



ESOPHAGEAL TUMORS

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BENIGN ESOPHAGEAL TUMORS AND CYSTS

- Esophageal benign tumors are rare (0.5-0.8% of all esophageal neoplasms)
- They are classified broadly into three groups

Classification of Benign Esophageal Tumors

Epithelial Tumors	Papillomas				
	Polyps 5%				
	Adenomas				
	Cysts 20%				
Nonepithelial Tumors	Myomas	Leiomyomas 60%	Fibromyomas	Lipomyomas	Fibromas
	Vascular Tumors	Hemangiomas 2-3%	Lymphangiomas		
	Mesenchymal and other tumors	Reticuloendothelial tumors	Lipomas	Myxofibromas	Giant cell tumors
		Neurofibromas	Osteochondromas		
Heterotopic Tumors	Gastric mucosal tumors Melanoblastic tumors Sebaceous gland tumors Granular cell myoblastomas Pancreatic gland tumors Thyroid nodules				

LEIOMYOMAS (1)

- Most common benign esophageal tumors.
- They are intramural (multiple in 3-10%).
- Occur between 20-50 years of age.
- > 80% occur in the middle and lower thirds.
- Calcification may occur within it (Ddx of a [calcified mediastinal mass](#))

LEIOMYOMAS (2)

- Vary greatly in size but seldom cause symptoms when < 5 cm
- Larger tumors cause **dysphagia**, retrosternal **pressure**, and **pain**
- Obstruction and **regurgitation** occur when these tumors encircle the esophageal lumen, and **bleeding** is a more common symptom of the malignant form of the tumor, **leiomyosarcoma**
- Potential for malignant degeneration of leiomyomas is **quite low**

LEIOMYOMAS (2)

- Appearance on **barium swallow** is a smooth concave defect with **intact mucosa** and sharp borders and abrupt sharp angles where the tumor meets the normal esophageal wall. Typically, half the tumor appears to lie within and half outside the esophagus
- **Esophagoscopy** is indicated to rule out Ca, but if a leiomyoma is suspected, a biopsy of the mass should **not** be performed so that subsequent extramucosal resection is not complicated by scarring at the biopsy site.
- **Treatment:** Enucleation.

MALIGNANT TUMORS OF THE ESOPHAGUS

Country	Incidence	Link
US	6 cases/100,000 men/year	(Black>white).
China (Henan Province)	0.9% in the population older than 30 years of age	Nitrosamine in the soil and contamination of foods by fungi (Geotrichum candidum) and yeast , which produce mutagens
India, Pakistan, Sri Lanka, and Yemen		Chewing tobacco
Singapore, Kurdistan		Hot beverages, Chinese tobacco and wine
South African Bantus and Zulus		Nitrosamine in the soil and contamination of food by molds , especially the Fusarium species
Normandy, Brittany		Alcohol and smoking

ETIOLOGY

Alcohol	Vitamin deficiencies
Tobacco	Anemia
Zinc	Poor oral hygiene and dental caries
Nitrosamine	Previous gastric surgery
Malnutrition	Chronic ingestion of hot foods or beverages

PREMALIGNANT ESOPHAGEAL LESIONS

Achalasia	Barrett's esophagus (CLE)
Irradiation esophagitis	Plummer-Vinson syndrome
Caustic burns	Esophageal diverticula
Leukoplakia	Ectopic gastric mucosa

There is an ↑ incidence of esophageal Ca in patients with **familial keratosis palmaris et plantaris (Tylosis)** (inherited as an autosomal dominant trait)

EPIDEMIOLOGY

- Estimated new cases and deaths from esophageal cancer during **2021** in the **USA**.

