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Navigated Retrograde Endoscopic Myotomy (REM) for the treatment of therapy-resistant achalasia

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Abstract

Background:

In achalasia, muscle spasm may involve the proximal esophagus. When the muscle spasm is located in the proximal esophagus, conventional Per Oral endoscopic Myotomy (POEM) may not be sufficient to relieve symptoms. In this paper, we describe Retrograde Endoscopic Myotomy (REM) as a novel approach to perform myotomy of the proximal esophagus, with the application of a navigation tool for anatomical guidance during REM. Our aim was to evaluate the feasibility and safety of REM, and usefulness of the navigation during REM.

Method:

A 42-year-old male with type III achalasia who was treated with laparoscopic myotomy with fundoplication, multiple pneumatic balloon dilations, Botox injections and anterior POEM of the middle and distal esophagus without symptomatic effect. Repeated high resolution manometry (HRM) revealed occluding contractions of high amplitude around and above the aortic arch. A probe based real time electromagnetic navigation platform was used to facilitate real-time anatomical orientation and to evaluate myotomy position and length during REM.

Results:

The navigation system aided in identifying the major structures of the mediastinum, and position and length of the myotomy. 12 weeks after REM, the Eckardt score fell from seven at baseline seven to two. We also observed improvement with reduction of the pressure at the level of previous spasms in the proximal esophagus from 124 mm Hg to 8 mm Hg on HRM.

Conclusion:

REM makes the proximal esophagus accessible for endoscopic myotomy. Potential indication for REM are motility disorders in the proximal esophagus and therapy failure after POEM.

Keywords: achalasia, esophageal motility disorder, endoscopic myotomy, POEM, real-time navigation

Introduction:

Achalasia is a rare motility disease of the esophagus, defined as incomplete relaxation of the lower esophageal sphincter (LES) and absence of propulsive esophageal contractions. The hallmark symptoms are dysphagia, chest pain, weight loss and regurgitation. By Chicago classification criteria of esophageal motility disorders (EMD), achalasia can be divided into three subtypes, based on high-resolution manometry in the untreated patient [1]. All subtypes have elevated residual pressure of the LES, but have different patterns of abnormal motility of the body of the esophagus. Type I is the classical achalasia, with absence of contractions, while type II has pan-esophageal pressuriazation, and in type III high-pressure spastic contractions may appear anywhere in the esophagus. Type III is least amenable to therapy, even to Per Oral Endoscopic Myotomy (POEM) [2,3].

Treatment options for patients not responding to primary POEM, could be to perform a re-do POEM [4]. When the muscle spasm is located at the proximal esophagus, conventional POEM is difficult, due to the limited access and requirement of a safe distance of the myotomy from the upper esophageal sphincter (UES). POEM requires a mucosal opening large enough for an endoscope to enter, and the myotomy should have an overlap of normal mucosa 2 cm away from the mucosal entry site for safety reasons. Placing clips to close the mucosal opening too close to the UES may also cause discomfort for the patient. The proximal limit for myotomy during POEM has therefore theoretically been around 5 cm from UES.

In this paper, we describe Retrograde Endoscopic Myotomy (REM) as a novel approach to perform myotomy of the proximal esophagus, with application of a navigation tools for anatomical guidance during REM. Our aim was to evaluate the feasibility and safety of REM, and usefulness of the navigation during REM.

Patient and methods:

The patient was a 42-year-old Caucasian male with type III achalasia diagnosed in 2010. His dominant symptoms were disabling attacks of chest pain and dysphagia. He was previously treated extensively in another tertiary center in 2011 with laparoscopic Heller´s myotomy combined with anterior fundoplication, and later with repeated pneumatic balloon dilations (PBD). Botox injections in the proximal esophagus were attempted twice, but resulted in larynx nerve paralysis without any improvement of symptoms. He was to our institution and was treated with anterior POEM in 2014 with 14 cm myotomy from the arch of the aorta to the cardia. The Eckardt score went from 9 to 7 points after POEM, with only slight improvement of dysphagia and regurgitation, but no improvement for pain.

On repeated high-resolution manometry (HRM) and barium swallow test (BST), occluding contractions of high amplitude around and above the aortic arch were recognized (Fig. 1), while the 4s IRP of the LES was normal (3.6 mmHg). During contractions, the patient experienced pain, which was reproducible on HRM and BST. During a pain attack, a maximum pressure of 123 mmHg was recorded. Despite above-mentioned treatments, he still had disabling symptoms. After informed oral and written consent, we performed REM in 2016.

