DIFFERENT SURGICAL OPTIONS IN TREATMENT OF CANCER CARDIA AND LOWER THIRD ESOPHAGEAL CANCER.

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ABSTRACT

Purpose: to study different techniques in resection of carcinoma of lower esophagus and cardia with regards to techniques, complications, morbidity, mortality, and survival.

Methods: from Feb. 2005 to Aug. 2006, this study included 33 patients with operable carcinoma of the lower esophagus or cardia as evident by clinical and investigatory tools including endoscopy and biopsy, patients were classified into: Type I (cancer of distal esophagus) included 10 cases, were treated by total esophagectomy in 5 cases, or distal subtotal esophagectomy in 5 cases. Type III (cancer of the subcardial area infitrating the esophago gastric junction) included 8 cases, were treated by total gastrectomy in 4 cases, and proximal gastrectomy in 4 cases. Type II (cancer of the gastric cardia) included 15 cases, were treated by the 5 types of operation as guided by the extent of the tumor and the proximity to either stomach or esophagus. The extent of lymphadenectomy was dependent on tumor type, node size, and gross involvement, approach, and general condition of the patient.

Results: Curative resection (R0) was performed in 25 patients (75.8%), 7 cases of type I, 11 cases of type II, and 7 cases with type III tumors, while incomplete resection (R1+R2) was done in 8 cases (24.2%), 5 cases of transhiatal esophagectomy in type I and II tumors, and 3 cases of proximal gastrectomy with less than D2 resection. Tumor free resection margins were achieved in 29 patients (88%), node metastasis were found in 24 cases (72.2%), 6 cases of type I, 12 cases of type II, and 6 cases of type III tumors. Two cases with type I tumor had >50% positive mediastinal nodes, and 2 cases with type III tumor had >50% positive abdominal nodes.

Significant complications occurred in 9 cases (27.3%), as anastomotic leak in 3 cases were managed conservatively, respiratory complications in 2 cases (6.1%), and wound infection in 4 cases (12.1%).

Mean hospital stay was comparable with no statistically significant difference (15.8, 15.2, and 14.8 days for type I, II, and III respectively). There was no significant difference in morbidity, mortality, and disease free survival (DFS) between cases of subtotal or total esophagectomy (transhiatal or 3 field approach) with P values 0.1, 0.95, 0.91 respectively. Similarly there was no significant difference between patients with type I and II who underwent proximal or total gastrectomy (P=0.6).

There was a better survival for patients with stage I & II compared to stage III & IV (P=0.001), for well and moderately differentiated grade I & II tumors than poorly and undifferentiated tumors grade III & IV (P=0.008), for negative nodes compared to those with positive nodes (P=0.03), while involvement of more than 50% of abdominal lymph nodes had a reverse action on the survival (P=0.001).

Conclusion: Type of the tumor had no influence on the survival (P=0.5),while the stage, node involvement, and operation were statistically significant. So efforts should be directed towards earlier diagnosis, better selection, and minimizing post operative complications, and R0 resection should be attempted.

Keywords: *Esophageal carcinoma, gastric carcinoma, esophagectomy, gastrectomy.*

INTRODUCTION AND AIM OF THE WORK

Esophageal cancer represents one of the most lethal malignancies with increasing incidence, and despite the numerous contributions to the surgical literatures, it remains a highly disputed topic (Blot et al., 1991).

While some consider all tumors arising in the esophago-gastric junction as esophageal cancer, others regard them as gastric cancer or even as a separate entity (Siewert and Stein, 1998). This confusion is due to the borderline location of the tumor, and inability to reach a consensus about classification and staging of these lesions (Sobin and Wittekind, 1997).

Esophago-gastric cancers are those which have their center within 5 cm proximal and distal to the anatomical cardia, and are differentiated into: **Type I** cancer of the distal esophagus which usually arises from an area of intestinal metaplasia (Barrett's esophagus) and may infiltrate the esophago-gastric junction from above. **Type II** cancer of the cardia that arises from short segment intestinal metaplasia of the cardia epithelium at the esophago-gastric junction. **Type III** cancer of the subcardial area which infiltrates the esophago-gastric junction and distal esophagus from below (Siewert and Stein, 1998).

Classification can be performed easily based on a combination of contrast radiography, endoscopy, computed tomography, endosonography, and intra-operative appearance (Clements et al., 2004).

Radical resection is the standard therapy, however local and distant failure remains high (Gunderson and Sosin, 1982), because of complicated anatomical and lymphatic structure, there are several surgical options for management (Hulscher et al., 2002). However the choice of treatment is influenced by patient age, coexisting conditions, site and extent of the tumor, anticipated life span of the patient, and wishes of the patient and his/her family (Siewert and Stein, 1998).

A number of approaches to esophageal resection had been described; each has its supporters and detractors despite the lack of sufficient objective evidence to clearly support one over another. The two most often reported are transthoracic approach (Lewis, 1946), and transhiatal approach (Orringer et al., 1993), the use of left thoracotomy in combination with division of the left hemi diaphragm had been also described with good results (Zhang et al.,1994).

