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SURGICAL TREATMENT OF ESOPHAGEAL CANCER, IS THERE ROOM FOR IMPROVING OUTCOME? RESULTS OF AN INDIVIDUALIZED PROTOCOL

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BACKGROUND

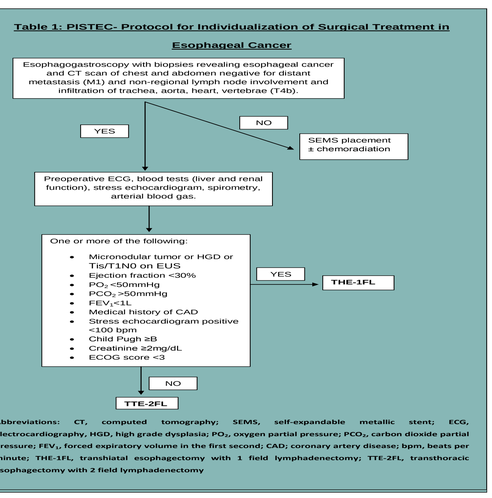
During the last decades, diagnostic tools, surgical technique and multidisciplinary management of esophageal cancer have led to improved results. However, overall survival of esophageal cancer (EC) remains approximately 20% [1]. In fact, only few randomized studies based on type of optimal surgery have been published. Therefore, the extent of surgery and lymphadenectomy in surgical treatment of esophageal cancer (EC) between transhiatal esophagectomy with 1-field lymphadenectomy (THE-1FL) and transthoracic esophagectomy with 2-field lymphadenectomy (TTE-2FL) is still controversial.

We evaluated the effect of patient's assessment and selection through individualized criteria for submission to each procedure on patients' overall survival, complication rate and recurrence rate.

METHODS

All patients with EC referred to our foregut surgical department were prospectively enrolled in a database. From January 2006, a protocol of individualized surgical treatment of EC (PISTEC) was applied to all patients with resectable disease. PISTEC is based on patient's physical status (PO_2<50mmHg, PCO_2>50mmHg, FEV_1<1L, ejection fraction<30%, medical history of coronary artery disease, stress echocardiogram positive at 100bpm, Child Phugh≥B, creatinine≥2mg/dl, ECOG score>3) and disease stage, with intent to select the appropriate surgical procedure (THE-1FL vs TTE-2FL) for each patient [Table 1]. Furthermore, preoperatively, all patients completed upper gastrointestinal (UGI) tract endoscopy with tumor biopsies and computed tomography (CT) of the chest, upper and lower abdomen with intravenous and oral contrast, while selected patients underwent endoscopic ultrasound (EUS). Patients with distant metastasis, non-regional lymph node enlargement or infiltration of adjacent organs identified during preoperative testing were excluded from the algorithm. Patients' demographics and characteristics were assessed [Table 2]. In terms of surgical technique, lymph node dissection in THE involves the removal of portal, celiac, left gastric artery and splenic artery lymph nodes and lower mediastinal lymph nodes (lymph node stations 1, 2, 3, 5, 7, 8a, 9, 11p, 12a). The dissection in TTE additionally involves the en bloc resection of all lymph nodes below the trachea bifurcation and the azygos vein.

Table 1: PISTEC- Protocol for Individualization of Surgical Treatment in Esophageal Cancer



Abbreviations: CT, computed tomography; SEMS, self-expandable metallic stent; ECG, electrocardiography, HGD, high grade dysplasia; PO_2, oxygen partial pressure; PCO_2, carbon dioxide partial pressure; FEV_1, forced expiratory volume in the first second; CAD; coronary artery disease; bpm, beats per minute; THE-1FL, transhiatal esophagectomy with 1 field lymphadenectomy; TTE-2FL, transthoracic esophagectomy with 2 field lymphadenectomy

TABLE 2. PATIENTS' DEMOGRAPHICS AND CHARACTERISTICS.

