Gastro-esophageal Junction Carcinoma

By

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Date-02/12/2017



The first parient to have transheracic exophageomery Notice patient has a rubber tabe as exugingue.

Biology

- The vast majority of esophageal cancers are of two subtypes: esophageal squamous cell cancer (ESCC) and esophageal adenocarcinoma (EAC). ESCC is preceded by squamous dysplasia.
- EAC is preceded by a Barrett esophagus (BE) or an incomplete intestinal metaplasia of the normal squamous epithelium of the esophagus.
- A BE undergoes transition from low-grade and high-grade dysplasia before progressing into EAC.

common and divergent genetic features as manifest by alterations in canonical oncogenes and tumor suppressor genes in somatic cells of tumors

Common Molecular Genetic Alterations Observed in Esophageal and Gastric Cancers

Oncogenes

Epidermal growth factor receptor (EGFR)

Cyclin D1

Tumor Suppressor Genes

P16INK4a

TP53

E-cacherin

p120 catenin

DNA Mismatch Repair Genes (hMLH1, hMSH2)

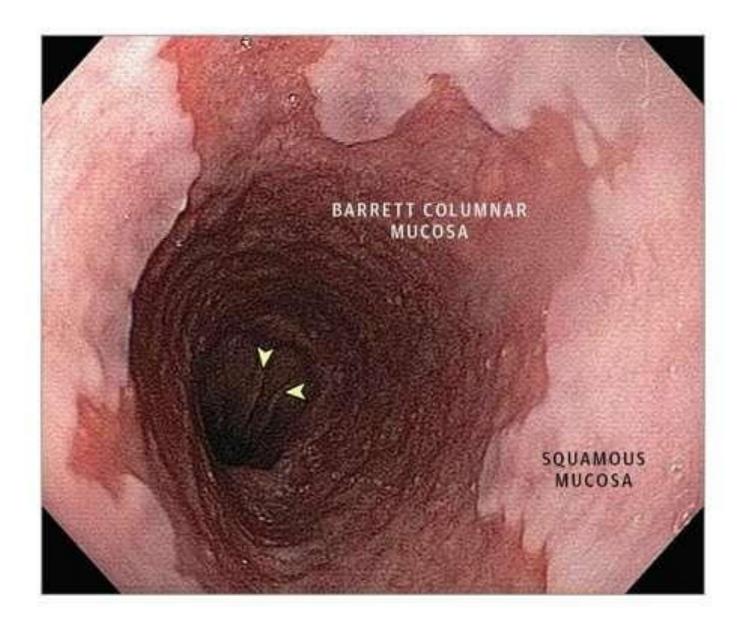
Mismatch repair instability

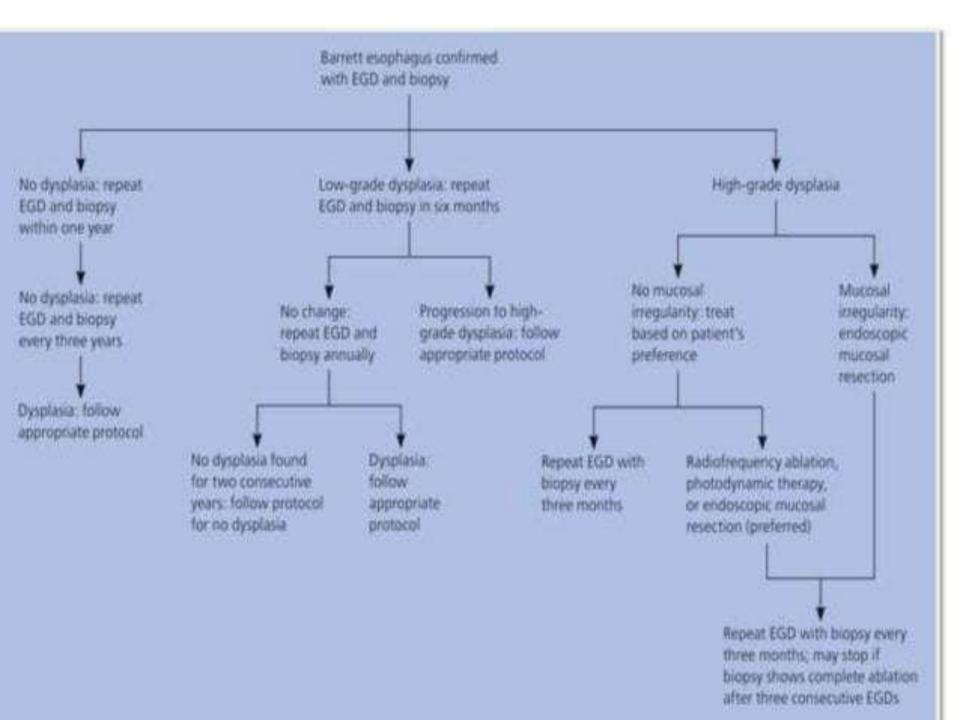
Normal esophagus → Squamous dysplasia → Squamous cell cancer

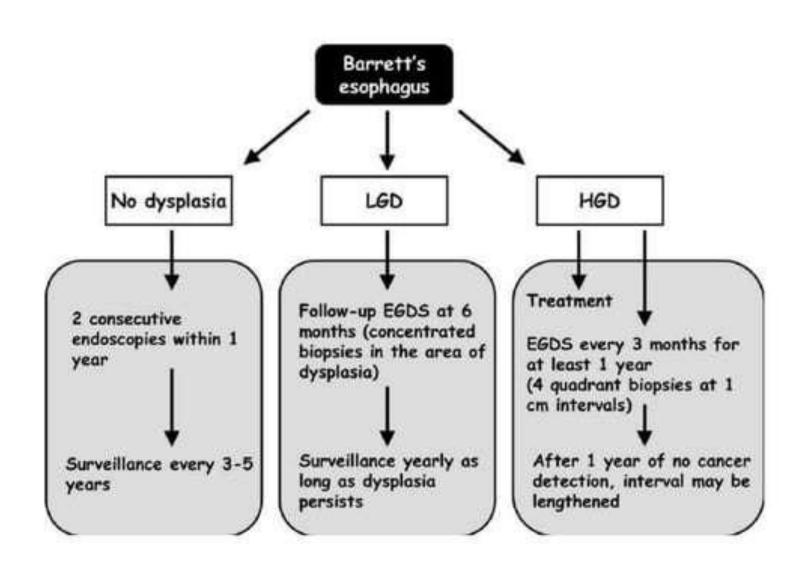
Normal esophagus → Intestinal metaplasia → Low-grade dysplasia → High-grade dysplasia → Adenocarcinoma

- Most adenocarcinomas of the esophagus occur in the area of the cardia and originate in islands of gastrointestinal mucosa, less often in the submucosal glands, and from the histological point of view are usually similar to gastric adenocarcinoma and its various histological patterns. Most tumors are welldifferentiated
- Adenocarcinomas extensively infiltrate the esophageal wall and often show perineural invasion, lymphatic and vascular invasion, and direct extension through the esophageal wall.

