

TRANSTHORACIC VERSUS TRANSHIATAL ESOPHAGECTOMY: COMPARATIVE STUDY REGARDING SURGICAL APPROACH IN ESOPHAGEAL CANCER

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TRANSTHORACIC VERSUS TRANSHIATAL ESOPHAGECTOMY: COMPARATIVE STUDY REGARDING SURGICAL APPROACH IN ESOPHAGEAL CANCER (Abstract):

BACKGROUND: Surgical resection can offer the best curative treatment for oesophageal cancer but is associated with high postoperative morbidity rates. Most common surgical approaches are transthoracic (TT) and transhiatal (TH) techniques. Transhiatal approach has the advantage of reducing the pulmonary morbidity in patients with impaired pulmonary function. AIM: The aim of this study is to compare the TT and TH approach, in terms of preoperative assessment and short term outcomes. MATERIALS AND METHODS: We performed an observational study on a prospective collected database which included all the patients diagnosed with oesophageal cancer in which surgery was performed. A detailed assessment of comorbidities was performed using several scales: Charlson and age adjusted Charlson score, physiological score of POSSUM. Postoperative complications were graded according to the Dindo-Clavien classification. RESULTS: During a 9 years period surgery was performed in 50 cases, 33 by TT approach and 17 by TH approach respectively. The mean age was 58.7 ± 2.21 years old (95% CI 56.3-61.2). Patients in the TH group had a higher Charlson score (3 vs 2, P = 0.01), age adjusted Charlson score (5 vs 4, P = 0.03) and physiological score (17 vs 15, P = 0.04). TT techniques were mainly used for middle oesophageal cancers (69.7%) and TH for lower oesophageal tumors (82.4%). The overall operative morbidity was 60% with no difference between the two groups even for minor and major complications. Pulmonary complications occurred in 23 cases (46%), cardiac complications in 5 cases (10%), anastomotic leakage in 6 cases (12%) and recurrent nerve paralysis in 6 cases (12%). Multivariate analysis showed that age adjusted Charlson score (OR = 2.77; 95% CI 1.114-6.9236) and physiological score (OR = 1.7601; 95% CI 1.2067-2.5674) were predictors for complications. CONCLUSION: In our study mortality and morbidity showed no statistical difference in relation to the surgical approach. An accurate preoperative assessment and tailoring an adequate surgical approach can limit the percentage of postoperative complications.

KEY WORDS: ESOPHAGUS; ESOPHAGEAL CANCER; SURGICAL TREATMENT; TRANSTHORACIC APPROACH; TRANSHIATAL APPROACH

SHORT TITLE: Transthoracic versus transhiatal esophagectomy

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BACKGROUND

Esophageal cancer is the seventh cancer related deaths with 482,300 new cases per year [1] and usually occurs as

either squamous cell carcinoma usually in the middle and upper part of the mediastinum or adenocarcinoma in the lower third and the gastroesophageal junction.

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There has been a shift in the incidence of the histological subtypes of oesophageal cancer with the incidence of adenocarcinoma rising in the past 3 decades. The greatest recent changes in the management of oesophageal cancer are related to the treatment and surveillance of Barrett esophagitis management of early stages oesophageal cancers. For locally advanced tumors surgery alone provides poor prognosis [2] and in these cases induction therapy is often used with the aim of increasing the R₀ resections rate, treatment of micrometastasis and improvement of survival. Surgical resection provides the best advantage for early stages and in tumors with good response after neoadjuvant treatment. The type of surgical approach depending on surgeon varies institutional preference; the two most utilised techniques are the transthoracic with cervical or mediastinal anastomosis and transhiatal techniques. The reference and largest randomised cited trial comparing the two surgical approaches included 220 patients with adenocarcinoma who were assigned to either transhiatal resection or Ivor Lewis technique [3,4]. The transhiatal group had shorter hospitalisation (19 vs 15 days), less blood loss and less overall morbidity (57 vs 27%, P < 0.001). In the other group more lymph nodes were resected (31 vs 16, P < 0.001) with no difference in terms of R0 resection rate, postoperative mortality (4 vs 2%, P = 0.4) and survival. The overall morbidity rate after esophagectomy ranges between 50 to 60% most common [5,6],the being cardiopulmonary complications.

