CLINICAL CASE

TOTALLY MINIMALLY INVASIVE ESOPHAGECTOMY 3D HD FOR THORACIC ESOPHAGEAL CANCER AFTER NEOADJUVANT CHEMORADIOTHERAPY

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Abstract

Esophagectomy is a major surgical procedure with morbidity, and mortality related to the patient's condition, stage of the disease at the moment of diagnosis, complementary treatments and surgical experience of the surgeon. Minimally invasive esophagectomy (MIE) may lead to a reduction in perioperative morbidity and mortality with an accepted quality of life and similar oncologic results to open approach.We present an experience of the Center of Excellence in Esophageal Surgery regarding totally MIE through thoracolaparoscopic modified McKeown triple approach, followed by esophageal reconstruction by gastric intrathoracic pull-up and cervical esophagogastric anastomosis and feeding jejunostomy in a patient with thoracic esophageal cancer who underwent preoperative neoadjuvant chemoradiotherapy. The short-term outcomes of the totally minimally invasive esophagectomy procedure were very encouraging. The overall operative times were: thoracoscopic - 120 minutes, laparoscopic - 130 minutes and cervical - 50 minutes with a total of 360 minutes. The intraoperative blood loss was 200 ml. The postoperative outcome was favorable with early feeding on the jejunostomy. The control of cervical anastomosiswas performed in the 6th day postoperative and the patient was discharged in the 10th day postoperative without any symptomatology. At the first and third-month follow-up were not reported any postoperative complications. The totally minimally invasive approach using advanced technology of endoscopic surgery allowed for this patient a simple postoperative evolution, no major complications and a good recovery after an extensive surgery. The solid experience in open esophageal surgery of Upper Gastro-Intestinal surgeons provides a fast learning curve of complex minimally invasive surgical procedures with reduced perioperative morbidity. Long-term follow-up can confirm the results from the literature regarding the survival, which are expected to be for these patients at least equivalent with outcomes after open esophagectomy.

Keywords*: totally minimally invasive esophagectomy, three-dimensional esophagectomy, chemoradiotherapy, the modified McKeown triple approach*

Introduction

Minimally invasive esophagectomy (MIE) has a history of 26 years of continuous development and improvement (first thoracoscopic esophagectomy – Cuschieri, 1992) and is a feasible alternative to the open approach for the treatment of resectable esophageal cancer, even after neoadjuvant chemoradiotherapy [1, 2]. The association of MIE with a lower incidence of postoperative complications, especially pulmonary infections, has increased the popularity of the technique, in the last years, in some countries, such as the Netherlands, MIE has become the standard indication for the treatment of esophageal cancer, where 82% of patients are treated with a minimally invasive approach [3]. Simplification of postoperative care (blood transfusions, postoperative antalgic treatment), shorter hospitalization and faster social reintegration recommend also the technique as the first indication in early esophageal neoplasms. The different localizations of the esophageal tumors may dictates also the type of minimally invasive approach.

Before to become totally minimally invasive procedure, MIE has benefited from the use of hybrid techniques including robotic-assisted for overcoming thoracoscopic difficult operative situations (video-assisted thoracoscopic surgery - VATS), for laparoscopic mobilization of the stomach (hand-assisted laparoscopic surgery-HALS) or for creation of the gastric conduit (extracorporeal preparation via an epigastric mini-laparotomy).

From the introduction of MIE into the current practice, all types of open esophagectomy were reproduced in minimally invasive approach [4-6].

The classic approach has been used for the treatment of resectable esophageal cancer in the Center of Excellence in Esophageal Surgery at the Clinical Hospital "St. Maria" Bucharest, in the last 30 years with very good results. Starting in 2015, we introduced minimal invasive esophagectomy using the modified McKeown triple approach in order to reduce the rate of postoperative pulmonary complications [7].

The triple modified McKeown thoracolaparoscopic approach provides an excellent visual field for mediastinal lymphadenectomy and avoids complications associated with intrathoracic anastomotic leakage that can cause significant postoperative morbidity and mortality. We prefer performing a cervical esophagogastric anastomosis, despite of increased risk of fistula, with significant swallowing difficulties, tracheobronchial aspiration and respiratory complications, but is not associated with high mortality as intratoracic anastomosis leakage. The management of cervical anastomotic fistula can be conservatively with nil per os and enteral nutrition via feeding jejunostomy until the complete closure of the fistula. In case of stenosis associated with leak healing, endoscopic dilatations with Savary bougies can be performed under interventional radiology control with good results.

We present an experience of the Center for Excellence in Esophageal Surgery using totally MIE through the triple modified McKeown approach, thoracolaparoscopic, as an initial experience, from a series of minimally invasive procedures for the treatment of esophageal cancer. Over the last 3 years, we have performed this operation using a 2D video camera and recently we are using a 3D HD camera. Our early results are very encouraging, there were fewer respiratory and parietal complications, a reduced duration of admission in Intensive Care Unit (ICU) and shorter hospital stay compared to open esophagectomy. The mortality rate was comparable to the open approach and was related to complications of anastomotic leaks. Short term oncological outcomes were also similar.

Case presentation

A 65 years old patient, smoker, alcohol user, diagnosed tomographic and endoscopic in another hospital with moderately differentiated inferior esophageal carcinoma was admitted in our clinic with grade I dysphagia and recent weight loss.

Clinical examination showed no significant abnormalities. The blood tests for evaluation of liver and kidney functions were within normal limits.

The upper digestive endoscopy revealed at 32-37 cm from incisors, an ulcerated tumor

about 1/4 -1/2 of the esophageal circumference and a gastric ulcer on the small curvature (1cm in size). The result of gastric ulcer biopsy did not detect malignant cells and the Helicobacter pylori test was positive 3+ (Figure 1).

The barium swallow showed in the lower third of the thoracic esophagus, a 5 cm large ulceration, as lacunar image, and a niche picture at the level of the small vertical curves, above the gastric angle (Figure 2).

