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ORIGINAL ARTICLE

MEDIASTINAL AND ABDOMINAL NODE DISSECTION FOR CARCINOMA OF THORACIC AND ABDOMINAL ESOPHAGUS

By

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Aim: To evaluate the safety and complications of mediastinal and abdominal dissection in association with subtotal and total esophagectomy for carcinoma of thoracic and abdominal esophagus.

Methods: 29 patients having curable carcinoma of the esophagus underwent mediastinal and abdominal node dissection. Subtotal esophagectomy was performed in 16 patients while total esophagectomy was performed in 13 patients.

Results: Pathological staging was: stage I 0%, stage IIA 24%, stage IIB 62% and stage III 13%. Positive mediastinal and celiac lymph nodes was found in 38% with a mean number of 6 (range1 -12). The mean number of dissected lymph nodes was 14 (range 8 - 34). Chest infection occurred in 27%. Early surgical complications were intrathoracic anastomotic leakage 6%, cervical leakage 10%, anastomotic bleeding in one patient and recurrent laryngeal nerve palsy in two patients. Postoperative mortality was 10%. Four patients had locoregional recurrence. Three-year survival rate were 21 % for stage IIA and ranged from 11- 0% for stage IIB and III.

Conclusion: The technique of mediastinal and abdominal dissection can be performed with subtotal and total esophagectomy with low rate of complications. This leads to more accurate staging, but it is unclear from this small study whether it has an impact on the survival or not.

Keywords: Esophageal cancer, lymph nodes, complications.

INTRODUCTION

Despite advances in various therapies for esophageal tumors, including the use of combined modalities; surgical resection remains the mainstay of treatment. However, surgery has historically been associated with high rates of morbidity and mortality; up to 33% mortality rates reported before 1980.(1) Although this figure fell substantially in the last major review of surgical results from 1980 to 1988 by Muller and colleagues,(2) certain institutions continued to report extremely high mortality rates for this commonly performed elective procedure.(3) Squamous cell carcinoma of the esophagus remains the predominant histological subtype.(4) Irrespective of histological subtypes, esophageal carcinoma presents at a

late stage with an overall poor prognosis even in the minority of patients in whom surgical resection is possible.[5]

Lymphatic metastasis in esophageal carcinoma is characterized by early and wide dissemination; metastasis from the neck to the abdominal cavity can be found. Irrespective of primary tumor location, lymph node metastasis is considered the most important prognostic factor.[6,7]

In an attempt to improve the dismal outlook for these patients, increasingly radical resections have been performed, making esophagectomy an ever more formidable procedure.[8] Radical surgery includes complete removal of the main tumor with extended node dissection in the mediastinal and abdominal nodes. Including lymph nodes in the neck in association with mediastinal node and abdominal node dissection has been performed in the Japanese since the mid 1950s to improve the survival of patients with carcinoma of the esophagus.[9]

However, no definite consensus has been reached concerning the extent of lymphadenectomy in esophageal carcinoma. The superiority of radical lymphadenectomy is unclear because the reported survival benefit varies.[10,11] The efficiency of 3- field nodal dissection procedure also, remains controversial. The preliminary and intermediate term results have shown that 3- field nodal dissection offers some patients significant survival benefits and reduces the incidence of recurrence in cervical and superior mediastinal lymph nodes.[12]

To have any impact on long-term survival and on accurate staging of these patients, it is essential to minimize morbidity and mortality by optimizing surgical technique and perioperative care.[13] In addition, high-risk patients must be identified to improve their preoperative status, tailor their operation and anesthetic, or alternatively, offer them a non surgical treatment.

At our institute, esophagectomy was performed by laparotomy and right thoracotomy (Ivor Lewis procedure) for thoracic esophageal carcinoma and transhiatal esophagectomy for abdominal esophagus till 2000; however, the lymphadenectomy during esophagectomy was not performed as a standard protocol. After 2000, complete mediastinal and abdominal node dissection in association with esophagectomy for carcinoma of esophagus has been practiced.