The aim of our study was to compare the two major approaches for oesophagectomy in a group of patients operated for oesophageal cancer in terms of preoperative assessment and early surgical outcome.

MATERIAL AND METHOD

We performed an observational study analysing all the patients who underwent esophageal resections for oesophageal cancer, from January 2004 until March 2013. Tumors of the cervical oesophagus as well as subcardial tumors (Siewert III type) were excluded from this analysis.

Preoperative workout consisted in medical history and examination, functional evaluation, barium contrast esophagogram, endoscopy with biopsy, thorax and abdominal CT scan, abdominal ultrasound. Functional status was assessed by means of routine blood tests, electrocardiogram and pulmonary function tests. Second line investigations such as: cardiac ultrasound and cardiopulmonary stress tests were performed when necessary.

After initial diagnosis and staging, patients with locally advanced tumors were submitted to a neoadjuvant protocol according to the functional status.

Comorbidities have been quantified accordingly to the Charlson comorbidity scale [7] and age adjusted Charlson comorbidity scale [8] and included: hypertension (systolic blood pressure higher than 140 and/or diastolic pressure higher than 90); cardiac dysfunction (history of ischemic heart disease, unstable angina, cardiac failure, atrial fibrillation), pulmonary dysfunction (FEV₁ < 70% of predicted values and/or vital capacity < 80%), vascular dysfunction (history of abdominal aortic aneurism, vascular bypass, carotid stenosis), neurological dysfunction (history of cerebrovascular accident or transitory ischemic attack, epilepsy or Parkinson), liver cirrhosis, chronic renal failure, diabetes mellitus on treatment. In order to have a more accurate information regarding functional status of the patients calculated the physiological score of the POSSUM (Physiological and Operative Severity Score for the enUmeration of Mortality and morbidity) based on the original description and codification of each component [9].

The POSSUM score was developed to allow risk-adjusted prediction of postoperative mortality and morbidity in surgery according to the physiological condition of the patients, severity of surgery,

age and general health and consists of a physiological part (12 factors with 4 grades score) and an operative part (6 factors with 4 grades).

Surgical procedures:

Transhiatal approach

The patient was placed in the supine position with the head turned toward the right and the neck extended. After laparotomy, the stomach was mobilised by dividing the gastrocolic ligament while preserving the right gastroepiploic vessels.

The short gastric vessels were divided. The esophagogastric junction was freed from the hiatus; the lesser omentum and the gastrohepatic ligament were divided. The left gastric artery was ligated and divided with celiac lymph nodes dissected. The oesophagus was dissected under direct vision through the widened hiatus of the diaphragm up to the inferior pulmonary vein.

A left cervical incision is made along the anterior border of the left sterno-cleido-mastoid muscle and dissection is carried out along the prevertebral space. When the cervical oesophagus was found, blunt dissection was performed down to the level of the thoracic outlet; blunt dissection was carried out along the oesophagus until the entire organ was mobilized. Several centimetres of oesophagus were gently pulled up into the cervical region and then transected.

The distal stump was carefully closed and the stomach and oesophagus were then removed through the diaphragmatic hiatus. After Kocher's manoeuvre and pyloroplasty, the oesophagus, cardia, and an area along the lesser curvature were resected and the stump was closed using a linear stapler or a running suture.

The stomach graft was delivered to the neck wound through the posterior mediastinal route by gentle traction using a silicone drain attached to the proximal part of the gastric tube and a hand sewn anastomosis was performed.