Figure 1 - Upper gastrointestinal endoscopy

Figure 2 - Barium swallow

The ultrasound endoscopy identified the lower esophageal hypoechogenic, non-homogeneous tumor located at about 34 cm from incisors in size of 4.2 / 2.2 cm and the invasion of muscularis propria up to the level of adventitia. Close to the tumor, a 1.5 cm well-defined oval hyperechogenic lymph node with malignant aspect was assessed and another adenopathy below the carina with a diameter of about 10 mm showed benign aspect (Figure 3).Computed tomography of the thorax, abdomen, and pelvis (CT TAP) confirmed the topography of the esophageal tumor and did not detect pulmonary or abdominal metastatic deposits. The final clinical staging was thoracic inferior esophageal squamous cell carcinoma moderately differentiated cT3N1M0 (Figure 4).

The multidisciplinary meeting recommended neoadjuvant treatment (CRT) and the patient underwent chemotherapy with Taxol-Carboplatin and radiotherapy with a modulated intensity of 45Gy / 25 fractions for 5 weeks.

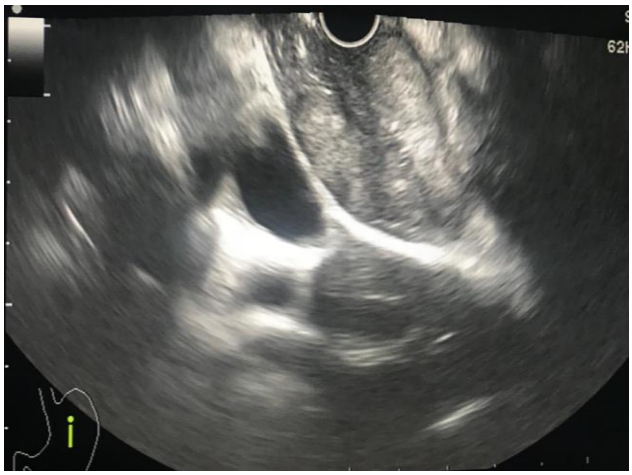

Figure 3 - Ultrasound endoscopy

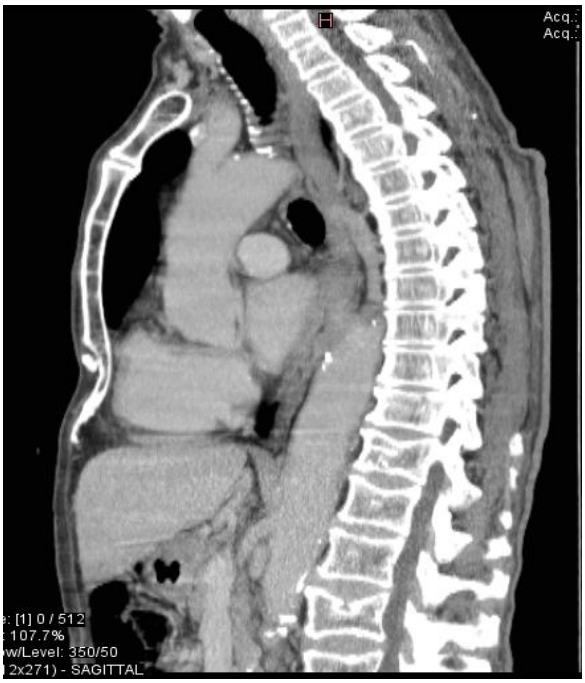

Figure 4 - CT thorax pre-irradiation sagittal view

Clinical and paraclinical evaluation post CRT

Six weeks after neoadjuvant treatment, the patient was re-assessed in our clinic. The

endoscopy revealed two small residual esophageal tumors at 33-35 centimeters from incisors and the complete healing of the gastric ulcer. The barium swallow revealed two lacunar images in the lower third of the thoracic esophagus. The CT TAP indicated a regression in dimensions of the esophageal tumor thickening without CT detectable metastasis (Figure 5).

Figure 5 - CT thorax post-irradiation transversal view. Dimensional regression of the esophageal tumour

Preoperative assesment

The patient was prepared for the operation and the renal and hepatic function, hemoleucogram and the coagulation were tested and were found within normal limits. The preoperative chest x-ray and an electrocardiogram were performed. The spirometry showed a mild obstructive ventilatory dysfunction. Also nasal, oropharyngeal and anal probes were taken. Preoperative preparation included administration of low molecular weight heparin (LMWH) and respiratory exercises.

Operative technique

Subtotal minimally invasive thoraco-laparoscopic esophagectomy with esophageal reconstruction with whole stomach was performed under AG IOT (16.07.2018 / CO 720) using the modified McKeown's triple approach with cervical esophagogastric anastomosis and feeding jejunostomy.

The surgical instruments set for minimally invasive interventions contains besides the standard 3D laparoscopic 3D HD camera, the trocars Thoracoport 11.5-12 mm for the thoracoscopic approach, the 45 mm EndoGIA vascular stapler with a white or gray cartridge (for azygos vein and left gastric artery and 5 mm endoscopic Ligasure, very useful in performing mediastinal lymphadenectomy and laparoscopic mobilization of the stomach. The duration of surgery can be reduced by using the use linear GIA or EndoGIA staplers with 45-60 mm blue or green cartridge depending on the thickness of the gastric wall for the preparation of the gastric conduit and the EndoFan which is very useful for retract of the right lung or the liver during dissection of the esophagogastric junction.

We present details of the technique of totally esophagectomy with thoracoscopic lymphadenectomy by modified triple approach and laparoscopically assisted gastric pull-up. For the thoracoscopic approach we used the position of the left lateral decubitus and for the laparoscopic and cervical approach the position of the dorsal decubitus.

