

## Esophageal Cancer

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## Esophageal cancer

Histology	Squamous cell	Adenocarcinoma
Anatomic location	Proximal and mid-portion	Distal third and gastroesophageal junction
Incidence	Decreasing	Increasing
	African American > Caucasian	Caucasian > African American
Risk factors	Tobacco and alcohol	Tobacco
	HPV	Obesity
	Ingestion of corrosives	GERD
	Plummer-Vinson Syndrome	Barrett's esophagus

## Esophageal cancer

- In the US (2012):
  - 17,460 new cases, 15,070 deaths
- Worldwide (2008)
  - 482,300 new cases, 406,800 deaths
  - 6<sup>th</sup> leading cause of cancer deaths
- Median age of diagnosis: 67 years
- Male predominance

## Barrett's esophagus

- Replacement of squamous epithelium with intestinal columnar epithelium
- Incidence:
  - 10-15% of endoscopies evaluating GERD
  - 40% patients with esophageal strictures
- 2% risk of adenocarcinoma over 10 yrs
- No therapy reverts (antacids, surgery, laser)

## Barrett's esophagus

- Consider screening if with risk factors for esophageal cancer:

- >50 years, Caucasian
- chronic GERD
- hiatal hernia
- high body mass index

Wang et al. Am J Gastroenterol 2008;103:788

## Chemoprevention for Barrett's Esophagus Trial

- ↑COX-2 in Barrett's esophagus
- U.S. trial with celecoxib
  - 100 pts with Barrett's esophagus: low or high grade dysplasia
  - Placebo vs Celecoxib 200 mg BID
  - No change in EGD findings at 48 weeks
  - No change in COX 1/2 mRNA

Heath et al. JNCI 2007;99:545

## Barrett's esophagus

Dysplasia	Repeat endoscopy
No dysplasia	3 years
Low-grade	6-12 months
High-grade	Every 3 months or local therapy

## Esophageal cancer

- Signs and symptoms:
  - Dysphagia and odynophagia (solids before liquid)
  - Weight loss
  - Abdominal pain
  - Cough and hoarseness
  - Supraclavicular adenopathy

## Diagnostic work-up

- CBC and chemistry
- Esophagogastroduodenoscopy
- CT chest/abdomen/pelvis with IV and PO contrast
- PET/CT
- Endoscopy with ultrasound
- Bronchoscopy (if above and at level of carina)

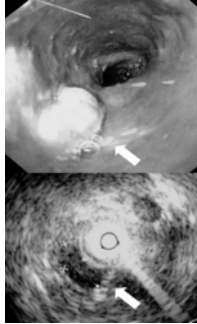


Image from: en.wikipedia

## Staging

### Tumor

- Tis – High grade dysplasia
- T1 – Tumor invades lamina propria, muscularis mucosae or 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

## PET/CT

- Utilized for preoperative staging
  - Correlate with EUS and CT scans
  - Upstages tumor to avoid surgery
- Prognostic
  - PET/CT responders after induction chemotherapy have improved survival

## Staging

### Node

- N0 – No regional LN involvement
- N1 – Metastasis in 1-2 regional nodes
- N2 – Metastasis in 3-6 regional nodes
- N3 – Metastasis in more than 7 regional nodes

### Metastasis

- M0 – No distant metastasis
- M1 – Distant metastasis

## 5 Year Survival by Stage

Stage	TNM	5-year Survival
Stage 0	TisN0M0	
Stage I	T1N0M0	80-90%
Stage IIA	T2-T3N0M0	50%
Stage IIB	T1-2N1M0	20%
Stage III	T3N1M0 T4N0-1M0	10-15%
Stage IVA	M1a	10%
Stage IVB	M1b	Anecdotal

## Resectable cancer

- Tumor location
- Tumor stage (nodal involvement, metastasis)
- Patient medically fit for esophagectomy