In this small prospective study, we have reviewed our experience with radical esophageal resection including mediastinal and abdominal node dissection to evaluate safety of the technique and to report the related early and late complications

PATIENTS AND METHODS

This prospective non-randomized study included 29 patients (22 men and 7 women) having curable carcinoma of the esophagus. They underwent Ivor Lewis subtotal esophagectomy with two-field lymphadenectomy under the care of the authors in National Cancer Institute, Cairo University over a 6-year period from January 2000 through January, 2006. The median age of the patients, at presentation, was 54 years, with a range (50-63 years). Patients subjected to palliative resection were excluded from this study. Diagnosis was confirmed through endoscopic biopsy. This included squamous cell carcinoma (22 patients), adenocarcinoma (5 patients) and adenosquamous carcinoma (2 patients). The site of the primary lesion was thoracic esophagus in 21 patients and abdominal esophagus in 8 patients. Patients were judged resectable for cure on the basis of spiral thoracoabdominal CT and cervical CT. No patients had enlarged cervical lymph nodes and so cervical lymphadenectomy was not done in our cases. No patients received preoperative neoadjuvant therapy.

Preoperative Assessment: Preoperative patient visits were performed to check history and physical examination; with special emphasis on cardiac and pulmonary symptoms and signs. The following investigations were checked: complete blood count, fasting blood sugar, liver function tests, urea, creatinine, electrocardiogram, and chest X ray. Pulmonary function tests (PFTs) were done for all patients; including forced vital capacity (FVC), forced expiratory volume in the first second (FEV1), and peak expiratory flow (PEF). PFTs were done using the computerized Zan 300 CO-Diffusion Apparatus (Zan MeBgerate GmbH, Germany). Echocardiography was ordered if there was a history of cardiac problems. Nutritional assessment of patients included anthropometric measurements (body weight, mid upper arm circumference and triceps skin fold thickness) and serum albumin level. Medical exclusion criteria included moderate to severe liver or renal dysfunction, severe malnutrion, PFTs < 50% of predicted values and if ejection fraction of stroke volume < 50%. Patients were asked to stop smoking once presented in NCI and any chest infection was treated

Anesthetic management: In the operating holding area, 18-G epidural catheter was inserted in the interspine space between T5 and T8. Monitoring of the patients included electrocardiography, noninvasive blood pressure, pulse oximetry, capnography (after intubation) and central venous pressure (after induction of anesthesia). Anesthesia was standardized in all patients. It was induced with fentanyl 2µg/kg, and thiopentone 4-7 mg/kg. Endotracheal intubation was facilitated by atracurium 0.5mg/kg. A Left double lumen endotracheal tube was inserted and its position was confirmed by chest auscultatation but, in few patients, fiberoptic endoscopy

was needed. Anesthesia was maintained by isoflurane 1-2%, oxygen 100% and boluses of atracurium 0.1-0.2 mg/kg. A shot dose of 20ml of bupivacaine of 0.1% plus fentanyl 50µg was injected into the epidural catheter.

Mechanical ventilation parameters were set at volume controlled mode, tidal volume 10ml/kg (reduced to 6ml if only one lung was ventilated), respiratory rate of 12 breath/min, and positive end expiratory pressure (PEEP) zero. During the intrathoracic part of the surgery, the right lung was deflated leading to hypoxemia. Such hypoxemia was minimized by continuous oxygen insufflation in the nonventilated lung or partial intermittent ventilation of the collapsed lung. At the end of the surgery, the double lumen tube was replaced with a single one. Fluid replacement during surgery was achieved by lactated Ringer´s solution to meet deficit, maintenance, and third space losses. Packed RBCs were given if blood loss exceeded about 1000ml.