 The prognosis of the esogastric junction carcinoma is worsened by the potential two-way route of spread in case of lymph node metastasis: mediastinum and abdomen.

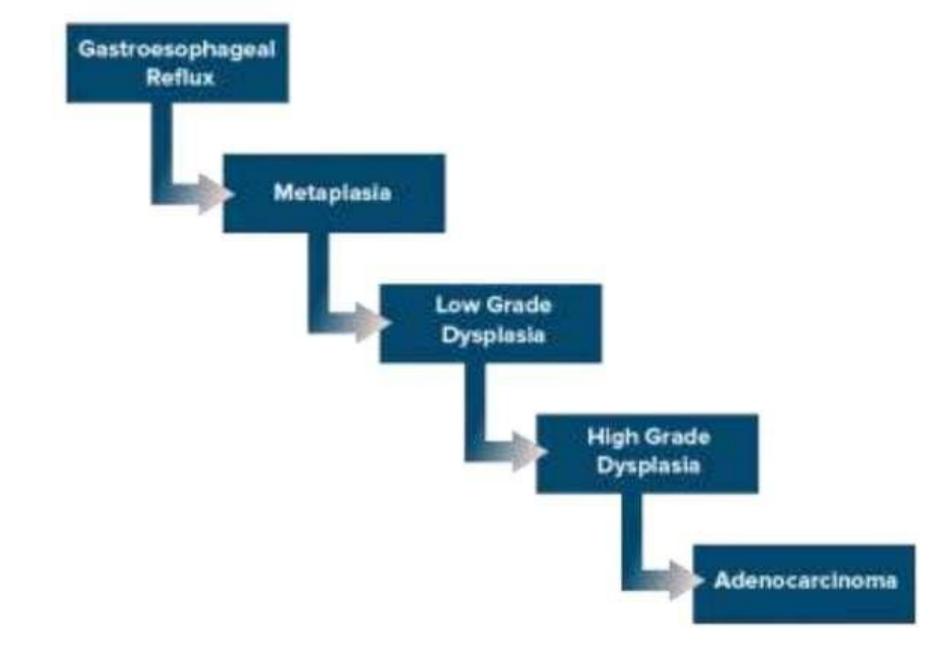






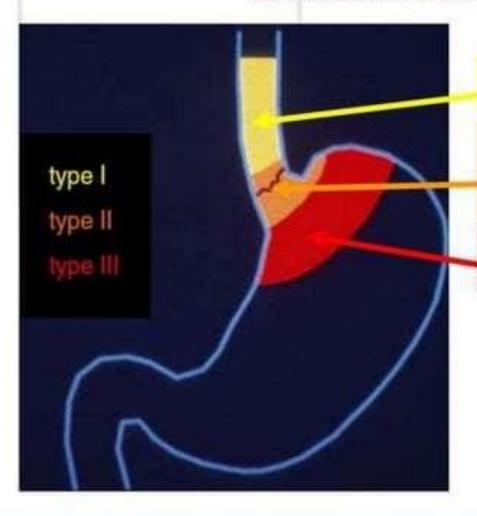
Who Should Be Screened?

 Evidence-based guidelines recommend against routine screening for Barrett esophagus.
 Patients with GERD who have alarm signs should undergo endoscopy. Screening may be considered in patients with multiple risk factors for Barrett esophagus.



Squamous cell carcinoma	Adenocarcinoma Gastro-esophageal reflux disease		
Cigarette smoking			
Alcohol drinking	Barrett's esophagus		
ALDH2 deficiency	Reflux symptoms		
Drinking very hot liquids	Obesity		
Achalasia	Cigarette smoking		
Caustic injury	Diet (high in processed meat, low in fruits, vegetables)		
History of thoracic radiation	History of thoracic radiation		
Tylosis	Anticholinergic agents		
Human papilloma virus infection	Family history		
N-nitrosamines	Helicobacter pylori infection (decreased risk)		

Classification



1cm to 5cm above OGJ

1cm above to 2 cm

below OGJ

2cm to 5cm below OGJ

Presentation

- Dysphagia
- Odynophagia
- Wt loss
- Dyspnea
- Cough
- Hoarseness
- Pain







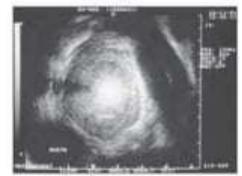


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DIAGNOSIS





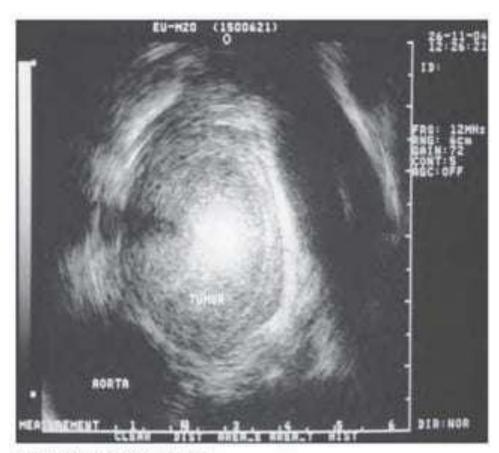


Endoscopic ultrasound examination (EUS)

- Endoscopic ultrasound (EUS) is helpful to determine the proximal and distal extent of the tumour and to assess tumour depth and lymph node status, although it is less useful in antral tumours.
- For clinical T1/T2 disease, EUS is recommended to clarify clinical T stage and to ascertain if preoperative chemotherapy is indicated.

EUS

- Only imaging that can distinguish the layers of the esophageal wall
- T staging 85% accurate
- N staging 75% accurate
 - Up to 2cm from esophagus
- 1/3 non-traversable stricture



Zoner HJ, Ackley SW: Mahpet's Abdomnel Operations, 13th Edition: Mtp://www.essessingerp.com Copyright & The Michael HJ Companies, Inc. All rights reserved.

Less accurate post-therapy

Esophageal Cancer

Endoscopic ultrasonography (EUS)



Unlike CT, EUS allows visualization of the distinct layers within the esophageal wall.

Alternating circumferential layers define:

the mucosal interface (hyperechoic),

the mucosa (hypoechoic),

the submucosa (hyperechoic),

the muscularis propria (hypoechoic),

and the adventitial interface (hyperechoic).

Diagnostic laparoscopy

- Laparoscopy may be useful in select patients in detecting radiographically occult metastatic disease, especially in patients with Siewert II and III tumors.
- Positive peritoneal cytology (performed in the absence of visible peritoneal implants) is associated with poor prognosis and is defined as M1 disease.
- In patients with advanced tumors, clinical T3 or N+ disease should be considered for laparoscopic staging with peritoneal washings.

