Challenges in the surgical management of gastric cancer

William H. Allum, MD, FRCS
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

Any surgeon can cure

Surgeon-dependent

No surgeon can cure

EMR, endoscopic mucosal resection.
T1 Tumours

- Protruding
- Superficial Elevated
- Superficial Flat
- Superficial Ulcerated
- Excavated
Endoscopic Resection - Indications

- well differentiated adenocarcinoma
- no lymphatic or venous invasion
- intramucosal cancer regardless of size without ulceration
- intramucosal cancer <30mm with ulceration
- minute submucosal penetration (sm1) and <30mm
LN Metastasis from EGC

About 10% of EGC

3% of M cancer

20% of SM cancer

5% of SM has N2

Multiple sections of the primary tumour detect SM

Multiple sections of LN detects metastasis
Surgery For Early Gastric Cancer

- T1 m      D1 alpha (Stations 7 & 8)
- T1 sm     D1 beta (D1 alpha + station 9 & 11p)
- Function preserving gastrectomy
Surgery for Early Gastric Cancer

D1

D1+
Locally Advanced Gastric Cancer

- Mass
- Ulcerative
- Infiltrative, ulcerative
- Infiltrative, diffuse
Japanese Rules
End Results of Surgical Resection

Medical Research Council

D1 vs D2 Trial

Operative Mortality
D1 13%
D2 6.5%

## Dutch Gastric Cancer Trial Results

<table>
<thead>
<tr>
<th></th>
<th>D&lt;sub&gt;1&lt;/sub&gt;</th>
<th>D&lt;sub&gt;2&lt;/sub&gt;</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.
## Morbidity And Mortality

<table>
<thead>
<tr>
<th>Complication</th>
<th>Oesophagectomy (n = 1220)</th>
<th>(95% CI)</th>
<th>Gastrectomy (n = 747)</th>
<th>(95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-hospital mortality</td>
<td>2.9%</td>
<td>1.9 to 3.9</td>
<td>2.2%</td>
<td>1.3 to 3.6</td>
</tr>
<tr>
<td>30-day mortality</td>
<td>1.7%</td>
<td>1.0 to 2.5</td>
<td>1.1%</td>
<td>0.5 to 2.1</td>
</tr>
<tr>
<td>≥1 complication</td>
<td>29.7%</td>
<td>27.1 to 32.2</td>
<td>14.7%</td>
<td>12.3 to 17.5</td>
</tr>
<tr>
<td>Anastomotic leak</td>
<td>7.4%</td>
<td>5.9 to 8.9</td>
<td>4.4%</td>
<td>3.1 to 6.1</td>
</tr>
<tr>
<td>Re-operation rate</td>
<td>8.9%</td>
<td>7.2 to 10.5</td>
<td>8.1%</td>
<td>6.2 to 10.5</td>
</tr>
<tr>
<td>Length of stay, days (median; IQR)</td>
<td>13; 10</td>
<td>N/A</td>
<td>11;7</td>
<td>N/A</td>
</tr>
</tbody>
</table>

CI, confidence interval; IQR, interquartile range; N/A, not available.

Italian Gastric Cancer Study Group

Operative Mortality
D1  3%
D2  2.2%

No. at risk
D1  129  117  107  100  91  82  75  67  49
D2  131  121  104  94  88  79  64  56  46

<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>R0 (proximal, distal circumferential margins)</td>
<td>D2 &gt; 25 lymph nodes</td>
</tr>
<tr>
<td></td>
<td>5cm intestinal</td>
<td></td>
</tr>
<tr>
<td></td>
<td>8cm diffuse</td>
<td></td>
</tr>
<tr>
<td>UK</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</td>
<td>cT1 diffuse – resect</td>
<td>D2 – without pancreatectomy or splenectomy</td>
</tr>
<tr>
<td></td>
<td>R0</td>
<td></td>
</tr>
</tbody>
</table>

SIGN, Scottish Intercollegiate Guidelines Network; TNM, tumour node metastases.
The Royal Marsden

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
Lymphadenectomy by Extent of Resection

- D1
- D1+
- D2
JCOG 9502

Randomized trial in Siewert type II and III cancers

Left thoraco-abdominal approach versus abdominal transhiatal approach

JCOG, Japan Clinical Oncology Group.
JCOG 9502
Scheme

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

AT: Abdominal (n=82)
LT: Thoraco-abdominal (n=85)

D2 lymphadenectomy alone or with para-aortic nodal dissection for gastric cancer

JCOG 9501 Scheme

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

Intraoperative Randomisation

Group A (standard)
D2

Group B (Extended)
D2 + PAND

Observation

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

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

D2 (n=263)
D2 + PAND (n=259*)

3-year Survival: 76.4% 76.4%
5-year Survival: 69.2% 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.

Overall Survival in pN(+)

Proportion Surviving

D2 (n=184)
71.7%
65.2%

D2 + PAND (n=164)
63.4%
54.9%

HR=1.38 (1.01-1.88)
one-sided \( P=0.979 \)

pN(+), node-positive.
Overall Survival in pN(-)

pN(-), node-negative.
Conclusion of JCOG 9501

PAND can be safely performed in fit patients by specialist surgeons.

PAND should not be used for prophylactic lymph node dissection for curable advanced gastric cancer.

Further research is needed to understand the paradoxical observation that patients with less advanced tumours seem to benefit from PAND.

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

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 + ß (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.
ADVANCED DISEASE
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)
Patient Selection

Natural history
Comorbidity and its assessment
Quality of life
Patient wishes
1. Initial assessment
   - Assessment of underlying cancer
   - Pre-operative health & risk assessment
   - Dietetic assessment
   - Patient information & expectations
   - Stratification of risk

2. Pre-surgery assessment
   Detailed discussions of
   - Surgical procedure
   - Physio assessment
   - Dietetic assessment
   - Patient information & expectations
   - Immunonutrition

3. Formal Pre-assessment
   - Anaesthetic review
   - CPEX
   - Physiotherapy instruction
   - Dietetic advice to optimise nutritional status

4. Admission day before surgery
   - Immunonutrition (Oral Impact®)
   - Carbohydrate loading

5. Intraoperative (Intra-op)
   - Optimise fluid management
   - Epidural
   - JEJ

6. Clinical daily assessment to determine progress along the pathway according to the protocol

7. Outpatient 2 weeks
   - Surgical review
   - Dietitian review
   - Dietary advice
   - JEJ removed if not used

CPEX, cardiopulmonary exercise testing; ERAS, enhanced recovery after surgery; JEJ, jejunostomy; MDT, multidisciplinary team.
Conclusions

- Role of surgical specialisation
- Standard approaches for gastric resection and lymphadenectomy
- Minimally invasive surgery is investigational
- Importance of patient selection and perioperative care
Thank you for your attention