Surgery for Gastric and GE Junction Cancer:

primary
palliative
where and when?

William Allum
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

Cumulative Survival Rate, %

Years

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

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

## European Guidelines Surgery

<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..

SURGERY FOR EARLY GASTRIC CANCER

T1 m  D1 alpha (Stations 7 & 8)

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

Function preserving gastrectomy
Indication and Division Lines for Distal Subtotal and Total Gastrectomy

**Distal subtotal gastrectomy**

- >2cm from cardia
- Early cancer or well-circumscribed advanced cancer
- <5cm

**Total gastrectomy**

- >5cm from cardia
- Infiltrative advanced cancer
- 3cm

- 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
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.
Randomized trial in Siewert type II and III cancers

Left thoraco-abdominal approach versus abdominal transhiatal approach

JCOG, Japan Clinical Oncology Group.
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

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)

D2 + PAND (n=259*)

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

D2

D2 + PAND

Years

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

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 or Not 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.**
Type I – Oesophago-gastrectomy

Type II – Oesophago-gastrectomy or
  – Extended Total Gastrectomy

Type I & II – Mediastinal Lymphadenectomy
  – 2 field

Type III – Extended Total Gastrectomy
Aim of Surgery for Junctional Cancer

- R0 resection
- Minimum 15 lymph nodes
- 5cm grossly normal in situ proximal oesophagus
Dutch Trial
THO vs TTO

- 220 patients with mid and lower oesophageal ACA
Dutch Trial
THO vs TTO

- TTO
  - More nodes
  - More respiratory complications
  - Lower oesophageal and LN 1-8 better outcome
Resection Margin and Procedure

- 171 AEG Patients
  - 16 Oesophagectomy
  - 71 Left Thoraco-abdominal
  - 84 Transhiatal

- Margin: proximal limit of tumour above junction
  - > 5cm – oesophagectomy
  - 3 – 5cm – left thoraco-abdominal
  - < 3cm - Transhiatal

Resection Margin and Survival

Circumferential resection margin (CRM) size correlates with overall survival

- 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

Landau et al., ESMO 2010 (Abstract 711PD)
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></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>D1 + β (n=103)</td>
<td>D2 (n=19)</td>
<td>P value</td>
<td></td>
</tr>
<tr>
<td>Operating time, mean, min ± SD</td>
<td>277 ± 86</td>
<td>350 ± 76</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>EBL, mean, mL ± SD</td>
<td>231 ± 190</td>
<td>350 ± 250</td>
<td>0.019</td>
<td></td>
</tr>
<tr>
<td>Harvested lymph nodes, mean, n ± SD</td>
<td>42 ± 16</td>
<td>44 ± 16</td>
<td>0.484</td>
<td></td>
</tr>
<tr>
<td>Morbidity, n %</td>
<td>19 (18.4)</td>
<td>10 (52.6)</td>
<td>0.003</td>
<td></td>
</tr>
<tr>
<td>Mortality, n %</td>
<td>0</td>
<td>2 (10.5)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Hospital stay, mean, d ± SD</td>
<td>10.8 ± 9.1</td>
<td>17.1 ± 20.8</td>
<td>0.032</td>
<td></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

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
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

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. 3** 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 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>$P_{\alpha}$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

*P values are calculated using a two-sample t-test.†Median and mean survival times are given in months.
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
Overall survival

<table>
<thead>
<tr>
<th></th>
<th>Chemotherapy n=86</th>
<th>Gastrectomy+Cx n=89</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of events</td>
<td>71</td>
<td>73</td>
</tr>
<tr>
<td>MST (95%CI)</td>
<td>16.6m (13.7-19.8)</td>
<td>14.3m (11.8-16.3)</td>
</tr>
<tr>
<td>1-year survival (95%CI)</td>
<td>66.4% (55.1%-75.4%)</td>
<td>57.1% (46.1%-66.6%)</td>
</tr>
<tr>
<td>2-year survival (95%CI)</td>
<td>31.7% (21.7%-42.2%)</td>
<td>25.1% (16.2%-34.9%)</td>
</tr>
</tbody>
</table>

One-sided p=0.70 by stratified log-rank test
HR for Gastrectomy+Cx, 1.09, 95%CI (0.78-1.52)

Yang et al ASCO 2015
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
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)
Thank you for your attention