Imaging

- MRI for T staging and invasion of adjacent structures.
- PET/CT scan can be considered for patients undergoing multimodality curative treatment.
- PET may not be helpful in some patients with mucinous or T1 tumours.
- False negative rates for PET are high in gastric cancer, due to the absence of the GLUT-1 transporter in mucinous and signet ring histologies.

downstatesurgery.org

PET

Detects mets not seen on CT

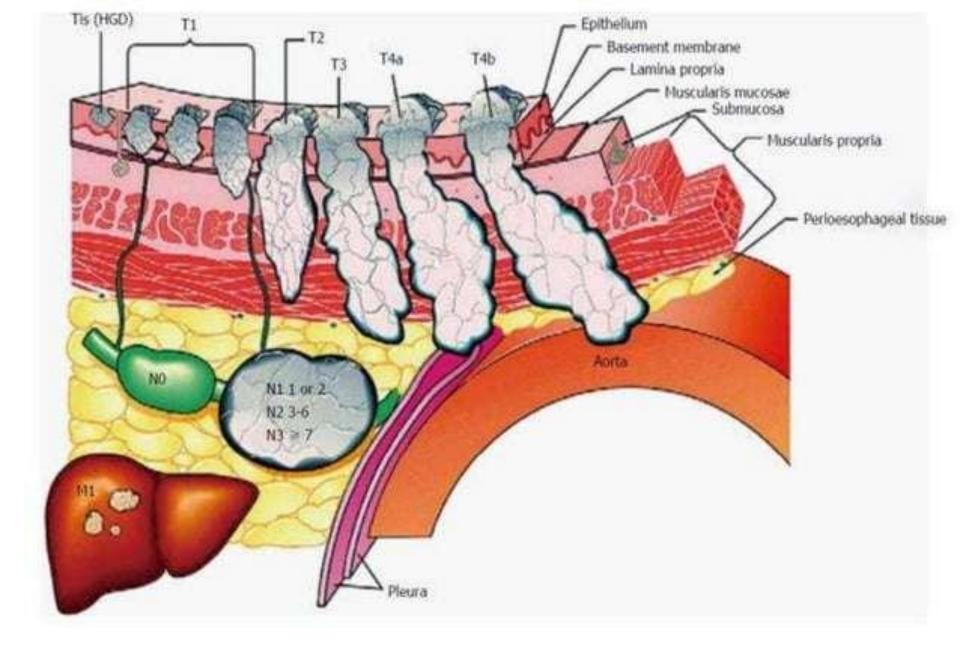
No value in T staging



Zinnar MJ, Ashley IIV: Manget's Abdomina' Operations. 11th Edition: https://www.accesssrargery.com Copyright & The McGraw-Hill Correlation. Inc. All rights reserved.

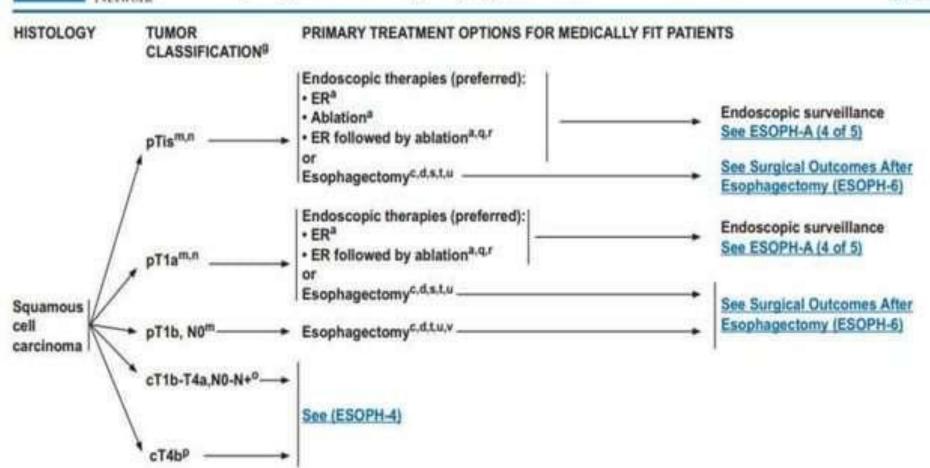
 Better for detecting higher nodes (cervical>thoracic>abdominal)

Assess response to chemoradiation



Cancer Esophageal and Esophagogastric Junction Cancers

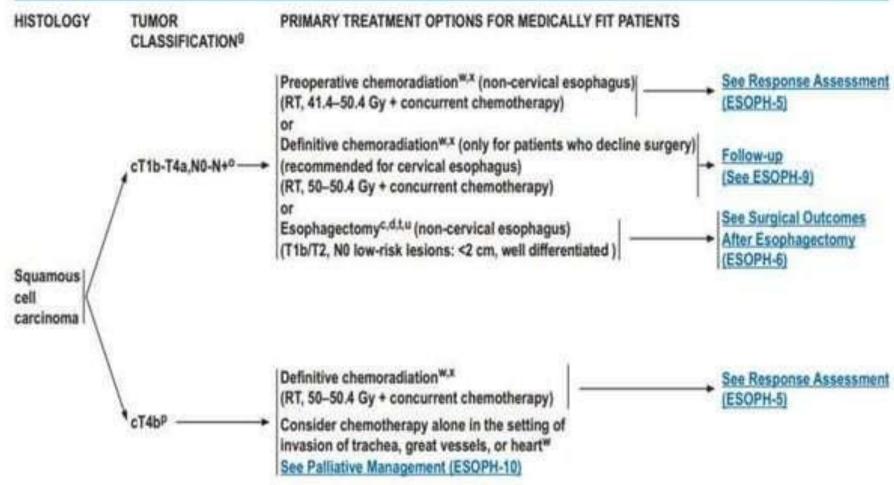
NCCN Guidelines Index Table of Contents Discussion

