Surgery for Gastric and GE Junction Cancer: 
primary 
palliative 
when and where?

William Allum
William Allum

Conflict of Interest

None
EMR, endoscopic mucosal resection.
R0 Resection

A surgical procedure in which there is no evidence of macroscopic residual tumour in the tumour bed, lymph nodes and/or distant sites with microscopic negative resection margins

Japanese Rules
End Results of Surgical Resection

Cumulative Survival Rate, %

- Absolute curative: 78.7 ± 1.7%; n=2706
- Relative curative: 39.6 ± 3.7%; n=823
- Relative non-curative: 16.5 ± 4.8%; n=281
- Absolute non-curative: 1.4 ± 0.9%; n=923

Indication and Division Lines for Distal Subtotal and Total Gastrectomy

Distal subtotal gastrectomy

- Early cancer or well-circumscribed advanced cancer
- Infiltrative advanced cancer

Total gastrectomy

- When the proximal distance from the cardia is less than the required length, total gastrectomy is indicated
- Total gastrectomy is always indicated in diffuse carcinoma (Borrmann type 4) regardless of its size

>2cm from cardia

>5cm from cardia

<5cm

3cm
Total Gastrectomy and Lymph Node Dissection

Japanese Gastric Cancer Association, 2011 Gastric Cancer 14: 113-23.
Distal Gastrectomy and Lymph Node Dissection

Japanese Gastric Cancer Association, 2011 Gastric Cancer 14: 113-23.
Western Trials

- **UK MRC D1 vs D2 (1996, 1999)**
  - 5 year survival  
    - D1: 35%  
    - D2: 33%
  - Operative mortality  
    - D1: 6.5%  
    - D2: 13%

- **Dutch Gastric Cancer trial (2010)**
  - Operative mortality  
    - D1: 4%  
    - D2: 10%
  - 15 year survival  
    - D1: 21%  
    - D2: 29% (NS)
  - Gastric cancer deaths  
    - D1: 48  
    - D2: 37 (p 0.01)

- **Italian trial (2014)**
  - Operative mortality  
    - D1: 3.0%  
    - D2: 2.2%
  - 5 year survival  
    - D1: 66.5%  
    - D2: 64.2%
  - pT2-4 / No  
    - D1: 38%  
    - D2: 59%
<table>
<thead>
<tr>
<th>Guideline</th>
<th>Gastric Resection</th>
<th>Lymphadenectomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIGN</td>
<td>R0 (proximal, distal circumferential margins)</td>
<td>D2 ≥ 25 lymph nodes</td>
</tr>
<tr>
<td></td>
<td>R0 (proximal, distal circumferential margins)</td>
<td>D2 &gt; 25 lymph nodes</td>
</tr>
<tr>
<td>German S3</td>
<td>5cm intestinal</td>
<td>&gt; 16 nodes for TNM</td>
</tr>
<tr>
<td></td>
<td>8cm diffuse</td>
<td>No pancreatectomy/splenectomy</td>
</tr>
<tr>
<td></td>
<td>R0</td>
<td>D2 for stage II &amp; III – if fit</td>
</tr>
<tr>
<td>UK</td>
<td>cT1 diffuse – resect</td>
<td>&gt; 15 nodes for TNM</td>
</tr>
<tr>
<td></td>
<td>R0</td>
<td>D2 – without pancreatectomy or splenectomy</td>
</tr>
<tr>
<td>St Gallen</td>
<td>cT1 diffuse – resect</td>
<td></td>
</tr>
</tbody>
</table>

SIGN, Scottish Intercollegiate Guidelines Network; TNM, tumour node metastases.
Post-operative survival by Resection Status
MRC UK ST03 trial

![Graph showing survival rates by resection status](image-url)

- **R0**
- **R1**
- **No resection**

**Number at risk (number censored)**
- **R0**: 626 (33) to 0 (0)
- **R1**: 208 (9) to 0 (0)
- **No resection**: 168 (2) to 0 (0)

**Survival rates**:
- HR 0.23 (95% CI 0.19-0.28), \( \chi^2 = 258.2 \);
- \( p < 0.0001 \) for R0 vs R1 or no resection.

**Survival curve**
- Time from surgery (months): 0 to 96 months.
European Chapter of IGCA

D2 Audit
Main findings

Early GC

The extent of lymphadenectomy is highly variable among European surgeons.

In cN+ cases a complete D2 dissection is performed only by 53% of surgeons.

- There is an impact of diffuse histology with a higher number of D2 performed in cN0 cases.

- The presence of comorbidity reduces the indication to D2 in cN+ cases.
Main findings

Advanced GC

Most surgeons perform a D2, but still some variations persist.