Operative technique: All resections were carried out by the same approach involving an initial midline laparotomy and mobilization of the stomach followed by a right-sided fifth interspace thoracotomy and resection of the esophagus and proximal stomach. The abdominal and thoracic approaches were carried out sequentially.[14] Patients were placed in the left lateral position and the right lung collapsed by endo-bronchial intubation during the thoracotomy phase. Gastrointestinal continuity was restored using the stomach as the conduit in all cases. A gastric tube (narrow tube was constructed in those having carcinoma of abdominal esophagus) was fashioned based on the right gastric and right gastroepiploic arteries (Fig. 1), with the anastomosis placed in the anterior fundus at the high point of the stomach. A circular staple device was introduced through the open lesser curve gastric resection line and the esophagogastric anastomosis fashioned at the apex of the thorax or at the level of azygous vein in 10 cases and hand sewn anastmosis using 3/0 vicryl in the rest of patients (19 patient). The open gastrotomy was closed with a TA90 staple gun in 10 cases and the staple line was oversewn with an absorbable suture. Esophago-gastric anastomosis was done with absorbable sutures in the other 19 cases. Two further absorbable anchor sutures were placed between the proximal part of the gastric conduit and the residual mediastinal pleura and muscles of the neck to decrease tension on the anastomosis (Fig. 2). Gastric drainage and decompression were achieved with a pyloroplasty and nasogastric tube placement. Two 32 FG chest drains were sited at the apex and base of the right hemi-thorax at the end of the procedure.

A radical upper abdominal and en-bloc mediastinal lymphadenectomy as described by Akiyama and associates[15] was routinely performed. The abdominal component of this lymphadenectomy comprised en-bloc resection of the nodal tissue along the common hepatic and proximal splenic arteries together with that at the origins of the left gastric artery and celiac axis (Fig. 3). The lesser omentum was divided, encompassing the nodes along the lesser curve and an en-bloc hiatal dissection was performed removing the left and right paracardial stations and the respective crura. Within the thorax the esophagus was mobilized with the middle and lower paraesophageal nodes, baring the aorta and pulmonary veins of any connective tissue and encompassing the mediastinal pleura. A meticulous lymphadenectomy of the left and right paratracheal, carinal, and left and right bronchial nodes was performed followed by ligation and en-bloc resection of the thoracic duct with the adjacent para-aortic nodes (Fig. 4). At this stage sleeve resection of the lesser curve and the associated nodes was undertaken and the other nodal stations were mobilized during the abdominal phase. The nodes in the aortopulmonary window were also removed but a full dissection of the left recurrent laryngeal nerve chain was not routinely carried out. No cervical lymphadenectomy was done in our cases because all of them had no evident cervical lymph nodes on cervical CT scanning. Splenectomy was not done routinely, however one patient had splenectomy due to iatrogenic trauma.

Postoperative care: Patients were routinely ventilated in the ICU overnight and if their clinical condition was satisfactory, they were extubated, and returned to the ward after 3 days. Blood transfusion was avoided unless hemoglobin level persistently fell below 8 g/dL or the clinical situation dictated otherwise. Similarly, if nutritional supplementation was required because of a protracted or complicated recovery, the unit policy was to deliver this by an enteral route (feeding jejunostomy) rather than by the parenteral route. Analgesia was provided through a thoracic epidural by continuous infusion of bupivacaine 0.1% and fentanyl 0.001% at a rate of 8 ml/hour. Thromboembolic prophylaxis was achieved throughout the hospital stay for all patients by subcutaneous endoxaparin 40mg once daily. The use of a nonionic contrast swallow on day 5 was not routinely done. Postoperative adjuvant radiotherapy or chemotherapy was individualized according to the pathological stage.

Statistical analysis: Analysis of preoperative and intra-operative risk factors for pulmonary complications was undertaken using the Chi-square or Fisher exact test (for categorical data) and unpaired t-test (for numerical data). P value < 0.05 was considered statistically significant.

