Surgical Resection of Gastric Cancer
Evidence & Issues

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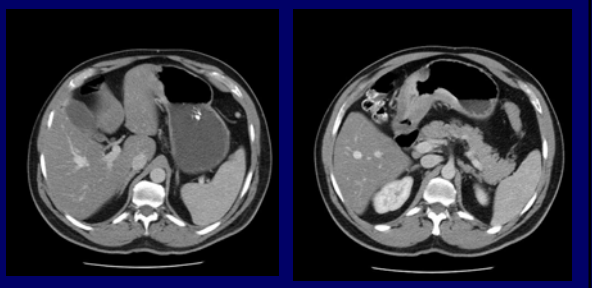
Surgical Problems in Proximal GI Cancer Management
BC Surgical Oncology Network Conference
Devember 3, 2005 Vancouver, BC

Surgical Resection of Gastric Cancer

I. Technical Issues
   - RCT
   - Other
II. Quality of Surgery
III. Adjuvant Treatment

Case #1

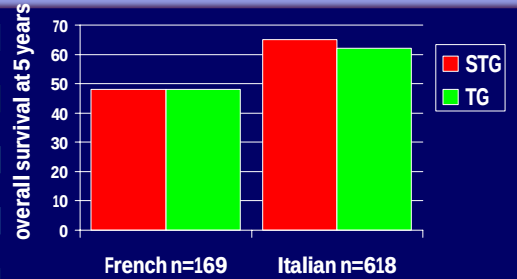
50 year old healthy man
2 years of dyspepsia
OGD: antral tumour
path: invasive adenoCa



I. Technical Issues

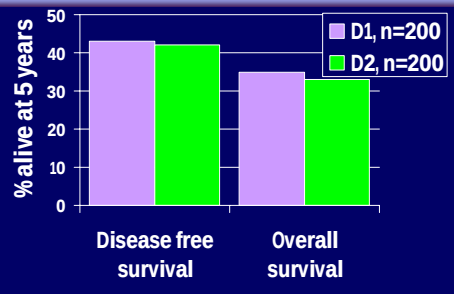
I. Extent of Gastrectomy
II. Extent of Lymphadenectomy
III. Lap vs. Open
IV. Margins
V. Other

French and Italian RCT Antral Ca TG vs STG: Longterm Survival



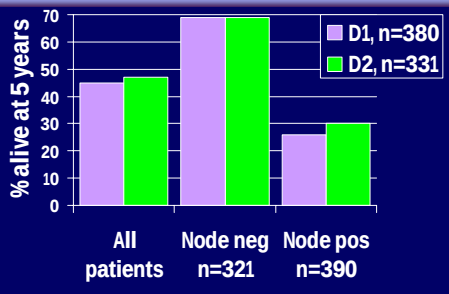
Ann Surg 1989 209:162; Ann Surg 1997 226:613

MRC RCT: D1 vs D2 Dissection Longterm Survival



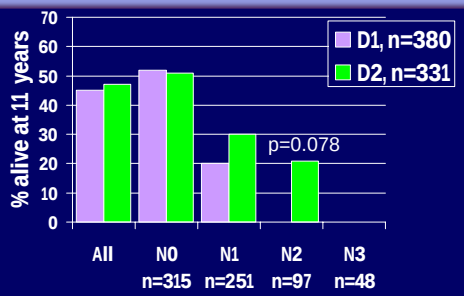
Br J Cancer 1999 79: 1522

Dutch RCT: D1 vs D2 Dissection Longterm Survival



NEJM 1999; 340:908

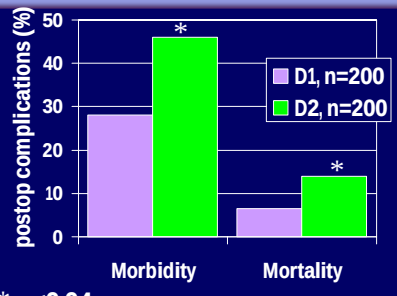
Dutch RCT: D1 vs D2 Dissection Very Longterm Survival