We used an epidural catheter for additional analgesia and after the onset of general anesthesia with selective orotracheal intubation with the Carlens tube, we introduced intraesophageal an thick Fauchet tube which is useful for identification of the esophagus during the mediastinal dissection. With the right lung ex-sufflated through selective intubation, the thoracoscopic stage begins after the positioning of the patient in the left lateral decubitus and the insertion of the trocars in the right hemithorax allowing enough distance between them avoiding as much as possible conflicts of the surgical instruments during the procedure. Five thoracoscopic trocars were used as follows: 10 mm optical trocar (10 mm camera) in the 8th intercostal space anterior to the middle axillary line. The place of first trocar has to be chosen very carrefully, because the table is bent from the middle to allow enlargement of intercostal spaces. If the trocar is too inferior, even in the corect intercostal space, it can be introduced in the abdomen with the risk of damage of the diaphragm muscle or the liver. The other working trocars are placed under direct vision: trocar of 10 mm in the 9th intercostal space behind the posterior axillary line; working trocar of 10 mm in the 7th intercostal space, ahead of the anterior axillary line and a 10 mm

work trocar in the 4th intercostal space on the anterior axillary line for the "fan" instrument endoscopic to retract anteriorly the lung and allows the exposure of the esophagus. Another working trocar 5 mm is placed anterior and inferior to the shoulder blade, used by instruments for left hand of the surgeon. If this trocar is too much posterior is useless for entire thoracoscopic stage because the instrument will have the vertebral bodies the way to mediastinum and in this case it have to be repositioned (Figure 6).

Figure 6 - The position of trocars during thoracoscopy

The positioning of working trocars is especially important during the thoracoscopic stage in which we have to fight also with the stiffness of the walls of the right thoracic cavity. After the right lung is collapsed, the anatomical elements are identified: the azygos vein, thoracic esophagus, the main right and left bronchi, the trachea and the pulmonary pedicles. For additional lung collapse, an insufflation with CO2 can be used up to a pressure of 8 mmHg. We have to assess the macroscopic appearance of the esophagus in order to highlight any signs of extra-adventitial invasion or presence of periesophageal lymph nodes. The triangular ligament and upper and lower mediastinal pleura are incised and the right lung adhesions are carefully cut to avoid damaging the lung, which may cause postoperatively the occurrence of an airway leak (Figure 7 and 8).