Transhiatal resection although less invasive, lymph node dissection is limited, in contrast to transthoracic resection the surgeon can perform en block dissection of mediastinal lymph nodes under unilateral ventilation (Hulscher et al., 2002).

The Ivory-Lewis approach is performed through upper abdominal incision and postero lateral thoracotomy that afford excellent exposure for both abdominal and thoracic portion of the operation, and allows more definitive oncologic procedure with superior margins and improved clearance of regional lymph nodes, but it had not been associated with significantly superior survival rates (Chu et al., 1997).

The transhiatal esophagectomy is accomplished via upper abdominal and cervical incision, the esophagus is bluntly dissected from above and below with avoidance of thoracotomy and that decreases morbidity (Orringer et al., 1993), moreover the performance of cervical anastomosis leaves the patient less vulnerable to the potentially lethal mediastinitis as a result of leakage. For this reason some surgeons perform transthoracic resection with a cervical anastomosis via a separate incision (King et al., 1987). Critics emphasize the difficulty of performing an adequate oncologic operation and the potential of hemorrhage with the blunt mediastinal dissection (Goldmine et al., 1993), however less morbidity and mortality was demonstrated by some authors (Bolton et al., 1994).

The aim of this work is to study and evaluate these different surgical techniques in treatment of cancer cardia and lower third esophagus, as regards indications, operative techniques, complications, morbidity, mortality, and survival.

PATIENTS AND METHODS

A selected sample of patients was collected from the out patient clinic, surgery department of Assiut university hospital and south Egypt cancer institute. All cases diagnosed as cancer cardia or cancer lower third esophagus by clinical data of abdominal sonar, barium swallow, upper endoscopy with biopsy, and CT scan. All patients were subjected to:

*-Complete history taking and meticulous examination.

*-Investigation for assessment of fitness e.g. ECG, blood picture, serum urea & creatinine, blood sugar, liver function, chest X-ray, and respiratory function test.

*-Investigation for diagnosis of tumor operability as upper endoscopy and biopsy, barium swallow and/or meal, abdominal sonar, CT scan of the chest and upper abdomen.

All cases included in the study were operable, and criteria of exclusion of the radical treatment included advanced cases either local or distant, unfit patient, patient refusal, and extremes of age.

Surgical management:

The choice of surgical approach was based on the tumor type and the goal to achieve complete tumor resection.

For all patients, laparotomy was done through upper midline incision and mobilization of the stomach was carried out, a standard dissection of the perigastric, paracardial, left gastric nodes, nodes along lesser curve, fundus with sampling of the common hepatic and splenic arteries nodes was also performed. Widening of the hiatus was carried out with splitting and dilatation of the crura or with excision of part of crura and diaphragm especially with type II tumor to achieve adequate radial margin. Postero-inferior mediastinal lymphadenectomy was carried out removing the para-esophageal lymph nodes.

Type I tumor: Total esophagectomy was carried out either transhiatal or through three field approach (abdominal, thoracic, and cervical). Reconstruction was done with esophago-gastric anastomosis after pull up of the stomach in the neck. In the others, distal subtotal esophagectomy through right thoracotomy (Ivory Lewis) was done with esophago-gastric anastomosis in the chest at the level of the azygos vein with safety margin 6-10 cm of the esophagus above the tumor.

Type III tumor: Total gastrectomy or proximal gastrectomy were done (T2and early T3 with grossly negative nodes and tumor size <5 cm). In some patients, abdominal and thoracic incision (Ivory Lewis) were done and reconstruction in the chest with esophago-gastric anastomosis or with esophago-jejunal anastomosis. In the other patients, only abdominal approach was performed with esophago-gastric or esophago-jejunal anastomosis.

Type II tumor: Guided by the extent of the tumor and proximity to either the esophagus or the stomach, the 5 types of operations were performed.

The extent of lymphadenectomy depended on the type of the tumor, the size of the lymph node, gross involvement of the lymph nodes, the approach, and the general condition of the patient.

For type I tumors underwent total esophagectomy through the 3 field approach and subtotal distal esophagectomy with Ivory Lewis approach, standard mediastinal lymphadenectomy included right bronchial nodes, nodes along azygos vein, paratracheal, carinal, and para-aortic nodes were resected if enlarged or palpated in addition to the abdominal nodes mentioned, with sampling of the celiac nodes.

For type III tumors underwent total gastrectomy, lymphadenectomy included lymph nodes station 1-11 of the Japanese classification with dissection of the splenic nodes, suprapyloric, infrapyloric nodes , and the spleen if grossly enlarged or involved with preservation of the pancreas (modified D2 dissection). In cases with proximal gastrectomy, lymphadectomy was done for lymph nodes station 1-7 without dissection of supra, or infra-pyloric nodes with the above mentioned abdominal lymph nodes that were removed as a standard for all cases.

