Surgery for Gastric and GE Junction Cancer:

primary palliative when and where?

William Allum
Consultant Surgeon
Any surgeon can cure

Surgeon - dependent

No surgeon can cure

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

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

Indication and Division Lines for Distal Subtotal and Total Gastrectomy

**Distal subtotal gastrectomy**

- >2cm from cardia
- Early cancer or well-circumscribed advanced cancer

**Total gastrectomy**

- <5cm
- When the proximal distance from the cardia is less than the required length, total gastrectomy is indicated

- 3cm
- Total gastrectomy is always indicated in diffuse carcinoma (Borrmann type 4) regardless of its size

- >5cm from cardia
- Infiltrative advanced cancer
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.
Medical Research Council

D1 vs D2

## Dutch Gastric Cancer Trial Results

<table>
<thead>
<tr>
<th></th>
<th>D₁</th>
<th>D₂</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 711</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morbidity, %</td>
<td>25</td>
<td>43</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mortality, %</td>
<td>4</td>
<td>10</td>
<td>0.004</td>
</tr>
<tr>
<td>5-year survival, %</td>
<td>45</td>
<td>47</td>
<td>NS</td>
</tr>
<tr>
<td>11-year survival, %</td>
<td>30</td>
<td>35</td>
<td>NS</td>
</tr>
<tr>
<td>15-year survival, %</td>
<td>21</td>
<td>29</td>
<td>NS</td>
</tr>
<tr>
<td>Gastric Cancer Deaths</td>
<td>48</td>
<td>37</td>
<td>0.01</td>
</tr>
</tbody>
</table>

*NS, not significant.
# Italian Gastric Cancer Study Group

## D1 vs D2 trial

<table>
<thead>
<tr>
<th></th>
<th>D1</th>
<th>D2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Operative Mortality</strong></td>
<td>3.0%</td>
<td>2.2%</td>
</tr>
<tr>
<td><strong>5 year Survival</strong></td>
<td>66.5%</td>
<td>64.2%</td>
</tr>
<tr>
<td><strong>pT1 (p=0.015)</strong></td>
<td>98%</td>
<td>83%</td>
</tr>
<tr>
<td><strong>pT2-4 N+ (p=0.055)</strong></td>
<td>38%</td>
<td>59%</td>
</tr>
</tbody>
</table>

<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>German S3</td>
<td>5cm intestinal 8cm diffuse</td>
<td>D2 &gt; 25 lymph nodes</td>
</tr>
<tr>
<td></td>
<td>R0 (proximal, distal circumferential margins)</td>
<td>&gt; 16 nodes for TNM</td>
</tr>
<tr>
<td>UK</td>
<td>cT1 diffuse – resect</td>
<td>No pancreatectomy/splenectomy</td>
</tr>
<tr>
<td>St Gallen</td>
<td>R0</td>
<td>D2 for stage II &amp; III – if fit</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt; 15 nodes for TNM</td>
</tr>
<tr>
<td></td>
<td></td>
<td>D2 – without pancreatectomy or splenectomy</td>
</tr>
</tbody>
</table>

SIGN, Scottish Intercollegiate Guidelines Network; TNM, tumour node metastases.
SURGERY FOR EARLY GASTRIC CANCER

T1 m  D1 alpha (Stations 7 & 8)

T1 sm  D1 beta (D1 alpha + station 9 & 11p)

Function preserving gastrectomy
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

Randomized trial in Siewert type II and III cancers

Left thoraco-abdominal approach versus abdominal transhiatal approach
Gastric carcinoma, oesophageal invasion (≤3 cm)  
T2-4, N0-2, M0

Preoperative randomisation of institution, macroscopic type, clinical T

Abdominal (AT)  
Total gastrectomy, D2  
+ left upper paraaortic dissection

Thoraco-abdominal (LT)  
Total gastrectomy, D2  
+ left upper paraaortic  
+ mediastinal dissection

Observation if curative resection

AT, abdominal transhiatal; LT, left thoraco-abdominal.  
JCOG 9502
Overall Survival