The patient was administered topical antifungal therapy for 7 days prior to REM. He was fasted for 12 hours, and given antibiotics the evening before REM with Metronidazole and Ceftriaxone, which was continued for 3 days. Postoperatively the patient was hospitalized for 6 days and followed up using Eckardt score, BST and HRM to evaluate the results of REM after 12 weeks.

Setup of the operation theater

General anesthesia with tracheal intubation was administered, with constant monitoring by a nurse anesthetist. The patient was placed in a supine position in a conventional laparoscopic setting with the right arm abducted 80-90 degrees. During REM, the endoscopist stood on the right side of the patient facing the head and monitors (Fig 2). A straight scope position could be easily achieved. Installation of water was used to identify the posterior portion of the esophagus.

Laparoscopic procedure, creation of gastrostomy

Abdominal entry was made with a 12mm trocar (Visiport, Medtronic, USA. Two additional 12 mm trocars were established. A 15mm trocar (B15LT, Endopath Xcel, Ethicon, Johnsson&Johnsson) was used to enter the gastric body, which was placed in a straight line to the cardia (fig.3). The gastroscope was inserted through this 15mm trocar. After endoscopic myotomy was performed, the gastrostomy was closed with two V-lock sutures.

Navigation system set up

A research navigation system for minimally invasive procedures (CustusX, SINTEF, Trondheim, Norway) was used for both preoperative planning and intraoperative navigation. The system has previously been implemented in a range of clinical areas [5].

Three-dimensional (3D) models of the mediastinal anatomy (esophagus, vessels, airways and spine) were reconstructed from the patient's own computer tomography (CT) images. The electromagnetic (EM) tracking system (Aurora®, Northern Digital Inc. Waterloo, ON, Canada) was used to facilitate intraoperative real-time position and orientation tracking. An EM transmitter box set up an EM field around the patient´s chest during the REM (Fig. 4a) and a navigation probe (Aurora® 6DOF Catheter, Type 2) was introduced through the working channel of the endoscope to locate the position of the endoscope tip in relation to the 3D CT images.

At the start of REM, the CT images were matched to the patient´s position on the operating table by sampling anatomical landmarks on the patient's chest using an EM pointer (Aurora®

6DOF Probe, Straight Tip, Standard) (Fig. 4b), and identifying the same landmarks in the CT images. The landmarks used were: the suprasternal notch, the sternal angle, the clavicles and the xiphoid process.

Preoperatively, the 3D visualization of the CT data in conjunction with the manometry data were used to select the optimal route for the myotomy and to avoid vital structures. The models were used to plan the procedure including the start and end for the submucosal tunnel and myotomy. Intraoperatively, the navigation probe was introduced in the working channel of the scope to visualize its positions and orientation in real-time in relation to the anatomical 3D CT models. It also facilitated evaluation of the myotomy position and length during REM by storing previous positions (e.g. the mucosal opening) and displaying the distance to the current sensor position (Fig. 5).

Retrograde Endoscopic Myotomy (REM) protocol

After the creation of the surgical gastrostomy, the gastroscope (HQ190, Olympus, Tokyo, Japan) was introduced through the trocar into the stomach. A nasogastric tube was placed to facilitate identification of the esophageal lumen within the fundoplication. The endoscope was introduced to the UES. The UES was marked as zero for further measurements and a calibration point for navigation.

A submucosal tunnel at the posterior (6 o´clock) position was made by first injecting 2-3 ml of saline with Indigocarmine to create a submucosal lift, and a mucosal incision with a diathermic knife (KD-640L, Triangle Tip, Olympus Tokyo, Japan) was created 14 cm from the UES. The setting for the diathermy (Erbe VIO 300) was Endocut Q Effect 2 for mucosal incision, and myotomy, while for submucosal dissection, spray coagulation 50w effect 2 was used. The mucosal opening and myotomy was aimed to overlap the proximal margin of the myotomy from the previous POEM, which was located at the lower edge of the aortic arch.

The submucosal tunneling was done in a standard fashion as in POEM, as one straight line along a cranial axis. At the level where spasms had been measured on HRM, we observed a markedly thickened muscular bundle and fibrosis in the submucosa, otherwise the creation of the submucosal tunnel was uneventful. Sterile water was used for irrigation and CO_2 for insufflation during REM. Gentamycin 80 mg was delivered in the submucosal tunnel with a spray catheter (PW-205V, Olympus, Tokyo, Japan) before myotomy. The myotomy was performed caudally to cranially toward the posterior aspect of the esophagus along the thoracic spine (Fig. 6). On the navigation, we could see that the distance from the proximal myotomy border to the UES was around 2 cm. The tunnel opening in the mucosa was then closed with four endoscopic clips (Instinct, Cook Medical, Limerick, Ireland). The REM procedure took 90 minutes.