For type II tumors, the extent of lymphadenectomy depended on the type of the operation and the approach.

The specimens were assessed pathologically and the removed lymph nodes were counted as mediastinal, abdominal, and total. Staging was reported

according to the most recent version of the Union International Contre Le Cancer (UICC) and American Joint Committee of Cancer (AJCC).

RESULTS

This study included 33 patients (27 males and 6 females), ages ranged from 24 to 67 years, complaining of cancer in the esophago-gastric junction who were studied from Feb. 2005 to Aug. 2006.

The most common complaint was dysphagia; however other presentations were also recorded as weight loss, vomiting, chest complaint, and bleeding.

Investigations:

*- By endoscopy and biopsy: adenocarcinoma was diagnosed in 21 patients (63.6%), squamous cell carcinoma in 8 patients (24.2%), and undifferentiated carcinoma in 4 patients (12.1%).

*- By combination of abdominal sonar, barium swallow or meal, and CT chest or abdomen, 10 cases (30.3%) were diagnosed as type I tumors, 15 cases (45.5%) were diagnosed as type II tumors, and 8 cases (24.2%) were diagnosed as type III tumors.

Management:

(1)- For type I tumors: Total esophagectomy was carried out for 5 cases either transhiatal in 2 patients (6.1%), or through three field approaches (abdominal, thoracic and cervical) in 3 cases (9.1%), reconstruction was done by esophago-gastric anastomosis after pull up of the stomach in the neck. And distal subtotal esophagectomy through right thoracotomy (Ivory lewis) in the other 5 patients (15.1%) with esophago-gastric anastomosis in the chest at the level of the azygos vein with safety margin 6-10 cm of the esophagus above the tumor.

(2)- For type III tumors: Total gastrectomy was carried out in 4 patients (12.1%), proximal gastrectomy in 4 patients (12.1%), in 5 cases (15.1%) abdominal and thoracic incision (Ivory Lewis) was done and reconstruction in the chest with esophago-gastric anastomosis in 3 cases (9.1%), and esophago-jejunal anastomosis in 2 cases (6.1%), however in 3 cases (9.1%) only abdominal approach was performed with esophago-gastric anastomosis in 1 patient (3%), and esophago-jejunal anastomosis in 2 cases (6.1%).

(3)- For type II tumors: guided by the extent of the tumor and the proximity to either the esophagus or the stomach, the 5 types of operations were performed as shown

Lymph node metastasis was found in 24 patients, 6 with type I tumors, 12 with type II tumors, and 6 with type III tumors. (Metastasis to celiac lymph nodes was discovered post operatively and considered by some as M1a).

When grouped as esophageal and gastric operations, the para-esophageal, left gastric and para-aortic nodes were the most commonly affected nodes for esophageal operations while left gastric, lesser curve, and para esophageal nodes were the most commonly involved for gastric operations.

Significant complications occurred in 9 patients (27.3%), as 3 cases had anastomotic leakage that was managed conservatively (2 leak in the neck, and 1 intrathoracic leak), 2 cases with respiratory complications, and wound infection occurred in 4 cases. However the mean hospital stay for all patients was 15.8 days for type I tumors, 15.2 days for type II, and 14.8 days for type III, but P value was not significant.

The post operative mortality was 9.1%, as 3 cases died within 30 days of the operation including 1 patient with anastomotic leakage, 1 patient with pneumonia, and 1 patient with heart failure. The surgical approach, method of reconstruction, and the type of the tumor did not influence the post operative mortality.

There was a siginficant survival advantage for patients with stage I and II tumors compared to patients with stage III and IV (P=0.001), and for patients with negative nodes compared to those with positive nodes (P=0.03). Involvement of more than 50% of the abdominal lymph nodes had a reverse action on the survival (P=0.001)

Survival was significantly better for patients with well and moderately differentiated grade I and II tumors than poorly and undifferentiated tumors grade II and IV (P=0.008).

In patients with type I tumors there was no significant difference in mortality, morbidity, and estimated DFS between those who underwent subtotal distal

esophagectomy and those who underwent total esophagectomy either transhiatal or with the three field approaches with P value 0.1, 0.95, and 0.91 respectively. There was also no significant difference in mortality and DFS between patients with type II and III who had proximal or total gastrectomy (P=0.6).

Follow up was completed for 28 patients with mean follow up period of 11.7 months (range 5: 31 months), with the overall survival for 1 and 2 years for 30 patients with resected carcinoma of esophagogastric junction tumors were 86.7% and 43.3% respectively and the median survival was 24 months (after exclusion of 3 cases died peri-operatively).

During follow up, 9 patients died (5 with metastatic disease, 3 with local recurrence, and 1 unrelated causes), and 19 (57.6%) patients were followed (3 with metastatic disease, 4 with local recurrence, 2 with both local and metastatic disease, and 10 patients were completely free), and 2 patients were lost during follow up.

The type of the tumor had no influence on the survival (P. = 0.5), while the stage, node involvement, and the type of operation were statistically significant.

