Minimally Invasive Esophagectomy for Cancer: A Safe Procedure in Oncological Surgery

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Abstract: Introduction: Minimally invasive surgery (MIS) in the surgical management of esophageal cancer is now accepted as a valid technique. The aim of this study is to show our initial experience with this approach.

Material and Methods: Observational study using data collected prospectively from a database, which includes 23 patients operated by MIS. Esophageal dissection was performed by videothoracoscopy, followed by laparotomy or laparoscopy. An Akiyama gastroplasty was made up, and pulled up through the posterior mediastinum and an side-to-side esophagogastric cervical anastomosis was then performed.

Results: Most of the patients (19) were male and the average age was 63.3 years. Most tumors were located underneath the carina. 17 were adenocarcinomas and 6 squamous cell type. 19 patients received neoadjuvant therapy. The average operating time was 377.5 minutes and in 5 patients it was necessary to make a thoracotomy to finish the esophageal dissection. An average of 18 lymph node were removed and the most frequent pathological stage was the IIA. The morbidity was 47.8%, 5 patients with respiratory complications and 7 patients presenting a anastomosis leakage or fistula. 3 patients died postoperatively. The average follow-up was 23.5 months and the estimated 5-year overall survival was 61.8%.

Conclusion: This study confirms previous reports about MIS which seems to be a valid technique if made by experienced teams. Our results support a satisfactory oncological outcome and a low rate of respiratory complications.

Keywords: Minimally invasive surgery, Thoracoscopy, Esophageal cancer, Laparoscopy, Outcome, Complications.

INTRODUCTION

Minimally invasive surgery (MIS) in esophageal cancer is a form of surgical approach that has been increasing over the last decade [1-7]. However, the high morbidity and mortality of this procedure [1-3, 8-13] and the complexities of the learning curve [1, 14, 15] have contributed to its underdevelopment. This procedure can be divided into two forms: the “non-total” minimally invasive surgery which includes thoracoscopy or laparoscopy, but not both, and the “total” minimally invasive surgery which includes thoracoscopy and laparoscopy in the same patient [2, 4, 8, 14,16-18]. The question about which procedure is better has been widely discussed without getting into specific rules for handling. It can be only concluded that the most important arguments are the preference and the experience of the surgical team, and a high volume of patients referenced to a center [5, 9, 10, 19-22]. Often it is not easy both match. Many studies support better outcomes for the MIS, describing a decreased in the respiratory complications rate [6, 8, 16, 19, 20, 23-28], a shorter recovery time, a shorter stay in the critical care unit (ICU) and an earlier hospital discharge [6, 8, 11, 19-21, 23]. On the other hand MIS has not been shown to have an impact on operative mortality or survival rates [3, 7, 8, 17, 19, 21, 23, 24, 29, 30]. Currently this approach is accepted as a valid technique that would not compromise the oncological results [3, 4, 29, 31], and it is especially indicated in the initial stages of the disease. The aim of this study is to show the experience in the surgical management of the esophageal cancer treated by minimally invasive surgery in our center.

MATERIAL AND METHODS

Patient’s Selection

This is an observational study of patients diagnosed of esophageal cancer collected prospectively from a database since 2002 in our unit of gastro esophageal surgery. Of the 139 patients diagnosed of esophageal

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cancer, 93 underwent surgery with curative intent. Esophagectomy using minimally invasive surgery began in 2007 in our center, and since then 23 patients have been operated by this approach, which are the object of this study. Patients flow diagram is shown in Figure 1. It includes patients diagnosed of adenocarcinoma or squamous cell carcinoma of the esophagus and those Siewert type I located in the gastro esophageal junction. Patients with metastasis, tumor located in the cervical esophagus, ASA greater than 3 and those whose respiratory function tests showed a FEV1 <70% and / or FEV1 / FVC <70% were excluded.

Diagnosis and Staging Studies

Diagnosis was always performed with endoscopy and biopsy. The staging study was performed using computed tomography (CT-scan). Endoscopic ultrasonography was used in those cases where the CT-scan could not discriminate between patients with local disease (T1 or T2, N0) of those with locoregional disease (T3 / T4 or N+), in order to define the candidates for neoadjuvant therapy. PET-scan and/or MRI was only performed in cases of doubt of metastatic disease and / or distant lymph nodes involvement. Tumor location was defined endoscopically as supracarinal, infracarinal or located in the esophagogastric junction (Siewert I). A bronchoscopy was performed in all patients with tumors classified as supracarinal or infracarinal.