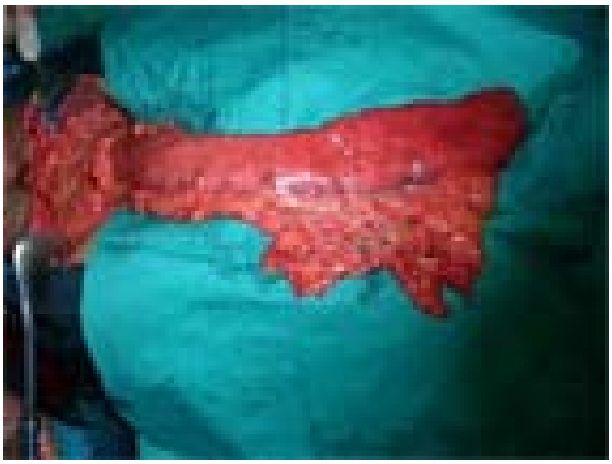

Fig 1. Gastric tube based on the RGA and RGEA.

Fig 2. Intrathorathic esophagogastric anastmosis.

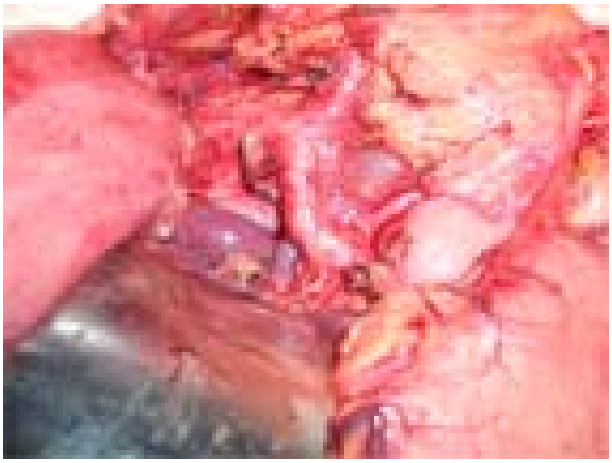

Fig 3. Abdominal node dissection around the celiac axis and its branches.

Fig 4. Paraesophageal, right partracheal and carinal lymph nodes are dissected en bloc with mobilization of the esophagus.

RESULTS

There were 29 patients (22 men and 7 women); the median age was 54 years with a range (50-63 years). Pathological study revealed squamous cell carcinoma in 22 patients, adenocarcinoma 5 patients, adenosquamous in 2 patients. Mean follow up period was25 months (range 9-56 months).

Operability and respectability: Out of 42 patients evaluated for carcinoma of esophagus during the period of January 2000 and January 2006, 29 were considered to be fit and have resectable disease. Of those 42 patients, 8 were found to either have distant metastases or unresectable hiatal disease at the time of abdominal surgery or were found to be inoperable because of direct invasion of essential mediastinal structures at the time of thoracotomy. Further 5 patients were deemed to have undergone a noncurative resection either as the result of incomplete resection with macroscopic residual disease, evidence of positive resection margins or accidental perforation of advanced lesion during mobilization. Those 13 patients were excluded from the study.

Preoperative status: A history of smoking was found in almost 50% of all male patients. Two patients had cardiovascular disease, with a history of previous myocardial infarction, or hypertension requiring treatment. Four patients suffered from noninsulin-dependent diabetes mellitus. The mean preoperative serum albumin was 40.1 g/L (range 25 to 49 g/L) and 30 % of patients reported weight loss greater than 10% of their normal body weight before surgery. Pulmonary disease was also prevalent, with variable

degrees of chronic obstructive airway disease, as judged clinically, radiologically and by spirometry in 5 patients.

Operative parameters: Mean total operative time (excluding anesthetic preparation and repositioning of the patient) was 270.5 minutes (median 250 minutes, range 180 to 450 minutes). Mean operative time for the abdominal phase of the procedure was 116 minutes (median 110 minutes, range 60 to 260 minutes) and 140.4 minutes for the thoracic phase of the procedure (median 140 minutes, range 90 to 270 minutes). Mean operative blood loss was 800 mL (median 900 mL, range 300 to 1,500 mL). Median ICU stay was 7 days (range 3 to 17 days) and the median postoperative hospital stay in patients surviving surgery was 16 days (range 10 to 39 days).