- Histology also have an impact:

  the number of surgeons performing a D2 and the number of total gastrectomies for tumours located in the lower third is higher in tumours with diffuse histology compared with the intestinal histology.
D2 lymphadenectomy alone or with para-aortic nodal dissection for gastric cancer

JCOG 9501
Scheme

Endpoints
1. Overall survival
2. Recurrence-free survival, morbidity/mortality

Adenocarcinoma
T2b/T3/T4, N0/N1/N2, Curative operation, Lavage cytology (-)

Intraoperative Randomisation

Group A (standard)
D2

Group B (Extended)
D2 + PAND

Observation

523 patients enrolled between July 1995 and April 2001
24 Institutions
Survival analysis performed April 2006

PAND, para-aortic nodal dissection.
JCOG 9501
Overall Survival

Overall Survival, %

D2 (n=263)
- 3-year Survival: 76.4%
- 5-year Survival: 69.2%

D2 + PAND (n=259*)
- 3-year Survival: 76.4%
- 5-year Survival: 70.3%

HR=1.03 (0.77-1.37)
one-sided P=0.57

HR, hazard ratio.
*One case was ineligible because of changed histologic diagnosis.
Extended Lymphadenectomy

Extended Lymphadenectomy

T3/4 cancers

Mixed or diffuse histology

Upper third of the stomach

## Subtypes of Gastric Cancer.

<table>
<thead>
<tr>
<th>Type</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diffuse, signet ring cancer</td>
<td>CDH-1 mutation</td>
</tr>
<tr>
<td></td>
<td>Lepidic growth</td>
</tr>
<tr>
<td></td>
<td>Peritoneal metastasis</td>
</tr>
<tr>
<td>Intestinal type, distal gastric cancer</td>
<td>Correa hypothesis – chronic inflammation</td>
</tr>
<tr>
<td></td>
<td>H. pylori associated</td>
</tr>
<tr>
<td>Proximal, non-diffuse cardia / junctional cancer</td>
<td>Obesity / GORD related</td>
</tr>
<tr>
<td></td>
<td>H. pylori protective</td>
</tr>
<tr>
<td></td>
<td>Poorest prognosis</td>
</tr>
<tr>
<td></td>
<td>HER2 strong expression</td>
</tr>
</tbody>
</table>
Minimally Invasive Surgery

- Shorter inpatient stay
- Less blood loss
- Quicker return to GI function
- ? Anastomotic leak rates
- Intraluminal bleeding
# Minimally Invasive Surgery

## Total Gastrectomy

<table>
<thead>
<tr>
<th>Variables</th>
<th>Extent of LND</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>D1 + β (n=103)</td>
<td>D2 (n=19)</td>
</tr>
<tr>
<td>Operating time, mean, min ± SD</td>
<td>277 ± 86</td>
<td>350 ± 76</td>
</tr>
<tr>
<td>EBL, mean, mL ± SD</td>
<td>231 ± 190</td>
<td>350 ± 250</td>
</tr>
<tr>
<td>Harvested lymph nodes, mean, n ± SD</td>
<td>42 ± 16</td>
<td>44 ± 16</td>
</tr>
<tr>
<td>Morbidity, n %</td>
<td>19 (18.4)</td>
<td>10 (52.6)</td>
</tr>
<tr>
<td>Mortality, n %</td>
<td>0</td>
<td>2 (10.5)</td>
</tr>
<tr>
<td>Hospital stay, mean, d ± SD</td>
<td>10.8 ± 9.1</td>
<td>17.1 ± 20.8</td>
</tr>
</tbody>
</table>

*EBL, estimated blood loss; LND, lymph node dissection; SD, standard deviation.*

Minimally Invasive Surgery

Early gastric cancer
Distal Gastrectomy

KLASS Trial
Comparison of laparoscopic vs open gastrectomy for gastric cancer: a prospective randomized trial

JCOG 0912
Phase III study of laparoscopy-assisted vs open distal gastrectomy with nodal dissection for clinical stage IA/IB gastric cancer: a multicenter study

KLASS, Korea Laparoscopic Gastrointestinal Surgery Study Group.
Minimally Invasive Surgery

KLASS and JCOG 0912 Trial

Safe – morbidity 14.8%, mortality 0%

Technically skilled surgeons

Long term outcomes awaited
Minimally Invasive Surgery

Advanced Disease

LAG vs Open – feasible D2 dissection

<table>
<thead>
<tr>
<th></th>
<th>Intraoperative Complications</th>
<th>Postoperative Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>LADG</td>
<td>1.1%</td>
<td>7.5%</td>
</tr>
<tr>
<td>LATG</td>
<td>1.9%</td>
<td>20.1%</td>
</tr>
</tbody>
</table>
OESOPHAGO-GASTRIC JUNCTIONAL ADENOCARCINOMA
TNM-8 Oesphagogastric Junction

Oesophagus and Gastric Carcinomas

- A tumour the epicenter of which is within 2 cm of the oesophagogastric junction and also extends into the oesophagus is classified and staged using the oesophageal scheme.

