Esophageal Cancer

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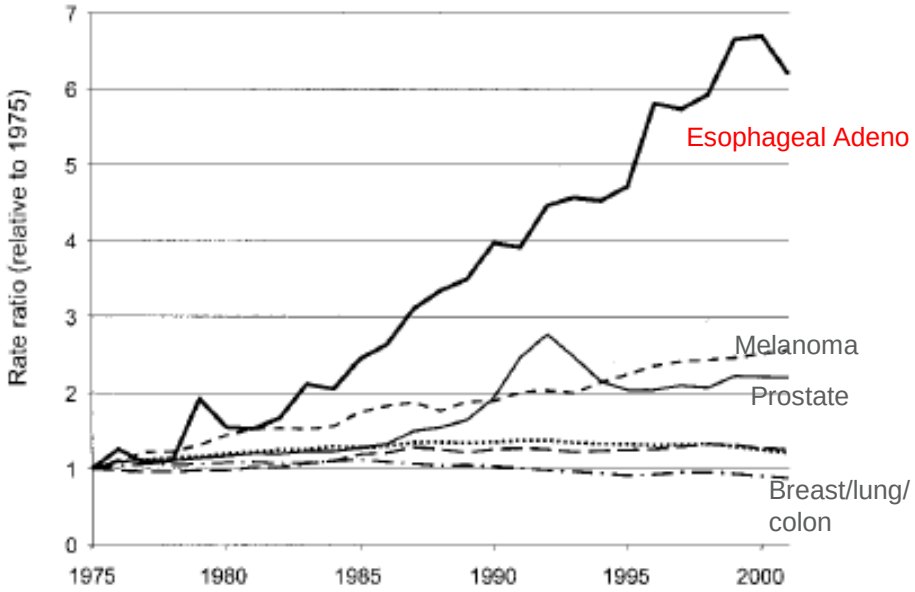
No Disclosures

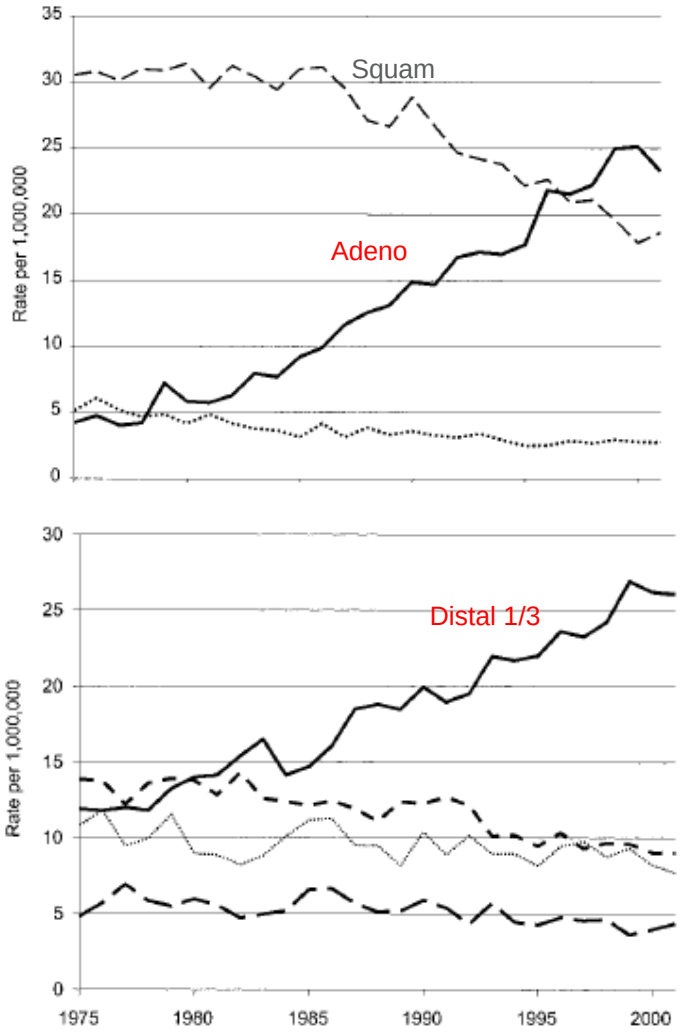
Learning Objectives

- Review the classification scheme for GE junction cancers
- Review workup and evaluation
- Review Minimally Invasive Esophagectomy

Epidemiology

- Esophageal Cancer is 6th leading cause of death worldwide
- Incidence has been rising in Western countries
  - ~17,000 cases anticipated 2015 in US
- Adenocarcinoma – 70%
  - Obesity, GERD, Barretts
- Squamous Cell Carcinoma – 30%
  - Tobacco, Alcohol