	Male	Female	Both sex
New cases	15310	3950	19260
Deaths	12410	3120	15530

PATTERN OF ESOPHAGEAL CANCER IN JORDAN 1996-2017

Year	Total No. of Cancer cases			Esophageal Ca-Male		Esophageal Ca-Female		Esophageal Ca-All	
	Male	Female	All	Freq.	%	Freq.	%	Freq.	%
1996	1704	1598	3302	19	1.1	11	0.6	30	0.9
1997	1699	1655	3354	17	1.0	4	0.2	21	0.6
1998	1777	1603	3380	16	0.9	9	0.5	25	0.7
1999	1560	1582	3142	17	1.1	10	0.6	27	0.9
2000	1680	1690	3370	21	1.2	5	0.3	26	0.8
2001	1740	1672	3412	16	0.9	7	0.4	23	0.7
2002	1760	1670	3430	16	0.9	10	0.6	26	0.8
2003	1743	1735	3478	7	0.4	5	0.3	12	0.3
2004	1763	1828	3591	14	0.8	11	0.6	25	0.7
2005	1818	1860	3678	15	0.8	4	0.2	19	0.5
2006	2047	2151	4198	17	0.8	12	0.6	29	0.7
2007	2048	2284	4332	14	0.7	9	0.4	23	0.5
2008	2274	2332	4606	10	0.4	9	0.4	19	0.4
2009	2280	2518	4798	18	0.8	5	0.2	23	0.5
2010	2330	2519	4849	18	0.8	11	0.4	29	0.6
2011	2194	2481	4675	15	0.7	11	0.4	26	0.6
2012	2346	2667	5013	17	0.7	7	0.3	24	0.5
2013	2564	2852	5416	13	0.5	11	0.4	24	0.4
2014	2718	2977	5695	21	0.8	18	0.6	39	0.7
2015	2668	2888	5556	20	0.7	5	0.2	25	0.4
2016	2815	3184	5999	17	0.6	9	0.3	26	0.4
2017	2990	3362	6352	19	0.6	9	0.3	28	0.4
Total	46518	49108	95626	357	0.8	192	0.4	549	0.6

Regarding the pattern of esophageal cancer in Jordan; between 1996 and 2017, there were **549** cases of esophageal cancer among Jordanians, accounting for **0.6%** of all newly diagnosed cancer cases. It affected **357** males (**0.8%**) and **192** females (**0.4%**). Esophageal cancer occurred more frequently in males than in females, with a male to female ratio of **1.9: 1**.

(1) SQUAMOUS CELL CARCINOMAS

- Disease of **men** (2-5 times more frequent) in the 6th-7th decades of life
- 95% of esophageal cancers worldwide

EARLY ESOPHAGEAL CANCER

- Constitute < 5% of all resected cases
- Are asymptomatic
- Endoscopically, Ca in situ most often presents as a slightly raised, granular, reddish plaque-like lesion, although superficial erosions or papillary lesions < 3 cm. may also be seen
- Microscopically, it is either **intraepithelial** (carcinoma in situ), **intramucosal** (no deeper than the lamina propria), or invading submucosa; varying degrees of dysplastic change are seen

ADVANCED ESOPHAGEAL CANCER

- The majority of esophageal Ca are diagnosed at an advanced stage.
- **Site:**
 - (a) Cervical esophagus (8%)
 - (b) Upper- and mid-thoracic segments (55%)
 - (c) Distal esophageal third (10 cm.) (37%).
- **Growth patterns:**
 - (a) Fungating (60%)
 - (b) Ulcerative (25%)
 - (c) Infiltrative (15%)

SPREAD

- Esophageal cancer is notorious for its aggressive biologic behavior, infiltrating **locally**, involving adjacent **lymph nodes**, and metastasizing widely by **hematogenous** spread
- **Lack of an esophageal serosal layer** tends to favor local tumor extension
- Upper- and middle-third tumors tend to involve the tracheobronchial tree, aorta, and left recurrent laryngeal nerve as it loops around the aortic arch
- Lower-third tumors may invade the diaphragm, pericardium, or stomach
- The extensive mediastinal lymphatic drainage, which communicates with cervical and abdominal collateral vessels, is responsible for the finding of mediastinal, supraclavicular, or celiac lymph node metastases in at least 75% of patients.