Adjuvant Therapy

Patients staged as T3 and/or N+ were treated with neoadjuvant therapy: chemoradiation (45 Gy + FEC(Fluorouracil (5FU), epirubicin and cyclophosphamide) in patients with esophageal squamous cell carcinoma and perioperative chemotherapy (mostly "XELOX" Oxaliplatin 130 mg / m2 / day for 3 weeks + Capecitabine 2000 mg / m2 / day for 15 days, three preoperative cycles) in patients diagnosed of adenocarcinoma. Response was assessed using the CT-scan. PET was only used in those cases where there was a doubt of the presence of metastasis and/or distant lymph nodes involvement in the CT-scan in order to identify patients with a progression of the disease. After 4 weeks of the completion of chemotherapy in cases of adenocarcinoma, and 6 weeks after the completion of radio chemotherapy in cases of squamous cell carcinoma, patients underwent esophagectomy using a minimally invasive approach.

Surgery

Surgery was performed using a selective bronchial intubation to exclude the right lung during the thoracoscopy approach. An epidural catheter for

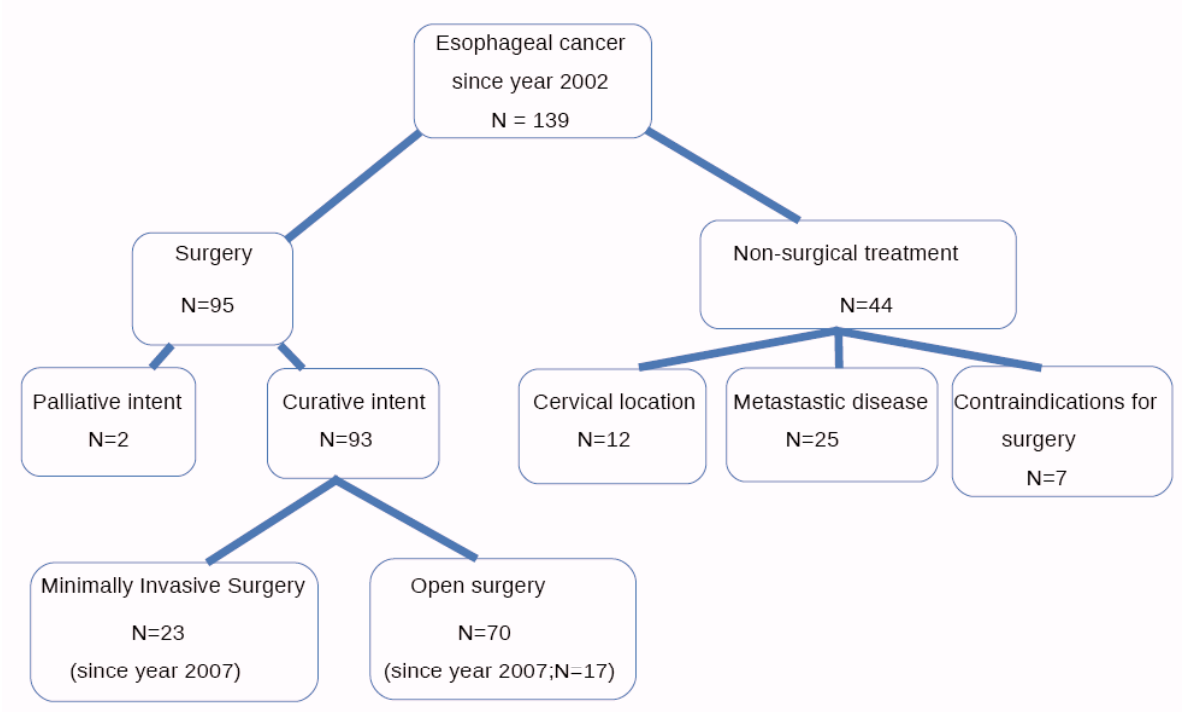

Figure 1: Flow chart of patients diagnosed of esophageal cancer.