Pohl & Welch, JNCI 2005

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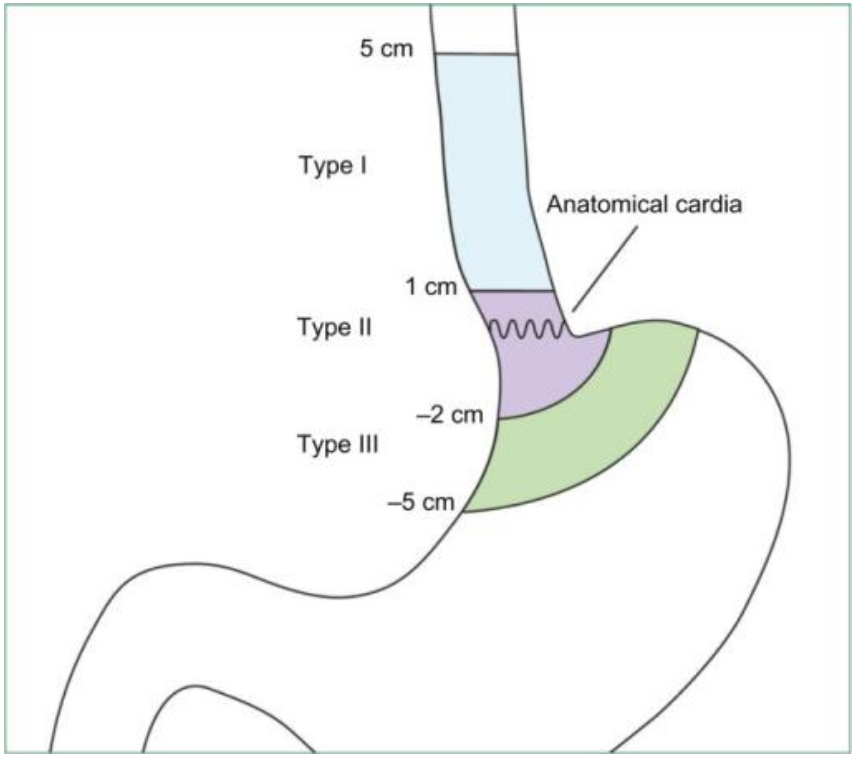
Cancer at the GE Junction

Siewart Classification

- I – located in the distal 5 cm of esophagus, but does not cross GE junction
- II – centered around the GE junction
- III – greater than 5 cm distal to the GE junction
  - Treated as Gastric Cancer



Marriette, Lancet Onc 2011

Patient Examples of GE Junction Cancer

Esophageal Cancer I/II

Gastric Cancer III

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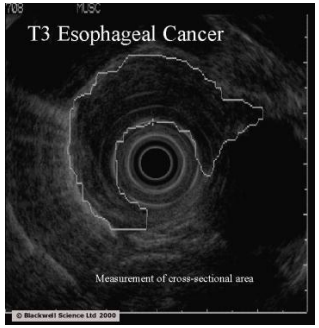
Evaluation of the Esophageal Mass

- High quality endoscopy
  - Defines the anatomic esophagogastric junction
  - Describes the anatomic location
- Endoscopic ultrasound (EUS)
  - Assessment of T-stage; Nodal involvement
  - FNA of suspicious node
- CT / PET



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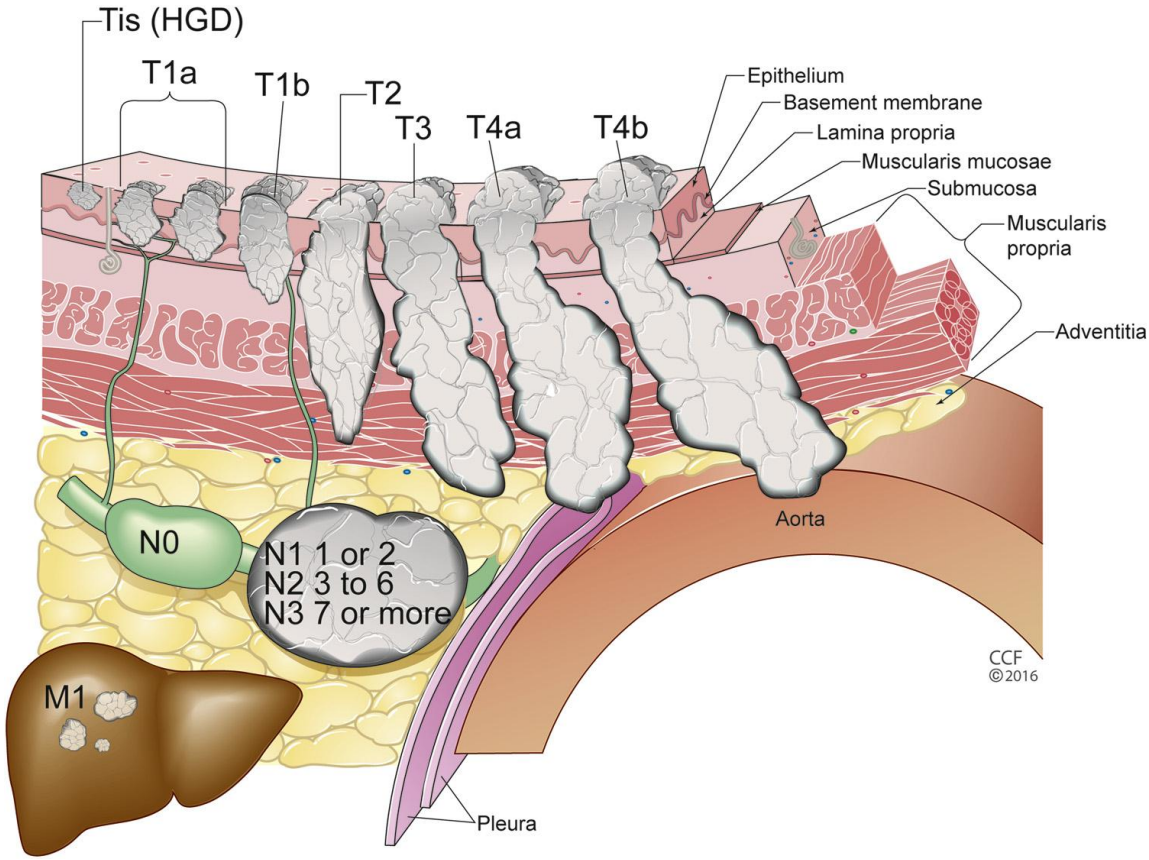
Staging of Esophageal Cancer