median f/u time = 11 years

J Clin Oncol 2004; 22:2069

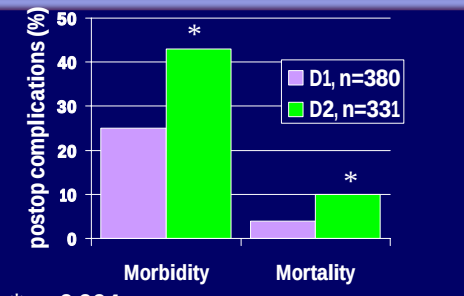
MRC RCT: D1 vs D2 Dissection Postoperative M & M Rates



* p<0.04

The Lancet 1996 347:995

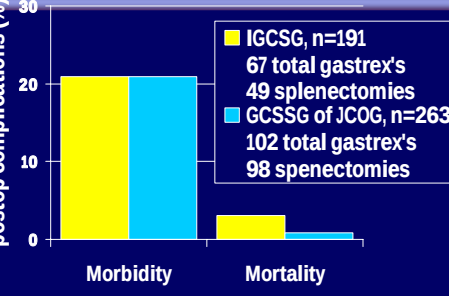
Dutch RCT: D1 vs D2 Dissection Postoperative M & M Rates



* p<0.004

NEJM 1999; 340:908

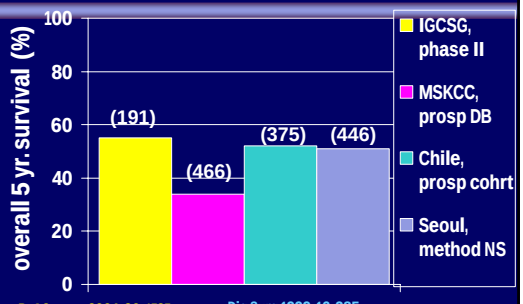
"Standard" D2 Dissection: Japanese RCT & Italian multicentre phase II trial



Br J Cancer 2004; 90: 1727

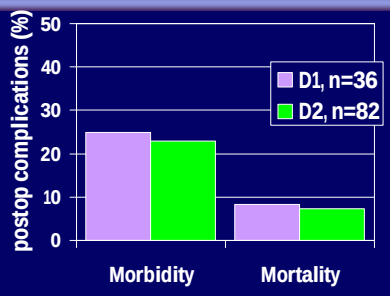
J Clin Oncol 2004; 22: 2767

Survival after "Standard" D2 Dissection



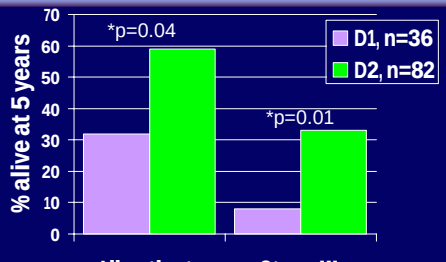
Br J Cancer 2004; 90: 1727
Gastrointest Surg 1999; 3: 24
Dig Surg 1999; 16: 385
Int J Radiat Oncol Biol Phys 2005; 63: 1279

UK postcode trial: D1 vs modified D2 Dissection Postoperative M & M Rates



Br J Cancer 2004; 90: 1888

UK postcode trial: D1 vs modified D2 Dissection Longterm Survival



Br J Cancer 2004; 90: 1888

Extent of Lymphadenectomy: Cochrane Review – D2

- more dangerous when
  - spleen/panc resected
  - surgeon inexperienced
- studies limited by
  - learning curves, poor compliance
  - contamination
- no PROVEN survival benefit
- MAY benefit
  - T3+
  - Stage II & IIIa

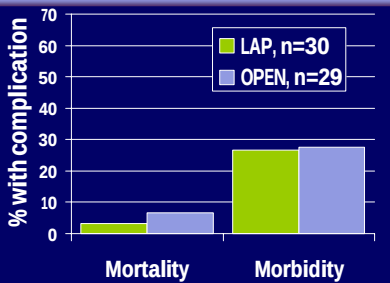
McCulloch et al,The Cochrane Collaboration, 2005

