

RESULTS OF THE APPLICATION OF A PROSPECTIVE PROTOCOL FOR INDIVIDUALIZATION OF SURGICAL TREATMENT OF ESOPHAGEAL CANCER.



Georgia Doulami, Nikolaos Kokoroskos, Zoi Vrakopoulou, Stamatina Triantafyllou, Eleftheria Kleidi, Georgios Zografos, Dimitrios Theodorou. Department of Foregut Surgery, 1st Propaedeutic Surgical Clinic, "Hippokration" General Hospital, National and Kapodistrian University of Athens, Greece.

OBJECTIVES

Despite improvements on diagnostic modalities, patient's preoperative preparation, surgical technique and multimodality approach have been made, overall survival of esophageal cancer (EC) remains still at approximately 20% [1]. Because of the rarity of the disease and the lack of large prospective studies, several controversies exist regarding the optimal surgical treatment of EC. The debate is on the extent of lymph node dissection, with transhiatal esophagectomy (THE) and transthoracic esophagectomy (TTE) being the two main surgical approaches. We have designed a protocol for individualized of surgical treatment of EC (PISTEC) and herein we present the results of its application in terms of patients' survival, complication rate and recurrence rate.

TABI	E 1. PATIENTS		S AND CHARAC	TERISTICS.	
PATIENTS	TOTAL	TTE (n=19)	THE (n=32)	UNRESCTABLE	
CHARACTERISTICS	(n=61)			(n=10)	р
Age (yrs)					
Median	60.26	49.84	63.66	69.2	<0.001
(range)	(24-83)	(24-68)	(39-83)	(58-81)	
<u>Sex</u>					
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%)	
<u>Histology</u>					
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%)	
DM	6 (9.8%)	2 (10.5%)	4 (12.5%)	0	
COPD	3 (4.9%)	0	2 (6.3%)	1 (10%)	NS
Cirrhosis	2 (3.3%)	1 (5.3%)	1 (3.1%)	0	
None	45 (73.8%)	16 (84.2%)	22 (68.8%)	7 (70%)	

PATIENTS AND METHODS

On January 2006 we initiated the application of PISTEC on patients with EC referred to our Department of Foregut Surgery. Preoperatively, all patients undergo upper gastrointestinal (UGI) tract endoscopy with tumor biopsies and computed tomography (CT) of the chest, upper and lower abdomen with intravenous and oral contrast and selected patients undergo endoscopic ultrasound (EUS). Patients with distant metastasis, non-regional lymph node enlargement or infiltration of adjacent organs according to preoperative evaluation are not included in PISTEC. Patients included in PISTEC are prospectively enrolled in a database and their demographics and characteristics are presented in table 1.

According to the PISTEC (table 2), we assess the patient's physical status and the presence of early disease in order to choose the appropriate surgical approach, THE or TTE. As for the extent of lymphadenectomy, 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.

Patients having on pathology examination disease stage greater than IIA undergo adjuvant chemotherapy with fluorouracil, oxaliplatin and capecitabine. In addition, patients with T4a disease and/or more than 6 metastatic lymph nodes receive adjuvant radiotherapy.

Statistical analysis was performed using the Statistical Package for the Social Sciences (IBM SPSS 19).

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



RESULTS

From January 2006 to December 2011, a total of 61 patients with EC were included in PISTEC. According to PISTEC, 31.1% of the patients (n=19) finally underwent a TTE and 52.6% (n=32) underwent a THE. All patients (n=51) with a resectable tumor 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 number of removed lymph nodes was 21 (range:4-60). Patients with TTE had a higher number of resected lymph nodes compared to THE (29.2 vs 23.2 respectively, p=0.161). Complications were recorded according to the Accordion Severity Grading System of Postoperative Complications [2]. The majority of complications were grade II (42.9%) and grade III (28.6%) and are presented in table 4. Thirty day mortality rate was 4.9% (n=3). Mean follow up time was 19.6 months (range 0-72 months). Recurrence occurred in 27.5% of the patients. Mean time of recurrence was 13.6 months and the 5-year survival of patients was 20.4% (figure 1).

The estimated 5-year overall (n=61) survival rate was 54.9% with a mean survival time (MST) of 44.6 months. The estimated overall survival rate of patients who finally underwent surgical resection of their tumor (n=51) was 65.7% with a MST of 52 months (figure 2). Patients who underwent THE (n=32) had an estimated 5-year survival rate of 63.1% and a MST of 43.9 months., whereas patients who underwent TTE (n=19) had an estimated 5-year survival rate of 69.5% and a MST of 54.6 months (figure 3).

According to disease stage, the estimated 5-year survival rate for stages 0 and I was 100%, for stage II was 92.9% with a MST of 66.9 months, for stage III was 45% with a MST of 30.4 months and for stage IV was 0% with a MST of 6.4 months. Patients without positive lymph nodes (N0) had an estimated 5-year survival rate of 88.7% with a MST of 64.7 months, patients with 1-8 positive lymph nodes had 55.5% with a MST of 40.4 months and patients with 9 or more positive lymph nodes had an 31.3% estimated 5-year survival rate 4).