Table (1): Distribution of different types of approaches and cancer.

Type►	**Type I**		**Type II**		**Type III**		**Total**	
Approach▼	No.	%	No.	%	No.	%	No.	%
Transthoracic	5	15.1	5	15.1	5	15.1	15	45.5
Transhiatal	2	6.1	6	18.2	0	0	8	24.2
3 Field	3	9.1	1	3	0	0	4	12.1
Abdominal	0	0	3	9.1	3	9.1	6	18.2
Total	10	30.3	15	45.5	8	24.2	33	100

Table (2): Distribution of operation and different types of cancer.

Type►	**Type I**		**Type II**		**Type III**		**Total**	
The operation▼	N.	%	N.	%	N.	%	N.	%
1-Subtotal gastrectomy	5	15.1	5	15.1	0	0	10	30..3
2-Transhiatal gastrectomy	2	6.1	6	18.2	0	0	8	24.2
3- 3 field approach	3	9.1	1	3	0	0	4	12.1
4-Proximal gastrectomy	0	0	2	6.1	4	12.1	6	18.2
5-Total gastrectomy	0	0	1	3	4	12.1	5	15.1
Total	10	30.3	15	45.5	8	24.2	33	100

Table (3): Shows the types of reconstruction (Es. = Esophageal).

The type ►	**Type I**		**Type II**		**Type III**		**Total**	
& reconstruction▼	N.	%	N.	%	N.	%	N.	%
Es.-gastrostomy cervical	5	15.1	7	21.2	0	0	12	36.2
Es.-gastrostomy thoracic	5	15.1	5	15.1	3	9.1	13	39.5
Es.-jejunostomy thoracic	0	0	0	0	2	6.1	2	6.1
Es.-gastrostomy abdominal	0	0	2	6.1	1	3	3	9.1
Es.-jejunostomy abdominal	0	0	1	3	2	6.1	3	9.1
Total	10	30.3	15	45.5	8	24.2	33	100

Table (4) Shows staging of the tumor in relation to type.

Staging		Type I		Type II		Type III		Total	
		No.	%	No.	%	No.	%	No.	%
Tumor	**T1**	0	0	0	0	0	0	0	0
	T2	2	20	2	13.3	1	12.5	5	15.2
	T3	7	70	11	73.3	6	75	24	72.7
	T4	1	10	2	13.3	1	12.5	4	12.1
Node	**N0**	4	40	3	20	2	25	9	27.3
	N1	6	60	7	46.7	3	37.5	16	48.5
	N2	0	0	5	33.3	3	37.5	8	24.2
Metast.	**M0**	9	90	15	100	8	100	32	97
	M1	1	10	0	0	0	0	1	3
Stage I		0	0	1	6.7	1	12.5	2	6.1
Stage II		5	50	1	6.7	2	25	8	24.2
Stage III		4	40	11	73.3	4	50	29	57.6
Stage IV		1	10	2	13.3	1	12.5	4	12.1

Table (5) Tumor pathology in relation to type (St. dev. =Standard deviation)

The tumor characteristics		Type I		Type II		Type II		Total	
		No.	%	No.	%	NO.	%	NO.	%
Tumor size	-Range	3-8 cm.		4-8 cm.		4-10 cm.		3-10 cm.	
	-Median	6 cm.		6cm.		7 cm.		6 cm.	
	-Mean	5.6 cm.		5.8cm.		6.8 cm.		6.2 cm.	
	-St.dev.	1.3		1.1		1.4		1.4	
Histological	-Grade I	3	30	0	0	2	25	5	15.1
	-Grade II	4	40	8	53.3	3	37.5	15	45.5
	-Grade III	2	20	5	33.3	2	25	9	27.3
	-Grade IV	1	10	2	13.3	1	12.5	4	12.1
The margin	-Negative	9	90	13	87.7	4	87.5	29	88
	-Positive	1	10	2	13.3	1	12.5	4	12
Resection type	-R0	7	70	11	73.3	7	87.5	25	75.8
	-R1+R2	3	30	4	26.7	1	12.5	8	24.2

Table (6) Distribution of tumor type to and nodal site involvement.

Lymph node groups, and involvement	Type I		Type II		Type III		Total		P.
	No.	%	No.	%	No.	%	No.	%	
	10	100	15	100	8	100	33	100	
Mediastinal -ve	4	40	10	66.7	6	75	20	66.7	0.06
<50%	4	40	5	33.3	2	25	11	33.3	
>50%	2	20	0	0	0	0	2	6	
Abdominal -ve	4	40	5	33.3	2	25	11	33.3	0.06
<50%	6	60	10	66.7	4	50	20	66.7	
>50%	0	0	0	0	2	25	2	6	
Abd. + Med. -ve	4	40	3	20	2	25	9	27.2	0.25
<50%	3	30	6	40	3	37.5	12	36.4	
>50%	3	30	6	40	3	37.5	12	36.4	

(Abd. = Abdominal, Med. = Mediastinal& P. = P value)

Table (7) Shows lymph node characteristics according to tumor type.