Extent of Lymphadenectomy: Current State of Play

- D2:
  - -not harmful in expert hands
  - -more nodes = better staging
  - -direct survival benefit unclear
- pending:
  - -Italian RCT D1 vs D2, 5 centres, n=162
  - -Japan RCT D2 vs D2+, 24 centres, n=523

Degiulu, EJSO 2004; 30: 303
Sano, J Clin Oncol 2004; 22: 2767

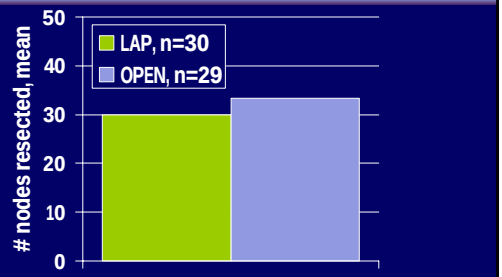
Laparoscopic vs Open Gastrectomy: RCT



STG for distal cancer

Huscher, Ann Surg 2005; 241:232

Laparoscopic vs Open Gastrectomy: RCT



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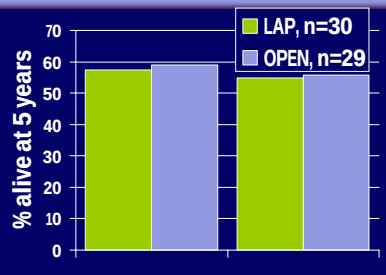
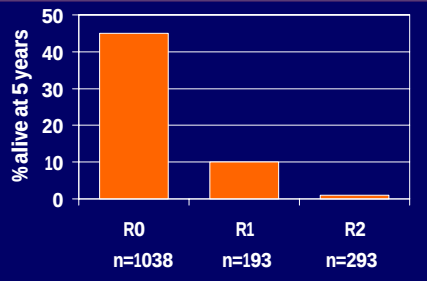
Laparoscopic vs Open Gastrectomy: RCT



STG for distal cancer

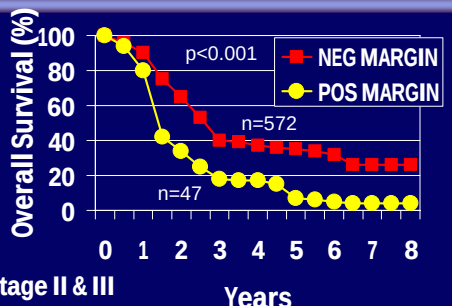
Huscher, Ann Surg 2005; 241:232

R Status Determines Prognosis



Karpeh et al., MSKCC

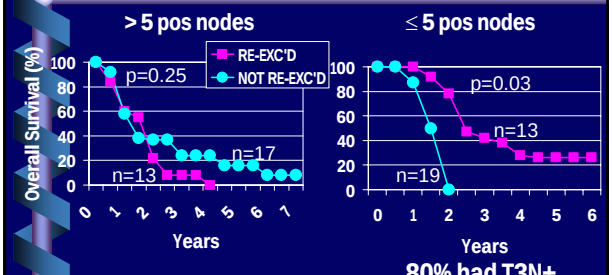
Positive Margins and Survival



Stage II & III

Kim et al, J Gastrointest Surg 1999; 3:24

Frozen Section Analysis and Re-Excision of Positive Margins



80% had T3N+

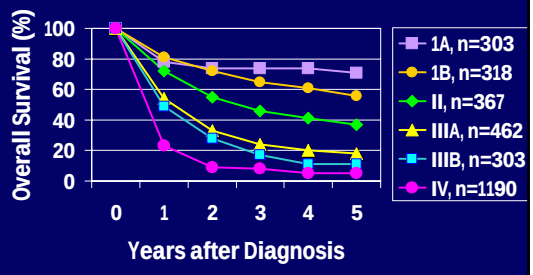
Kim et al, J Gastrointest Surg 1999; 3:24

