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

William Allum
William Allum

Conflict of Interest

None
Any surgeon can cure

Surgeon - dependent

No surgeon can cure

EMR, endoscopic mucosal resection.
Algorithm of Standard Treatment

Neoadjuvant Chemotherapy
## 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 strongest expression</td>
</tr>
</tbody>
</table>
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**

<table>
<thead>
<tr>
<th>Years</th>
<th>Cumulative Survival Rate, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>1</td>
<td>88</td>
</tr>
<tr>
<td>2</td>
<td>75</td>
</tr>
<tr>
<td>3</td>
<td>63</td>
</tr>
<tr>
<td>4</td>
<td>51</td>
</tr>
<tr>
<td>5</td>
<td>40</td>
</tr>
</tbody>
</table>

- **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**

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

- >5cm from cardia
  - Infiltrative 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
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 (2006)</td>
<td>R0 (proximal, distal circumferential margins)</td>
<td>D2 &gt; 25 lymph nodes</td>
</tr>
<tr>
<td>German S3 (2011)</td>
<td>R0 (proximal, distal circumferential margins)</td>
<td>D2 &gt; 25 lymph nodes</td>
</tr>
<tr>
<td></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>UK (2011)</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>St Gallen (2012/2018)</td>
<td>cT1 diffuse – resect R0</td>
<td>D2 – without pancreatectomy or splenectomy</td>
</tr>
<tr>
<td>ESMO (2016)</td>
<td>T1a</td>
<td>D1 alpha / beta</td>
</tr>
<tr>
<td></td>
<td>T1b - III</td>
<td>D2</td>
</tr>
</tbody>
</table>
## Surgery in ST03
### Radicality of Resection

<table>
<thead>
<tr>
<th>Extent of resection</th>
<th>ECX (n=533)</th>
<th>ECX+B (n=530)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>R0</td>
<td>315 (74%)</td>
<td>301 (75%)</td>
<td>0.844</td>
</tr>
<tr>
<td>R1</td>
<td>108 (26%)</td>
<td>100 (25%)</td>
<td></td>
</tr>
<tr>
<td>No resection</td>
<td>86</td>
<td>105</td>
<td></td>
</tr>
<tr>
<td>Unavailable</td>
<td>24</td>
<td>24</td>
<td></td>
</tr>
</tbody>
</table>

895 (84%) underwent surgical resection

**Operative mortality** 2.7%

**Operative morbidity** 52%

- Respiratory 24%,
- Sepsis 18%,
- Wound healing 10%
# Lymph node resection status

<table>
<thead>
<tr>
<th>Number of nodes</th>
<th>ECX</th>
<th>ECX+B</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>24 (17 - 33)</td>
<td>25 (18 - 34)</td>
<td>24 (17 - 34)</td>
</tr>
<tr>
<td>Range</td>
<td>0 - 96</td>
<td>0 - 89</td>
<td>0 - 96</td>
</tr>
<tr>
<td>None</td>
<td>5</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>&lt;15</td>
<td>74</td>
<td>17</td>
<td>57</td>
</tr>
<tr>
<td>15-24</td>
<td>146</td>
<td>33</td>
<td>137</td>
</tr>
<tr>
<td>25-34</td>
<td>109</td>
<td>25</td>
<td>110</td>
</tr>
<tr>
<td>35-44</td>
<td>56</td>
<td>13</td>
<td>60</td>
</tr>
<tr>
<td>45+</td>
<td>42</td>
<td>10</td>
<td>37</td>
</tr>
<tr>
<td>Unknown</td>
<td>4</td>
<td>&lt;1</td>
<td>3</td>
</tr>
<tr>
<td>TOTAL</td>
<td>436</td>
<td></td>
<td>409</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>845</td>
</tr>
</tbody>
</table>

**Take home message**

- >15 nodes 82%
- >25 nodes 49%

Acknowledgment: Bill Allum for help with these slides
Post-operative survival by Resection Status

HR 0.23 (95% CI 0.19–0.28), $\chi^2=258.2$; $p<0.0001$ for R0 vs R1 or no resection.
Left thoraco-abdominal approach versus abdominal transhiatal approach in Siewert type II and III (JCOG 9502)

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.  
D2 lymphadenectomy alone or with para-aortic nodal dissection for gastric cancer (JCOG 9501)

**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) 76.4% 69.2%
D2 + PAND (n=259*) 76.4% 70.3%

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

*One case was ineligible because of changed histologic diagnosis.
JCOG 0110 “Splenectomy or Not”

Endpoints

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

Intraoperative randomisation

Group A (Splenectomy)
Total gastrectomy, D2

Group B (Spleen preserve)
Total gastrectomy, D2

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

Extended Lymphadenectomy

- T3/4 cancers
- Mixed or diffuse histology
- Upper third of the stomach

Extended Lymphadenectomy

“Splenectomy or Not” (JCOG 0110)

Similar operative mortality with or without splenectomy

Greater postoperative morbidity with splenectomy

Greater intraoperative blood loss with splenectomy

Minimally Invasive Surgery

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

KLASS 01 Trial

Laparoscopic Distal Gastrectomy in early disease

Morbidity 14.8%,
Mortality 0%

Survival LADG
95.8% vs ODG 95.9%
Minimally Invasive Surgery

Advanced Disease – KLASS 02

LADG vs Open – feasible D2 dissection

Complications

LADG  16.4%
ODG   24.3%

KLASS 06

Lap Total Gastrectomy
Robotic vs Laparoscopy

Obesity and Type of Gastrectomy

No difference
- estimated blood loss,
- retrieved lymph nodes,
- complication rates,
- open conversion,
- length of stay