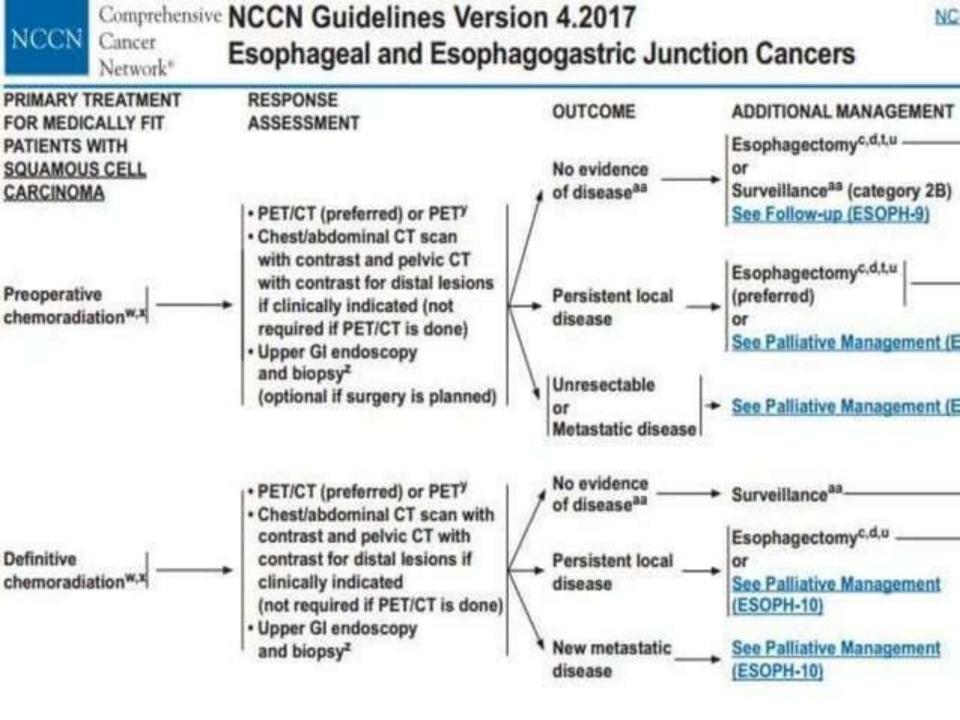




Comprehensive NCCN Guidelines Version 4.2017 Cancer Esophageal and Esophagogastric Junction Cancers

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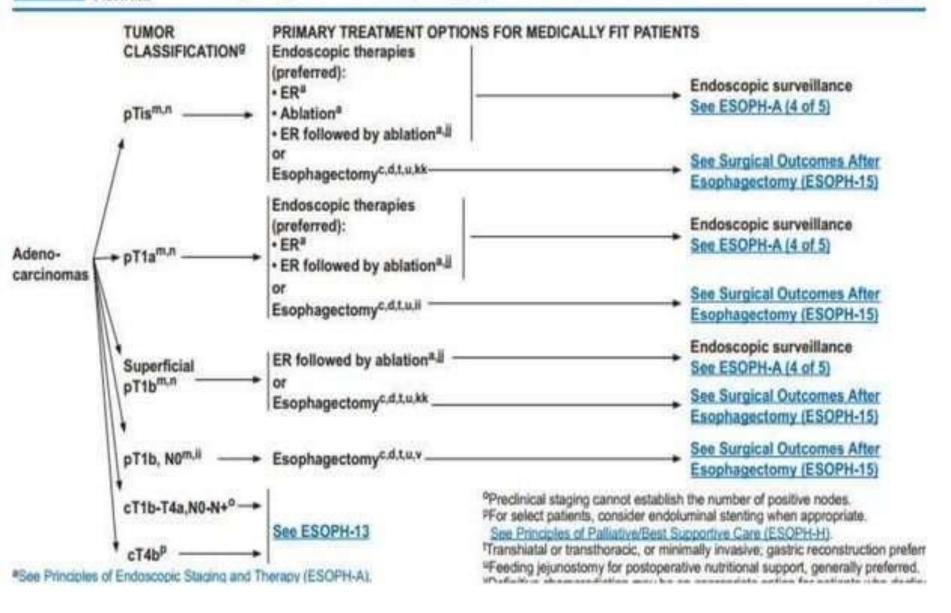






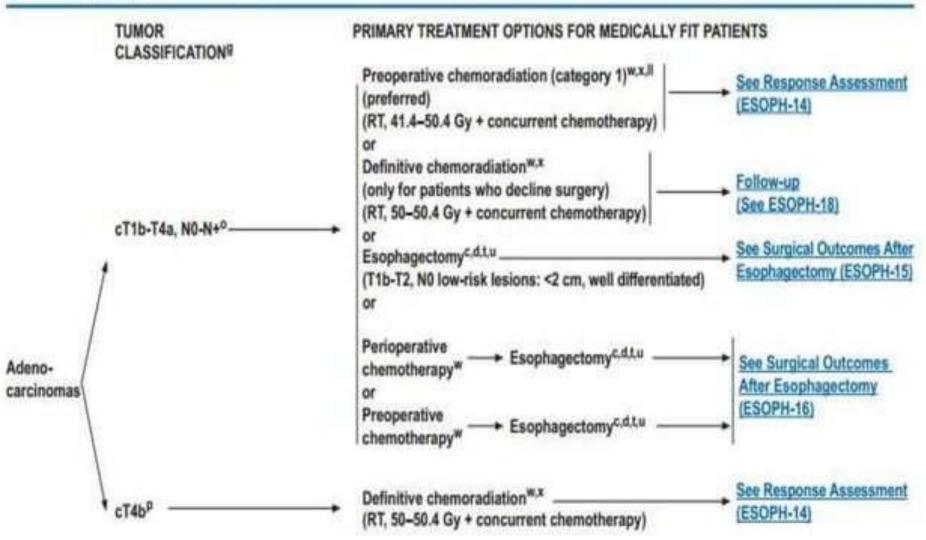
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PRINCIPLES OF SURGERY

Type I	Transthoracic Esophagectomy better than Transhiatal Esophagectomy		
		T Hulscher 2002/2005	
Type II	Transhiatal Esophagectomy or Transhiatal extended total Gastrectomy		
	Extended total Gastrectomy better than Esophagectomy	(French-Trial 2004	
	Transhiatal extended Gastre better than Left Thoracic Resection	HE POST OF THE PERSON	
Type III	Total Gastrectomy better than LT Gastrectomy Total Gastrectomy	(Jacob-Trial 2005	
	better than Extended total Gastrec	tomy (French-Trial)	

Source: Sugarbaker DJ, Bueno R, Krasna MJ, Mentzer SJ, Zellos L: *Adult Chest Surgery:* http://www.accesssurgery.com

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Resectable EGJ cancer

- T1a tumors, defined as tumors involving the mucosa but not invading the submucosa, may be considered for EMR + ablation or esophagectomy in experienced centers.
- Tumors in the submucosa (T1b) or deeper may be treated with esophagectomy.
- T1-T3 tumors are resectable even with regional nodal metastases (N+), although bulky; multi-station lymphatic involvement is a relative contraindication to surgery, to be considered in conjunction with age and performance status.
- T4a tumors with involvement of pericardium, pleura, or diaphragm are resectable.

Unresectable esophageal cancer:

- cT4b tumors with involvement of the heart, great vessels, trachea, or adjacent organs including liver, pancreas, lung, and spleen are unresectable.
- Most patients with multi-station, bulky lymphadenopathy should be considered unresectable, although lymph node involvement should be considered in conjunction with other factors, including age and performance status and response to therapy.
- Patients with EGJ and supraclavicular lymph node involvement should be considered unresectable.
- Patients with distant (including nonregional lymph nodes) metastases (stage IV) are unresectable.

- The type of esophageal resection is dictated by the location of the tumor, the available choices for conduit, as well as by the surgeon's experience and preference and the patient's preference.
 - In patients who are unable to swallow well enough to maintain nutrition during induction therapy, esophageal dilatation or a feeding jejunostomy tube are preferred to a gastrostomy (which may compromise the integrity of gastric conduit for reconstruction).