TNM Staging of Gastric Cancer

Stage 1	A	T1; N0
	B	T1; N1
		T2; N0
Stage 2		T1; N2
		T2; N1
		T3; N0
Stage 3	A	T2; N2
		T3; N1
		T4; N0
	B	T3; N2
Stage 4		T4; N1, N2, N3
		T1, T2, T3; N3
		M1

AJCC, 2002

National Cancer Data Base (USA)
Report on Gastric Cancer (Dx 1987 - 88)



Cancer 1997; 80: 2333

Gastric Cancer
Surgical RCT Pot- Pourri

Au, Inst, Date	Question	n	Answer
Doglietto, Rome, 2004	± NJT in TG	237	no diff
Inaba, Tokyo, 2004	midline vs transv	54	less pain, pneumonia, SBO in transv
Mochiki, Maebashi, 2003	JI ± pouch	26	less caloric intake in pouch
Hori, Chiba, 2004	stapled vs HS gastroduod	187	stapled faster by 11 min, no other diff
Fiori, Rome, 2004	pall stent vs gastroent	18	shorter op time, time to food, hosp stay with stent

Case #1: Pathology Report

- poorly differentiated adenocarcinoma
- tumour penetrates through muscularis propria into adjacent greater omentum, but not through visceral peritoneum
- proximal and distal margins negative
- 0 of 12 nodes positive

WHAT STAGE IS THIS?

TNM Staging of Gastric Cancer: T Stage

T1	Lamina propria, submucosa
T2	Muscularis propria, subserosa
T3	Penetrates serosa
T4	Adjacent structures

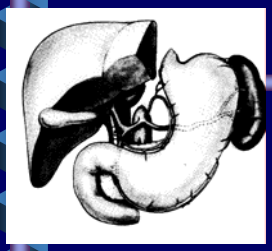
TNM Staging of Gastric Cancer: N Stage

N0	no regional nodes involved
N1	1 to 6 nodes
N2	7 to 15 nodes
N3	> 15 nodes

TNM Staging of Gastric Cancer

Stage 1	A	T1; N0
	B	T1; N1
		T2; N0
Stage 2		T1; N2
		T2; N1
		T3; N0
Stage 3	A	T2; N2
		T3; N1
		T4; N0
	B	T3; N2
Stage 4		T4; N1, N2, N3
		T1, T2, T3; N3
		M1

AJCC 2002, 6th edition



1997 AJCC, 5th Ed.

N0- No regional LN metastases

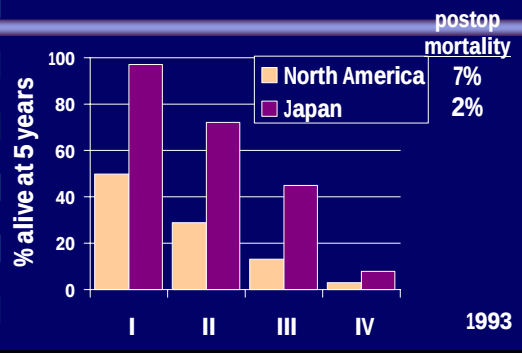
N1- Metastasis in 1-6 regional LN

N2- Metastasis in 7-15 regional LN

N3- Metastasis in > 15 regional LN

"…it is suggested that at least 15 regional nodes be assessed..."

The Question of Quality: Outcomes of Resection for Gastric Cancer



The Question of Quality: What is the Secret of Japan?