## Treatment Options

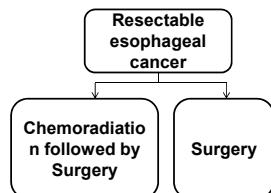
- **Resectable cancer**
  - Surgery
  - Radiation
  - Chemotherapy
- **Unresectable cancer**
  - Radiation
  - Chemotherapy
- **Metastatic cancer**
  - Chemotherapy
  - Radiation therapy
  - Photodynamic Therapy
  - Laser Ablation
  - Stents
  - Nutrition (PEG, TPN)

## Meta-analysis: Survival benefit from neoadjuvant chemoradiation vs. chemotherapy

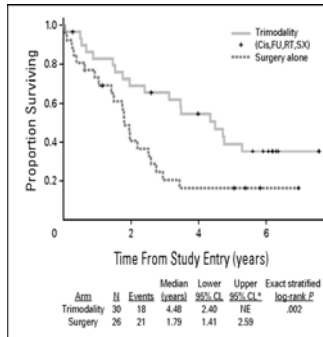
	Neoadjuvant chemoradiation	Neoadjuvant chemotherapy
Number	10 studies, total n = 1209	8 studies, total n = 1724
HR for all-cause mortality	0.81 (p=0.002)	0.90 (p=0.05)
Absolute survival difference at 2 years	13%	7%
Comments	Similar results for SCC and AC	Benefit only in AC, not SCC

Gebski et al, Lancet Oncol 2007; 8:226-34.

## CALGB 9871 trial



**Trimodality vs surgery:**  
**Median OS :4.5 vs 1.8 years**  
**5-yr survival: 39% vs. 16%**  
**Median PFS: 3.5 vs. 1 yr**



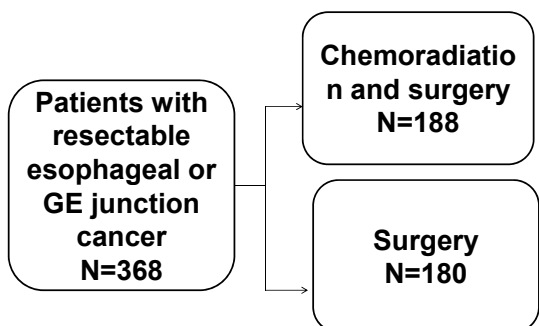
Tepper et al. J Clin Oncol 2008; 26:1086

## CROSS trial results

Surgery		Trimodality
67%	R0 resection	92.3%
3.8%	In hospital mortality	3.4%
26 months	Median survival	49 months
70%	1 year survival	82%
52%	2 year survival	67%
48%	3 year survival (HR 0.67, p=0.011)	59%

Van Hagen et al, NEJM 2012;366:2074

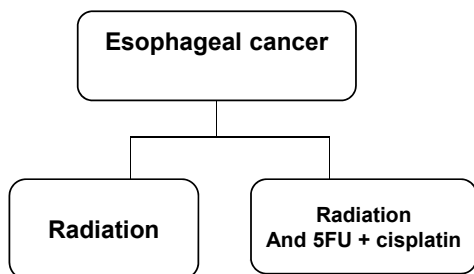
## CROSS trial



Van Hagen et al, NEJM 2012;366:2074

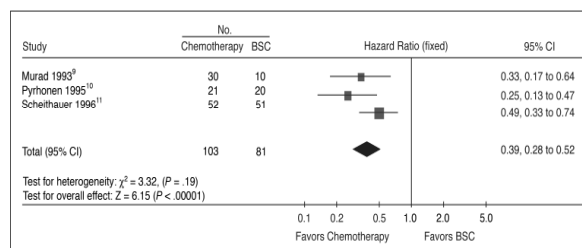
**Unresectable tumor**

### Non-operative trial: RTOG 85-01



Cooper et al. JAMA 1999;281:1623.

### Metastatic esophageal cancer: Best Supportive Care vs Chemotherapy



Wagner et al. JCO 2006;24:2903.

