Surgical Management of Esophageal and Gastric Cancers

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Leading cancer Types and Deaths by Sex

Estimated New Cases

Males				Females		
Prostate	268,490	27%		Breast	287,850	31%
Lung & bronchus	117,910	12%		Lung & bronchus	118,830	13%
Colon & rectum	80,690	8%		Colon & rectum	70,340	8%
Urinary bladder	61,700	6%		Uterine corpus	65,950	7%
Melanoma of the skin	57,180	6%		Melanoma of the skin	42,600	5%
Kidney & renal pelvis	50,290	5%		Non-Hodgkin lymphoma	36,350	4%
Non-Hodgkin lymphoma	44,120	4%		Thyroid	31,940	3%
Oral cavity & pharynx	38,700	4%		Pancreas	29,240	3%
Leukemia	35,810	4%		Kidney & renal pelvis	28,710	3%
Pancreas	32,970	3%		Leukemia	24,840	3%
All Sites	**983,160**	**100%**		**All Sites**	**934,870**	**100%**

Estimated Deaths

Males				Females		
Lung & bronchus	68,820	21%		Lung & bronchus	61,360	21%
Prostate	34,500	11%		Breast	43,250	15%
Colon & rectum	28,400	9%		Colon & rectum	24,180	8%
Pancreas	25,970	8%		Pancreas	23,860	8%
Liver & intrahepatic bile duct	20,420	6%		Ovary	12,810	4%
Leukemia	14,020	4%		Uterine corpus	12,550	4%
Esophagus	13,250	4%		Liver & intrahepatic bile duct	10,100	4%
Urinary bladder	12,120	4%		Leukemia	9,980	3%
Non-Hodgkin lymphoma	11,700	4%		Non-Hodgkin lymphoma	8,550	3%
Brain & other nervous system	10,710	3%		Brain & other nervous system	7,570	3%
All Sites	**322,090**	**100%**		**All Sites**	**287,270**	**100%**

Esophageal Cancer

Very poor survival (overall ratio of mortality to incidence of 0.88), and the esophageal cancer mortality closely follows the geographical patterns for incidence

- Eighth most common cancer worldwide with an estimated 456,000 new cases (3.2% of the total)
- Sixth most common cause of death from cancer with an estimated 400,000 deaths (4.9% of the total)

Esophageal Cancer Statistics: 2022

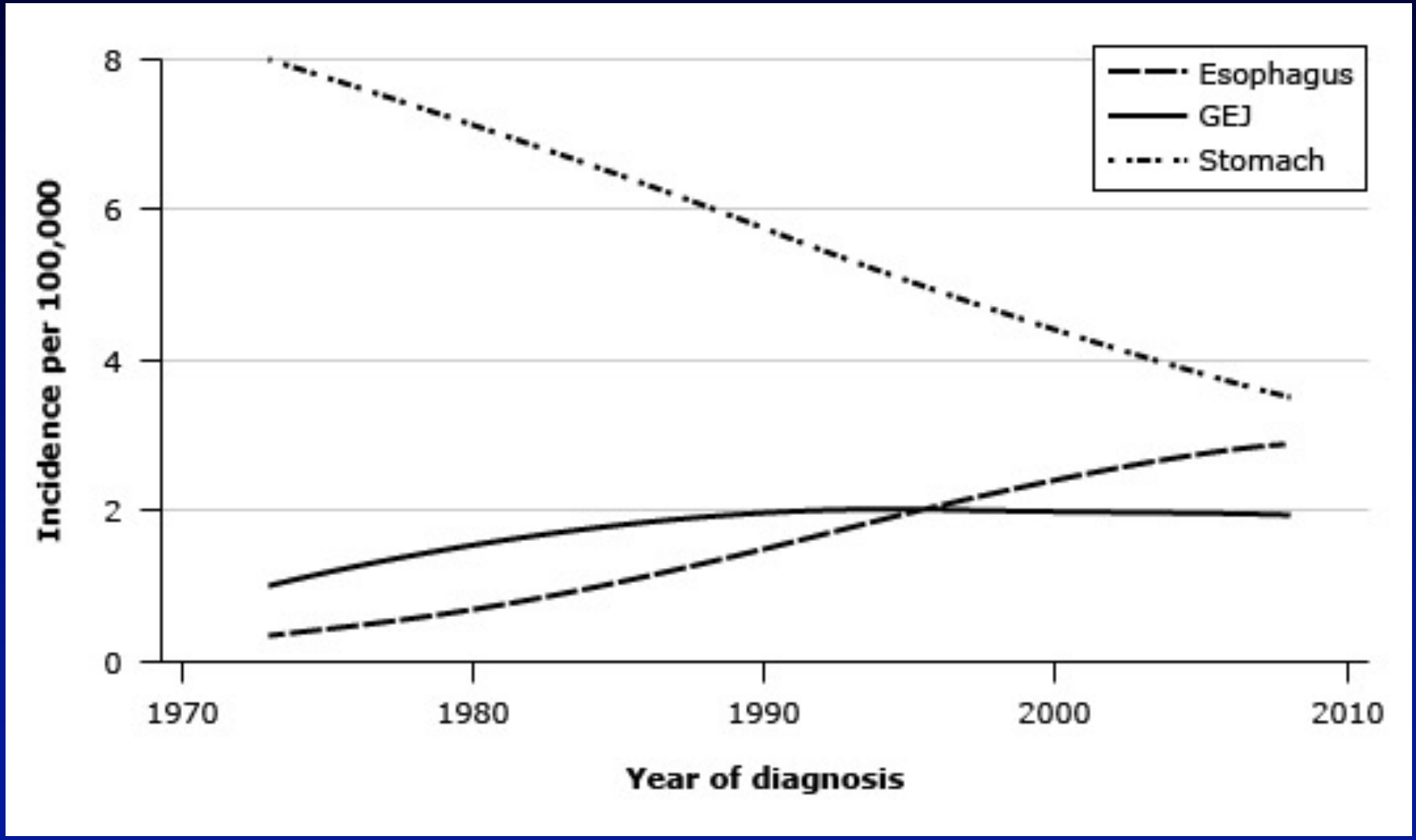
- 20,640 new cases
- 16,410 deaths

- Average incidence is 4.7/100,000
- Coastal regions of South Carolina and metropolitan areas including New York City, Detroit, Washington D.C and Los Angeles incidence is 30/100,000 (mostly squamous cancer)

Demographics / Epidemiology

- Over last 3 decades there has been a progressive increase in the incidence of adenocarcinoma of the distal esophagus and GE junction
  - 30% of all cases in mid-1990s
  - 50 - 60% today
- Adenocarcinoma affects mostly white men and the pathogenesis is linked to GERD

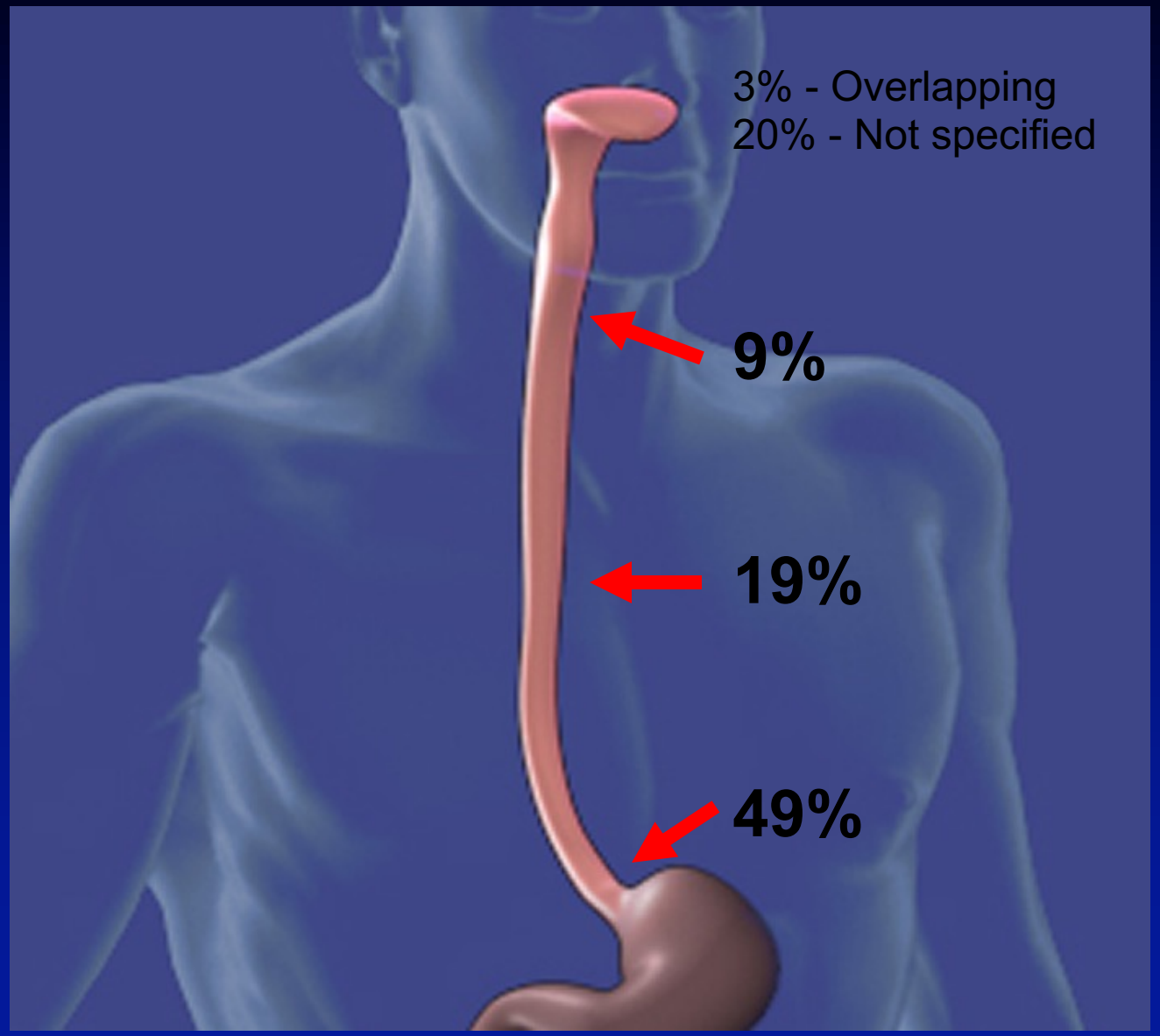
Incidence of Adenocarcinoma of the Stomach, Esophagus and GEJ, 1973 – 2008, USA



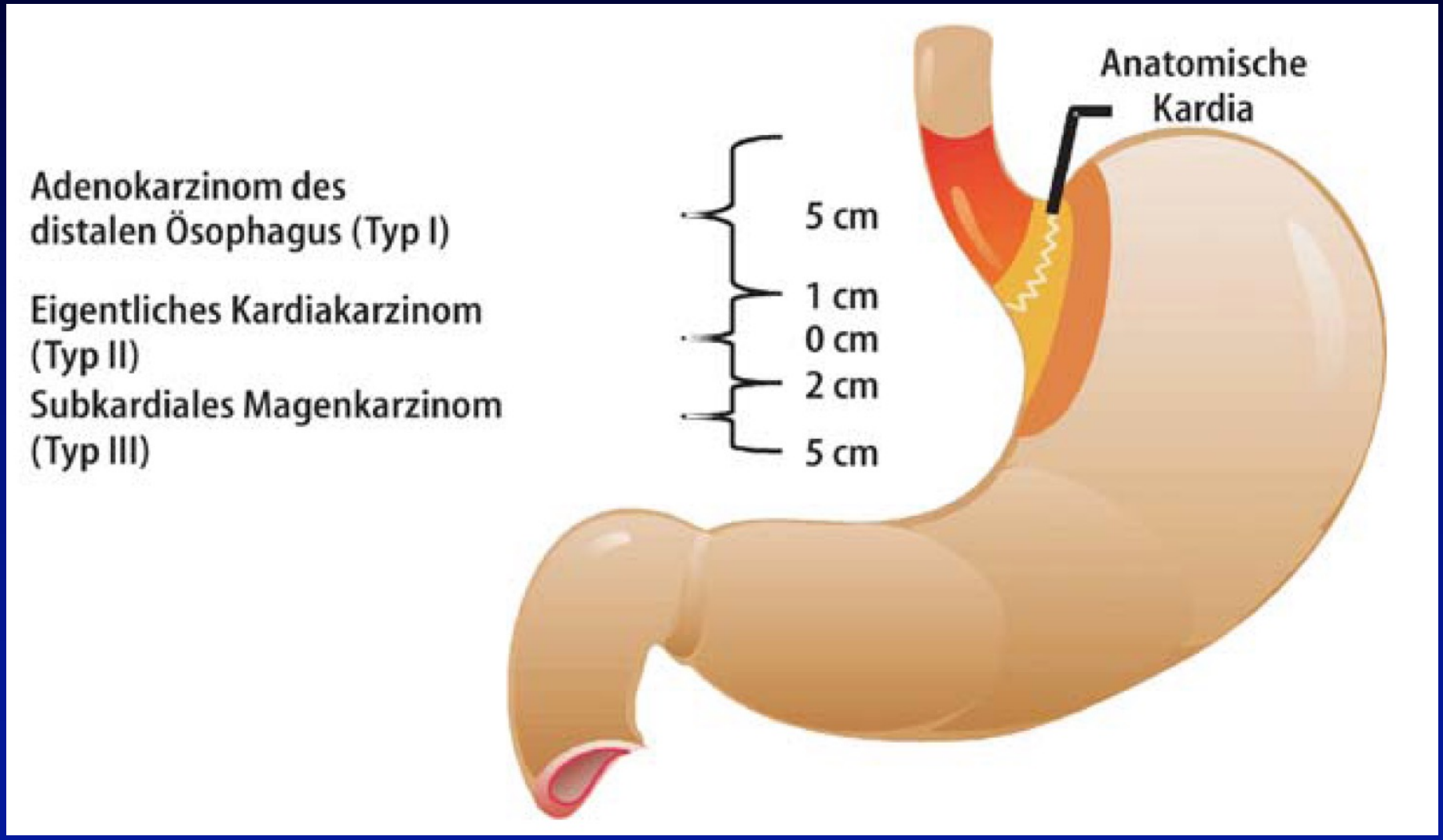
Etiology

- Adenocarcinoma
  - GERD, Obesity, Smoking
- Squamous
  - History of alcohol and tobacco abuse
  - Plummer-Vinson syndrome
  - Nutritional factors
    - Vitamin deficiencies, High nitrosamine intake

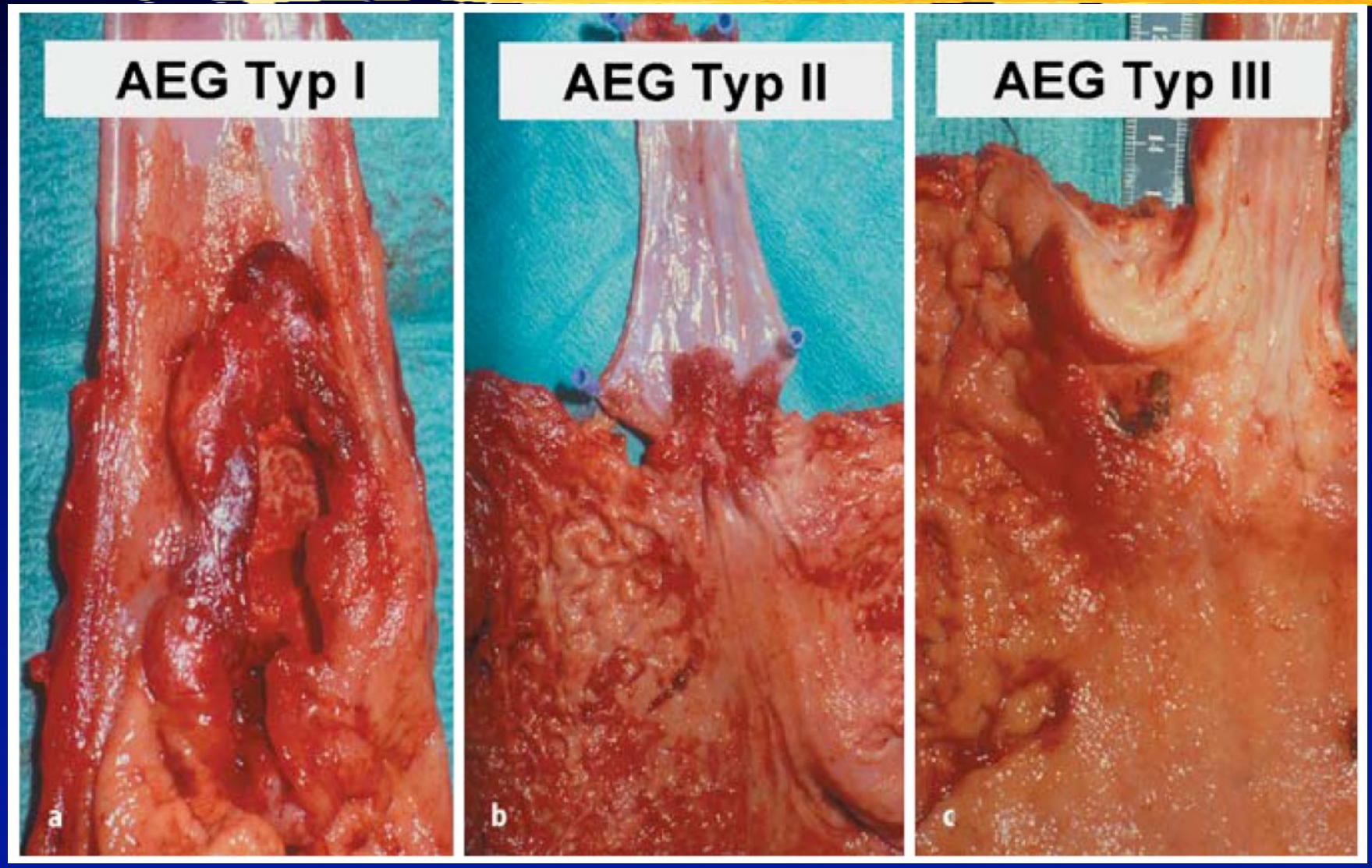
Distribution of Tumors



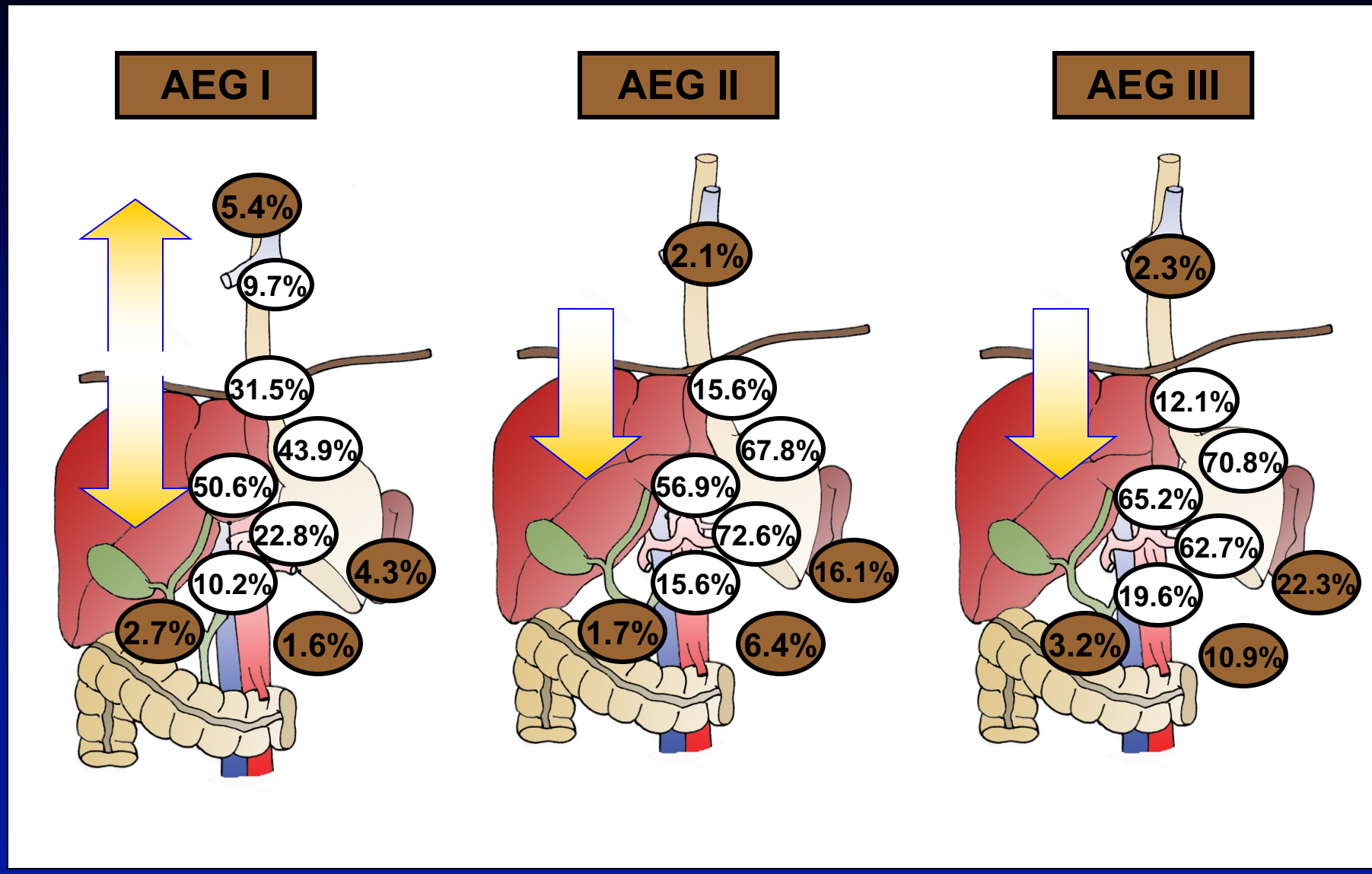
GE Junction Adenocarcinoma



Adenocarcinoma of the GE Junction

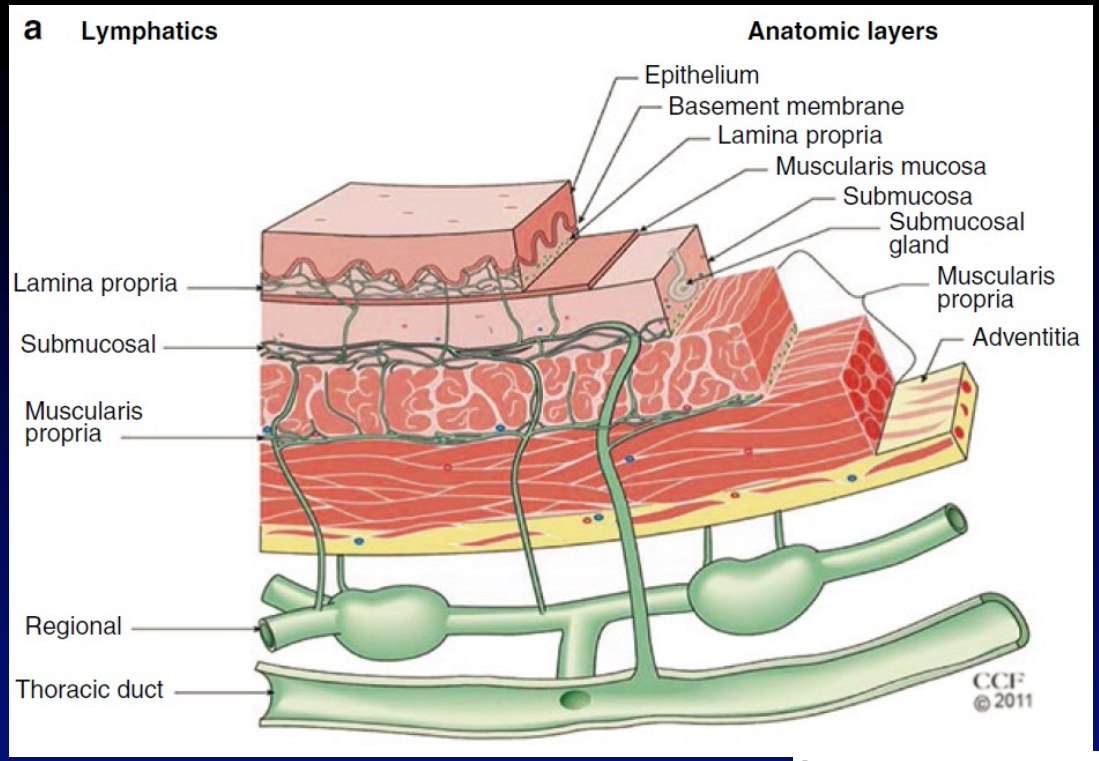


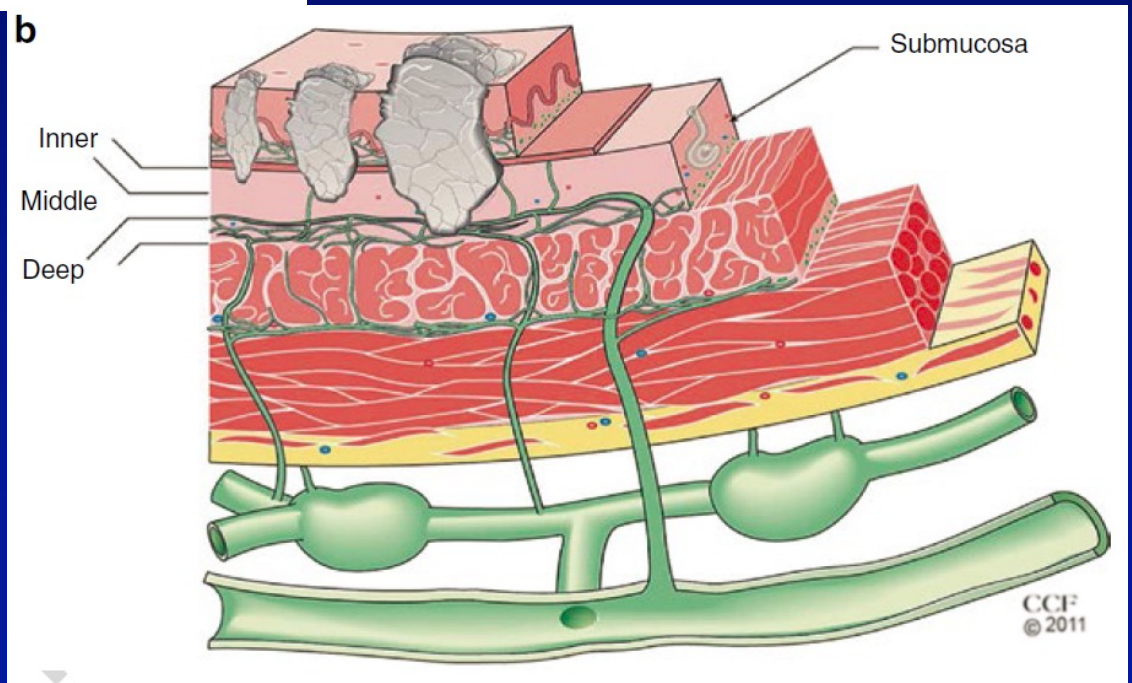
Pattern of Lymphatic Spread of AEG Tumors