DISCUSSION

The idea of treatment individualization is not novel. Nowadays, clinical practice encourages tailored treatment in order to

Stage	·	6 (9.8%)	2 (10.5%)	4 (12.5%)	0
Stage		14 (23%)	5 (26.3%)	9 (28.1%)	ο
Stage		30 (49.2%)	11 (57.9%)	18 (56.3%)	1 (10%)
Stage	IV	9 (14.8%)	0	о	9 (90%)
No lyn	nph node	20 (39.2%)	7 (36,8%)	13 (40,6%)	n.a
1-8 po	ositive	25 (49%)	9 (47.4%)	16 (50%)	n.a
lymph ≥9 pos	nodes sitive	6 (11.8%)	3 (15.8%)	3 (9,4%)	n.a
lymph	h nodes				
Tab	ole 4: Com	plications of e	esophagectomy in	total and accord	ing to type of
Comp	olications	Total	THE-1	FL TTI	E-2FL
Respi	iratory	(n=27) 4 (14.8%)	(n=17) 2 (11.8	%) 2 (2	: 10) 20%)
infect	ion				
arrhyt	ac thmia	4 (14.8%)	4 (23.5	%) 0	
Pleura	al effusior	ם 4 (14.8%)	3 (17.6	%) 1 (*	10%)
Laryn palsy	geal nerv	e 5 (18.6%)	3 (17.6	%) 2 (2	20%)
Chylo	othorax	2 (7.4%)	0	2 (2	20%)
Intern	al hernia	2 (7.4%)	1 (5.9%	6) 1 (*	10%)
Gastri	ic conduit	t 1 (3.7%)	1 (5.9%	6) O	
Anast	tomotic	1 (3.7%)	1 (5.9%	6) O	
ieakag Anast	ge tomotic	4 (14.8%)	2 (11.8	%) 2.(3	20%)
strictu	ure				
tients				- Iym	phadenectomy
Number of patients					Figure 1. Recurrence of EC according to type of surgery.
Number of patients	Loc	al recurence Place of	Systematic r	recurrence	Figure 1. Recurrence of EC according to type of surgery.
-0 -0 -0 -0 -0 -0	Loc	al recurence Place of	Systematic r	recurrence	Figure 1. Recurrence of EC according to type of surgery.
	Loc	al recurence Place o	Systematic r	recurrence	Figure 1. Recurrence of EC according to type of surgery.
-0 -0 -0,1 -0,1	Loc	al recurence Place of	Systematic r of recurrence	recurrence	Figure 1, Recurrence of EC according to type of surgery.
Durvival	Loc	al recurence Place of	Systematic r of recurrence	recurrence	Figure 1. Recurrence of EC according to type of surgery.
Number of patients -9.0 -9.0 -9.0	Loc	al recurence Place of	Systematic of recurrence	recurrence	Figure 1. Recurrence of EC according to type of surgery.
Cumulative Survival		Place of	Systematic r of recurrence	recurrence	Figure 1. Recurrence of EC according to type of surgery.
Cumulative Survival		al recurence Place of	Systematic r of recurrence	recurrence	Figure 1. Recurrence of EC according to type of surgery. Figure 2. 5- year overall survival of patients with resectable EC
Cumunative Survival		al recurence Place of	Systematic r of recurrence 65	5.7% ••••••	Figure 1. Recurrence of EC according to type of surgery. Figure 2. 5- year overall survival of patients with resectable EC included in PISTEC

achieve better results in terms of perioperative morbidity and mortality and overall survival. In EC treatment individualization has been previously proposed [3,4]. 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, having in mind the oncological benefit and the surgical risk.

CONCLUSION

Our study proposes an algorithm in order to balance perioperative risks and oncological benefit. Both types of surgery are useful and should be selectively applied. This individualized approach may result in favorable outcomes regarding survival.

REFERENCES

- 1. Gavin AT, Francisci S, Foschi R, et al. Oesophageal survival in Europe: A EUROCARE-4 study. Cancer Epidemiol 2012; 36(6):505-12
- 2. Strasberg SM, Linehan DC, Hawkins WG. The accordion severity grading system of surgical complications. Ann Surg 2009; 250(2):177-86..
- 3. Hulscher JBF, van Lanschot JJ. Individualized surgical treatment of patients with an adenocarcinoma of the distal oesophagus or gastro-oesophageal junction. Dig Surg 2005; 22(3):130-4.
- 4. Donohoe CL, O'Farrell NJ, Ravi N, Reynolds JV. Evidence-based selective application of transhiatal esophagectomy in a high-volume esophageal center. World J Surg 2012; 36(1):98-103.

