RECENT ADVANCES IN MANAGMENT OF CANCER ESOPHAGUS

Essay

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LIST OF ABBREVIATIONS

ACA	Esophageal Adenocarcinoma
AJCC	American Joint Committee of Cancer
BE	Barrett's esophagus
BMI	Body mass index
COX-٢	Cyclooxygenase- ٢
EGF	Epidermal growth factor
EGF-R	Epidermal growth factor receptor
EMR	Endoscopic mucosal resection
EUS	Endoscopic ultrasonography
FDG	Fluorodeoxyglucose
FNA	Fine needle aspiration
GERD	Gastro esophageal reflux disease
HPV	Human papilloma virus
MRI	Magnetic Resonance Imaging
NSAIDs	Nonsteroidal anti-inflammatory agents
PDT	Photodynamic therapy
PET	Positron Emission Topography
PLE	Pharyngo-laryngo-esophagectomy
RR	Relative risk
SCC	Squamous cell carcinoma
SCC-RA	Squamous cell carcinoma-related antigen
SEMS	Self-expanding metallic stents
TGF	Transforming growth factor
VATS	Video-Assisted Thoracic Surgery
RTOG	Radiation Therapy Oncology Group
FFCD	Federation Francophone de Cancerologie Digestive
MRC	Medical Research Council

INTRODUCTION

Esophageal cancer is one of the most lethal human solid malignancies. In contrast, early-stage esophageal cancer is a highly curable tumour although it is relatively uncommon, comprising less than ١٠% of patients in most published surgical series (**Griffin and Raime,** ٢٠٠٥).

Approximately ٤٠٠٠٠٠ new cases of esophageal cancer occur each year, and esophageal cancer is the sixth leading cause of cancer death worldwide (**Pisani et al.,** ١٩٩٩).

In the United States, the overall incidence is approximately ٣–٤ per ١٠٠٠٠٠, with a steady decline over the past ٢٥ years (**Vizcaino et al.,** ٢٠٠٢).

But in Africa, cancer esophagus is more prevalent and is the sixth most common cause of cancer in adult males (**Nasser et al.,** ١٩٩٦).

More than ٩٠% of esophageal cancer is squamous cell carcinoma (SCC) or adenocarcinoma (ACA); despite their histologic differences, the clinical presentation, testing leading to diagnosis, and treatment of esophageal SCC and ACA are similar (**Vizcaino et al.,** ٢٠٠٢).

Chronic inflammation, epithelial hyperplasia, and stasis of food may contribute to malignant transformation. The interval between the onset of symptoms of achalasia and the development of cancer is approximately ١٥-٢٠ years (**Mark et al.,** ٢٠٠٠).

The annual incidence of ACA in patients with Barrett's esophagus is ٠.٥–٠.٨%, a ٣٠–٦٠ fold increase over that in the general population (**Lagergren et al.,** ١٩٩٩).

Most patients with esophageal cancer do not develop symptoms until the tumor is large enough to cause mechanical obstruction. Although patients presenting with dysphagia may undergo barium esophagography, it is now more common to perform endoscopy, with tissue biopsy and, if appropriate, treated (**Jacobson et al.,** ٢٠٠٣).

Chromoendoscopy, the endoscopic evaluation of mucosa after application of a dye, can be used to highlight neoplastic tissue that is not visible to the naked eye (**Dawsey et al.,** ١٩٩٣).

Computed tomography (CT) of the chest and abdomen with intravenous contrast is recommended to detect metastatic disease as well as endoscopic ultrasonography (EUS) for local invasion and regional lymph nodes (**Romagnuolo et al.,** ٢٠٠٢).

The treatment of esophageal cancer is dependent on the stage of disease. Unfortunately, esophageal cancer is rarely detected in the early stages and over half of patients have irresectable disease at the time of diagnosis. The overall ٥ years survival rate is ١٣% (**Ajani et al.,** ٢٠٠٣).

Usually the choice of operative approaches for management of cancer esophagus depends on four factors (١) surgical intent (curative/ palliative), (٢) anatomic location of the cancer (cervical or upper, middle and lower thoracic), (٣) the preferred method of esophageal replacement and reconstruction, (٤) line of management either surgery alone or multidisciplinary methods (surgery with chemotherapy and or radiotherapy) (**Ajani et al.,** ٢٠٠٣).