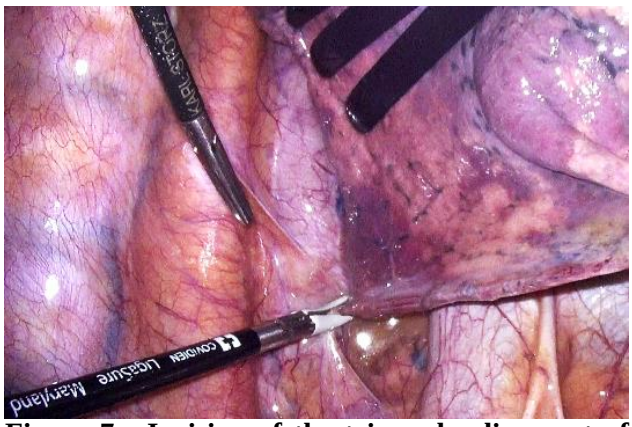

Figure 7 - Incision of the triangular ligament of the lung

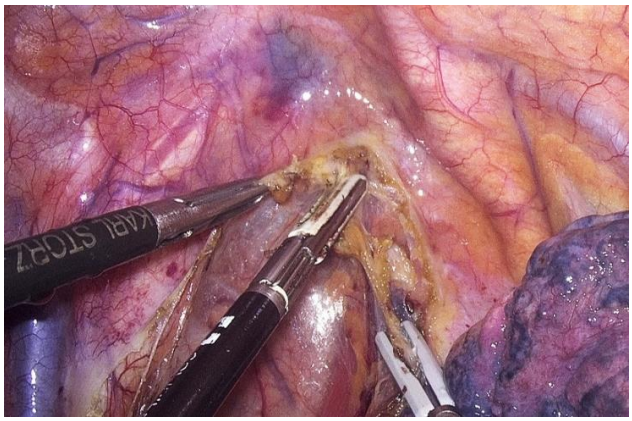

Figure 8 - Incision of mediastinal pleura

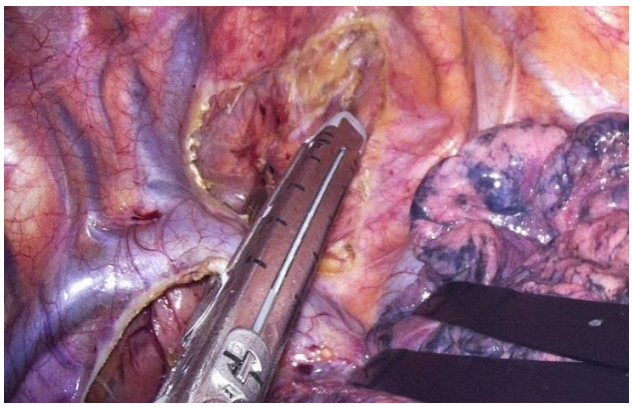

Figure 9 - Section of the azygos vein

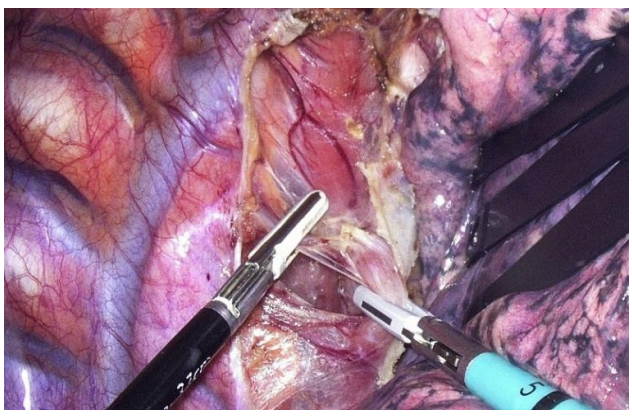

Figure 10 - Section of esophageal arteries using the Ligasure

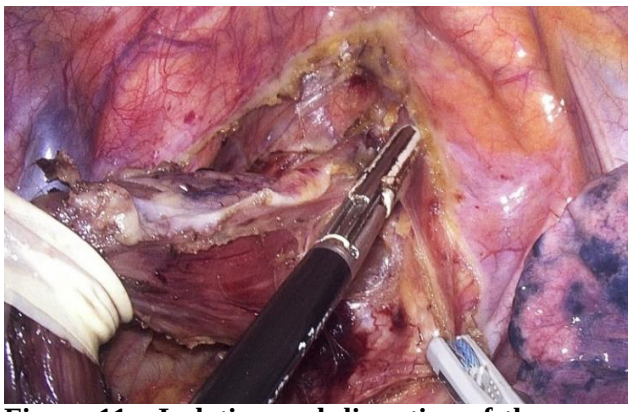

Figure 11 - Isolation and dissection of the upper esophagus

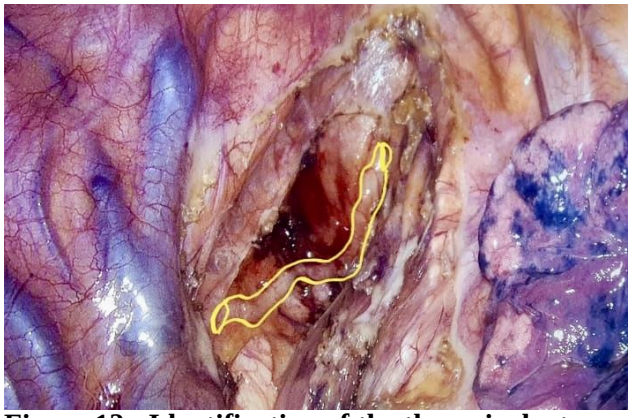

Figure 12 - Identification of the thoracic duct

Figure 13 - Disection of inferior esophagus

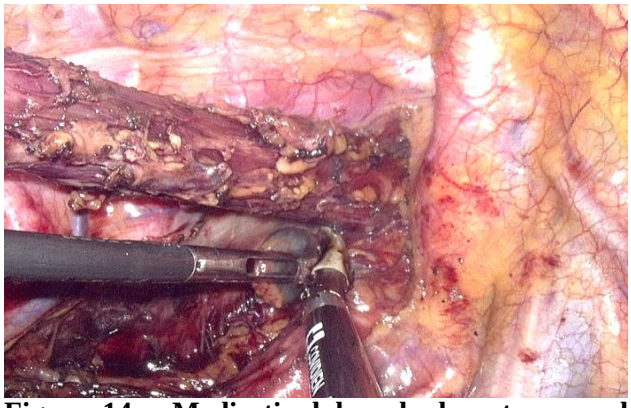

Figure 14 - Mediastinal lymphadenectomy and thoracic duct clipped

Figure 15 - Pleural drainage

After complete esophagus dissection, the pleural cavity is reviewed for definitive hemostasis and two drain tubes are installed at Beclaire drainage, one at the base of the lung and the other at the apex. The lavage of pleural cavity is not routinely performed especially if is not large amount of blood loss (figure 15). The pulmonary expansion is directly observed and the instruments and the trocars are removed, the thoracic skin wounds were sutured.

The laparoscopic stage begins with patient positioned in dorsal decubitus in French position, insufflation of the peritoneal cavity with Veres needle and inserting the 10 mm optical trocar supraumbilical on the xifo-umbilical line. The position of the rest of the trocars during the laparoscopic procedure is the following: 10 mm working trocar, subxiphoidian for EndoFan endoscopic retractor; 10 cm trocar, supraumbilical in the right upper quadrant on the right of medial-clavicle line; 10 cm trocar, supraumbilical in the left upper quadrant on the left medial-clavicle line; a 5 mm trocar in the left upper quadrant lateral as possible to allow a good working angle of the instruments (figure 16). After insertion of the trocars, the entire peritoneal cavity is explored, carefully to detect other pathologies or metastatic deposits, especially when the tumor is located in the distal esophagus. The table is placed in the Fowler position. The small omentum is incised, the abdominal esophagus is dissected and the hiatus is enlarged by sectioning of right crus of diaphragm using the Ligasure to allow the gastric conduit to pass in the thorax (figure 17). The gastro-colic ligament is dissected, starting in the middle and continuing with the gastro-

splenic, gastrophrenic ligament (figure 18). The dissection of the left crus and the esophagogastric junction is performed and the left gastric pedicle is identified. The right part of the gastrocolic ligament is sectioned and gastro-epiploic arcade is followed up to the antro-pyloric region. Laparoscopic gastric mobilization is continued by sectioning of the coronary pedicle with a vascular stapler and the perigastric lymphadenectomy is performed with the preservation of the right gastro-pedicle as vascular suply for the gastric conduit (figure 19, 20, 21 and 22). For supplementary mobilization of the stomach a Kocher maneuver is performed laparoscopically.