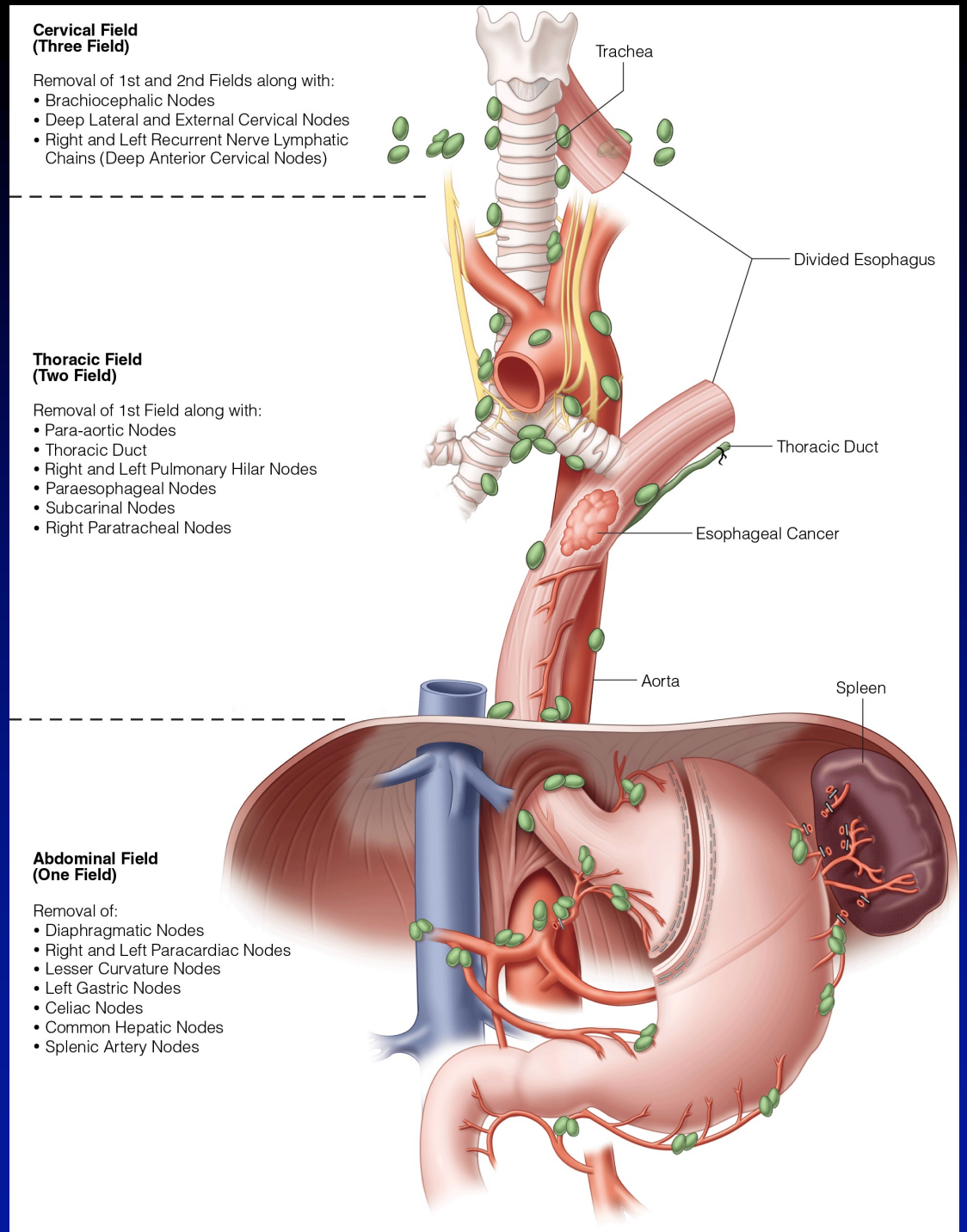
Siewert RJ 2004

Lymphatics in Esophageal Cancer





Lymph node Dissection in Esophageal Cancer



Goals of Surgical Approach

- Esophagectomy - Obtain R0 resection
- Adequate lymphadenectomy
- Decrease complications

Neoadjuvant Chemotherapy for Esophageal Cancer

Table 1
Results of phase III preoperative or perioperative chemotherapy trials in esophageal and gastroesophageal junction cancer

Treatment	Histology	No. of Patients	R0 Resection Rate (%)	Pathologic CR Rate (%)	Survival		Local failure (%)	Reference
					Median	Overall		
Perioperative ECF + surgery	Adeno	250	69	0	24 mo	5-y 36%	14	Cunningham et al,[5] 2006
Surgery		253	66	N/A	20 mo	5-y 23%	21	
Perioperative 5FU/Cis + surgery	Adeno	109	87	NS	NS	5-y 38%	24	Ychou et al,[6] 2011
Surgery		110	74	N/A	NS	5-y 24%	26	
Preoperative ECX + surgery	Adeno	446	67	11	25.8	3-y 42%	NS	Alderson et al,[7] 2015
Preoperative 5FU/Cis + surgery		451	60	3	24.2	3-y 39%	NS	
Perioperative 5FU/Cis + surgery	Adeno	213	62	2.5	14.9 mo	3-y 23%	32	Kelsen et al,[12] 1998
Surgery	(54%) + SCC	227	59	N/A	16.1 mo	3-y 26%	31	
Preoperative 5FU/Cis + surgery	Adeno	400	60	NS	16.8 mo	5-y 23%	19	Medical Research Council,[48] 2002; Allum et al,[13] 2009
Surgery	(66%) + SCC	402	54	N/A	13.3 mo	5-y 17%	17	
Preoperative 5FU/LV/Cis + surgery	Adeno	72	82	7.1	64.6 mo	2-y 73%	NS	Schuhmacher et al,[14] 2010
Surgery		72	66.7	N/A	52.5 mo	2-y 69.9%	NS	

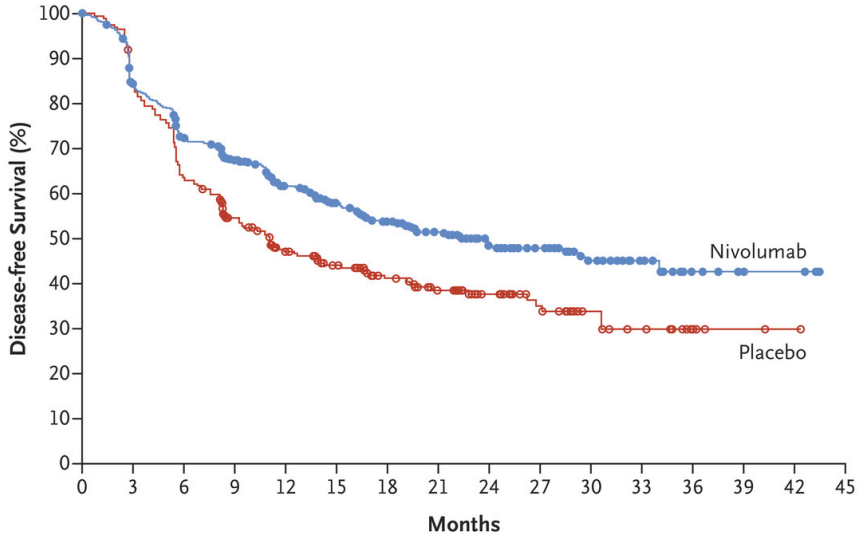
CheckMate 577 Trial

- 794 patients with residual disease after neoadjuvant CRT
- Randomized to Nivolumab 480 mg or placebo every 2 weeks for 16 weeks -> every 4 weeks. Treatment duration was 1 year
  - Enrollment irrespective of PD-L1 status
- Median follow-up 24.4 months
  - Survival was twice as long for nivolumab (22.4 vs 11 months)
    - Effect seen irrespective of histology, location, initial stage of PD-L1 status

Kelly RJ et al. N Engl J Med 2021; 384:1191

CheckMate 577 Trial

A Disease-free Survival in the Overall Population



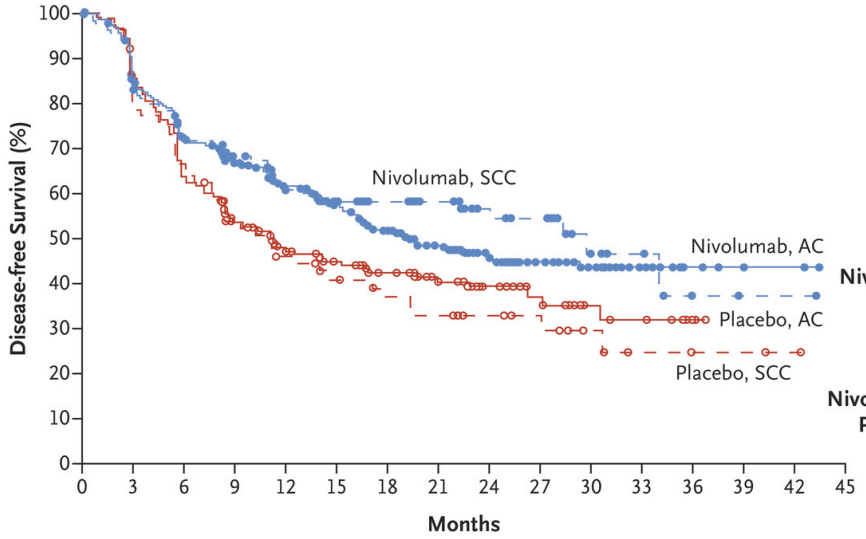
	No. of Patients	Median Disease-free Survival (mo (95% CI))
Nivolumab	532	22.4 (16.6–34.0)
Placebo	262	11.0 (8.3–14.3)

Hazard ratio for disease recurrence or death, 0.69 (96.4% CI, 0.56–0.86)
P<0.001

No. at Risk

Nivolumab	532	430	364	306	249	212	181	147	92	68	41	22	8	4	3	0
Placebo	262	214	163	126	96	80	65	53	38	28	17	12	5	2	1	0

B Disease-free Survival According to Histologic Type



	No. of Patients	Median Disease-free Survival (mo (95% CI))
Nivolumab, AC	376	19.4 (15.9–29.4)
Placebo, AC	187	11.1 (8.3–16.8)

Hazard ratio for disease recurrence or death, 0.75 (95% CI, 0.59–0.96)

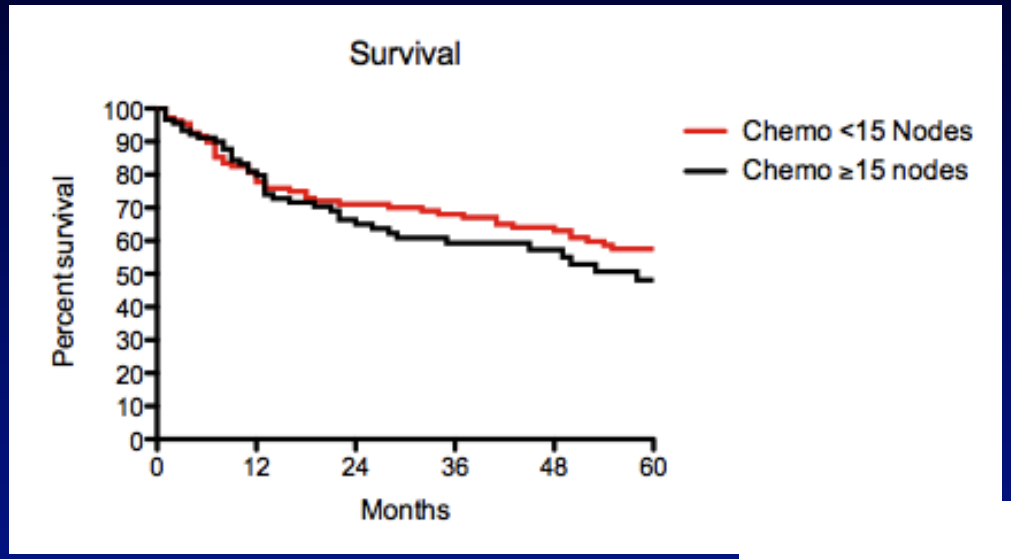
Nivolumab, SCC	155	29.7 (14.4–NE)
Placebo, SCC	75	11.0 (7.6–17.8)

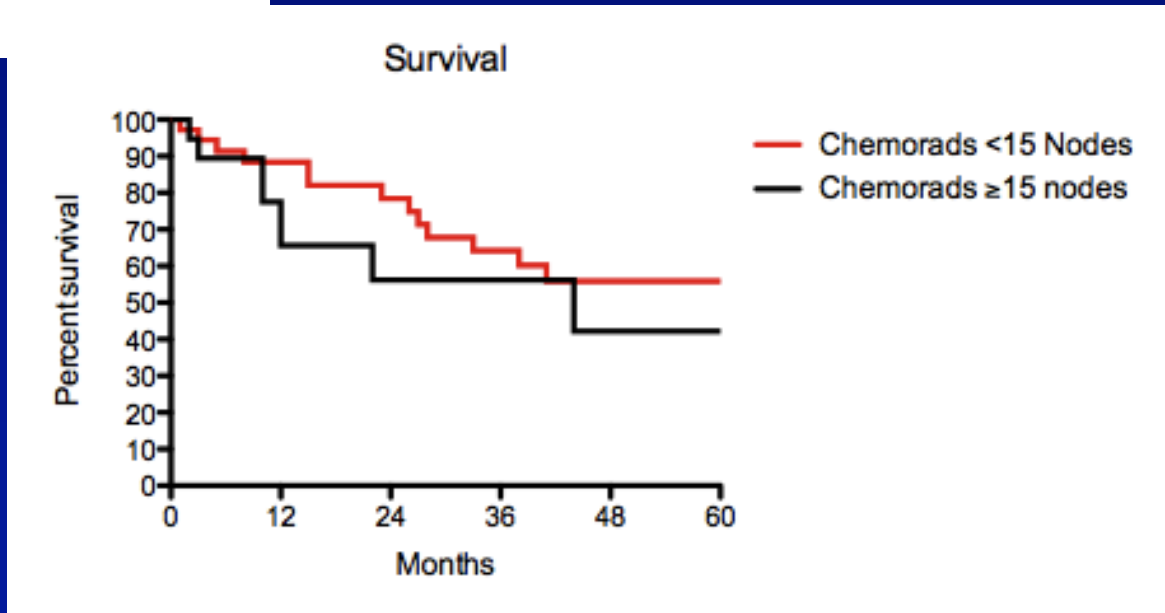
Hazard ratio for disease recurrence or death, 0.61 (95% CI, 0.42–0.88)

No. at Risk

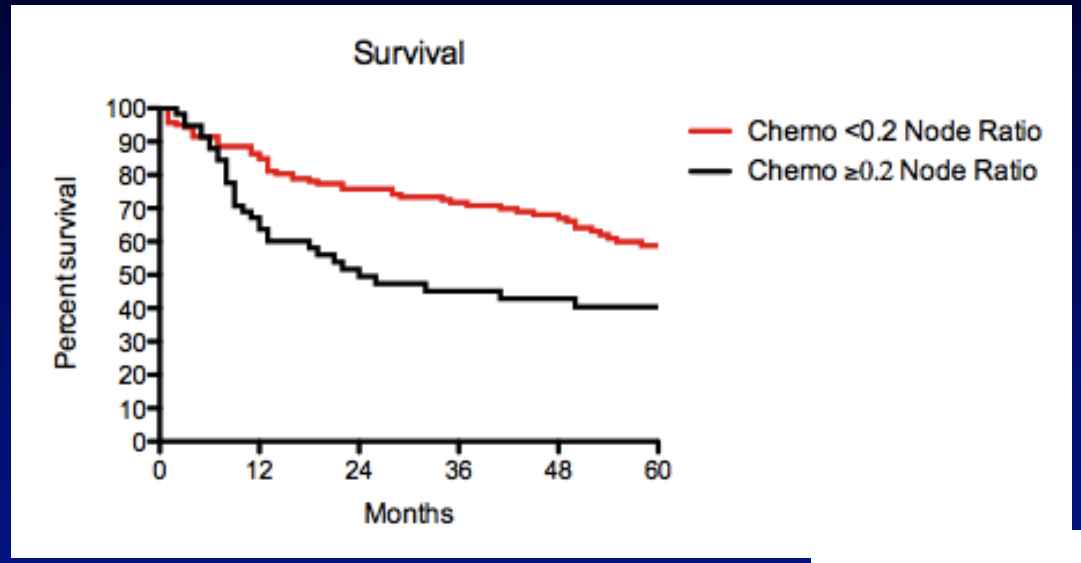
Nivolumab, AC	376	305	257	219	178	151	125	99	65	45	32	16	6	3	2	0
Nivolumab, SCC	155	124	106	87	71	61	56	48	27	23	9	6	2	1	1	0
Placebo, AC	187	156	114	92	68	57	47	37	26	18	11	9	3	0	0	0
Placebo, SCC	75	58	49	34	28	23	18	16	12	10	6	3	2	2	1	0

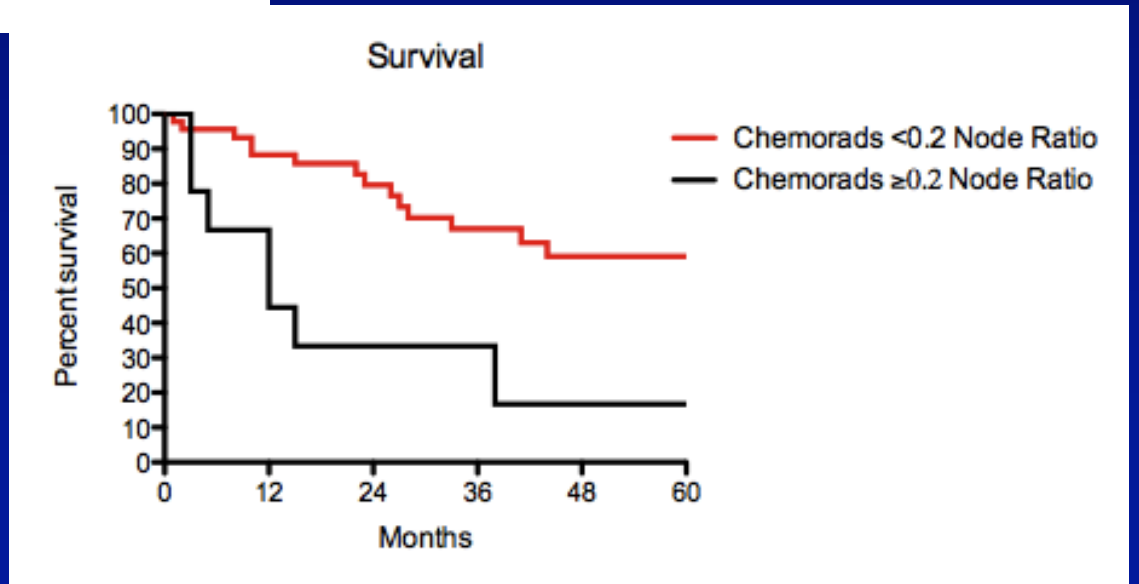
Extent of Lymphadenectomy in Patients Receiving Neoadjuvant Treatment