Type of tumor► ▼Lymph nodes	**Type I (10)**	**Type II (15)**	**Type III (8)**	**Total (33)**
Total (abdom. + mediast.):				
*-Number	179	301	173	653
*-Mean	17.8	20.4	21.6	20
+ve (Abdom. + mediast.):				
*-Number	31(17.4%)	84(27.9%)	41(23.7%)	156(24%)
*-Mean	3.1	5.6	5.1	4.6
Abdominal nodes:				
*-Number	110(61.5%)	228(75.6%)	126(72.8%)	464(71%)
*-Mean	11	15.5	15.8	14.2
+ve abdominal nodes:				
*-Number	16(15%)	74(32.5%)	34(27%)	124(26.9%)
*-Mean	3	5.9	5.7	5.2
Mediastinal nodes:				
*-Number	69(38.5%)	73(24.4%)	47(27.2%)	189(29%)
*-Mean	6.9	4.9	5.9	5.7
+ve mediastinal nodes:				
*-Number	15(21.3%)	10(13.6%)	7(14.9%)	32(16.8%)
*-Mean	2.6	1.8	1	2

Table (8) shows lymph node characteristics according to the type of operation

The operative	**Esophageal operations**				**Gastric operations**		
technique►	1	2	3	Total	4	5	Total
No. of cases	10	8	4	22	6	5	11
Abd.+ mediast.							
*-Number	120	74	48	242	107	123	230
*-Mean	17.1	16	18.3	17.2	17.8	23.4	21.6
+ve Abd. + mediast.							
*-Number	22	14	8	44	23	33	56
*-Mean	3.1	3.3	3	3.1	3.8	6.9	5.9
Abdominal nodes:							
*-Number	73	40	33	146	81	99	180
*-Mean	10.4	11	10	10.4	13.5	18.2	16.7
+ve abd. nodes:							
*-Number	13	8	5	26	19	30	40
*-Mean	1.9	2.6	1.3	1.9	3.2	6.2	5.2
Mediastinal nodes:							
*-Number	47	34	15	96	26	24	50
*-Mean	6.7	5	8.5	6.9	4.3	4.5	4.4
+ve mediast. nodes:							
*-Number	9	6	3	18	4	3	7
*-Mean	1.3	1	1.5	1.3	0.7	0.8	0.7

Table (9) Distribution of DFS at 12 & 24 months and median survival with lymph node involvement and stage.

DFS ► & node involved▼		No.	12 months	24 months	Median survival	P.
Total nodes	-ve	9	88.9	66.7	ND	0.002*
	<30%	12	66.7	8.3	16	
	>30%	12	58.3	0.00	14	
Mediastinal	-ve	20	65	35	16	0.2
	<50%	11	63.6	0.00	16	
	>50%	2	50	0.00	18	
Abdominal	-ve	11	81.8	54.5	ND	0.001*
	<50%	20	65	10	16	
	>50%	2	0.00	0.00	7	
Stage	I and II	10	80	55.4	ND	0.001*
	III and IV	23	65.2	4.3	15	

(DFS: Disease Free Survival, ND: Not Detected, *: Significant)

Table (10) Distribution of DFS at 12& 24 months and median survival with tumor type and operative data.

DFS► & Tumor type and operative data▼		No.	12 months	24 months	Med. Survival	P.
Tumor type:	I	10	90	20	19	0.5
	II	15	46.7	26.7	11	
	III	8	62.5	25	15	
Approache:	Abd. Th.	15	73	33.3	18	0.4
	Abd. C.	8	62.5	0.00	16	
	Abd. Th. C.	4	75	0.00	16	
	Abd.	6	66.7	33.3	15	
Operation:	Transhiatal	8	62.5	0.00	24	0.03*
	Subtotal	10	70	0.00	16	
	3 Field	4	75	50	16	
	Prox. Gastr.	6	66.7	16.6	11	
	Total Gastr.	5	60	20	16	
	Esohageal	22	86.4	27.3	21	
	Gastric	11	63.6	18.2	14	
Resection:	R0	25	68	24	16	0.06
	R1+R2	8	62.5	0.00	13.5	

DISCUSSION

In the present study, the surgical approach was determined by the classification of Siewert and Stein (Siewert and Stein, 1998). Although this classification is based purely on anatomical and topographic parameters, many analyses have shown that it provides a useful tool to differentiate tumors entities arising in the vicinity of the esophagogastric junction and thus helps in selection of the surgical approach (Aikou et al., 1987).