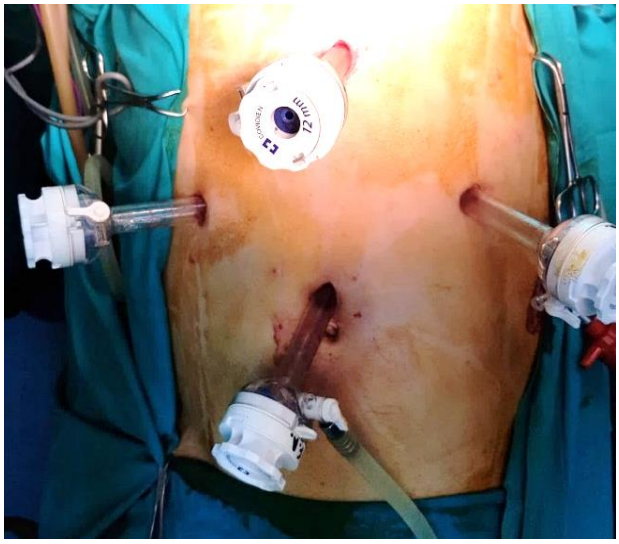

Figure 16 - Position of the trocars during laparoscopic stage

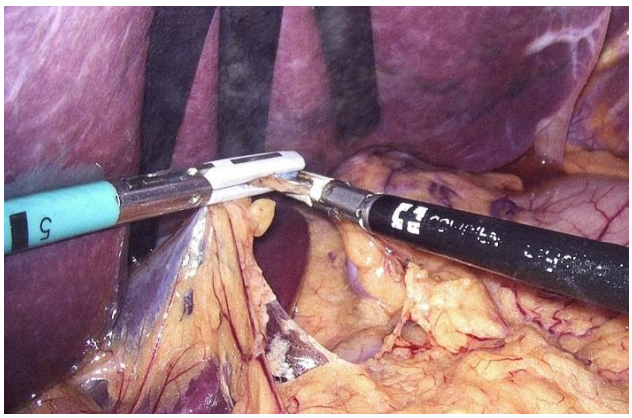

Figure 17 - Section of hepato-gastric ligament

The cervical stage begins with an incision at the anterior margin of the left sternocleidomastoid muscle, the dissection is continued medio-vascularly to the carotid artery and posteriorly to the prevertebral fascia. The cervical esophagus is isolated and is sectioned above the jugular incision of the sternum. We used for esophageal reconstruction the whole stomach after the Nakayama technique. The thoracic esophagus along with the future gastric conduit were ascended through the posterior mediastinum in the cervical region under direct visual laparoscopic control and is extracted through the left latero-cervical incision (figure 23 and 24).

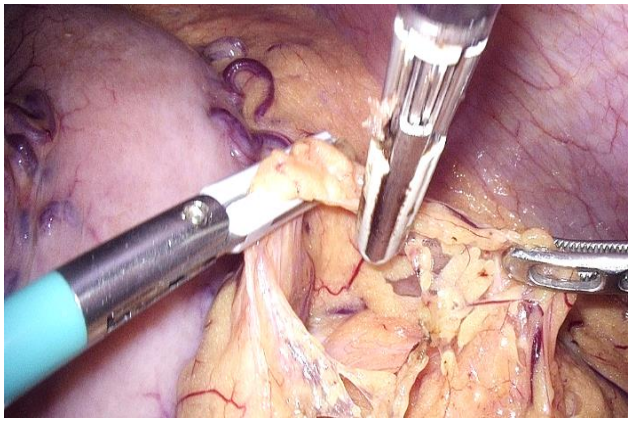

Figure 18 - Section of gastro-colic ligament

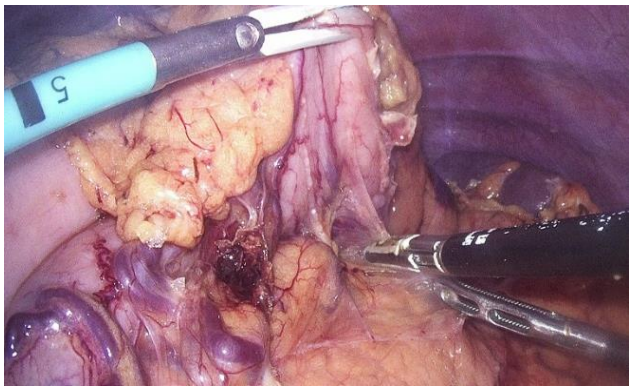

Figure 19 - Dissection of posterior gastric adhesions

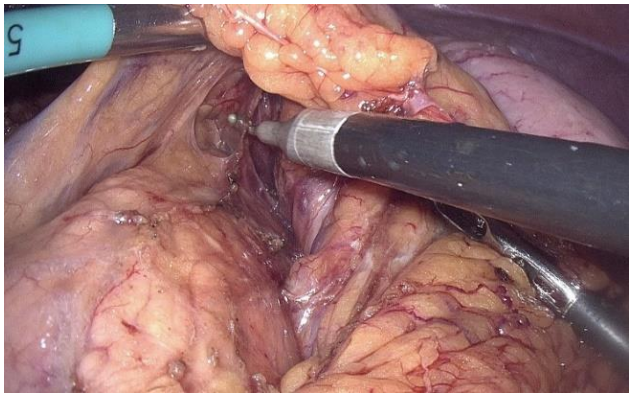

Figure 20 - Perigastric lymphadenectomy

The cardia was sectioned with a linear EndoGIA stapler with a blue cartridge after the stomach was secured at the cervical level, the esophagectomy specimen is sent to histology

(figure 31). After cutting and closing the cardia with the linear stapler, the esophagogastric cervical single layer anastomosis end-to-side was performed between the cervical esophagus and the gastric fornix with monofilament suture PDO 3-0 (figure 25, 26 and 27). We use a naso-gastric tube to decompress postoperative the gastric conduit.