Lymph Node Ratio in Esophageal Cancer





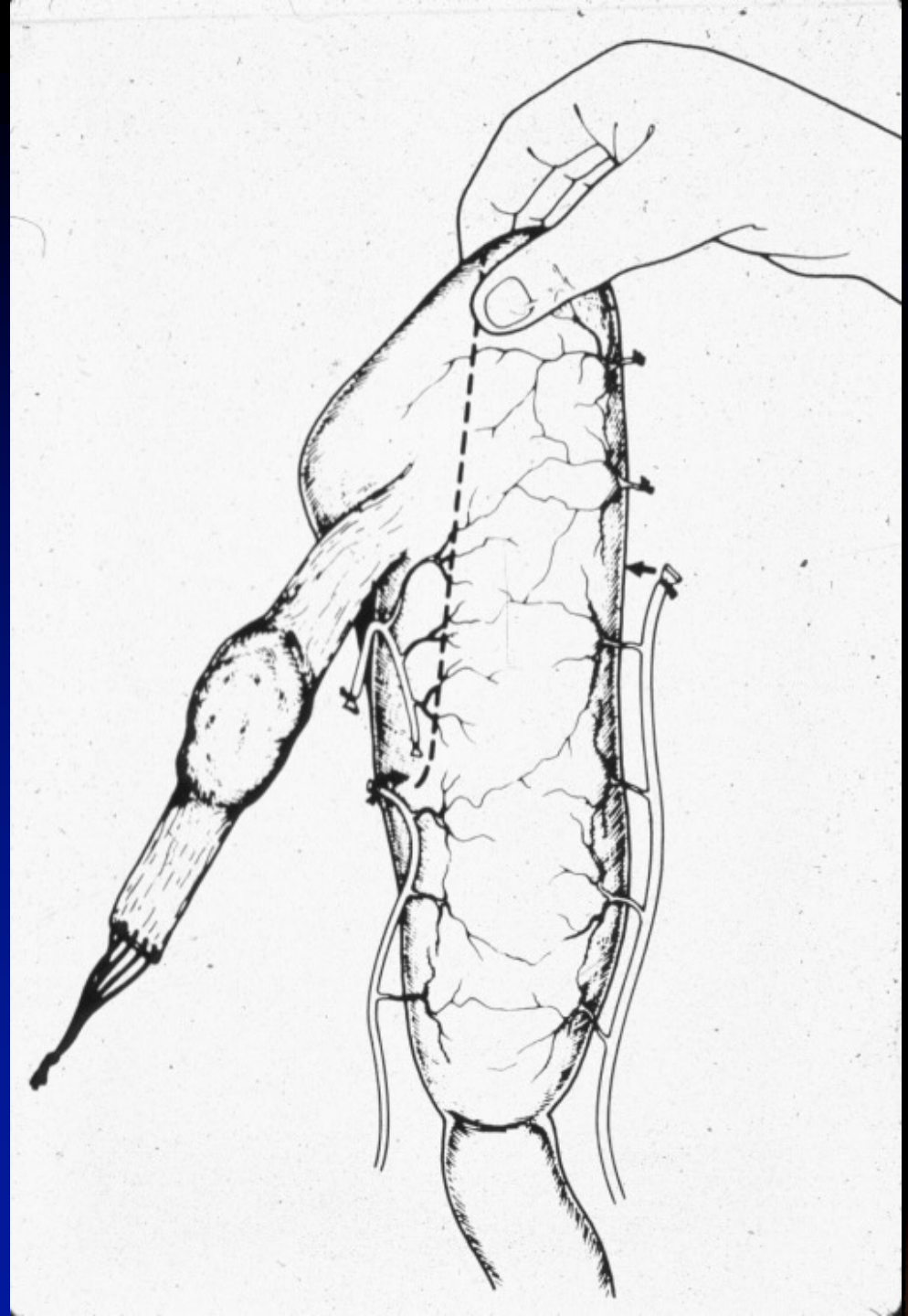
Gastric Replacement

ADVANTAGES

- Excellent blood supply
- One anastomosis
- Any level
- Good functional results

DISADVANTAGE

- Reflux



Colon Interposition

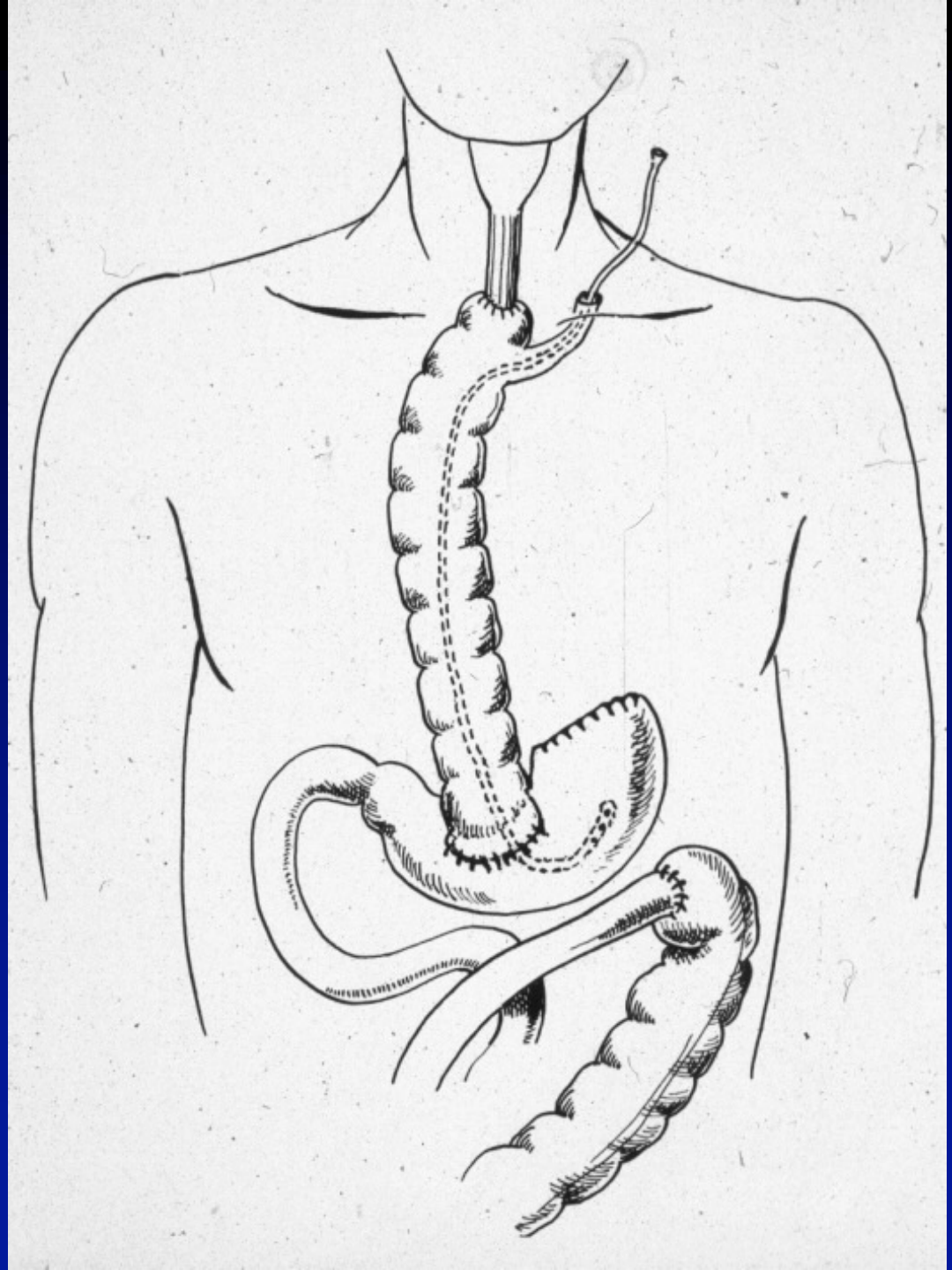
ADVANTAGES

- Any level

DISADVANTAGES

- 3 anastomoses
- Redundancy
- Blood supply variable

Colon Interposition



Jejunal Replacement

ADVANTAGES

- Effective peristalsis

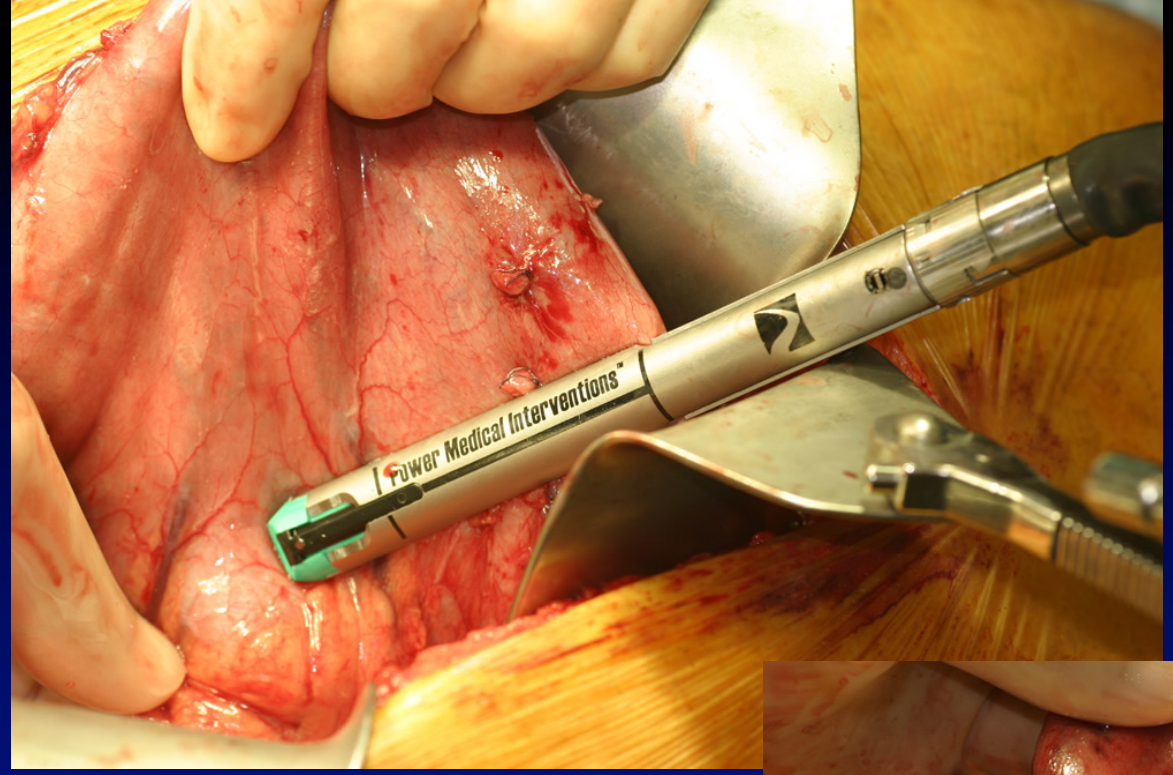
DISADVANTAGES

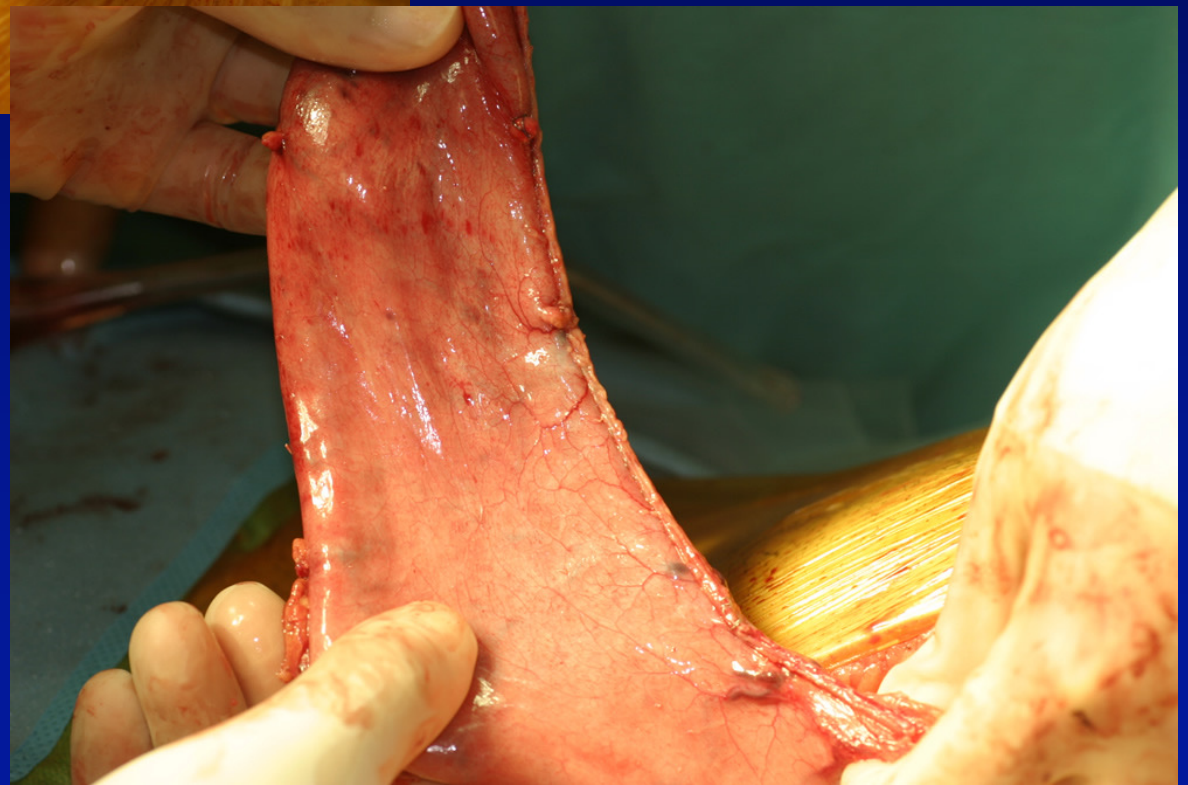
- 3 anastomoses
- Redundancy
- Level uncertain
- Technical difficulty

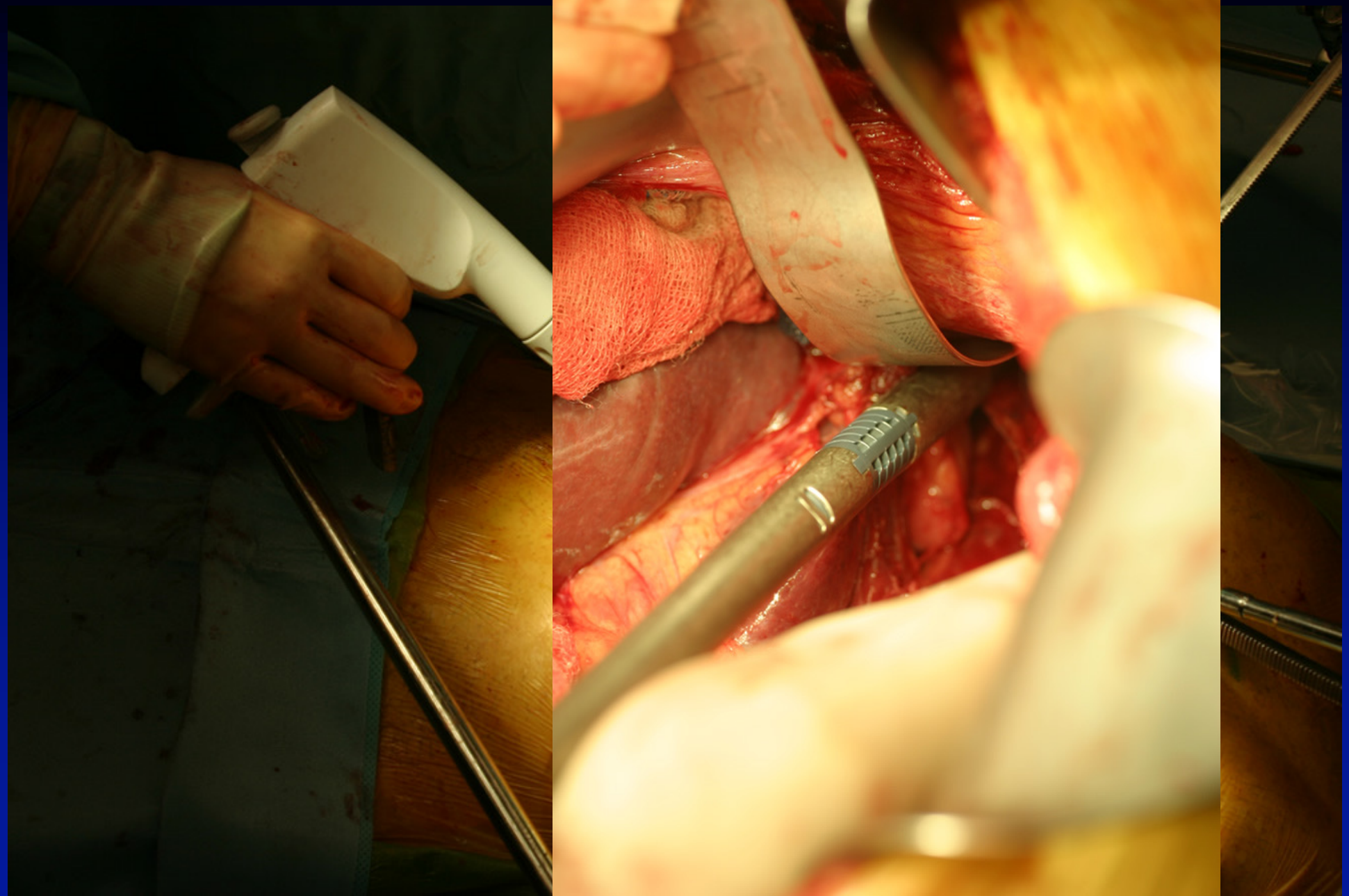
Transhiatal vs Transthoracic Approach – Randomized Trials

- No statistically significant differences were found in morbidity and in (short-medium term) survival between both techniques
- Hulscher's study suggested that a THE was associated with a significantly lower morbidity, while there was a trend towards improved medium-term survival with the extended approach