T Stage

- T1a : lamina propria, muscularis mucosa
- T1b : submucosa
- T2 : muscularis propria
- T3 : adventitia
- T4 : adjacent structures

N Stage

- N1 : 1-2 nodes
- N2 : 3- 6 nodes
- N3 : ≥ 7 nodes



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J Thoracic Surg 2017

Accuracy of EUS for T Stage / Nodes

- Operator dependent
- Very good at early vs late (ie T1 vs T3/4)
- More difficult discerning between earlier lesions (ie T1a vs T1b vs T2)

- Review of 107 patients with early stage (Tis, T1) compared to final pathology
- Understaging:
  - 30% of T1a
  - 49% of T1b
- Overstaging:
  - 29% of T1a
  - 51% of T1b

J Thor and Cardiovas Surg 2014

Risk of Nodal Disease Based on T stage

- Lymph node involvement greatest predictor of prognosis
- T stage is best predictor of lymph node involvement

	T1	T1a	T1b	T2	T3	T4
Squamus	20%	0-3%	5-40%	40%	60%	80%
Adeno	10%	0-2%	0-40%	50%	80%	90%

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Clin Endosc 2014

Staging Laparoscopy

- Used selectively in patient with Type II/III tumors
- Yield is variable (5%-30%)
- Extraluminal assessment of tumor location
- Evaluate future conduit
- Placement of feeding jejunostomy

Early Stage (T1, N0)

- Endoscopic Therapies for Tis or T1a
  - EMR / ESD followed by ablation
- Esophagectomy

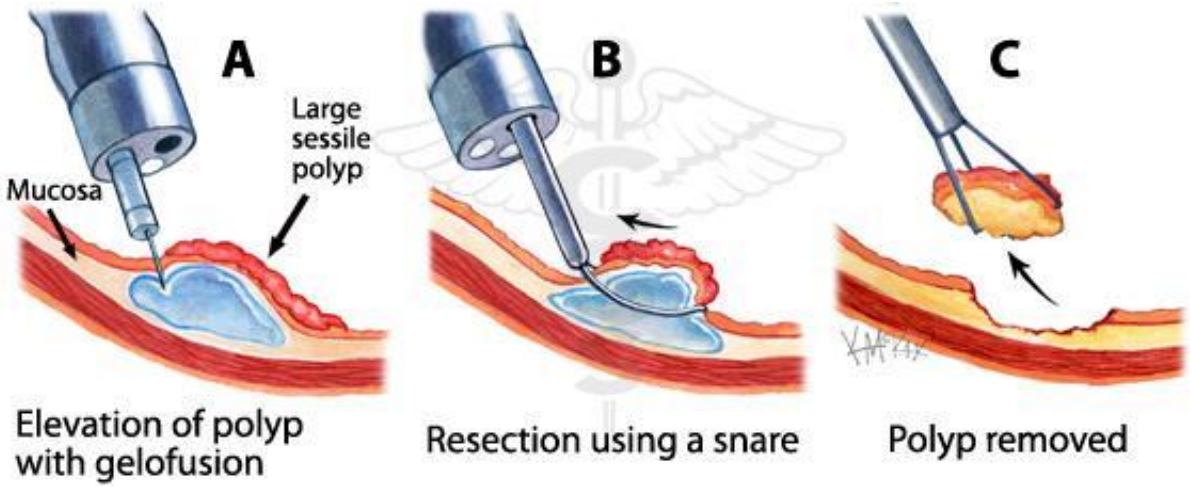
Locally Advanced (T2 or N+)

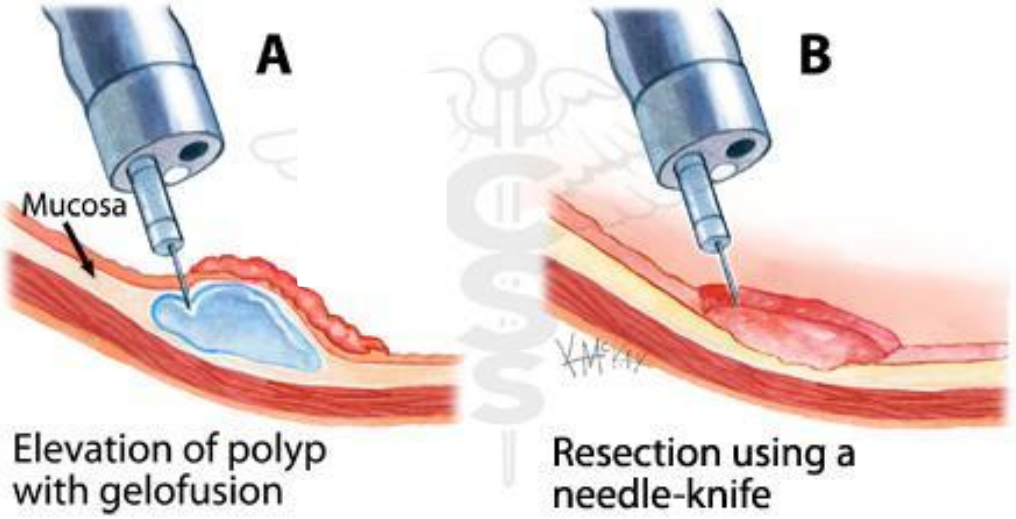
- Neoadjuvant therapy

Metastatic

- Definitive Chemotherapy

Endoscopic Mucosal Resection
Endoscopic Submucosal Dissection
Ablation of Surrounding Barrett's