Transthoracic approach

Based on a surgeon's preference, when a triple approach was chosen, a right thoracotomy is performed as an initial step of the procedure and included removal of the azygous arch, low paratracheal, subcarinal, paraesophageal and parahiatal nodes in continuity with the resected esophagus. For tumors of the middle part of the thoracic oesophagus, the right reccurential lymph nodes were removed. The pleural cavity was drained and the chest wall was closed. Afterwards, the patient was placed in a supine position, in the same manner as for the transhiatal approach. The cervical and abdominal part of the intervention was similar to the transhiatal technique described above. This represents a modified McKeown technique; we prefer to perform thoracotomy as the first step to allow a better assessment of resectability in order to avoid potential unresectable locally advanced tumors. The stomach graft is pulled to the neck incision in similar fashion as in the transhiatal technique.

When the Ivor-Lewis technique is performed, the initial step was a median laparotomy with gastric mobilisation with preservation of the right gastric and gastroepiploic vessels and resection of the upper third of the stomach. After the abdominal stage, a right posterolateral thoracotomy is done allowing resection of oesophagus the and mediastinal lymphadenectomy. The intrathoracic anastomosis is performed manually.

In all patients a pyloroplasty and a jejunostomy feeding tube inserted at the end of surgery in order to provide accurate nutrition in the early postoperative period were performed. In patients with previous gastric surgery a colic interposition was preferred.

Pathologic examination was recorded in all patients and tumors were classified using the UICC TNM 7th classification.

Postoperatively, patients were transferred to the intensive care unit and extubated when they were hemodinamically

and respiratory stable; jejunostomy feeding was administered in the first postoperative day, swallow X-ray studies were performed on the 7th postoperative day to assess the anastomosis and gastric tube passage and a liquid diet was initiated when there were no signs of leakage. Postoperative complications in any of the patients undergoing either of the two approaches were noted. Postoperative morbidity and mortality were defined as any complication or death which occurred within 30 days after surgery.

Complications were graded according to the Dindo Clavien classification [10] based on the therapeutic consequences. Grade I and II were considered minor complications and grade III and IV as major complications, grade V complications was considered any major complications leading to the death of the patient.

Based on these considerations, patients were divided in two groups: patients who underwent transhiatal approach (TH group) and respectively, patients who underwent transthoracic approach (TT group).

Statistical analysis

Statistical analysis was performed using MedCalc v 9.2.0.1. Medians and interquartile ranges at the 25^{th} and 75^{th} percentile were calculated and subsequently depicted when relevant. Mann-Whiney U tests and Chi-square testes were used when appropriate. Significance was set at P < 0.05.

RESULTS

Between January 2004 and March 2013, fifty consecutive patients diagnosed with oesophageal cancer underwent surgical resections.

Table I Baseline characteristics

	TH $(n = 17)$	TT $(n = 33)$	Total $(n = 50)$	<i>P</i> -value
Age	60±1.48 (51.6-67.68)	57±2.17 (54-62)	58.7±2.21 (56.3-61.2)	0.53
Charlson score (CS)	3 (2-4)	2 (2-3)	3 (2-4)	0.01
Age adjusted CS	5 (3.75-6.25)	4 (3-5)	4 (2-7)	0.03
POSSUM	17 (15.75-18.25)	15 (14-17.25)	16 (15.23-16.64)	0.04
Cardiac	7 (41.2%)	8 (24.2%)	15 (30%)	
Pulmonary	9 (52.9%)	10 (30.3%)	19 (38%)	0.13
Renal	1 (5.9%)	0	1 (2%)	-
Diabetes	4 (23.5%)	1 (3%)	5 (10%)	0.04
Liver disease	4 (23.5%)	1 (3%)	5 (10%)	0.04
ASA score				
2	8 (47%)	26 (78.8)	34 (68%)	0.02
3	9 (53%)	7 (21.2%)	16 (32%)	0.02
Radiotherapy	2 (11.7%)	4 (12.1%)	6 (12%)	
Chemotherapy	2 (11.7%))	8 (24.2%)	10 (20%)	0.46
Radio-chemotherapy	2 (11.7%)	6 (18.2%)	8 (16%)	0.69
Hemoglobin	12±1.46 (10.86-13.46)	11.3±0.9 (10.84-12.26)	11.89±0.44 (11.4-12.4)	0.16
White Blood Cells	8044±548 (6484-9419)	8640±444 (7417-9944)	8440±456 (7743-9136)	0.36

Patients' characteristics are summarised in Table I. There were no significant differences between the groups in terms of age. All of the patients were considered on preoperative assessment by the anaesthesiologist of being ASA 2 or 3.

