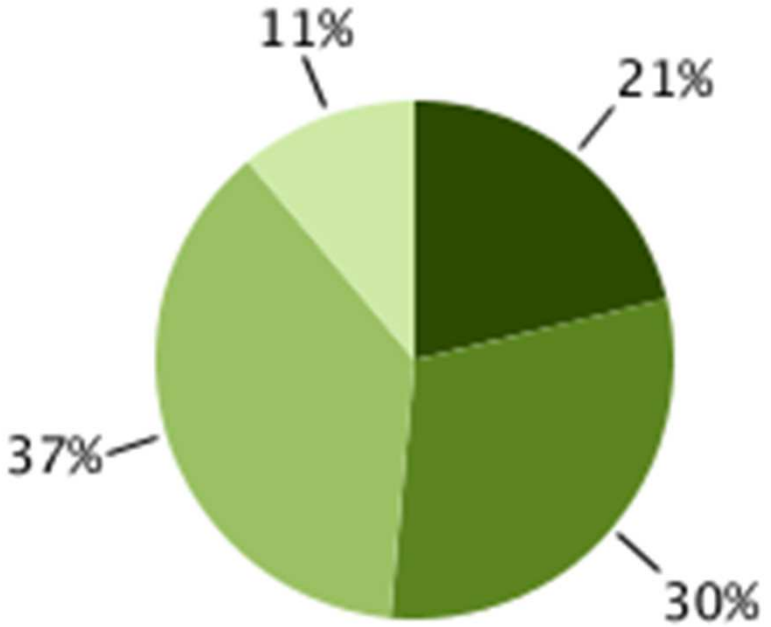
ROLE OF SURGERY IN OESOPHAGEAL CANCER

Dr.M.Iqbal ahamed
Prof Surgical Oncology
Regional Cancer Cenre
Thiruvanandapram

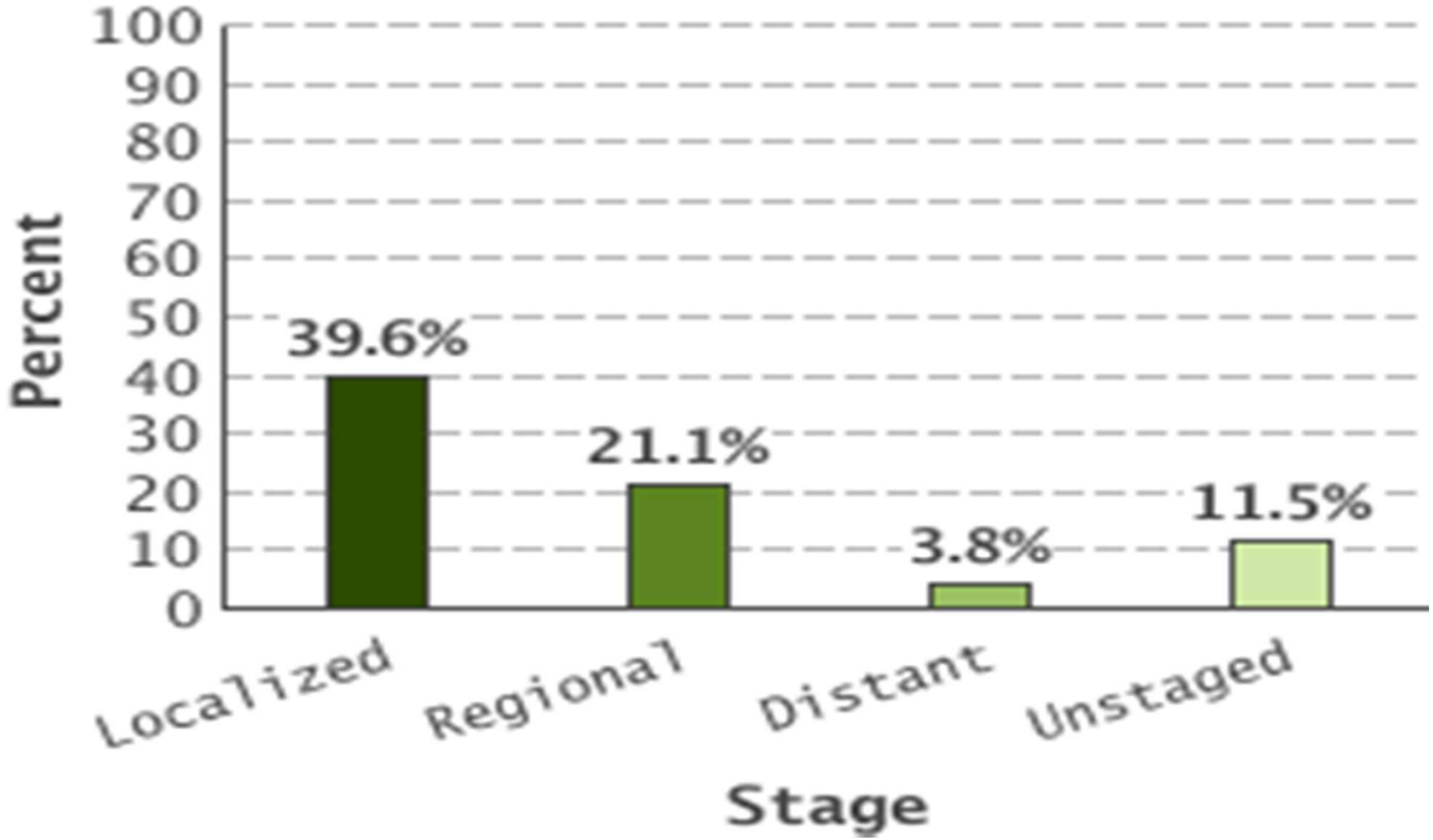
Percent of Cases by Stage Esophageal Cancer

- **Localized (21%)**
  Confined to Primary Site
- **Regional (30%)**
  Spread to Regional Lymph Nodes
- **Distant (37%)**
  Cancer Has Metastasized
- **Unknown (11%)**
  Unstaged
-

SEER 18 2004-2010, All Races, Both Sexes by SEER Summary Stage 2000



5-Year Relative Survival



How Many People Survive 5 Years Or More after Being Diagnosed with Esophageal Cancer?

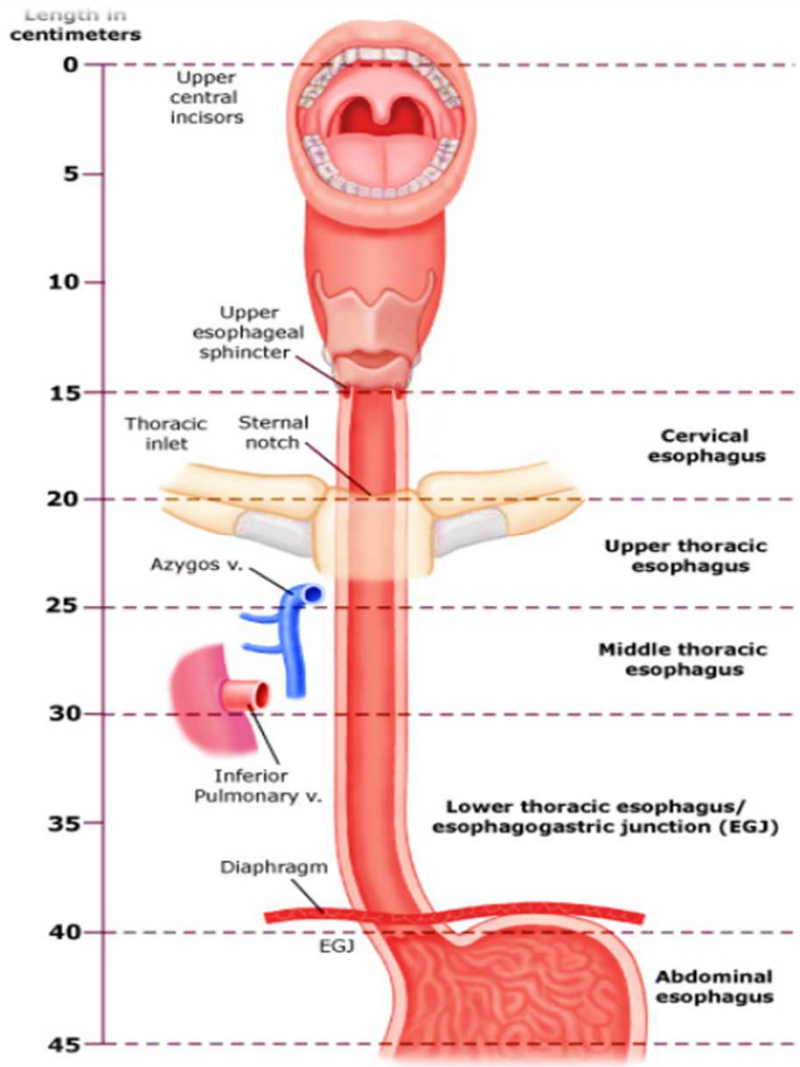
- **Percent Surviving 5 Years** **17.5%**

- Based on data from SEER 18 2004-2010

Surgical Objecives

- Potentially curative R0 resection
- No role of resection in metastatic disease
- Survival related to stage of disease

Anatomical Regions



SCC Vs ADENOCARCINOMA- Two Different tumors at one location?

- The patient of SCC is usually emaciated alchoholic and smoker ,Poor GC
- Precursor lesion of SCC is epithelial dysplasia, while for adenocarcinoma it is barretts
- 65 percent of SCCs are located above carina while 94 percent of adenocarcinoma occur below carina
- SCCs tend to arise 10 years earlier, on average, than adenocarcinomas
- SCC Skip lesions and LN spread are more with SCC
- SCCs tend to recur locoregionally first, while distal esophageal adenocarcinomas more commonly recur with distant dissemination.

Pre treatment work up

NCCN guidelines

- H&P
- Upper GI scopy and biopsy
- CT –abdomen/chest with oral and IV contrast (pelvis as indicated)
- EUS (if no suspicion of M1)
- PET CT (if no suspicion of M1)
- Her 2 neu testing (M1 suspicion)
- Nutritional counseling
- CBC and chemistries
- Biopsy of metastasis as indicated
- Assign Sievert category
- EMR- if done for early lesions
- Diagnostic laparoscopy (if no M1,EGJ lesions)

Staging

- CT scan for metastatic disease
- Endoscopic ultrasonography (EUS)
- Integrated PET/CT scans
    - Suspicious PET findings should be confirmed before excluding a patient from surgical consideration.
- Staging laparoscopy is controversial
    - NCCN guidelines suggest that diagnostic laparoscopy is optional- EGJ tumours
- Preoperative bronchoscopy - tumors that are located at or above the level of the carina.

PRIMARY TUMOR (T)	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	High grade dysplasia*
T1	Tumor invades lumina propria, muscularis mucosae, or submucosa
T1a	Tumor invades lamina propria or muscularis mucosae
T1b	Tumor invades submucosa
T2	Tumor invades muscularis propria
T3	Tumor invades adventitia
T4	Tumor invades adjacent structures
T4a	Resectable tumor invading pleura, pericardium, or diaphragm
T4b	Unresectable tumor invading other adjacent structures, such as aorta, vertebral body, trachea, etc. *High-grade dysplasia includes all noninvasive neoplastic epithelium that was formerly called carcinoma *in situ*, a diagnosis that is no longer used for columnar mucosae anywhere in the gastrointestinal tract
REGIONAL LYMPH NODES (N)	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Regional lymph node metastasis involving 1 to 2 nodes
N2	Regional lymph node metastases involving 3 to 6 nodes
N3	Regional lymph node metastases involving 7 or more nodes
DISTANT METASTASIS (M)	
M0	No distant metastasis (no pathologic M0; use clinic M to complete stage group)
M1	Distant metastasis

TNM-7

Anatomic Stage/Prognostic Groups

Squamous Cell Carcinoma*

Stage	T	N	M	Grade	Tumor Location**
Stage 0	Tis (HGD)	N0	M0	1, X	Any
Stage IA	T1	N0	M0	1, X	Any
Stage IB	T1	N0	M0	2–3	Any
	T2–3	N0	M0	1, X	Lower, X
Stage IIA	T2–3	N0	M0	1, X	Upper, middle
	T2–3	N0	M0	2–3	Lower, X
Stage IIB	T2–3	N0	M0	2–3	Upper, middle
	T1–2	N1	M0	Any	Any
Stage IIIA	T1–2	N2	M0	Any	Any
	T3	N1	M0	Any	Any
	T4a	N0	M0	Any	Any
Stage IIIB	T3	N2	M0	Any	Any
Stage IIIC	T4a	N1–2	M0	Any	Any
	T4b	Any	M0	Any	Any
	Any	N3	M0	Any	Any
Stage IV	Any	Any	M1	Any	Any

Anatomic Stage/Prognostic Groups

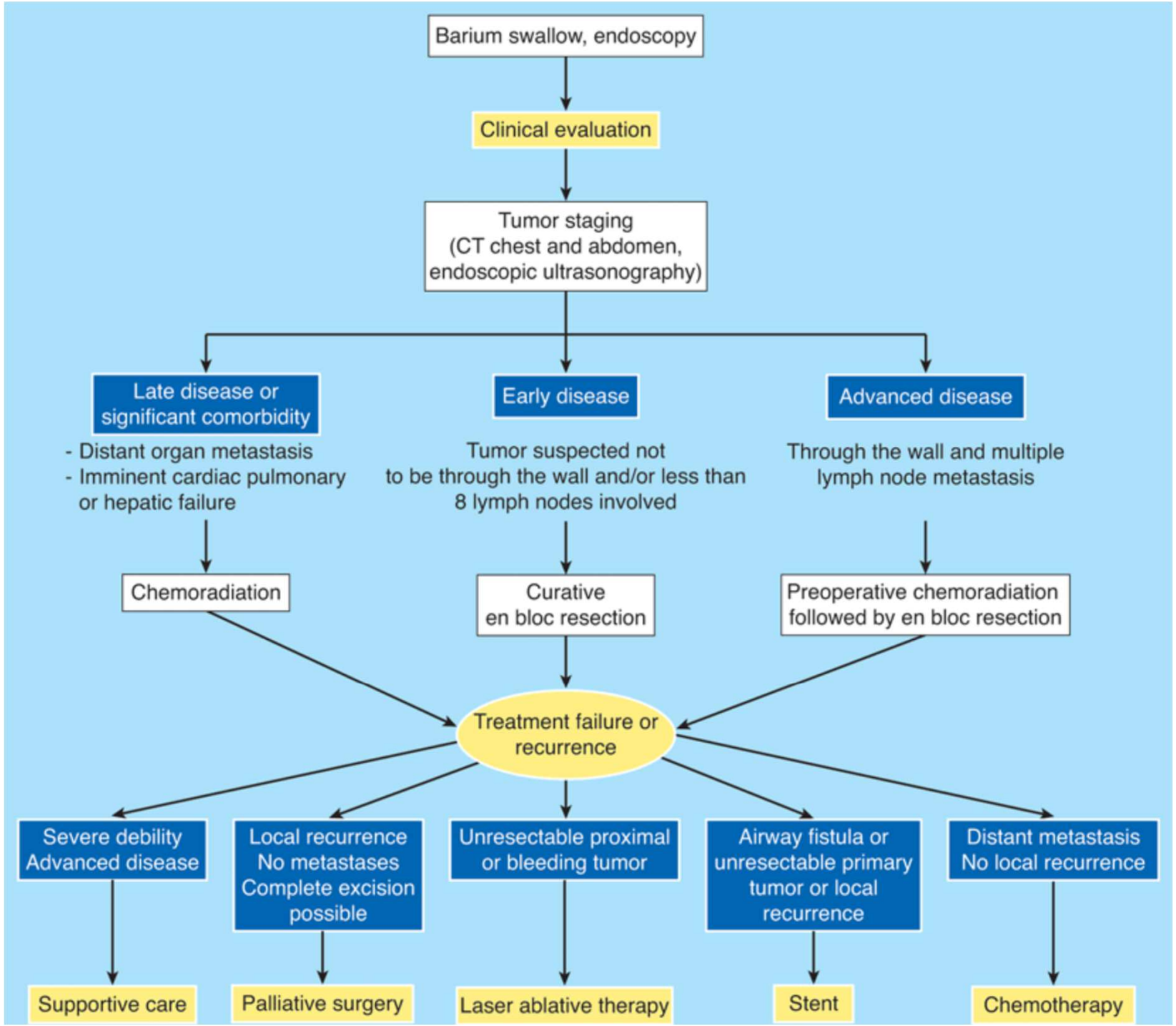
Adenocarcinoma

Stage	T	N	M	Grade
Stage 0	Tis (HGD)	N0	M0	1, X
Stage IA	T1	N0	M0	1-2, X
Stage IB	T1	N0	M0	3
	T2	N0	M0	1-2, X
Stage IIA	T2	N0	M0	3
Stage IIB	T3	N0	M0	Any
	T1–2	N1	M0	Any
Stage IIIA	T1–2	N2	M0	Any
	T3	N1	M0	Any
	T4a	N0	M0	Any
Stage IIIB	T3	N2	M0	Any
Stage IIIC	T4a	N1–2	M0	Any
	T4b	Any	M0	Any
	Any	N3	M0	Any
Stage IV	Any	Any	M1	Any