The approach:

A lot of debate was noticed with and against the transhiatal approach for the treatment of esophageal cancer (Fok et al., 1993; Goldmine et al., 1993; Jakl et al.,1995; Chu et al., 1997 and Ellis et al.,1997), in contradistinction to other authors (Skinner et al., 1986 and Hulscher et al., 2000), who advised thoracotomy for distal esophageal tumors in order to allow radical enbloc dissection to be performed. Moreover the relatively high incidence of positive resection margins is another cause of concern, so several investigators have postulated that 6-10 cm of macroscopically tumor free esophagus in the resected specimen is required to ensure a negative microscopic margin (Mandard et al., 1981; Husemann, 1989 and Stipa et al., 1996). To fulfill this, either the left thoraco-abdominal approach or Ivory-Lewis (right thoracotomy and abdominal approach) have been advocated. Despite such a curative approach, microscopic tumor at the resection margin was reported in as many as 16% of the patients undergoing resection with curative intent, resulting in loco regional recurrences (Jakl et al., 1995).

In the present study, thoraco-abdominal approach was used in 15 cases and the abdominal approach alone was used in 6 cases (table 1), the thoraco-abominal approach provides the best operative field, enabling a wide resection of esophageal hiatus and crura, complete dissection of lower mediastinal lymph nodes (Kodama et al., 1998) and permits a safe esophago-jejunostomy under direct vision (Sasako, 1999). However, the 5-year survival rates of those who had mediastinal metastases were less than 10% (Kodama et al., 1998 and Kodera et al., 1999) Partly because of limited treatment effect of lymphadenectomy in the mediastinum and the improved safety of high esophago-jejunostomy without thoracotomy, using staple guns, so thoracotomy could be avoided for the treatment of cancer cardia (Sasako, 2000).

On the other hand, several reports have suggested that thoracotomy is associated with considerable respiratory complications (Mandard et al., 1981; Husemann, 1989; Stipa et al., 1992; Orringer et al., 1993; Stark et al., 1996; DeManzoni et al., 1998 and Wayman et al., 1999), and wound pain (Stark et al., 1996). So many surgeons favor transhiatal approach for lower esophageal cancer resection on the grounds that the survival benefit from the extended lymphadenectomy in advanced disease is outweighed by the added morbidity associated with thoracotomy (Orringer et al., 1993).

The operative techniques:

Total gastrectomy was performed in 5 cases in this study (12.1%) and proximal gastrectomy in 6 cases (18.2%) for type II and III tumors as shown in table (2).In agreement with the controversy about the extent of gastric resection for the treatment of carcinoma of the cardia, advocates of total gastrectomy stress the possible benefit of a more radical lymphadenectomy as evident by the number of lymph nodes retrieved that total gastrectomy does result in a more complete lymphadenectomy (Kodera et al., 1999). Moreover, some patients also had metastases to the peri-gastric stations at the distal portion of the stomach (node groups 4d, 5 and 6) that required total gastrectomy. Although the incidence was low, a higher incidence of metastases to these lymph nodes was detected in the advanced cancer (DeManzoni et al., 1998).

On the other hand, current data show no 5-year survivors among those with metastases to the distal peri-gastric nodes, implying that resection of these nodes is likely to have little impact on the survival of patients with type II and III cancer (Kodera et al., 1999). If these nodes need not to be resected, the blood supply to the distal stomach through the right gastric and gastro-epiploic arteries can be

preserved, and proximal gastrectomy emerges as an alternative to total gastrectomy, provided that the tumor size and location permit preservation of an adequately large remnant of stomach without compromising distal tumor clearance (Harrison et al., 1998). These findings contradict what has been long considered that total gastrectomy is the standard procedure for all advanced cancer of the proximal third of the stomach.

Siewert's classification identified a subgroup of carcinoma of the proximal third of the stomach (types II and III) that can be treated by proximal gastrectomy when limited to the upper stomach with no invasion to the serosa, the size of the lesion being not greater than 4 cm, a surgical margin of 3 cm for the localized type and 5 m in infiltrative lesions is needed, and with no metastases to the superior or inferior pyloric lymph nodes or lymph nodes on the right side of the greater curvature (Harrison et al., 1998). However previous retrospective studies have suggested that no difference in survival has been associated with total gastrectomy when compared with proximal gastrectomy (Launois et al., 1993 and Jakl et al.,1995).

Lymphadenectomy procedures:

In this study 72.8% of cases had positive lymph nodes (table 6), the highest incidence was for type II cancers (80%), followed by type III (75%), then type I (60%), and the presence of this malignant lymph nodes whether abdominal or total (abdominal + mediastinal) was associated with a significantly worse prognoses, as the 2 year DFS for negative abdominal and total nodes were 54.5% and 66.7% respectively. While it was only 10% and 8.3% for patients with less than 50% involvement (as shown in table 7). None of our patients with more than 50% involvement of abdominal or total nodes were alive after 2 years (table 7). This is evident by Hagen and colleagues who identified lymph node metastases in 63% of patients with carcinoma of the cardia, the 2 year actuarial survival was 90% , 65% , and 38% for patients with -ve nodes, patients with 1 to 4 positive node, and the group with more than 4 +ve nodes respectively (Hagen et al., 2001).