SPREAD

- Cervical esophageal Ca drain to the deep cervical, paraesophageal, posterior mediastinal, and tracheobronchial lymph nodes
- Lower esophageal tumors spread to paraesophageal, celiac, and splenic hilar lymph nodes
- Distant spread to liver and lungs is common
- Prognosis of invasive Ca is poor (overall 5-year survival for treated tumors is 5-12%)
- Extraesophageal tumor extension is present in 70% of cases at the time of diagnosis, and the 5-year survival is only 3% when lymph node metastases are present, compared with 42% when there is no lymph node spread.

(2) ADENOCARCINOMAS

- 2.5-8% of primary esophageal cancers
- Its frequency is ↑ dramatically in the US at a rate surpassing that of any other cancer
- Disease of **men** (male-to-female ratio of 3:1), in the 6th-7th decades of life
- They occur most commonly in the distal third
- It have one of three origins:
 - (1) Malignant degeneration of Barrett's mucosa (CLE)
 - (2) heterotopic islands of columnar epithelium
 - (3) the esophageal submucosal glands
- Patients with CLE are at least **40 times** more likely to develop adenocarcinoma than the general population.
- Adenocarcinoma arises in 8-15% of patients with a CLE. The finding of dysplasia in Barrett's mucosa is an ominous sign of impending malignant degeneration, with severe dysplasia being virtually synonymous with carcinoma in situ and being an indication for resectional therapy

ADENOCARCINOMAS

- Exhibits an aggressive behavior, with frequent **transmural** invasion and **lymphatic** spread
- Because many of these tumors arise in the distal esophagus, spread to paraesophageal, celiac axis, and splenic hilum lymph nodes is common
- Metastases to the lung and liver are most frequent
- The 5-year survival is only 0-7%, with the presence of lymph node metastases exerting a significant negative effect on survival

OTHER TYPES OF ESOPHAGEAL CANCERS

- (3) Anaplastic small cell (oat cell) carcinoma
- (4) Adenoid cystic carcinoma
- (5) Malignant melanoma
- (6) Carcinosarcoma

CLINICAL PRESENTATION

- Typically occurs in the 6th-7th decades of life, and a history of excessive use of tobacco and alcohol is common
- Symptoms may be of insidious onset, beginning as nonspecific retrosternal discomfort or indigestion.
- As the tumor enlarges, the initially intermittent dysphagia becomes progressive and the predominant symptom, with weight loss, odynophagia, chest pain, and occasionally hematemesis
- Because dysphagia is the presenting complaint in 80-90% of patients, any adult who complains of progressive dysphagia warrants both a barium esophagogram and esophagoscopy to rule out Ca

DIAGNOSIS

- **Esophagoscopy and biopsy** to establish the diagnosis are mandatory in every patient with an esophageal stenosis
- **Esophageal biopsy and cytology:** establishes a diagnosis in 95% of patients with malignant strictures
- **Double contrast barium swallow:** can demonstrate lesions as small as 5-15 mm. The majority of patients present with irregular mucosal filling defects, distortion of the esophageal lumen, or annular constrictions on barium studies

EVALUATION (1)

- Once the diagnosis has been established histologically, **staging** of the tumor is the next step in determining the therapeutic option.
- **Barium swallow** examination should be the first study in the patient with dysphagia because it provides information regarding the location and length of the tumor and the degree of associated obstruction.
- **Endoscopic ultrasound** to define the depth of mural invasion and to assess associated paraesophageal lymph nodes (it has 86% accuracy in defining involved mediastinal lymph nodes).
- **Chest X-ray** is abnormal in only 50% of patients, with findings such as an **air-fluid level** in the obstructed esophagus in the posterior mediastinum, a **dilated esophagus**, abnormal mediastinal soft tissue representing adenopathy, a pleural effusion, or pulmonary metastases being most common. The chest film, however, may be deceptively normal even with advanced disease.