AJCC-7

- Major changes have been made in this edition
- Separate staging for Adeno/squamous(SCC-poor prog)
- Grade and site have been incorporated
- LN numbers are more important than location
- Regional LN defined as periesophageal from cervical to Coeliac
- LN ratio has not found any role in staging

Treatment Overview


Barium swallow, endoscopy
Clinical evaluation
Tumor staging
(CT chest and abdomen,
endoscopic ultrasonography)
Late disease or
significant comorbidity
- Distant organ metastasis
- Imminent cardiac pulmonary
or hepatic failure
Early disease
Tumor suspected not
to be through the wall and/or less than
8 lymph nodes involved
Advanced disease
Through the wall and multiple
lymph node metastasis
Chemoradiation
Curative
en bloc resection
Preoperative chemoradiation
followed by en bloc resection
Treatment failure or
recurrence
Severe debility
Advanced disease
Local recurrence
No metastases
Complete excision
possible
Unresectable proximal
or bleeding tumor
Airway fistula or
unresectable primary
tumor or local
recurrence
Distant metastasis
No local recurrence
Supportive care
Palliative surgery
Laser ablative therapy
Stent
Chemotherapy

Esophageal Cancer

- Treatment Overview
  - Proximal
    - Definitive Chemoradiation therapy
  - Metastatic
    - Definitive Chemoradiaiton therapy
    - No role for palliative resection
  - HGD, T1, maybe T2
    - Primary Treatment is Surgical
  - All others
    - Multimodality approach

Esophageal Cancer

Treatment Overview

Proximal

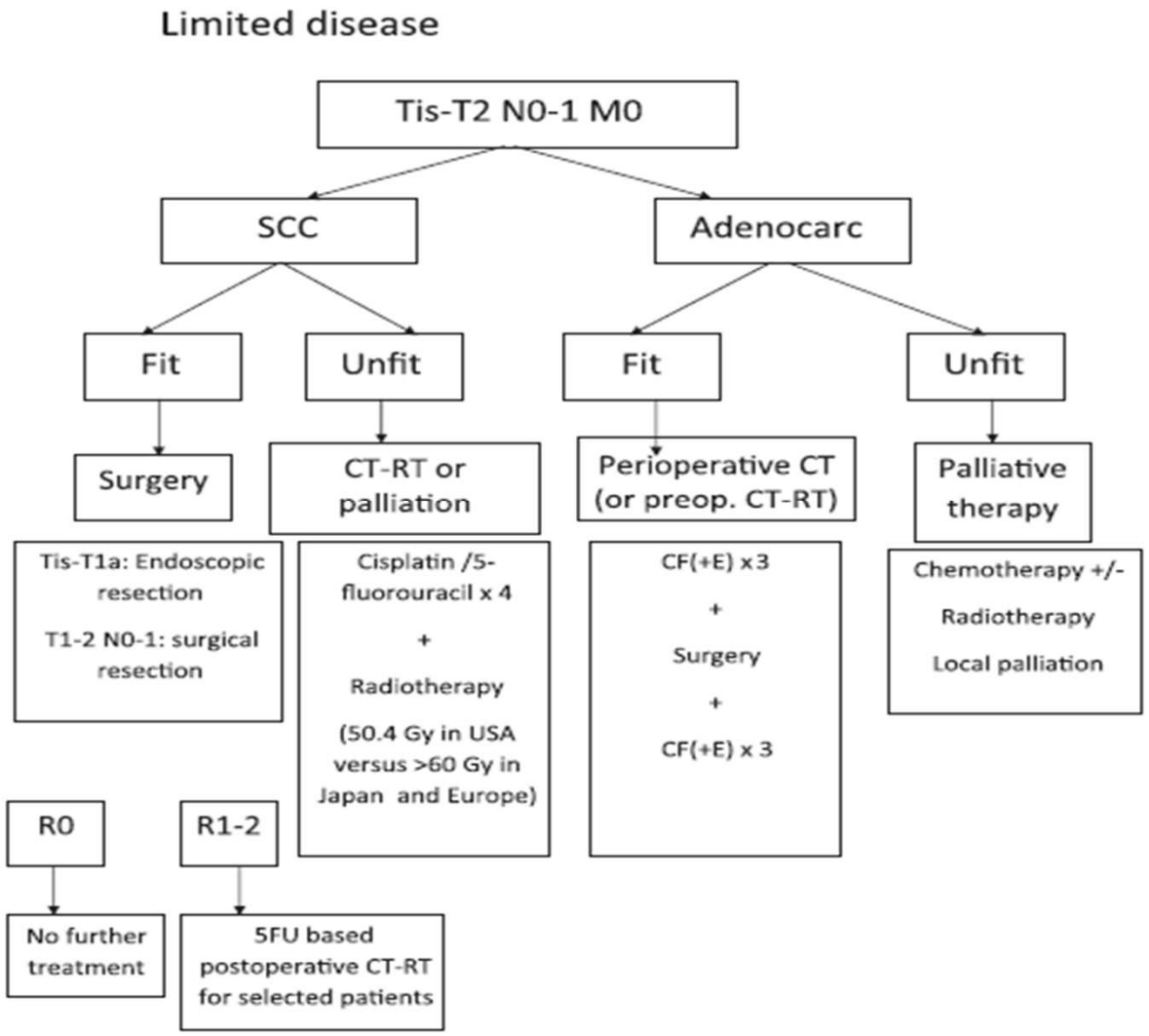
Definitive Chemoradiation therapy

CERVICAL ESOPHAGEAL CANCER

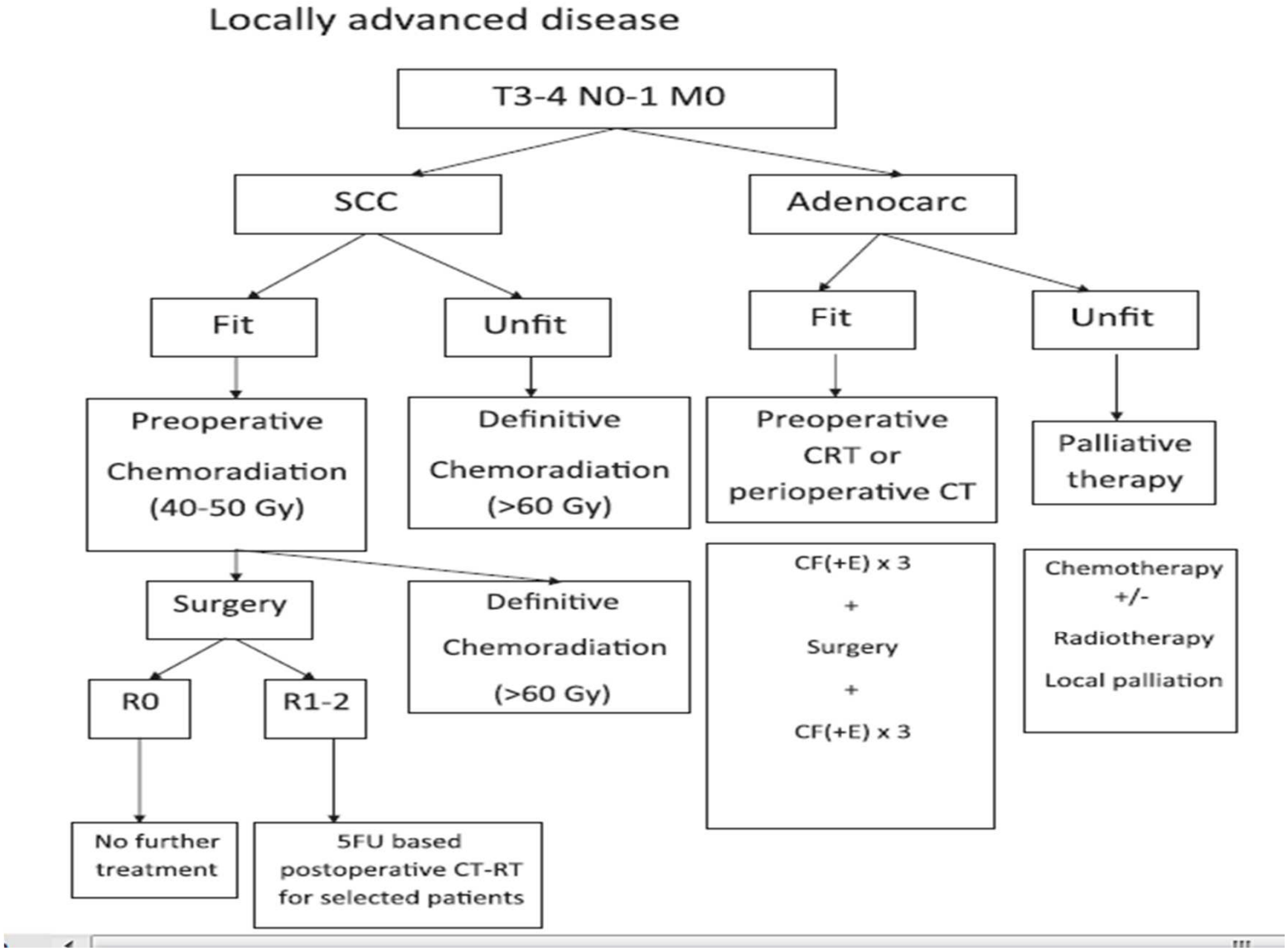
- 6 to 8 cm long
- Cricopharyngeus to the thoracic inlet

- Locally advanced disease at diagnosis.
    - tracheal invasion 35 %
    - vocal cord paralysis 24%
- ChemoRT preferred over surgery
    - survival comparable and
    - major morbidity is avoided

Guidelines-ESMO2010



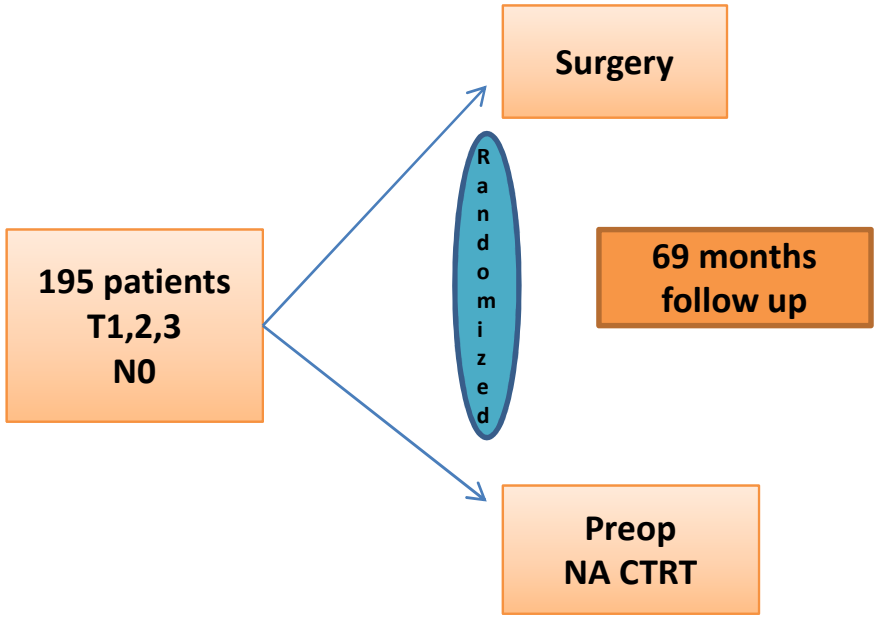
Guidelines-ESMO2010



- Early stage-
  1. Surgery alone

- Locally advanced-
  1. Neoadjuvant chemo → surgery (± post-op chemo)
  2. Neoadjuvant chemoradiation → surgery

Treatment -Early stage disease



	Survival	Adverse events	Mortality
	44 months	35%	1%
	32months	65%	7.3%

- No role of Trimodality treatment in early stage
- Surgery alone adequate in the majority of these patients.

French FFD Trial,J Clin Oncol 2010; 28:302s.

Principles of Oesophagectomy

- Spreads longitudinally in submucosal lymphatics
- Crucial to achieve longitudinal resection margin
- Debate on optimum surgical margin
- What surgical approach?

Margins

- Proximal ,distal and lateral margin
- Axial margin
  - Propensity for intramural spread , multicentric , skip mets.
  - Taking to account shrinkage of specimen after resection, in situ margin of 10 cm [fresh contracted specimen – 5 cm /SCC]
  - This allows < 5 % of recurrance .

Extent of surgery

- Controversial/Surgeons choice
- Conventional view margin-
  - Adenocarcinoma-5cm –Partial esophagectomy
  - SCC-10-12 cm-Total esophagectomy

CRM

- The College of American Pathologists (CAP) defines a positive CRM as the presence of esophageal cancer at the resection margin .