In this study, the median survival was not detected in cases with negative abdominal and negative total nodes as more than 50% of those patients were alive and free after 2 years with P = 0.001, 0.002 respectively indicating better prognosis. This was also proved by authors that the ratio of involved to uninvolved nodes is a predictor of survival (Roder et al., 1994 and Hulscher et al., 1995), Hagen and colleagues found that the presence of 10% nodal involvement was associated with a poor survival (Hagen et al., 2001).

The total mediastinal and positive mediastinal nodes were significantly higher for type I in comparison to those resected in type II and III, and it was detected by Siewert and colleagues that there are several pronounced differences between type I and II tumors where as similarities between type II and III tumors were predominant (Siewert et al., 1996). The mean number of the nodes dissected when grouped as esophageal and gastric operations were 17.2 and 21.6 respectively as shown in table (8), this difference may be because we have performed modified D2 dissection for the majority for gastric operations and Dl dissection in few cases, while we have performed standard and not radical dissection in esophageal operation especially with transhiatal esophagectomy, and the term Dl describes removal of the lymph nodes compartment 1 that includes for proximal tumors (type III) lymph nodes located peripheral and parallel to the greater and lesser curvature (station 1 -7).On the other hand and D2 dissection includes Dl + central lymph nodes along the large vessels and towards the celiac vessels (station 7-11) and include the distal esophagus (Siewert et al., 1996 and Siewert et al., 2000). Although, lymphadenectomy in this area can be achieved by pancreas preserving splenectomy, removal of the spleen may increase the rate of postoperative septic complications and thus adversely influence survival (Griffith et al., 1995; Kitamura et al., 1997 and Bonenkamp et al., 1999).Therefore, splenectomies should only be performed in patients with frank lymph node metastases or infiltration of splenic hilum, and was only done in three cases in this study.

Dresner and colleagues had counted a mean of 22, 23 nodes for gastric and esophageal operations respectively (Dresner et al., 2001). While Japanese researchers have correlated increasing radicality of resection with improved survival with their dissection (Akiyama et al.,1981), and their description of the lymph node tier is based on meticulous

dissection of specimen with the recovery and histopathological assessment of all associated lymph node groups. So that lymph nodes yield from such an approach is impressive with 40 to 50 lymph nodes routinely identified in D2 gastrectomies and similar numbers from enbloc esophagectomies (Akiyama et al.,1981 and Dresner et al., 2001). Worthwhile attempts to replicate this is level of lymph node recovery have met with only partial success (Dresner et al., 2001). Because of lack of controlled studies, the benefits, risks and optimal extent of lymphadenectomy for esophagogastric carcinoma still are being debated (Gamal et al., 2004).

Most surgeons accept that extended lymphadenectomy in the lower posterior mediastinum and along the celiac axis may improve the prognosis of the subgroup of patients who have a limited number of positive lymph nodes (Clark et al., 1994 and DeManzoni et al., 1998), although, survival benefit has not been confirmed in randomized trials (Bonenkamp et al., 1999). Several studies indicated that systematic lymphadenectomy may improve the prognosis of the subgroup of patients at the early stage of lymphatic spread (stage II and III tumors) (Siewert et al., 2000).

When the operations performed were grouped as esophageal and gastric, the most commonly involved nodes in the esophageal group was the para-esophageal in 9 (27.3%) cases, the left gastric in 6 (18.2%), the para aortic in 5 (15.2%)cases and the para-tracheal and carinal in 4 (12.1%) cases. While for gastric operations, they were the left gastric in 13 (39.4%) cases, lesser curve in 9 (27.3%), para-esophageal in 7(21.2%) and both left para cardial and greater curve in 6 (18.2%) cases. This distribution of nodal metastases is similar to the pattern of dissemination reported by the Japanese researchers(Maruyama et al., 1989).

In this study, 5 para-aortic positive nodes were retrieved from 3 patients of type 1, and 2 of type II tumors, while 3 positive bronchial nodes were resected from 2 patients of type I, and 1 of type II. In the contrary, Dresner and colleagues found that in the abdominal field for type 1 cancer, the right and left para-cardial nodes and left gastric nodes are the most common sites involved whereas the greater and lesser curvatures together with the celiac, common hepatic and splenic artery nodes are rarely involved. In the mediastinum, they found that the para-esophageal nodes (middle and lower) were involved in 60% of cases and the bronchial and para aortic nodes were less frequently involved (Dresner et al., 2001).

The incidence of nodal disease at the origin of left gastric artery (N2) in this series was considerably higher than that at the greater curvature station, as described by the Japanese as Nl station (Japanese, 1998). Based on this pattern of dissemination, a D2 nodal clearance is a logical approach and this technique is popular in Japan, and has been adopted by several specialized centers in Europe and North America (Jatsko et al ., 1992 and Sue-Ling et al., 1993). In the hands of experienced surgeons who adopt these meticulous techniques, the associated mortality and morbidity is not higher

Neither for patients with esophageal cancer nor patients with gastric cancer has a clear overall survival benefit been demonstrated for extended lymphadenectomy in randomized trials. D2 resections appear to offer a survival advantage over Dl resection with a lower incidence of local recurrence (Dresner et al., 2001). In our study, there was no statistical significant difference in the morbidity, mortality or recurrence between the cases subjected to modified D2 and Dl dissection which were considered as RO and Rl resection.