Lymph node dissection
- Lower blood loss for robotic after D2 but not <D2

Cost
- Robotic more expensive 250%

Park et al. EJSO 42 (2016) 1944-1949
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

- 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 / 2018

– 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

![Graph showing survival rates for THO and TTO over time with numbers at risk for each group: THO 52, TTO 63]
Dutch Trial
THO vs TTO

Cumulative Disease-free Survival (%)

Years

No. at Risk
Transhiatal esophagectomy
106 69 47 32 20 15 11 4

Transhiatal esophagectomy
114 69 53 39 31 20 13 7
Minimally Invasive Oesophagectomy

101 open; 65 MIO; 9 Conversion

pT1a & pT1b. No

<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
Minimally Invasive Oesophagectomy

**MIRO trial**

<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>

**TIME trial**

<table>
<thead>
<tr>
<th></th>
<th>Respiratory Complications</th>
<th>Survival 3 yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>OE (n=56)</td>
<td>19 (34%)</td>
<td>40.4%</td>
</tr>
<tr>
<td>HMIE (n=59)</td>
<td>7 (12%)</td>
<td>50.5%</td>
</tr>
</tbody>
</table>

Mariette et al ESMO 2017


Mariette et al ESMO 2017
Operation Selection

Surgical Approach

Margins

Lymphadenectomy
Resection Margin and Survival

Longitudinal

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

Landau et al., ESMO 2010 (Abstract 711PD)
# 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>
</tr>
</thead>
<tbody>
<tr>
<td>OEO2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25%</td>
<td></td>
<td>28%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OEO5</td>
<td></td>
<td></td>
<td>41%</td>
<td>33%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CROSS</td>
<td></td>
<td></td>
<td></td>
<td>8%</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

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

Dutch Gastric Cancer Trial (D1 – D2)
Palliative Resection

Patients
palliative resections

996
285 (26%)

Survival benefit of Surgery:

patients < 70 and 1 metastatic site

\( H^+ \) liver metastasis
\( P^+ \) peritoneal metastasis
\( N4^+ \) distant lymph nodes

Hartgrink Br J Surg 2002
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)
Gastrectomy plus chemotherapy versus chemotherapy alone for advanced gastric cancer with a single non-curable factor (REGATTA): a phase 3, randomised controlled trial

Kazumasa Fujitani*, Han-Kwang Yang*, Junki Mizusawa, Young-Woo Kim, Masanori Terashima, Sang-Uk Han, Yoshiaki Iwasaki, Woo Jin Hyung, Akinori Takagane, Do Joong Park, Takaki Yoshikawa, Seokyung Hahn, Kenichi Nakamura, Cho Hyun Park, Yukinori Kurokawa, Yung-Jue Bang, Byung Joo Park, Mitsuru Sasako, Toshimasu Tsujinaka, for the REGATTA study investigators†

<table>
<thead>
<tr>
<th></th>
<th>Chemotherapy alone (n=86)</th>
<th>Gastrectomy plus chemotherapy (n=89)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>59 (49-67)</td>
<td>62 (54-66)</td>
</tr>
<tr>
<td>Country</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Japan</td>
<td>46 (53%)</td>
<td>49 (55%)</td>
</tr>
<tr>
<td>South Korea</td>
<td>40 (47%)</td>
<td>40 (45%)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>56 (65%)</td>
<td>61 (69%)</td>
</tr>
<tr>
<td>Female</td>
<td>30 (35%)</td>
<td>28 (31%)</td>
</tr>
<tr>
<td>Non-curable factor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver metastasis (H1)</td>
<td>5 (6%)</td>
<td>11 (12%)</td>
</tr>
<tr>
<td>Peritoneal metastasis (P1)</td>
<td>66 (77%)</td>
<td>65 (73%)</td>
</tr>
<tr>
<td>Para-aortic lymph node metastasis (16a1/b2)</td>
<td>11 (13%)</td>
<td>13 (15%)</td>
</tr>
<tr>
<td>Missing</td>
<td>4 (5%)*</td>
<td>0</td>
</tr>
</tbody>
</table>

Lancet Oncology 2016
Figure 3: Subgroup analyses

Hazard ratios (HRs) for death in the patients assigned to gastrectomy plus chemotherapy are shown with 95% CIs. HR = hazard ratio. * Data missing for four patients in the chemotherapy alone group.
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

Yoshida, Kodera et al Gastric Cancer 2016
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 and gastric cancer

William Allum\textsuperscript{a}, Florian Lordick\textsuperscript{b}, Maria Alsina\textsuperscript{c}, Elisabeth Andritsch\textsuperscript{d}, Ahmed Ba-Salamah\textsuperscript{e}, Marc Beishon\textsuperscript{f}, Marco Braga\textsuperscript{g}, Carmela Caballero\textsuperscript{h}, Fatima Carneiro\textsuperscript{i}, Fernando Cassinello\textsuperscript{j}, Jan Willem Dekker\textsuperscript{k}, Roberto Delgado-Bolton\textsuperscript{l}, Karin Haustermans\textsuperscript{m}, Geoffrey Henning\textsuperscript{n}, Bettina Hutter\textsuperscript{o}, József Lövey\textsuperscript{p}, Irena Strnglová Netíková\textsuperscript{q}, Radka Obermannová\textsuperscript{r}, Simon Oberst\textsuperscript{s}, Siri Rostoft\textsuperscript{t}, Tiina Saarto\textsuperscript{u}, Thomas Seufferlein\textsuperscript{v}, Sapna Sheth\textsuperscript{w}, Venetia Wynter-Blyth\textsuperscript{x}, Alberto Costa\textsuperscript{y}, Peter Naredi\textsuperscript{z,*}
Overall Survival by Site and Period of Surgery

Fontana et al *Gastric Cancer* 2016
Thank you for your attention