EVALUATION (2)

- **Abdominal and Chest CT scan:** is the standard radiographic means of staging esophageal cancer. CT permits evaluation of the esophageal wall thickness (which normally should not exceed 5 mm.), assessment of direct mediastinal invasion by the tumor and the presence of regional lymphadenopathy and distant metastases. Regional adenopathy that can be resected with the esophagus does not preclude esophagectomy. However, histologically documented distant metastatic (Stage IV) (e.g., liver, pulmonary, or supraclavicular lymph node) **contraindicates** esophagectomy, since the expected survival is only 6-12 months.
- **Bronchoscopy** is an integral part of the evaluation of esophageal Ca, which are in proximity to the trachea or mainstem bronchi (i.e., upper- and middle-third tumors), because endoscopic evidence of invasion of the airway precludes a safe esophagectomy.
- Additional studies such as **MRI** to evaluate mediastinal structures, **bone and brain scans** to detect metastatic disease, or staging **mediastinoscopy** are not performed routinely unless indicated by specific symptoms or findings.

TNM CLASSIFICATION FOR STAGING ESOPHAGEAL CA

- The esophagus is divided into four sections:
- (a) The **cervical** (from the lower border of the cricoid cartilage to the thoracic inlet, 15-18 cm. from the upper incisor teeth)
- (b) The **upper thoracic** (from the thoracic inlet to the level of the carina at approximately 24 cm.)
- (c) The **middle thoracic** (from the carina to half the distance to the EGJ, or approximately 32 cm.)
- (d) The **lower** (to the EGJ at approximately 40 cm.)

The TNM classification

- (a) **“T”** (depth of invasion of the primary tumor).
- (b) **“N”** (regional lymph involvement).
- (c) **“M”** (presence or absence of distant metastases).

PRIMARY TUMORS (T)

- **T_x** Primary tumor cannot be assessed (cytologically positive tumor not evident endoscopically or radiographically)
- **T₀** No evidence of primary tumor (e.g., after treatment with radiation and chemotherapy)
- **T_{is}** Carcinoma in situ
- **T₁** Tumor invades lamina propria or submucosa, but not beyond it
- **T₂** Tumor invades muscularis propria
- **T₃** Tumor invades adventitia
- **T₄** Tumor invades adjacent structures (e.g., aorta, tracheobronchial tree, vertebral bodies, pericardium)

REGIONAL LYMPH NODES (N)

- **Nx** Regional nodes cannot be assessed
- **N0** No regional node metastasis
- **N1** Regional node metastasis

DISTANT METASTASIS (M)

- **M0** No metastasis
- **M1** Distal metastasis

STAGE GROUPING

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage IIA	T2 T3	N0 N0	M0 M0
Stage IIB	T1 T2	N1 N1	M0 M0
Stage III	T3 T4	N1 Any N	M0 M0
Stage IV	Any T	Any N	M1

- Regional lymph nodes for tumors of the **cervical esophagus** are cervical and supraclavicular nodes; those for the **thoracic esophagus** are the mediastinal and perigastric nodes along the lesser curvature, fundus, and left gastric artery.
- The TNM categories are grouped into stages, which have been shown to reflect the prognosis of the tumors, the 5-year survival for Stage I Ca being approximately **60%** while that for Stage IV disease is **<5%**.

TREATMENT

- Local tumor invasion or distant metastatic disease precludes cure.
- Esophageal Ca is almost uniformly a systemic disease when it is diagnosed; and local therapy (radiation or operation) is simply unable to eradicate this malignancy.
- The 5-year survival rate in Western countries from esophageal Ca treated by either radiation or surgery is generally < 10%; more than 80% of the patients die within 1 year of diagnosis. Consequently, until very recently, the primary aim of therapy for esophageal carcinoma has been palliation (restoring the patient's ability to swallow).
- Esophageal Ca is notorious for its ability to spread in the submucosal lymphatics well beyond the gross extent of the tumor, and the maximum proximal and distal margins of resection beyond gross tumor are therefore desirable to minimize the possibility of recurrent tumor at the anastomotic suture line.

SURGERY

- **Resection** provides the best palliation for most patients with localized carcinoma.
- **Esophageal resection and reconstruction** remain **formidable** operations in patients whose nutritional and pulmonary status have been compromised by impaired swallowing.