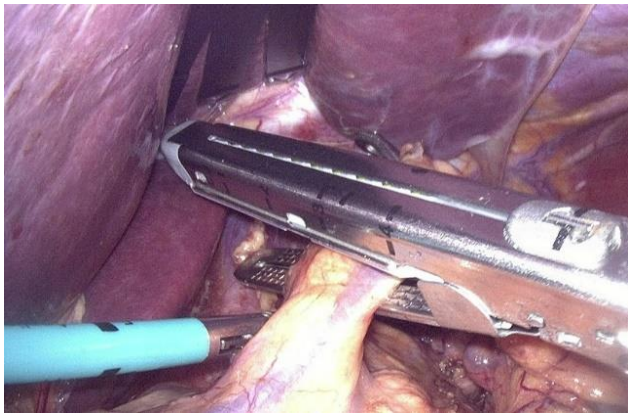

Figure 21 - Section of coronary pedicle

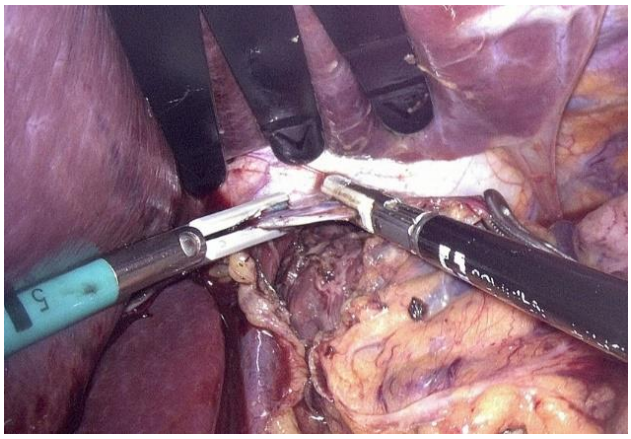

Figure 22 - Partial section of the hiatus

Figure 23 - Gastric conduit ascensioned through enlarged hiatus

The cervical wound was sutured and we returned to the abdominal cavity where a feeding jejunostomy was inserted using a Foley 28Ch catheter, exteriorized in the left upper quadrant and fixed with 3-0 Silk to the parietal peritoneum. For laparoscopic jejunostomy, we use the trocar incision on the left midclavicular line. Also, jejunostomy can be mounted in a classic manner, a mini-laparotomy allows a enough working space. After anchoring the first jejunal loop to the peritoneum on anterior abdominal wall, behind the trocar hole, we made a purse string using 3-0 Silk. The intestinal wall was opened using a Hook and the Foley catheter is inserted in the jejunum through the mentioned trocar. We check the position of the catheter at the level of the jejunum both visually and by instillation of physiological serum. The jejunal loop is additionally anchored in several points to the anterior abdominal wall and the trocar is extracted and the jejunostomy is fixed to the skin as well (figure 28).

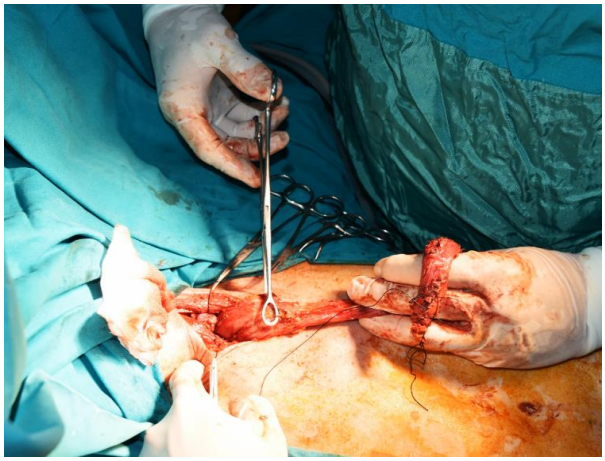

Figure 24 - Extraction of the esophagus specimen

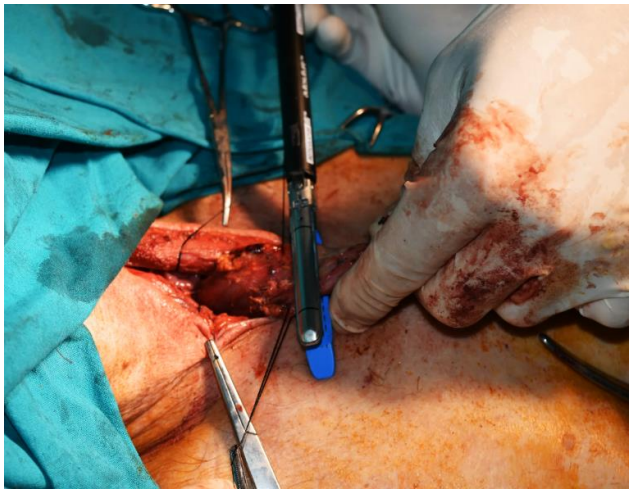

Figure 25 - Section of the cardia

The pyloroplasty performed as extra-mucosal myomectomy is often optional while insertion a

feeding jejunostomy to facilitate enteral nutrition during the postoperative period is mandatory. We practice drainage of peritoneal cavity at the diaphragmatic hiatus, with a drain tube exteriorized by the working trocar incision on the right midclavicular line (figure 29). The working trocars are removed under direct vision and the wounds are sutured.

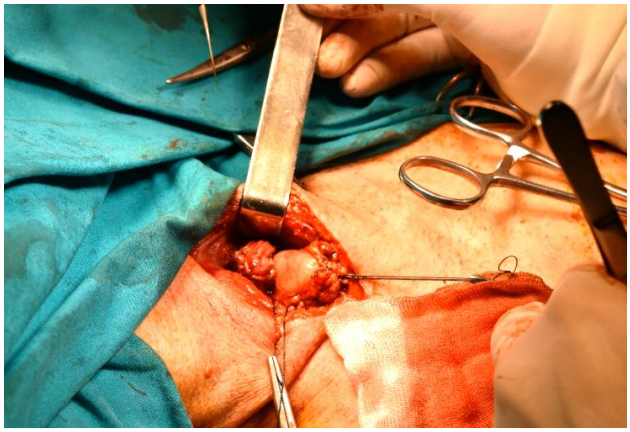

Figure 26 - Preparing end-to-side cervical anastomosis -distal cervical esophagus and the gastric fornix