analgesia was placed in all patients. The minimally invasive techniques used were a combination of videothoracoscopy (VTC) and laparoscopy, with an intrathoracic esophagogastric anastomosis in cases of tumors located in the lower esophagus, or a cervical anastomosis in those tumors located in the middle and upper thoracic esophagus. For the VTC approach, the patient is placed in the left lateral or prone position, and 3 ports are placed in the infrascapular region, in the anterior axillary line on the 5th right intercostal space and in the mid-axillary line on the 8th intercostal space. An additional fourth port was used if needed. Conversion was considered in cases where dissection of the esophagus via VTC could not be completed and a formal thoracotomy was required. For the abdominal approach, the patient is placed in the supine position and five ports (1 in the supraumbilical midline, 2 in the right upper quadrant, and 2 in the left upper quadrant) were placed. An Akiyama tubular gastroplasty was performed and conducted through the posterior mediastinal route. An esophagogastric side-to-side mechanical anastomosis was then performed. If the patient has no stomach or has a previous stomach surgery, the transverse colon was used.

Postoperative Period

During the first postoperative 24 hours, the patient remains in the intensive care unit (ICU) and depending on the clinical conditions is transferred to the surgical ward. Operative mortality and morbidity were defined as those occurred within 30 days after surgery. Patients with anastomotic leakage were classified as dehiscence (associated sepsis that can not be controlled by drains) or fistula (filtration that can be controlled by a drain placement or by puncturing).

Follow-Up

Follow-up was performed through clinical evaluation and CT-scan every six months for two years and then annually for five years. Gastroscopy was only performed in those cases where a local recurrence was suspected.

The following clinical variables were collected: age, sex, clinical features (presence of dysphagia and preoperative hemoglobin, ASA), medical history (smoking, alcoholism, gastroesophageal reflux disease (GERD), Barrett's disease), parameters of nutritional status (albumin , prealbumin, BMI), tumor location, response to neoadjuvant therapy , type of surgery, transfusion, operative time, conversion rate and causes, intraoperative complications, reoperations, 30-days related operative morbidity and mortality, ICU and hospital stay, pathological tumor characteristics , tumor stage, disease-free survival and overall survival. The 6th edition of the TNM, 2002 was used for staging. For the statistical analysis, the Kaplan-Meier test and t-test were used.

RESULTS

Of the 23 patients operated by MIS, 19 were male and 4 were female. The mean age was 63.3 years. Clinical features, medical history and nutritional status are shown in Table 1. There were 2 patients with previous history of neoplasia; one operated of a squamous cell cancer of the mouth, and one with a sigmoid colon cancer. 8 (35%) patients underwent EUS for staging purpose. The tumors location were: 4 (17%) supracarinal, 11 (48%) infracarinal and 8 (35%) at the esophagogastric junction. 17 (74%) were adenocarcinomas and 6 (26%) squamous cell type.

Table 1: Clinical Features, History and Nutritional Status

	N	%
Clinical features		
Presenting dysphagia	21	91
ASA I II III	1 13 9	4 57 39
Haemoglobin (□11 mg/dl)	3	13
Medical History		
Smoking	16	70
Alcoholism	8	35
GORD	5	22
Barrett	6	26
Nutritional markers		
Albumin (□3,5g/dl)	3	13
Prealbumin (□20 mg/dl)	3	13
BMI (<20 Kg/mt2)	2	9

19 (83%) patients received neoadjuvant therapy . Of these, 4 (21%) received radiotherapy and chemotherapy and 15 (79%) chemotherapy alone. The 4 patients who received radiation and chemotherapy presented a partial response to treatment. Of those receiving chemotherapy alone, 1 (7%), 12 (80%) and 2 (13%) presented a complete, a partial response and no response respectively.