Results

Clinical course

After REM, the patient fasted for 24 hours, then we performed fluoroscopy of the esophagus with water-soluble contrast (Iomeron, Bracco Imaging, Milano, Italy) to exclude contrast leakage outside the esophagus. We observed pain related to hematoma at entry site of the laparoscopic ports. The patient did not experience any symptoms from the esophagus or its surroundings. The patient was admitted for 6 days. CRP and leucocyte counts remained in the normal range (Tab 1)

Adverse events

During the laparoscopic procedure, minor bleeding occurred perioperatively, and hematoma developed at the entry site for the gastrostomy trocar, causing local pain postoperatively. For the REM procedure, we did not observe any adverse events.

Outcome measures

The primary outcome measure was reduction of symptoms, which was evaluated with Eckardt score. Secondary outcome is reduction of contractions observed near the aortic arch during BST, and measurable reduction of pressure at the high-pressure zone with HRM.

Ten weeks after the procedure, the Eckardt score fell from seven at baseline to two, with the dominant symptoms still being pain attacks, but no dysphagia or regurgitation. The pain attacks were, however, described as less intense and more infrequent compared to the pre-REM situation. The patient could resume his full-time occupation.

After 12 weeks, we performed a new HRM and BST. On the BST, we could no longer locate occlusive contractions in the proximal esophagus. We also observed improvement with reduction of contractions at the HRM, and the pressure at the level of previous spasms in the proximal esophagus was reduced from 124 mm Hg to 8 mm Hg. The reduction of mean DCI was from 249 to 0.9 mmHgxcmxs.

Discussion

To our knowledge, this is the first report of REM for the treatment of a motility disorder affecting the proximal esophagus. REM significantly reduced the symptoms of our patient, which is reflected in the reduction in Eckard score. It shows the feasibility and safety of treating EMD of the proximal esophagus, which is not accessible using an oral route. REM may be an approach to treat patients with other EMDs who have findings on BST and HRM that show spasms in the proximal esophagus after POEM. When indicated, combined REM and POEM will allow myotomy of the entire length of the esophagus. A potential indication for REM is therapy failure after POEM with a long myotomy.

The posterior route for myotomy was chosen based on the findings on CT scan. The lateral and anterior directions are close to many vital structures. In the posterior direction, above the aortic arch, the esophagus is close to the thoracic vertebral column, with the anterior longitudinal ligament as the closest structure. The ligament is robust, and would probably tolerate more trauma in case of accidental dissection and dislocation of instruments. During the myotomy, we visualized the anterior longitudinal ligament, which also facilitated orientation together with the navigation system. We could not observe any other vital structures during the myotomy.

The main drawback of REM is the need of surgical assisted gastrostomy as entrance port. This procedure required a surgical team and operation room. The patient experienced also complication with a heamatoma at the trochar site, with was recognized by slight fall of Hb, without clinical manifestation. REM should be tried as last resort.

The navigation system was in this case particularly helpful in the planning phase to mark the area for myotomy based on HRM and the 3D anatomy models. Intraoperatively, the system visualized the position of the sensor located in the endoscope's working channel, in relation to preoperative images and the planned myotomy length. The navigation probe had to be introduced in the working channel of the endoscope intermittently, thus it could not provide feedback to the user continuously during the procedure since the working channel had to be available for other equipment. An integrated probe, or even fastening the probe on the outside of the scope, would overcome this problem.

A drawback using the tracking system for this specific procedure was the reduced accuracy resulting in the image-to-patient alignment being around 1 cm. This was compensated by marking new reference points at the mucosal opening and at the end of the myotomy from the luminal side and inside the submucosal tunnel. The operator could thus monitor the length and position of the endoscope in relation to these positions. The reduced navigation accuracy could be explained by the registration procedure. Most of the anatomical landmarks used in the registration were located proximal to the myotomy area, where the accuracy appeared superior to more distal positions. It is also difficult to pinpoint identical positions in the CT and on the patient surface, and there might be changes in positions between the patient anatomy compared to the 3D-CT data. A future improvement in the navigation system accuracy would be to introduce more landmarks in a larger area, positions along the inside of the esophagus or fiducial markers placed on the patients' skin. Further studies are required to confirm our findings. Based on our experience, we believe that REM at the posterior route is feasible and can be done safely without navigation in the hands of an expert endoscopist with experience with POEM.