### Definitive Chemoradiation or Radiation for Esophageal Cancer

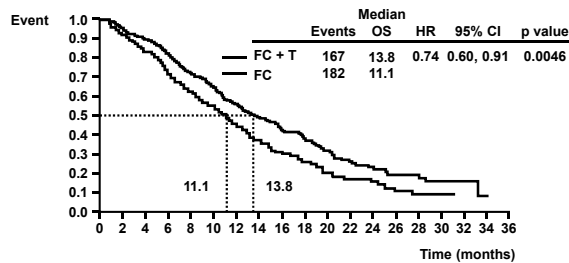
	Chemoradiation	Radiation
Median survival	12.5 months	8.9 months
1- year survival	52%	34%
2-year survival	36%	10%
5-year survival	26%	0%

Cooper et al. JAMA 1999;281:1623.

### Targeted therapy-HER2

- Human epidermal growth factor receptor-2
- HER2 is over-expressed in 20% gastro-esophageal and gastric cancers
- Antibody to HER2- trastuzumab

## Primary end point: OS



Bang et al, Lancet 2010;376:687.

## Surgical Intervention for Esophageal Cancer

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## In summary

- Incidence: Adenocarcinoma ↑, squamous cell ↓ carcinoma
- Risk factors:
  - Adenocarcinoma: tobacco, obesity, GERD, Barrett's esophagus
  - Squamous cell carcinoma: tobacco, alcohol, HPV, corrosive ingestion
- Signs and symptoms:
  - Dysphagia/odynophagia, weight loss, pain, and cough
- Work-up: CBC + CMP, EGD, CT chest/abdomen/pelvis
- Treatment: Multi-modality- surgery, radiation, chemotherapy
- Prognosis:
  - Poor prognosis (1/3 patients have metastatic disease at diagnosis)
  - Improved prognosis if localized, resectable cancer

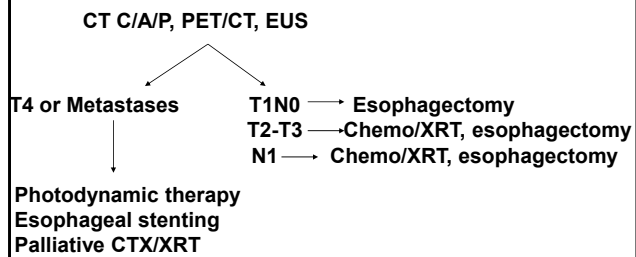
## Overview

- OSU approach to esophageal cancer
- Morbidity and mortality after esophagectomy
- Approaches to esophageal resection

Using evidence-based medicine, has the ideal operative approach been determined?

**Answer: No**

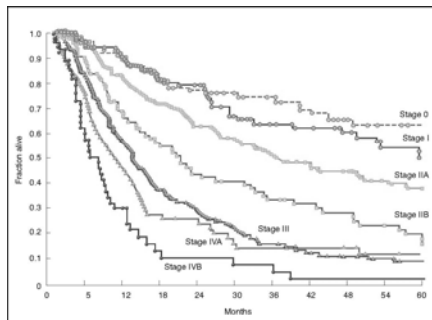
## Algorithm for Esophageal Cancer: OSU Approach



## Esophagectomy and Survival

Author (year)	N	Approach	1 year survival	5-year survival
Swanson (2001)	250	Three hole	44	NR
Bailey (2003)	1777	Varied	NR	NR
Rizk (2004)	510	Varied	44	NR
Lerut (2005)	394	Varied	63	30
Portale (2006)	263	Varied	NR	46.5
Orringer (2007)	2007	THE	70	29
Mathisen (1998)	104	Varied	NR	15%

## Survival by Stage



## Esophagectomy and Mortality

- Open esophagectomy mortality rates range from 8% at high volume centers to 23% in low volume centers (NEJM 2002)
- Published series from experienced centers report a mortality rate of 5%



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

*ROL in last 10 years w/13 papers:*

- 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*

### High Volume Centers for Esophagectomy: What is the number needed to achieve low post-operative

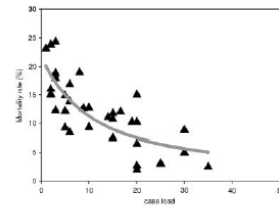


Fig. 2 Correlation between number of esophagectomies and hospital mortality rate.

