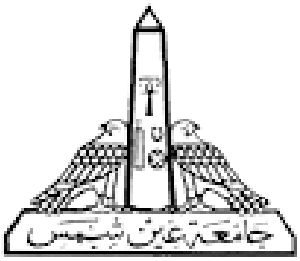

Recent Trends in Management of Esophageal Carcinoma

An Essay

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Contents

List of Figures

List of Tables

List of Abbreviations

AJCC	American Joint Committee on Cancer
AMPK	AMP activated protein kinase
BMI	Body mass index
CDDP	Cis-diamminedichloroplatinum
CDKs	Cyclin-dependent kinases
CDKI	Cyclin-dependent kinases Inhibitors
CGR	Cell growth ratio
CPT1	Carnitine Opalmitoyltransferase-1
EAC	Esophageal adenocarcinoma
EEMR-T	Endoscopic esophageal mucosal resection tube
EGFR	Epidermal growth factor receptor
EMR	Endoscopic mucosal resection
EMR-C	Endoscopic mucosal resection cap
ESCC	Esophageal squamous cell carcinoma
ESD	Endoscopic submucosal dissection
FAS	Fatty acid synthase
FDG	Fluorodeoxyglucose
FFCD	Fédération Francophone de Cancérologie Digestive
FREGAT	French Eso-Gastric Tumors
GERD	gastro-esophageal reflux disease
HER2	Human epidermal growth factor receptor 2
HGD	High-grade dysplasia
HGF	Hepatocyte growth factor
HNSCC	Head and neck cancer squamous cell cancers
HPV	Human papillomavirus
ICC	Interstitial cells of Cajal
KRAS	Kirsten rat sarcoma viral oncogene homolog

LES	lower esophageal sphincter
MECC	Middle East Cancer Consortium
MIE	Minimally invasive esophagectomy
MTORC1	Mammalian target of rapamycin complex 1
NBI	Narrow-band imaging
NCI	National Cancer Institute
NSAIDs	Nonsteroidal anti-inflammatory drugs
PAR	Population attributable risk
PCNA	Proliferating cell nuclear antigen
PPI	Proton pump inhibitor
RCT	Radio-chemotherapy
RFA	Radiofrequency ablation
RTK	Receptor tyrosine kinase
SCC	Squamous Cell Carcinoma
SLPI	Secretory leukoprotease inhibitor
SRC	Signet ring cell
THE	Trans-hiatal esophagectomy
TKIs	Tyrosine kinase inhibitors
TTE	Trans-thoracic esophagectomy
TTS	Through-the-scope
UES	Upper esophageal sphincter
UICC	The International Union Against Cancer
VEGF	Vascular endothelial growth factor

Introduction

Esophageal cancer is the eighth most common cause of cancer death worldwide, and it is one of the least studied and deadliest cancers worldwide because of its extremely aggressive nature and poor survival rate. The overall 5-year relative survival is 17%, Reason to explain this poor outcome stands on the fact that esophageal cancer is diagnosed at rather late stage. ***(Jemal et al; 2011)***

There are two main histological types: squamous cell carcinoma and adenocarcinoma, Worldwide, squamous cell carcinoma is the predominant histological type. Adenocarcinoma is mainly a disease of developed countries as squamous cell carcinoma accounted for more than a quarter (28%) of all esophageal cancer cases, while Adenocarcinoma accounted for more than half (55%) especially in Europe. ***(Cook et al; 2009)***

Tobacco use increases the risk of both squamous cell carcinoma and Adenocarcinoma. Squamous cell carcinomais also strongly linked with alcohol consumption, while Adenocarcinoma is linked with excess body weight, and long-term acid reflux (which can lead to the pre-cancerous condition Barrett's esophagus). ***(Zhang, 2013)***

Esophageal cancer is generally associated with poor outcomes. However, over the last decades the treatment algorithms have changed considerably shifting from single mode treatments to complex multimodal approaches. ***(Chak et al; 2012)***

An esophagectomy has long been a mainstay treatment for esophageal cancer. However, the prognosis of patients with esophageal cancer remains extremely poor even after a "curative" esophagectomy. The results for an esophagectomy of esophageal cancer still remain unsatisfactory. ***(Berger and Belka, 2009)***