- United Kingdom Royal College of Pathologists (RCP) defines a positive CRM as the presence of esophageal cancer within 1 mm of the resection margin
- Negative CRM-independent predictor of survival

Lateral margin

- Concept of En bloc resection
- Less suitable for upper and middle esophageal cancers – close proximity to trachea and bronchi
- Applicable to adeno ca – lower esophagus

Surgery

- Perioperative mortality is <5%
- Local recurrance has decreased further
- Surgery after Neoadjuvant CT/CRT is a very promising option
- Surgery restores the nutritional intake and restore QOL

Reasons for Improved results for resection

- Increase in specialist units
- Multidisciplinary approach
- Earlier diagnosis
- Better patient selection
- Improved perioperative management
- Enhanced recovery programmes

The surgical option

Stage wise management

In general

- Stage I-IIA(T1,T2,N0,M0)-Upfront surgery if the candidate is fit
- Stage II B-III –Multimodality therapy
  1. Neoadjuvant chemo → surgery (± post-op chemo)
  2. Neoadjuvant chemoradiation → surgery
- Stage IV - Palliative

Superficial cancer (HGD /T1a/T1bN0M0)

- Rate of conversion of barretts
- 0.6%/year – Low grade dysplasia
- 5%/year – High grade dysplasia

Esophagectomy- Gold standard
ER+ Ablation – reasonable alternative
RADIATION +/- CT(Investigational)

EMR

- Early T1a
- Confined to mucosa
- < / =2cm
- Non ulcerated
- Not P/D
- No LVI

Depth of invasion				
			% of LN	% of LN
Mucosa	m1	barely breaks the basement membrane	0%	
	m2		3.3%	
	m3	infiltrates the lamina muscularis mucosae	12.2%	
Submucosa	Sm1		26.5%	7.5%
	Sm2		35.8%	10%
	Sm3		45.9%	45%

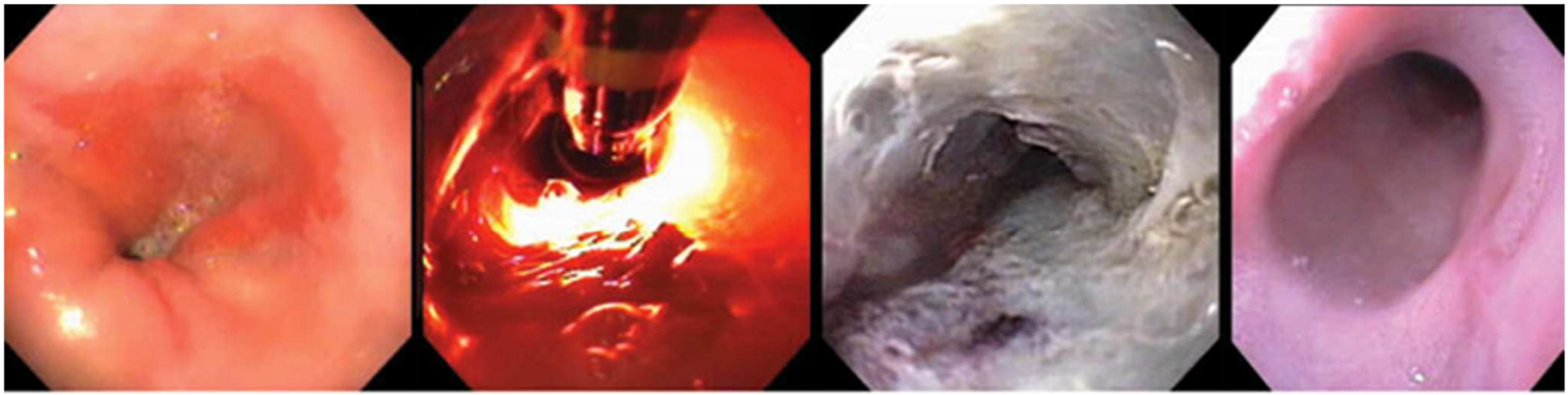
Kodama Met al, Surgery 1998;123(4):432–9.
Raja S et al,J Thorac Cardiovasc Surg. 2011 Dec;142(6):1403-11.e1.

Endoscopic Ablation

- **Thermal Forms**
  - **Multipolar coagulation**
  - **Heat probe therapy**
  - **Argon plasma coagulation**
  - **Laser therapy (many types)**
  - **Radiofrequency ablation**
- **Photodynamic Therapy**
  - **Systemic photosensitizer**
    - **Preferentially taken up by dysplastic tissue/tumor**
  - **Expose tissue to light of specific wavelength**
  - **Debride devitalized tissue**

Endoscopic Ablation

- **Deficiencies**
  - **No tissue removed to assure adequate targeting**
  - **Islands of Barrett's esophagus +/- cancer can still exist under ablated tissue**
  - **Surveillance afterward difficult**

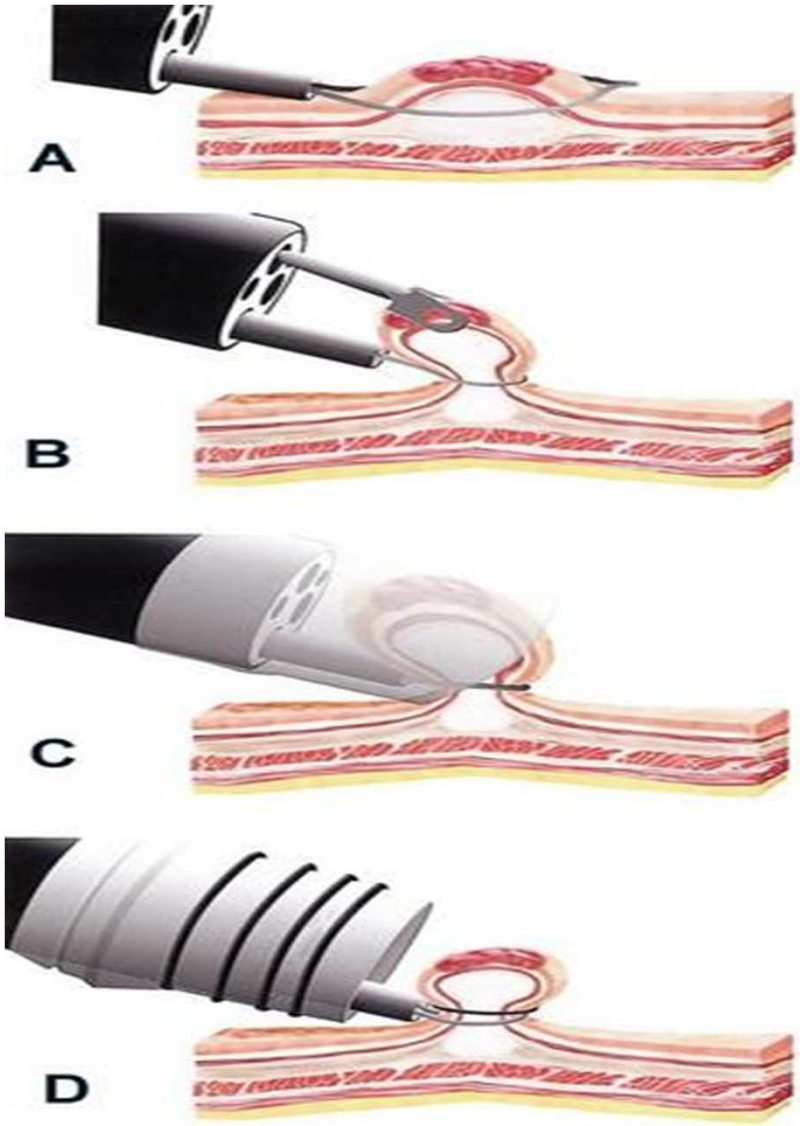


Barrett esophagus with intramucosal cancer | Cylindrical laser fiber and light | Severe esophagitis 48h after treatment | Surveillance endoscopy at 2 years

Endoscopic Mucosal Resection

- **Technique**
  - **– Create pseudo polyp with epinephrine**
  - **– Snare**
- **Shortcomings**
  - **– Technically difficult**
  - **– Difficult to perform in long segment Barrett's**
  - **– High recurrence rate (30%)**
- **May have diagnostic value**

Endoscopic Mucosal Resection



Inject and Cut

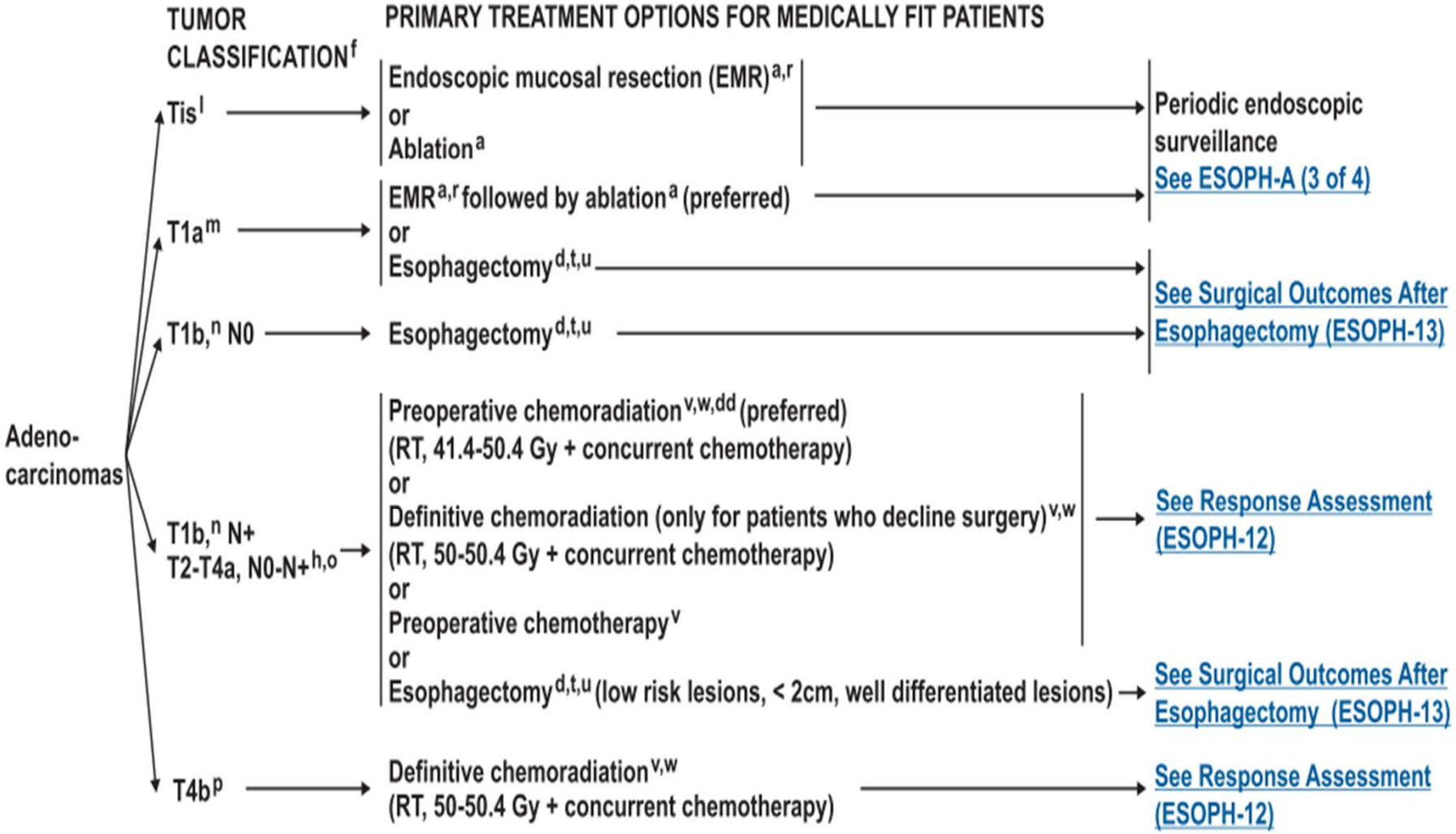
Inject, Lift, and Cut

Inject, Suction, and Cut

Ligate, then Snare

NCCN Guidelines Version 2.2013
Esophageal and Esophagogastric Junction Cancers

NCCN Guidelines Index
Esophageal/EGJ Table of Contents
Discussion



Post treatment surveillance

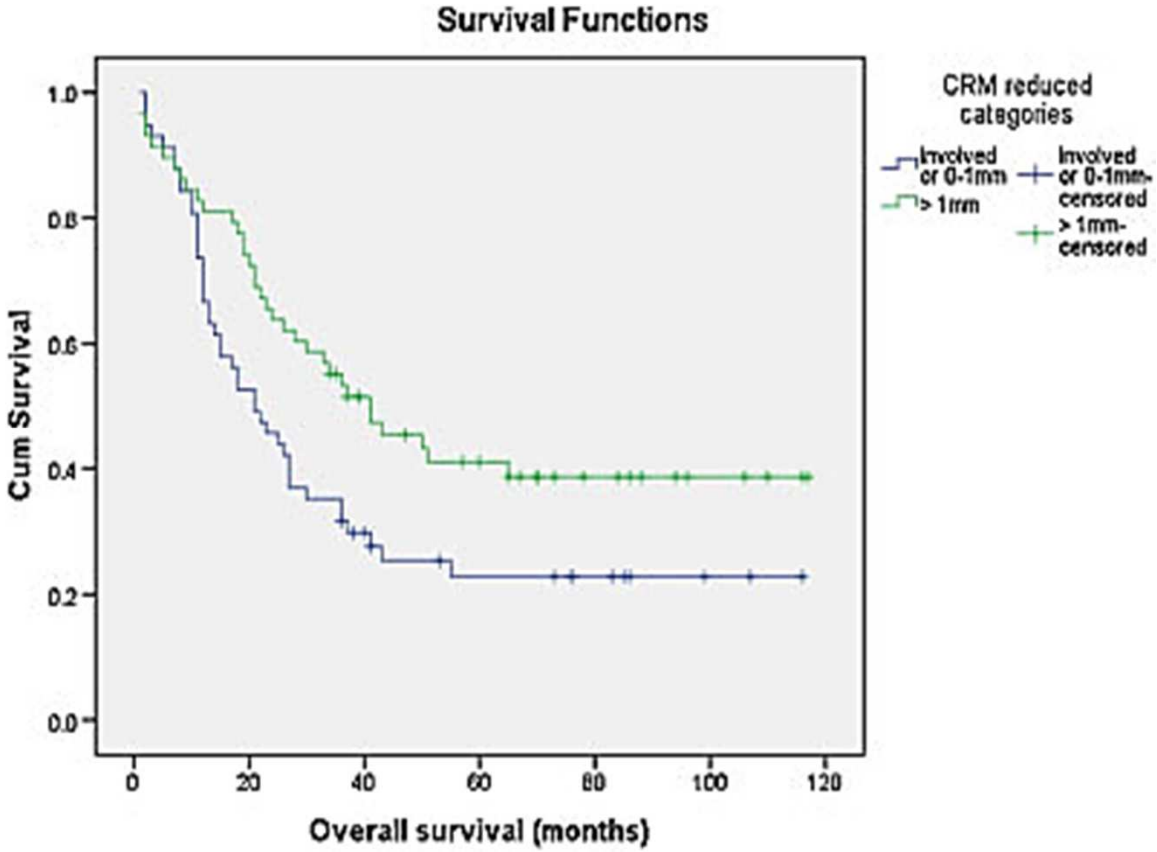
- Check endoscopy 5-6 weeks
- Biopsy of all mucosal abnormalities , strictures (Combination with EUS increases sensitivity)
- Look for barretts- 4 quadrant biopsy
- Biopsy neo squamous areas(buried glands)
- Every 3 months → 1 year →Annually

Methods of Esophagectomy

CRM

optimal free CRM should be >1 mm.