Aim of the work

Evaluation of new techniques and updates in management of esophageal carcinoma.

CHAPTER ١:

Anatomy

ANATOMY OF THE ESOPHAGUS

The esophagus is a muscular tube about ٢٥ cm (١٠ in) long, connecting the pharynx to the stomach. It begins in the neck, level with the lower border of the cricoid cartilage and the sixth cervical vertebra; descending largely anterior to the vertebral column through the superior and posterior mediastina. It traverses the diaphragm, level with the tenth thoracic vertebra, and ends at the gastric cardiac orifice level with the eleventh thoracic vertebra (**Orringer et al.,** ١٩٩٩).

Generally vertical in its course, it has two shallow curves. At its beginning it is median but inclines to the left as far as the root of the neck, gradually returns to the median plane near the fifth thoracic vertebra, and at the seventh deviates left again, finally turning anterior to traverse the diaphragm at the tenth. The tube also bends in an antero-posterior plane to follow the cervical and thoracic curvatures of the vertebral column (**Orringer et al.,** ١٩٩٩). It is the narrowest part of the alimentary tract, except for the vermiform appendix (**Bannister,** ١٩٩٩).

Parts:-

It is arbitrarily divided into four segments :(١) pharyngesophageal, (٢) cervical, (٣) thoracic, and (٤) abdominal (**Orringer et al.,** ١٩٩٩).

(١) The pharyngesophageal segment:

The pharyngeal musculature includes the superior, middle, and inferior constrictors, as well as the stylopharyngeus muscles. The inferior pharyngeal constrictor, or thyropharyngeus muscle, passes obliquely and superiorly from its origin on the thyroid cartilage to its posterior insertion in the median raphe (**Orringer et al.,** ١٩٩٩).

The esophageal introitus (*the cricopharyngeus muscle or upper esophageal sphincter*) is the most inferior portion of the inferior pharyngeal constrictor and is clearly identifiable by the transverse direction of its fibers. The transition between the oblique fibers of the thyropharyngeus muscle and the transverse fibers of the cricopharyngeus muscle creates a point of potential weakness in the pharyngoesophageal segment, which is the site of origin of a pharyngoesophageal (***Zenker's***) diverticulum as well as a common site of perforation during esophagoscopy. The cricopharyngeal sphincter is unique to the gastrointestinal tract because it does not consist of a circular ring of muscle but rather a bow of muscle connecting the two lateral borders of the cricoid cartilage (**Orringer et al.,** ١٩٩٩).

(٢) Cervical esophagus

The cricopharyngeus muscle fibers blend into the longitudinal and circular muscle of the muscle of the cervical esophagus, a ٥- to ٦-cm. long segment that extends to the beginning of the first thoracic vertebra. Although the cervical esophagus is a midline structure positioned posteriorly to the trachea, it tends to course more to the left of the trachea. It is attached to it by loose connective tissue; the recurrent laryngeal nerves ascend on each side in or near the groove between the trachea and the esophagus; posterior are the vertebral column, longus colli and prevertebral layer of deep cervical fascia; lateral on each side are the common carotid artery and posterior part of the thyroid gland. In the lower neck, where the esophagus deviates left, it is closer to the left carotid sheath and thyroid gland than it is on the right. The thoracic duct ascends for a short distance along its left side ***(Patti et al., ١٩٩٧)***.

(٣)Thoracic Part

At first situated a little to the left in the superior mediastinum between the trachea and the vertebral column, this passes behind and to the right of the aortic arch to descend in the posterior mediastinum along the right side of the descending thoracic aorta. Below, as it inclines left, it crosses anterior to the aorta to enter the abdomen through the diaphragm at the level of the tenth thoracic vertebra (**Peter,** ١٩٩٩).

Anterior (from above downwards) are: the trachea, right pulmonary artery, left principal bronchus, pericardium (separating it from the left atrium) and the diaphragm; posterior are the vertebral column, longus colli muscles, right posterior (aortic) intercostal arteries, thoracic duct, azygos vein and the terminal parts of the hemiazygos and accessory hemiazygos veins and, near the diaphragm, the aorta. In the posterior mediastinum there is a long recess of the right pleural sac between the esophagus in front and the vena azygos and vertebral column behind (**Peter,** ١٩٩٩).