Early postoperative Complications: These included surgical and medical complications Table 1.

Table 1. Postoperative complications (in 29 patients).

Complications	Number of patients
Early	
Bronchopneumonia	8
Respiratory failure	1
Pulmonary embolism	1
Mediastinal leak	2
Cervical anastomotic leak	3
Lt recurrent laryngeal palsy	2
Late	
Benign anastomotic stricture	6
Loco-regional recurrence	4

Medical complications

Respiratory complications: Eight patients (26%) developed variable degrees of chest infection. Most patients were successfully managed with intravenous antibiotics and physiotherapy. Only one patient had to be readmitted to the ICU for respiratory support. This patients required ventilatory support as the result of respiratory insufficiency. Risk factors of statistical significance ($p<0.05$) for occurrence of respiratory complications are listed in Table 2. History of active smoking and poor preoperative spirometry were found as risk factor of bronchopneumonia in this patient.

Table 2. Risk factors associated with respiratory complications.

Risk factor	Respiratory complication (N=8)	Non-respiratory complications (N=21)	P value
Active smoking(N)	6	5	0.028
FVC(L)	3.1± 0.9	4.1± 1.2	0.042
FEV1(L)	2.2± 0.6	2.9± 0.8	0.034
PEF(L/s)	5.4± 1.3	6.7± 1.4	0.031

FVC: forced vital capacity, FEV1: forced expiratory volume in the first second, PEF: peak expiratory flow; values presented as mean±SD.

Thromboembolic complications developed in one patient and this patient died at day 5 after being ventilated due to massive pulmonary embolism.

Surgical complications:

Mediastinal leak: Two patient developed mediastinal leak. Early flexible video endoscopy had been undertaken in patients with evidence of mediastinal leaks to distinguish between that originated from the anastomosis, that from the gastrotomy line, and that developed as a result of partial or total necrosis of the mobilized stomach. No patient had gastric ischemia or necrosis .The cause of early mediastinal leak was anastomotic in one patient who was clinically stable, demonstrated a degree of tolerance, and managed conservatively with persistent chest drainage, nasogastric suction, intravenous antibiotics, and enteral hyperalimentation. The fistula gradually resoluted and the patient discharged on day 31. The cause of leak in the second patient was due to disruption of part of gastrotomy line. This patient rapidly developed mediastinal sepsis requiring thoracic lavage and repair of the gastrotomy suture line, but despite intensive supportive care eventually died of multiorgan failure and sepsis on day 26. Both patients received enteral hyperalimentation through feeding jejunostomies.

Cervical anastmotic leak: Cervical anastomotic leak was seen in 3 cases. The leak was minor in all the cases, and those patients were treated conservatively. The leak stopped at a maximum of 25 days.

Bleeding: No patients had intrathoracic hemorrhage, However, one patient had minor bleeding from the gastrotomy line that was evident on endoscopic evaluation

He was haemodynamically stable and was controlled conservatively.

Chyle leak was not seen in our patients.

Recurrent laryngeal nerve palsy: Two patient having cervical esophagogastric anastmoses developed partial left vocal cord palsy. They developed hoarseness of voice. No tracheostomy was needed.

Mortality: The overall early postoperative mortality was 10% (3/29). The causes of death included, mediastinal sepsis in one patient, pulmonary embolism in the second patient and bronchopneumonia in third patient.