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

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**

![Graph showing overall survival](image)

- **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 case was ineligible because of changed histologic diagnosis.*


**HR, hazard ratio.**
Extended Lymphadenectomy

Extended Lymphadenectomy

T3/4 cancers

Mixed or diffuse histology

Upper third of the stomach
JCOG 0110 “Splenectomy or Not”

Endpoints
1. Overall survival
2. Morbidity, operation time, blood loss

Adenocarcinoma in upper 1/3
T2/T3/T4, N0/N1/N2, Not greater curve, Curative operation, Lavage cytology (-)

Intraoperative randomisation

Group A (Splenectomy)
Total gastrectomy, D2

Group B (Spleen preserve)
Total gastrectomy, D2

Observation
(S-1 adjuvant for Stage II/III)

JCOG 0110 “Splenectomy or Not”

505 patients

Similar operative mortality with or without splenectomy

Greater postoperative morbidity with splenectomy

Greater intraoperative blood loss with splenectomy

5 year survival

Splenectomy 75.1%

Splenectomy preservation 76.4%

OESOPHAGO-GASTRIC JUNCTIONAL ADENOCARCINOMA
EGJ tumor (TNM 7th ed.)

**Oesophagus**
*(ICD-O C15)*
Includes Oesophagogastric junction (C16.0)

**Rules for Classification**

- A tumour the epicenter of which is within 5 cm of the oesophagogastric junction and also extends into the oesophagus is classified and staged using the oesophageal scheme.

- Tumours with an epicenter in the stomach greater than 5 cm from the oesophagogastric junction or those within 5 cm of the oesophagogastric junction without extension in the oesophagus are classified and staged using the gastric carcinoma scheme.
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
Dutch Trial
THO vs TTO
Minimally Invasive Oesophagectomy

101 open;
65 MIO;
9 Conversion

pT1a & pT1b. N0

<table>
<thead>
<tr>
<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>
</tr>
<tr>
<td>OPEN</td>
<td>Shorter time</td>
<td>Respiratory</td>
</tr>
</tbody>
</table>

Nafteux et al 2011 Eur J Cardio Surgery 40: 1455
Operation Selection

Surgical Approach

Margins

Lymphadenectomy
Resection Margin and Survival

The Royal Marsden

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

Kaplan-Meier curves of OS by margin size:

<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>
</tr>
</tbody>
</table>

Landau et al., ESMO 2010 (Abstract 711PD)
Operation Selection

Surgical Approach

Margins

Lymphadenectomy
Survival by Nodal Volume

Bollschweiler et al 2006
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?
Symptom Control

Obstruction

Stenting

Bleeding

XRT

Nutritional Support
Palliative Resection

Dutch D1 vs D2 trial

295 / 996 (29%) incurable

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

**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 $\alpha = 0.05; 80\%$ power

Yang et al ASCO 2015
REGATTA

- Single non-curable factor defined by:
  - Liver metastases – >2 liver lesions or requiring extended lobectomy
  - Peritoneal metastases – any number of peritoneal lesions
  - Para-aortic lymph node metastases
<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>
Overall survival

Yang et al ASCO 2015

- **Chemotherapy**
  - Number of events: 71
  - MST (95%CI): 16.6m (13.7-19.8)
  - 1-year survival (95%CI): 66.4% (55.1% - 75.4%)
  - 2-year survival (95%CI): 31.7% (21.7% - 42.2%)

- **Gastrectomy+Cx**
  - Number of events: 73
  - MST (95%CI): 14.3m (11.8-16.3)
  - 1-year survival (95%CI): 57.1% (46.1% - 66.6%)
  - 2-year survival (95%CI): 25.1% (16.2% - 34.9%)

One-sided p=0.70 by stratified log-rank test
HR for Gastrectomy+Cx, 1.09, 95%CI (0.78-1.52)
13 countries affiliated to EURECCA upper GI group

Data source
- Registry
- National audit
- National society
- National audit
# SURGERY STOMACH

