes, applications, and complication managements of POEM are summarized.

INDICATIONS AND CONTRAINDICATIONS

All patients with achalasia can be treated by POEM. Although its role and efficacy are not clearly validated, POEM has also been successfully performed in other hypertensive motor disorders associated with dysphagia and chest pain, such as diffuse esophageal spasm,⁵ nutcracker esophagus,⁶ and hypercontractile (jackhammer) esophagus⁷ (Table 1). The obvious dilation of esophagus (sigmoid-type esophagus, megaesophagus), recurrence/persistence of symptoms after HM or previous POEM, as well as other previous endoscopic treatments (including botulinum toxin injection, pneumatic dilation, and self-expanding metallic stents) may make subsequent endoscopic tunneling and myotomy more challenging, but usually does not prevent successful POEM.

Contraindications for POEM include severe cardiopulmonary disease or other serious disease leading to unacceptable surgical risk, pseudoachalasia, and failure in creating the submucosal tunnel because of severe fibrosis and adhesion. Despite that mild or moderate esophagitis that does not induce stricture of the esophagus is not excluded, severe esophagitis and/or very large

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Table 1. Indications and Contraindications for Peroral Endoscopic Myotomy

Indications	
Absolute indications	
Idiopathic achalasia	
Relative indications	
Other hypertensive motor disorders (diffuse esophageal spasm, nutcracker esophagus, jackhammer esophagus)	
Contraindications	
Absolute contraindications	
Severe cardiopulmonary disease or other serious disease	
Pseudoachalasia	
Failure in creating the submucosal tunnel because of severe fibrosis and adhesion	
Relative contraindications	
Severe esophagitis and/or very large ulcer in the lower esophagus	

ulcer in the lower esophagus or esophagogastric junction (EGJ) should be considered as the relative contraindication (Table 1).

OPERATORS

There is a substantial learning curve in performing POEM,⁸ and the best outcomes are likely to be achieved in medical centers with extensive experiences of endoscopic treatment. Experiences are needed for not only the operator, but also the assistant and nurse. The main operator should have received regular endoscopic training, owned the experiences of endoscopic resection (endoscopic mucosal resection [EMR], endoscopic submucosal dissection [ESD], and endoscopic retrograde cholangiopancreatography [ERCP], etc.), completed at least 30 cases of esophageal ESD, and been with rich experiences in managing the complications such as bleeding and perforation. The beginner is suggested to perform POEM under the close supervision of an experienced operator at the beginning; after performing a sufficient number of supervised POEM procedures, easy cases, such as patients with shorter course of disease and untreated before, can be performed independently. Difficult and advanced cases, such as patients with sigmoid-type esophagus or recurrent symptoms, should be only performed by very experienced operators.

CONVENTIONAL POEM PROCEDURE

Conventional POEM procedure majorly includes four steps:³

(1) Step 1: Mucosal incision. The point of entry usually lies on the anterior wall of the esophagus. A 1.5- to 2-cm longitudinal incision is performed in the 2-o'clock position about 10 cm above the EGJ after injection of saline mixed with indigo carmine and epinephrine.

(2) Step 2: Submucosal tunnel. The tunnel is created distally by using a technique similar to ESD. The tunnel is passed over the EGJ and 3 to 4 cm down to cardia.

(3) Step 3: Endoscopic myotomy. Under the direct endoscopic view, 2 cm below the mucosal entry point, the circular muscular layer is selectively dissected until 2 to 3 cm below the EGJ.

We routinely divide muscle fibers over a minimum length of 6 to 8 cm in the esophagus and at least 2 cm onto the cardia according to the surgical standards of HM. Substantial reduction of lower esophageal sphincter (LES) tonus is confirmed by opening the EGJ with gentle insufflation through the endoscope and easily passing an endoscope through the lumen of the esophagus. In patients with chest pain caused by the abnormal contractions of hypertrophied muscle within the esophageal body (often considered as type III achalasia on high resolution manometry), a long myotomy is made and all abnormal contractions (endoscopically visible and measured with manometry) are incorporated into the site of myotomy.

(4) Step 4: Closure of mucosal entry. After careful hemostasis, the mucosal incision site is closed with several hemostatic clips.

TECHNIQUE CHANGES

POEM has achieved remarkable initial outcomes for treating achalasia. Apart from the undoubted need to evaluate the clinical efficacy of POEM in prospective multicenter studies, attempts to simplify the procedure are underway. Technique changes introduced by us include posterior wall incision, full-thickness myotomy, a "push-and-pull" technique for myotomy, and water-jet assisted POEM. Using these techniques, the mean POEM procedure time was just about 35 minutes in our center, and the age of patients with POEM ranged from 3 to 98 years. An example of the POEM procedure using these technique changes is shown in Fig. 1.