All patients underwent VTC initially. VTC + VLC was performed in 5 (22%) patients and VTC + laparotomy in 18 (78%) patients. Conversion into thoracotomy or minithoracotomy occurred in 5 patients (22%); 4 for technical difficulties due to an inflammatory reaction and/or tumor invading surrounding structures, and 1 for bleeding that could not be controlled via VTC. The average operating time was 377.5 minutes (range, 225-590 minutes). The average time in the VTC + laparotomy group was 350 minutes and 469 minutes in the VTC + VLC group. 22 (96%) patients underwent subtotal resection + gastric lesser curvature esophagectomy and cervical anastomosis, and 1 (4%) patient had a partial esophagectomy + lesser curvature gastric resection with intrathoracic anastomosis due to a previous cervical cancer surgery. In 22 (96%) patients, an Akiyama's tubular gastroplasty were performed, and in 1 (4%) patient an isoperistaltic transverse colon loop was used because a previous gastrectomy for benign disease. During surgery, 10 (43%) patients were transfused (8 patients received 2 packets of red blood cells, and 2 patients received 3 packets of red blood cell). None of the 23 patients presented serious operative complications during surgery. The median stay in the ICU was 1 day (range 1-90), and median hospital stay was 15 days (range 11-98). 11 (48%) patients presented postoperative morbidity and 3 (13%) patients died. Comparing groups (VTC+ LAP vs VTC + VLC), morbidity was higher in the first group, 56% and 40% respectively. Table 2 shows the operative morbidity and mortality of the serie. No patients presented with recurrent laryngeal nerve injury, postoperative bleeding or chylothorax. Of the seven patients presenting an anastomotic leakage, three were handled succesfully by conservative management; two were sealed off with sealant glue by endoscopy (one died), and one by suturing and placement of drainages. One patient presented a necrosis of the coloplasty which was resected and a jejunostomy performed. The mortality was associated with sepsis secondary to anastomotic leakage.

R0 surgery was performed in 22 (96%) patients and only 1 (4%) patient presented the margin affected by tumor, which corresponded to a supracarinal pT4 squamous cancer located at 25 cm distal from the dental arch. The mean of lymph nodes resected was 18; 6.9 in the mediastinal area and 11.1 in the abdomen. Pathological staging of the serie is as follow: 4 (17%) stage I, 10 (43%) Stage II A, 4 (17%) Stage II B, 4 (17%) stage III, and 1 (4%) Stage IV. The average follow-up was 23.5 months. 7 patients (35%) presented a recurrence. Table 3 shows the evolution of patients

Table 2: Morbidity and Mortality

Patient No	Respiratory Complications	Sepsis	Anastomosis Leakage/fistula	Air Leakage	Abdominal Wound Dehiscence	Management	Mortality
1	ARDS	YES	Leakage			Endoscopic sealing	YES
2		YES	Coloplasty necrosis			Coloplasty resection + jejunostomy	YES
3		YES	Leakage	Bronchial fistula		Suture of the fistula + drainage placement	YES
4	ARDS + Pleural effusion	YES	Leakage			Drainage placement + endoscopic stent	NO
5		NO	Fístula			Medical	NO
6		NO	Fístula			Medical	NO
7	Pneumonia + Pulmonar abscess	NO	Fístula			Medical	NO
8	Pneumonia + ARDS	YES				Medical	NO
9	Pneumonia	NO				Medical	NO
10		NO			YES	Surgery	NO
11		NO		Air leakage		Drainage placement	NO
Total N = 23	22 %	22%	30%	9%	4 %		13%

* ARDS: Adult Respiratory Distress Syndrome.

Table 3: Patients Presenting Recurrence

Patient No	Recurrence Location	Disease-free Survival	Management	Actual Status	Survival	Stage (yp TNM)
1	Lymph node recurrence	7	Palliative chemotherapy	Dead	22	II A
2	Mediastinum + Lung	11	Palliative care	Dead	17	II B
3	Bone metastasis	7	Palliative care	Dead	15	II B
4	Peritoneal	14	Palliative care	Dead	14	II B
5	Liver + peritoneal	6	Palliative care	Live	8	III
6	Pleural	18	Palliative chemotherapy	Live	30	II B
7	Lung	22	Intent curative Lobectomy	Disease-free live	35	II A

presenting the recurrence. Figure 2 and 3 show the overall survival and the disease-free survival of the serie respectively. The estimated 5-year overall survival was 61% and 5-year disease-free survival was 53%.