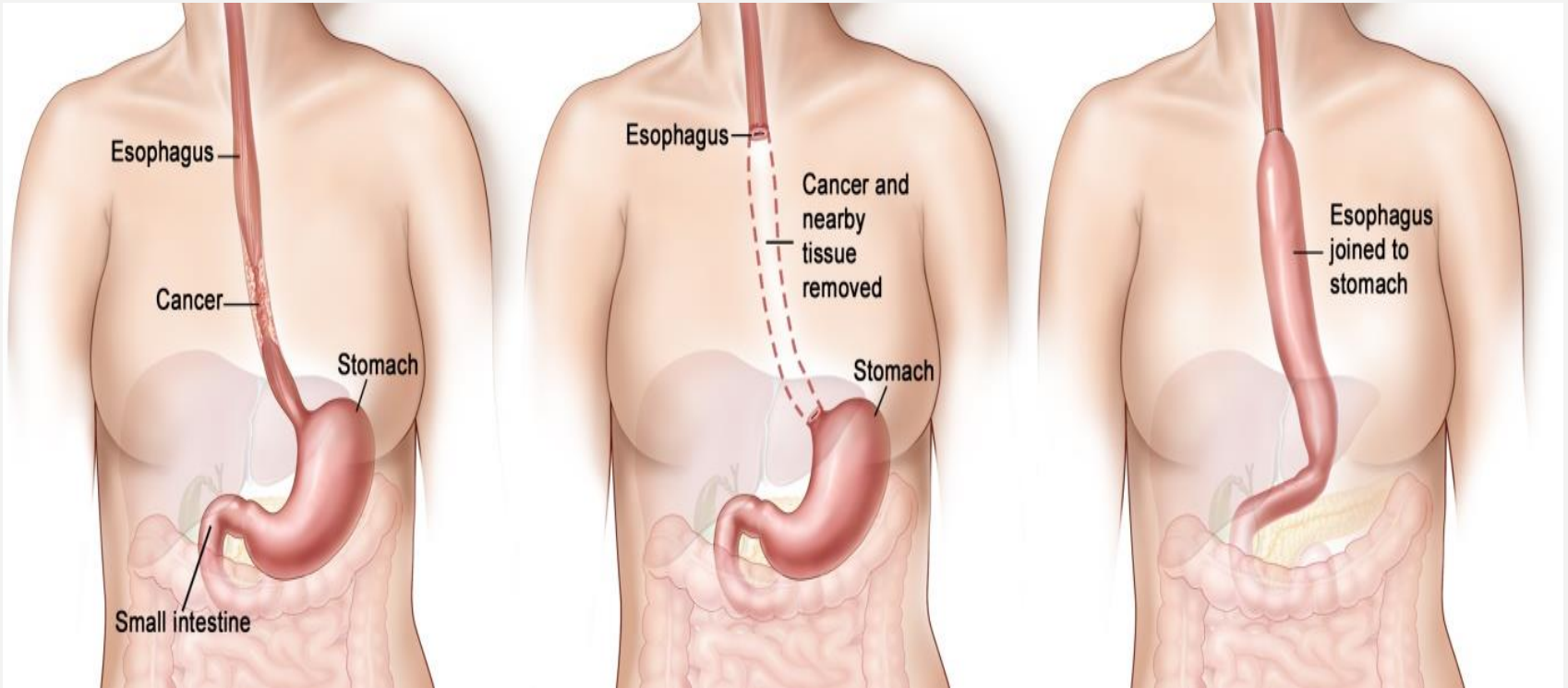
SURGERY

Left thoracoabdominal incision. Is the approach to distal esophageal Ca. The distal esophagus, proximal stomach, and adjacent lymph node-bearing tissues are resected, and an intrathoracic esophagogastric anastomosis is performed.