- The surgical approach for Siewert Type I and II EGJ tumors are similar to esophageal cancer.
- Type III tumors are considered as gastric cancers and the surgical approach for these tumors is similar Gastric Cancer.
- In some cases, additional esophageal resection may be necessary to obtain adequate surgical margins.



Mediastinal lymph node dissection and distal esophagectomy is not essential in early esophagogastric junction adenocarcinoma

In-Seob Lee^{1,2}, Ji-Yong Ahn^{3,4}, Jeong-Hwan Yook^{1,2} and Byung-Sik Kim^{1,2*}

Abstract

Background: Optimal extent of surgery remains controversial in types 2 and 3 adenocarcinoma of esophagogastric junction (AEG). We aimed to determine whether the extended procedure including mediastinal lymphadenectomy is essential in all patients with AEG by comparing prognosis and recurrence of proximal gastric adenocarcinoma based on total gastrectomy with intra-abdominal lymphadenectomy.

Methods: The clinicopathologic characteristics of 672 patients (type 2: 90, type 3: 211, upper third of the stornach: 371 cases) who underwent curative total gastrectomy with lymphadenectomy between 2003 and 2009 were reviewed.

Results: Recurrence was observed in 36.7, 16.1, and 16.1% of cases of type 2 AEG, type 3 AEG, and cancer of the upper third of the stomach, respectively. The 5-year disease-free survival rates were 62.6, 82.5, and 84.6%, respectively. Subgroup analysis revealed that in early cancers, there was no difference in survival between the groups (93.2 vs. 96.7 vs. 98.7%) but in advanced cancers, there was a difference (47.9 vs. 75.4 vs. 71.8%, P < 0.001). There was no survival difference in stage 1 (97.5 vs. 98.7 vs. 98.3%), but, in stage 2, type 2 AEG had a worse prognosis (41.9 vs. 92.1 vs. 83.0%). Types 2 and 3 advanced AEG had higher rates of locoregional recurrence, especially in the vicinity of the esophagojejunostomy and mediastinal lymph nodes compared to proximal gastric cancer.

Conclusions: Total gastrectomy without mediastinal lymphadenectomy might produce favorable outcomes in early AEG and acquisition of a greater length of proximal margin, and removal of mediastinal lymph nodes might be helpful in advanced cancers.

Keywords: Esophagogastric junction, Adenocarcinoma, Mediastinal lymphadenectomy, Total gastrectomy

EXTENDED TRANSTHORACIC RESECTION COMPARED WITH LIMITED TRANSHIATAL RESECTION FOR ADENOCARCINOMA OF THE ESOPHAGUS

JAN B.F. HULSCHER, M.D., JOHANNA W. VAN SANDICK, M.D., ANGELA G.E.M. DE BOER, Ph.D., BAS P.L. WUNHOVEN, M.D., JAN G.P. TUSSEN, Ph.D., PAUL FOCKENS, M.D., PEEP F.M. STALMEIER, Ph.D., FIEBO J.W. TEN KATE, M.D., HERMAN VAN DEKKEN, M.D., HUUG OBERTOP, M.D., HUGO W. TILANUS, M.D., AND J. JAN B. VAN LANSCHOT, M.D.

 Transhiatal esophagectomy was associated with lower morbidity than transthoracic esophagectomy with extended en bloc lymphadenectomy.
 Although median overall, disease-free, and qualityadjusted survival did not differ statistically between the groups, there was a trend toward improved long term survival at five years with the extended transthoracic approach.

ORIGINAL ARTICLE

The optimal extent of lymph node dissection for adenocarcinoma of the esophagogastric junction differs between Siewert type II and Siewert type III patients

Hironobu Goto · Masanori Tokunaga · Yuichiro Miki · Rie Makuuchi · Norihiko Sugisawa · Yutaka Tanizawa · Etsuro Bando · Taiichi Kawamura · Masahiro Niihara · Yasuhiro Tsubosa · Masanori Terashima

- The IEBLDs were similar between Siewert type II and III AEGs at all stations except for lower perigastric lymph nodes.
- •Total gastrectomy should be selected as a standard treatment for Siewert type III AEG, whereas in Siewert type II AEG, preservation of the distal part of the stomach may be an acceptable procedure.

Optimal Extent of Lymph Node Dissection for Siewert Type II Esophagogastric Junction Adenocarcinoma

Jun Peng, MD, Wen-Ping Wang, MD, Yong Yuan, MD, Yang Hu, MD, Yun Wang, MD, and Long-Qi Chen, MD, PhD

Department of Thoracic Surgery, West China Hospital of Sichuan University, Chengdu, Sichuan, China

Background. The optimal surgical approach and extent of lymphadenectomy for Siewert type II adenocarcinoma of the esophagogastric junction (AEG) is controversial. The aim of this study was to identify its optimal extent of thoracic and abdominal lymph node dissection, and the appropriate surgical approach.

Methods. The clinicopathologic data of 192 patients with Siewert type II AEG who were admitted to our center during January 2007 through October 2011 were retrospectively analyzed. We used the index of estimated benefit from lymph node dissection to assess the therapeutic value of lymph node dissection of each station.

Results. Overall, for the thoracic lymph node dissection, the left thoracic route and Ivor-Lewis procedure are better choices than the abdominotranshiatal route. While for the abdominal lymph node dissection, the abdominotranshiatal achieved a better dissection extent. No significant difference was found in metastatic frequency for each station except the 16th station. The multivariate analysis found only N stage (p = 0.000) and number of resected lymph nodes of 12 or more (p = 0.035) were prognostic factors for Siewert type II AEG. Furthermore, we identified two thoracic lymph node stations (5M and 5L) and six abdominal lymph node stations (16, 17, 19, 20, G3, G4) that have a high therapeutic value for the patients.

Conclusions. We recommend the 8M, 8L, 16, 17, and G3 should be excised for Siewert type II AEG. Considering the lymphadenectomy, the Ivor-Lewis procedure is the optimal choice for patients with Siewert type II AEG.

> (Ann Thorac Surg 2015;100:263-70) © 2015 by The Society of Thoracic Surgeona

The 8M, 8L, 16, 17, and G3 should be excised for Siewert type II AEG.
 Considering the lymphadenectomy, the Ivor-Lewis procedure is the optimal choice for patients with Siewert type II AEG.