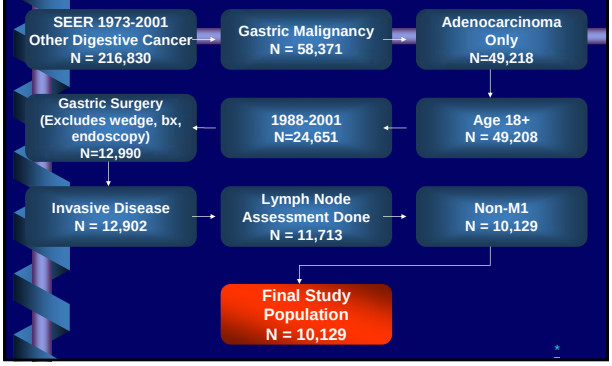
- younger, less CV disease
- less obese
- stage migration 2° to better N staging
- TECHNIQUE

Significant Regional Variation in Staging and Survival of Gastric Cancer- An Analysis of the SEER Database

Natalie G. Coburn, MD, MPH
Carol J. Swallow, MD, PhD
Calvin Law, MD, MPH

Proc ASCO, 2005

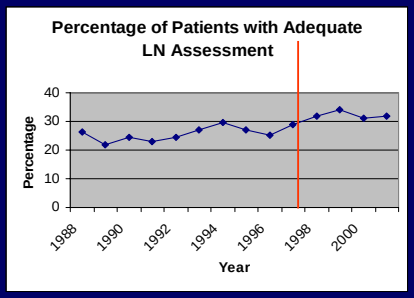
Defining the Study Population



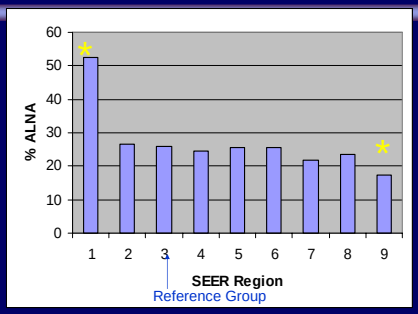
Overall Results

- 10,129 cases
- Male: 64%
- Age
  - Median: 70 years
  - Mean: 68.3±12.5 years
- Median # of LN assessed: 9
- Overall percentage of patients with Adequate LN assessment: 28.6%
  - Improved to 32.7% 1998-2001 (p<0.05)

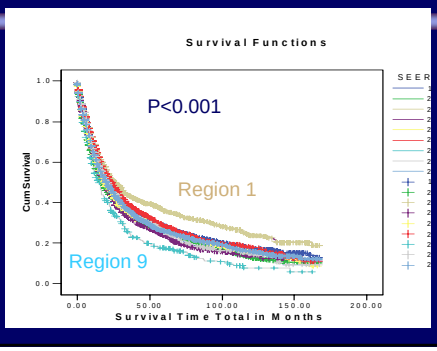
Odds of Adequate LN Assessment- Year of diagnosis



Odds of Adequate LN Assessment- SEER Region



Factors Predictive of Survival- SEER Region



Cox HR of Death Final Model (p<0.05 for all)

- SEER Region
- Age (vs. 60-74)
  - 18-59: HR=0.8
  - >74: HR=1.4
- Race
  - Japanese: HR=0.8
  - Other Asian: HR=0.8
  - African-American, Islanders, Other: HR=NS
- Female Gender
  HR= 0.8
- Marital Status
  HR=0.9
- T-Stage
  HR=1.4, 2.2, 3.4
- Grade
  HR= NS, 1.4, 1.4
- Radiation
  - Neoadjuvant: HR=NS
  - Adjuvant: HR=0.9
- Surgery Type (v. Distal)
  - Total: HR=0.8
  - Gastrectomy NOS: HR=1.2
  - En bloc: HR=1.12
- >15 LN assessed
  HR=0.86

Gastric Cancer Lymph Node Retrieval in the Province of Ontario and at a Tertiary Care Cancer Centre

Anirban Gupta, Riad Haddad, Julinor Bacani, Catherine O'Brien, Aaron Pollett, Steven Gallinger and Carol Swallow

Departments of Surgical Oncology and Pathology, Mount Sinai and Princess Margaret Hospitals, University of Toronto