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

### 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*

### Hospital Volume and Mortality

Author	Study period	Low volume	High volume
Begg (1998)	1984-1993	17.3 (<5)	3.4 (>11)
Patti (1998)	1990-1994	16 (<8)	4.8 (>30)
Swisher (2000)	1994-1996	12.2 (<5)	3 (>5)
Dimick (2001)	1989-1999	16 (<3)	2.7 (>15)
Von Lanachot (2001)	1993-1998	12.1 (<10)	4.9 (>50)
Birkmeyer (2002)	1994-1999	23% (<2)	8.1 (>19)
Dimick (2003)	1994-1998	15.4	2.5%
Finlayson (2003)	1995-1997	15 (<4)	6.5 (>9)
Dimick (2005)	1998-1999	24.3 (<5)	11.4 (>12)

### Esophagectomy and Perioperative Mortality

Author (year)	N	Approach	LOS	Mortality
Swanson (2001)	250	Three hole	13	3.6
Bailey (2003)	1777	Varied	NR	9.8
Rizk (2004)	510	Varied	11	6.1
Lerut (2005)	394	Varied	NR	2.1
Portale (2006)	263	Varied	NR	4.5
Orringer (2007)	2007	THE	10	3.0
Mathisen (1998)	104	Varied	NR	2.9

### Lowering the Morbidity of Esophagectomy

- Limit rib spreading to 5 cm during transthoracic esophagectomy (Skinner 1967)
- Avoid thoracotomy and perform transhiatal approach (Orringer 1980)
- Perform only in high volume centers (Birkmeier 2002)
- Perform minimally invasive esophagectomy in high volume center (Luketich 1996)

### 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

### Surgical Options

#### Approach

- Transhiatal
- Transthoracic
- Three Field
- Minimally Invasive
- En Bloc

#### Anastomosis

- Neck
- Chest
- Abdomen

#### Conduit

- Stomach
- Colon
- Jejunum
- Skin Tube

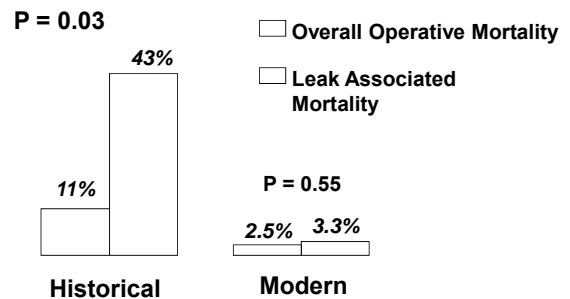
#### Route

- Post. Mediast.
- Retrosternal
- Subcutaneous

## 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%

## Perioperative Mortality After Intrathoracic Leak

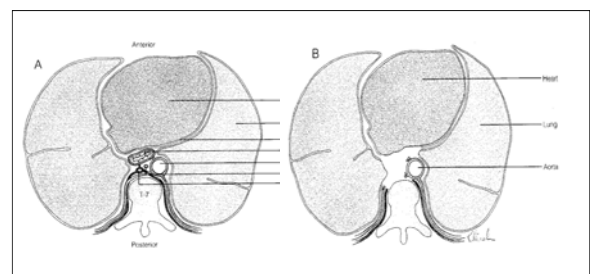


## Comparison of Approach Transhiatal vs. Transthoracic

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

Putnam et al., Ann Thor Surg, 1994

## En-Bloc Esophagectomy



### Extended Surgical Resection *Transhiatal vs. Transthoracic "En Bloc"*

	THE	TT "En Bloc"	
No. Pts.	106 pts	114 pts	
Pulm Cxns	29 (27%)	65 (57%)	< 0.001
ICU Days	2 (0-38)	6 (0-79)	<0.001
Op Mort	2 (2%)	5 (4%)	0.45
Relapse	62 (58%)	57 (50%)	0.60
5-yr Surv.	27%	39%	0.12

Hulscher et al., NEJM, 2002

### MIE Techniques

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

### 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

### 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

- Luketich, 2003
- 222 patients
- High grade dysplasia 47 pts
- Esophageal cancer 175 pts
  - Neoadjuvant chemotherapy 78 pts
  - Neoadjuvant radiotherapy 36 pts