All scores which included a thoroughly assessment of the physiological status or of the co-existing comorbidities were statistically significant between the two subgroups of patients. Patients in which thoracotomy was performed had a better

Charlson score (P = 0.01), age adjusted Charlson score (P = 0.03) and a better physiological score of POSSUM (P = 0.04). In terms of pre-existing conditions patients in which thoracotomy was performed had a lower incidence of cardiac, pulmonary, liver diseases and diabetes.

There was no difference in terms of neoadjuvant treatment, although there was a tendency for performing the induction therapy on the patients from the last 5 years included in the study.

The pathological characteristics of all the patients are summarised in Table II. In the vast majority of cases the tumor was localised in the middle and lower part of the esophagus, tumors considered Siewert I and II were encountered in 14% of all cases (n = 7). There were differences in terms of surgical approach based on tumor site: the transthoracic approach was more frequent used for tumors located in the middle third of the oesophagus and the transthoracic approach, for tumors located in the lower part of the oesophagus. The predominant histology (72%, n = 36) was squamous cell carcinoma. As a rule, tubulised stomach was used for reconstruction, in 6 cases it was used colon interposition graft due to the previous gastric surgery. In 44 cases anastomosis was performed in the neck, the remaining 6 cases being intrathoracic

anastomosis, all of the cases were hand sewn anastomosis. Final pathological staging showed a predominance of the locally advanced tumors (stage III, 52%, n = 26), with no difference in terms of surgical approach. The patients were usually transferred intubated in the Intensive Care Unit and were extubated the next day.

Postoperative morbidity occurred in 60% of the cases (n = 30) and was mostly represented by cardiac and pulmonary complications (Table III). Eighteen patients developed minor complications according to Dindo-Clavien classification developed major complications. There were no differences in terms of overall, minor or major complications between the two subgroups of patients. Postoperative mortality rate was 10%, with no difference based on surgical approach. In these cases death was due to the: sepsis secondary to anastomotic leakage, bilateral bronchopneumonia, massive myocardial infarction, stroke and severe pancreatitis. Mean hospital stay was 14±1.06 days and ICU stay 6±0.55 days with no difference between surgical approaches. Multivariate analysis as seen in Table IV showed that age adjusted Charlson score and physiologic score of POSSUM independent prognostic were affecting postoperative complications.

Table II Tumor and reconstruction characteristics

	TH $(n = 17)$	TT $(n = 33)$	Total $(n = 50)$	P-value
Tumor site				
Thoracic esophagus	3 (17.6%)	23 (69.7%)	26 (52%)	0.0007
Inferior esophagus	14 (82.4%)	10 (30.3%)	24 (48%)	0.0007
Histology				
SCC	10 (58.8%)	26 (78.8%)	36 (72%)	0.10
ADK	7 (41.2%)	7 (21.2%)	14 (28%)	0.18
Stage				
1	4 (23.5%)	3 (9%)	7 (14%)	
2	4 (23.5%)	13 (39.5%)	17 (34%)	0.67
3	9 (53%)	17 (51.5%)	26 (52%)	
Reconstruction				
Gastric graft	15 (88.2%)	29 (87.9%)	44 (88%)	0.85
Colon interposition	2 (11.8%)	4 (12.1%)	6 (12%)	0.83

SCC squamous cell carcinoma; ADK adenocarcinoma

DISCUSSION

Despite the recent shift in management of oesophageal cancer to perform neoadjuvant chemo-radiotherapy, surgical resection remains the most important part of multimodal treatment for early stages and locally advanced disease [11]. The best surgical approach, in terms of outcomes and quality of lymphadenectomy is still a subject of debate. Although the minimally invasive techniques recently developed are used, the traditional surgical approaches are still the most used in surgical practice.

Several variables as comorbidities, tumoral stage, surgical technique (especially the type of approach) and surgeon and hospital experience should be considered when an audit of operative outcomes is performed.