Canadian Society of Surgical Oncology

12th Annual Scientific Meeting, Montreal

Friday, April 1, 2005

Methods

Inclusion Criteria

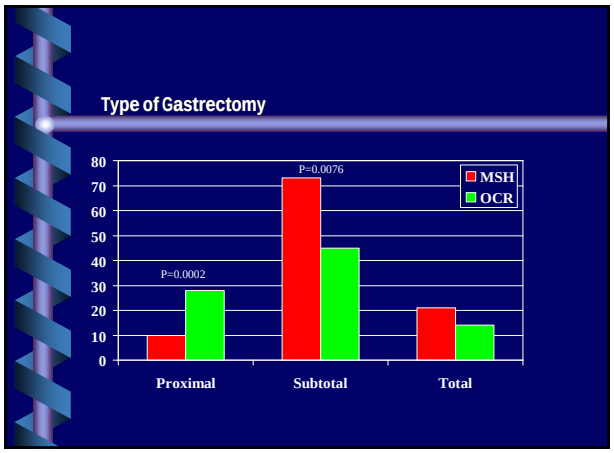
- Gastric cancer between 1989-2001
- Curative Resection attempt, no distant mets
- Surgical pathology report

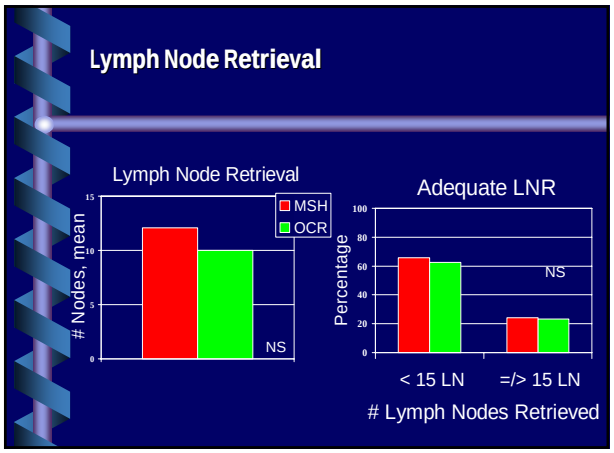
Exclusion Criteria

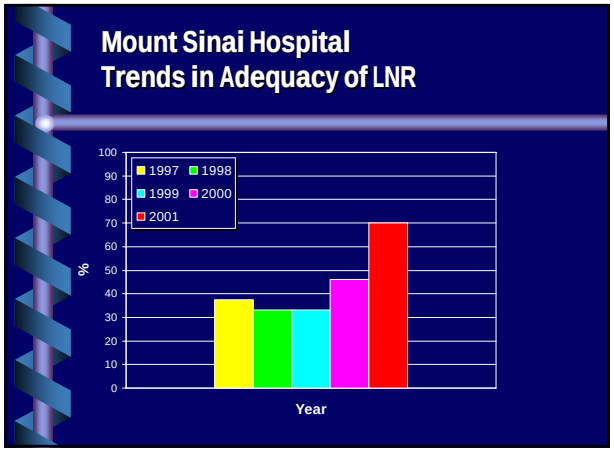
- biopsy only

Mount Sinai Hospital (MSH)
108 patients
Mount Sinai Hospital
(Dept Pathology Database)
1990-2001

Province of Ontario
91 patients
across Ontario, age<56
(OCR Database)
1989-1993







The Question of Quality: What do Ontario surgeons strive for?