Patients with unfavorable CRM involvement (1 mm) may be considered for adjuvant



V S R Rao et al, J. Surg. Oncol. 2012

Prerequisites for surgery

- Complete (R0) resection
- 4 cm distal gastric margin
- 5 cm esophageal margin
- At least 15 nodes - appropriate for the primary tumor location

Early stage carcinoma esophagus is surgically curable disease – **No controversy**

I:Surgery alone

cT1N0M0 lesions

cT2N0M0 lesions(some centres)

CHOICE OF SURGICAL APPROACH

- DEPENDS UPON :
  - Tumor location and length, submucosal extension, and adherence to surrounding structures
  - The type of lymphadenectomy desired
  - The conduit to be used for replacement
  - The preference of the surgeon

Surgical Options

Approach

- Transhiatal
- Transthoracic
- Tri incisional
- Minimally Invasive

Conduit

- Stomach
- Colon
- Jejunum
- Skin Tube

Anastomosis

- Neck
- Chest
- Abdomen

Route

- Post. Mediast.
- Retrosternal
- Subcutaneous

Approach

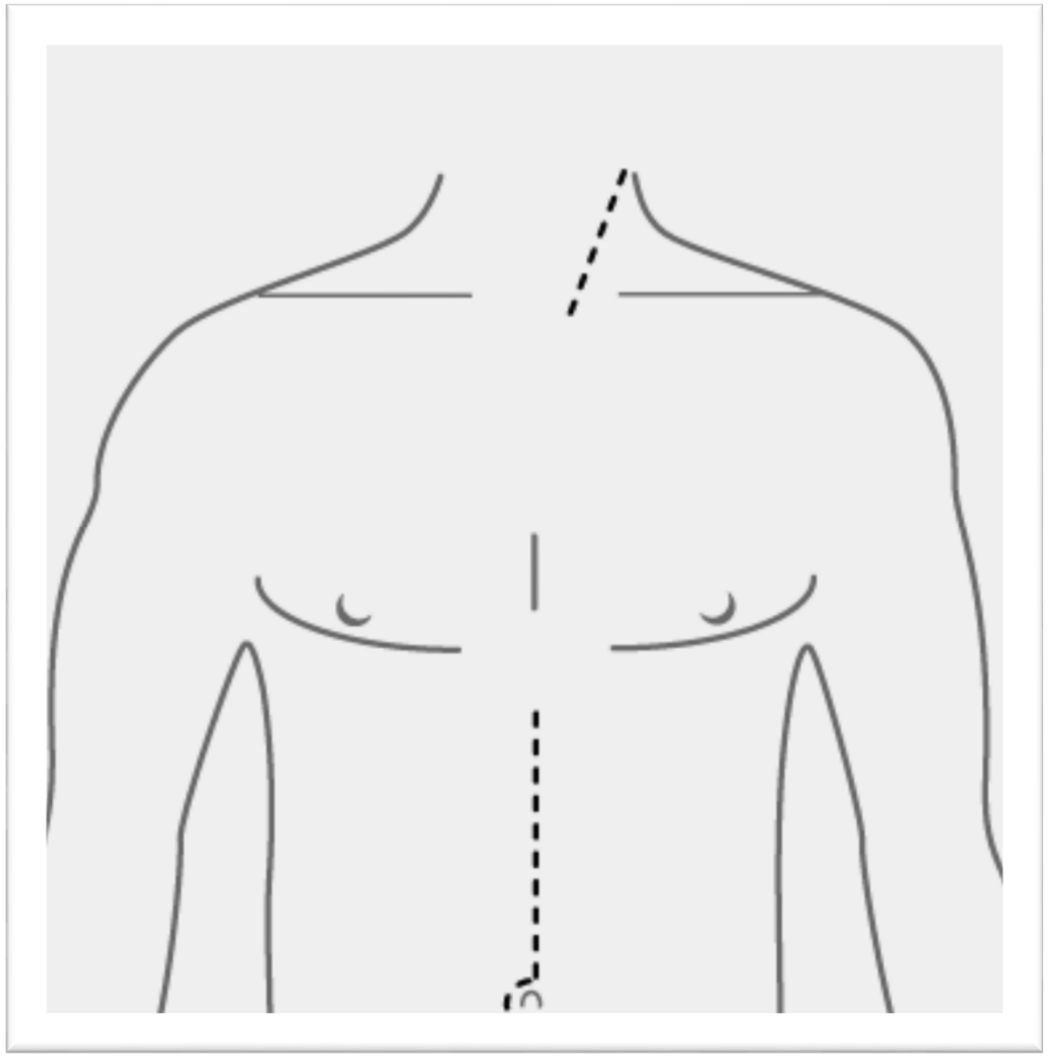
TRANSHIATAL-Orringer

- Laparotomy and cervical approach

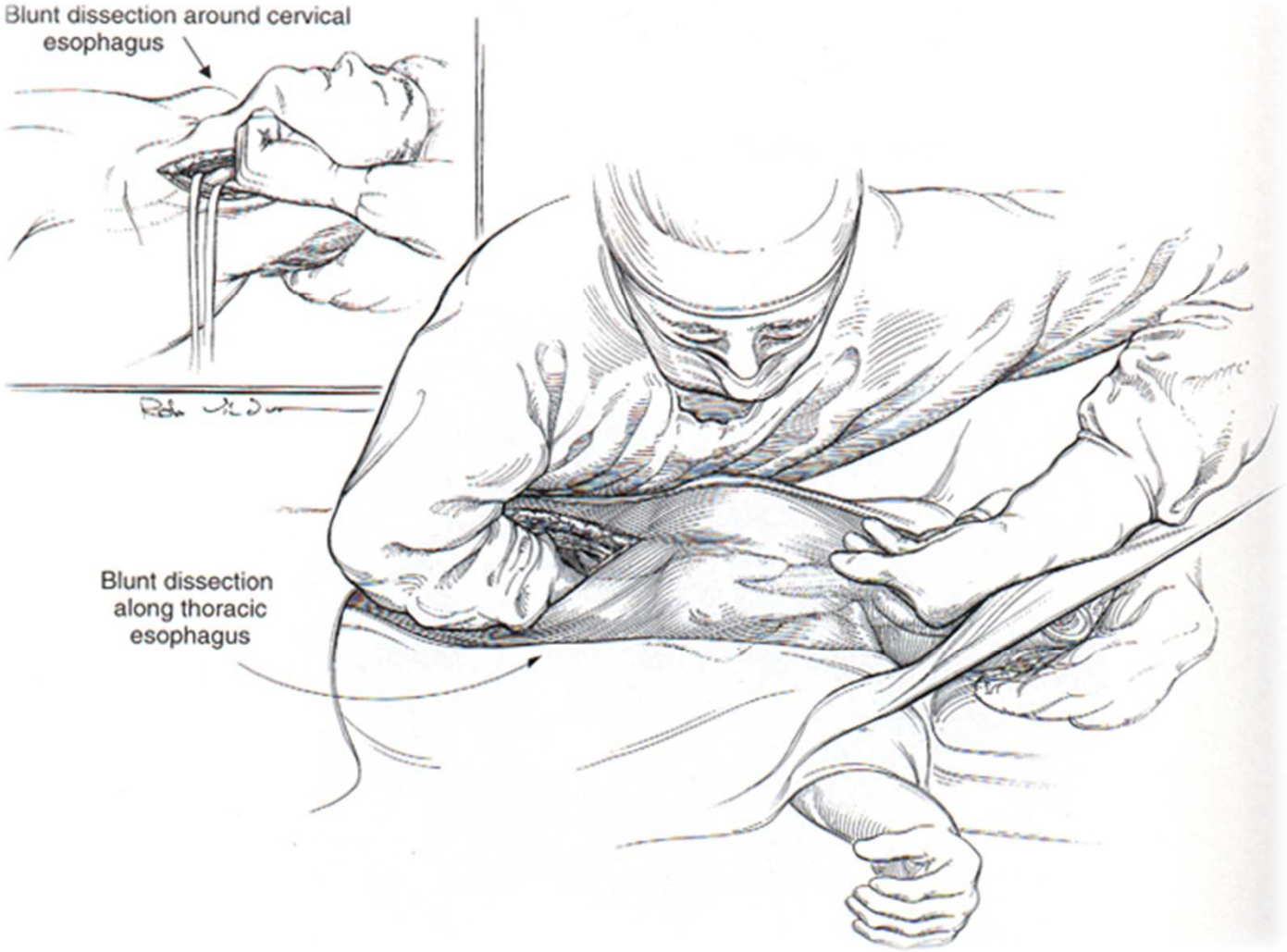
TRANSTHORACIC

- Ivor Lewis
  - Right thoracotomy and laparotomy
- McKeown or “three hole”
  - Right thoracotomy, laparotomy, cervical approach
- Left thoracotomy/Left thoracoabdominal

Transhiatal Esophagectomy



Transhiatal Esophagectomy



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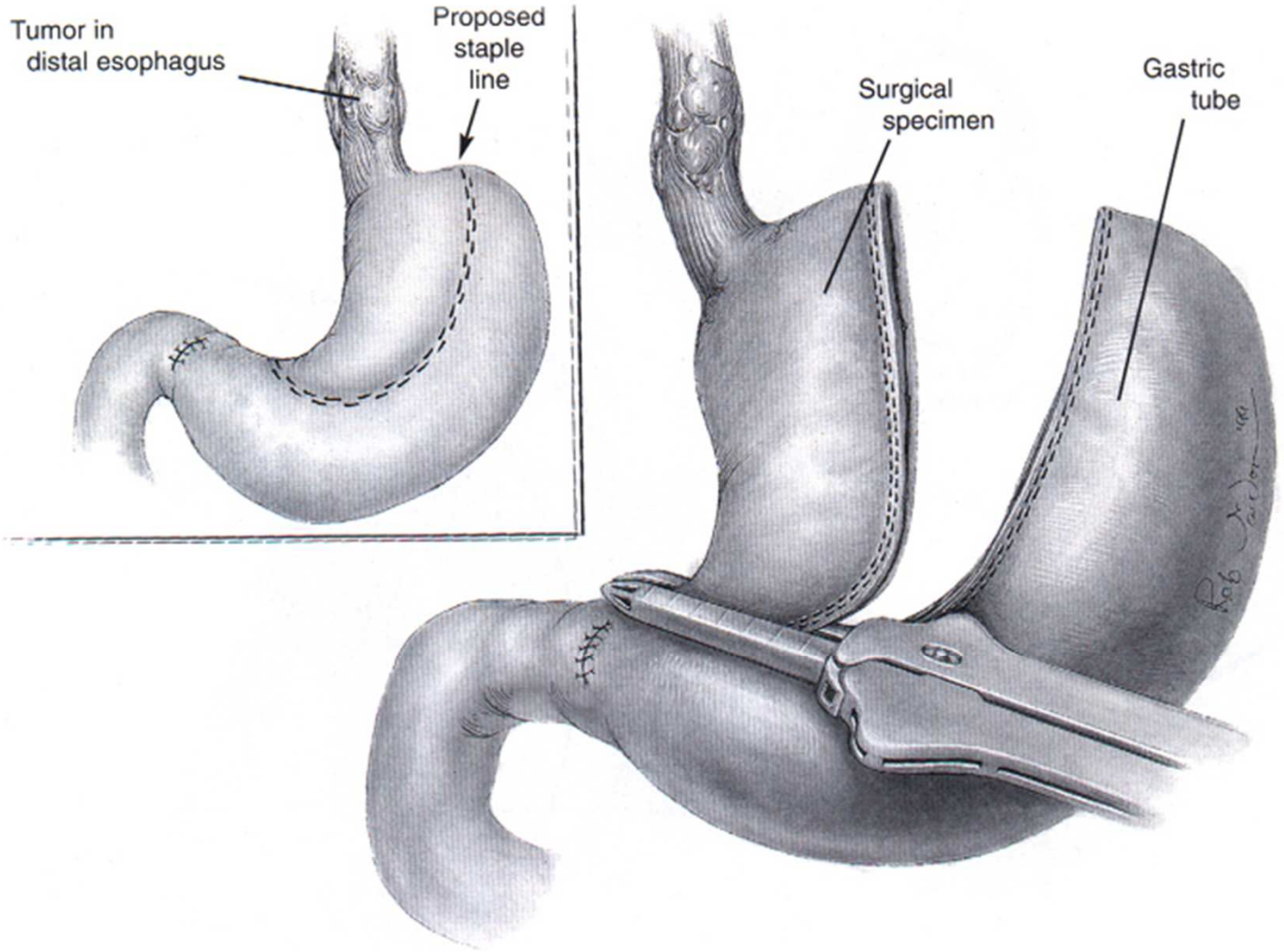
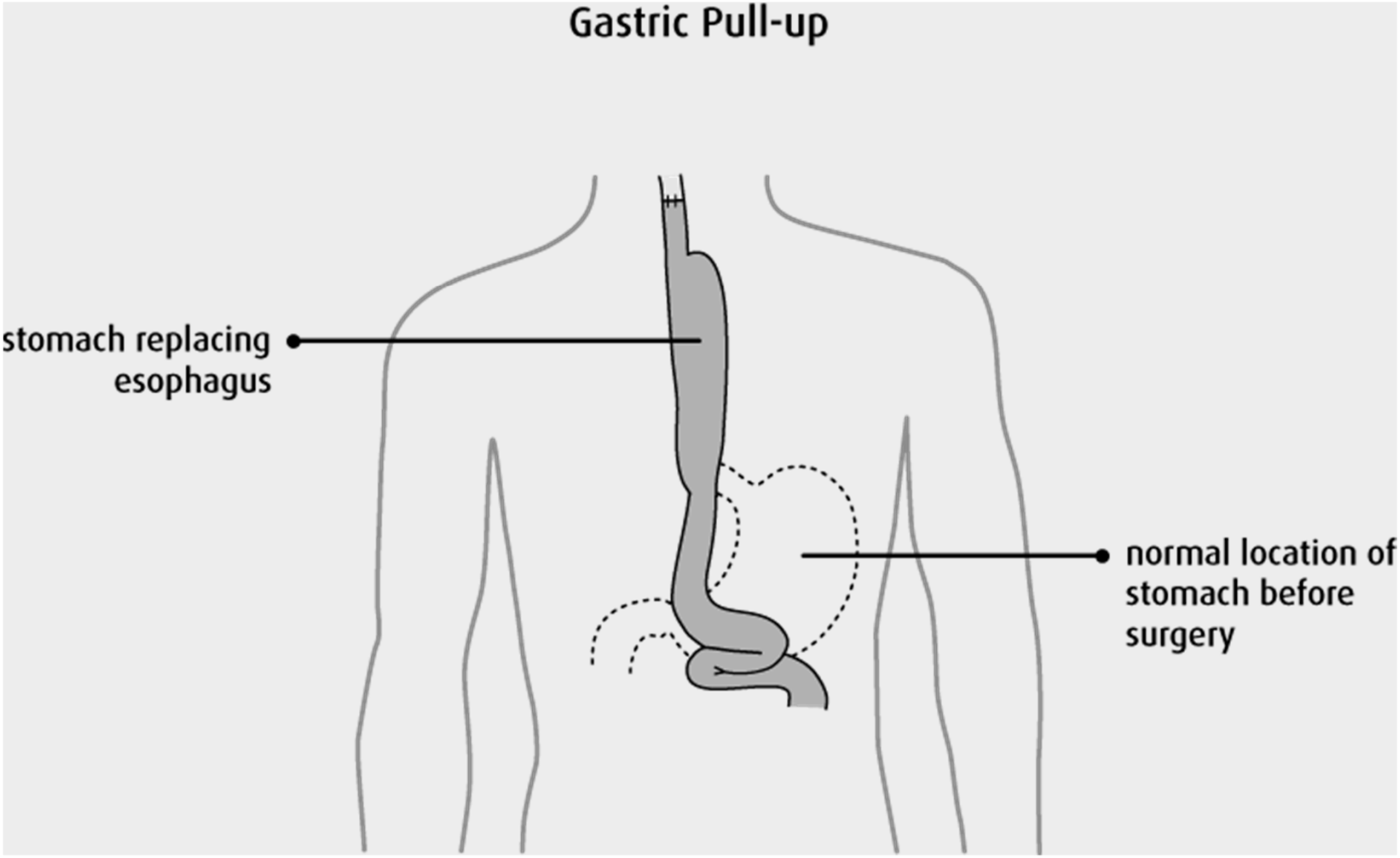
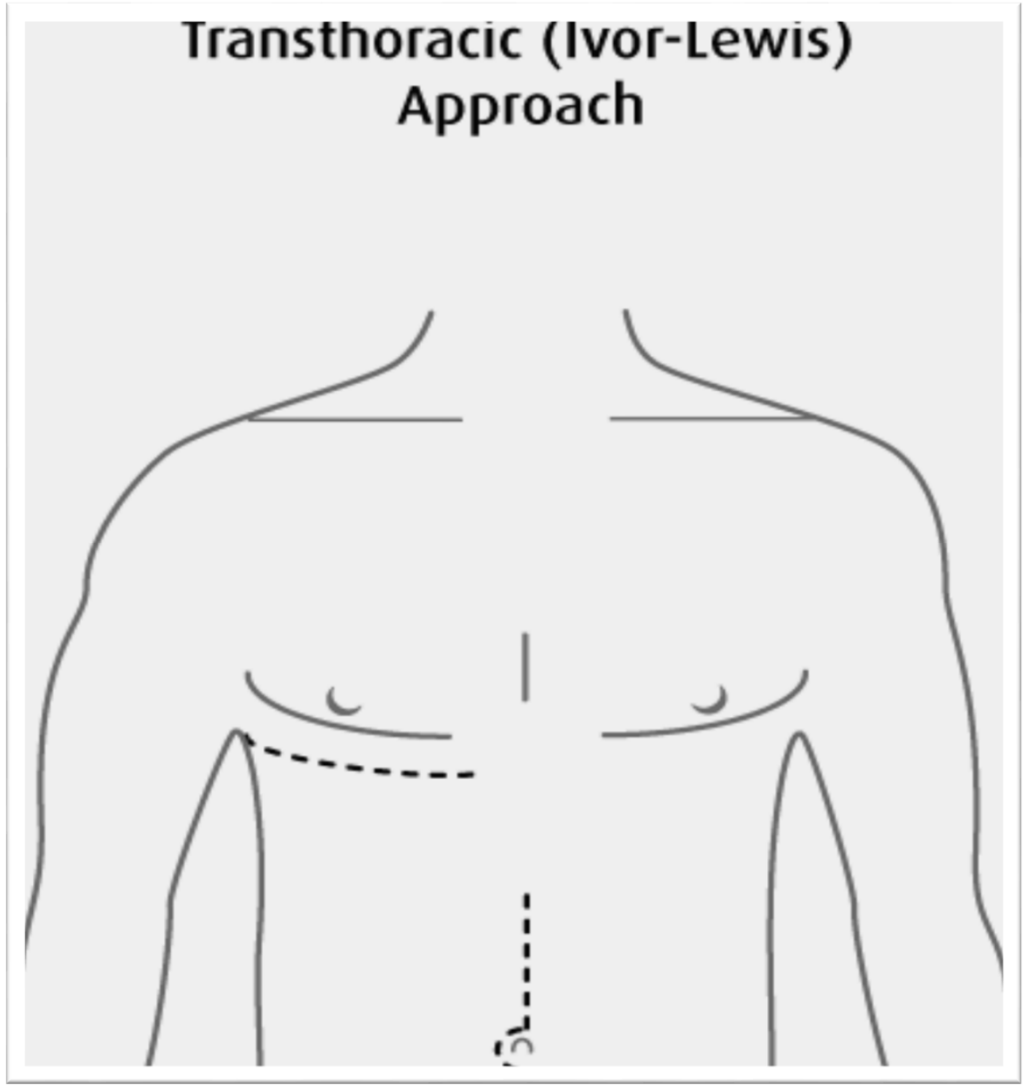