Locally Advanced Disease

- T2 tumors
- N+ disease

Neoadjuvant Chemotherapy & Radiation

- Paclitaxel and Carboplatin weekly x 5 weeks
- 50.4 Gy over 28 fractions

CROSS Trial

- Randomized patients to preop chemoxrt + surgery vs. surgery alone
  - Carboplatin & Paclitaxel
  - 41.4 Gy radiation over 23 fractions
- R0 resection rate (92% vs 69%)
- 29% complete pathologic response
  - 23% adenocarcinoma
  - 49% squamous

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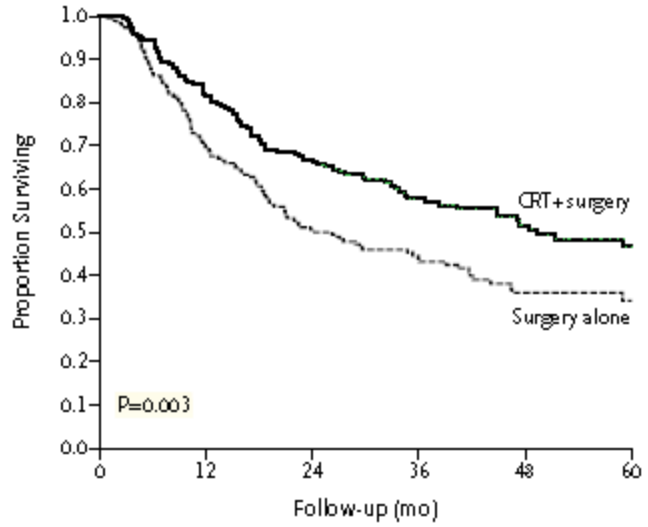
Van Hagen, NEJM 2012

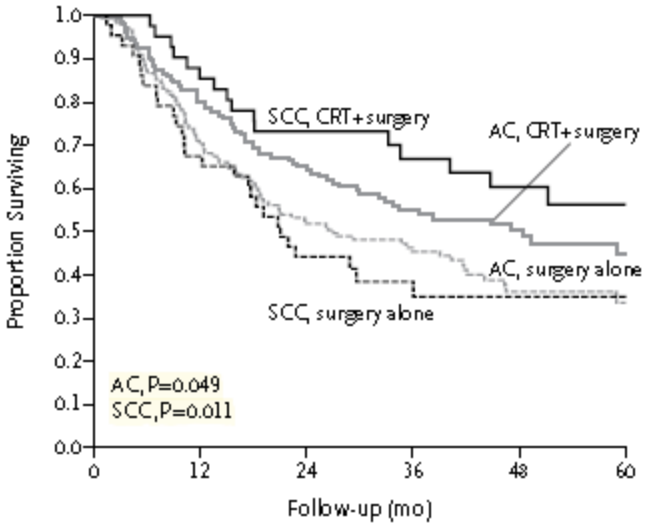
CROSS Trial

A Survival According to Treatment Group



No. at Risk						
CRT + surgery	178	145	119	75	49	28
Surgery alone	188	131	94	62	33	17
Total	366	276	213	137	82	45

B Survival According to Tumor Type and Treatment Group



No. at Risk						
AC, CRT+surgery	134	107	87	53	34	18
AC, surgery alone	141	99	73	50	25	10
SCC, CRT+surgery	41	35	30	21	15	8
SCC, surgery alone	43	29	19	11	8	4
Total	359	270	209	135	82	40

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CROSS Patterns of Recurrence

- CRT had lower local recurrence rate
  - Anastomosis: 2.8% vs 8.7%
  - Mediastinum: 7.0% vs 20.5%
- CRT had lower distant recurrence rate
  - Carcinomatosis: 4.2% vs 13.7%
  - Hematogenous: 28.6% vs 35.4%
- No difference in Nodal recurrence
  - Celiac, Periaortic, Supraclavicular