Surgical Approach - PreOp

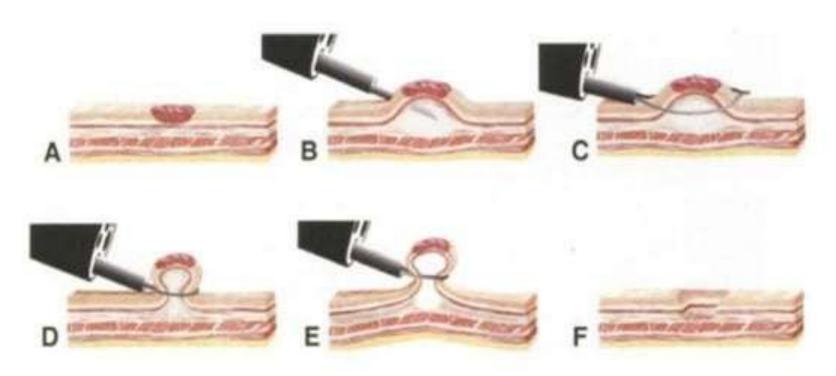
- Consider age typically not done if >80 y/o
- Cardiopulmonary reserve
 - FEV-1: >2L is ideal; >1.25 for thoracotomy
 - Clinical eval, EKG, echo
- Nutritional status
 - Most predictive of postop complications (wt loss >20lb, albumin
 <3.5)
- Clinical staging
 - Paralysis of diaphragm
 - Bronchiotracheal involvement
 - Malignant pleural effusion



Treatment approach for GEJ cancer

- Type 1: Treat as esophageal cancer
 - Esophagectomy
- Type 2: controversial
 - Total gastrectomy + distal esophagectomy
 - Esophagectomy + proximal gastrectomy
- Type 3: Treat as gastric cancer
 - Gastrectomy

Endoscopic mucosal resection(EMR)



- T1a (mucosal), <1cm cancer
- >1cm cancer: piecemeal resection

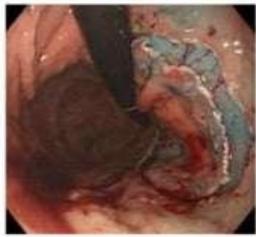
Gastrointestinal Endoscopy 2003

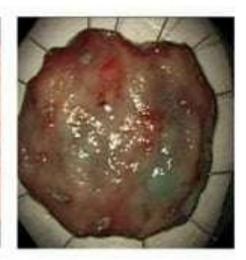
Absolute indications for endoscopic resection

- Macroscopically intramucosal (cT1a) differentiated carcinomas measuring less than 2 cm in diameter
- Macroscopic type does not matter but no ulceration scar (UL[-])

Endoscopic Submucosal Dissection





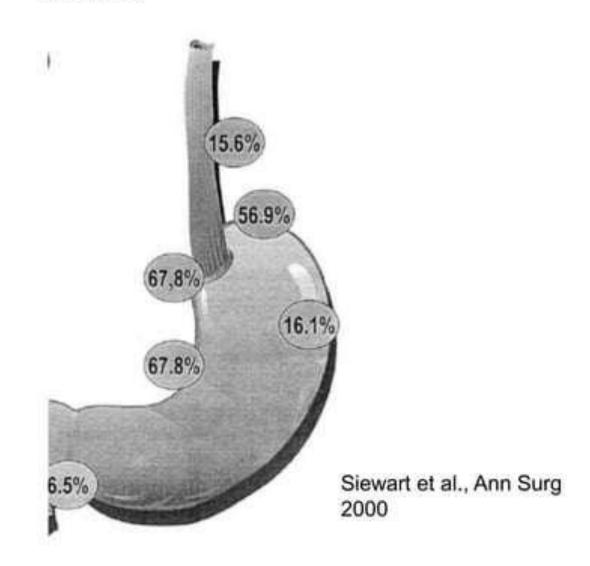


[Concept]

Simple.

'Inject, Cut & Dissect,' 'Remove tumor in one Pifbfoc resection, less risk of local recurrence

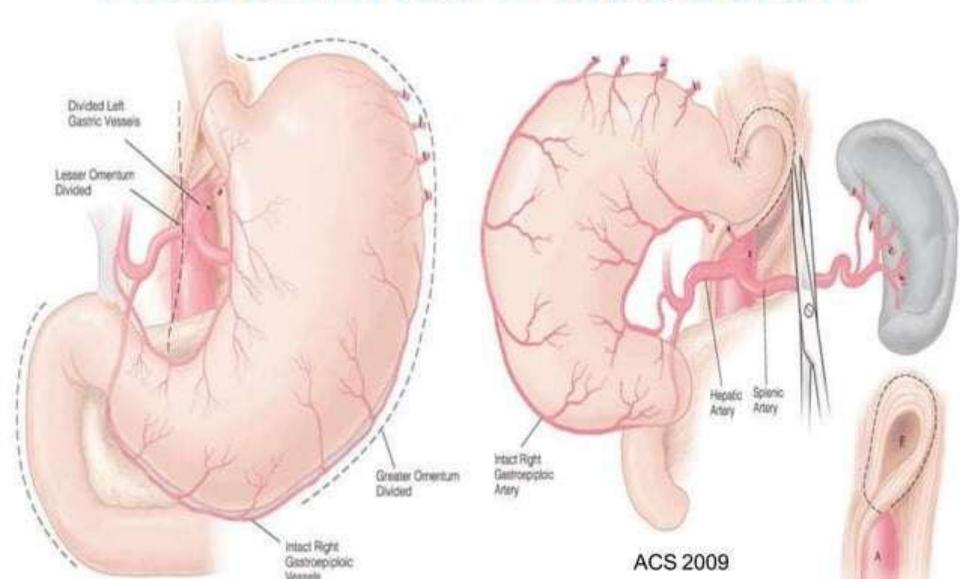
Lymph nodes spread in Type II tumors



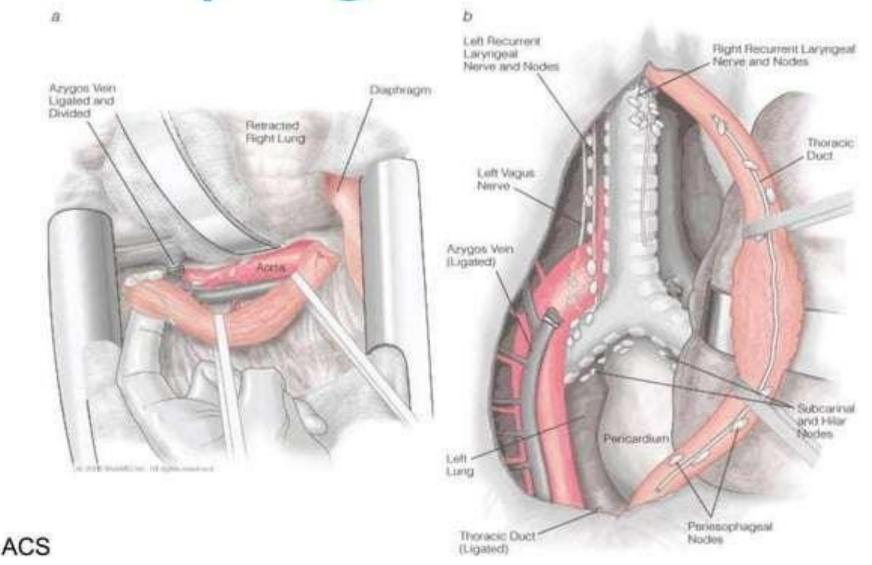
Different Surgical Approaches

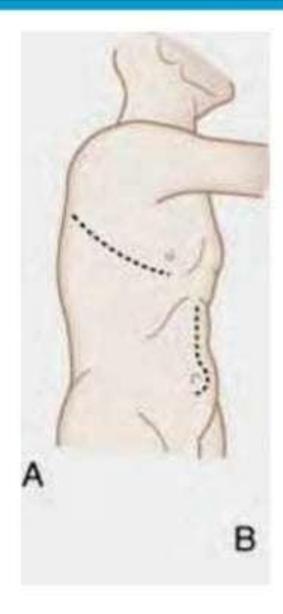
- Ivor Lewis
 - Abdominal/thoracic dissection
 - Thoracic esophagogastrostomy
- Left Thoracoabdominal
- Transhiatal
 - Cervical and upper midline incisions
 - Blind chest dissection
 - Cervical esophagogastrostomy
- Feeding jejunostomy