POSTERIOR WALL INCISION

Posterior wall incision in the 5- to 6-o'clock position is the one of important modifications introduced by us.⁹ This modification makes the operation more convenient and faster because it is much easier to control your knife to create the tunnel and myotomy on the posterior wall versus the anterior wall. The spine located behind the esophagus does not restrict the appropriate positioning of the endoscope tip during posterior myotomy. According to our experience, posterior myotomy is also safe and has a comparable complication rate as with anterior myotomy (including bleeding and gastroesophageal reflux). Posterior myotomy in the 5- to 6-o'clock position also achieves myotomy from the luminal side without disturbing the acute angle of His, which is located at the 8-o'clock position; this is important to prevent reflux.

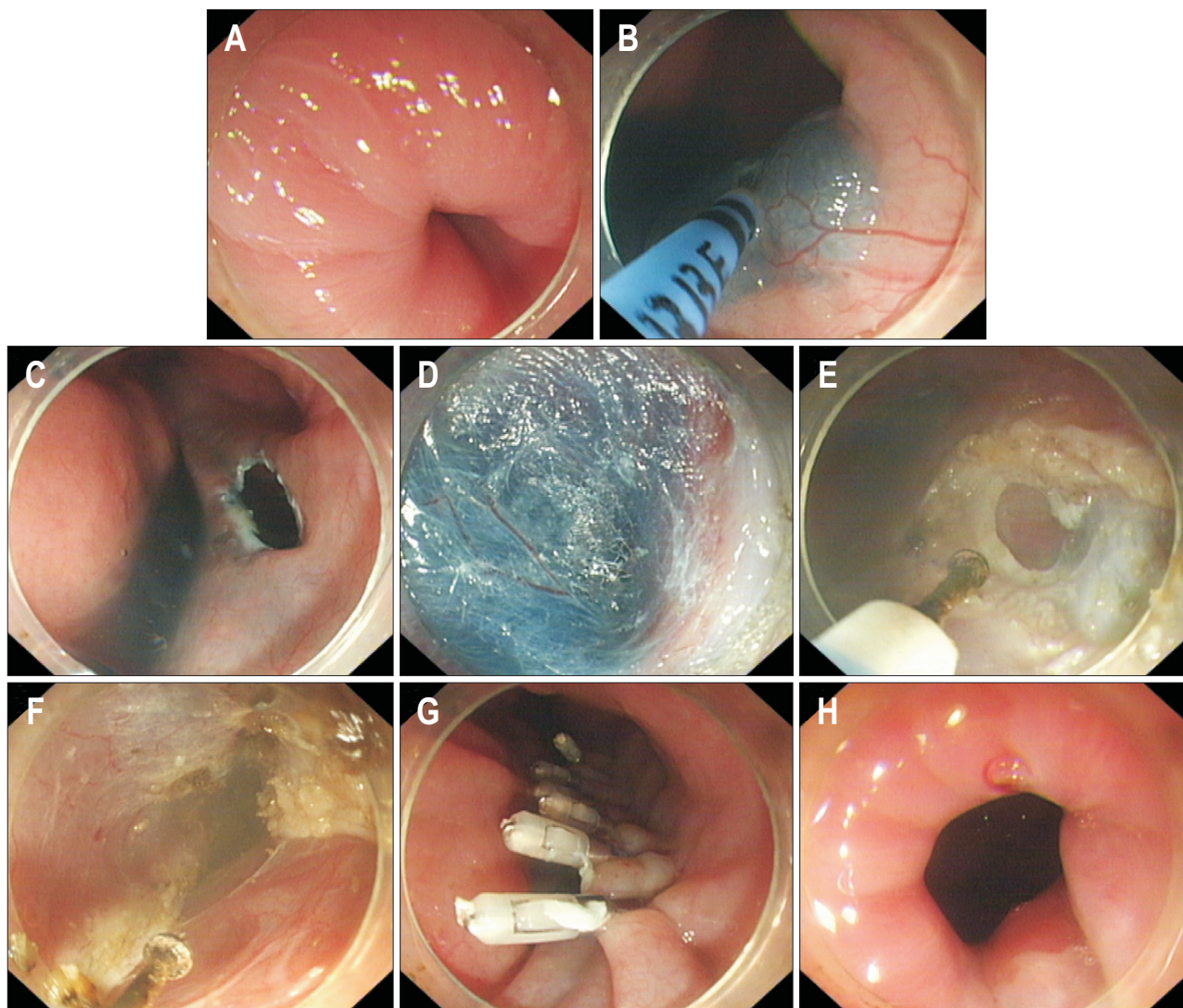


Fig. 1. Water-jet assisted peroral endoscopic myotomy (POEM) using the changes in technique that we introduced. (A) Cardiac stricture. (B) Submucosal injection in the 5- to 6-o'clock position using a water jet-assisted hybrid knife. (C) Mucosal incision on the posterior wall. (D) Creation of the submucosal tunnel. (E, F) Full-thickness myotomy. (G) Closure of the mucosal entry point. (H) Substantial reduction of lower esophageal sphincter tone after POEM.

FULL-THICKNESS MYOTOMY

Although a circular muscle myotomy preserving the longitudinal outer esophageal muscular layer is often recommended, which is different from the usual full-thickness myotomy performed surgically and designed in order to avoid entering the pleural space and decrease morbidity, it is often hard to achieve since the longitudinal muscle fibers of the esophagus are extremely thin which led frequently to an unintentional splitting of the muscle fibers during POEM. Either a minor electrocautery damage, mechanical trauma from maneuvering the endoscope in the tunnel, or air insufflation alone can result in spreading of the longitudinal muscle fibers, and adventitia and transmural openings into the mediastinum. In fact, a clear separation of circular (to be completely dissected) and longitudinal (to be

left) muscular layers cannot be found any more at the EGJ and stomach. Moreover, completeness of myotomy is a prerequisite for sufficient and long-term reduction of LES pressure and is the basis for the excellent result. Given the fact that an incomplete myotomy with possible fibrotic healing may be considered as a major reason for postoperative recurrence, a full-thickness myotomy may reduce the incidence of fusion by further spreading of the cut muscular wall and theoretically induce long-term symptom remission. For these considerations, POEM with a full-thickness myotomy including the internal circular and longitudinal muscular layer has been performed in about half of the achalasia patients in our center. On the basis of more than 1,300 cases' experiences in our center, short-term symptom relief and manometry outcomes were comparable between patients undergoing full-thickness and circular muscle myotomy. Full-

thickness myotomy significantly reduced the procedure time but did not increase the procedure-related adverse events or clinical reflux complications.⁹