<table>
<thead>
<tr>
<th>Country</th>
<th>Proximal Gastrectomy</th>
<th>Total Gastrectomy</th>
<th>Distal Gastrectomy</th>
<th>Laparotomy only</th>
</tr>
</thead>
<tbody>
<tr>
<td>Netherlands</td>
<td>33%</td>
<td>33%</td>
<td>54%</td>
<td>12%</td>
</tr>
<tr>
<td>France</td>
<td>23%</td>
<td>49%</td>
<td>28%</td>
<td></td>
</tr>
<tr>
<td>Spain</td>
<td>1%</td>
<td>38%</td>
<td>61%</td>
<td></td>
</tr>
<tr>
<td>UK</td>
<td>3%</td>
<td>39%</td>
<td>44%</td>
<td>5%</td>
</tr>
<tr>
<td>Ireland</td>
<td>42%</td>
<td>57%</td>
<td></td>
<td>1%</td>
</tr>
</tbody>
</table>
Hospital volume over time

Oesophageal and Gastric Resection
HR according to hospital volume

Adjusted for sex, age, deprivation, co-morbidity score, type of cancer and resection quintile
Overall Survival by Site and Period of Surgery

Fontana et al *Gastric Cancer* 2016 In Press
Thank you for your attention
Surgeon Outcome 2012-2014

Adjusted 30 day mortality rate by consultant

Adjusted 90 day mortality rate by consultant
163 (2011-12) 177 (2012-13) surgeons

40 (2011-12) 51 hospitals (2012-13)
median volume 56 (19-141)

2381 (2011-12), 2354 (2012-13) cases,
281 (12%) dual operations

Median volume: 14
(13 before accounting for dual surgery)

Max volume: 40
(39 before accounting for dual surgery)

Surgeons with a volume <10: 56
(65 before accounting for dual surgery)
### Palliative Resection Morbidity and Mortality

<table>
<thead>
<tr>
<th></th>
<th>No. of patients</th>
<th>Morbidity*</th>
<th>Hospital stay (days)†</th>
<th>Mortality*</th>
<th>Survival (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Median</td>
</tr>
<tr>
<td><strong>All ages</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No resection</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exploration</td>
<td>78</td>
<td>9 (12)</td>
<td>9 (3–93)</td>
<td>8 (10)</td>
<td>5.4</td>
</tr>
<tr>
<td>Gastroenterostomy</td>
<td>51</td>
<td>7 (14)</td>
<td>11 (7–27)</td>
<td>5 (10)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>129</td>
<td>16 (12)</td>
<td>10 (3–93)</td>
<td>13 (10)</td>
<td></td>
</tr>
<tr>
<td>Resection</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Partial gastrectomy</td>
<td>93</td>
<td>28 (30)</td>
<td>14 (7–154)</td>
<td>12 (13)</td>
<td>8.1</td>
</tr>
<tr>
<td>Total gastrectomy</td>
<td>63</td>
<td>31 (49)</td>
<td>17 (11–82)</td>
<td>7 (11)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>156</td>
<td>59 (38)</td>
<td>15 (7–154)</td>
<td>19 (12)</td>
<td></td>
</tr>
<tr>
<td>$P^*$</td>
<td>$&lt; 0.001$</td>
<td>$&lt; 0.001$</td>
<td>n.s.</td>
<td>$&lt; 0.001$</td>
<td></td>
</tr>
</tbody>
</table>
Survival by CRM

![Graph showing survival rates by CRM categories.](image)

**No. at risk**

<table>
<thead>
<tr>
<th>CRM Category</th>
<th>0 mm</th>
<th>0.1–0.9 mm</th>
<th>≥ 1 mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRM 0 mm</td>
<td>42</td>
<td>32</td>
<td>13</td>
</tr>
<tr>
<td>CRM 0.1–0.9 mm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CRM ≥ 1 mm</td>
<td></td>
<td></td>
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</table>

*O’Neill et al. BJS 2013; 100:1055-63*