Left lateral, in the superior mediastinum, are the terminal part of the aortic arch, the left subclavian artery, thoracic duct, the left pleura and the recurrent laryngeal nerve which ascends in or near the groove between the esophagus and trachea. In the posterior mediastinum the esophagus is related to the descending thoracic aorta and left pleura. Right lateral it is related to the right pleura, with the azygos vein intervening as it arches forwards above the right principal bronchus to join the superior vena cava. Below the pulmonary roots the vagus nerves descend in contact with the esophagus, the right chiefly behind and the left in front, uniting to form an esophageal plexus around it. Low in the posterior mediastinum the thoracic duct is behind and to the right; higher, it is posterior, crossing to the left at

about the level of the fifth thoracic vertebra and then ascending on the left. On the right of the esophagus, just above the diaphragm, a small serous infracardiac bursa may occur, representing the detached apex of the right pneumato-enteric recess (**Thomas and Tom,** ١٩٩٦).

The diaphragmatic esophageal hiatus is a sling of muscle fibers that arise from the right crus in approximately ٤٥% of patients. At times, however, both the left and right crura contribute to the hiatus (**Thomas and Tom,** ١٩٩٦).

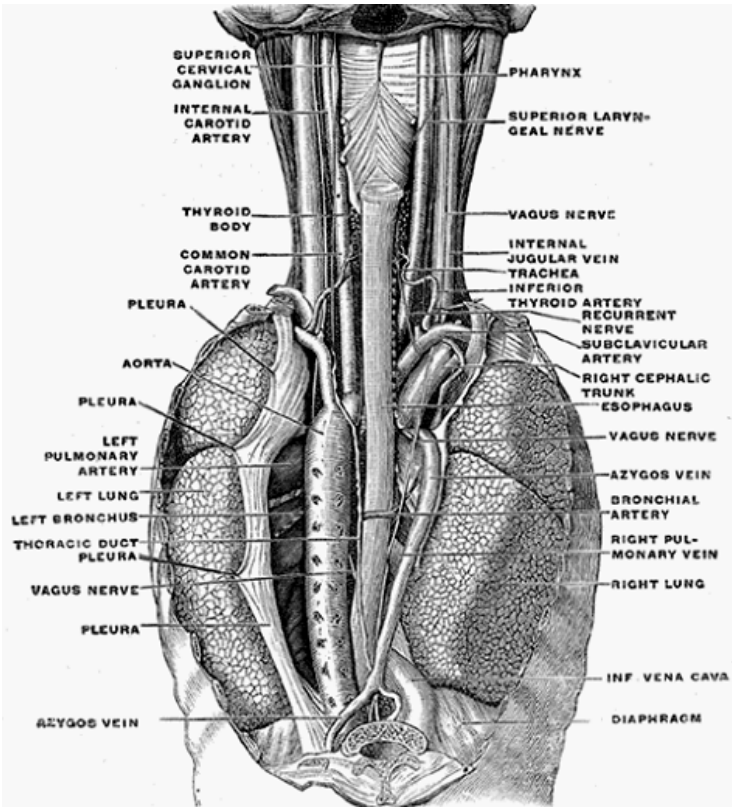

Figure: ١ the position and relation of the esophagus in the cervical region and in the posterior mediastinum. Seen from behind (**Poirier and Charpy,** ٢٠٠٥)

(٤)Abdominal Part

This emerges from the right diaphragmatic crus, slightly left of the midline and level with the tenth thoracic vertebra, grooving the posterior surface of the left lobe of the liver. It forms a truncated cone, about ١ cm long, curving sharply left, its base continuous with the cardiac orifice of the stomach; its right side continues smoothly into the lesser curvature, while the left is separated from the gastric fundus by the cardiac notch. Covered by peritoneum on its front and left side, it is contained in the upper left part of the lesser omentum; the peritoneum reflected from its posterior surface to the diaphragm is part of the gastrophrenic ligament, through which esophageal branches of the left gastric vessels reach it. Posterior are the left crus and left inferior phrenic artery. The relations of the vagus nerves vary as the esophagus traverses the diaphragm. Usually the left vagus is composed of two or three trunks firmly applied to the anterior aspect of the esophagus; the right vagus is usually single, a thick cord some distance from the posterior aspect of the esophagus (**Liebermann-Meffert and Duranceau,** ١٩٩١).