A multicentre study regarding the preferred surgical techniques in oesophageal cancer [12] showed that the most common approaches are the transhiatal (35-44%) and Ivor Lewis (36-50%) with variability regarding the site of the tumor. In a small number of cases "en bloc" resection (3.9-6.5%) and the three fields lymphadenectomy (13% for proximal tumors and 1.3% for gastroesophageal junction tumors) were preferred.

Table III Outcomes after surgery

	TH $(n = 17)$	TT (n = 33)	Total $(n = 50)$	P-value
Overall morbidity	10 (58.8%)	20 (60.6%)	30 (60%)	0.99
Pulmonary	8 (47%)	15 (45.4%)	23 (46%)	0.99
Cardiac	1 (5.9%)	4 (12.1%)	5 (10%)	0.64
Fistula	2 (11.8%)	4 (12.1%)	6 (12%)	0.99
Haemorrhage	2 (11.8%)	3 (9.1%)	5 (10%)	0.99
Neurologic	1 (5.9%)	1 (3%)	2 (4%)	0.99
Hepatic failure	-	1 (3%)	1 (2%)	-
Sepsis	2 (11.8%)	8 (24.2%)	10 (20%)	0.46
Recurrent palsy	5 (29.4%)	2 (6%)	6 (12%)	0.037
Minor complications	6 (35.2%)	12 (36.3%)	18 (36%)	0.95
Major complications	4 (23.5%)	11 (33.3%)	15 (30%)	0.53
Mortality	1 (5.9%)	4 (12.1%)	5 (10%)	0.64
ICU stay	6±1.15 (4.6-8.8)	6±0.62 (5-7)	6±0.55 (5-7)	0.70
Hospital stay	14±1.58 (10.6-20.2)	14±1.29 (12-17.4)	14±1.06 (12-16)	0.81

Table IV Multivariate analysis for postoperative complications

Variable	Odds Ratio (OR)	95% CI	<i>P</i> -value
Age adjusted Charlson score	2.7772	1.1140 - 6.9236	0.028
Charlson score	0.3491	0.0865 - 1.4090	0.139
ASA	1.7347	0.2202 - 13.6674	0.60
Physiologic score POSSUM	1.7601	1.2067 - 2.5674	0.0033
Thoracotomy	1.2469	1.2067 - 2.5674	0.80
Tumor site	0.6258	0.1284 - 3.0504	0.5619

Te prognostic scores based on general evaluation of the patient (ASA score) and on the overall comorbidities (POSSUM, Charlson and age adjusted Charlson scores)

were significantly different in the two groups of patients (Table I). This is probably explained by the selection of patients suitable for a transthoracic resection; basically, the thoracotomy was not performed in a patient with an impaired cardiac and pulmonary function and this was directly reflected in the scores for functional assessment.

Age did not differ in the two groups, result which is concurent with literature data [13]. Comorbidities and overall functional capacity are more likely to affect perioperative morbidity more than age alone [14]. Patients with poor pulmonary status (forced vital capacity of less than 80% and forced expiratory volume in one second less than 70% of predicted value) have been associated with higher risk for pulmonary complications [15].

In our series patients suffering from an impaired pulmonary function were not considerate suitable for thoracotomy, and a transhiatal approach was used.

Other organ dysfunction can increase the risk of postoperative morbidity and mortality.

Liver cirrhosis can be a contraindication for surgery in some centres although Child A cirrhotic patient can undergo esophagectomy with acceptable mortality and morbidity [16]. All the patients in our series with a preoperative impaired liver function developed a major complication and death occurred in two cases, no matter the type of surgical approach.

Based on the results of a metaanalysis, the mortality rate after esophagectomy varies from 0 to 22% depending on the selection of the patients, experience of surgical team and the level of postoperative care [17]. Low volume centres (less than 5 cases per year) had a median of 18% mortality and high-volume centres (more than 20 cases per year) a median 4.9% mortality. We had a 10% mortality rate by performing 5 to 6 oesophagectomies per vear.