A “PUSH-AND-PULL” TECHNIQUE FOR MYOTOMY

After successfully creating tunnel in the 5- to 6-o'clock position on the posterior esophagus, we can use a “push-and-pull” technique for full-thickness myotomy. After clinging the knife tip to the longitudinal muscle fibers and lifting them up toward the esophageal lumen, the full-thickness muscle bundles can be sectioned. Continuous cutting can be done just by pushing the scope. There is often no need to adjusting the insertion length of the knife. While in the confined area like cardia, pulling the knife and cutting the muscles from internal to external are usually needed in order to avoid mucosal injury. The technique makes the myotomy more convenient and faster.

WATER-JET ASSISTED POEM

Water-jet assisted HybridKnife is a new knife that combines high-pressure injection with electrical cutting. During POEM, the use of the HybridKnife leads to a significant decrease in POEM procedure time and facilitates reinjection, possibly contributing to a lower rate of minor intraprocedural bleeding.^{10,11}

POEM FOR SPECIAL CASES

POEM can be also performed in surgical failed or re-POEM cases. In these cases, the submucosal space may be obliterated and an obvious esophageal diverticulum may occur at the original myotomy site as a result of previous surgery; it may therefore be very difficult to confidently and easily create the

submucosal tunnel, as can be accomplished easily in those who have not had prior surgery. The myotomy should therefore be placed in an unscarred area that has not been previously myotomized. Given that it may be difficult to identify the original myotomy site, an initial mucosal incision is often empirically done in the 5- to 6-o'clock position on the posterior esophagus because primary HM is often done on the anterior or left lateral esophagus.^{12,13}

The sigmoid type of achalasia is considered to be difficult to treat, in which the esophageal lumen is significantly dilated and tortured. In patients with such megaesophagus, treatments include interventional ones and surgery ones, both thoracotomy and laparoscopy, are relatively harder. POEM can be also performed in these cases despite it is very difficult and time-consuming to make the tunnel.¹⁴

Achalasia is an extremely uncommon pediatric disease, with an estimated annual incidence of 0.02 to 0.11 cases per 100,000 children; however, it can lead to complications such as malnutrition, as well as mental and physical stunting. According to our relatively long-term follow-up study, POEM seems to be a promising new treatment for pediatric patients with achalasia resulting in long-term symptom relief in all cases and without serious complications after a mean of 24.6 months. POEM could become a real alternative to laparoscopic HM in pediatric patients once these results are confirmed in multicenter larger studies with a longer follow-up.¹⁵

COMPLICATION MANagements

Common complications of POEM consist mainly of gas-related complications, pneumonitis, and mucosal injury.¹⁶ Other rare but severe complications include delayed bleeding and gastrointestinal (GI) tract leakage (Table 2).