## MIE

- ICU stay 1 day ( 1 – 30)
- Time to oral intake 4 days (1 – 40)
- Hospital stay 7 days (3 – 75)
- Median follow-up 9 months

## MIE

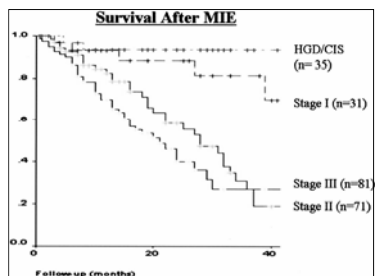
- MIE completed in 206 (92.8%) pts
- Conversion to open
  - Thoracotomy 12 pts
  - Laparotomy 4 pts

## MIE

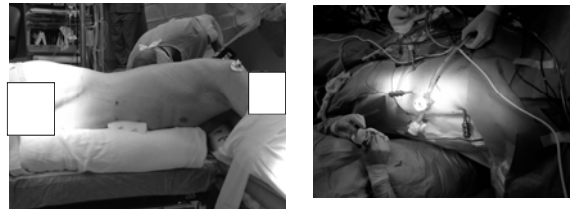
- Minor complications 53 (24%)
- Major complications 71 (32%)

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 emptying	4 (1.8)
Pleural effusion	14 (6.3)	Tracheal injury	4 (1.8)
Recurrent nerve palsy	8 (3.6)	ARDS	4 (1.8)

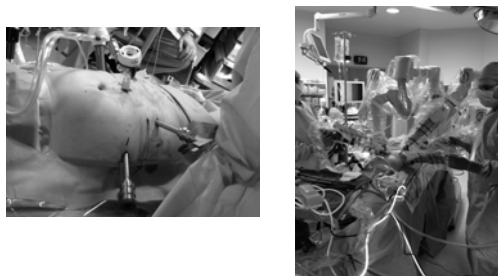
## MIE Survival



## Totally Robotic Ivor Lewis Esophagectomy



## Totally Robotic Ivor Lewis Esophagectomy



## Totally Robotic Ivor Lewis Esophagectomy

- Two patients completed thus far
- Mean age 59 years
- Mean operative time 10 hours
- Mean blood loss <100 cc
- Mean LOS 7 days
- No anastomotic leak

## 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

- Three field esophagectomy and 'en-bloc' esophagectomy increase morbidity without improving survival
- MIE
  - ? Decrease in peri-operative complications
  - Not proven to be superior to open approach
  - Long term outcomes similar to open approach

## 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

## Esophagectomy

### Techniques

	Transhiatal	Ivor Lewis	Three field
Advantages	Shorter operation ↓ Pulm Comp ↓ Pain	↓ Neck morbidity Lower leak rate Increased lymph node yield ? Increased complete resection	↓ Chest Leak
Disadvantages	↓ Node dissection Double the leak rate Recurrent nerve injury Injury to thoracic structures Neck morbidity		Increased pulmonary comp Increased pain

## Summary

- Overall survival still poor in patients with esophageal cancer
- Surgery remains mainstay of treatment
- In order for surgery to have an impact on survival peri-operative mortality and morbidity must be low

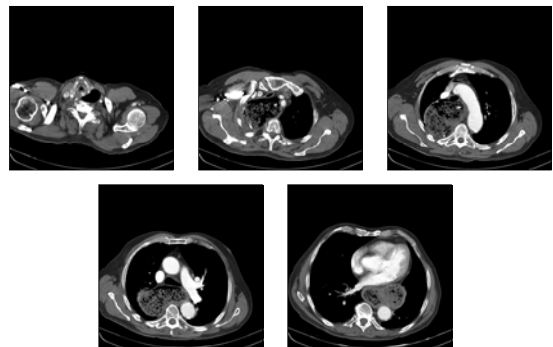
## Jejunal Interposition

- 79 year old male with esophageal cancer in the setting of end stage achalasia
- History of multiple dilations and Botox injections
- History of subtotal gastrectomy
- New onset dysphagia and dyspnea