Late complications:

Benign anastomotic stricture: After a mean follow up period of 14 months (range 6 to 21 months), eight patients (31 %) out of 26 patients surviving the operation presented again with dysphagia. Six patients (23%) were found to have a benign anastomotic stricture as defined by the presence of dysphagia and an esophagogastric anastomosis that would not allow the passage of an 11-mm diameter endoscope. Four patients had a historyof early anastmotic leakage (3 cevical, 1 intrathorthic). The median time to the development of benign anastomotic stricture was 100 days and all patients underwent X-ray controlled endoscopic dilatation without complication. Recurrent benign anastomotic stricture formation occurred in three cases and required repeated endoscopic dilatation. One patient having cervical anastmosis required refashioning of the anastmosis.

Locoregional recurrence: Locoregional recurrence was defined as recurrence at the site of the primary tumor, anstomotic line, or lower in the neck nodes. Four of surviving patients (4/26) developed locoregional recurrence after a mean follow up period of 9.3 months. Two patients having carcinoma of midthoracic esophagus developed isolated unilateral cervical lymph node metastasis .They were salvaged with bilateral anterolmedial node dissection. One patient (1/8) developed isolated anastomotic recurrence; this patient was treated with radiotherapy because his general condition could not tolerate resurgery. Another patient developed posterior mediastinal local recurrence that had infiltrated the anastomotic line. The recurrence was extensive and was not amenable to treatment.

Post operative staging: Post-surgical pathological staging was done according to TNM classification (16): Stage I 0%, Stage IIA (7/29 patients) 24%, Stage II B (18/29patient) 62%, and Stage III (4/29 patients) 13 %. The mean nodal harvest was 14 nodes (range 8 to 34) .Thirty eight % of all patients (11/29) were node positive. The mean number of lymph positive nodes was 6 (range 1 -12). We did not study the frequency and number of lymph node metastasis in relation to the exact location of primary tumor, size, grade or depth of infiltration.

Survival: Three-year survival for 26 patient discharged from the hospital was 21 % for stage IIA and ranged from 11- 0% for stage IIB and III respectively.

DISCUSSION

D´ Journo and colleagues,[17] reported in a comparative study between groups of standard and extended two field lymph node dissection that disease free survival was found to differ significantly according to lymphadenectomy group, and were 10% and 41% in each group. Improved long term survival was also found to be associated with extensive lymphadenectomy in a meta-analysis; in which, it was observed that extensive lymphadenectomy decreased the locoregional recurrence and improved long term survival.[18] Several reports insist that aggressive lymphadenectomy can improve long term outcome.[19-21] The effect of three field radical esophagectomy including lymph nodes dissection of the neck in addition to mediastinal and abdominal node dissection on survival remains controversial but the preliminary and intermediate term results have shown that 3-field nodal dissections offers some patients significant survival benefits and reduces the incidence of recurrence in cervical and superior mediastinal lymph nodes.[21,22] Conversely, others have found no survival benefit for extensive lymphadenectomy,[10] and no survival benefit in a randomized study of three-field lymphadenectomy versus two-field lymphadenectomy.[11]

Extensive lymphadenetomy has several advantages that may influence long term survival; including accurate staging and decrease in the regional recurrence rate.[19,20] In this small present study, more than 70% of all patients completing resection had stage IIB and III disease. In addition to the bad nutritional status and physiologic problems associated with extensive surgery, it was not surprising that the survival rate was poor .A larger study with multidisplanary approach is required to have better results. We routinely requested cervical CT scan to all patients and the results showed no evidence of cervical lymph nodes, therefore we did not perform 3-field node dissection. However, cervical node relapses had been seen in 2/26 patients (8%). This warranted further study to justify cervical node dissection in NO neck.

The number of positive lymph nodes is a recognized factor of long term survival. Extensive nodal involvement is considered an indication of systemic disease and cannot be cured by extensive lymphadenectomy,[23] however a nodal involvement of less than 4 and a positive lymph node ratio

of less than 0.2 are regarded as a favorable prognostic factors in N1 disease.[24,25] Therefore, for reduced tumor burden, nodal involvement is regarded as an indicator of cure by curative surgical resection of primary tumor and metastatic lymph nodes. The mean number of positive lymph nodes in the present study was 6 which signifies late presentation. We did not study the pattern of lymph node metastasis in relation to the location of primary tumor, size, grade or depth of infiltration because this requires a large number of patients.