IVOR-LEWIS esophagectomy. Is the approach for higher thoracic esophageal tumors. A high intrathoracic esophagogastric anastomosis is performed. In either case, a gastric drainage procedure (pyloromyotomy or pyloroplasty) is recommended to prevent subsequent postvagotomy gastric outlet obstruction due to pylorospasm.

Transhiatal esophagectomy without thoracotomy (limited exposure of the intrathoracic esophagus and its blood supply and the risk of hemorrhage and the inability to carry out a complete mediastinal lymph node dissection).

laryngopharyngoesophagectomy. For treatment of Ca involving the cervicothoracic esophagus (and frequently the larynx).



CHEMOTHERAPY

- No data proving that chemotherapy alone provides improved survival or palliation. Partial response, not long-term remission, is the rule
 - **Single-agent chemotherapy** used to treat many patients with esophageal Ca who present with distant disease, with **cisplatin**, **mitomycin**, and **5-fluorouracil** achieving reported response rates of 35%.
 - **Combination chemotherapy** regimens such as **cisplatin**, **bleomycin**, and **vindesine** or **methotrexate**; cisplatin, mitoguanzone, and vindesine or vinblastine; and cisplatin and 5-fu used for metastatic or unresectable esophageal Ca, with reported response rates of 11-55% for 3-9 months.
 - Combination chemotherapy has been used **preoperatively** in a combined modality approach to esophageal Ca in hopes of controlling occult metastatic disease and improving the resectability rate.

RADIATION THERAPY

- Although squamous cell Ca is **radiosensitive**, as a single modality of treatment seldom achieves cure. Radiation therapy is used in the treatment of esophageal carcinoma with one of three theoretical objectives: **palliation**, **cure**, or as an **adjunct** to esophagectomy
 - (a) **Palliative course of radiation.** One half of patients with advanced Ca and severe dysphagia are able to swallow sufficiently after receiving a palliative course of radiation (4000-5000 cGy over a 3-4 weeks).
 - (b) **Supervoltage radiation therapy.** Delivers larger doses (5000 to 7000 cGy) over a 5-7 weeks with **curative intent**. The 5-year survival ranges only from 3-9%. Either the local is not controlled by radiation or a stricture is left in its place; or continued progression of tumor outside the field of irradiation causes the patient's death.

MULTIMODALITY THERAPY

Because most patients have systemic or locally invasive disease that precludes cure, there is efforts to improve survival with multimodality therapy. Experience with combined **preoperative radiation therapy and chemotherapy**, as well as **preoperative chemotherapy and postoperative adjuvant radiation**, are encouraging. This therapy provide better local-regional control of the tumor than can be achieved by radical resection of the esophagus alone

TRANSORAL INTUBATION

- Transoral intubation of esophageal Ca, using a variety of tubes (Souttar, Mackler, Mousseau, Fell, and Celestin) and the Wilson-Cook and **self-expanding stents**, have been used to provide palliation.
- Esophageal intubation carries an overall reported mortality that ranges from 3-15% and a complication rate of 20%, largely the result of **perforation** of the esophagus, **migration** of the tubes, or **obstruction** of the tubes by food or tumor overgrowth.

OTHER MODALITIES

- **Endoscopic laser therapy:** improves dysphagia, but multiple treatments are required and long-term benefit is seldom achieved.
- **Palliative internal bypass:** Bypass of unresectable Ca with **colonic interposition, gastric tubes** or **retrosternal gastric bypass** as a method of palliation. These procedures are of considerable magnitude and carry a high mortality rate and survival in these patients' averages < 6 months.

PREOPERATIVE PREPARATION FOR ESOPHAGECTOMY

- **Pulmonary physiotherapy.**
- **Abstinence from cigarette smoking** and use of an incentive spirometer.
- **Antibiotics** for associated pneumonitis may be required.
- **Nutritional build-up.**
- **Oral hygiene**
- **Barium enema** should be done, if there is a history of prior gastric operations that may preclude the use of the entire stomach as an esophageal substitute, to assess the suitability of the colon for esophageal replacement. **The colon should be prepared in the event that a colonic interposition is required.**