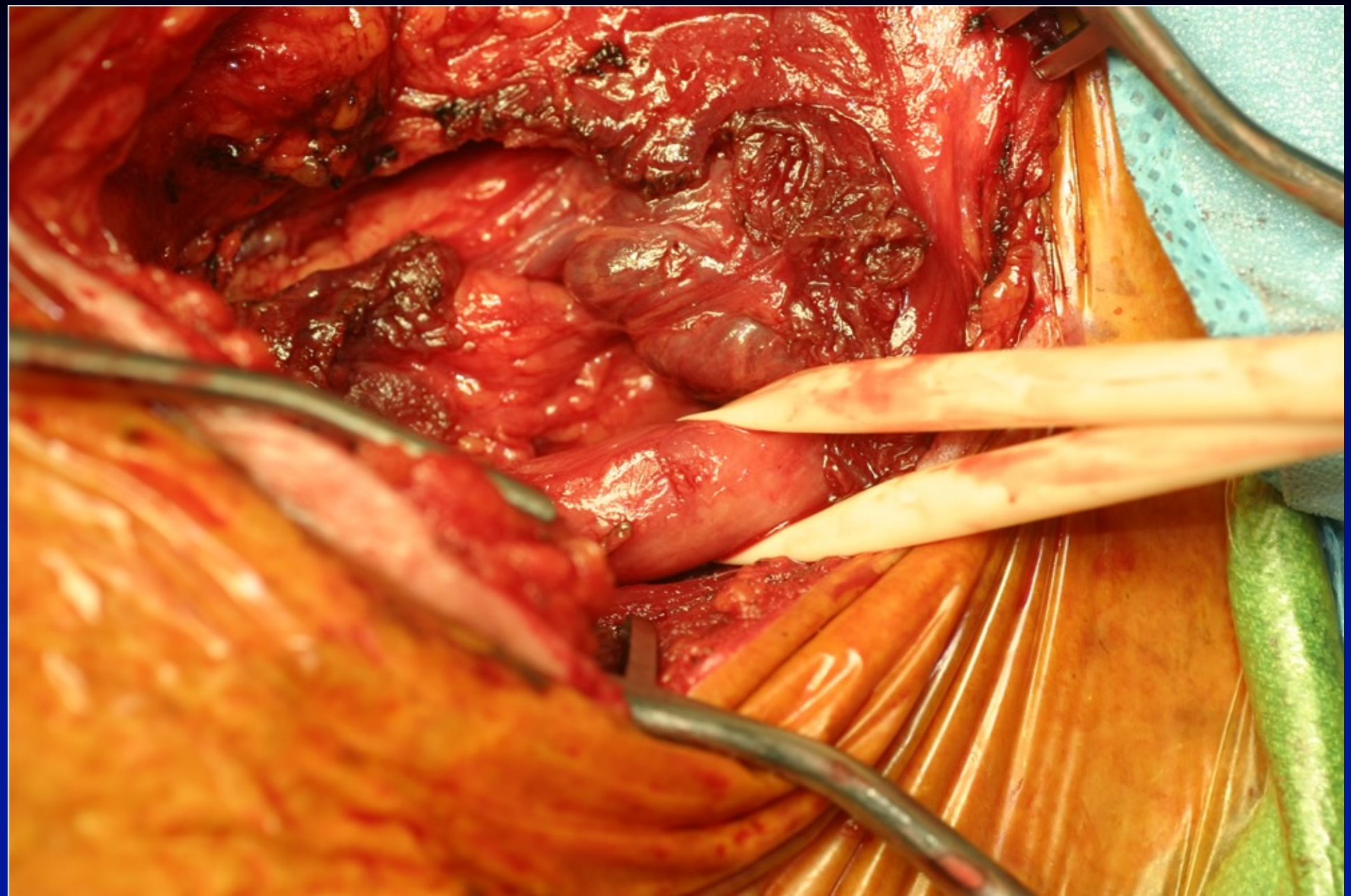
Creation of Gastric Tube



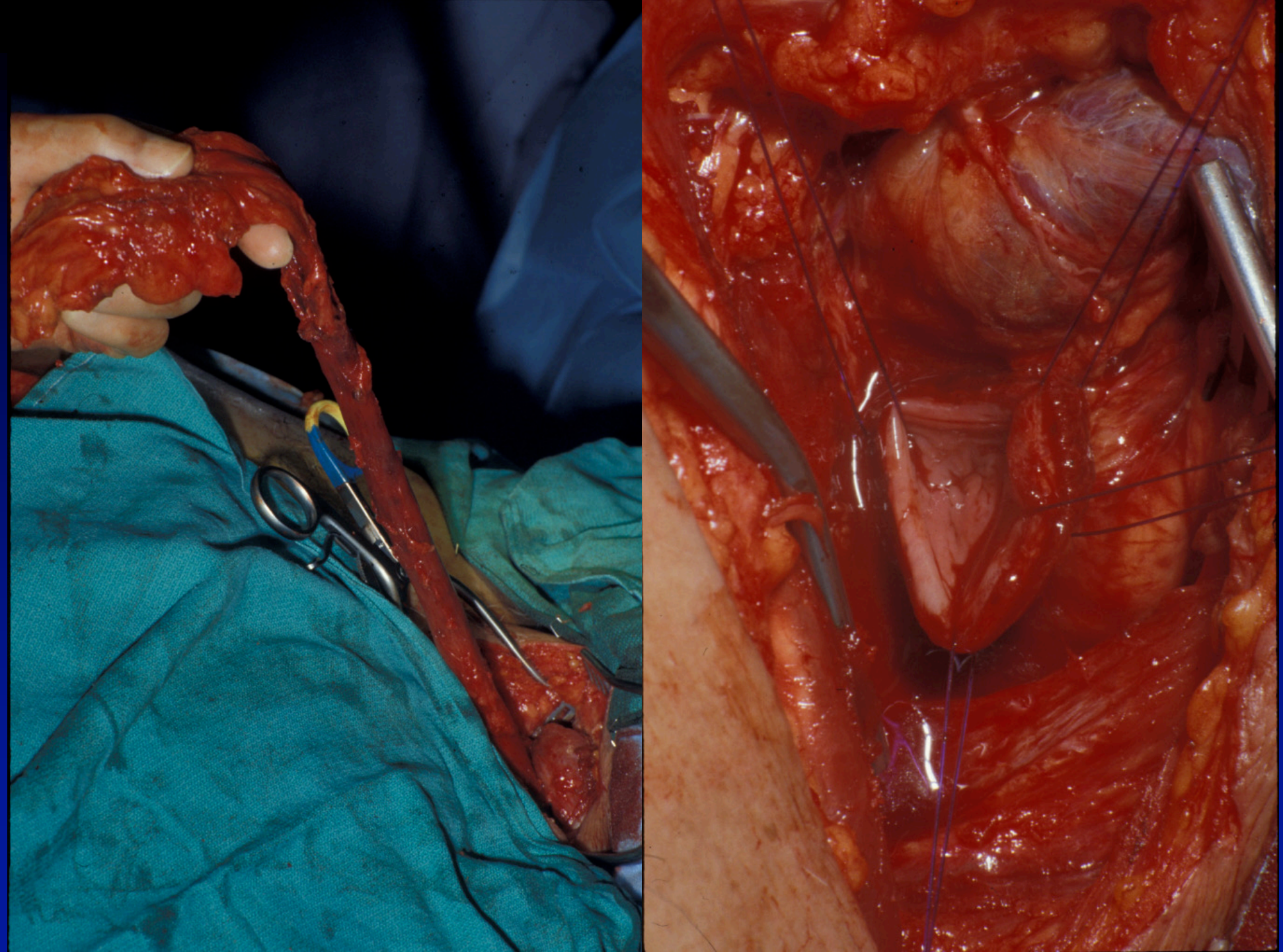


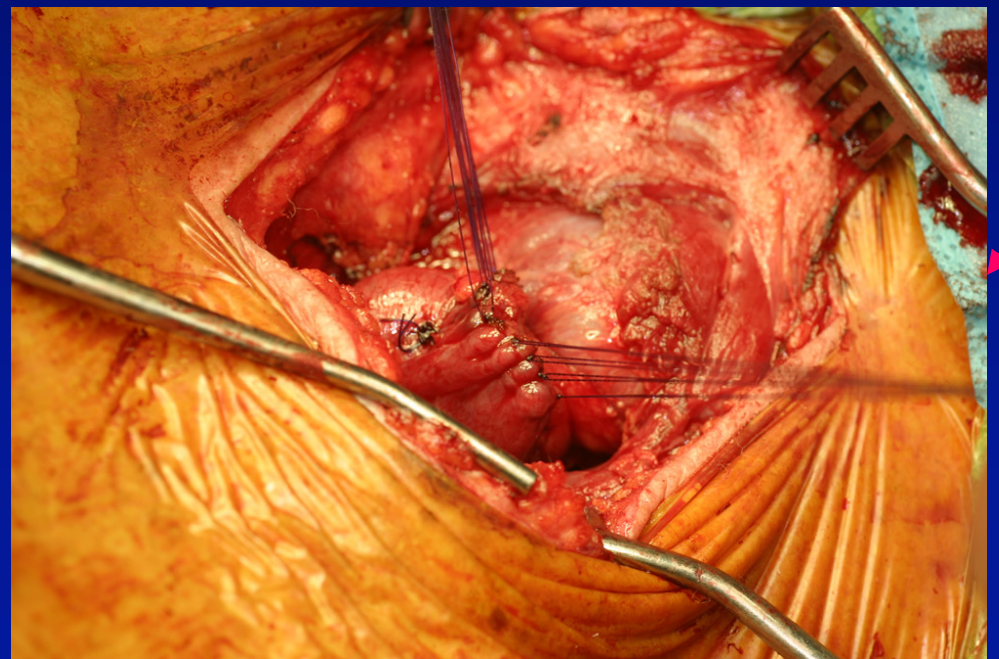


Transhiatal Esophagectomy – Isolation of esophagus in the neck

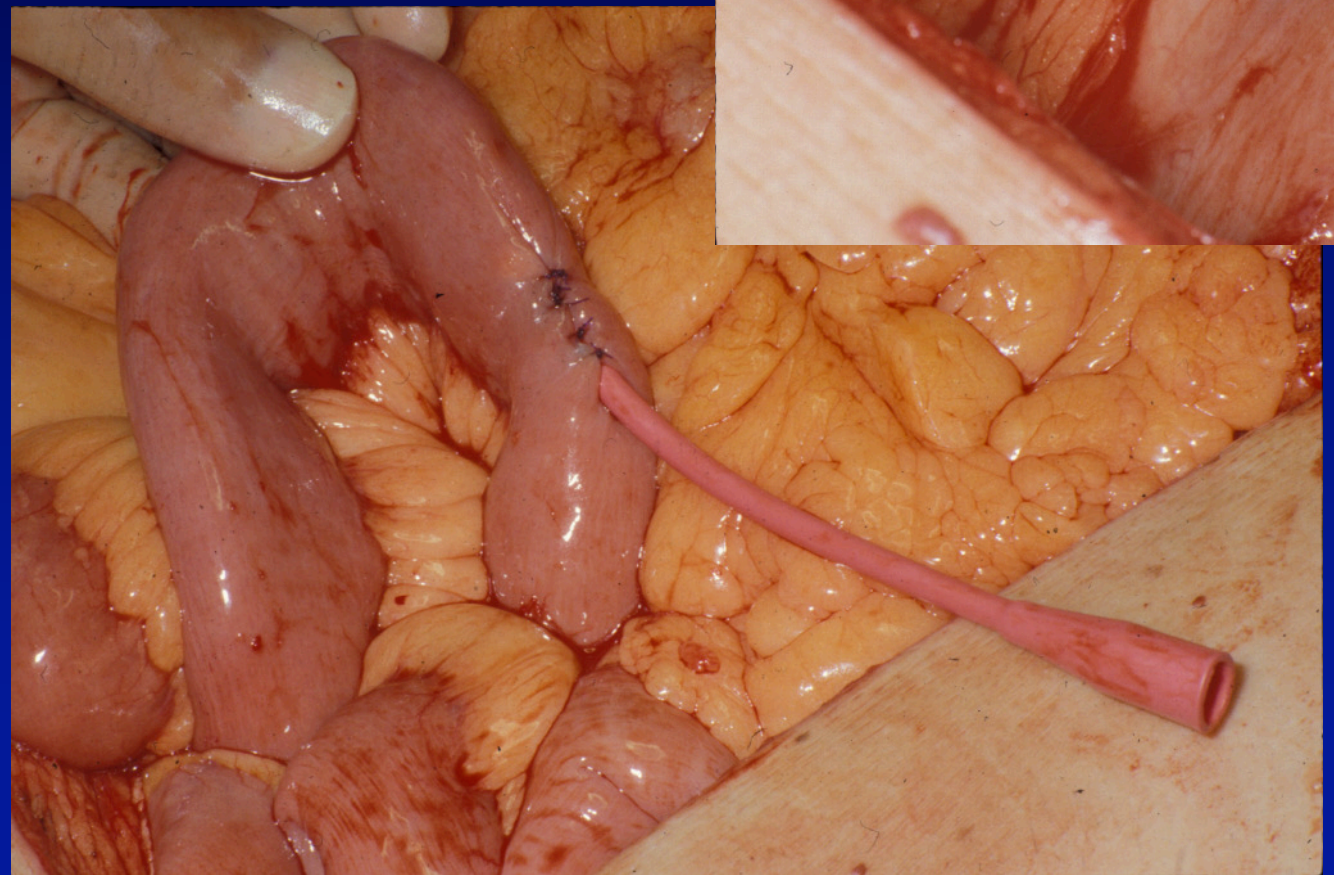


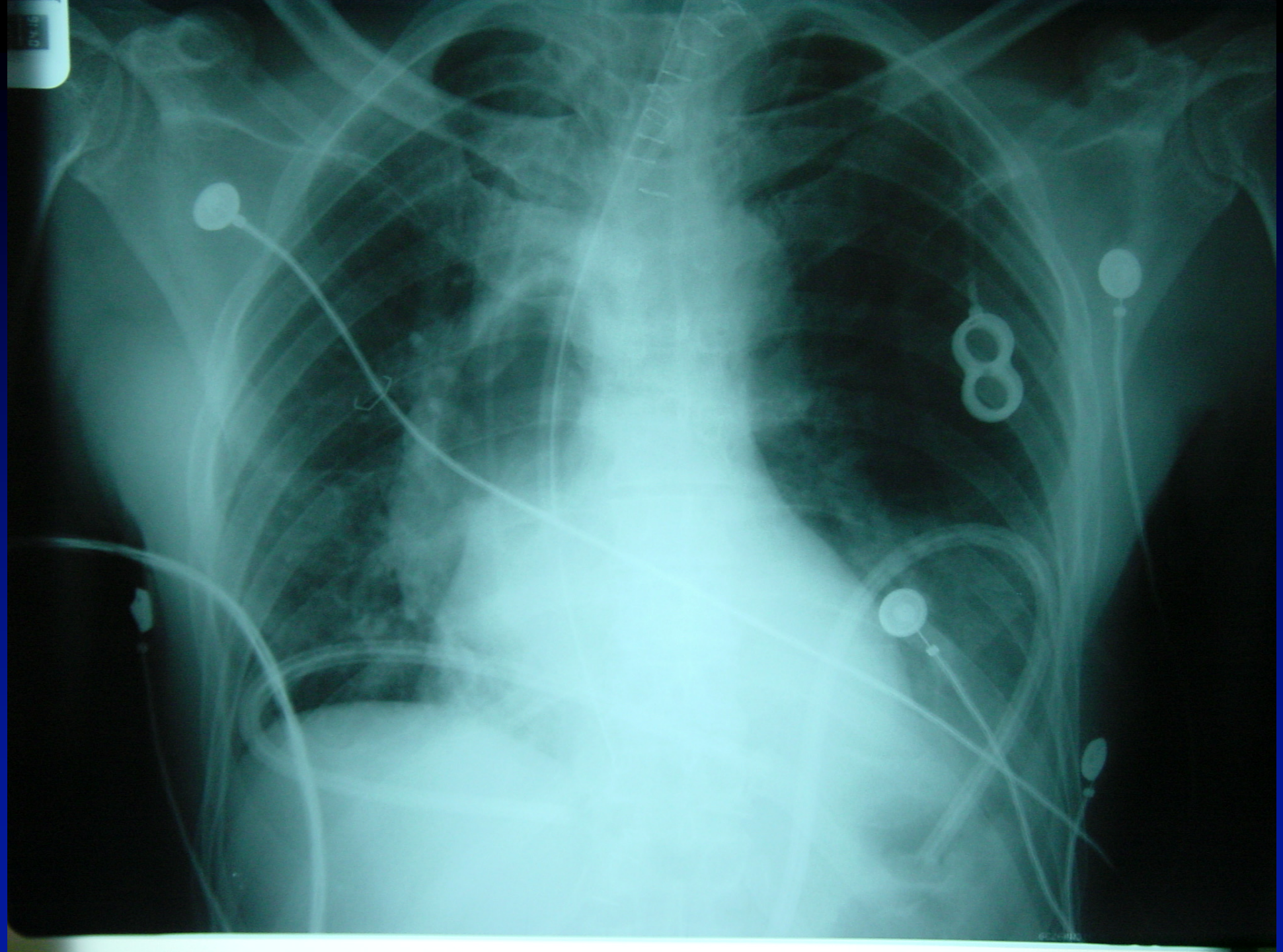
Transhiatal Esophagectomy – Blunt mediastinal dissection



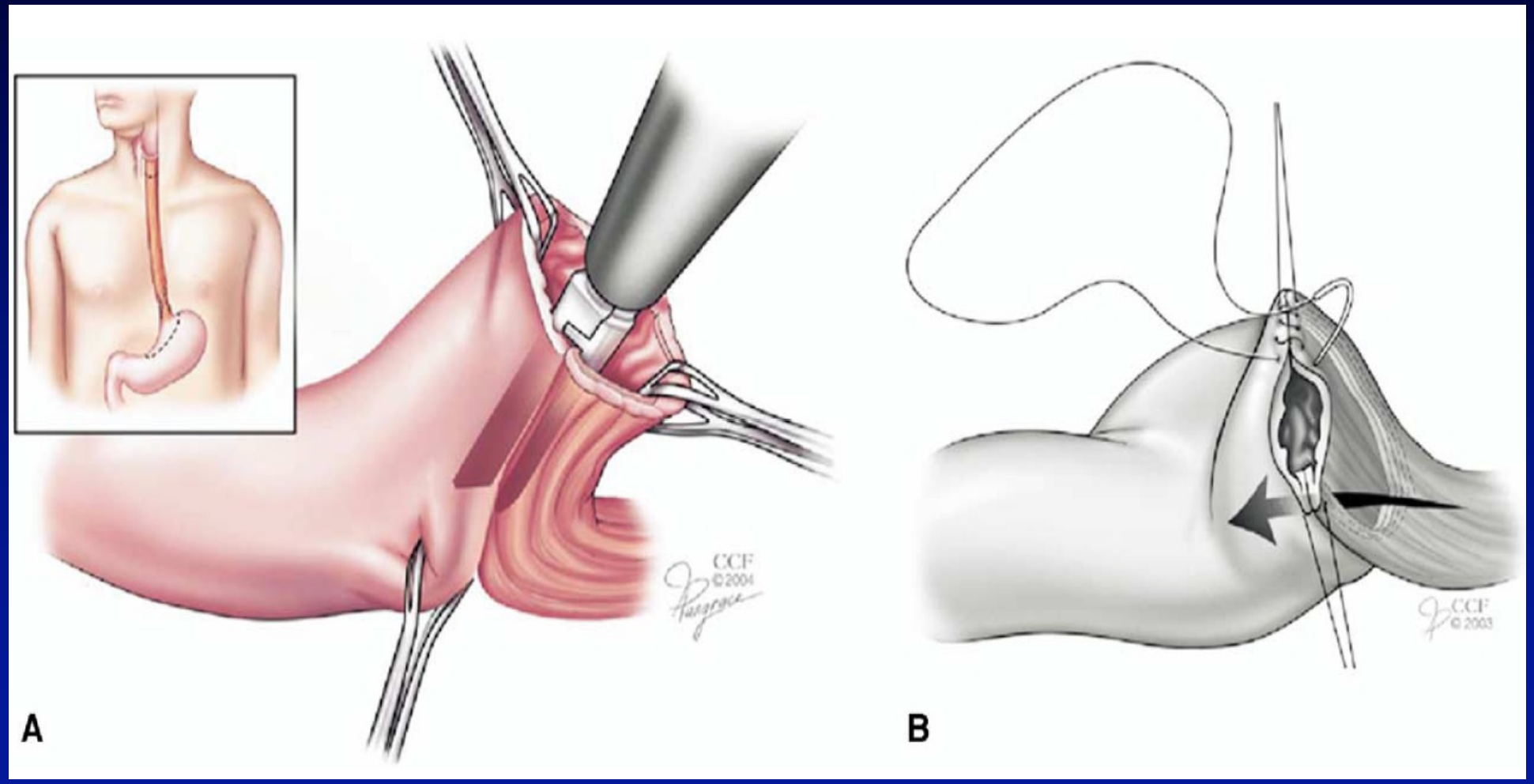


Transhiatal Esophagectomy: Pyloroplasty and Feeding Jejunostomy





Gastroesophageal Anastomosis



Laparoscopic Esophagectomy

- First reported by DePaula et al.
  - 1996
  - 48 patients
- Swanstrom and Hansen
  - 1997; 9 patients
- Luketich et al.
  - 2000; Over 100 patients
  - Laparoscopic + Thoracoscopic approach

Minimally Invasive Esophagectomy

- Thoracoscopy combined with laparotomy
- Thoracoscopy combined with laparoscopy
- Hand-assisted thoracotomy
- Hand-assisted laparotomy
- Laparoscopic transhiatal or hand-assisted laparoscopic transhiatal

Minimally Invasive Esophagectomy

- 1011 patients
- 30 day mortality: 1.7%
- Median LOS: 8 (6-14) days
- Anastomotic leak rate – 5%

Luketich et al. Ann Surg 2012;256:95-103

- Reduced overall morbidity – respiratory
- Data in literature has significant heterogeneity

MIE vs Open Esophagectomy

- Randomized 56 patient to open esophagectomy and 59 patients to MIE
- 16 (29%) - Open vs 5 (9%) –MIE: pulmonary infections in first 2 weeks
- 19(34%) – Open vs 7(12%) – MIE: pulmonary infection in the whole hospital stay

Biere SS, et al. Lancet 2012; 379:1887-92

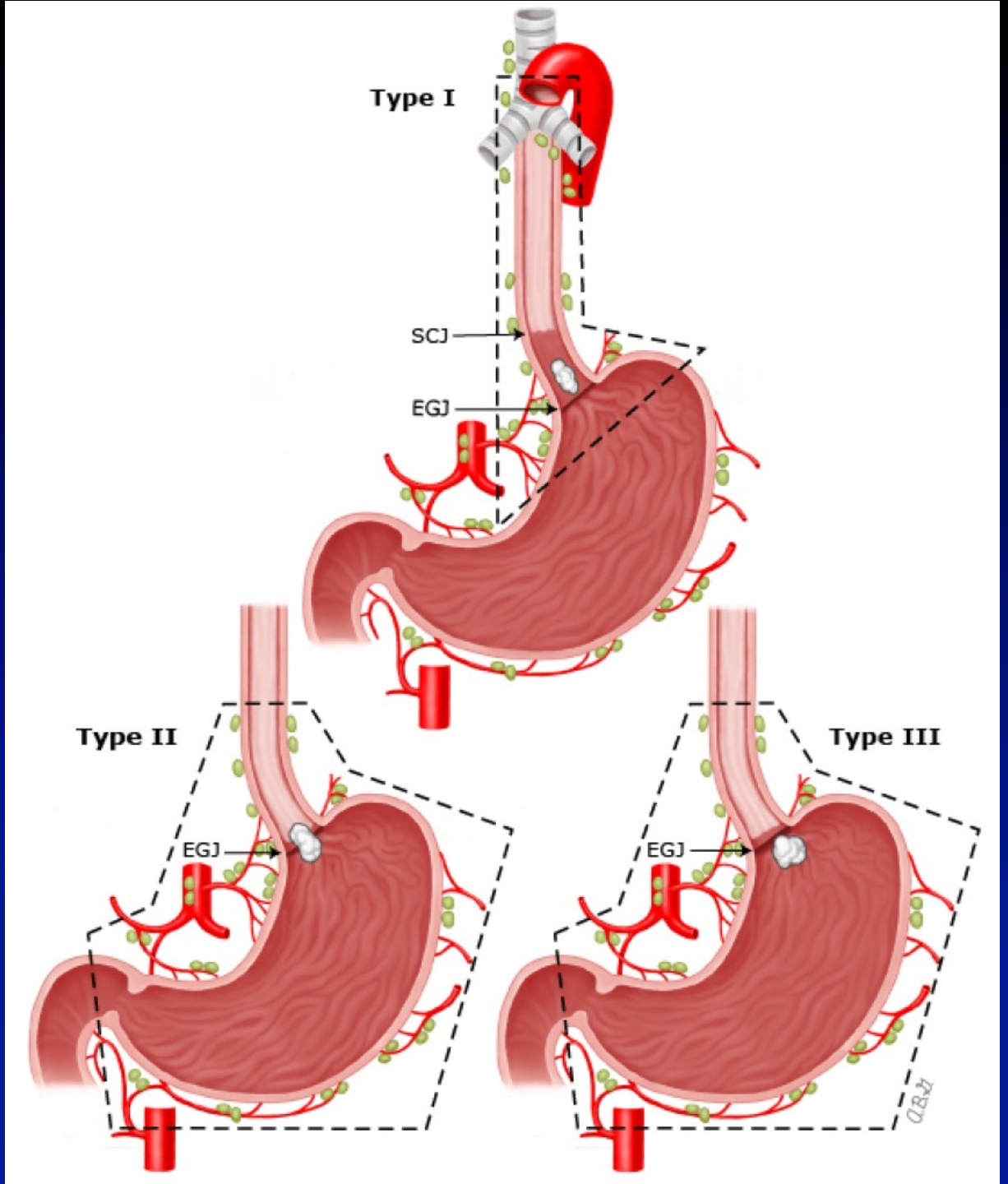
Short Term Results for Laparoscopic Transhiatal Esophagectomy

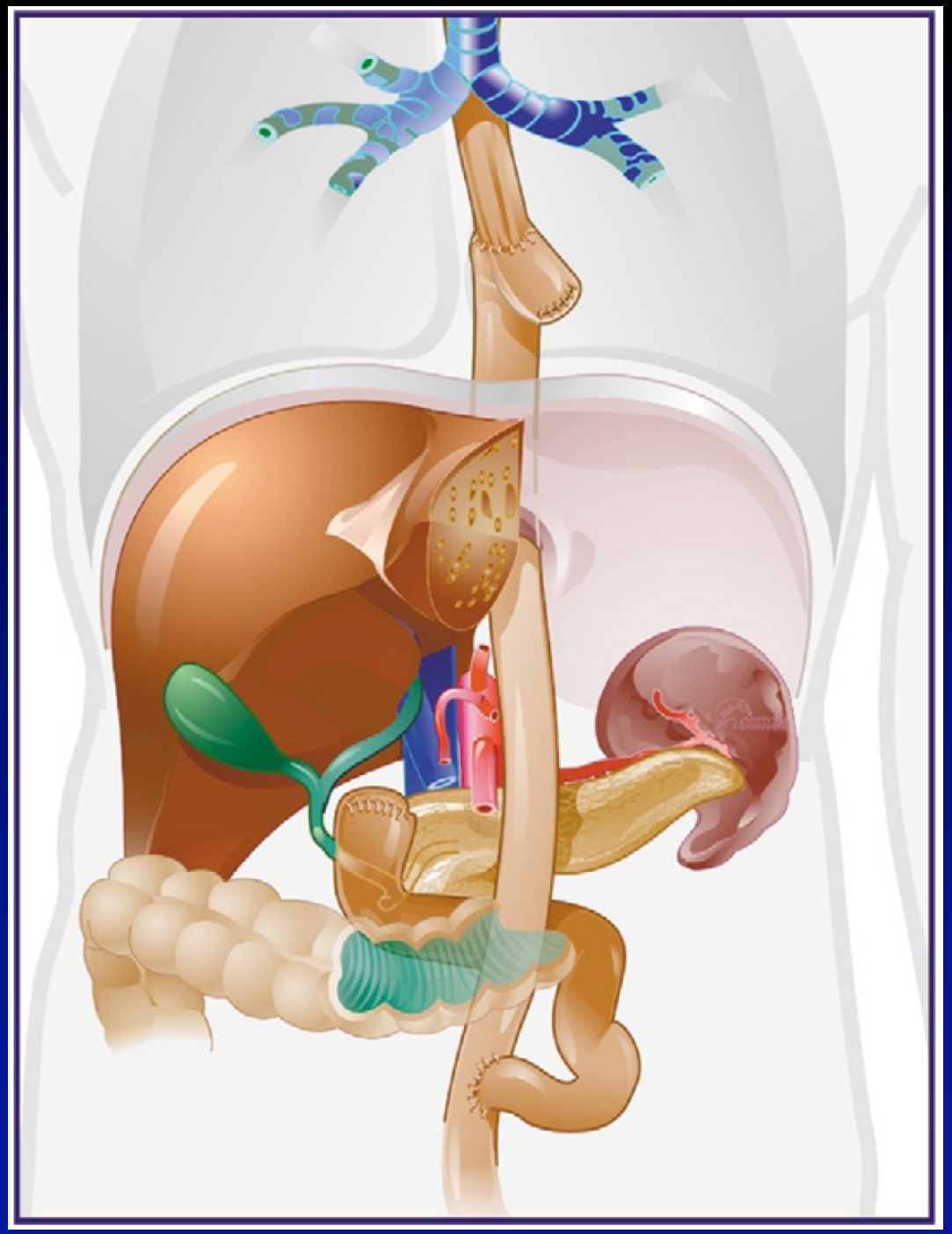
PARAMETER	RESULT
Mean Operative Time	160 - 390 minutes
Mean Blood Loss	220 - 400 cc
Conversion Rate	0 - 16.6%
Anastomotic Leak	0 - 8.3%
Mean Number of Retrieved Lymph nodes	8-14
Mean Hospital Stay	6.4 to 12.1 days
Thirty Day Mortality	0 - 13.6%