Abdominal Dissection



Esophageal Dissection



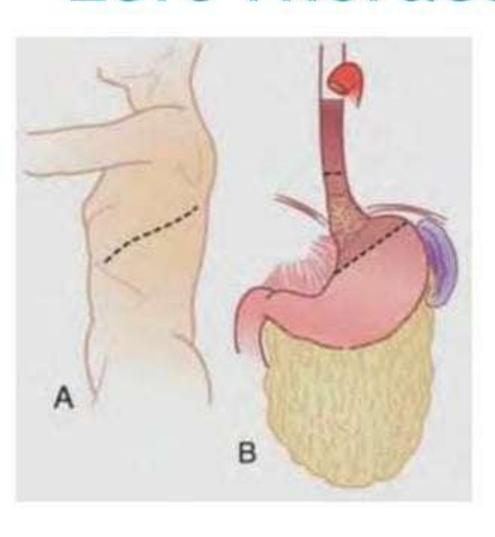


Ivor Lewis

- Abdominal/thoracic dissection
- Direct visualization

- Leak rate ~5%
 - □ Difficult to manage → empyema

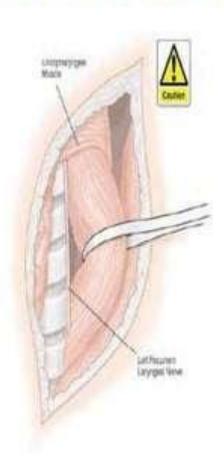
Left Thoracoabdominal



- Indicated for GEJ, distal esophageal, proximal stomach tumors
 - especially if using intestinal conduit
 - obese
- Thoracic esophagogastrostomy

Transhiatal







Einner NJ, Ashlay EN: Malogot's Abdoninal Operations, 11th Edition: http://www.accesssurgers.com

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Reconstruction

- Tubularized or whole stomach
 - Preferred b/c blood supply
 - Proximity
 - Single anastomosis

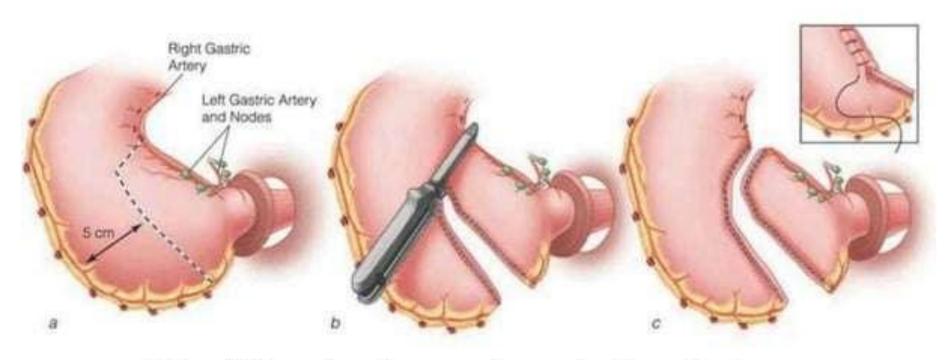
Colon

- Stomach can't be used
 - · Prior Sx, PUD scarring, tumor involvement
- L colon preferred b/c
 - Diameter closer to that of esophagus, more length, less variation of blood supply
- Problems w/ L. colon
 - · most affected by diverticular Dz, IMA most affected by atherosclerosis

Jejunum

- Cannot replace entire esophagus
- Free graft, pedicled graft, or Roux-en-Y

Creating the Gastric Tube



➤ Don't forget pyloromyotomy/pyloroplasty

Surgical Approach Which way do I go?



- Transhiatal esophagectomy (THE) is may be safer
 - One major incision instead of 2
 - Shorter OR time
- Transthoracic esophagectomy (TTE) may be a better oncological procedure
 - Extended lymph node dissection in the posterior mediastinum
 - Better for tumors close to tracheobronchial tree & after neoadjuvant Tx especially mid & upper esophagus



Transthoracic

The transthoracic approach provides direct visualization and exposure of the intrathoracic esophagus, facilitating a wider dissection to achieve a more adequate radial margin around the primary tumor and more thorough lymph node dissection, which theoretically results in a more sound cancer operation.

In patients with significant comorbid conditions, the combined effects of an abdominal and thoracic incision may compromise cardiorespiratory function.

Transthroacic

An intrathoracic anastomotic leak can lead to mediastinitis, sepsis, and death.

In addition, esophagitis in the nonresected thoracic esophagus may occur secondary to bile reflux.

The threeincision (cervical, thoracic, and abdominal) modification of the procedure effectively eliminates the potential for complications associated with an intrathoracic esophagogastric anastomosis

Transhiatal

Limitations and disadvantages of transhiatal esophagectomy, increased anastomotic leak rate with subsequent stricture formation, the possibility of chylothorax, and the possibility of recurrent laryngeal nerve injury.

Outcomes after Transhiatal & Transthoracic Esophagectomy

Linked SEER-Medicare Database
All patients with esophageal cancer
N=8312

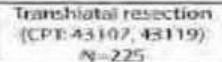


Patients undergoing esophageal resection (ICD-9: 42.4, 42.5, 42.6, 43.5) N=882



Study population N=866 Non-Medicare part 6; Esophagostomy (CPT: 43124), Complex reconstruction (CPT: 43108, 43113, 43116,

43118, 43123) N=14



Transthoracic resection CPT: 43112, 43117, 43121, 43122 N=643

Outcomes after Transhiatal & Transthoracic Esophagectomy

Pts s/p THE had:

- Lower operative mortality (30 days)
 - 6.7% vs 13.1%, p = 0.009
- Trend towards higher 5-yr survival
 - No statistically significant difference
- More likely to require endoscopic dilatation w/in 6months
 - 43.1% vs 34.5%, p = 0.02