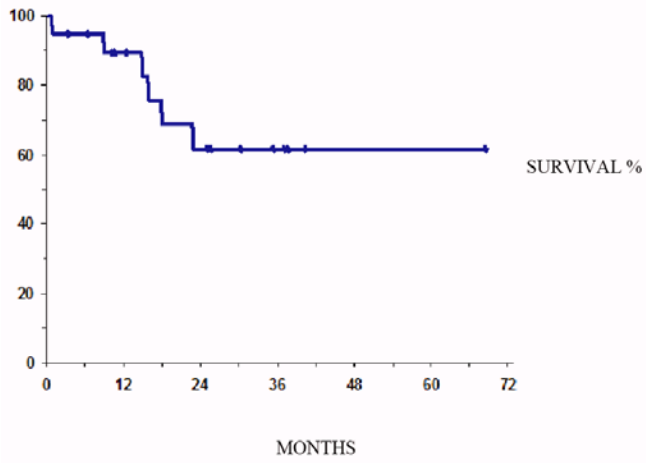

Figure 2

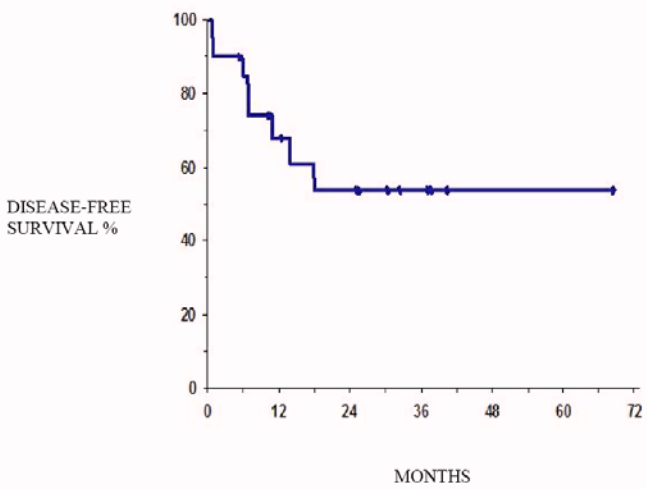

Figure 3

DISCUSSION

Current treatment of esophageal cancer must be multidisciplinary. Much progresses have been made in the field of adjuvant therapy for improving survival. But surgery remains the cornerstone in the curative treatment of this disease, although the percentage of patients eligible for surgery with curative intent remains being low. This has made that the team experience is related to a small number of patients, with the consequent delay in the application of the new techniques. On the other hand, it is considered a very aggressive surgery, often in elderly patients who usually present comorbidities. This makes that surgical outcome results poor, with high morbidity and mortality rates. It has been reported that the main causes of morbidity and mortality are secondary to the development of respiratory complications and to dehiscence of the anastomosis. So one of the goals of the treatment has focused on improving these aspects. Although MIS has failed to show an impact on reducing the mortality, it has a role reducing the pulmonary complications rates. Respiratory complications rate reported for open surgery ranges from 30 to 38.7% while MIS ranges from 6,7 to 20% [18,24,25] , which results quite similar to those described by us.

Our experience in the esophageal dissection went smoothly, without serious complications, although two patients presented a persistent air leak in the immediate postoperative period. The conversion rate to minithoracotomy was 22%, which may be attributable to the learning curve, where large tumors should not be candidates for MIS, especially in early stages of the learning curve. We believe it is valid to apply mixed techniques (laparotomy/thoracoscopy or thoracotomy/laparoscopy). Our experience in totally

minimally invasive techniques was favorable, except for an increase in the operating time which has been already described by other authors. Oncologic outcomes are also acceptable and comparable to high-volume series, 96% of R0 resections, 15 or more lymph nodes removed and quite similar survival rates. Concerning to the dissection of the esophagus, our experience resulted quite similar to those described by other authors which advocate that VTC could facilitate the esophageal dissection compare to the open approach.

VTC must be performed by experienced teams in the classical open approach since it has an important impact on the surgical outcome. Our dehiscence and mortality rate are slightly higher according to the latest reports [4, 9, 24, 26, 33, 34], however we believe this is not attributable to the minimally invasive approach, considering that the most complicated patients were approached by laparotomy. The VTC approach facilitates the dissection of the esophagus especially in smaller tumors, with a similar oncological outcome and reducing the aggression of a thoracotomy. This involves the consequent decrease of pulmonary complications.

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