Surgical Resection of Gastric Cancer
Evidence & Issues

Carol J. Swallow
Department of Surgical Oncology
Princess Margaret and Mount Sinai Hospitals
University of Toronto

Surgical Resections in Proximal GI Cancer Management
BC Surgical Oncology Network Conference
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I. Technical Issues
- RCT
- Other

II. Quality of Surgery
III. Adjuvant Treatment

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

Case #1
50 year old healthy man
2 years of dyspepsia
OGD: antral tumour
path: invasive adenoCa

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

**MRC RCT: D1 vs D2 Dissection Longterm Survival**

- Disease free survival
- Overall survival

% alive at 5 years

D1, n=200
D2, n=200

*Br J Cancer 1999 79: 1522*

**Dutch RCT: D1 vs D2 Dissection Longterm Survival**

- All patients
- Node neg
- Node pos

% alive at 5 years

D1, n=380
D2, n=331

*NEJM 1999; 340:908*

**Dutch RCT: D1 vs D2 Dissection Very Longterm Survival**

- All
- N0
- N1
- N2
- N3

% alive at 11 years

D1, n=380
D2, n=331

* p=0.078

*median f/u time = 11 years*

*J Clin Oncol 2004; 22:2069*

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

- Morbidity
- Mortality

% postop complications (%)

D1, n=200
D2, n=200

* p<0.04

*The Lancet 1996 347:995*

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

- Morbidity
- Mortality

% postop complications (%)

D1, n=380
D2, n=331

* p<0.004

*NEJM 1999; 340:908*

**“Standard” D2 Dissection: Japanese RCT & Italian multicentre phase II trial**

- IGCSG, n=191
  - 67 total gastrectomies
  - 40 splenectomies

- GCSSG of JCOG, n=263
  - 102 total gastrectomies
  - 98 splenectomies

Survival after “Standard” D2 Dissection

UK postcode trial: D1 vs modified D2 Dissection

Postoperative M & M Rates

UK postcode trial: D1 vs modified D2 Dissection

Longterm Survival

Extent of Lymphadenectomy: Cochrane Review – D2

• more dangerous when
  - spleen/pancreas resected
  - surgeon inexperienced

• studies limited by
  - learning curves, poor compliance
  - contamination
  - no PROVEN survival benefit
  - MAY benefit
  - T3+
  - Stage II & III

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

Laparoscopic vs Open Gastrectomy: RCT

- McCulloch et al, The Cochrane Collaboration, 2005

- Degiuli, EJSO 2004; 30: 303

Laparoscopic vs Open Gastrectomy: RCT


STG for distal cancer

LAP, n=30
OPEN, n=29

# nodes resected, mean

0 10 20 30 40 50

R Status Determines Prognosis

Karpeh et al, MSKCC

R0
n=1038

R1
n=193

R2
n=293

% alive at 5 years

0 10 20 30 40 50 60 70

Positive Margins and Survival

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

Stage II & III

Overall Survival (%)

0 1 2 3 4 5 6 7 8

Years

n=572

n=47

p<0.001

Frozen Section Analysis and Re-Excision of Positive Margins

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

> 5 pos nodes

≤ 5 pos nodes

Overall Survival (%)

0 100

Years

n=13

p=0.25

n=19

p=0.03

n=17

80% had T3N+

p=0.01

p=0.08

TNM Staging of Gastric Cancer

AJCC, 2002

Stage 1

A

T1; N0

Stage 2

T1; N2

T2; N1

T3; N0

Stage 3

A

T2; N2

T3; N1

T4; N0

T3; N2

Stage 4

A

T4; N1, N2, N3

T1, T2, T3, N3

M1
### National Cancer Data Base (USA) Report on Gastric Cancer (Dx 1987–88)

![Graph showing overall survival (%) over years after diagnosis]