Extended TTE vs Limited THE for AdenoCa of the mid/distal Esophagus

- 1994-2000; randomly assigned 220 pts w/ THE (n=95) or TTE (n=110); 15 pts excluded b/c unresectable
- 5-yr survival THE 34% vs TTE 36%, p = 0.71
- Survival benefit 14% in Type I tumor w/ TTE (51% vs 37%, p = 0.33)
 - Not seen in pts w/ Type II tumor, no positive nodes, or >8 + nodes
- TTE higher perioperative morbidity but no difference in mortality

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ORIGINAL ARTICLE

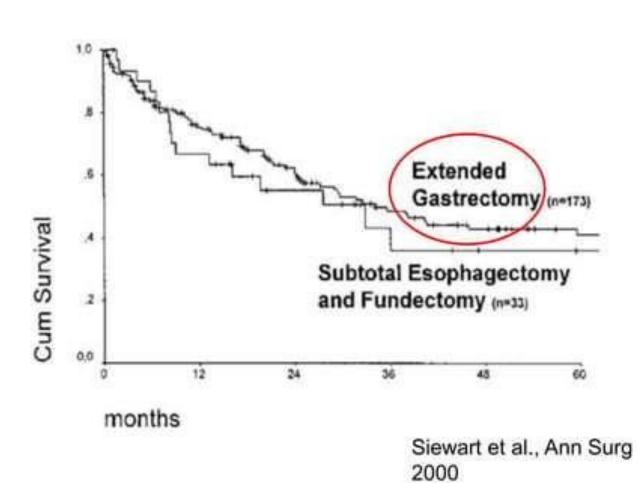
Retrospective Cohort Study

Optimal treatment for Siewert type II and III adenocarcinoma of the esophagogastric junction: A retrospective cohort study with long-term follow-up

Kei Hosoda, Keishi Yamashita, Hiromitsu Moriya, Hiroaki Mieno, Masahiko Watanabe

LN along the lesser curvature, right and left paracardial LN, and LN along the left gastric artery should be dissected in patients with Siewert type II or III adenoca rcinoma of the esophagogastric junction.

Survival for Type 2 Cardia cancer



Current recommendation for Type 2

- For tumor with esophageal invasion
 <2cm
 - Extended gastrectomy
- For tumor with esophageal invasion
 >2cm
 - Esophagectomy

Surgical Treatment of Adenocarcinomas of the Gastro-esophageal Junction

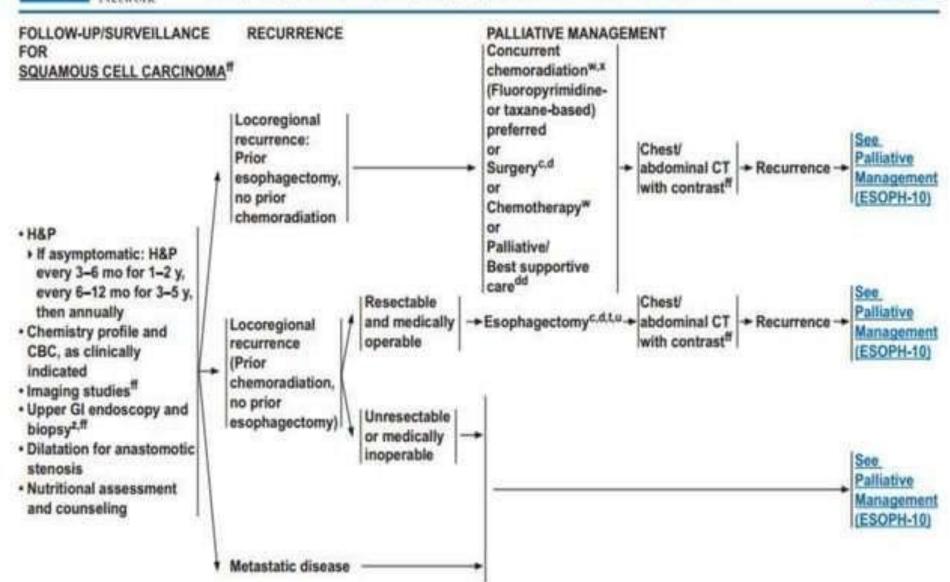
- Kevin Parry, Leonie Haverkamp, Rutger C. G. Bruijnen, PhD P. D. Siersema MD, PhD J. P. Ruurda MD, PhD R. van Hillegersberg MD.
- Published 2014 in Annals of Surgical Oncology

A positive CRM was more common with gastrectomy in patients with a type II GEJ adenocarcinoma.

Esophagectomy provides for a more complete paraesophageal lymphadenectomy. Furthermore, the high prevalence of mediastinal nodal involvement indicates that a full lymphadenectomy of these stations should be considered in type II tumors

Comprehensive NCCN Guidelines Version 4.2017 Cancer Esophageal and Esophagogastric Junction Cancers

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Assessment of Treatment Response

- Residual primary tumor in the resection specimen following neoadjuvant therapy is associated with shorter overall survival for both adenocarcinoma and squamous cell carcinoma of the esophagus.
- Sizable pools of acellular mucin may be present after chemoradiation but should not be interpreted as representing residual tumor.

RECIST 1.1

Response category	WHO	RECIST 1.1
CR	Disappearance of all lesions	Disappearance of all lesions and pathologic lymph nodes
PR	≥50% decrease in sum of the area (longest diameters multiplied by longest perpendicular diameters)	≥30% decrease in the sum of longest diameters of targeted lesions
SD	Neither PR nor PD	Neither PR nor PD
PD	>25% increase in sum of the area	>20% increase in the sum of longest diameters and ≥5 mm absolute increase in the sum of longest diameters

CR: Complete response, PR: Partial response, SD: Stable disease, PD: Progressive disease, WHO: World Health Organization, RECIST: Response evaluation criteria in solid tumors

Role of PET Scans in the Assessment of Treatment Response

- The NCCN guidelines recommend consideration of PET/CT or PET only for the assessment of response to preoperative or definitive chemoradiation therapy before surgery or initiation of postoperative treatment (category 2B).
- However, the guidelines emphasize that PET scans should not be used for the selection of patients to surgery following preoperative chemoradiation.

Tumor Regression Score

Tumor Regression Score ⁹	Wu et al ⁶ Description	Ryan et al ⁸ Description
0 (Complete response)	No residual cancer cells, including lymph nodes	No cancer cells, including lymph nodes
1 (Moderate response)	1%-50% residual cancer; rare individual cancer cells or minute clusters of cancer cells	Single cells or small groups of cancer cells
2 (Minimal response)	More than 50% residual cancer cells, often grossly identifiable at primary site	Residual cancer cells outgrown by fibrosis
3 (Poor response)		Minimum or no treatment effect; extensive residual cancer

Summary

- Tumors of the esophagogastric junction seem to be a distinct
 pathophysiologic entity, separate from esophageal and gastric carcinomas
 yet with some oncologic features of each.
- Accurate preoperative staging is crucial in the management of these tumors

Thank You