

Contents

Foreword	xi
Ronald F. Martin	
Preface: Surgical Challenges of the Foregut	xiii
Sushanth Reddy	
The Molecular Biologic Basis of Esophageal and Gastric Cancers	403
Arjun Pennathur, Tony E. Godfrey, and James D. Luketich	
<p>Esophageal cancer and gastric cancer are leading causes of cancer-related mortality worldwide. In this article, the authors discuss the molecular biology of esophageal and gastric cancer with a focus on esophageal adenocarcinoma. They review data from The Cancer Genome Atlas project and advances in the molecular stratification and classification of esophageal carcinoma and gastric cancer. They also summarize advances in microRNA, molecular staging, gene expression profiling, tumor microenvironment, and detection of circulating tumor DNA. Finally, the authors summarize some of the implications of understanding the molecular basis of esophageal cancer and future directions in the management of esophageal cancer.</p>	
Multidisciplinary Therapy of Esophageal Cancer	419
Matthew R. Egyud, Jennifer F. Tseng, and Kei Suzuki	
<p>Multimodality therapy is the standard of care for locoregional esophageal cancers (greater than clinical T3 or Np), including Siewert type 1 and 2 gastroesophageal junction tumors. Induction regimen, chemotherapy only or chemoradiation, is an area of controversy and often institution-specific, as neither has shown to be superior. Response to induction therapy is an important prognostic marker. For esophageal squamous cell carcinoma, it may be acceptable to observe clinical complete responders after chemoradiotherapy and perform salvage esophagectomy for recurrent disease. Clinical T2N0 esophageal cancer presents a unique challenge given its inaccuracy in clinical staging; management of this particular subset is controversial.</p>	
Management of Early Stage Gastric and Gastroesophageal Junction Malignancies	439
Feredun S. Azari and Robert E. Roses	
<p>Esophageal and gastric carcinomas are prevalent malignancies worldwide. In contrast to the poor prognosis associated with advanced stages of disease, early stage disease has a favorable prognosis. Early stage gastric cancer (ESGC) is defined as cancer in which the depth of invasion is limited to the submucosal layer of the stomach on histologic examination, regardless of lymph node status. ESGC that meets standard or expanded criteria can be treated via endoscopic mucosal resection and endoscopic submucosal dissection. Similar indications for endoscopic interventions exist for gastroesophageal junction and esophageal malignancies.</p>	

What Is the Best Operation for Proximal Gastric Cancer and Distal Esophageal Cancer?

457

Laura M. Mazer and George A. Poultsides

Cancer of the gastroesophageal junction (GEJ) is increasing in incidence, likely as a result of rising obesity and gastroesophageal reflux disease rates. The tumors that arise here share features of esophageal and gastric cancer, and are classified based on their location in relationship to the GEJ. The definition of the GEJ itself, as well as optimal resection strategy, extent of lymph node dissection, resection margin length, and reconstruction methods are still very much a subject of debate. This article summarizes the available evidence on this topic, and highlights specific areas for further research.

The Difficult Esophageal Conduit

471

Rajat Kumar and Benjamin Wei

A variety of esophageal diseases are treated with esophagectomy, from benign to esophageal cancer. Careful attention must be given to management of the difficult conduit, including patients who have had prior gastric surgery and other procedures, patients with conditions such as diabetic gastroparesis, which can affect the stomach as a future usable conduit, and patients who have an absent or unusable stomach. In these situations, consideration should be raised for the use of alternative conduits, including jejunal and colonic interposition conduits. The esophageal surgeon should also be adept at management of intraoperative difficulties with the conduit.

Combined Modality Therapy for Management of Esophageal Cancer: Current Approach Based on Experiences from East and West

479

Omeed Moaven and Thomas N. Wang

Human evolutionary genetic divergence and distinctive environmental exposures have contributed to the development of clinicopathologic variations of esophageal cancer in Eastern and Western countries. Different treatment strategies have derived from the disparate regional experiences. Treatment strategy is more standardized in the West. Trimodality treatment with neoadjuvant chemoradiation followed by surgery is widely accepted as the standard treatment of locally advanced esophageal adenocarcinoma and esophageal squamous cell carcinoma. Trimodality treatment has not been adopted in many Eastern countries, and standard treatment is neoadjuvant chemotherapy. Several randomized trials are ongoing that may alter the standard management of esophageal cancer worldwide.

Complications After Esophagectomy

501

Igor Wanko Mboumi, Sushanth Reddy and Anne O. Lidor

Esophagectomy is the mainstay for treating esophageal cancers and other pathology. Even with refinements in surgical techniques and the introduction of minimally invasive approaches, the overall morbidity remains formidable. Complications, if not quickly recognized, can lead to significant long-term sequelae and even death. Vigilance with a high degree of suspicion remains the surgeon's greatest ally when caring for a patient who has recently undergone an esophagectomy. In this review, we highlight different

approaches in dealing with anastomotic leaks, chyle leaks, cardiopulmonary complications, and later functional issues after esophagectomy.

Next-generation Sequencing in the Management of Gastric and Esophageal Cancers 511

Jill C. Rubinstein, Norman G. Nicolson, and Nita Ahuja

Next-generation sequencing has enabled genome-wide molecular profiling of gastric and esophageal malignancies at single-nucleotide resolution. The resultant genomic profiles provide information about the specific oncogenic pathways that are the likely driving forces behind tumorigenesis and progression. The abundance of available genomic data has immense potential to redefine management paradigms for these difficult disease processes. The ability to capitalize on the information provided through high-throughput sequencing technologies will define cancer care in the coming decades and could shift the paradigm from current stage-based, organ-specific treatments toward tailored regimens that target the specific culprit pathways driving individual tumors.

Managing Squamous Cell Esophageal Cancer 529

Rishi Batra, Gautam K. Malhotra, Shailender Singh, and Chandrakanth Are

This article reviews the pathophysiology, risk factors, clinical presentation/diagnosis, and management of SCC.

Gastrointestinal Stromal Tumors of the Stomach and Esophagus 543

Lauren Theiss and Carlo M. Contreras

Gastrointestinal stromal tumors (GISTs) arise anywhere along the gastrointestinal tract, most commonly as a result of c-kit or PDGFRA proto-oncogene mutations. Surgical resection is an important component of treatment. However, molecular profiling of GISTs has provided many insights into adjuvant and neoadjuvant therapy options. Imatinib, the most frequently studied medical therapy, has been shown in numerous studies to provide benefit to patients in both the neoadjuvant and adjuvant setting. Interval imaging is an important component of the treatment of GISTs and national surveillance recommendations should be followed.

Palliative Management of Gastric and Esophageal Cancer 555

Alison L. Halpern and Martin D. McCarter

In patients with advanced esophageal or gastric cancer, it is highly likely that palliation of symptoms will become a focus of treatment. Dysphagia and obstruction are the most common complaints, and many of these patients can be treated with endoscopic interventions to alleviate symptoms. Bleeding, perforation, and nutritional issues are common problems. Attempts at palliation should be guided by thoughtful discussions regarding patients' goals of care. Owing to the high morbidity and mortality in patients with limited life expectancy, a strategy of working from the least invasive to the most invasive interventions should be guided by the patient's goals.