Pulmonary complications are the most frequent complication after esophagectomy and have been the leading cause of two-thirds of postoperative mortality [18]. In a 10 year review of 1,777 oesophagectomies it

was reported a 49.5% rate of complications of which pneumonia represented 21.4%, failure which required respiratory reintubation in 16.2% [5]. The choice of approach may also have a direct impact on respiratory complications. In a randomised study of 220 patients to a transthoracic versus a transhiatal approach for mid to distal oesophageal cancer, the comparison revealed a significantly higher rate of complications pulmonary in transthoracic group (57% 27%, VS P < 0.001), but with the same 5-year survival [3].

In our study we noted similar rates of pulomary complications. Given the study type (observational) we cannot conclude that both surgical approaches are similar in term of pulmonary morbidity rate. However we can conclude that a tailoring surgical approach can decrease the pulomonary complications.

Cardiovascular complications after esophagectomy includes a large group of events, in which atrial fibrillation remains the most common, with reported rates from 11.5% until 22% [6,19]. It is very important to prevent this type of complication because of the concern that conduit perfusion can be altered in the periods of relative hypotension precipitated by atrial fibrillation. In our series we encountered atrial fibrillation as a direct effect of another major complication, such as sepsis following anastomotic leak.

Recurrent nerve injury occurs during dissection of the cervical oesophagus and it is associated with the site of the anastomosis. The results of a meta-analysis [20] showed that the cervical anastomosis increases this risk (OR = 7.14; 95%CI: 1.75-29.14; P = 0.006). In our series we found to have significantly higher rates of recurrent nerve injury following the transhiatal approach, although the major part of the anastomosis was performed in the cervical region.

One of the most challenging steps of the esophagectomy is the preservation of an accurate perfusion at the site of the anastomosis; compromised conduit perfusion can lead to a reduced blood flow with an impaired healing and a high risk for fistula [21]. This is important when performing a cervical anastomosis that requires a longer gastric conduit with a high of diminished blood flow. anastomotic leakage rates are reported in the literature from 10.9% to 16% [3,6,22,23]. A large study [24] reported a 2% rate of gastric tip necrosis that required reintervention. The evaluation endoscopic of oesophageal replacement revealed gastric conduit ischemia in 9.2% of patients [23]. The thoracic anastomosis requires a shorter conduit length and less tension which are the key elements for a lower leak rate. The disadvantages of this site of the anastomosis are the opening of thoracic cavity and the possible consequences of an intrathoracic fistula. Although in our series there were no differences in terms of surgical approach we encountered only one fistula by performing an intrathoracic anastomosis, all the others were cervical site fistulas after either transhiatal or McKeown techniques. So, the choice of anastomotic location remains surgeon dependent based on personal experience and awareness of outcomes.

Our study has several drawbacks. The first one is that represents a small number of patients and this can limit the accuracy of the results. This is the direct result of relatively low percentage of patients suitable for surgery in Romania; many of the newly diagnosed cases are locally advanced or metastatic lesions in a patient with severe comorbid conditions. The second major drawback is the heterogeneous cohort of patients, we had a relatively long inclusion period and this induced a bias in the appliance of multimodal treatment. perioperative management in terms of early extubation, fluid restriction management, management and respiratory pain rehabilitation. Also, the management of postoperative complications was relatively different during the inclusion period, with a clinical suspicion toward occurrence of a complication after even a minor change in the postoperative course of a patient.

CONCLUSIONS

Surgery is still the standard of care and the best way to cure or palliate patients with oesophageal cancer. Significant improvement in oncologic staging and functional preoperative evaluation has led to better patient selection and better outcomes. Despite these improvements, esophagectomy is still associated with high morbidity and mortality risks. In order to minimalize the surgical trauma to the patient a various surgical approaches are used to treat patients. The surgeon should put in balance oncologic principles of (complete removal of the tumor with negative longitudinal and circumferential margins and adequate lymph node removal) and the risks of a specific surgical approach. The best way to reduce the surgical impact is to personalise the surgical approach to patient and tumor characteristics.

CONFLICT OF INTERESTS

None to declare.

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