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- KDCP got the idea for REM and use of navigation during REM, performed REM, and wrote the paper
- RFH, OHG, JGH and AV reviewed the paper, and contributed as scientific supervisors
- TL, EFH, GAT prepared and set up the navigation system
- TP performed the laparoscopic surgery
- RM reviewed the paper

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Abbreviations:

REM: Retrograde Endoscopic Myotomy

BST: Barium swallow test

POEM: Per oral endoscopic myotomy

PBD: Pneumatic balloon dilation

CT: Computer tomography

HRM: High resolution manometry

EMD: Esophageal motility disorder

LES: Lower esophageal sphincter

UES: Upper esophageal sphincter

EM: Electromagnetic

Legends

- Fig. 1 High-resolution manometry showing occluding contractions of high amplitude around and above the aortic arch.
- Fig. 2 During REM, the endoscopist stood on the right side of the patient facing the head and monitors.
- Fig. 3 Position of 12 mm trocars (blue) and 15 mm trocar (red) on the abdomen.
- Fig. 4: a: The navigation system EM field generator mounted to cover the myotomy area. b: Positioning of the 3D image-to-patient anatomical landmarks.
- Fig. 5: 3D model reconstructed from CT presented in the navigation system, CustusX. Left: The navigation system showing the sensor in the endoscope (white), esophagus (green), vessels and heart (red), airways (blue) and axial skeleton in 3D (white-brown). Right: Axial and coronal CT slices are visualized with segmented structures overlay. The center of the yellow cross indicates the real-time sensor position.
- Fig. 6 The proper muscle layer (yellow arrow) in relation to the thoracic spine (red arrow)

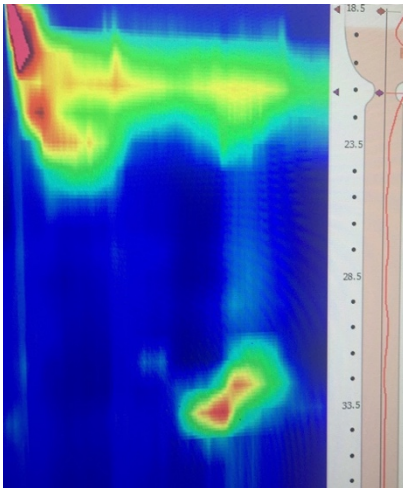


Fig 1 High resolution manometry showing occluding contractions of high amplitude around and above the aortic arch.

Fig 2. During REM, the endoscopist stood on the right side of the patient facing the head and monitors.

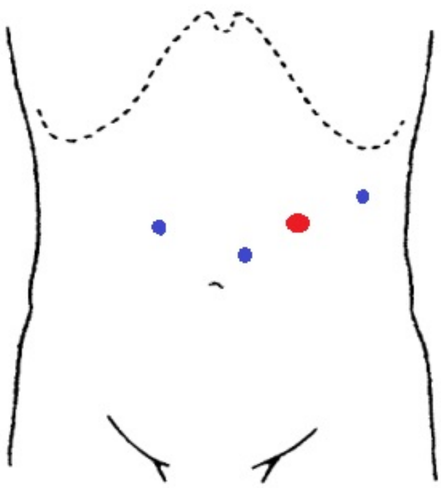


Fig. 3 Position of 12 mm trocars (blue) and 15 mm trocar (red) on the abdomen.