Surgical Treatment Options - Siewert

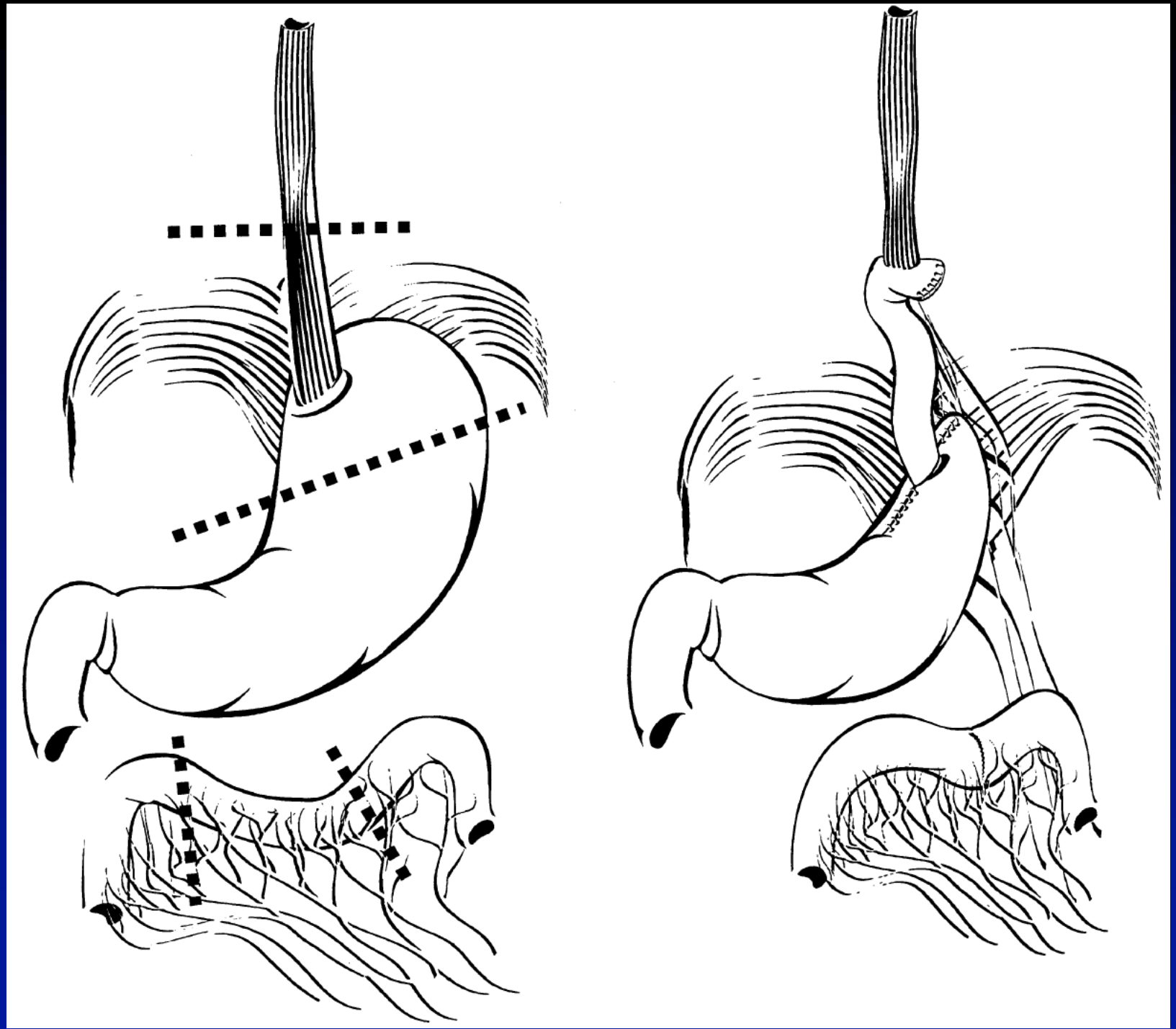
- Type I
  - Ivor Lewis procedure vs transmediastinal esophagectomy
- Type II
  - Extended gastrectomy with distal transhiatal esophageal resection vs transmediastinal esophagectomy
- Type III
  - Extended gastrectomy with distal transhiatal esophageal resection

Extent of resection for type I, II, and III adenocarcinoma of EGJ





Extended Total Gastrectomy



Performance indicators in esophageal cancer surgery Quality-of-care Indicators

Structural measures

- Hospital volume
- Surgeon volume
- Centralization

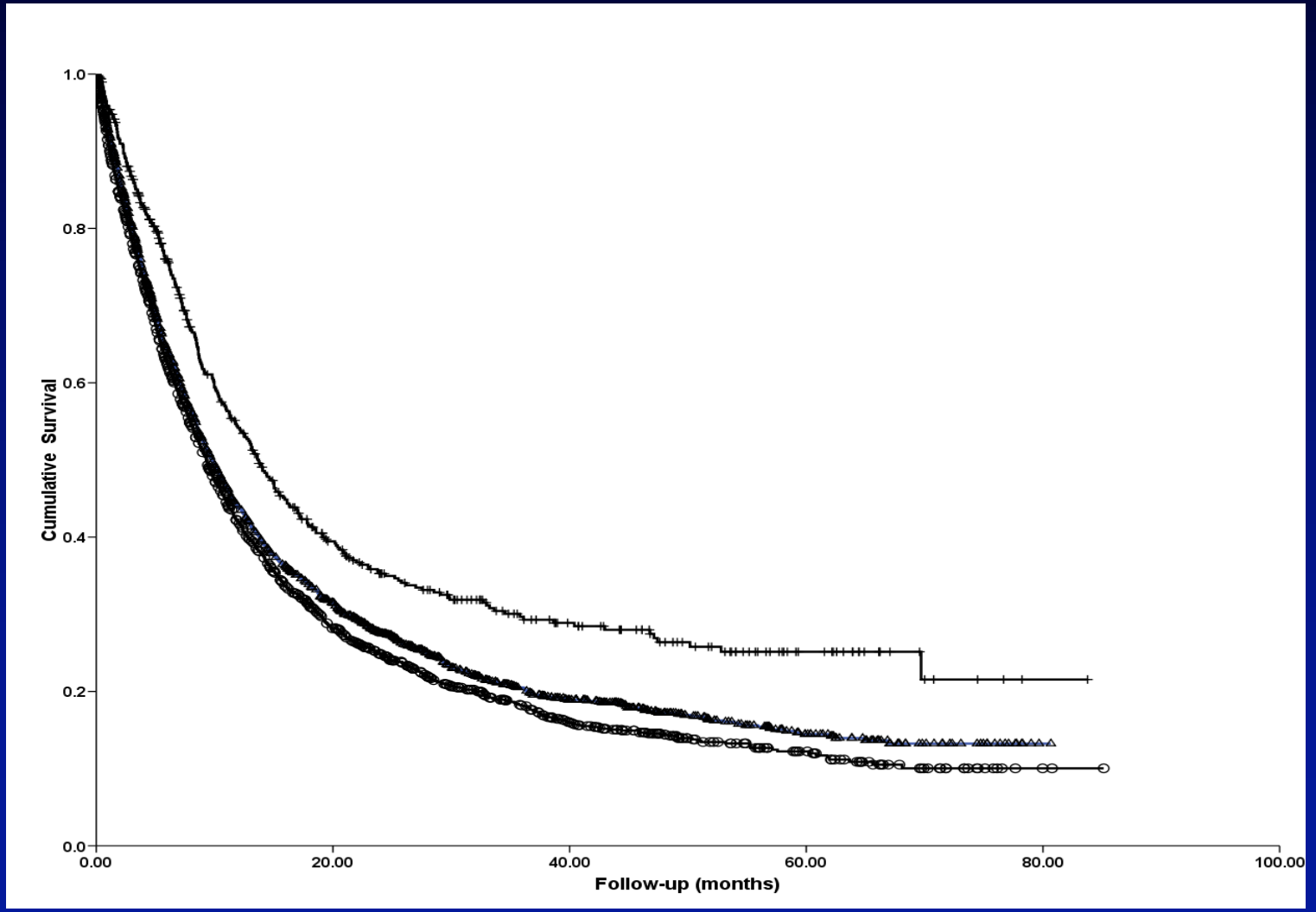
Outcome measures

- Postoperative complications
- Radicality of resection
- Number of resected lymph nodes

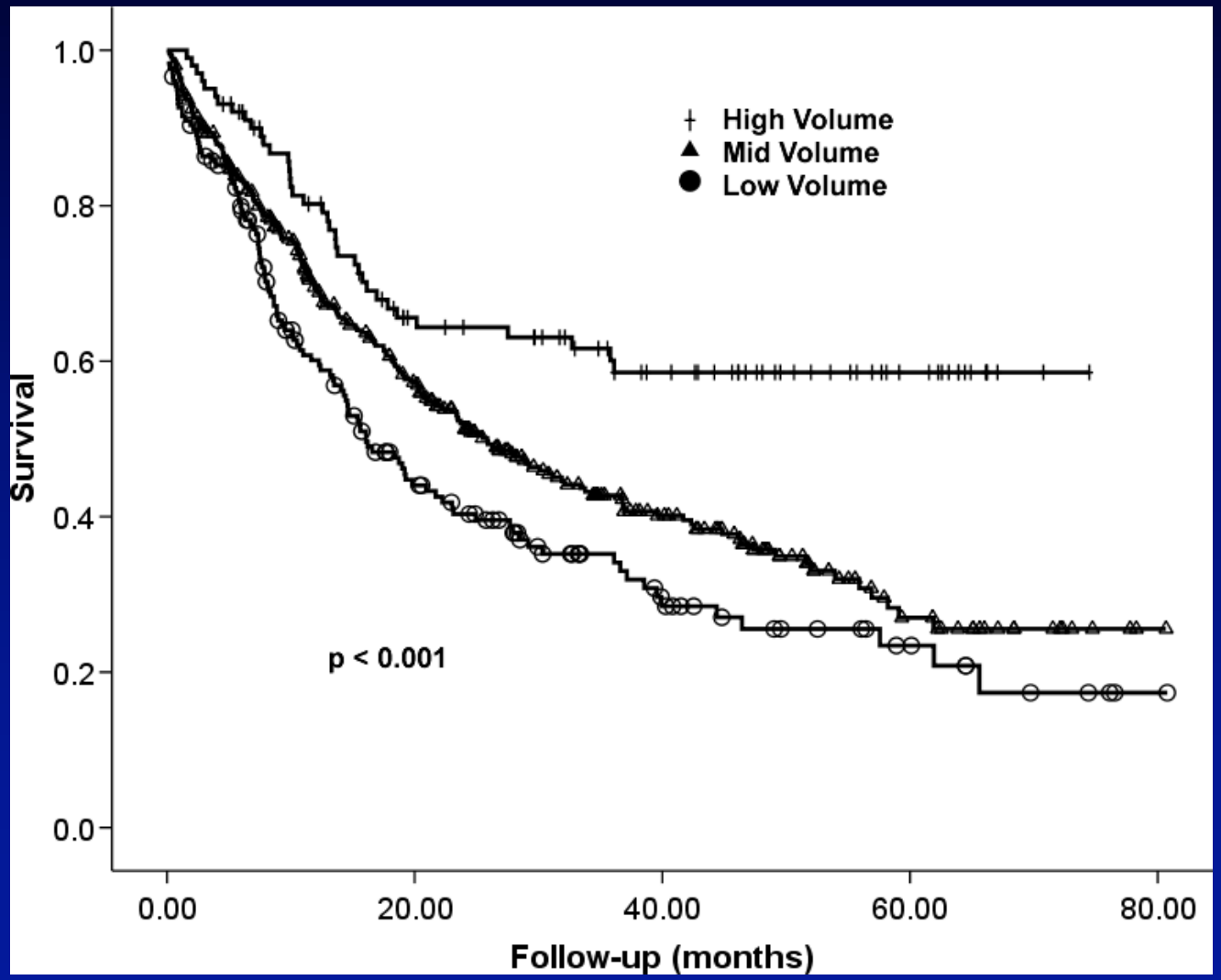
Process measures

- Discussion in multidisciplinary board
- Age
- Preoperative quality of life
- Staging (FDG-PET vs. FDG-PET)
- Lymphadenectomy
- Neoadjuvant chemoradiation
- Surgical approach

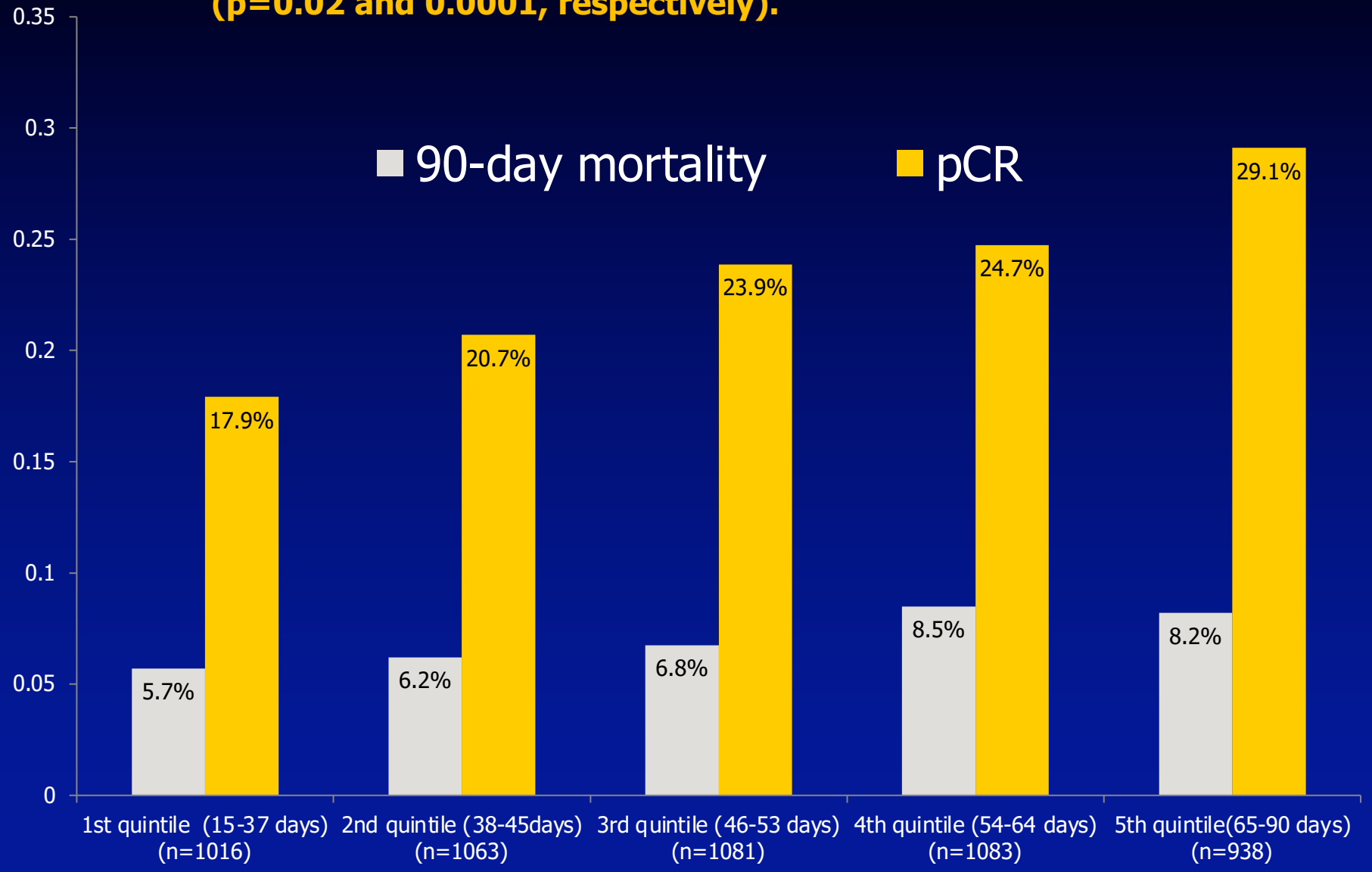
Overall Survival by Treatment Center Volume



Survival of Surgical Patients with Adenocarcinoma by Center Volume



The 90-day mortality and pathological complete response (pCR) according to the neoadjuvant chemoradiation->surgery intervals (p=0.02 and 0.0001, respectively).



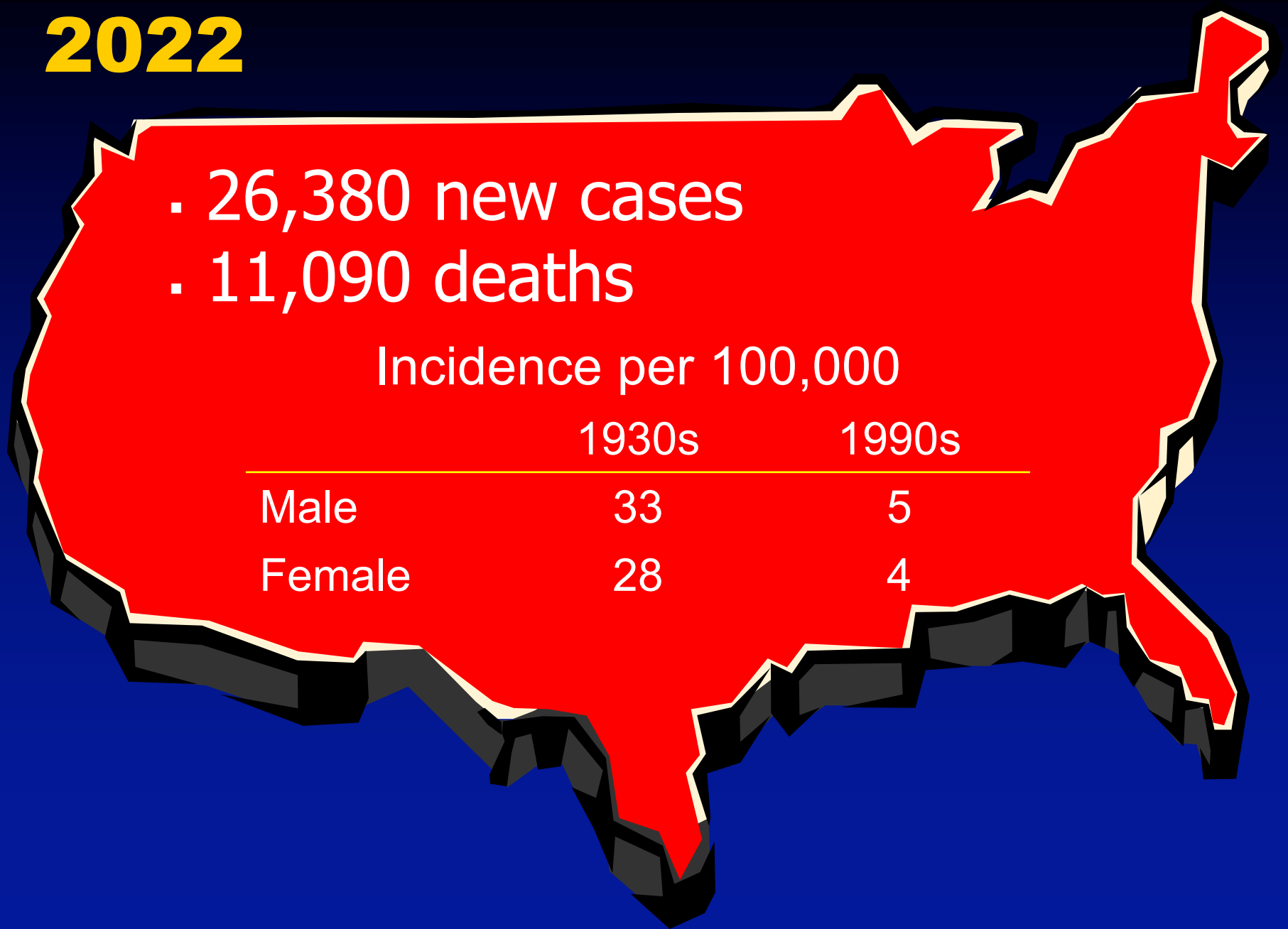
Conclusions

- Surgery remains the standard of care for the treatment of operable esophageal cancer
- Technological advances have allowed for minimally invasive approaches that closely emulate and potentially improve traditional open approaches.
- These surgeries should be done in high volume centers

Gastric Cancer

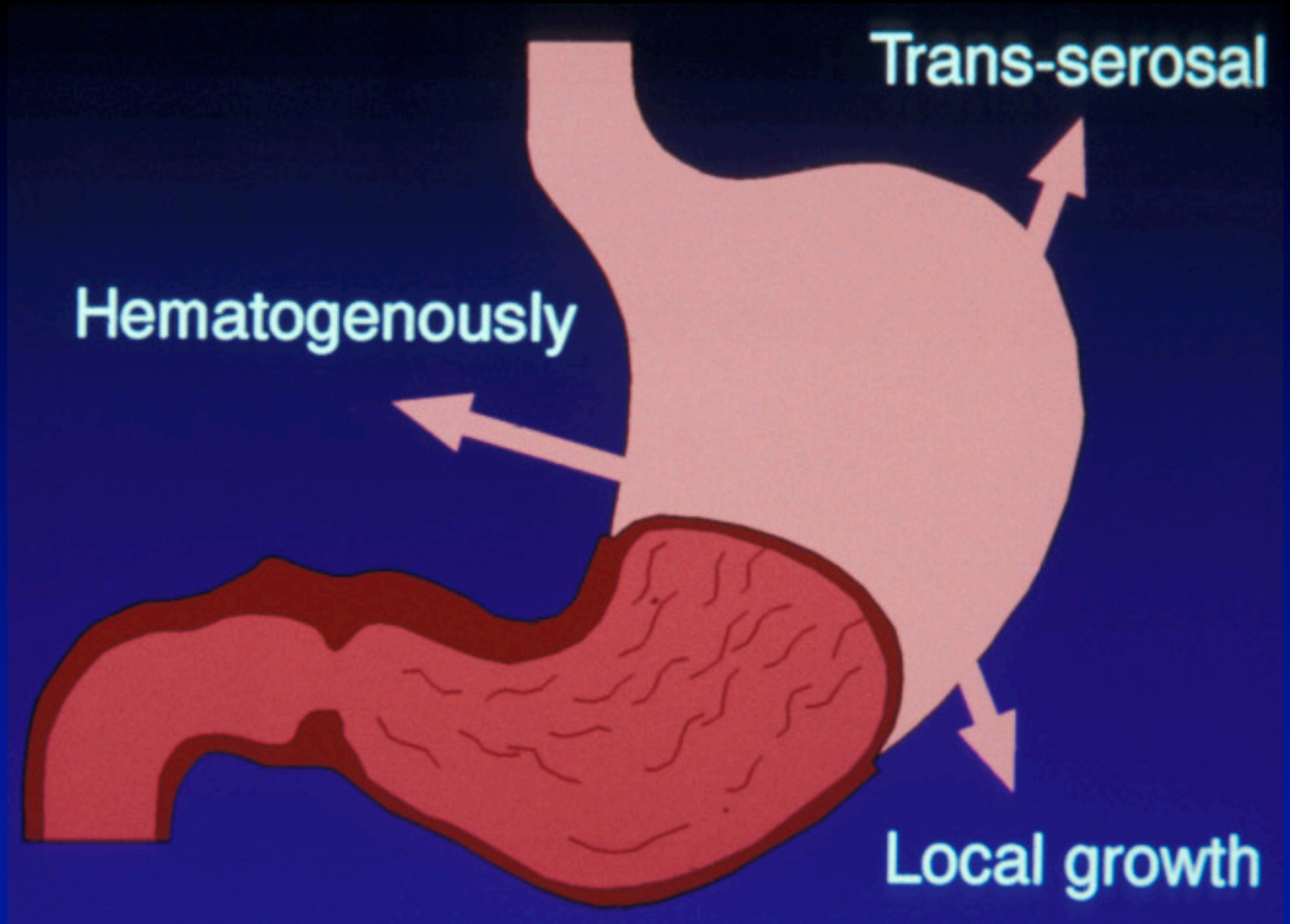
- Third leading cause of cancer-related deaths worldwide
- Over 95% of gastric cancers are adenocarcinomas, typically classified based on anatomic location and histologic type
- Usually carries a poor prognosis because it is often diagnosed at an advanced stage.