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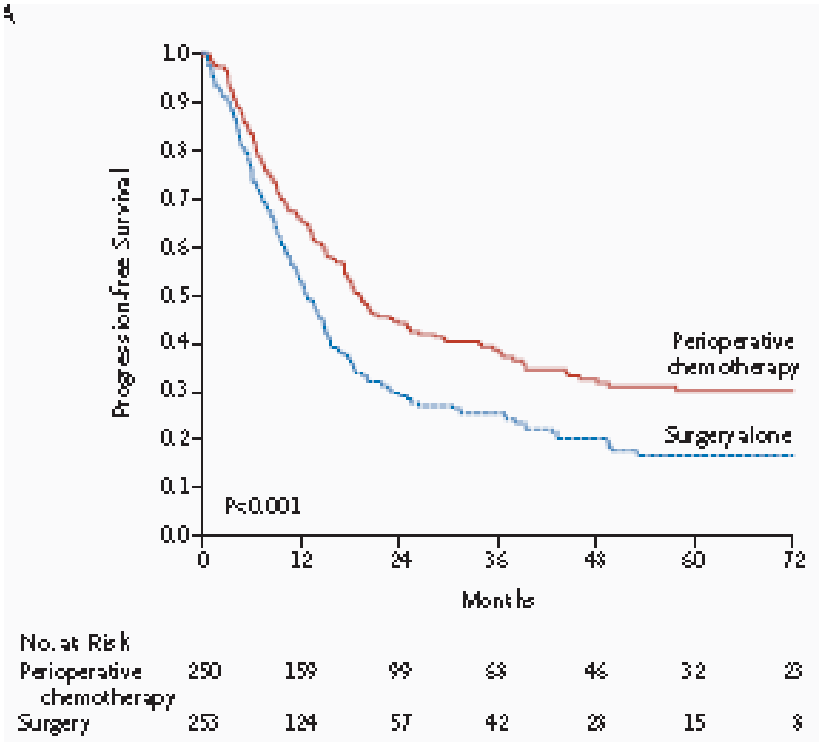
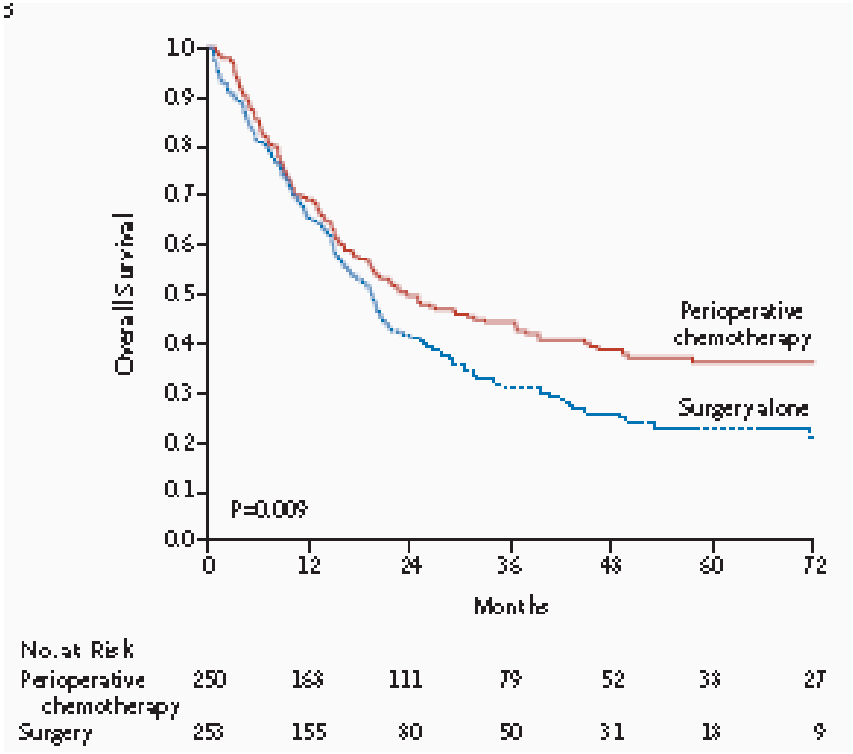
Oppedijk et al. JCO 2014 32:385

Evaluated Perioperative Chemotherapy vs Surgery Alone

- Gastric Cancer including the lower 1/3 of esophagus
  - 25% were GE Jxn (11%) or Esophageal (14%)
- Epirubicin/Cisplatin/Fluoruracil – 3 cycles preop / 3 cycles post op
  - 86% of patients completed preop chemo
  - 55% started post op chemo
  - 41% of patients assigned to the chemotherapy group completed all 6 cycles





Cunningham et al, NEJM 2006

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FLOT

FLOT

- Fluorouracil / leucovorin
- Oxaliplatin
- Docetaxel

Phase 3 FLOT 4 - abstract

- FLOT vs ECF/ ECX
- Improved OS (50 v 35 mo)
- Improved PFS (30 v 18 mo)
- Improved R0
- Smaller tumors

FLOT vs Cross

- Propensity matched study
- No survival benefit
- CRT had better tumor response, fewer nodes

ESOPEC

- Randomizing pts to FLOT vs CROSS
- Opened 2016
- Expected 2023
- https://clinicaltrials.gov/show/NCT02509286

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ESMO 2017 – Abs LBA27
Eur J Surg Onc 2017
BMC Cancer 2016

Surgical Approaches to Esophagectomy

- Transhiatal
  - Abdominal incision
  - Neck incision
  - Anastomosis in the Neck
- Ivor Lewis
  - Abdominal incision
  - Right chest incision
  - Anastomosis in the Chest
- Minimally Invasive Esophagectomy