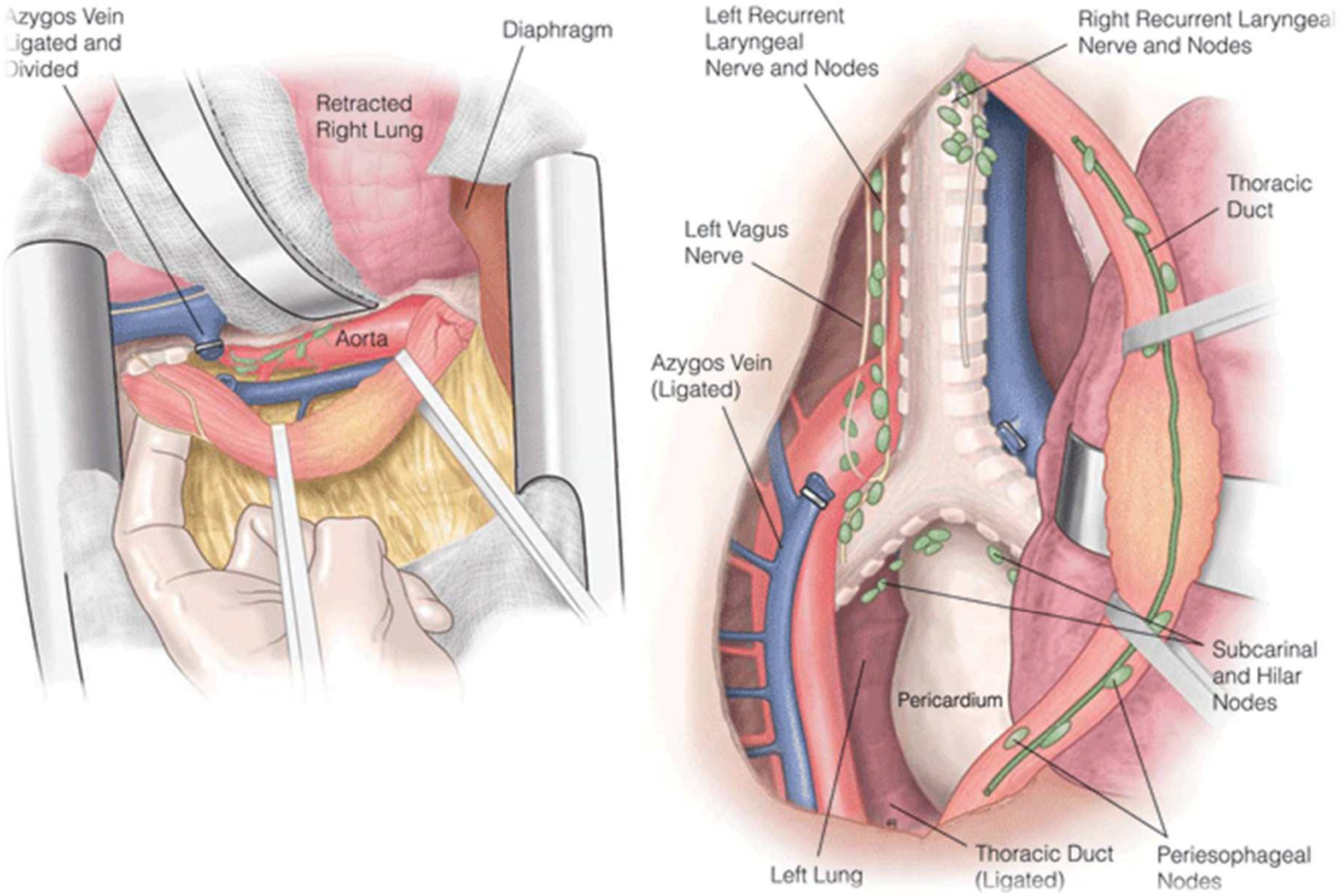
Transhiatal Esophagectomy



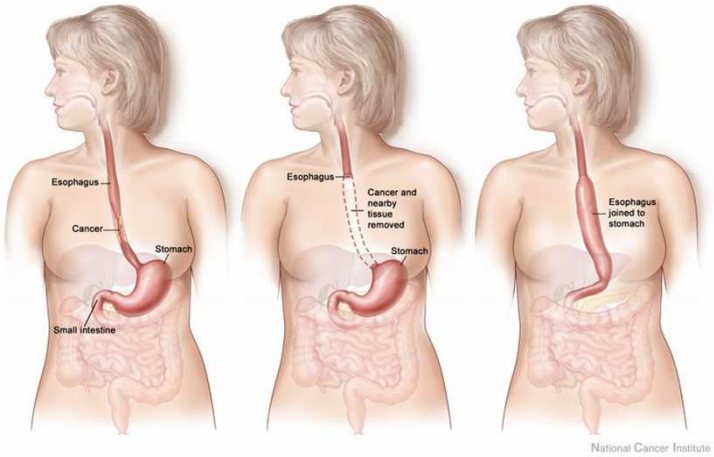
Ivor-Lewis Esophagectomy

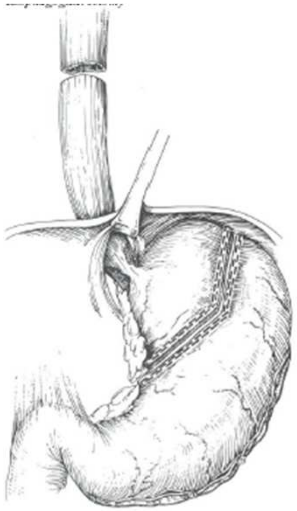


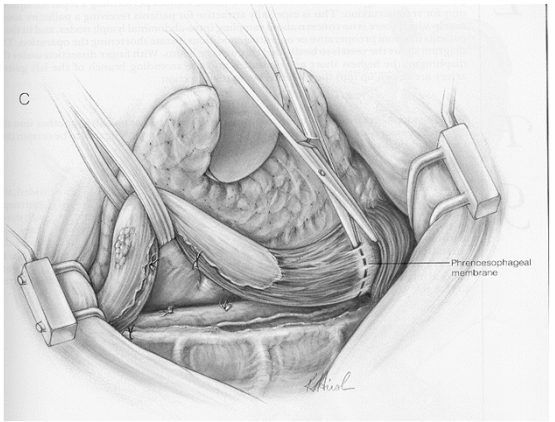
Ivor-Lewis Esophagectomy

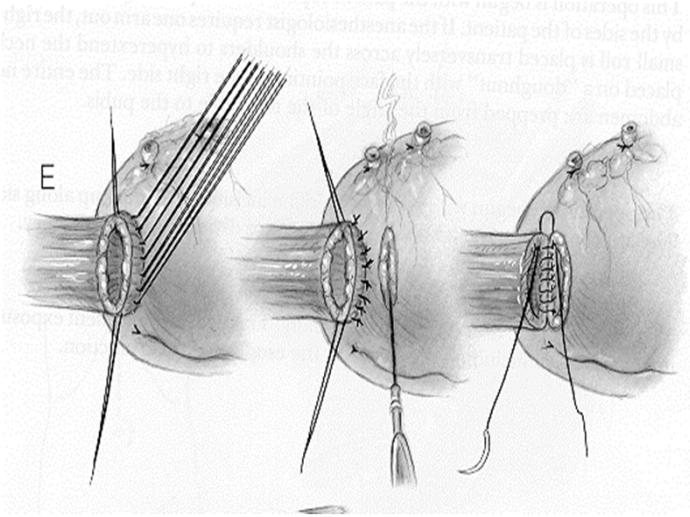


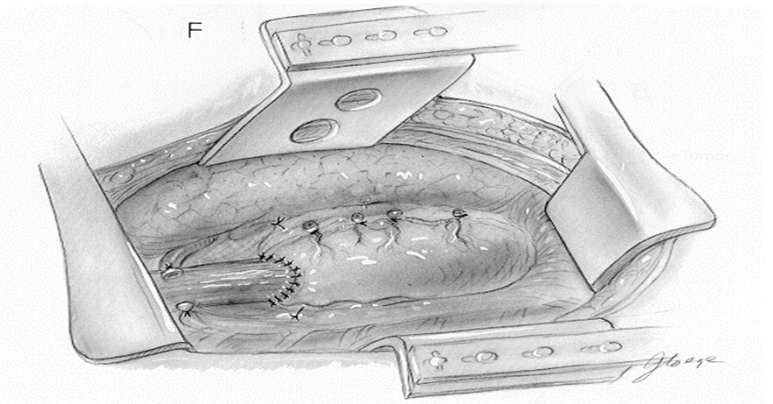
Ivor Lewis Esophagectomy











Type of anastamosis

- Hand sewn-single/double layer
- Stapler
- Circular –EEA
- Linear side to side
- Hybrid –Modified Collard technique
- Circular stapled anastomosis - significantly higher rate of anastomotic stricture
- Leak rates similar

	TH	TTS
lymph nodes retrieved	31	16
OS at completed 5 years	34%	36%

Hulscher JB, van Sandick JW, de Boer AG, et al . N Engl J Med 2002;347: 1662–9.

Comparison of Approach

Transhiatal vs. Transthoracic

- No difference in operative time, blood loss, morbidity or mortality
- 5 year Survival similar
- Anastomotic Leak rate
  - Cervical 11%
  - Thoracic 6%

Putnam et al., Annal Thor Surg, 1994

Table 4. Complications: morbidity and mortality.

	ILO (n = 33)		THO (n = 65)	
Complications	No.	%	No.	%
Death	2	6.1	3	4.6
Bleeding	1	3.0	1	1.5
Wound	6	18.2	7	10.8
Sepsis	4	12.1	4	6.2
Leak	3	9.1	3	4.6
Stricture	4	12.1	18	27.7
RLN	2	6.1	8	12.3
Respiratory problems				
Minor	5	15.2	13	20.0
Intermediate	7	21.2	17	26.2
Major	4	12.1	4	6.2

RLN: recurrent laryngeal nerve.

There were no significant differences between the two groups for any of the parameters according to Fisher's exact test.