**Cases:**
- IA, n=303
- IB, n=318
- II, n=367
- IIA, n=462
- IIB, n=303
- IV, n=1190

**Years after Diagnosis:**
- 0
- 1
- 2
- 3
- 4
- 5

**Overall Survival (%)**
- 100
- 80
- 60
- 40
- 20
- 0

**Cancer 1997; 80: 2333**

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### Gastric Cancer Surgical RCT Pot–Pourri

<table>
<thead>
<tr>
<th>Ac, Inst, Date</th>
<th>Question</th>
<th>n</th>
<th>Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doglietto, Rome, 2004</td>
<td>NJT in T1</td>
<td>237</td>
<td>No diff</td>
</tr>
<tr>
<td>Inaba, Tokyo, 2004</td>
<td>midline vs transv</td>
<td>54</td>
<td>Less pain, pneumonia, SBO in transv</td>
</tr>
<tr>
<td>Mochiki, Maebashi, 2003</td>
<td>JJ vs pouch</td>
<td>26</td>
<td>Less caloric intake in pouch</td>
</tr>
<tr>
<td>Hori, Chiba, 2004</td>
<td>stapled vs HS gastroduodenal pouch</td>
<td>167</td>
<td>Staped faster by 11 min, no other diff</td>
</tr>
<tr>
<td>Fiori, Rome, 2004</td>
<td>pall stent vs gastroend</td>
<td>16</td>
<td>Shorter op time, time to food, hosp stay with stent</td>
</tr>
</tbody>
</table>

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### 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?**

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### TNM Staging of Gastric Cancer: T Stage

<table>
<thead>
<tr>
<th>Stage</th>
<th>T1</th>
<th>T2</th>
<th>T3</th>
<th>T4</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Lamina propria, submucosa</td>
<td>Muscularis propria, subserosa</td>
<td>Penetrates serosa</td>
<td>Adjacent structures</td>
</tr>
<tr>
<td>B</td>
<td>T1; N0</td>
<td>T1; N1</td>
<td>T2; N0</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>T2; N2</td>
<td>T2; N1</td>
<td>T3; N0</td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>T3; N1</td>
<td>T4; N0</td>
<td>T3; N2</td>
<td></td>
</tr>
<tr>
<td>E</td>
<td>T4; N1, N2, N3</td>
<td>T1, T2, T3; N3</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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### 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

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**TNM Staging of Gastric Cancer: AJCC 2002, 6th edition**
"...it is suggested that at least 15 regional nodes be assessed..."

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

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

**Defining the Study Population**

- SEER 1973-2001
- Other Digestive Cancer
  - N = 216,830
- Gastric Malignancy
  - N = 58,371
- Adenocarcinoma Only
  - N = 49,218
- Gastric Surgery (Excludes wedge, bx, endoscopy)
  - N = 12,980
- Invasive Disease
  - N = 12,902
- 1988-2001
  - N = 24,651
- Age 18+
  - N = 49,208
- Lymph Node Assessment Done
  - N = 11,713
- Non-M1
  - N = 10,129
- Final Study Population
  - N = 10,129

**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)

**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
Odds of Adequate LN Assessment

- Year of diagnosis
- Percentage of Patients with Adequate LN Assessment

- 0 10 20 30 40

- SEER Region
- Reference Group

Factors Predictive of Survival

- SEER Region
- Survival Functions

- 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=L2
  - En bloc: HR=L2
- >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
**Type of Gastrectomy**

- **Proximal**
- **Subtotal**
- **Total**

**Lymph Node Retrieval**

- **Proximal**
- **Subtotal**
- **Total**

**Mount Sinai Hospital Trends in Adequacy of LNR**

- **1997**
- **1998**
- **1999**
- **2000**
- **2001**

**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 propia into adjacent greater omentum, but not through visceral peritoneum, T2
- proximal and distal margins negative
- 4 of 20 nodes positive, N1

**Intergroup-0116 RCT of Postoperative Adjuvant Chemoradiation**

- **Overall Survival**
- **Disease-free Survival**

* p<0.001
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