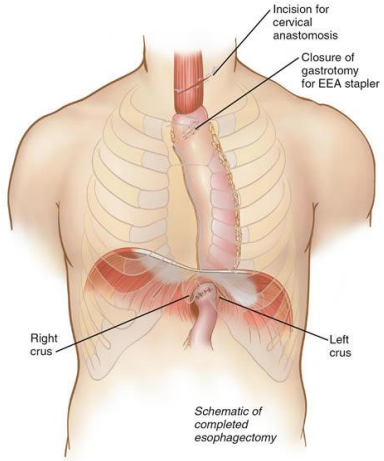
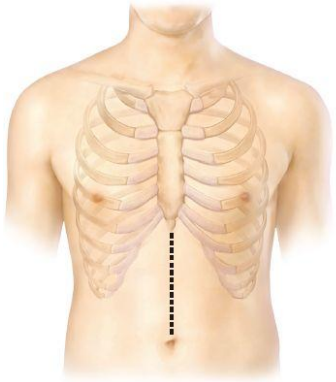
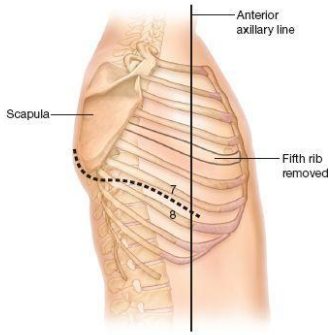


FIGURE 1-17 Completed minimally invasive esophagectomy.





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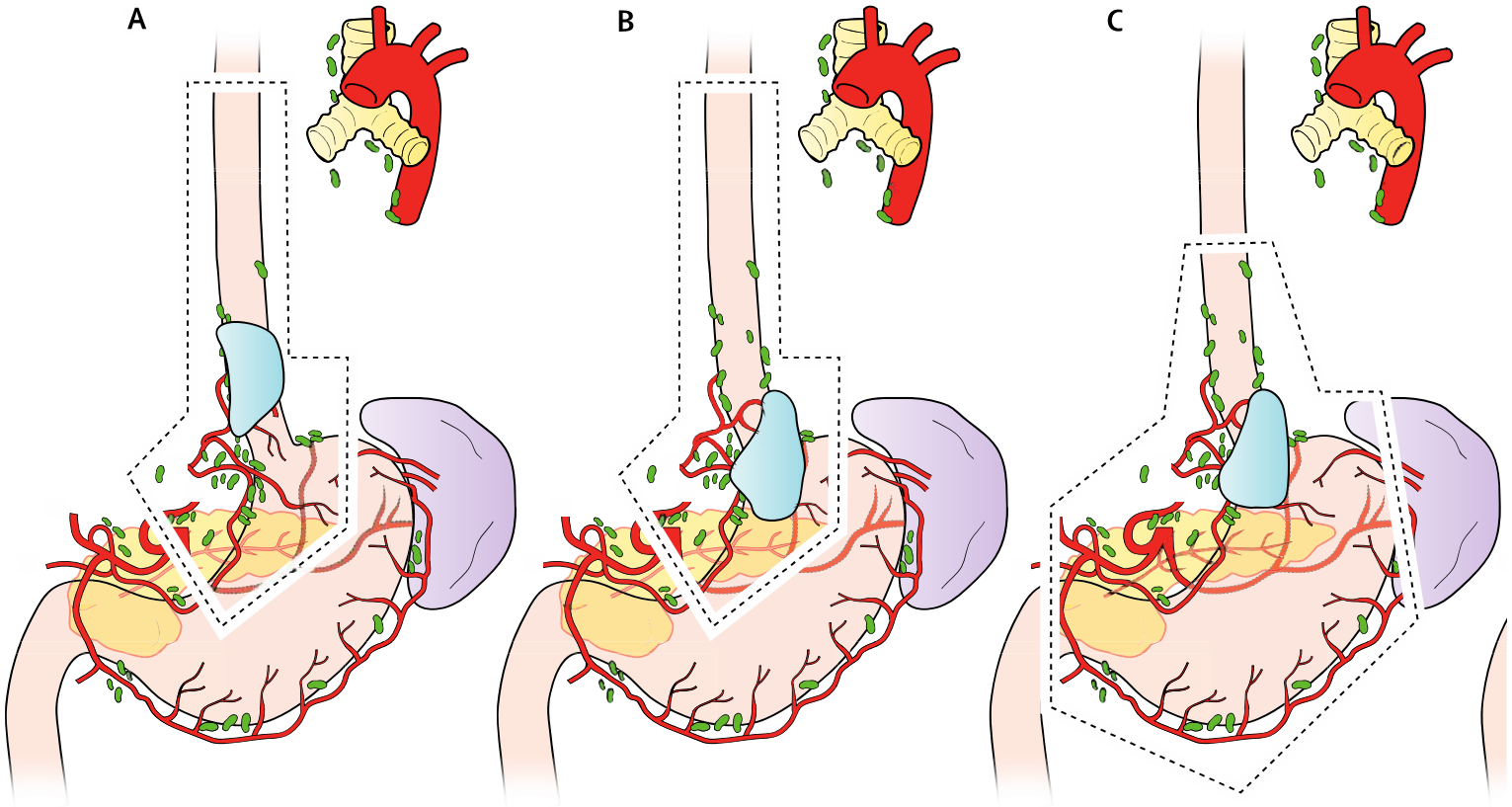

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Marriette, Lancet Onc 2011

Comparison of Open Approaches

	Transhiatal %	Ivor Lewis %	P-Value
Pneumonia	14	16	NS
Sepsis/Shock	17.8	20.9	NS
Return to OR	10.9	14.5	0.046
Morbidity	49.1	49.4	NS
Serious Morbidity	39.6	43.5	NS
Mortality	2.9	4.7	0.095