Gluch et al. Comparison of Outcomes following Transhiatal or Ivor Lewis Esophagectomy for Esophageal Carcinoma. World J. Surg. 23, 271–276, 1999

Transhiatal Esophagectomy

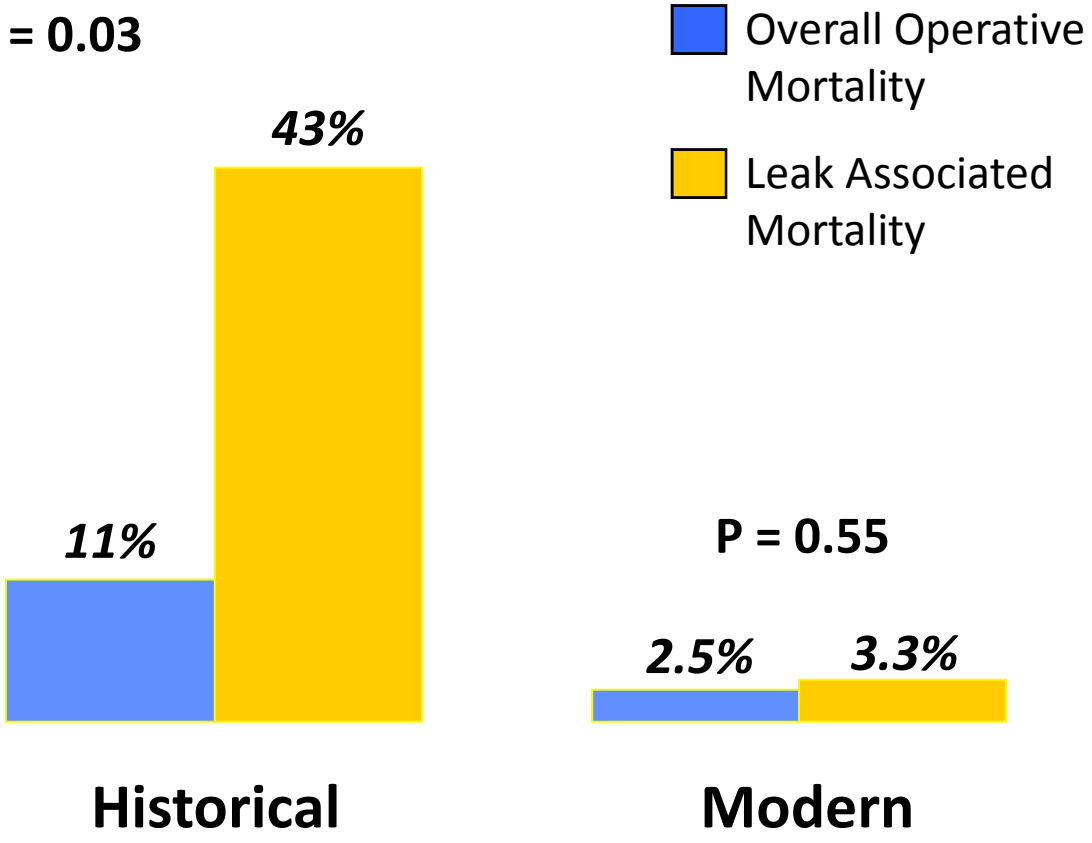
- Experienced centers report <5% mortality
- Overall survival: 20-25%
- Stage I: 60-70%
- Stage III: 5%
- 40% rate of local recurrence
- Major complication rate of 30-40%

Summary

- Transthoracic (Ivor Lewis)
  - Pros: Lower rate of leaks, More extensive lymphadenectomy, decreased stricture rate, no risk to recurrent laryngeal nerve
  - Cons: Increased pain (thoracotomy)
- Intrathoracic leak not associated with increased mortality

The Ohio State University Medical Center

Perioperative Mortality After Intrathoracic Leak



Martin et al., Ann Surg, 2006

Summary

- Debate continues as to optimal approach
  - Transhiatal
    - Pros: Avoid thoracotomy
      Technically easier operation
    - Cons: Increase rate of anastomotic leak
      Recurrent laryngeal nerve injury (aspiration)
      Limited thoracic lymphadenectomy

Summary

- There is no ideal approach to esophagectomy
- Outcomes are best when performed in high volume centers

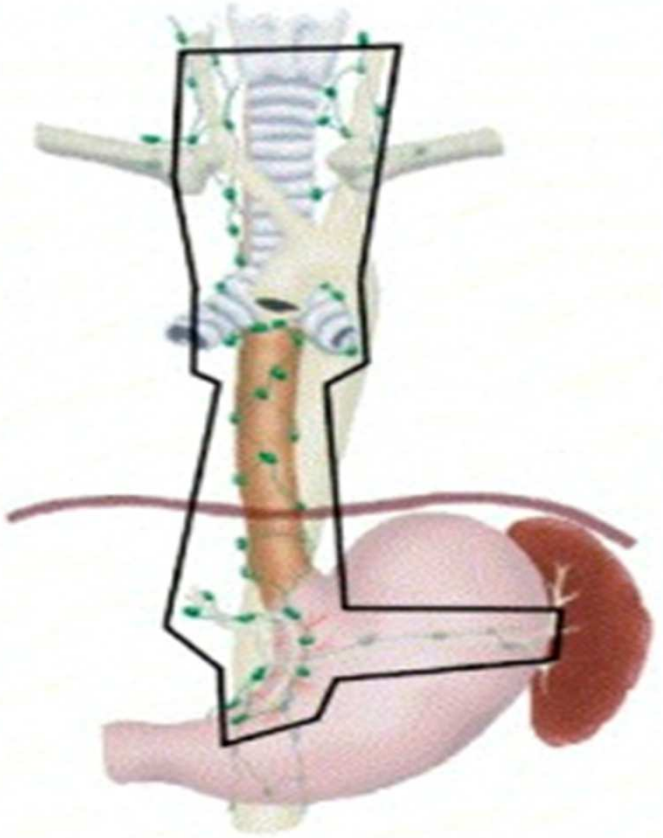
The Ohio State University Medical Center

Problem

- Both TTE and THE are equally effective in Carcinoma esophagus
- Both are an accepted form of management
- The problem is dismal 5 year survival that ranges from 25-35% in various studies.(Even lesser for locally advanced lesions)

The answer-Extended Esophagectomy

- *Two concepts*
  - *en bloc*
  - *Lymph node dissection*



Rationale for lymphadenectomy

- A rich network of submucosal lymphatics
- Prone to longitudinal spread of tumor.
- Intramural metastases
  - subepithelial spread
  - skip lesions
  - satellite nodules
- The incidence of intramural metastasis and multiple tumors is up to 30%
- Adequate axial margin in esophagectomy is important to prevent anastomotic recurrence

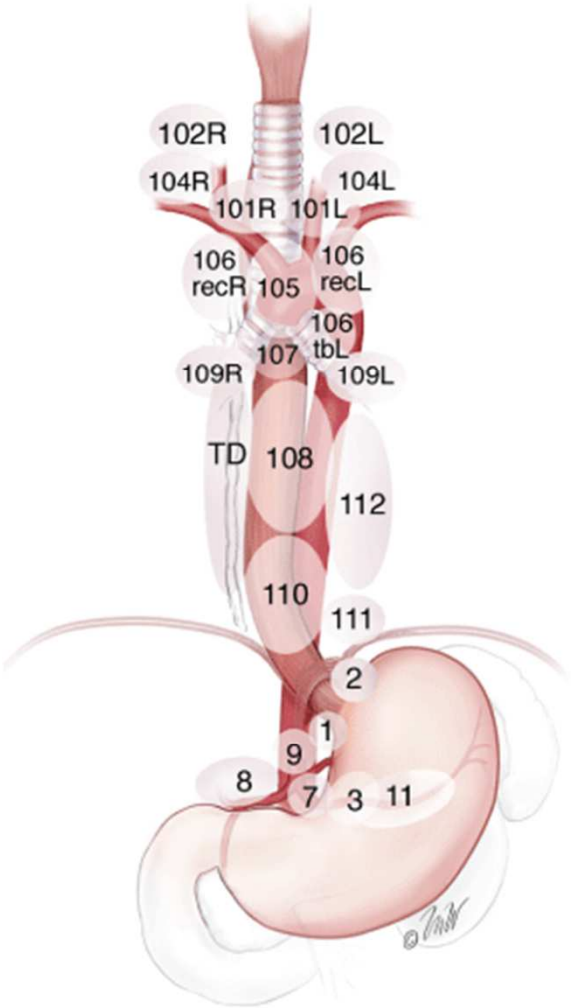
Lam KY, Ma LT, Wong J. Measurement of extent of spread of oesophageal squamous carcinoma by serial sectioning. J Clin Pathol 1996;49:124–9.

- Rationale of 3 field lymphadenectomy
  - Overall involvement of cervical nodes – 30%
  - Cervical lymph nodes are involved in 60%, 20%, and 12.5% of upper-, middle-, and lower-third tumors respectively
  - Radical esophagectomy should encompass all lymph node stations having a greater than 10% incidence of metastases.

Akiyama H, Tsurumaru M, Udagawa H, et al. Radical lymph node dissection for cancer of the thoracic esophagus. Ann Surg 1994;220(3):364–72.

Radical Three Field Esophagectomy

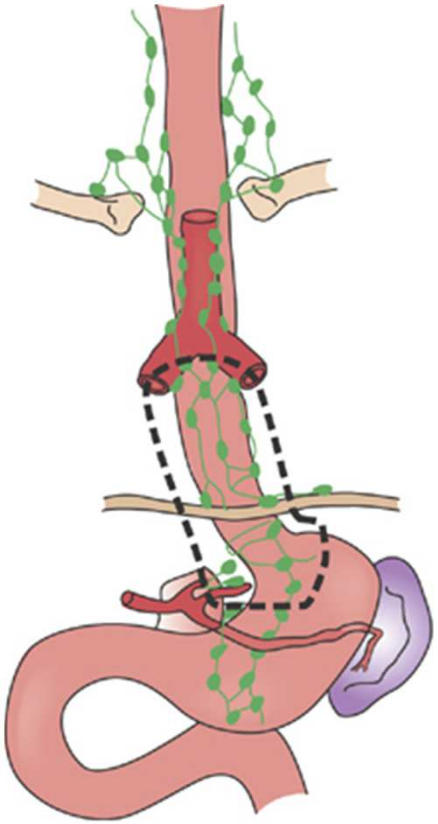
- Thoracic, abdominal and cervical incisions
- Three field lymphadenectomy
- Increased complications:
  - RLN Injury: 56 vs 30%
  - Tracheostomy: 53 vs 10%
  - Phrenic nerve injury: 13 vs 0%
  - No difference in 5-year survival
- Significant increase in morbidity with no improvement in survival



101:	Cervical paraesophageal lymph nodes
102:	Deep cervical lymph nodes
104:	Supraclavicular lymph nodes
105:	Upper thoracic paraesophageal lymph nodes
106-rec:	Recurrent nerve lymph nodes
106-tbL:	Left tracheobronchial lymph nodes
107:	Subcarinal lymph nodes
108:	Middle thoracic paraesophageal lymph nodes
109:	Main bronchus lymph nodes
110:	Lower thoracic paraesophageal lymph nodes
111:	Supradiaphragmatic lymph nodes
112:	Posterior mediastinal lymph nodes
TD:	Lymph nodes along the thoracic duct
1:	Right cardial lymph nodes
2:	Left cardial lymph nodes
3:	Lymph nodes along the lesser curvature
7:	Lymph nodes along the left gastric artery
8:	Lymph nodes along the common hepatic artery
9:	Lymph nodes along the celiac artery
11:	Lymph nodes along the splenic artery

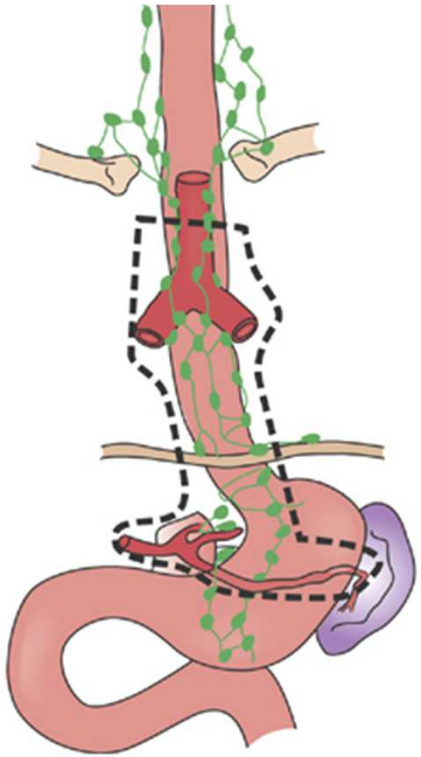
Source: Sugarbaker DJ, Bueno R, Krasna MJ, Mentzer SJ, Zellos L: *Adult Chest Surgery:*
http://www.accesssurgery.com

Standard esophagectomy



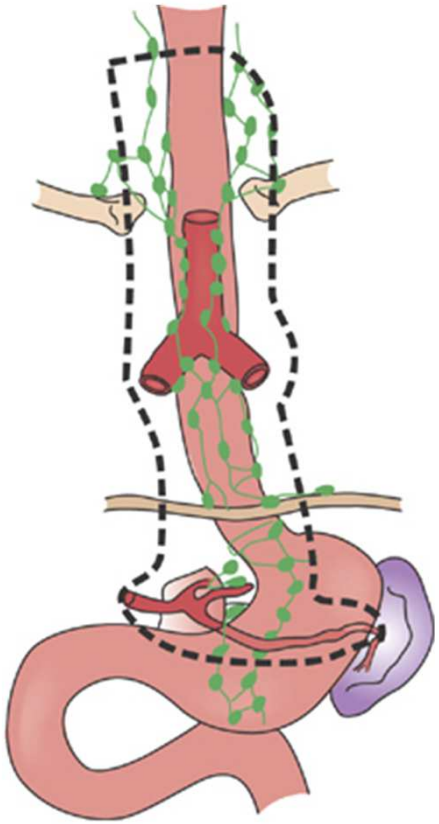
- Paraesophageal nodes
- Subcarinal nodes
- Right and Left bronchial nodes below the tracheal bifurcation

Two field Esophagectomy



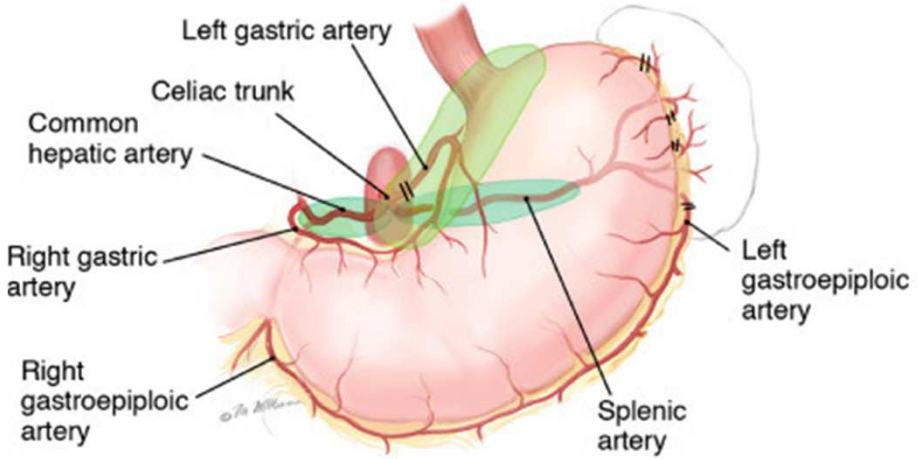
All nodal groups between the tracheal bifurcation superiorly to the celiac axis inferiorly

Three field esophagectomy



Excision of the nodes along both recurrent nerves as they course through the mediastinum and neck, as well as a modified cervical node dissection

Includes the nodes posterior and lateral to the internal jugular vein and an infraomohyoid node dissection bilaterally



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

ABDOMINAL FIELD:

Lymph nodes around the celiac trifurcation should be resected

Rationale of 3 field lymphadenectomy

- Overall involvement of cervical nodes – 30%
  - Upper- 60%,
  - Middle-20%
  - Lower-12.5%
- Radical esophagectomy should include all lymph node stations having a greater than 10% incidence of metastases.

Akiyama H, Tsurumaru M, Udagawa H, et al. Radical lymph node dissection for cancer of the thoracic esophagus. Ann Surg 1994;220(3):364–72.

DISADVANTAGES OF 3-FIELD DISSECTION

- The greater the extent of dissection, the better the prognosis and local control might be; but the higher would be the surgical risks.

- Double edged sword

Three field lymphadenectomy

- Early stage esophageal carcinoma
- SCC of cervical and thoracic esophagus
- Backup of extremely good ICU care
- Careful selection of cases

- Although the optimal extent of lymph node clearance has always been under debate, the superiority of extended lymphadenectomy has rendered it a standard procedure in more than 70% of institutions in Japan

Isono K, Sato H, Nakayama K. Results of a nationwide study on three-field lymph node dissection of esophageal cancer. Oncology 1991;48:411–20

Kato H, Watanabe H, Tachimori Y, Iizuka T. Evaluation of neck lymph node dissection for thoracic esophageal carcinoma. Ann Thorac Surg 1991;51:931–5.