  Cancers involving the oesophagogastric junction (OGJ) whose epicenter is within the proximal 2 cm of the cardia (Siewert types I/II) are to be staged as oesophageal.

- Cancers whose epicenter is more than 2 cm distal from the OGJ will be staged using the Stomach Cancer TNM and Stage even if the OGJ is involved.
OESOPHAGO-GASTRIC JUNCTIONAL ADENOCARCINOMA

Type I

Type II

Type III

• The problem of large tumours
• Accuracy of preoperative endoscopy and imaging techniques
• Location of the epicenter of the tumour vs. length of esophageal or gastric involvement
Operation Selection

Surgical Approach

Margins

Lymphadenectomy
EORTC Consensus
St Gallen 2012

- Type I – Oesophago-gastrectomy

- Type II – Oesophago-gastrectomy or
  - Extended Total Gastrectomy

- Type I & II – Mediastinal Lymphadenectomy
  - 2 field

- Type III – Extended Total Gastrectomy
Dutch Trial
Trans Hiatal Oesophagectomy vs Trans Thoracic Oesophagectomy

220 patients with mid and lower oesophageal ACA

THO
Lower morbidity

TTO
More nodes
More respiratory complications

Dutch Trial
THO vs TTO

Numbers at risk:

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>25</th>
<th>45</th>
</tr>
</thead>
<tbody>
<tr>
<td>THO</td>
<td>52</td>
<td>25</td>
<td>9</td>
</tr>
<tr>
<td>TTO</td>
<td>63</td>
<td>28</td>
<td>11</td>
</tr>
</tbody>
</table>
Dutch Trial
THO vs TTO
Minimally Invasive Oesophagectomy

101 open; 65 MIO; 9 Conversion

pT1a & pT1b. No

<table>
<thead>
<tr>
<th></th>
<th>Intraoperative</th>
<th>Morbidity</th>
<th>Medium Term</th>
</tr>
</thead>
<tbody>
<tr>
<td>MIO</td>
<td>Less blood loss</td>
<td>Gastroparesis</td>
<td>Less pain</td>
</tr>
<tr>
<td>OPEN</td>
<td>Shorter time</td>
<td>Respiratory</td>
<td>More fatigued</td>
</tr>
</tbody>
</table>

Nafteux et al 2011 Eur J Cardio Surgery 40: 1455
Minimally Invasive Oesophagectomy

MIRO trial

Open right thoraco-abdominal oesophago-gastrectomy (OE) vs Hybrid – laparoscopic mobilisation / open thoracotomy (HMIE)

<table>
<thead>
<tr>
<th></th>
<th>Major Complications</th>
<th>Respiratory Complications</th>
<th>Survival 3 yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>OE (n=104)</td>
<td>67 (64.4%)</td>
<td>31 (30.1%)</td>
<td>54.8%</td>
</tr>
<tr>
<td>HMIE (n=103)</td>
<td>37 (35.9%)</td>
<td>18 (17.7%)</td>
<td>67.0%</td>
</tr>
</tbody>
</table>

Mariette et al ESMO 2017
Operation Selection

Surgical Approach

Margins

Lymphadenectomy
Resection Margin and Survival

Circumferential resection margin (CRM) size correlates with overall survival

Prospective database, single institution study, N = 229

- CRM size is a significant prognostic factor for overall survival
- 40.6% of patients in this study had a CRM <1mm
- Post operative chemoradiation did not alter survival in patients with CRM <1mm
- BUT smaller CRM may just reflect a larger tumour

<table>
<thead>
<tr>
<th>CRM</th>
<th>n</th>
<th>Median Survival (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>45</td>
<td>1.2 yrs (0.9-1.4)</td>
</tr>
<tr>
<td>&lt;1mm</td>
<td>48</td>
<td>1.9 yrs (1.4-3.2)</td>
</tr>
<tr>
<td>1.0-1.9mm</td>
<td>31</td>
<td>3.5 yrs (2.0–no upper CI)</td>
</tr>
<tr>
<td>≥ 2.0mm</td>
<td>105</td>
<td>Not reached</td>
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</table>
CRM in Neoadjuvant Trials