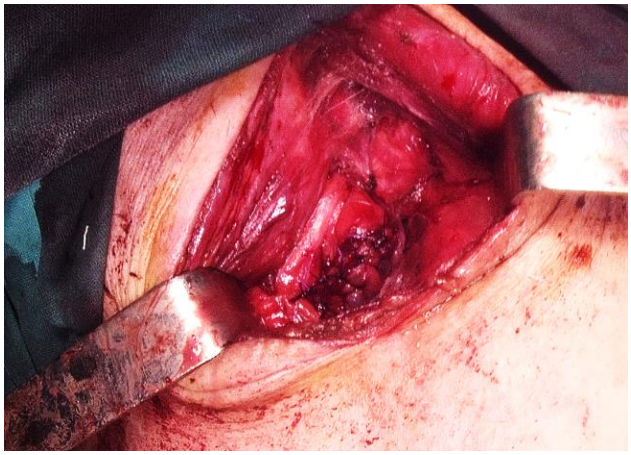

Figure 27 - Eso-gastric end-to-side cervical anastomosis - final aspect

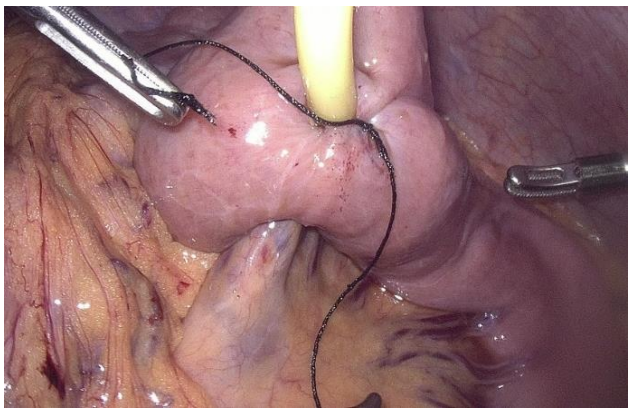

Figure 28 - Laparoscopic-assisted feeding jejunostomy

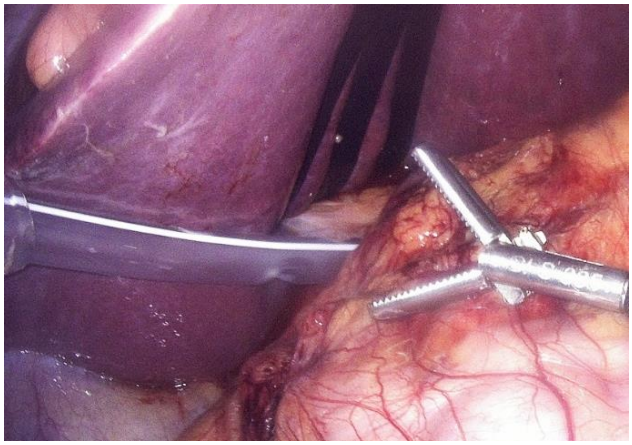

Figure 29 - Subhepatic abdominal drainage

The communication between the surgical team and anesthesia in order to prevent accidents that can lead to conversion to open surgery is a very important aspect of intraoperative management. Also, to reduce the rate of postoperative lung complications, the anesthetist uses a lung protection strategy during operation with fluid restriction (gold directed fluid therapy - GDFT), while maintaining hemodynamic stability not to affect the viability of the gastric graft [8].

Results

The overall operative time was: in the thoracoscopic approach -120 minutes, laparoscopic - 130 minutes, cervical - 50 minutes, in total 300 minutes. The blood loss associated with the procedure was 200 ml. The postoperative evolution was favorable, the patient was extubated at the end of the surgery, a chest x-ray was performed to assess the position of the drainage tubes and the pulmonary expansion. The patient was transferred to the ICU for 48 hours. The patient followed an integrated post-esophagectomy care protocol that included intensive physiotherapy, early bed mobilization and early enteral nutrition in the first day postoperative on the feeding jejunostomy (figure 30). The nasogastric tube was used in the first postoperative days for gastric conduit drainage. On the 6th postoperative day, a digestive transit with iodate contrast substance was performed which revealed a high esophagogastric anastomosis with normal appearance without

leakage and a delayed emptying of the gastric conduit.

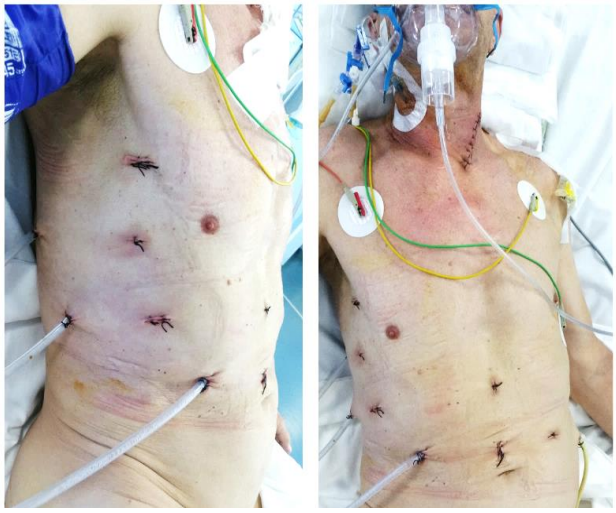

Figure 30 - Postoperative aspect day 1

Figure 31 - Subtotal esophagectomy specimen

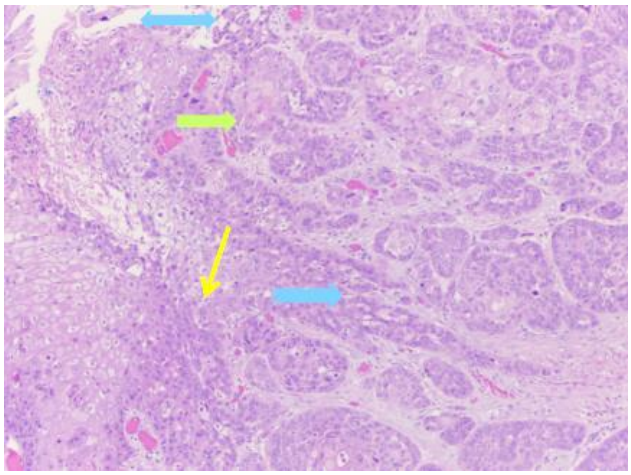

Figure 32 - Microscopic view. Hematoxylin eosine stain x20, (Leica ICC 50 HD) The green arrow - the keratin pearl characteristic of the keratinized squamous cell carcinoma. Yellow arrow - non-keratinized squamous epithelium with cyto-architectural disruption with tachycromatic nucleus and nucleotide cytoplasmic ratio with disposition in ½ inferior of the epithelium (low-grade intraepitelial neoplasia). Blue arrow- cyto-architectural disruption with polar loss and cyto-nuclear ratio in favor of the nucleus in all the thickness of the epithelium (high-grade intraepithelial neoplasia). Double arrow - in the surface, ulceration and fibrino-leucocyte exudate

Figure 33 - The 30-days postoperative aspect

Figure 34 - Barium swallow 30-days postoperative

The final histology result revealed that the tumor was invasive to muscularis propria with the distal limit at 31 mm, the proximal limit without tumor infiltration and angio-lympho-perineural invasion was present (figure 32). All the lymph nodes found on the specimen or sent separately were reactive - 15 reactive lymph nodes periesophageal (thoracic) and 23 lymph nodes periesophageal and left gastric

(abdominal). Final stage of the disease was ypT2N0M0.