- It provides more accurate tumor staging

- Japanese Association of Esophageal Oncology Group carried out a nationwide survey on lymphadenectomy among 96 institutions in 1991

Isono K, Sato H, Nakayama K. Results of a nationwide study on three-field lymph node dissection of esophageal cancer. Oncology 1991;48:411–20.

	2-field	3 – field
Rate of lymph node metastasis	58.7%	72.9%
Rate of mediastinal metastasis	40.8%	55.8%

Indicates more thorough lymph node clearance

Predicting systemic disease in patients with esophageal cancer after esophagectomy: study on the significance of the pN+

- Multinational retrospective review
- 700 Adenoca, 353 SCC undergoing oesophagectomy alone
- Systemic disease recurrance:
  - 40% Overall
  - 16% if pN0 Lymph nodes
  - 93% with >8 involved

Peyre CG, Hagen JA, DeMeester SR et al.
Ann Surg 2008 Dec;248(6):979-85

MERITS OF EXTENDED LYMPH NODE DISSECTION FOR ESOPHAGEAL CANCER

- The chance of cure would be increased
- Risk of early local-regional recurrence reduced
- Lack of other effective adjuvant therapies, it is not surprising to observe a high recurrence rate in mediastinal or cervical lymph nodes shortly after surgery

Ilson DH, Kelsen DP. Combined modality therapy in the treatment of esophageal cancer [Review]. Semin Oncol 1994; 21:493–507.

Lymphadenectomy-

How many?
Which all?
Does it make a difference?

Optimum Lymphadenectomy for Esophageal Cancer

Nabil P. Rizk, MD, Hemant Ishwaran, PhD,† Thomas W. Rice, MD,† Long-Qi Chen, MD,‡ Paul H. Schipper, MD,§ Kenneth A. Kesler, MD,¶ Simon Law, MD,‖ Toni E. M. R. Lerut, MD, PhD,** Carolyn E. Reed, MD,†† Jarmo A. Salo, MD,‡‡ Walter J. Scott, MD,§§ Wayne L. Hofstetter, MD,¶¶ Thomas J. Watson, MD,‖‖ Mark S. Allen, MD,*** Valerie W. Rusch, MD,* and Eugene H. Blackstone, MD†*

(*Ann Surg* 2010;251: 46–50)

From the *Memorial Sloan-Kettering Cancer Center, New York, NY; †Cleveland Clinic, Cleveland, OH; ‡West China Hospital of Sichuan University, Chengdu, Sichuan, People's Republic of China; §Oregon Health and Science University, Portland, OR; ¶Indiana University, Indianapolis, IN; ‖Queen Mary Hospital, University of Hong Kong Medical Center, Hong Kong, China; **University Hospital Leuven, Leuven, Belgium; ††Medical University of South Carolina, Charleston, SC; ‡‡Helsinki University Central Hospital, Helsinki, Finland; §§Fox Chase Cancer Center, Philadelphia, PA; ¶¶University of Texas MD Anderson Cancer Center, Houston, TX; ‖‖University of Rochester. Rochester. NY: and the ***Mavo Clinic. Rochester. MN.

Method

- Deta base : Worldwide Esophageal Cancer Collaboration data.
- The entire project was approved by the Case Cancer Institutional Review Board of Case Western Reserve University.
- Method : total of 4627 patients who had esophagectomy alone for esophageal cancer. (no pre- or postoperative adjuvant therapy) for esophageal cancer and had follow-up for all-cause mortality.)
- Risk-adjusted 5-year survival was averaged for each number of lymph nodes resected.

Result

pN0M0 Cancers

pTis cancers

regardless of histopathologic cell type, survival was excellent and **not associated** with extent of lymphadenectomy.

T1N0M0 cancers

G1 : survival **was unrelated** to extent of lymphadenectomy

G2/G3 cancers : survival was increased with more extensive lymphadenectomy

Result

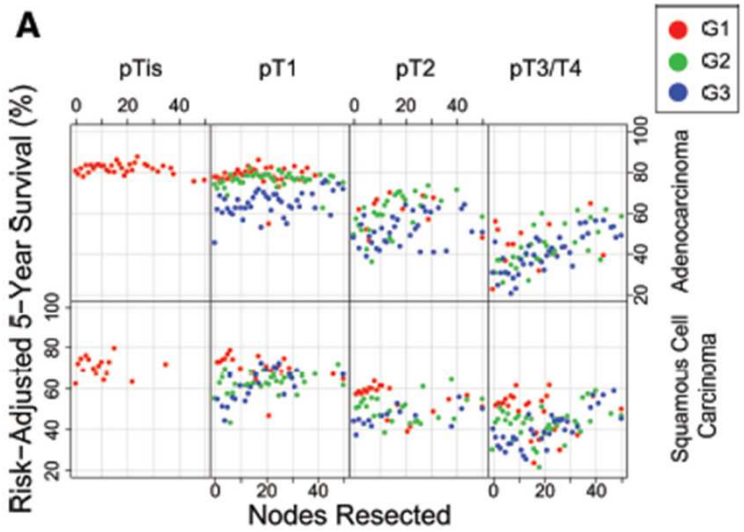
pN0M0 Cancers

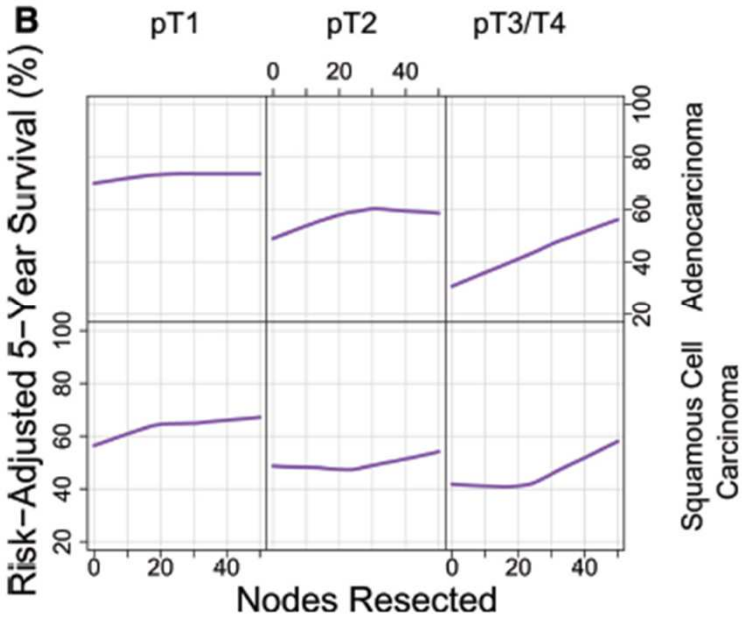
T2N0M0 and T3/T4N0M0 cancers

G1 : limited data , due to few case number

<u>G2/G3 cancers : survival was increased with more extensive lymphadenectomy</u>

•.





Result

N+M0 Cancers

1 to 6 nodes positive (N1~2)

survival increased with extent of lymphadenectomy for all T classifications

7 or more nodes positive

T2 and T3/T4 cancers : Survival increased, albeit minimally, with extent of lymphadenectomy

T1 : very few case number to assessing the survival value

Discussion

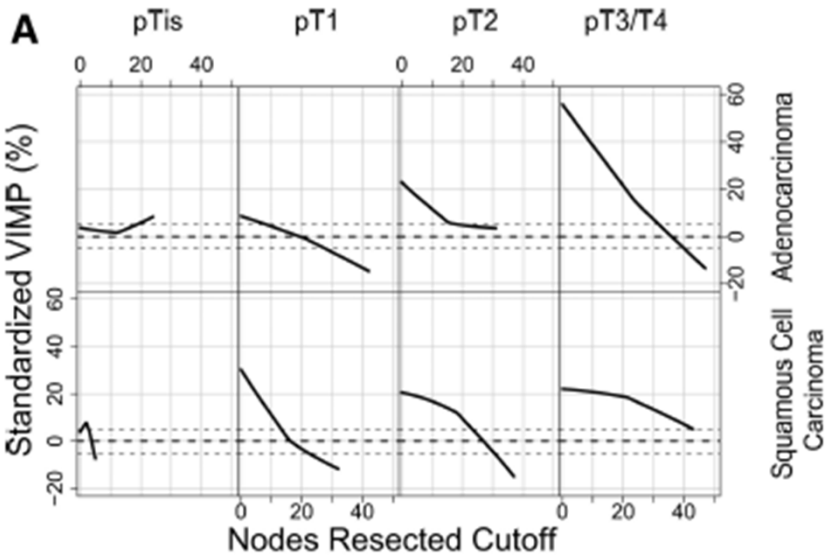
- Extent of lymphadenectomy was either unassociated with or minimally increased survival for patients with **extremes of esophageal cancer (TisN0M0 and T2N3 lesion)** and those with **well-differentiated(G1) pN0 cancer.**
- pN+ cancers
  - improved survival!!
  - more accurate determination of number of positive nodes (stage purification), or therapeutic effect of removing micrometastases.

Recommendations

- If there is uncertainty as to T and histopathologic grade, it is recommended that 30 or more nodes be resected to maximize 5-year survival.
  - It is recommended that to maximize 5-year survival, a minimum of 10 nodes be resected for T1 cancer, 20 nodes for T2 cancer, and 30 or more nodes for T3/T4 cancers.

Optimum Lymphadenectomy

- pTis
  - no optimum extent of lymphadenectomy
- pT1 N0M0 cancers
  - 10 for adenocarcinomas
  - 12 for squamous cell carcinomas
- pT2 N0M0 cancers
  - 15 for adenocarcinomas
  - 22 for squamous cell carcinomas
- T3/T4N0M0 cancers
  - 31 for Adenocarcinomas
  - 42 for squamous cell carcinomas



Optimum number of nodes resected was determined by the value at which standardized VIMP first dropped below 5%.

Lymphadenectomy-AJCC 7

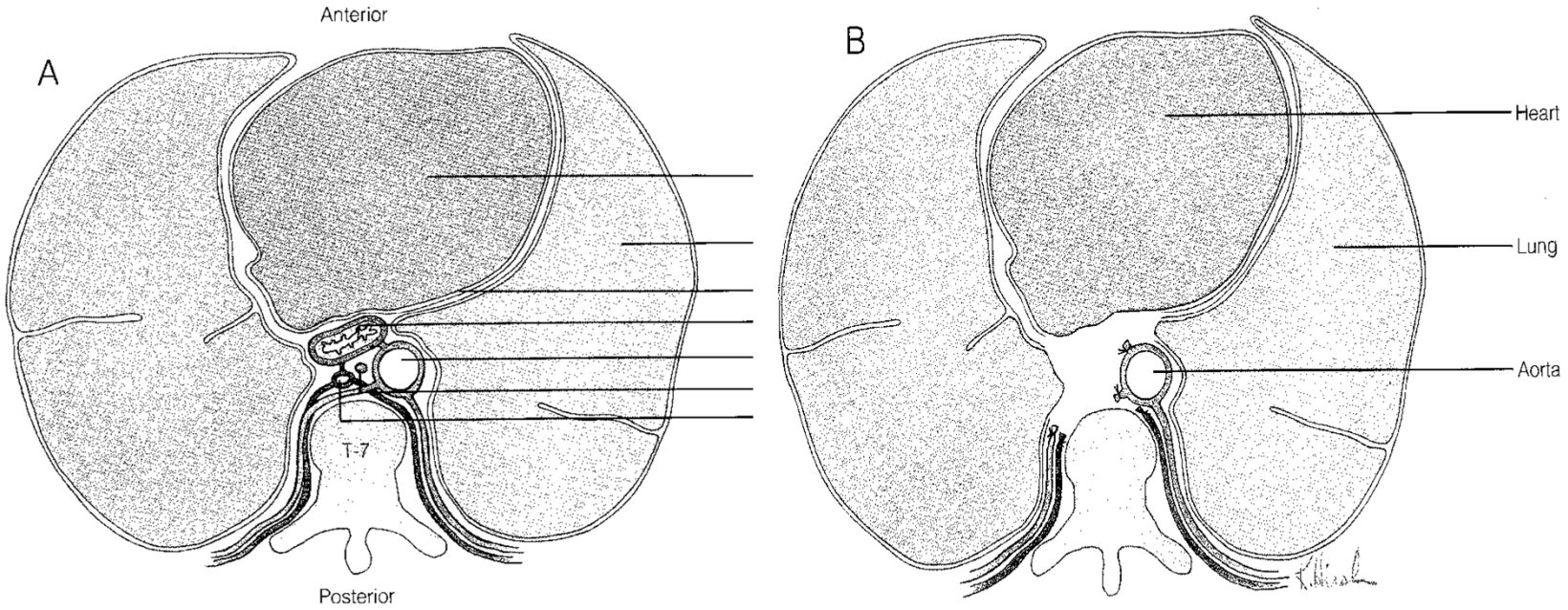
- Prognosis is Dichotomized between LN positive and LN negative
- Based on pooled data of 7800 esophagectomy predominantly squamous cell type
- The data has been validated in adenocarcinoma
- Worldwide Esophageal Cancer Collaboration (WECC)

Stage	***LN No.***
T1	**10**
T2	**20**
T3-4	**30**

En-Bloc Esophagectomy

- Concept of en-bloc resection, as originally proposed by Logan and later reintroduced by Skinner 1968
- Resecting the tumor-bearing esophagus within a wide envelope of surrounding tissues
- ***Pericardium anteriorly and both pleural surfaces laterally, as well as the azygous vein, thoracic duct and all other lympho-areolar tissue wedged posteriorly between the esophagus and the spine***
- ***1-in cuff of diaphragm is excised circumferentially for GE junction tumor***
- Concept is valid for lower thoracic and GE junction tumor
- Aims to maximize local tumor control
- Can be combined with a two field or three field esophagectomy

En-Bloc Esophagectomy



COMPLICATIONS

Mortality rate	4%
Anastomotic leaks	19% to 30%
Sepsis	27%
Recurrent laryngeal nerve palsy	>50%
	long-term quality of life in terms of speech, swallowing, and respiratory functions
Tracheal ischemic necrosis is specific for extensive superior mediastinal dissection	