One patient with type I tumor proved after surgery to have celiac positive nodes, and as evident by TNM staging system for esophageal cancer (Kelly et al., 2001), the nodal metastases at the celiac axis (station 9) are deemed Ml disease, and interference for palliation rather curative resection should be attempted (Hardwick and Williams, 2002). But these nodes are considered N2 in cases of gastric cardia cancer therefore all are considered as loco regional lymph nodes from both distal esophagus as well as gastric cardia and both carcinomas are regarded as one entity (Wijnhoven et al., 1999 and Dresner et al., 2001). So there is an urgent need for reviewing the staging system for gastro-esophageal junction tumors (Dickson et al., 2001), that takes in account that the number of nodal metastases influences outcome. Furthermore N staging should use a number based assessment of positive nodes instead of the current anatomical one, bringing it into line with rules of staging gastric cancer. This would help to ensure that adequate numbers of lymph nodes must be examined to improve the prognostic information derived from pathological staging, and proposals for

new staging system be made (Dolan et al., 1999).

In our study, 10 patients developed post operative metastases during follow up, leading to death in 5 of them, and metastases occurred in the liver (4 patients), the lung (2 patients), the bones (2 cases), and multiple sites (2 patients) and unfortunately despite optimal treatment, most patients with clinically manifest esophago gastric carcinoma die from metastatic disease within 3 years of presentation (O'Sullivan and Shahnan ,2000). So the clinical outcome is predetermined by the presence of wide spread occult metastatic cancer cells that are disseminated before treatment (O'Sullivan et al., 1999). These cancers have traditionally been thought to spread sequentially in a stepwise manner from the esophageal wall to the regional lymph nodes and finally to systemic dissemination. Staging investigators define the nodal status of the tumor as a surrogate indicator for systemic spread but the majority of patients with node negative cancer also die of metastases. This indicates the biologically aggressive nature of this disease with haematogenous involvement. A finding confirmed by analysis of bone marrow from resected rib for micro metastases that were detected in 80% of the patients (O'Sullivan et al., 1999).

Mortality and morbidity rates:

In the present study, postoperative mortality was 9%, and major morbidity occurred in 9 patients (27.3%) in the form of anastomotic leak, respiratory complications and wound infection, in agreement with a similar percent reported for a large series of patients with esophageal and gastric cardia tumors (Bytzer et al., 1999). However, Siewert and colleagues reported 3.8% postoperative mortality, and found that transthoracic esophagectomy was associated with a significant higher postoperative 30 days mortality compared with extended total gastrectomy (Siewert et al., 2000). In another study, hospital mortality and morbidity rates were 4.8% and 34.1% respectively (Mariette et al.,2002). A comparable morbidity and mortality incidence of 17% and 5.4% was detected by Solerio et al., 2003. On the other hand, McCulloch and colleagues had an overall mortality of 12% and morbidity of 43% for gastric resection, and the commonest problems they reported were respiratory infection or failure, cardiac failure and anastomotic leak and 10% of patients needed a second operation (Mc Culloch et al., 2003).

The surgical approaches in our study was not associated with any statistically significant difference in hospital death or frequency of complications (P = 0.4) as shown in table (8). However the number of patients undergoing transthoracic approach (abdomino thoracic or abdominal-thoracic-cervical) was high in the present randomized study (19 cases representing 57.5%) making definitive conclusions difficult. In agreement with us, other similar randomized trials showed no difference in morbidity or mortality between a transhiatal, transthoracic and three field approach (Chu et al., 1997 and Ellis et al., 1997).

We also found that the DFS was unaffected by surgical approach except between the group that underwent distal subtotal esophagectomy compared to those who underwent total gastrectomy (P = 0.035). This difference may reflect better outcome for the site of the lesion than the approach or the type of operation. So that patients with distal esophageal cancer had better DFS than patients with cardial and subcardial tumors due to early presentation and better T stage as (20% of patients of type I were T2 in comparison to 13.3% and 12.5% for type II and III respectively) as shown in table 4.

The long term survival with adenocarcinoma of the cardia, even in patients selected for surgical resection, remains poor. In the present study the median overall survival was 24 months and the median DFS was 16 month. However other studies reported median survival 2.9 months and higher survival rate in patients with negative nodes (Wijnhoven et al., 1999). On the other hand, other studies have reported 5-year survival rates of 16.0 - 32.3% (Launois et al.,1993 , Ellis et al., 1997 and Hagen et al., 1993).

Patients with carcinoma of the cardia usually have a dismal prognosis, and the tumor is often far advanced at diagnosis. So that long term survival is still low. To improve the results, efforts should be directed towards earlier diagnosis, better selection, and minimizing post operative

complications. A R0 resection should be attempted.

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