To improve this dismal situation, great endeavors to establish better curative resection procedures have been made by esophageal surgeons over the last two decades. An extensive esophagectomy is highly invasive and places a great operative burden on patients with esophageal cancer, who are frequently compromised by poor nutrition. ***(Wolf et al; 2011)***

Therefore, minimally invasive surgery using thoracoscopy and laparoscopy has been recently introduced into the field of esophageal cancer surgery, and are associated with equivalent functional results compared with open procedures. ***(Sihag et al; 2012)***

The application of minimally invasive surgery has been explored and found to be feasible in the management of esophageal cancer, as these techniques offer the potential advantages of its safety, efficacy, oncologic value, enhanced recovery, a reduction in pain, a quicker return to normal function, and other advantages that justify longer operative times and higher costs. ***(Barreto and Posner, 2010)***

Furthermore, recent improvements in chemo-radiotherapy using potent anti cancer agents for esophageal cancer have led surgeons to reevaluate an esophagectomy as the treatment of choice for this disease. ***(Sjoquist et al; 2011)***

Recently, the development of gene therapy systems as new treatment or prevention strategies for various malignant diseases has been explored, Based on the genetic background of esophageal cancer, several molecular therapies have been developed, p53 abnormalities are observed in 40–60% of patients with esophageal cancer, even in an early precancerous lesion.Indeed, p53 genetic alteration is a good predictor for treatment responses and survival in esophageal cancer. ***(Ribeiro et al; 1998)***

Therefore, the current standard for patients with locally advanced esophageal cancer who receive neo adjuvant chemo-radiation is esophagectomy, and the minimally invasive approach may be offered to these patients without compromising surgical or oncologic outcomes. ***(Merritt et al; 2011)***

Aim of the Work

The aim of this work is to illustrate the recent trends in diagnosis and management of esophageal carcinoma, and recent guidelines.

Embryology and surgical anatomy of the Esophagus

The oesophagus is a muscular tube connecting the pharynx to the stomach and measuring 25-30 cm in the adult. Its primary function is as a conduit for the passage of swallowed food and fluid, which it propels by ante-grade peristaltic contraction. It also serves to prevent the reflux of gastric contents whilst allowing regurgitation, vomiting and belching to take place. It is aided in these functions by the upper and lower esophageal sphincters sited at its proximal and distal ends. Any impairment of esophageal function can lead to the debilitating symptoms of dysphagia, gastro-oesophageal reflux or oesophageal pain. ***(Muller et al; 1990)***

The apparently simple basic structure of the esophagus belies both physiological importance and the dangers associated with surgical intervention. As a consequence of its location deep within the thorax and abdomen, a close anatomical relationship to major structures throughout its course and a marginal blood supply, the surgical exposure, resection and reconstruction of the esophagus are complex. Despite advances in peri-operative care, oesophagectomy is still associated with the highest mortality of any routinely performed elective surgical procedure. ***(Griffin and Raimes, 2001)***

Embryological development Of The Esophagus

The first stages of life are divided into the embryonic and fetal periods. The embryonic period extends from fertilization to week 9. The fetal period lasts from the end of the week 9 to birth. From days 0 to 14, the human embryo develops into a bilaminar disk of ectoderm and endoderm, with the endoderm forming the lining of the yolk sac. The endoderm is the scaffold for the future digestive tract. The ectoderm gives rise to epidermis and neural plates. Through the neurulation process, the neural plates evolve to neural tube and neural crest cells. ***(Sherman et al; 2001)***

Mesoderm proliferation and segmentation, which takes place between the endoderm and ectoderm, induces numerous transformations in the endoderm. At the same time, the human embryo elongates cranio-caudally and folds laterally. The dorsal part of the yolk sac, composed of endoderm, is compressed by the lateral folding of the embryo and is incorporated as a rim during the fourth week. Thus the human embryo becomes a "body cylinder" dividing the yolk sac into intra-embryonic and extra-embryonic parts. The intra-embryonic part is the origin of digestive tube and its accessory glands. The extra-embryonic part regresses and disappears around week 12. At this point, the early digestive system divides into foregut, midgut, and hindgut. ***(Kedinger et al; 1988)***