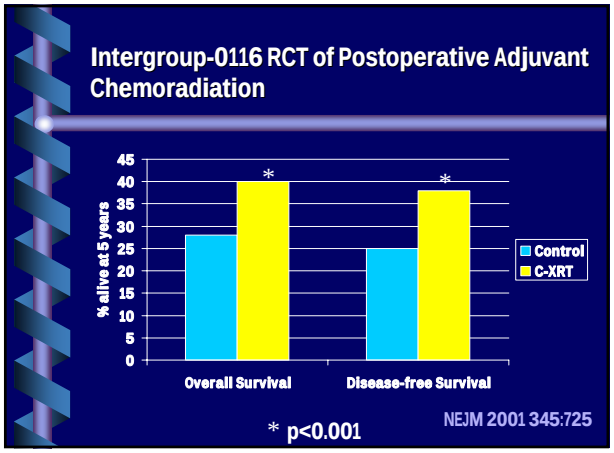
- n=188 who perform gastric surgery
- # nodes desired
  - mean = 11
  - median = 10 (2-30)
- routine intraop frozen section
  - proximal 53%
  - distal 34%

Helyer, O'Brien, Swallow 2005 unpub

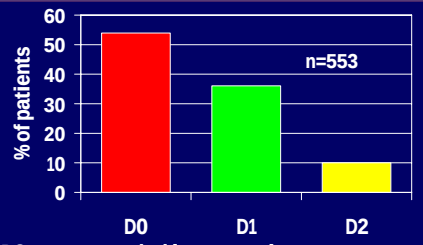
Case #1: Revised Pathology Report

- poorly differentiated adenocarcinoma
- tumour penetrates through muscularis propria into adjacent greater omentum, but not through visceral peritoneum, T2
- proximal and distal margins negative
- 4 of 20 nodes positive, N1

NOW WHAT?



Extent of LND in Intergroup 0116



D2 recommended in protocol
LND assessed from surgical checklist

Hundahl et al, Ann Surg Oncol 2002; 9: 278

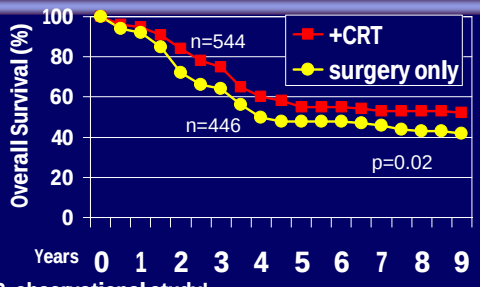
D1 Dissection

- Level 1 nodes (perigastric, stations 1 - 6)
  - right & left cardiac (1 & 2)
  - lesser & greater curve (3 & 4)
  - supra- and infra- pyloric [5 & 6]
- omentum

D2 Dissection

- Level 1 nodes (perigastric, stations 1 - 6)
- Level 2 nodes (intermediate, stations 7 - 9)
  - left gastric (7), common hepatic (8), celiac (9)
- stations 10 (splenic hilum) and 11 (splenic artery) nodes
- omental bursa, anterior leaf of mesocolon

THE HOT QUESTION OF TODAY: What is the role of postoperative adjuvant chemoradiation with D2 dissection?



NB: observational study!

Kim et al, Int J Radiation Oncol Biol Phys 2005; 63: 1279

THE HOT QUESTION OF TODAY: What is the role of postoperative adjuvant chemoradiation with D2 dissection?

Korean Protocol: D2

- 5 cycles 5-FU and leucovorin
- 45 Gy RT concurrent from 2nd cycle
- n=291, median f/u 48 mos.
- in-field recurrence rate= 16% (1/3 of all recurrences)

Br J Cancer 2004; 91: 11

Intergroup-0116 RCT of Postoperative Adjuvant Chemoradiation: M & M

32% needed change in XRT plan

30% couldn't complete Rx

1% mortality in C-XRT arm

PMH Protocol for Postoperative Adjuvant Chemoradiation

Eligibility Criteria:

- R0 resection
- < 5 cm into esophagus
- stage 1B - IV, no distant mets
- start 20-90 days post-op

CCO Updated Practice Guideline

" after surgical resection, patients whose tumours have penetrated the MP or involve regional lymph nodes **should be considered** for adjuvant combined chemoradiotherapy "

December, 2002

Management of Resectable Gastric Cancer – Summary

- Goals in the resection of localized disease
  - R0 resection
  - accurate staging
  - STG > TG
  - D1+ dissection
  - adjuvant treatment stage 1B - IV