<table>
<thead>
<tr>
<th></th>
<th>CS</th>
<th>S</th>
<th>CF</th>
<th>ECX</th>
<th>CXRT</th>
<th>S</th>
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<tbody>
<tr>
<td>OEO2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>25%</td>
</tr>
<tr>
<td>OEO5</td>
<td></td>
<td></td>
<td>28%</td>
<td>41%</td>
<td>33%</td>
<td></td>
</tr>
<tr>
<td>CROSS</td>
<td></td>
<td></td>
<td>8%</td>
<td></td>
<td>30%</td>
<td></td>
</tr>
</tbody>
</table>

Radical Surgery – 13% - 2/62
Operation Selection

Surgical Approach

Margins

Lymphadenectomy
Risk of Systemic Disease and Number of Nodes Involved

Peyre et al 2008

INCURABLE DISEASE
Palliative Intent

Quality of life  vs Quantity of life

Patient Wishes
Quality of Life

Resection vs Chemotherapy?

Subtotal vs Total Gastrectomy?
Palliative Resection

Dutch D1 vs D2 trial

295 / 996 (29%) incurable

T+ macroscopically irresectable
H+ liver metastasis
P+ peritoneal metastasis
N4+ distant lymph nodes

**Palliative Surgery**

**Fig. 2** Survival following resection and no resection in patients aged 70 years or less and with two or more positive signs of incurability. $P = 0.07$ (log rank test)

**Fig. 4** Survival following resection and no resection in patients aged more than 70 years and with two or more positive signs of incurability. $P = 0.82$ (log rank test)
Palliative Surgery Selection

ASA I & II

Non – Ro resection

Single site solid organ metastasis

Localised peritoneal disease without signet ring cancer

(Robb et al 2012)
**REGATTA study design**

**Recruitment:** 330 patients
**To detect an 10% improvement in 2-yr OS from 20-30%**
**HR = 0.75; 1-side \( \alpha \text{=} 0.05; 80\% \text{ power} \)**  

_Yang et al ASCO 2015_
Overall survival

Yang et al ASCO 2015
<table>
<thead>
<tr>
<th>Metastasis Site</th>
<th>Chemotherapy</th>
<th>Gastrectomy + Chemotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver</td>
<td>5 (6%)</td>
<td>11 (12%)</td>
</tr>
<tr>
<td>Peritoneum</td>
<td>66 (77%)</td>
<td>65 (73%)</td>
</tr>
<tr>
<td>Para-aortic node</td>
<td>11 (13%)</td>
<td>13 (15%)</td>
</tr>
<tr>
<td>Missing</td>
<td>4 (5%)</td>
<td>0</td>
</tr>
</tbody>
</table>
Hepatic Resection for Gastric Cancer Liver Metastases: A Systematic Review and Meta-Analysis

FAUSTO PETRELLI, MD, ANDREA COINU, MD, MARY CABIDDU, MD, MARA GHILARDI, MD, KAREN BORGONOVO, MD, VERONICA LONATI, AND SANDRO BARNI, MD
Department of Oncology, Division of Medical Oncology, Azienda Ospedaliera Treviglio, Treviglio (BG), Italy

23 trials including 870 patients
Median survival 22 months
5-y-surv. all 23.9%
synchronous 22.6%
metachronous 30.0%
OLIGOMETASTATIC DISEASE
Surgery

Quality Assurance
- 13 countries affiliated to EURECCA upper GI group

**Data source**
- Registry
- National audit
- National society
- National audit
ECCO ESSENTIAL REQUIREMENTS FOR QUALITY CANCER CARE

OESOPHAGEAL / GASTRIC CANCER

Multidisciplinary standards for service and management of oesophageal and gastric cancer
HR according to hospital volume

Adjusted for sex, age, deprivation, co-morbidity score, type of cancer and resection quintile
## Nodal Yield

**MAGIC vs ST03**

### MAGIC (2006)

<table>
<thead>
<tr>
<th></th>
<th>&lt; 15</th>
<th>15 - 20</th>
<th>20 - 25</th>
<th>&gt; 25</th>
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</thead>
<tbody>
<tr>
<td>Count</td>
<td>104</td>
<td>47</td>
<td>24</td>
<td>43</td>
</tr>
<tr>
<td>Percent</td>
<td>48%</td>
<td>22%</td>
<td>11%</td>
<td>19%</td>
</tr>
</tbody>
</table>

### ST03 (2017)

<table>
<thead>
<tr>
<th></th>
<th>&lt;15</th>
<th>15-24</th>
<th>&gt;25</th>
</tr>
</thead>
<tbody>
<tr>
<td>Count</td>
<td>141</td>
<td>277</td>
<td>410</td>
</tr>
<tr>
<td>Percent</td>
<td>17%</td>
<td>33%</td>
<td>50%</td>
</tr>
</tbody>
</table>
Thank you for your attention