Gastric Cancer Statistics: 2022

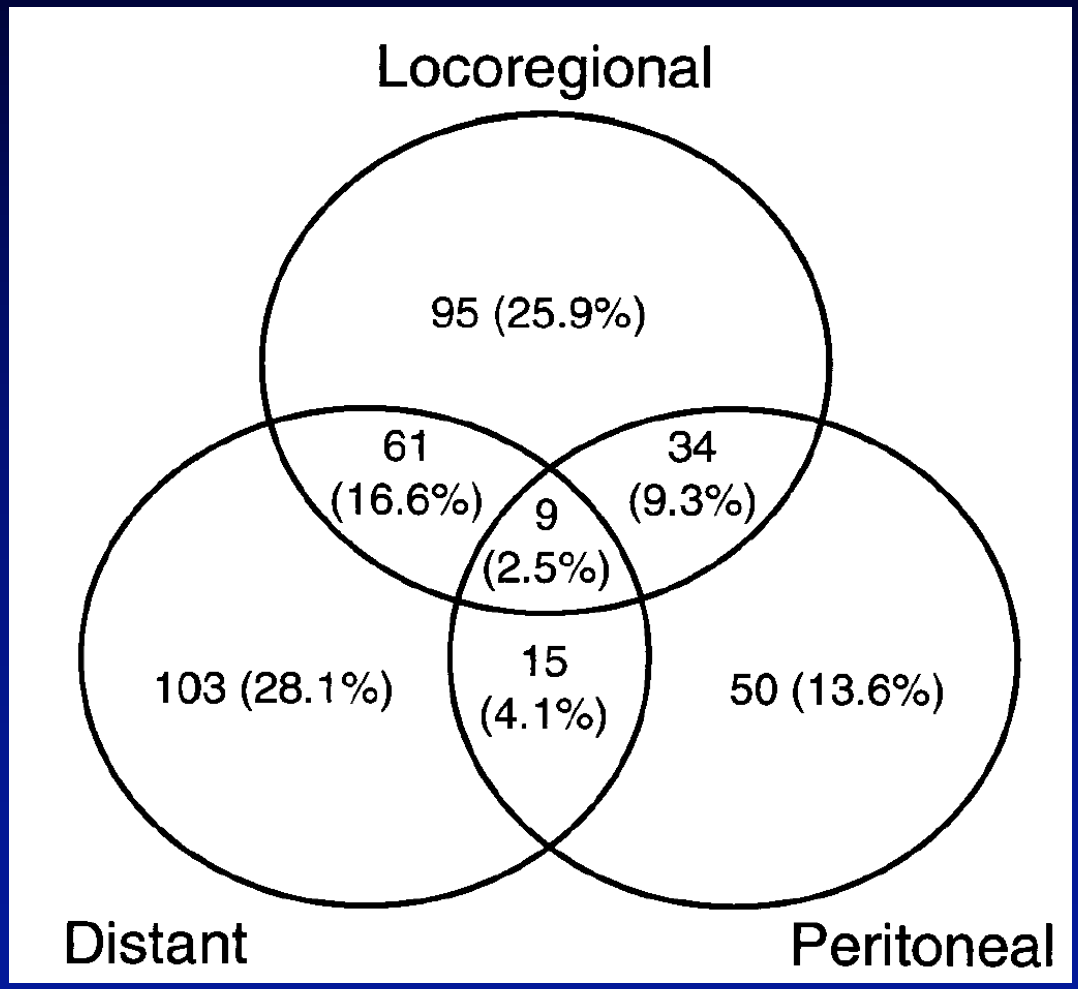


Gastric Cancer

- Dramatic shift in the type and location of upper gastrointestinal tract tumors has occurred in North America and Europe
- Marked decline in intestinal type gastric cancers of the distal stomach
  - Enhanced access to clean drinking water
  - Improved food preservation
  - Average diet with low promotion of gastric cancer
  - *H Pylori* eradication
- Incidence rates of diffuse type gastric cancer of the proximal stomach are rising (multifactorial)


Trans-serosal
Hematogenously
Local growth

Recurrence patterns in 367 patients with documented recurrence after complete resection of gastric adenocarcinoma



D'Angelica M, et al. Ann Surg 2004; 240:808-816

Diagnostic Laparoscopy - Gastric Cancer

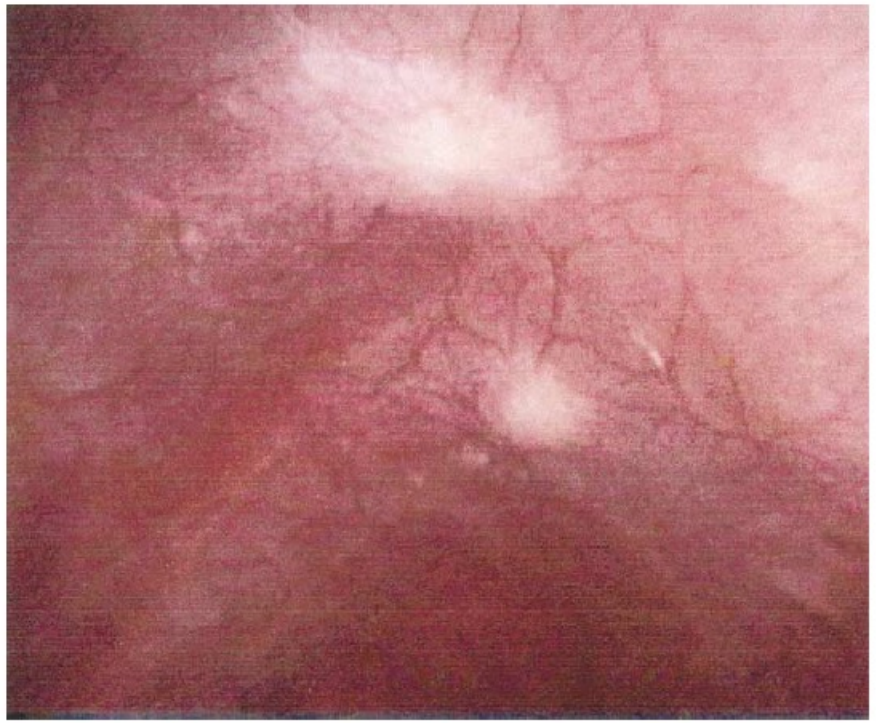


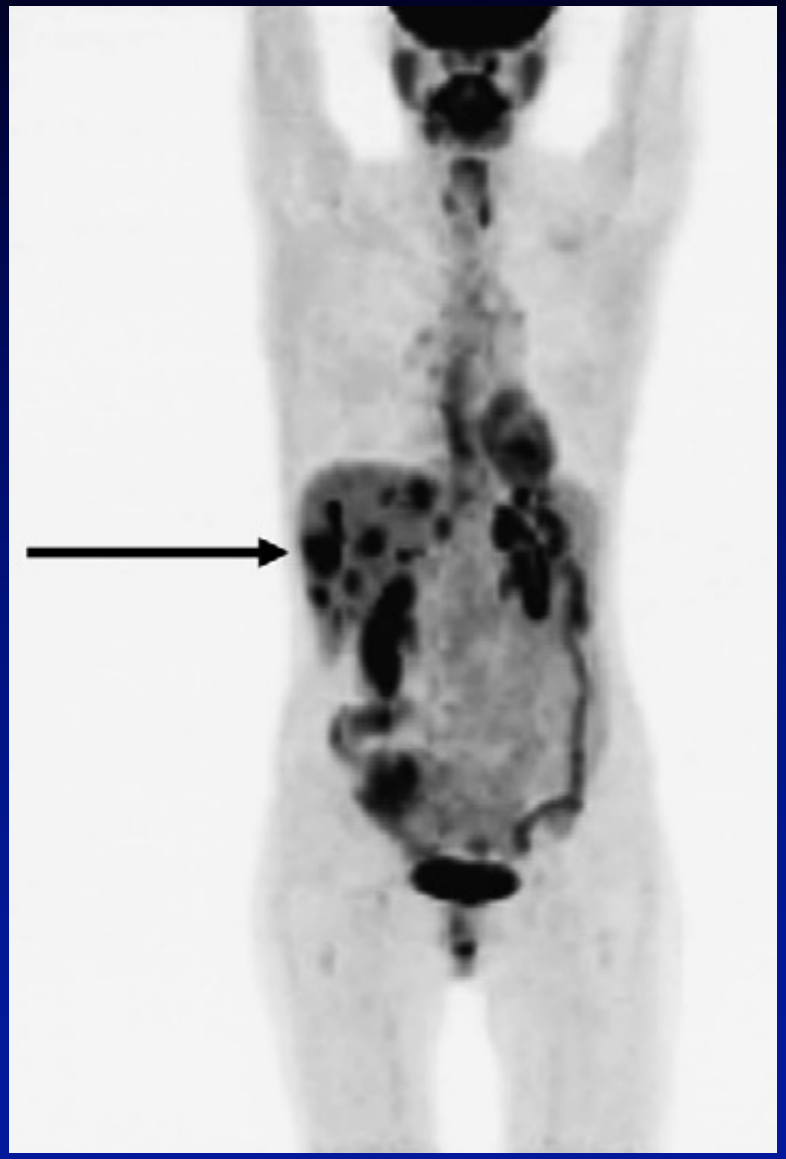
Figure 1. Peritoneal carcinomatosis.

Figure 2. Carcinomatosis of round ligament.

Diagnostic Laparoscopy

- Laparoscopy shows reasonable correlation with final pathology in identifying T stage, but there are insufficient data to comment on the benefit of laparoscopy in identifying lymph node involvement.
- Laparoscopy is additive to conventional imaging in detecting overall metastatic disease and peritoneal carcinomatosis, and therefore shows significant benefit in changing management (8.5–59.6%) and avoiding unnecessary laparotomy. Laparoscopic ultrasound has minimal additional value in this regard.

PET Scan



PET in Gastric Cancer

- Limited number of studies
- Poor sensitivity for detection of mucinous tumors, lower grade tumors and small volume disease
- The normal, moderately intense physiologic FDG uptake in the stomach may obscure tumors that have low-level uptake
- There are insufficient data to recommend its routine use for staging, restaging, or treatment monitoring of this disease.

Surgical Treatment:
Strategies to Minimize Locoregional Failure

- Complete resection of the primary lesion to ensure that all resection margins are free of malignant cells. This includes extending the resection line in continuity to adjacent structures and organs if feasible and safe.
- En bloc resection of all potentially involved lymph nodes
- Prevention of implantation of free cancer cells in gastric bed.

Early Gastric Cancer

Limited to mucosa or submucosa (T1)

- cT1a
- < 2 cm in diameter
- Lack ulceration
- Differentiated histology
- No lymphovascular invasion
- Lack clinical evidence of locoregional node involvement

  1% to 5% risk of + nodes

* EMR or ESMR recommended

- Noncurative endoscopic resections (positive margins), lymphovascular invasion, poorly differentiated histology

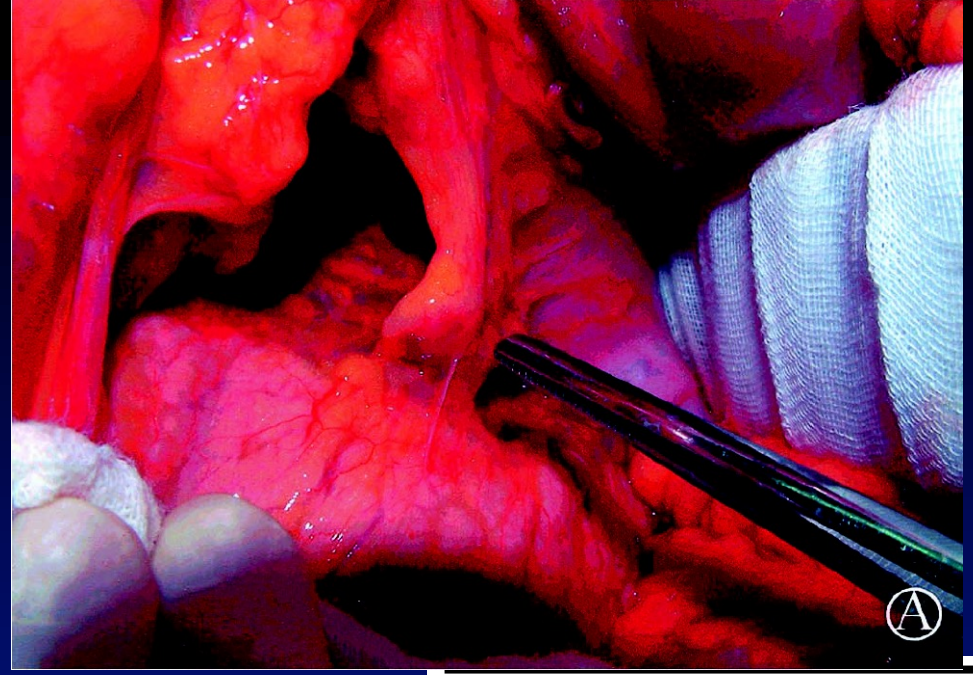
  14% rate of + nodes
- cT1b

  18% - 32% risk of + nodes

* Radical gastrectomy with formal lymphadenectomy

IN SITU AND T-1 DISEASE: ROLE OF ENDOSCOPIC MUCOSAL/SUBMUCOSAL RESECTION

- For selected superficial T-1 cancers, EMR performed by experienced personnel can generate superb results and can be recommended, especially because any local recurrences can be addressed with salvage gastrectomy.
- Laparoscopic resection with D1 lymphadenectomy and D1 pylorus-preserving gastrectomy represent valid options for T1 tumors not meeting EMR/ESR criteria.



Lymphatic Mapping

	Number of patients and T category	Method	Detection rate (%)	Sensitivity (%)	Node positive patients (%)
Kitagawa[96]	127 T1 18 T2	m99Tc Sn-colloid	95%	92%	17%
Ichikura[97]	62 T1/2	dye ICG	100%	87%	24%
Hiratsuka[98]	44 T1 30 T2	dye ICG	99%	90%	14%

ICG=indocyan green

Table 4: **Results of sentinel node detection gastric cancer**

Sentinel Lymph Nodes in Gastric Cancer

- Sentinel lymphadenectomy using isosulfan-blue was studied in 144 patients and 97.2% were found to have a stained lymph node
- In 99 patients with D2 surgery, the false-negative rates were:
  - T1-SN0 11%
  - T1-+N 29%
  - T2-T3 44%
- The authors conclude that only patients with T1 gastric cancers and sentinel nodes that are macroscopically negative should have this technique

(From: Izozaki, et al, Gastric Cancer 7:149, 2004)

Sentinel Node Biopsy with Function-Preserving Resection

- For centers that perform sentinel lymph node biopsy, a negative biopsy is followed by a function-sparing gastric resection.
  - Gastric wedge resection
  - Segmental gastric resection, in which the gastric body is resected, the vagal nerve branches are preserved, and a gastrogastric anastomosis is performed between the proximal and distal stomach
- Segmental gastric resections are performed primarily in East Asia, but long term quality of life for patients appears to be better than that of patients who undergo subtotal or total gastrectomy.
- Patients with EGC who have had margin-negative endoscopic resection but tumors with high-risk pathologic features may be candidates for sentinel lymph node biopsy alone without additional gastric resection if the sentinel nodes are negative.

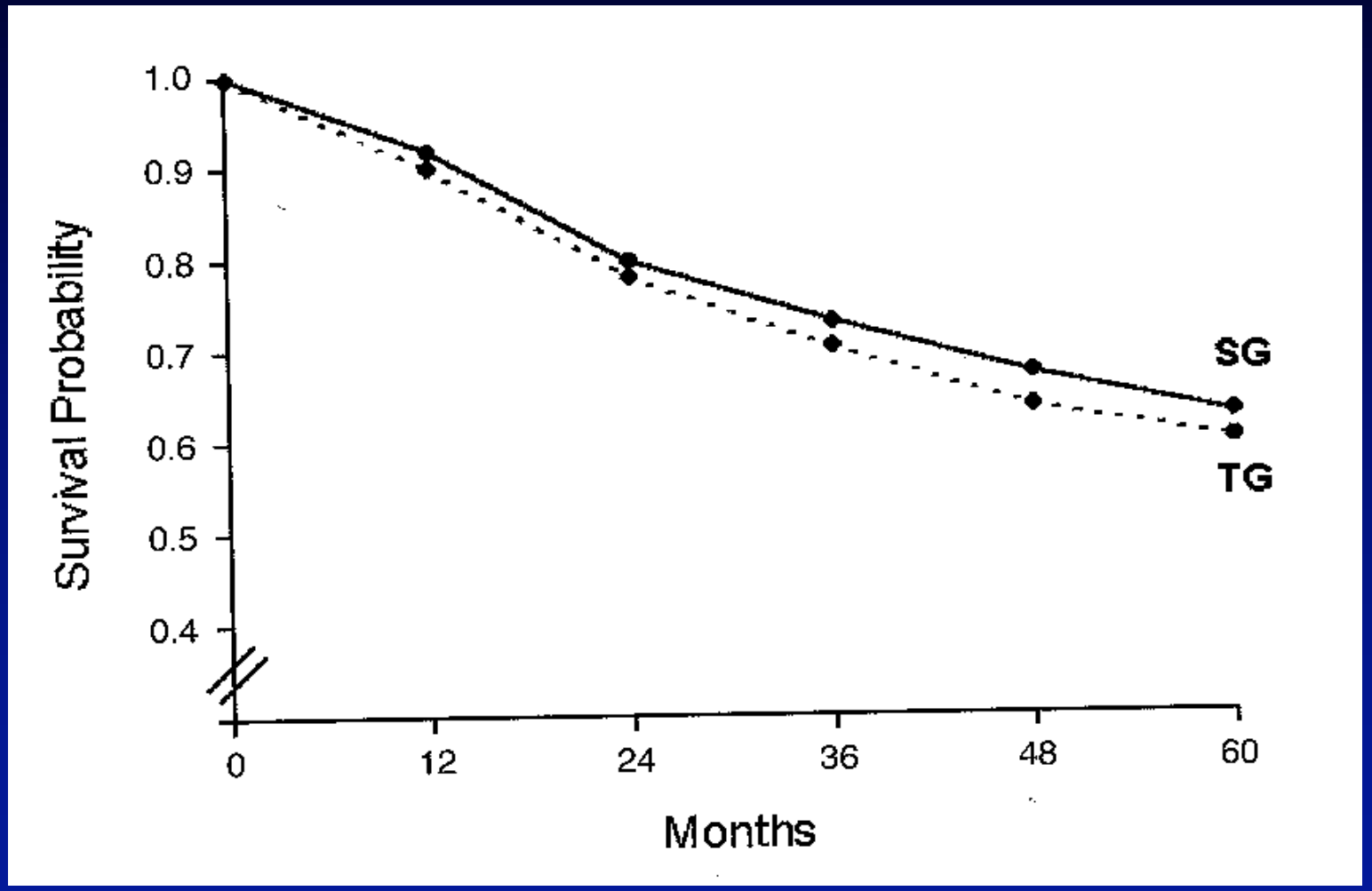
Li GZ, Doherty GM, Wang J. Jama Surgery 2022, e1-e9

Total vs Subtotal Gastrectomy

Table 1
Prospective randomized clinical trials: total versus subtotal gastrectomy

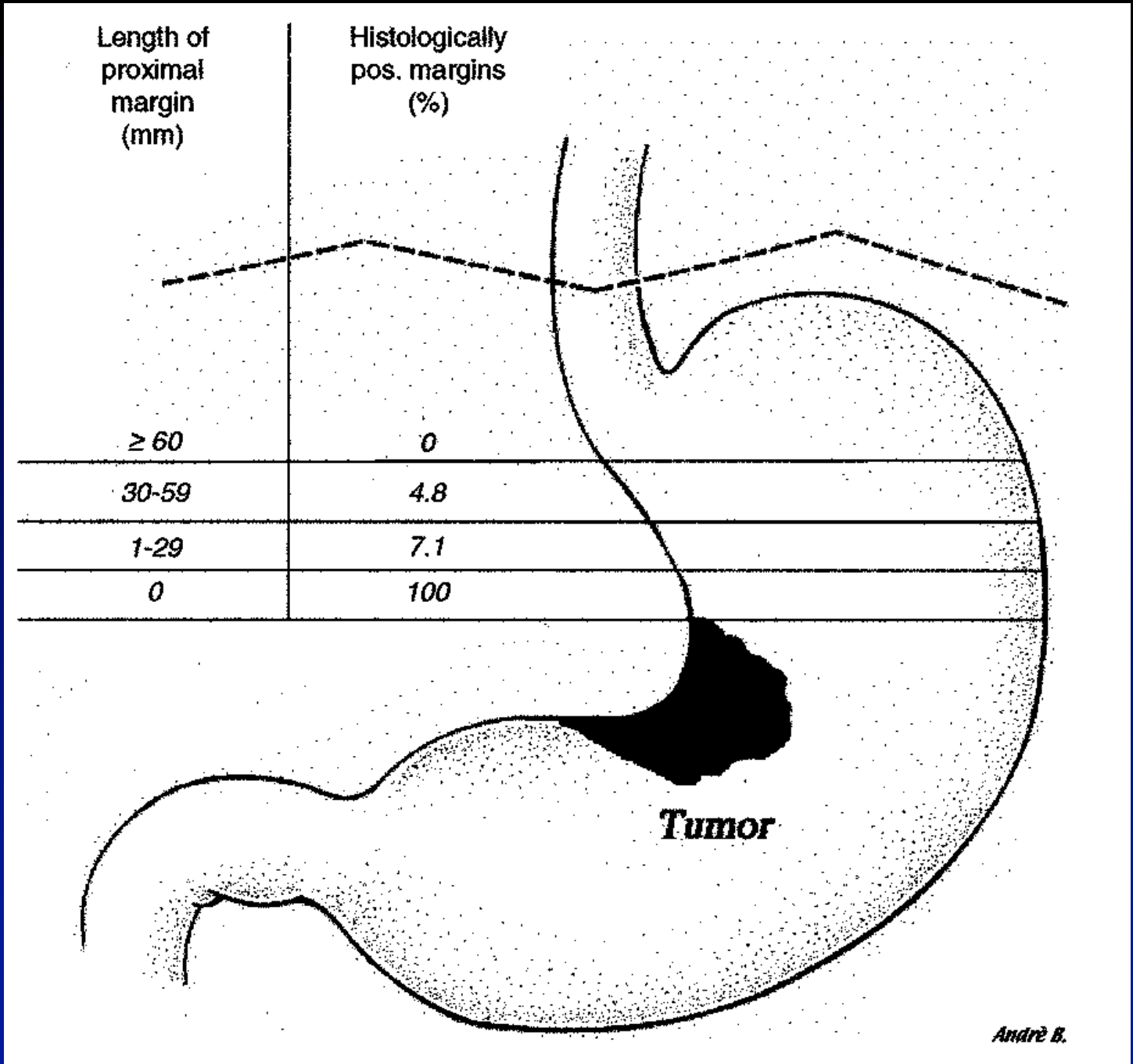
Total vs Subtotal Trials		Inclusion Criteria	Mortality/ Survival	Mortality/ Survival	*P* Value (Survival)
			Subtotal	Total	
Gouzi et al[12]	N = 169	Antral tumor M-0	3%/48% (5-y survival)	1%/48% (5-y survival)	ns
Bozzetti et al[15]	N = 618	>6 cm proximal margin possible M-0	1%/65% (5-y survival)	2%/62% (5-y survival)	ns
			Subtotal+D1	Total+D = 3	
Robertson et al[18]	N = 55	Antral >6 cm margin M-0, age <75 y	0%/1511 d median survival	3%/922 d median survival	0.04 0.07