MUCOSAL INJURY

One refinement of POEM is the application of the ESD technique to create the submucosal tunnel. This precaution is vital to avoid injuring the overlying mucosa while tunneling because the mucosal injury may put the patient at the risk for a potential fistula with mediastinal sepsis, especially in those patients who have a full thickness myotomy. It is important to create the tunnel as close as possible to the muscular layers not only to avoid injury to the mucosal flap but also due to the lower vascularity adjacent to the muscle. However, as a consequence of tissue adhesions and limited space, the mucosal injury or even perforation sometimes occurs, especially at the cardia. This area can be clipped with metallic clips after myotomy. The endoscope assisted nasogastric tube placement can also be used for decompression when the injury occurred at the EGJ, especially at the stomach. If the mucosal tear area is large or there are multiple ruptures which cannot be clipped, using of a covered

Table 2. Complications of Peroral Endoscopic Myotomy

Common complications
Mucosal injury
Gas-related complications (intraoperative and postoperative)
Subcutaneous emphysema
Pneumomediastinum
Pneumothorax
Pneumoperitoneum
Pleural effusion
Pneumonitis
Fever (temperature $\geq 38^{\circ}\text{C}$)
Severe postoperative pain
Rare complications
Delay bleeding
Submucosal infection
Gastrointestinal tract leakage

retrievable stent or fibrin sealant can be alternative options for sealing the rupture. After mucosal integrity repaired, the mucosal injury often does not induce any clinical complications, even in those patients who have a full thickness myotomy. The use of blunt dissection for submucosal tunnelling, either balloon or a novel gel, may be considered as an alternative to facilitate the procedure and decrease the risk of incidental mucosal injury, especially for operators without sufficient ESD experience.^{9,15,16}

COMPLICATIONS ON COMPUTED TOMOGRAPHY SCAN

Early routine chest computed tomography (CT) scan for achalasia patients who received POEM procedure can detect a number of the common sequelae, postoperative gas-related complications, and noninfectious pneumonitis. Gas-related complications of POEM, including subcutaneous emphysema, pneumothorax, and pneumoperitoneum, are often of limited clinical significance, and can be resolved with conservative treatments. Because of the rapid diffusion, CO₂ gas instead of room air should be advocated for insufflation to reduce the incidence of gas-related complications. The radiographic and clinical features of pulmonary inflammation on CT scan were more consistent with pneumonitis rather than a frank infection. We also did not treat any of the patients for an infectious related pneumonia. In our opinion, the pneumonitis is majorly mostly caused by the irritation and inflammation due to operation injury, rather than aspiration and postoperative factors. Thus, routine CT scan after POEM is probably not warranted due to the high rate of minor and clinically irrelevant findings. Adverse event requiring intervention always has clinical correlate, and we want to stress that the most important parameter in the management of POEM adverse events such as pneumothorax is always the patients' clinical status. We therefore suggest post-POEM CT should be selectively used in symptomatic post-POEM patients.¹⁷

For pneumothorax with a volume of more than 30%, thoracic drainage should be carried out. A central venous catheter is inserted at the 3rd or 4th intercostal space instead of regular chest tube for drainage. After 2 to 3 days of the drainage, the decompressed lung comes back to normal condition and the drainage tube can be removed. If the CT image or the X-ray film shows

a small amount of free gas under the diaphragm, by maintaining the conservative treatments mentioned above, the gas will be absorbed automatically. If abdominal bloating is severe, a 20-gauge needle should be used for drainage of the gas from the abdominal cavity and a stomach tube is inserted simultaneously when necessary. Pleural effusion occurs in about 40% of the patients after POEM. If the patient only has small volume of pleural effusion and is absence of fever, the spontaneous absorption of the effusion is often observed without further intervention. For the patient who suffers from large amounts of pleural effusion or has persistence of the high temperature, ultrasound-guided thoracentesis and drainage should be performed to prevent further infection.¹⁶