The pitfall of mediastinal lymphadenectomy is its high rate of morbidity due to injury of bronchial artery, tracheobroncheal tree, thoracic duct or recurrent laryngeal nerve.[17,26] In the present study we had no tracheobroncheal tree injury. The two cases of left recurrent laryngeal nerve palsy might be related to the dissection of left recurrent nerve chain nodes in the aortopulmonary window or injury during performing cervical esophagogastric anastomosis. Those using a cervical anastomosis[27] or an extended three-field clearance[28] reported a higher rate of injury of the nerve. Routine ligation of the thoracic duct is associated with low incidence of chylothorax. This avoids repeated thoracotomy or medical problems as lymphopeia associated with conservative management.[29]

Most reports concerning the management of surgical complications have focused on anastomotic leak because its incidence was high and often fatal. There is a wide variation in reported anastomotic leak rate after esophagectomy, although much of this variation can be attributed to the different techniques (hand sewn versus mechanical) and sites (neck versus thorax) of esophagogastric anastomoses.[26] Incidence of anastmotic leak in the present series was 16% which was higher in cervical anastmosis.

The positioning of the esophagogastrostomy within the neck is believed to reduce the extent of morbidity arising from an anastomotic leak by preventing mediastinal contamination. However, cervical anastomoses tend to have a higher leak rate than intrathoracic anastomoses and the seriousness of cervical leaks should not be underestimated because sepsis may track into the mediastinum.[31] Also, the risk of regurgitation and aspiration in the early post operative period may be high. The potential additional morbidity of a cervical approach should also be taken into account before selecting this site for routine use.

Of all risk factors associated with postoperative pulmonary complications, the surgical site was the most important,[32] with the risk being highest for upper abdominal surgery and for thoracic surgery. The combination of these two approaches, as in Ivor Lewis esophageal resection, made the incidence of pulmonary complications high,[13] especially if coupled with risk independent patient-related factors as chronic lung disease and smoking. In the present study we had a high incidence of chest infection (26%). Cessation of smoking, preoperative chest treatment, routine use of thoracic epidural catheter and postoperative physiotherapy markedly reduced the bad sequence of chest infection. We had one case of mortality due to chest infection. Routine practice of performing a pyloroplasty to facilitate gastric drainage helps to prevent early outlet obstruction and possible aspiration. Early removal of nasogastric tube might also reduce the incidence of post operative chest infection.

The association between poor preoperative spirometric parameters as predictive measures for pulmonary complications after esophagectomy has been identified.[19] Although spirometry is the best way to define chronic lung disease,[20] some authors reported that clinical findings alone are generally more predictive than spirometry.[33,34] Although there might be an absolute spirometric threshold below which consideration for anesthesia and esophagectomy can be rejected, it is unlikely that such a decision will be taken based solely on these routine pulmonary function tests.

Considerable attention has focused on the nutritional aspects of risk prediction because patients being considered for esophageal resection are often malnourished. Protein depletion is associated with poor respiratory muscle strength and a subsequently higher incidence of postoperative pulmonary complications. Preoperative hyperalimentation can provide clinical benefit, however this remains to be proved.[35] The lack of association between major pulmonary morbidity and crude measures of nutrition such as serum albumin and percentage weight loss merely reflects the inadequacy of these parameters in assessing protein energy malnutrition.[26] More exact anthropometric, biochemical, and immunologic measurements can prove more useful.

In conclusion, complete mediastinal and abdominal dissection with subtotal and total esophagectomy can be performed safely with very low rate of surgical complications. This technique leads to more accurate staging, but it is unclear from this small study whether it has an impact on improvement of disease free survival or overall survival or not.

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