PATIENTS CHARACTERISTICS	TOTAL (n=61)	TTE (n=19)	THE (n=32)	UNRESCTABLE (n=10)	p
Age (yrs)					
Median (range)	60.26 (24-83)	49.84 (24-68)	63.66 (39-83)	69.2 (58-81)	<0.001
Sex					
Male	51 (83.6%)	16 (84.2%)	27 (84.4%)	8 (80%)	NS
Female	10 (16.4%)	3 (15.8%)	5 (15.6%)	2 (20%)	
Histology					
EAC	51 (83.6%)	13 (68.4%)	29 (90.6%)	9 (90%)	NS
ESCC	7 (11.5%)	5 (26.3%)	1 (3.1%)	1 (10%)	
EAC/ESCC	2 (3.3%)	1 (5.3%)	1 (3.1%)	0	
Neuroendocrine	1 (1.6%)	0	1 (3.1%)	0	
Tumor place					
EGJ	51 (83.6%)	13 (68.4%)	30 (93.8%)	8 (80%)	NS
ME	10 (16.4%)	6 (31.6%)	2 (6.3%)	2 (20%)	
Concomitant diseases					
CAD	5 (8.2%)	0	3 (9.4%)	2 (20%)	NS
DM	6 (9.8%)	2 (10.5%)	4 (12.5%)	0	
COPD	3 (4.9%)	0	2 (6.3%)	1 (10%)	
Cirrhosis	2 (3.3%)	1 (5.3%)	1 (3.1%)	0	
None	45 (73.8%)	16 (84.2%)	22 (68.8%)	7 (70%)	

Abbreviations: EAC, esophageal adenocarcinoma; ESCC, esophageal squamous cell carcinoma; ME, middle esophagus; CAD, coronary artery disease; DM, diabetes mellitus; COPD, chronic obstructive pulmonary disease; TTE-2FL, transthoracic esophagectomy with 2 field lymphadenectomy; THE-1FL, transhiatal esophagectomy with 1 field lymphadenectomy.

RESULTS

From January 2006 to January 2012, individualized surgical treatment according to PISTEC was applied on 61 patients with EC. Of them, 52.5% (n=32) were submitted to THE-1FL and 31.1% (n=19) to TTE-2FL. All patients with a resectable tumor (n=51) had a R0 resection. The pathological examination as corrected according to the 7th edition of TNM classification - which was introduced on January 2010- is shown in table 3. Mean follow up time was 21.06 months. Adjuvant therapy was administered tin 73.8% (n=45) of patients. Recurrence was observed in 35.4% (n=17) of patients [TTE=33.3% (n=6), THE=36.7% (n=11), p=0.534]. Among them, 17.6% (n=3) had local recurrence. Mean time of recurrence was 14.24 months. The 5-year overall survival rate was 45.3%, with mean survival time (MST) estimated 40.25 months (fig.1). The 5-year survival of patients who finally underwent surgical resection (n=51) was 56.4% with MST of 50.11 months (fig.2).

Patients who underwent THE had an estimated 5-year survival rate of 46.5 % and a MST of 41.29 months, whereas patients who underwent TTE had an estimated 5-year survival rate of 77.8% and a MST of 58.22 months (fig.3).

The estimated overall 5-year survival of patients with stage 0, I, II, III and IV was 100%, 100%, 92.3%, 23.6% and 0%, respectively. Patients without positive lymph nodes (N0) had an estimated 5-year survival rate of 71.3% with a MST of 60.72 months, patients with 1-8 positive lymph nodes had 58.1% with a MST of 41.5 months and patients with 9 or more positive lymph nodes had an 30% estimated 5-year survival rate with a MST of 19 months (fig.4).

The estimated overall 5-year survival of patients with stage II who underwent THE was 88.9% and of patients who underwent TTE was 100% (fig.5). For patients with stage III, overall 5-year survival was 0% and 61.4%, respectively (fig.6).