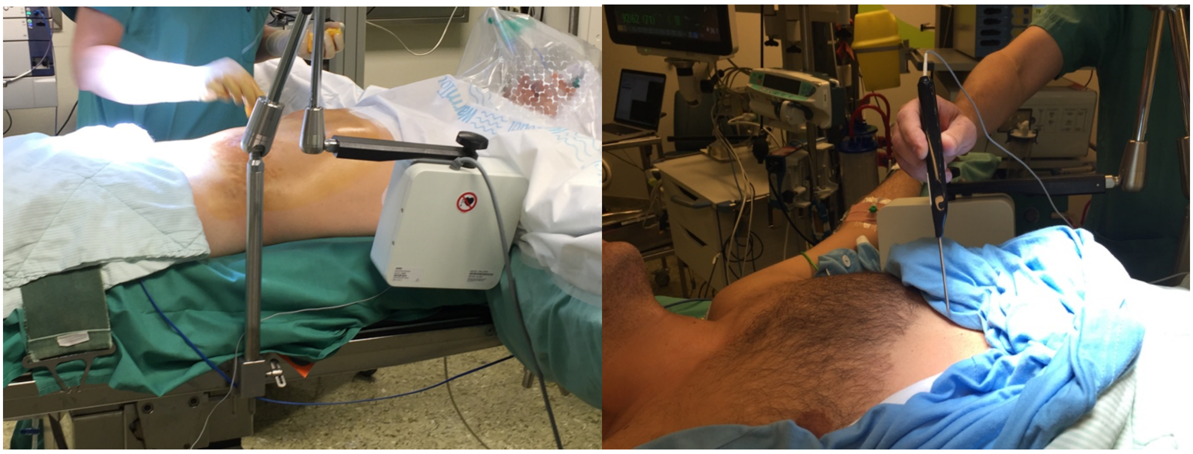
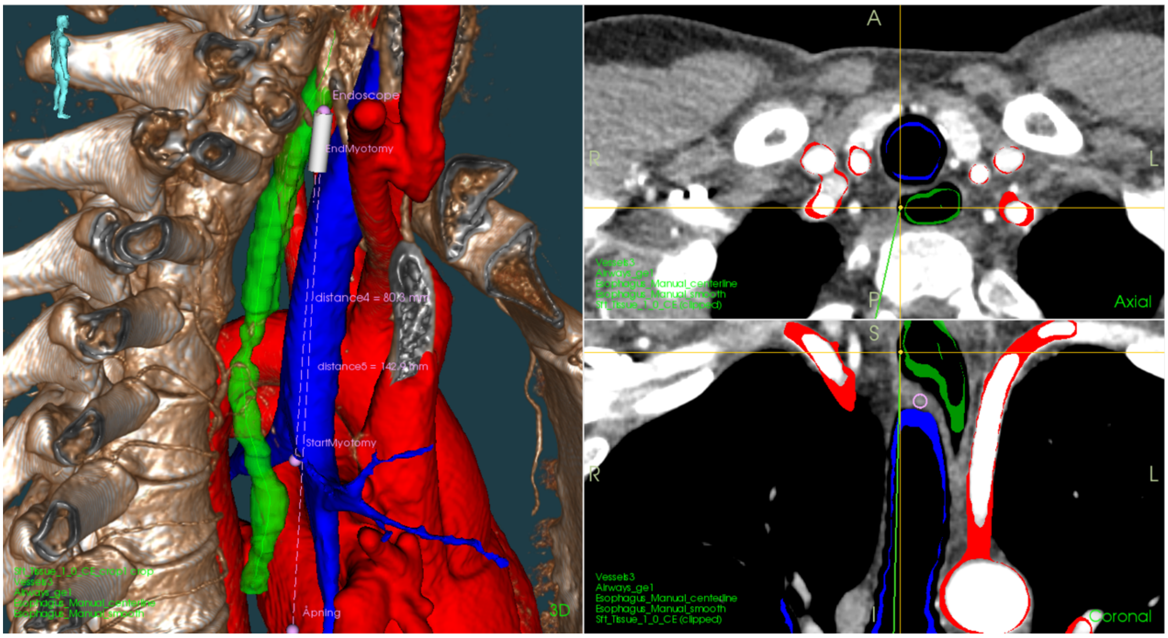


Figure 4: a: The navigation system EM field generator mounted to cover the myotomy area. b: Positioning of the 3D image-to-patient anatomical landmarks.



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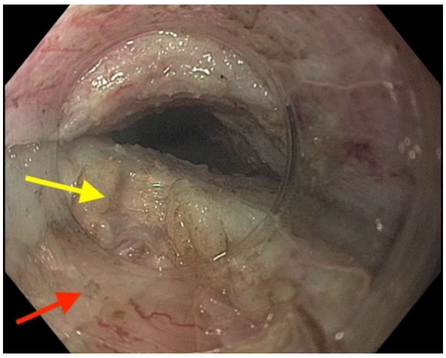

Fig. 6 The proper muscle layer (yellow arrow) in relation to the thoracic spine (red arrow)

Table 1

Day	CRP	Leucocytes	Hb
0	1	5,2	14.4
1	32	5,9	12.4
2	48	5,5	11.9
3	26	5,0	12.9