On the 8th postoperative day, a digestive transit with barium sulfate was performed, which revealed a normal postoperative appearance, no leakage and a slow emptying of the stomach gastric at 5 minutes post-ingestion. The patient was discharged on the day 10 postoperative without subjective symptoms with feeding jejunostomy in place. During the clinical and paraclinical re-evaluation at the 30th day postoperative, the feeding jejunostomy was extracted after a preliminary swallowing control. There were no long-term complications at 90 days postoperatively follow up (figure 33, 34 and 35).

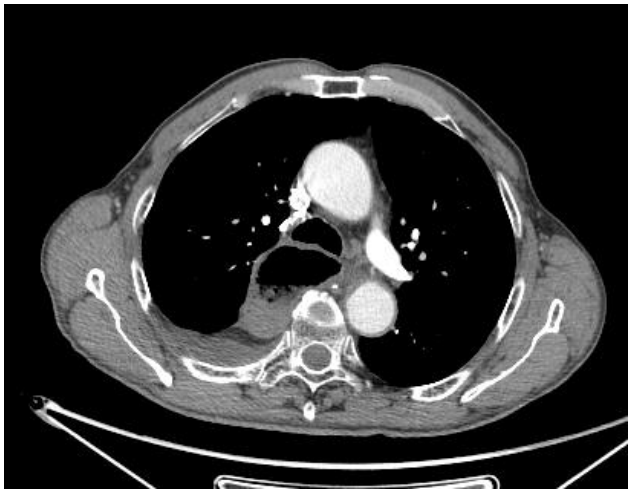

Figure 35 - CT TAP 90-days postoperative - transversal view

Discussions

The recent increasing incidence of inferior esophageal and esophageal junction adenocarcinoma, made the use of 2-stage Ivor Lewis MIE more frequent in current practice in the Western world, but is not applicable for the entire world where the squamous cell carcinoma is still diagnosed more frequently than adenocarcinoma. The modified 3-stage McKeown approach remains the indications for thoracic esophageal tumors because allows an extended mediastinal lymphadenectomy.

Currently, in the selection of cases: age, body mass index, non-adjuvant RCT does not affect the decision for MIE. Barium swallow is very important for assessing tumor localization and topography and for assessing the future gastric conduit. The ultrasound endoscopy is routinely used in our practice for establishing the local tumor invasion in the esophageal wall and the evaluation of mediastinal lymph nodes Tomography combined with positron emission (CT-PET) is not routinely performed in our clinic, but it can prevent a surgery without an oncological benefit especially when histology is adenocarcinoma and the tumor is located in the distal esophagus. We are still in the learning curve of this type of minimally invasive approach, and for this patient, we used the left lateral decubitus to be able to convert to open surgery via emergency thoracotomy in case of an accident during surgery. Also, the extracorporeal preparation of the gastric conduit that we practiced at the first esophagectomies through minimally invasive approach reduces the risks associated with the learning curve and has a positive impact on postoperative outcomes.

Performing the pyloroplasty on vagotomised stomach is not absolutely necessary and we do not recommend it routinely, usually, the emptying of the gastric conduit is improving in the first few weeks postoperatively [9]. We use high epidural anesthesia to control pain in the immediate post-operative period, that facilitates early extubation and mobilization of the patient which reduces the rate of respiratory complications, duration of hospitalization and improves quality of life [10].

We support active respiratory physiotherapy and start of early feeding on the jejunostomy on the first day after surgery which, in our experience, is well tolerated by the patient. The changes in consciousness and infectious risk are carefully assessed by repeating laboratory tests and pulmonary x-rays to identify possible postoperative medical or surgical complications [11].

Image augmentation in the operative field and the use of a 3D High Definition video camera provides an excellent visual field for accurate aproximation of the dissection plans and overcome difficult moments by reducing the risk of intraoperative accidents and also enables an extensive periesophageal and perigastric lymphadenectomy facilitating a better staging [12]. The 3D thoracoscopic and laparoscopic HD approach is promising and appears, in our experience, to be superior to 2D

during thoracoscopic stage and laparoscopic gastric mobilization, which could lead to an improvement of postoperative outcomes.

Simplifying postoperative care and reducing the incidence of postoperative complications, especially pulmonary infections, may determine a shorter duration of hospitalization and allows faster social reintegration [13].

The long learning curve of MIE is much easier to overcome in the presence of an experience in open esophagectomy. Also, advanced technical skills in minimally invasive surgery and the supervision of a mentor are mandatory for the first operations [14].

Difficulties encountered at certain operative stages, such as the presence of intrathoracic or intraperitoneal adhesions with the prolonged incidence of surgical incidents or intraoperative accidents, can determine the conversion to open surgery. The literature reports an average conversion rate of 5-7% [15].

The advantages of the MIE are evident in the immediate postoperative period, but also at a distance, oncological results are comparable to those of classical esophagectomy, proven by comparative studies on large cohort of patients operated and randomized clinical trials such as TIME, MIRO or ROBOT who compared the results of classical surgery with those of the MIE starting with 2012 and have recently published long-term oncological results [16-22]. It remains to be demonstrated as the accumulation of minimally invasive cases in our clinic will decreases the incidence of local recurrences.

Conclusions

Advanced technology and optics of endoscopic surgery allow better assessment of anatomical plans, a very good access to narrow spaces, and therefore a more precise dissection with lower trauma in esophageal cancer surgery.

The long-term outcomes of surgical treatment of esophageal cancer are an additional motivation for treatment orientation in order to obtain good results in quality of life of the patients in the first postoperative year, results in which MIE is surpassing open technique.

The modern Upper Gastro-intestinal surgeon should offer to the patients the opportunity of benefit of the MIE and he should perform an esophagectomy with low morbidity and mortality.

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