Papenfuss et al, J Surg Onc 2014

Minimally Invasive Esophagectomy

- Improvement in Morbidity
- Extent of Lymphadenectomy
- Multiple approaches described

>1000 MIE

- 48% Neck Anastomosis
- 52% Chest Anastomosis

	Neck	Chest	P value
RLN	8%	1%	<0.001
Leak	5%	4%	0.4
Mortality	2.5%	0.9%	0.08

Luketich, Ann Surg 2012

MIE vs Traditional Esophagectomy

- RCT of 115 patients to MIE (prone) vs Right Thoractomy, Laparotomy, Cervical incision
- > 90% had modern neoadjuvant chemoradiation: carboplatin, paclitaxel, XRT
- Significant difference in early postoperative pulmonary complications favoring MIE
  - 34% vs 12% in hospital
- No difference in LN, RO, Mortality

Bierre, Lancet 2012

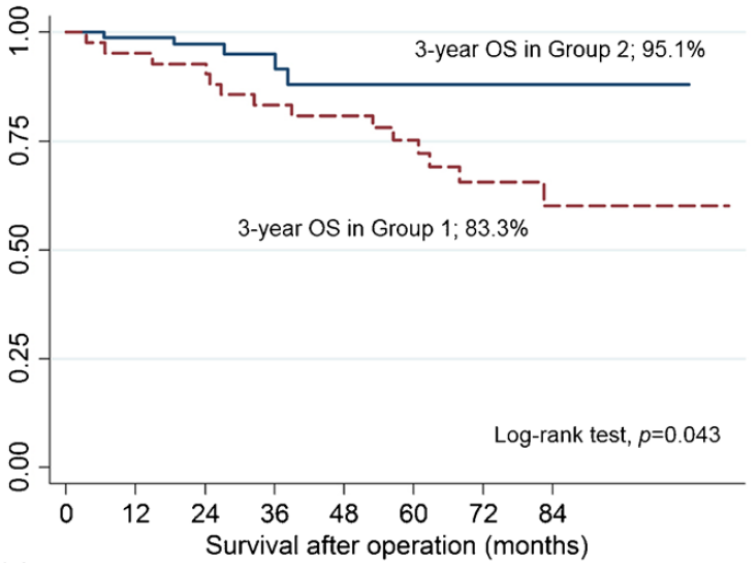
Extent of Mediastinal Lymphadenectomy and Survival in Superficial Esophageal Squamous Cell Carcinoma

Seong Yong Park[1] · Dae Joon Kim[1] · Taeil Son[2] · Yong Chan Lee[3] · Chang Young Lee[1] · Jin Gu Lee[1] · Kyung Young Chung[1]

- Single-institution retrospective study of 129 patients undergoing curative-intent esophagectomy for pT1 ESCC
  - Group 1 (n=42): standard MLND
  - Group 2 (n=87): Extensive MLND

Table 3 Surveillance data

Variable	Group 1 (n = 42)	Group 2 (n = 85)	p value
Recurrence	10 (23.8%)	3 (3.5%)	0.001
Loco-regional	6 (14.3%)	0	0.001
Distant	2 (4.8%)	0	0.108
Combined	2 (4.8%)	3 (3.5%)	1.0
Death	14 (33.3%)	5 (5.9%)	<0.001
Cancer related	7 (16.7%)	3 (3.5%)	0.015
Intercurrent disease	5 (11.9%)	2 (2.4%)	0.039
Unknown	2 (4.8%)	0 (0%)	0.108



J Gastrointest Surg (2017)

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The Aurora Approach

THE TEEM

Trans
Hiatal
Esophagectomy

Transcervical
Endoscopic
Esophageal
Mobilization

****Da Vinci Xi Robot-Assisted**

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THE TEEM Approach

- Aurora one of few centers around the world to use this technique
- Combines the oncologic advantage of transthoracic approach with the morbidity advantage of the transhiatal approach

Video / Graphic

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THE TEEM

Year	Author	Country	N	Operative Data Abdomen	OR time	No of LNs	Complications Pulmonary	Leak	RLN Palsy	LOS	30d Mort
1993	Bumm	Germany	30	Open			4 (13.3%)	6 (20%)	2 (6.6%)		2 (6.6%)
2004	Tangoku	Japan	41		269		10 (24.4%)	4 (9.8%)	15 (36.6%)		
2010	Wu	China	40	Open 32 (80%), Lap 8 (20%)	220	12.6	1 (2.5%)	3 (7.5%)	2 (5%)	11.4	
2011	Parker	US (Mayo Florida)	8	Laparoscopic	292	23		2 (25%)	2 (25%)	7	0
2012	Feng	China	27	Open	194	11.4	7 (26%)	5 (18%)	5 (18%)	11.1	1 (3.7%)
2014	Wang	China	70		150	13.8	4 (5.7%)	5 (7.1%)	2 (2.9%)	10	
2015	Okumura et al	Japan	63	Open	403	22.9	4 (6.3%)	14 (22.2%)	6 (11.5%)		1 (1.6%)
2016	Nomura	Japan	20	Open	315	8.2					
2016	Mori	Japan	22	DaVinci S for mediastinum	524	30		4 (18%)	1 (4.5%)	18	0
2017	Fujiwara	Japan	60		363	38	4 (6.7%)	9 (15%)	20 (33.3%)	31	0
2018	Aurora Health Care	US									