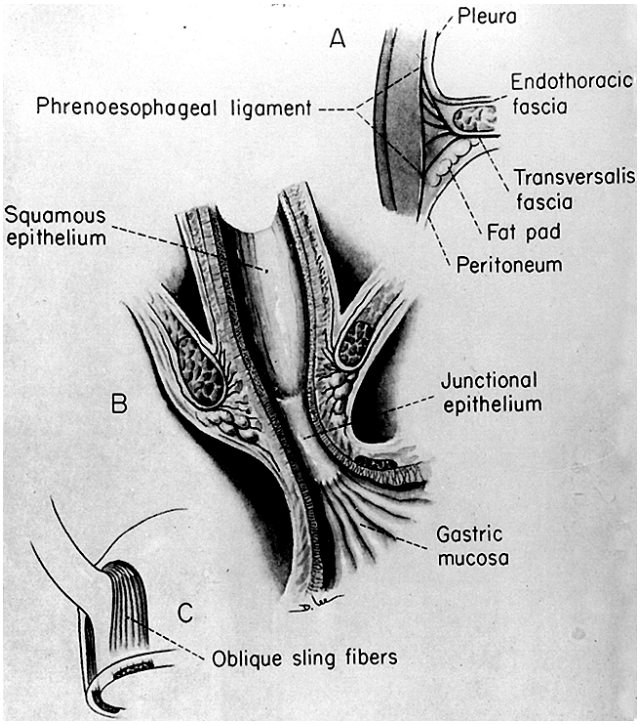

Figure ٢ Gross anatomy of the esophagogastric junction area. *A*, Details of origin and insertion of phrenoesophageal membrane or ligament. *B*, Cross-section of distal esophagus and proximal stomach. *C*, Oblique gastric sling fibers (**Courtney et al.,** ٢٠٠٤).

The precise location of the esophagogastric junction is a matter of considerable controversy, because this area has been defined in at least three different ways: (١) the junction of esophageal squamous and gastric columnar epithelium; (٢) the point at which the tubular esophagus joins the gastric pouch; and (٣) the junction of the esophageal circular muscle layer with the oblique sling fibers of the stomach (the loop of Willis or the collar of ***Helvetius***). Each definition has its merit as well as its shortcomings. Clinically, however, the squamocolumnar epithelial junction (the ora serrata or Z-line), as identified endoscopically, is the most practical definition of the gastro esophageal junction, provided that the patient does not have a columnar-lined lower esophagus (**Orringer et al.,** ١٩٩٩).

Sphincters of the esophagus

There is anatomical sphincter at the upper end of the esophagus and a physiological sphincter at the lower end of the esophagus (**Deker and Du Plessis,** ١٩٩٦).

Anatomy of Upper Esophageal Sphincter

The opening of esophagus is collared by cricopharyngeal muscle (inferior constrictor of the pharynx) this muscle of two parts a lower transverse part (cricopharyngeus) and upper oblique part (thyrophanyngeus) the lower transverse fibers arise from the cricoid cartilage and pass horizontally backward around pharynx to be inserted to the median raphe at the back of this tube . Its function is to prevent regurgitation of the esophageal contents into the pharynx. The upper oblique fibers arise from cricoid and thyroid cartilage and encircle the hypopharynx ending in the median raphe. In the act of swallowing the upper oblique part of this muscle propels the content downwards and the lower transverse part relaxes to allow the content to pass into the esophagus (**Deker and Du Plessis,** ١٩٩٦).

Anatomy of Lower Esophageal Sphincter

Radiological studies show that swallowed food stops momentarily in the gastric end of the esophagus, before entering the stomach suggesting the presence of a sphincter at this point. In the past there was much controversy about the reason for this behaviour, since only slight thickening of the muscle coat has been found in humans. There is now ample physiological and clinical evidence that closure depends on two major mechanisms operating at the lower end of the esophagus (**Bannister,** ١٩٩٩).