Total vs Sub-total Gastrectomy



Bozzetti et al, Ann Surg 230:170-178, 1999

Margins of Resection



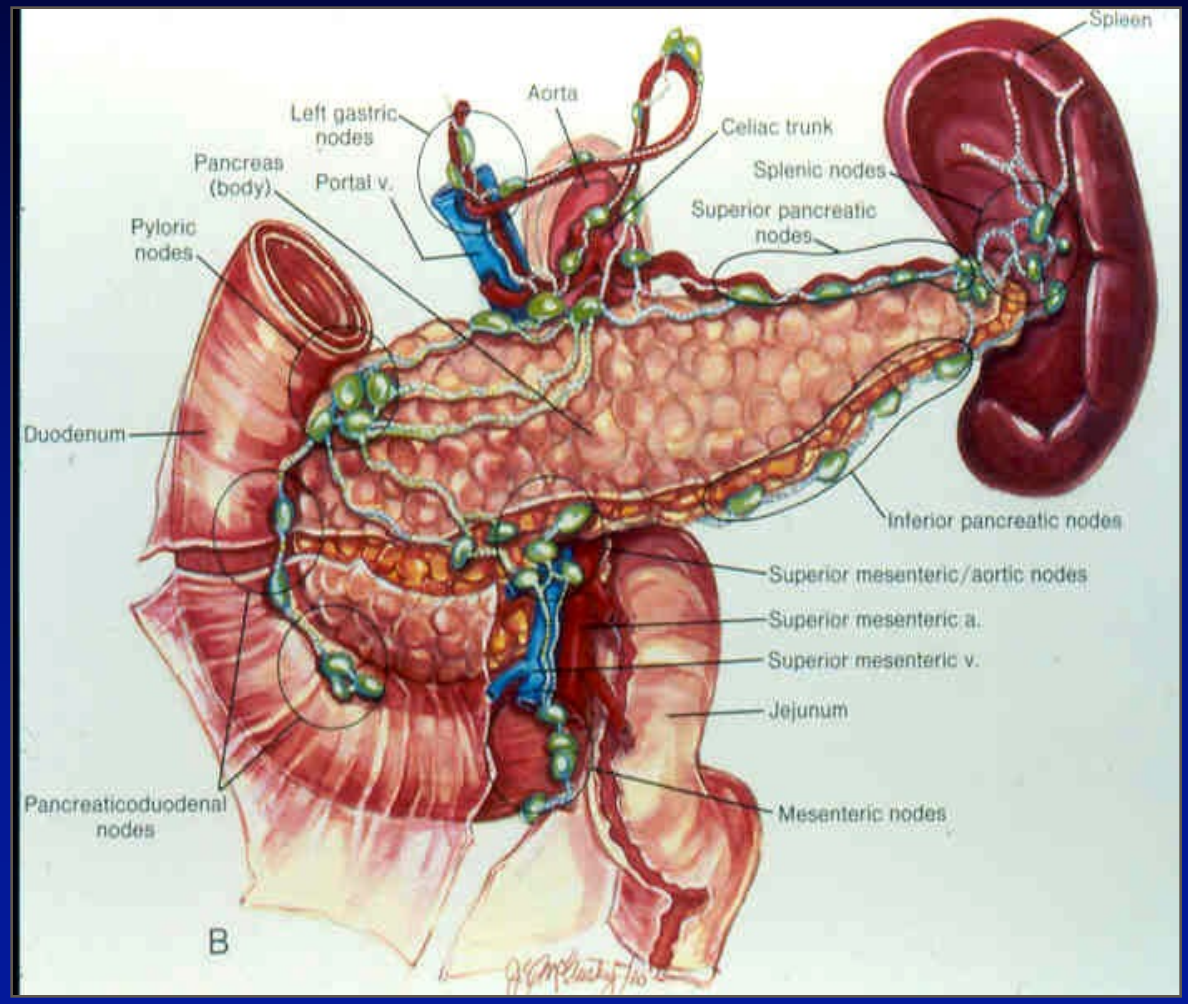
- The NCCN no longer specifies a minimum margin length, but the Japanese Gastric Cancer Association recommends aiming for gross margins of at least 3 cm for T1 to T2 tumors and at least 5 cm for T3 to T4 tumors to improve the chances of an R0 resection which is ultimately the goal.

- European Society of Medical Oncology guidelines recommend a proximal margin of at least 5 cm, or 8 cm for diffuse-type gastric cancer, if considering less than a total gastrectomy

Splenectomy in Gastric Cancer

- Increases early and late complications and the length of stay
- Splenectomy has a deleterious effect on oncologic outcome
- Should only be performed if there are adenopathies along the splenic vessels o in the splenic hilus that cannot be removed without splenectomy

Lymphatic Drainage in Gastric Cancer



Types of lymphadenectomy for gastric cancer

D0	-	No lymph nodes resected
D1	-	Perigastric
D2	-	Second echelon: hepatic, splenic, celiac, peripancreatic
D3	-	Third echelon nodes: retro-pancreatic, retroduodenal
D4	-	Para-aortic lymphadenectomy

Lymphadenectomy in gastric cancer

- The central concept of radical lymphadenectomy is to remove the nodal chain beyond the level of metastatic lymph nodes (Anatomic theory)

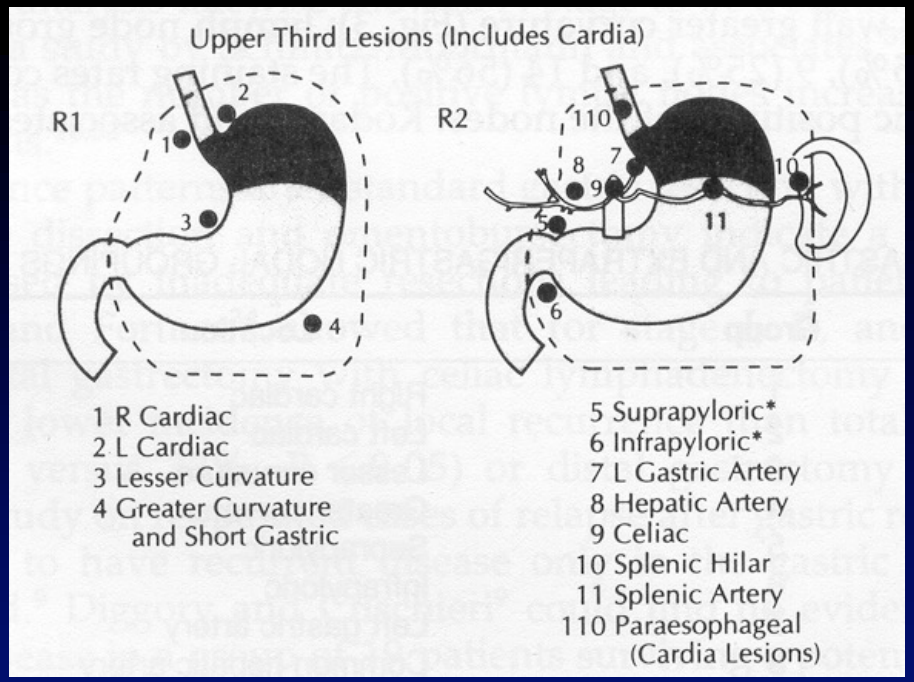
- Lymph node metastasis are prognostic markers, not instigators of metastatic disease (Biologic theory)

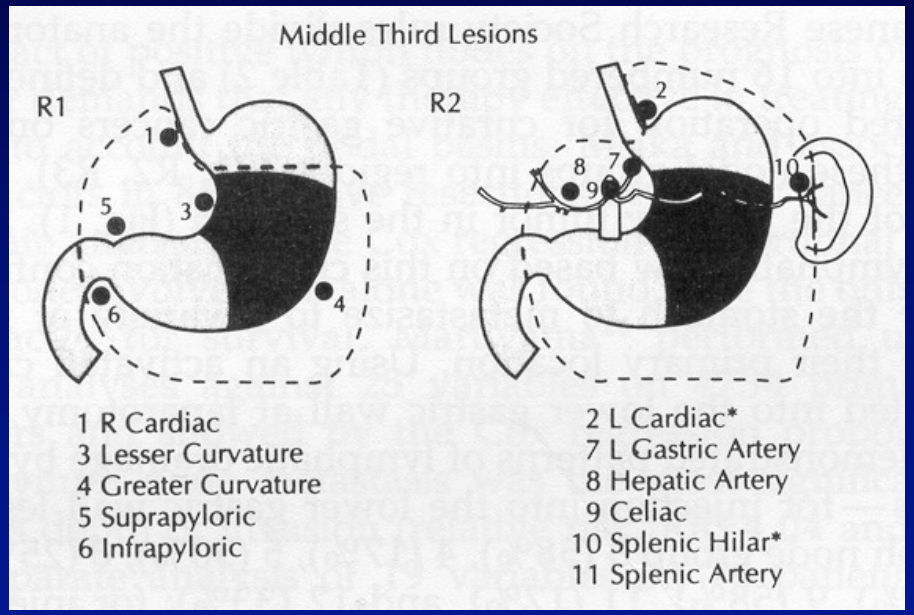
Radical Lymphadenectomy (D2) for Gastric Cancer

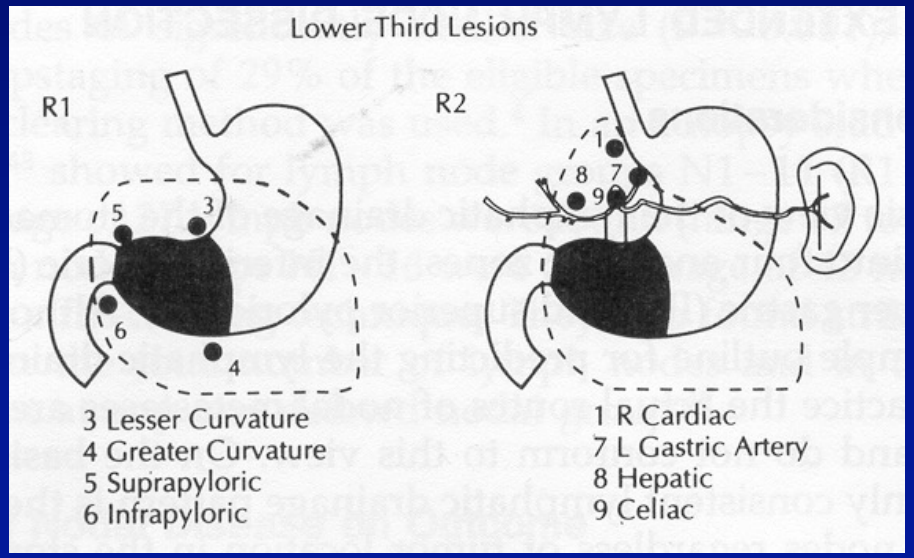
Makes no biologic sense in:

1. Serosa-positive gastric cancer (T3)
2. Incomplete primary tumor resection (R1-2)
3. Positive peritoneal cytology
4. When morbidity and mortality are increased by the radical operation

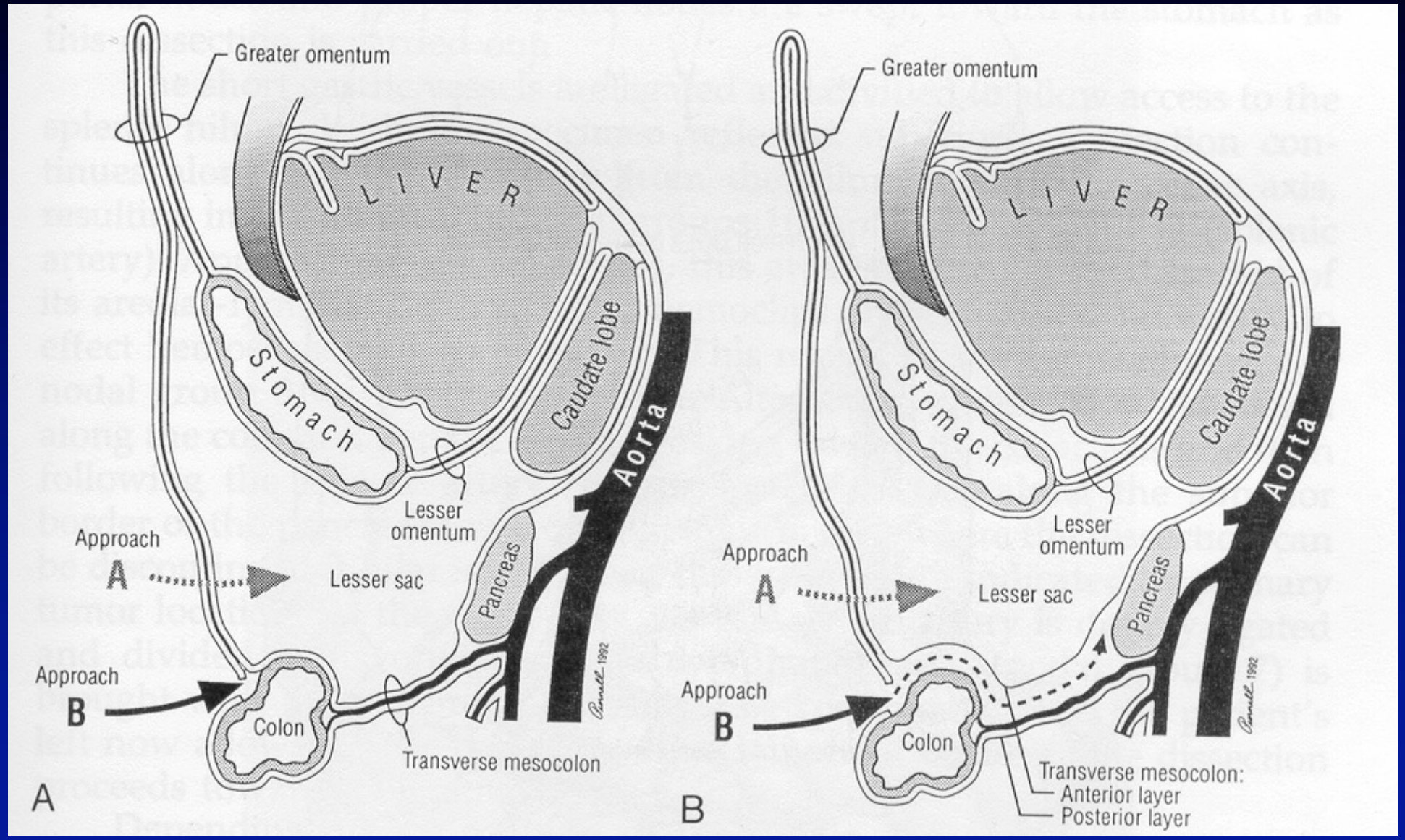
Extent of D1 and D2 Lymph Node Dissections

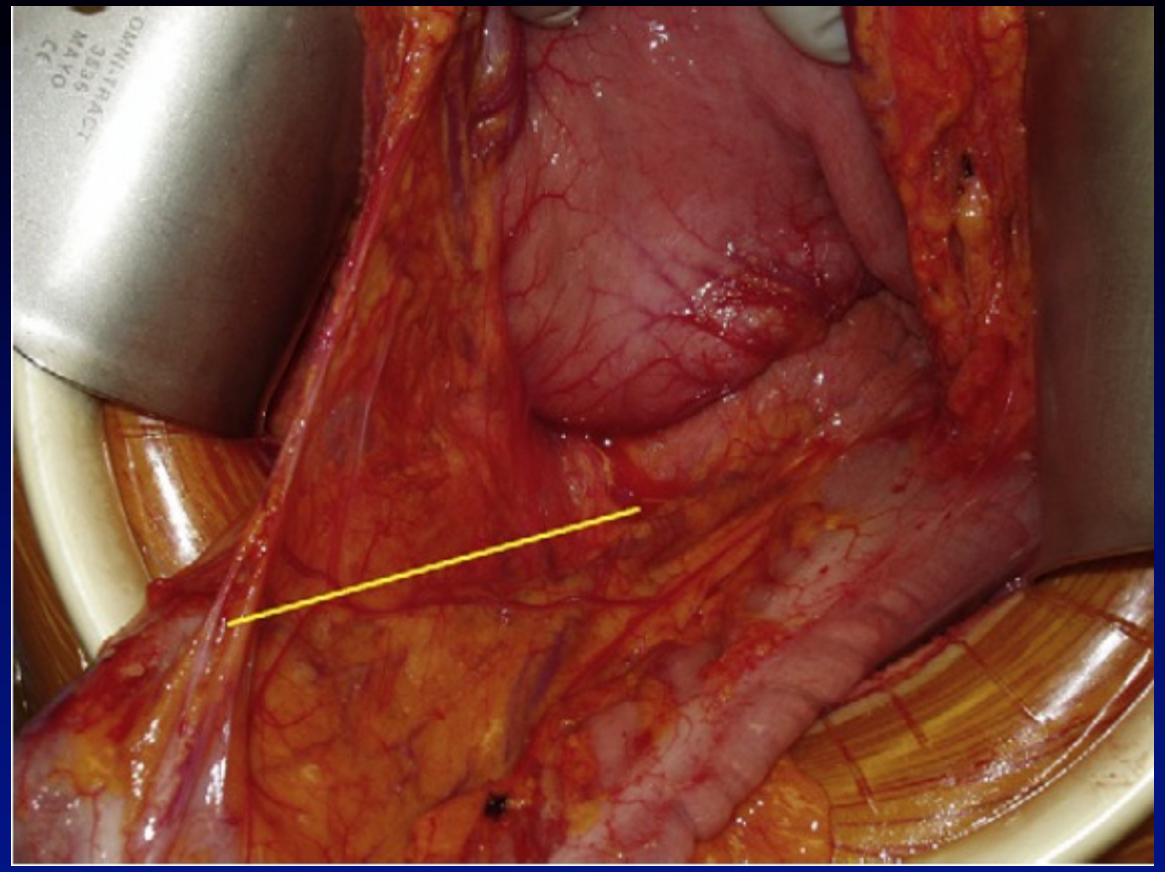




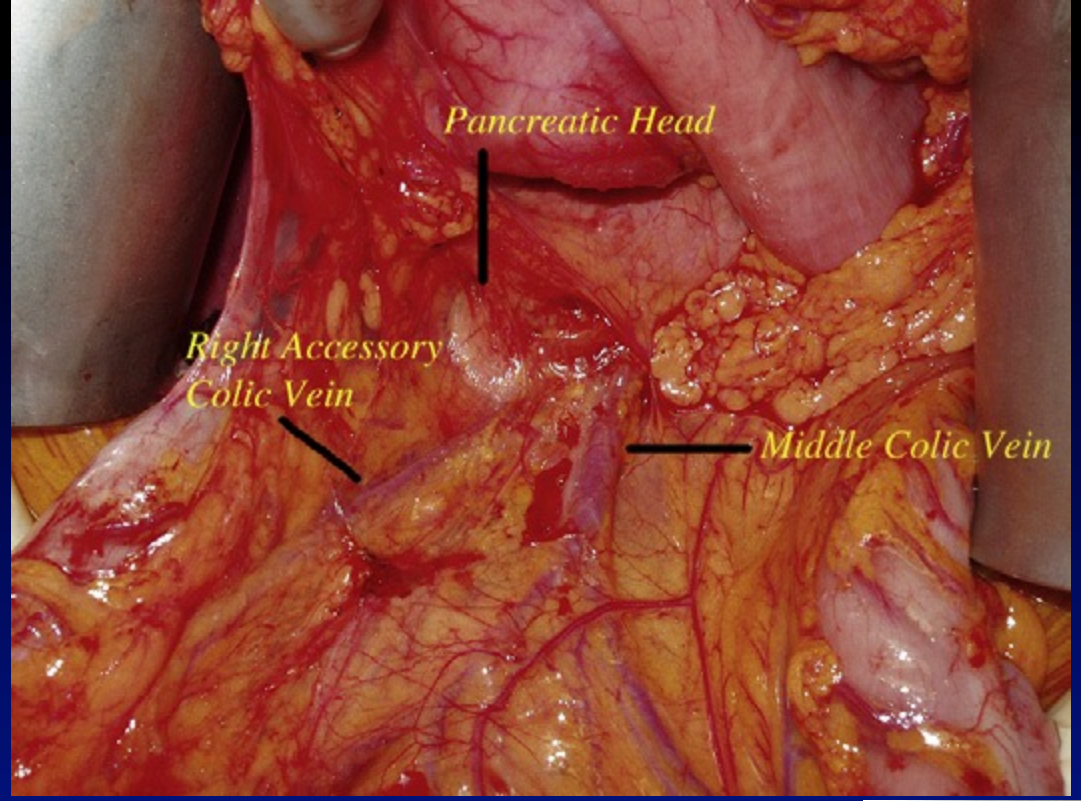


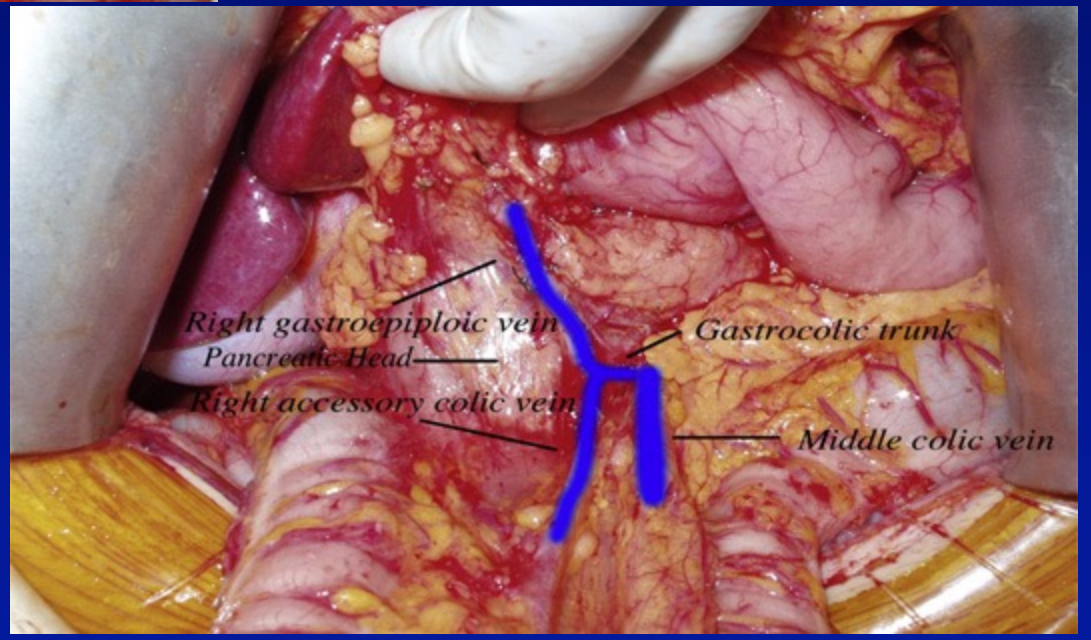
Plane of Dissection for Complete Lesser Bursectomy