Aurora 2015-2016	Time	Afib	Leak	VC	Pneum	Bleed	30 d mort
N= 26	221 min	37%	6%	15%	7%	7%	0

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Bierre, Lancet 2012

Thank You

Management of Complete response for SCC

- Complete pathologic response is higher in SCC than Adeno
- Progression free survival is better in patients treated with surgery
- Overall survival is not improved
- Cancer specific survival was improved in surgery groups
- ? High mortality rate in surgery arm (10%)

81 patients from 2001 – 2012

Endoscopic resection of T1a patients

Ablation of associated Barrett's

7 patients had T1b disease (all negative margins)

3.25 years of follow up

84% eradication of HGD

One patient developed invasive carcinoma

Treated endoscopically

100% cancer specific survival

Nurkin, Surg End 2013

Human epidermal growth factor (HER2)

- Associated with cell proliferation
- Amplified in 10-25% of GE Jxn cancers

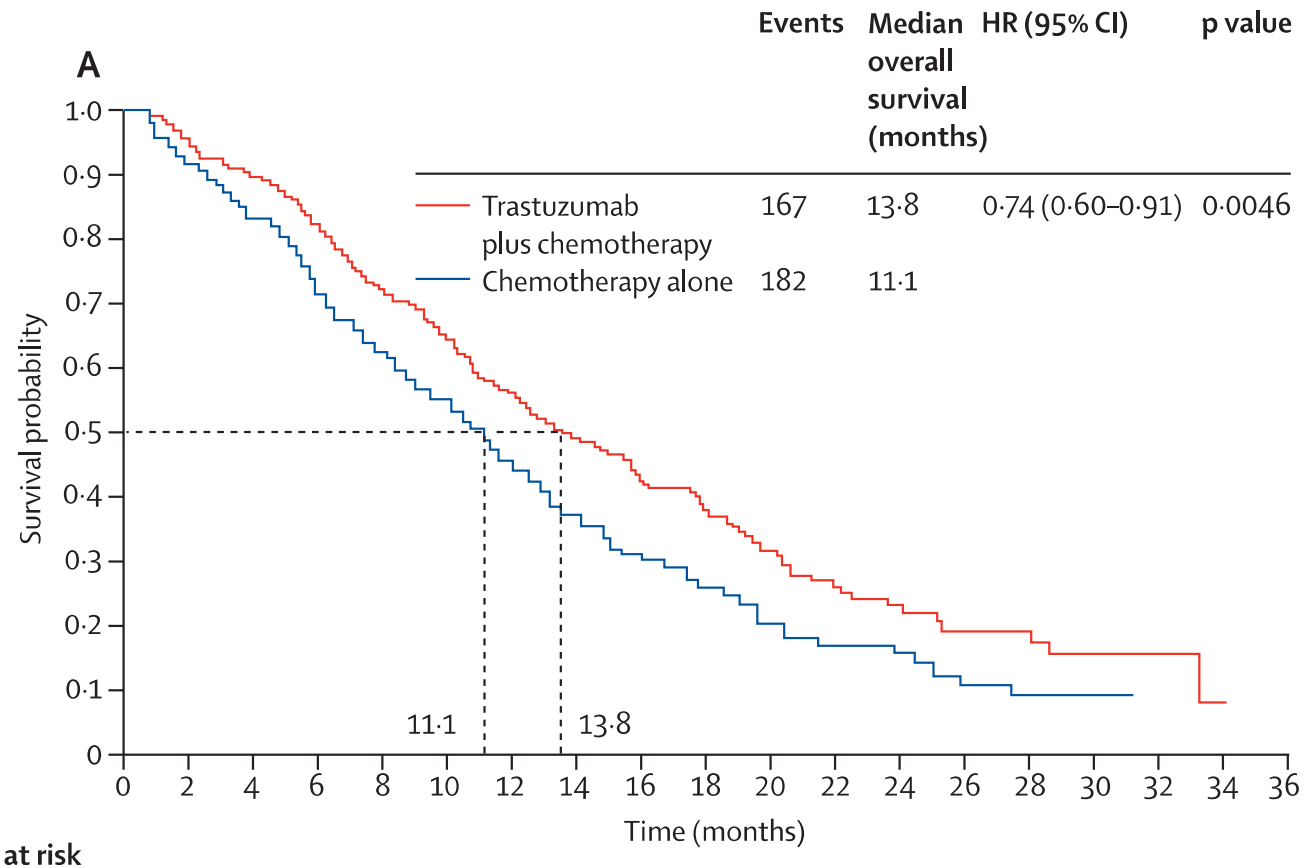
Trastuzumab

- Monoclonal antibody to HER2

Trastuzumab for Gastric Cancer Study (ToGA)

- Compared Chemotherapy +/- trastuzumab
  - Capecitabine/fluorouracil plus cisplatin
- Locally advanced or Metastatic Gastric/EGJ cancers
  - Approximately 20% were EGJ
- Improvements in OS, PFS

ToGA, Lancet 2010



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ToGA, Lancet 2010

RTOG 1010

Evaluate the addition of Trastuzumab to Neoadjuvant therapy for GE Jxn cancer

Carboplatin, Paclitaxel, XRT +/- trastuzumab

Anticipated 480 Enrollees

2010 – 2018

http://clinicaltrials.gov/show/NCT01196390

Local PI: Dr. Robert Behrens

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