Table 3. Post-surgical pathological disease stage and number of positive lymph nodes

Disease stage (pathological)	Total (n=61)	TTE (n=19)	THE (n=32)	Unresectable (n=10)
Stage 0	2 (3.3%)	1 (5.3%)	1 (3.1%)	0
Stage I	6 (9.8%)	2 (10.5%)	4 (12.5%)	0
Stage II	14 (23%)	5 (26.3%)	9 (28.1%)	0
Stage III	30 (49.2%)	11 (57.9%)	18 (56.3%)	1 (10%)
Stage IV	9 (14.8%)	0	0	9 (90%)
No lymph node metastasis	20 (39.2%)	7 (36.8%)	13 (40.6%)	n.a.
1-8 positive lymph nodes	25 (49%)	9 (47.4%)	16 (50%)	n.a.
≥9 positive lymph nodes	6 (11.8%)	3 (15.8%)	3 (9.4%)	n.a.

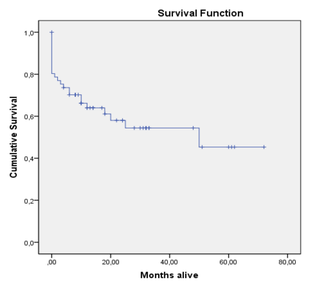


Fig.1

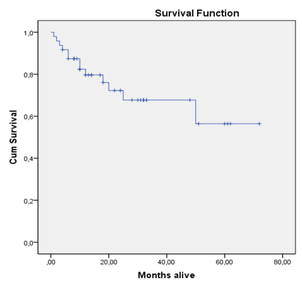


Fig.2

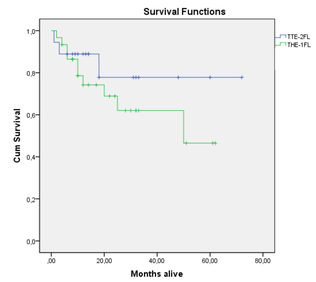


Fig.3

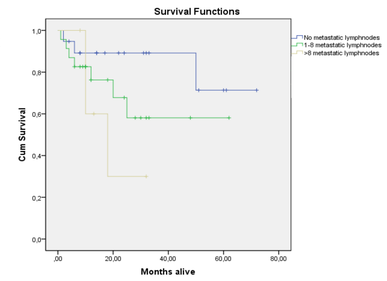


Fig.4

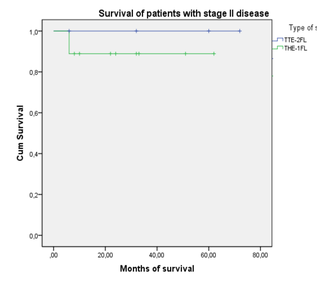


Fig.5

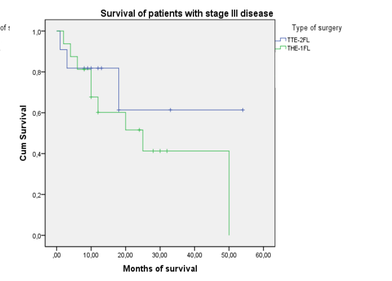


Fig.6

DISCUSSION

The idea of treatment individualization is not novel. Tailored treatment has become mandatory in order to achieve better results decreasing perioperative morbidity and mortality, while targeting to optimal overall survival. In EC treatment individualization has been previously proposed [2,3]. The protocol we present is mainly based on patient's clinical characteristics and less in tumor's characteristics. Since it is not yet possible to accurately estimate the number of positive lymph nodes preoperatively, the decision on the appropriate surgical management has to be made according to the patient's physical status, in order to offer the lowest perioperative morbidity and mortality combined with the maximum oncological benefit. Surgical units that manage EC should have the ability to perform both operations, taking under consideration the oncological benefit and the surgical risk.

CONCLUSION

The proposed algorithm aims at balancing perioperative risks and oncological benefit. Individualization of surgical treatment of EC seems to provide favorable outcomes regarding survival. This effect could probably be enhanced with the concurrent application of neoadjuvant treatment.

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