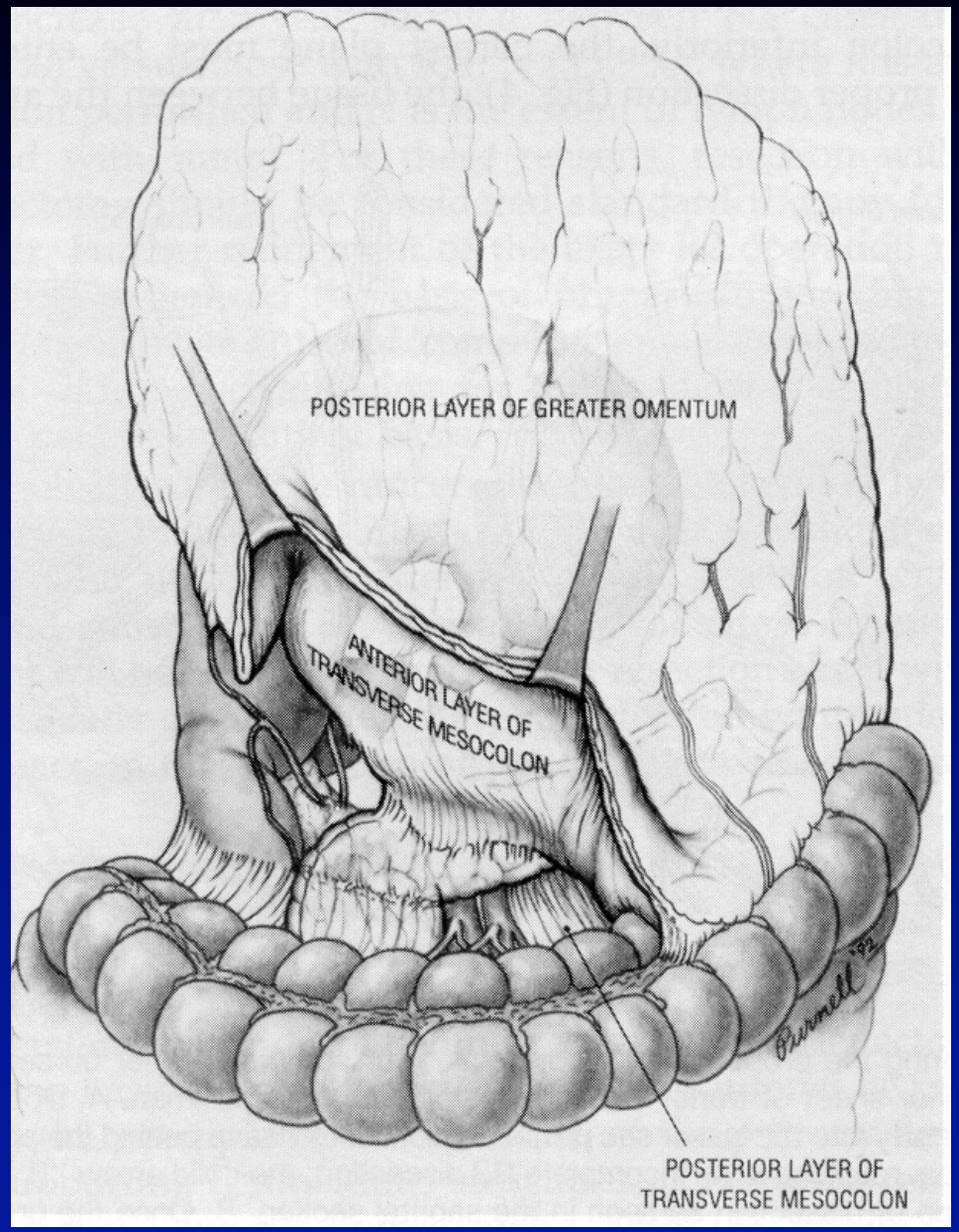


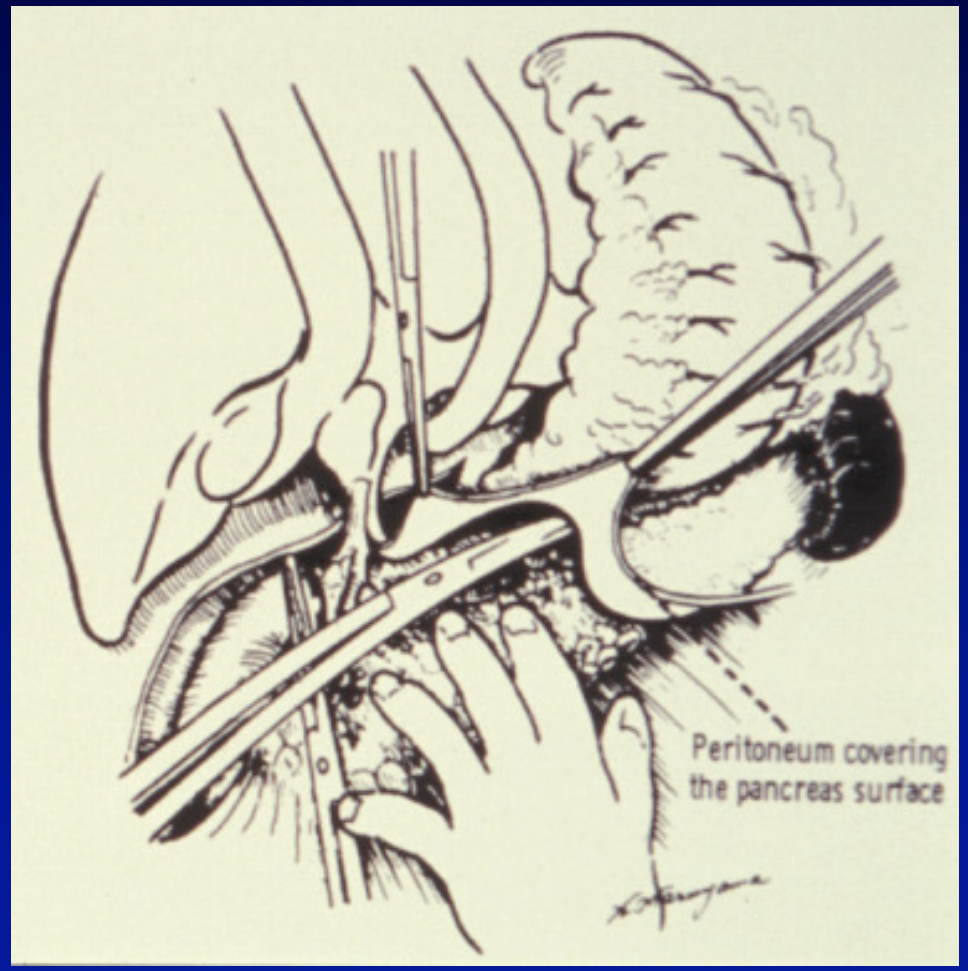
Right side border of lesser sac. The yellow line indicates the peritoneal incision to
further separate the greater omentum and the transverse colon mesentery.

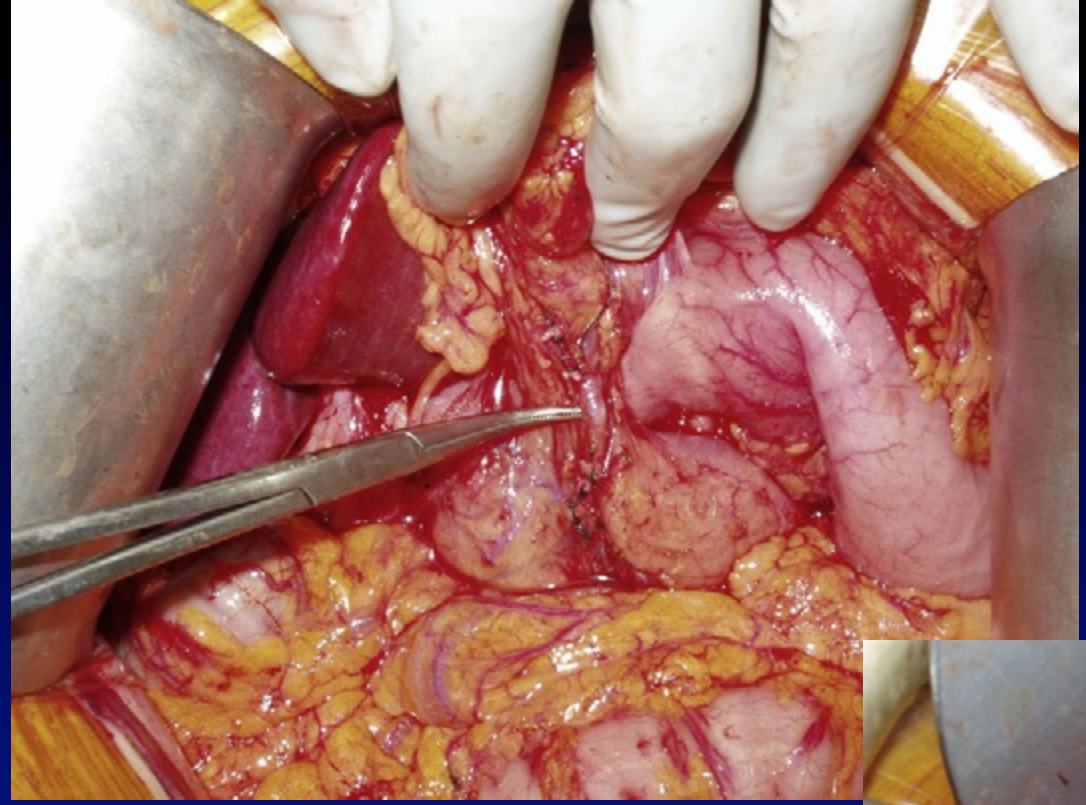

Pancreatic Head
Right Accessory
Colic Vein
Middle Colic Vein

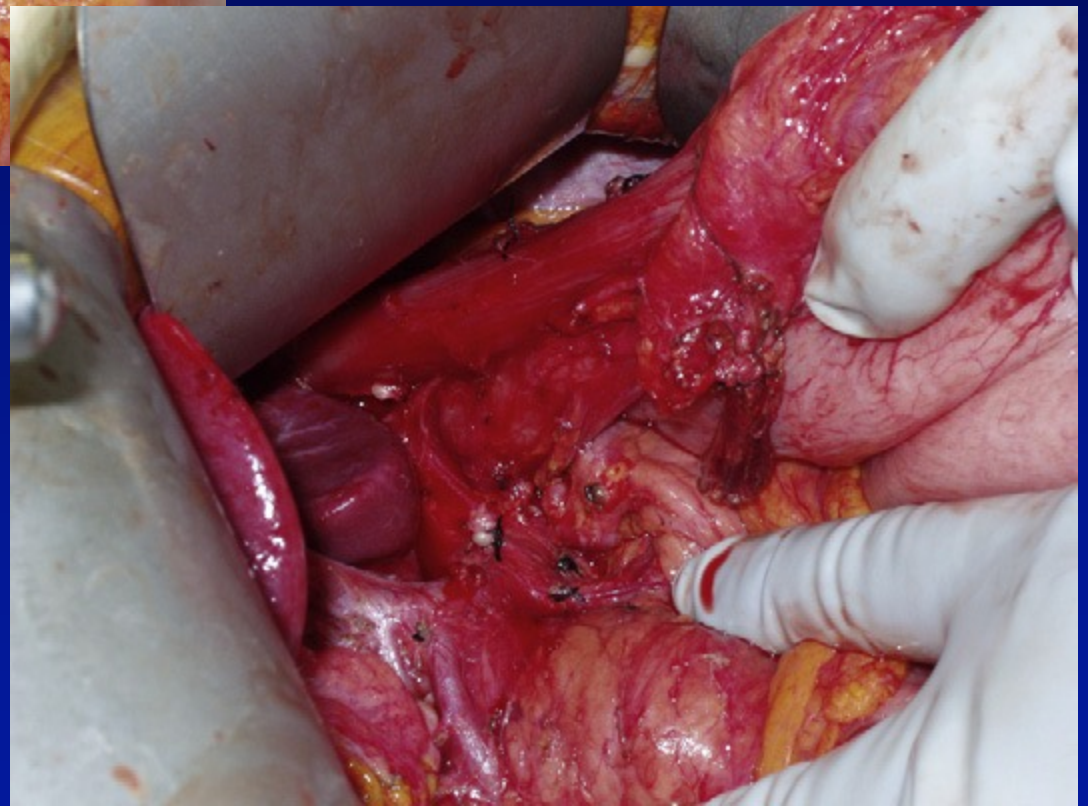

Right gastroepiploic vein
Pancreatic Head
Right accessory colic vein
Gastrocolic trunk
Middle colic vein

D2 Dissection – Lesser Bursectomy





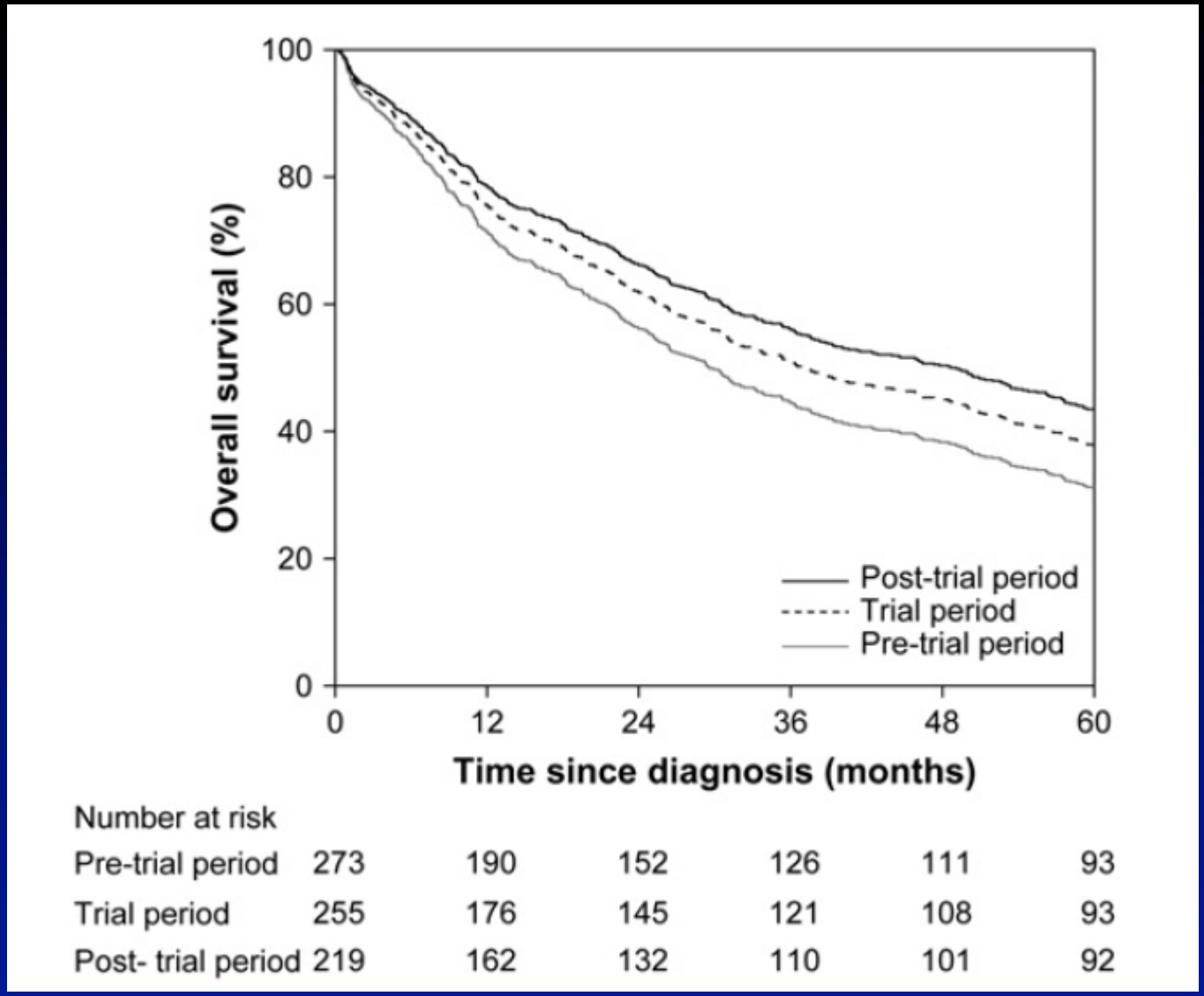




Learning Curve for Total Gastrectomy with D2 Lymph Node Dissection

- The success rate was >90% after completing 2 years of subspecialty training
- Operating time decreased as operative experience increased
- The learning period for total gastrectomy with D2 lymph node dissection was 23 - 35 cases

Lee JH et al., Ann Surg Oncol 2006; 13:1175-81



Krijnen P, den Dulk M, Meerchoek-Klein E, et al. Improved survival after resectable non-cardia gastric cancer in the Netherlands: the importance of surgical training and quality control. Eur J Surg Oncol 2009;35(7):718

Radical Lymphadenectomy: Pros and Cons

FOR

- Survival depends on nodal stage
- Eradicates cancer
- Removes occult nodal disease
- Achieves loco-regional control
- Superior and more extensive surgery
- No excess morbidity, mortality
- Better survival (Japan)

AGAINST

- Advanced disease is not amenable to surgery
- Biological predeterminism
- Survival advantage of radical surgery merely and artifact of more accurate staging
- Excess morbidity, cost
- Every surgeon unlikely to perform it
- No survival advantage (in the West)

Neoadjuvant/Perioperative Therapy

- Patients with cT2 or higher tumors or clinically positive nodes should undergo multimodality therapy

Perioperative Chemotherapy and Chemoradiotherapy Trials for Gastric Cancer

Source study name and location	Patients	Groups	Results, HR (95% CI)
Perioperative chemotherapy			
MAGIC[50] 2006; UK	cT ≥2 or cN >0; gastric/GEJ (n = 503)[a]	ECF + surgery + ECF (n = 250); surgery (n = 253)	Improved OS for perioperative ECF: 0.75 (0.6-0.93)
FLOT4-AIO[51]; Germany	cT ≥2 or cN >0; gastric/GEJ (n = 716)	FLOT + surgery + FLOT (n = 356); ECF + surgery + ECF (n = 360)	Improved OS for perioperative FLOT: 0.77 (90.63-0.94); median OS 35 mo vs 50 mo
Perioperative chemotherapy + CRT			
CRITICS[52]; the Netherlands	Stage IB-IVA; gastric/GEJ (n = 788)	ECX/EOX + surgery + CRT (n = 395); ECX/EOX + surgery + ECX/EOX (n = 393)	OS not different 1.01 (0.84-1.22); median OS 37 mo vs 43 mo

Adjuvant Therapy

- Patients who undergo upfront resection without neoadjuvant chemotherapy and are subsequently found to have gastric cancer categories pT3 to pT4 or pN greater than 0 should receive adjuvant chemotherapy.

Adjuvant Chemotherapy and Chemoradiotherapy Trials for Gastric Cancer

Source study name and location	Patients	Groups	Results, HR (95% CI)
Adjuvant chemotherapy			
CLASSIC[56]; China, Taiwan, South Korea	Stage II-IIIB; resected/D2; gastric (n = 1035)	CAPOX (n = 520); observation (n = 515)	Improved DFS for adjuvant CAPOX; 0.56 (0.44-0.72); 3-y DFS 74% vs 59%
ACTS-GC[58]; Japan	Stage II-III; resected/D2; gastric (n = 1034)	S-1 (n = 515); observation (n = 519)	Improved OS for adjuvant S-1 0.67 (0.54-0.83); 5-y OS 72% vs 61%
Adjuvant CRT plus chemotherapy			
INT 0116[59]; US	Resected; gastric/GEJ (n = 556)	CRT + 5-FU/LV (n = 281); observation (n = 275)	Improved OS with CRT 1.35 (1.09-1.66)[a]; median OS 36 mo vs 27 mo
ARTIST[60]; South Korea	Resected/D2; gastric (n = 458)	XP + CRT (n = 230); XP (n = 228)	OS not different; 1.13 (0.78-1.65)
ARTIST-2[61]; South Korea	Stage II-III; pN>0; resected/D2 gastric (n = 546)[b]	SOX + CRT (n = 183); SOX (n = 181); S-1 (n = 182)	DFS not different between SOX and SOX + CRT; 0.97 (0.66-1.42); 3-y DFS 73% SOX + CRT vs 74% SOX vs 65% S-1

Metastatic Gastric Cancer

- The traditional paradigm that stage IV gastric cancer is not a surgical disease has been replaced by a more nuanced patient-specific approach. However, systemic therapy remains the backbone of treatment for these patients and most surgical approaches discussed here remain investigational. Indeed, expansion of surgical indications for metastatic disease is being driven by advances in systemic therapy
  - Resectable Metastatic Disease
  - Peritoneal Disease
  - Palliation

Peritoneal Carcinomatosis from Gastric Cancer

- Malignant ascites
- Intestinal obstruction
- Palpable abdominal masses
- General symptoms of malignant diseases

Cytoreductive Surgery + HIPEC

- Combined cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (HIPEC) might be an additional therapeutic option for highly selected patients with peritoneal carcinomatosis arising from gastric cancer
- Complete macroscopic cytoreduction (CC-0/1) is a precondition for a possible survival benefit.

Peritoneal Carcinomatosis – Preoperative Diagnostics

Selection criteria

- PCI <12
- Complete macroscopic cytoreduction probable
- No evidence of distant organ metastasis
- ECOG performance status 1
- Limited clinical relevant comorbidities

Exclusion criteria (STOP signs)

- Disseminated small bowel infiltration
- Ureteral stenosis
- Bilary tract stenosis/cholestasis

Gastric Peritoneal Carcinomatosis: CRS + HIPEC

Table 1
Median and overall survival after CRS and HIPEC

Author, Year	n	Median Survival, mo	Survival Rate, %
Fujimoto et al,[27] 1997	48	16	31 (5 y)
Loggie et al,[28] 2000	17	10	0 (1 y)
Hall et al,[29] 2004	34	11	21 (5 y) CC-0/1
Glehen et al,[30] 2004	49	10	29 (5 y) CC-0/1
Yonemura et al,[31] 2005	107	11.5	27 (5 y) CC-0/1
Cheong et al,[33] 2007 (EPIC)	154	11	32 (5 y) CC-0/1
Yang et al,[34] 2010	21	43.4 (CC-0) 9.4 (CC-1)	43 (2 y) CC-0/1
Glehen et al,[22,35] 2010	159	9 (CC-0/1: 15)	23 (5 y) CC-0/1
Yang et al,[23] 2011	34	11	15 (2 y)

Ongoing Randomized Trials in Gastric Cancer

Source study name and location	Patients	Groups	Primary end point
SENORITA[21]; phase 3; South Korea	cT1N0M0 gastric cancer ≤3 cm[a]; target enrollment 580	SLNB + stomach-preserving resection; standard gastrectomy	3-y Disease-free survival
CRITICS-II[22]; phase 2; the Netherlands	Stage IB-IIIC gastric cancer	DOC + CRT + surgery; CRT + surgery; DOC + surgery	Event-free survival
TOPGEAR[23]; phase 3; Australia, Europe, Canada	Stage IB-IIIC gastric cancer; target enrollment 752	ECF + CRT + surgery + ECF; ECF + surgery + ECF	Overall survival
PILGRIM (HIPEC-01)[24]; phase 3; China	T3-4NxM0 gastric cancer (n = 648)	Surgery + HIPEC + XELOX/SOX (n = 317); surgery + XELOX/SOX (n = 331)	Overall survival
RENAISSANCE (AIO-FLOT5)[25]; phase 3; Germany	M1 gastric cancer: retroperitoneal metastasis only or 1 potentially resectable/controllable organ site met with or without retroperitoneal metastasis; no disease progression on FLOT ×4 cycles; target enrollment = 271	Surgery + FLOT; continue FLOT; alone	Overall survival

Conclusions

- Despite marked decreases in incidence over the last century, particularly in developed countries, gastric cancer is still the second most common tumor worldwide.
- Surgery remains the gold standard for the cure of locoregional disease. However, in most countries, the diagnosis is made at an advanced stage, and the 5-year survival for surgically resectable disease stays far below 50%.

Conclusions

- Chemotherapy and radiation therapy have had increasingly important roles for treating these malignancies, such that their inclusion in treatment schema is now considered standard.
- Their use as pre- or peri-operative treatments in particular has been supported by several recent trials.

Conclusions

- As new drugs and biologic therapies are developed, and as the ability to assess tumor response to induction therapy continues to improve, strategies for managing gastric cancer will continue to evolve.