## Summary

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

## CT Chest

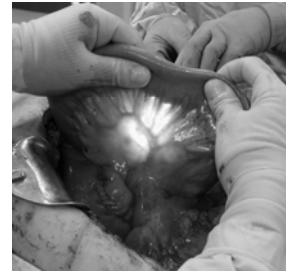




### **Jejunal Interposition for Esophageal Replacement**

- **Advantages**
  - Readily available
  - Limited physiologic impact
  - Sterile conduit
  - Generally free of intrinsic disease
  - Approximates diameter of esophagus
  - Maintains intrinsic peristalsis

### **Technique**



### **Jejunal Interposition for Esophageal Replacement**

- **Disadvantages**
  - Anatomic limitations of mesenteric arcades
- Limited to short segment interpositions
- Longer segment risks ischemia

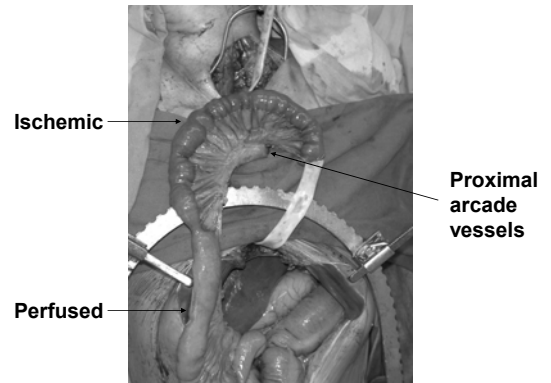
### **Technique**



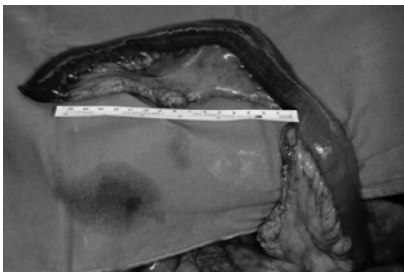
## Technique



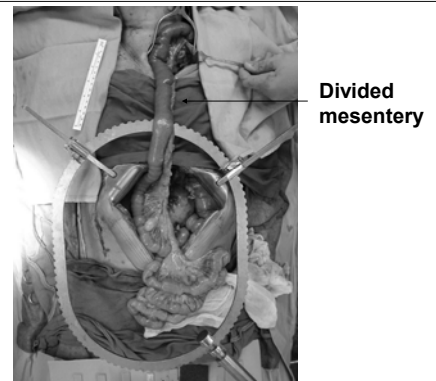
## Technique



## Technique



## Technique

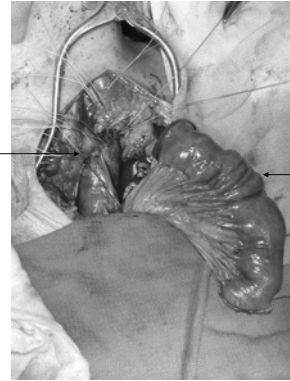


## Technique



## Technique

Proximal  
anastomosis



Bowel  
divided,  
mesentery  
intact

## Technique

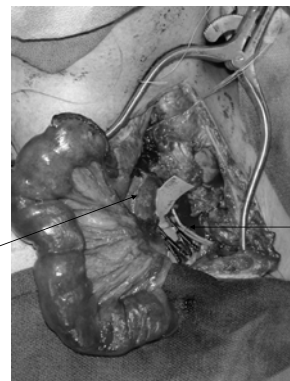
Divided  
esophagus



Redundant  
ischemic  
jejunum

## Technique

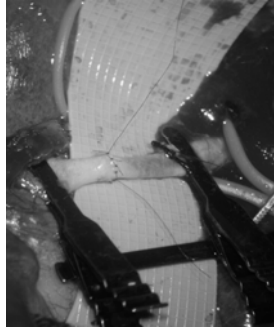
Ischemic



Microvascular  
augmentation

## **“Supercharging”**

- Microvascular augmentation
- Internal thoracic or cervical vessels



## **Technique**



## **Technique**



Perfused  
interposition

Monitor flap