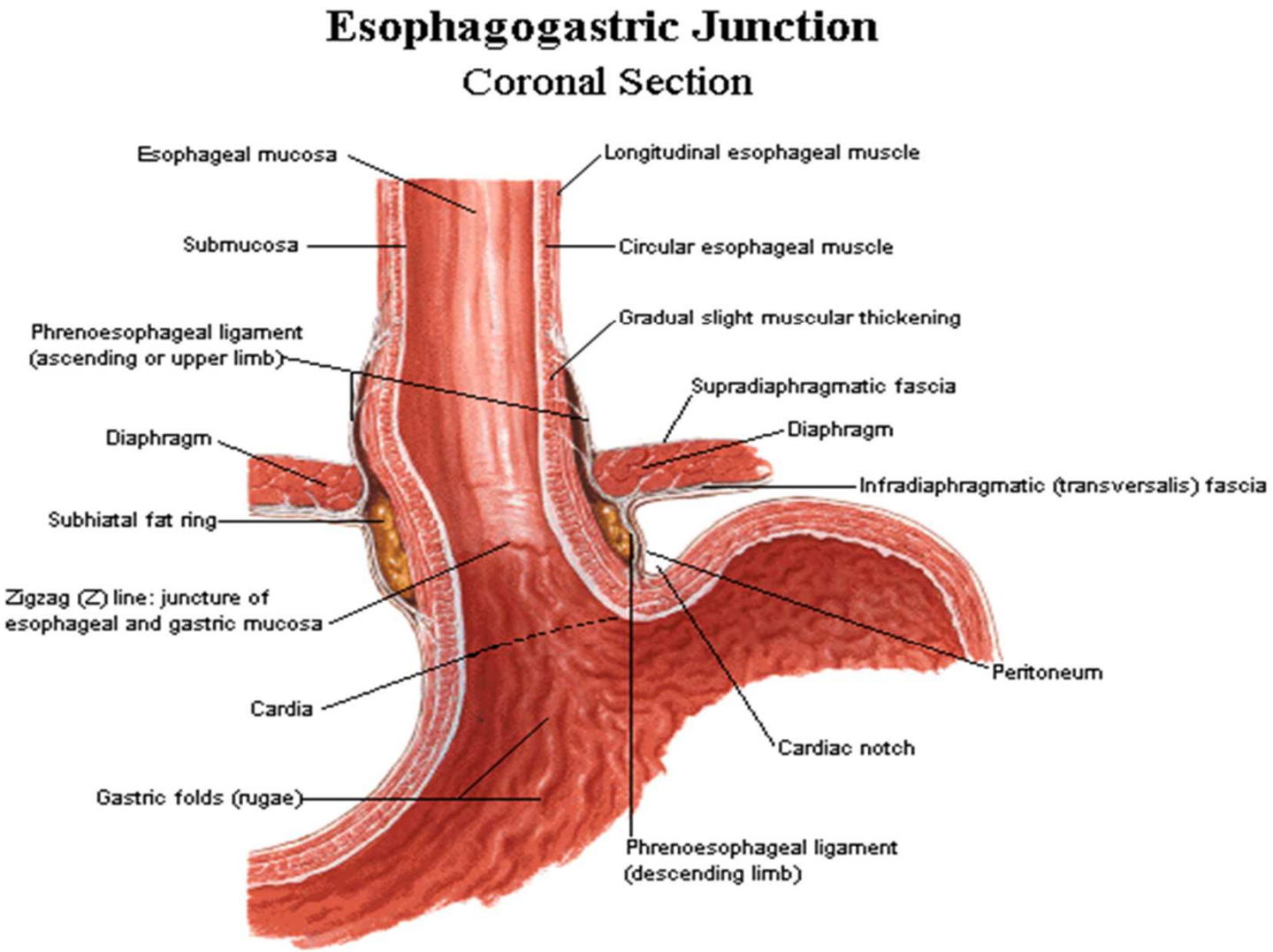
Tachibana M et al. Arch Surg 2003;138(12):1383–9.

GE JN CANCER

- Incidence of adenocarcinoma of the EGJ has been increasing at 5 to 10 percent annually since the mid 1970s

- Most rapidly increasing cancer in many Western countries

What is the GE Junction



Definition

- Anatomical: EGJ is localized at the level of the angle of His , paraesophageal pad of fat
- Physiological: Distal border of the lower esophageal sphincter, as determined by manometry.
- Endoscopically :

  -Z line- squamo columnar junction - 3 to 10 mm proximal to the anatomically defined EGJ

  -Proximal most extent of gastric rugosal folds →transitioning to smooth lined esophageal mucosa
- Pathological: In an opened esophagogastrectomy specimen as the most proximal aspect of the gastric folds.

Classification

- Siewert's classification

Professor
J Rudger Siewert

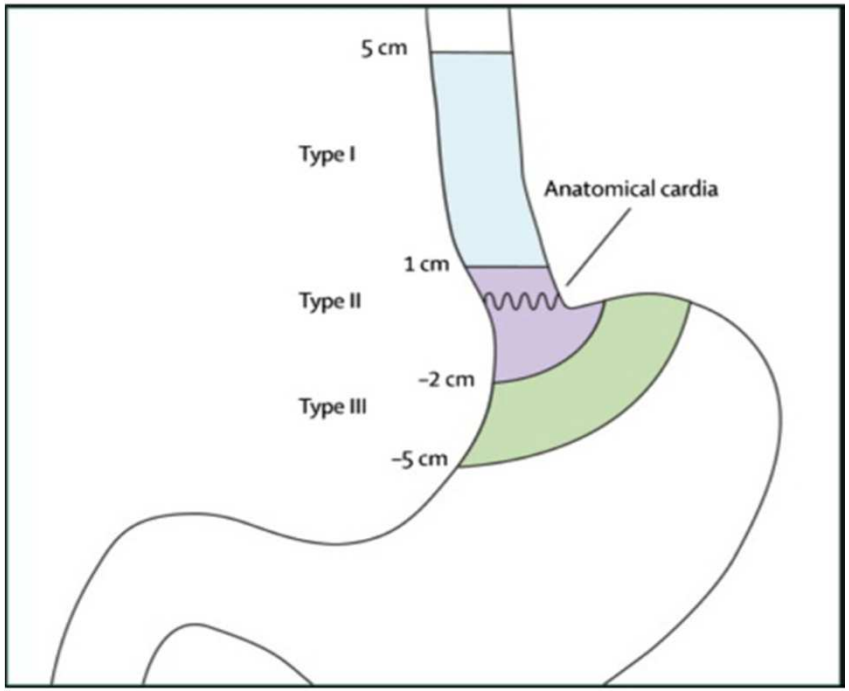
Adenocarcinoma of the Esophagogastric Junction

Results of Surgical Therapy Based on Anatomical/Topographic Classification in 1,002 Consecutive Patients

J. Rüdiger Siewert, MD, FACS(Hon), FRCS, FASA,* Marcus Feith, MD,* M. Werner, MD,† and Hubert J. Stein, MD*

*From the *Chirurgische Klinik und Poliklinik and †Institut für Pathologie und Pathologische Anatomie, Klinikum rechts der Isar, Technische Universität München, Munich, Germany*

2000 Modified
Siewert's classification



AJCC 7th edition

Siewert Types I and II- esophageal cancer

Siewert Type III - gastric cancer

Esophagectomy Morbidity

	Michigan	VA	MSKCC	Duke
Leak	12%	NR	21%	14%
Pneumonia	2%	21%	21%	16%
RLN Injury	4.5%	NR	4%	NR
Conduit Necrosis	2%	NR	NR	NR
Chylothorax	1%	0.02%	NR	NR
MI	NR	1.2%	NR	NR
Tracheal Injury	0.4%	NR	NR	NR
Splenectomy	2%	NR	NR	NR
Diaphragm Hernia	NR	NR	1.2%	NR

High Volume Centers for Esophagectomy: Number needed to achieve low post-operative mortality

- Reduction in post-op mortality with increasing case volumes per year
- Post-op complication rates are lower in high-volume hospitals

Metzger, R. et al. Dis of the Esophagus, Vol17(4)310,Dec, 2004

The Ohio State University Medical Center

Surgery , future…?

MIE Techniques

- Thoracoscopic; laparotomy
- Laparoscopic; thoracotomy
- Laparoscopic; transhiatal
- Thoracoscopic; laparoscopic

The Ohio State University Medical Center

MIE vs Open

	MIE	Transthoracic	Transhiatal
Operative time	364	437	391
Blood Loss	297	1046	1142
Intraop Transfusion	0.3	1.8	2.9
ICU Stay	6.1	9.9	11.1
Hospital Stay	11.3	23.0	22.3
No. LN's Removed	10.8	6.3	6.9

MIE

- Minor complications 53 (24%)
- Major complications 71 (32%)

Complication	N (%)	Complication	N (%)
Death	3 (1.4)	Chylothorax	7 (3.2)
Leak	26 (11.7)	Gastric necrosis	7 (3.2)
Pneumonia	17 (7.7)	Delayed gastric empying	4 (1.8)
Pleural effusion	14 (6.3)	Tracheal injury	4 (1.8)
Recurrent nerve palsy	8 (3.6)	ARDS	4 (1.8)

Minimally invasive versus open -RCT

- Multicentre,RCT –Only RCT available
- June 1, 2009, and March 31, 2011
- Primary outcomes-Pulmonary infections

	Open(n=56)	MIS(n=59)	*p*
Pulm Infection	29%	9%	0.005
Pulm Infection (Hosp)	34%	12%	0.005

Surya S A Y Biere,et al, Lancet 2012

Minimally invasive versus open -RCT

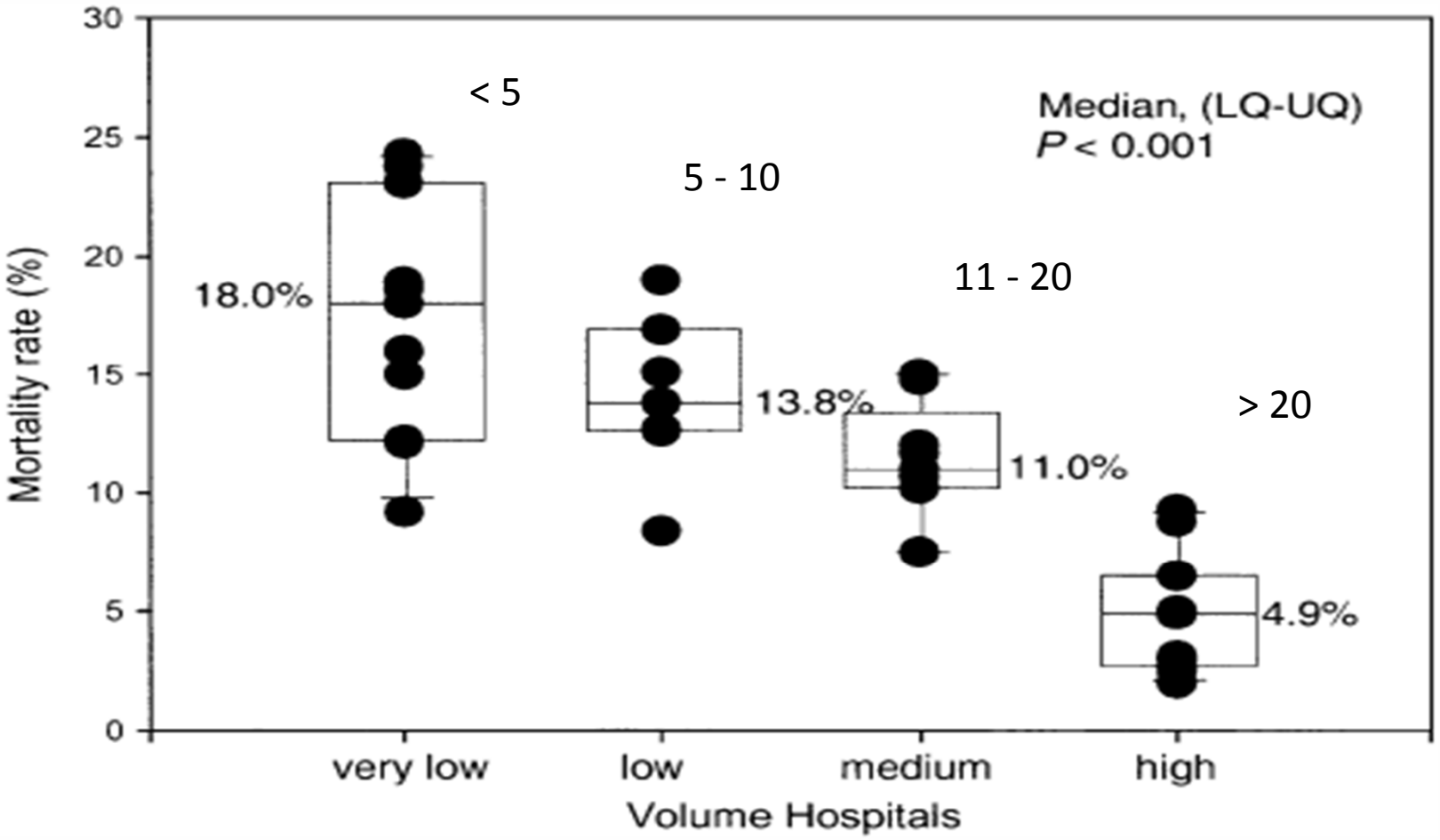
Secondary outcomes

Secondary outcomes	Open(n=56)	MIS(n=59)	p
Hospital stay	14 Days	11 Days	0.04
SF-36	36	42	0.007
Lymphnode	21	20	0.8
Margins			
R0	84%	92%	
R1	9%	2%	

Surya S A Y Biere,et al, Lancet 2012

Hospital-Volume Outcome: Esophagectomy

Metzger et al. *Dis Esoph*; 2004, 17:310-314



High Volume Centers: What is the number needed to achieve low post-operative mortality

- Management of complications is more successful in high-volume hospitals
- Long-term prognosis is also correlated to case-volume
- With the experience of > 20 esophagectomies/yr mortality <5% can be achieved

Metzger, R. et al. Dis of the Esophagus, Vol17(4)310,Dec, 2004

The Ohio State University Medical Center

Results of surgery alone

Surgical mortality	<10 %
Med survival	16m
Med survival - R0	27m
3 yr survival	26 %

Underscores need for adjuvant therapy

Most recurrences following esophagectomy are systemic

	Pattern of Recurrence post Esophageal Cancer Resection (%)		
	Locoregional	Hematogenous / distant	Mixed
Osugi Oncol Rep 2003	11	58	-
Kato Anticancer Rsrch 2005	22	51	27
Fahn ATS 1994	33	61	-
Abate JACS 2010	30	60	10

Results of surgery alone patterns of failure

Local recurrence	30 %
Distant mets	50 %

Underscores need for adjuvant therapy

Neoadjuvant

- **NA Chemotherapy**
- **NA Radiotherapy**
- **NA chemoradiotherapy**
- **Chemoradiotherapy Vs Chemotherapy**

Neoadjuvant Chemotherapy +/- Radiation Therapy

- **Rationale**
  - **Down-staging of tumor**
    - **Increase “resectability” rate**
    - **Improve the ability of surgeon to perform a complete (R0) oncologic resection**
  - **Potentially prevent systemic spread at the earliest time-point of treatment**
  - **Tumor “oxygenation” may be better prior to surgery, thus enhancing effectiveness**
  - **Better compliance than if given post-operative**
  - **Better assessment of biology of tumor**
    - **20% have complete pathologic response**
  - **Recent data has shown a survival advantage**

Meta-analysis

- Ten randomised comparisons of neoadjuvant chemoradiotherapy versus surgery alone (n=1209) and
- Eight neoadjuvant chemotherapy versus surgery alone (n=1724) in patients with local operable oesophageal carcinoma

- Survival benefit was evident for preoperative chemoradiotherapy (13% at two years)
- No survival benefit of chemotherapy in squamous cell carcinoma and lesser survival benefit (7%) with adenocarcinoma of the oesophagus.

Lancet Oncol 2007

Palliative Therapy

- **Epidemiology**
  - **>50% patients are inoperable due to:**
    - **Unresectable tumor**
    - **Metastatic disease**
    - **Poor medical condition**
- **Goal**
  - **Relieve dysphagia rapidly with no hospital stay**
- **Basic principles**
  - **Currently, no indication for “palliative esophagectomy”**
  - **Treatment should be individualized**
    - **Wide range of options**