DELAYED BLEEDING

Postoperative delayed bleeding in the submucosal tunnel is a rare complication after POEM. Despite of the low incidence, delayed bleeding can result in serious conditions, such as massive bleeding and hemorrhagic shock, once it occurs it can be fatal. Thus, early prevention, prompt diagnosis, and effective management are most critical for the patient outcome. In summary, vomiting of fresh blood and progressive serious retrosternal pain are the major early manifestations in patients with delayed bleeding in the submucosal tunnel after POEM. When delayed bleeding is suspected, emergency gastroscopy should be performed immediately for exploration and a hematoma is often found along the mucosa covering the submucosal tunnel. Chest CT scan can also be used to detect early signs of postoperative bleeding. A hematoma can be often observed on CT scan before any clinical manifestation occurs. Emergency endoscopic hemostasis should be performed immediately after symptom emergence. Blood and any blood clots at the wound and in the tunnel should be patiently and meticulously cleared to expose the bleeding site(s). When the active bleeding points are identified, coagulation using hemostatic forceps can be performed as is done for delayed bleeding after ESD. It should be worth mentioning that a Sengstaken-Blakemore tube is particularly effective for providing compressive hemostasis to staunch post-POEM bleeding.¹⁸

Table 3. Tunnel Endoscopic Surgery

Novel procedure	Disease
Peroral endoscopic myotomy	Achalasia
Submucosal tunneling endoscopic resection	Gastrointestinal submucosal tumors originating from the muscularis propria layer
Peroral endoscopic submucosal pyloromyotomy	Pyloric stenosis
Endoscopic submucosal tunnel dissection	Large esophageal neoplastic lesions
Retrograde submucosal tunneling technique	Complete esophageal obstruction

GI TRACT LEAKAGE

GI tract leakage post-POEM include esophagomediastinal fistula, esophagothoracic fistula, and so forth. The maintenance of mucosal integrity is critical for the prevention of GI tract leakage. The clips on the tunnel entry breaking off early might be an important reason to result in the GI tract leakage as the leakage orifice was detected at the entrance of the tunnel in the patients. Early diagnosis is difficult as the lack of typical symptoms of esophageal leakage before the oral intake. Leakage should be considered if there is any unusual or slow course of recovery. Endoscopy is recommended as a safe and sensitive method to detect small leakage and an effective treatment for the closure of the leakage in the early stage. Patients with esophageal leakage after POEM could achieve complete recovery in a short time by the endoscopic closure of the leakage, sufficient drainage and optimal conservative management without surgical intervention. Adequate nutrition support by enteric feeding tube is another important factor to significantly reduce the morbidity and healing time.

OFFSHOOTS OF POEM

The emergence of POEM marks the rising of a new branch of therapeutic endoscopy. Our group defines it as tunnel endoscopic surgery which includes several novel procedures utilizing a submucosal tunnel as an operating space (Table 3).¹⁹ In 2010, we innovated a new procedure that takes advantage of the submucosal tunneling technique popularized by POEM in order to achieve complete, full thickness endoscopic resection of GI submucosal tumors (SMTs) originating from the muscularis propria layer. Our group coined the acronym STER (submucosal tunneling endoscopic resection) for this procedure.^{20,21} The advantage of STER is maintenance of GI tract mucosal integrity while achieving an en bloc resection of SMTs. This method will possibly reduce the risk of postoperative GI tract leakage and secondary infection. In contrast to conventional endoscopic procedures and NOTES, this technique is unique because it uses the submucosal space between the mucosal and muscular layers. Other reported applications of tunneling technique include peroral endoscopic submucosal pyloromyotomy for pyloric stenosis, endoscopic submucosal tunnel dissection for large esophageal neoplastic lesions, retrograde submucosal tunneling technique for management of complete esophageal obstruction, and so forth.²² In the future, other applications may include sampling of the enteric nervous system and muscle, submucosal implantation of devices (such as microstimulators and drug delivery pumps), and bulking agents for reflux and incontinence. In our center, endoscopic sympathectomy using submucosal tunneling technique has been attempted in a porcine model. This procedure may further be considered as a treatment option for palmar hyperhidrosis.

CONCLUSIONS

POEM seems to be a safe and effective surgical myotomy option for treating achalasia, even for special cases such as pediatric patients, patients with sigmoid-type esophagus, and recurrent symptoms after previous surgery. In order to achieve long-term symptom remission and simplify the procedure, several technique changes of POEM are introduced by us including posterior wall incision, full-thickness myotomy, a “push-and-pull” technique for myotomy, and water-jet assisted technique. Apart from the undoubted need to evaluate the clinical efficacy of POEM in prospective multicenter studies, attempts to simplify the procedure are still underway.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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