Surgical management of localized gastric cancer

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Multidisciplinary interactive session
Management of localized gastric cancer
Case Presentation

Chest CT-scan: no lung or mediastinal mets

Abdominal and pelvic CT-scan:
- No liver mets or peritoneal mets
- Thickening of the whole gastric wall without invasion of any surrounding local structures
- Multiple perigastric lymphonodes of 2 cm size, but no extraperigastric and paraortic lymph nodes.

A laparoscopy and an endoscopic ultrasonography were not considered

cT3 cN+ cM0
Case

- Questions
  - What is the most appropriate surgical treatment for this patient?
  - What is the most appropriate hospital to refer this patient to?
The role of Surgery for gastric cancer

Pean and Billroth
Advanced gastric cancer

Surgery

• Goal: R0 resection
• Options:
  • Limited lymphadenectomy
  • extended lymphadenectomy
  • super extended lymphadenectomy
Definition of lymphadenectomy

D1 nodes adjacent to the stomach
D2 + branches celiac axis
D3 nodes along the aorta

Station #10: in splenic hilus:
Difficult to remove without splenectomy
## Randomized trials on extent of lymph node dissection

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Comparing</th>
<th>Conclusion</th>
<th>Journal</th>
</tr>
</thead>
<tbody>
<tr>
<td>South Africa</td>
<td>43</td>
<td>R1/R2</td>
<td>R1</td>
<td>Br J Surg 1998;110-2</td>
</tr>
<tr>
<td>Hong Kong</td>
<td>55</td>
<td>R1/R3</td>
<td>R1</td>
<td>Ann Surg 1994;176-82</td>
</tr>
<tr>
<td>UK-MRC</td>
<td>400</td>
<td>D1/D2</td>
<td>D1</td>
<td>Lancet 1996;995-9</td>
</tr>
<tr>
<td>Dutch</td>
<td>996</td>
<td>D1/D2</td>
<td>D1</td>
<td>Lancet 1995;745-8</td>
</tr>
<tr>
<td>Taiwan</td>
<td>221</td>
<td>D1/D2,3</td>
<td>D2,3</td>
<td>Lancet Oncol 2006;309-15</td>
</tr>
<tr>
<td>Japan</td>
<td>520</td>
<td>D2, D2+PAND</td>
<td>D2</td>
<td>NEJM 2008;359:453-62</td>
</tr>
<tr>
<td>Italy</td>
<td>267</td>
<td>D1/D2</td>
<td>No difference in mortality</td>
<td>Br J Surg 2010; 97: 643–649</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>No survival data yet</td>
<td></td>
</tr>
</tbody>
</table>
Dutch Gastric Cancer Trial – 5-year follow-up

- 996 Patients
- D1 vs D2
- Mortality
  - D1: 4%
  - D2: 10%
- 5-Year Survival
  - D1: 45%
  - D2: 47%

Conclusion: D1 dissection recommended

Dutch Gastric Cancer Trial – 15-year follow-up

711 Patients with curative resection

15-Year OS
D1: 21%
D2: 29%
P = 0.34

Local recurrence
D1: 22%
D2: 12%

Regional recurrence
D1: 19%
D2: 13%

Songun, vd Velde et al, Lancet Oncology 2010
Dutch Gastric Cancer Trial – 15-year follow-up

711 Patients with curative resection

Conclusion

D2 dissection should be recommended as standard surgical approach in resectable gastric cancer

Death of Gastric Cancer
D1: 48%
D2: 37%
P=0.01

Death of Other Causes
HR=1.22
P=NS

Songun, vd Velde et al, Lancet Oncology 2010
Taiwanese trial

- 221 Patients: small trial
- D1 vs D2,3

5-Year Overall Survival
D1: 54%
D2,3: 60%

5-Year Recurrence Rate
D1: 51%
D2,3: 40%

Conclusion: in Asian population, extended lymphadenectomy brings improved survival

Wu et al., Lancet Oncology 2006
Japanese Trial

- 523 Patients
- D2 vs D2 + PAND

Morbidity
- D2: 20.9%
- D2 + PAND: 28.1%
  \[ P = 0.067 \]
Japanese Trial

- 5-Year overall survival
  - D2: 69%
  - D2 + PAND: 70%
  - \( P = 0.85 \)
- Conclusion: D2 + PAND should not be recommended

Sasako et al., NEJM 2008
Italian D1-D2 study

• 267 patients
• D1 vs D2 dissection in 5 specialized centers
• Only mortality data have been published

• Mortality
  • D1: 3.0%
  • D2: 2.2%

• Conclusion: D2-LND is safe in experienced centers
• Survival data to be awaited, but only 267 patients included
Lymphadenectomy in recent Western trials

• **Intergroup 0116 Trial:**
  - D2 recommended
    - D0: 54%
    - D1: 36%
    - D2: 10%

• **MAGIC Trial:**
  - Surgeons decided extent of lymphadenectomy
    - D1: 19%
    - D2: 40%

• **Majority of patients: limited lymph node dissection**

MacDonald, NEJM 2001, Cunningham, NEJM 2006
Lymphadenectomy in Japan

- Differentiation extent of lymphadenectomy
- Different recommendation for every combination of T-stage and N-stage

Table 5. Japanese guidelines for surgical treatment (curative intention) by stage

<table>
<thead>
<tr>
<th>T1 (M)</th>
<th>N0</th>
<th>N1</th>
<th>N2</th>
<th>N3</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>IA</td>
<td>IB</td>
<td>II</td>
<td>IV</td>
</tr>
<tr>
<td>A) ER (differentiated type, ≤2 cm, UL(-))</td>
<td>A) MGB (≤2 cm)</td>
<td>D2</td>
<td>D3</td>
<td></td>
</tr>
<tr>
<td>B) MGA (remainder)</td>
<td>B) D2 (&gt;2 cm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IA</td>
<td>IA</td>
<td>IB</td>
<td>II</td>
<td>IV</td>
</tr>
<tr>
<td>A) MGA (differentiated type, ≤1.5 cm)</td>
<td>A) MGB (≤2 cm)</td>
<td>D2</td>
<td>D3</td>
<td></td>
</tr>
<tr>
<td>B) MGB (remainder)</td>
<td>B) D2 (&gt;2 cm)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>T1 (SM)</td>
<td>T1</td>
<td>T1</td>
<td>T1</td>
<td>T1</td>
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<td>T2</td>
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<td>T4</td>
</tr>
</tbody>
</table>

ER, endoscopic resection; MGA, modified gastrectomy A; MGB, modified gastrectomy B; UL, with ulcerated lesion

Tanizawa, Gastric Cancer 2010
### D1 vs D2: Results without splenectomy

<table>
<thead>
<tr>
<th></th>
<th>D1</th>
<th>D2</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morbidity (%)</td>
<td>23</td>
<td>35</td>
<td>0.001</td>
</tr>
<tr>
<td>Mortality (%)</td>
<td>3.8</td>
<td>6.3</td>
<td>NS</td>
</tr>
<tr>
<td>Survival</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean (yrs)</td>
<td>5.77</td>
<td>6.67</td>
<td>0.018</td>
</tr>
<tr>
<td>5 year (%)</td>
<td>47</td>
<td>56</td>
<td></td>
</tr>
<tr>
<td>7 year (%)</td>
<td>42</td>
<td>52</td>
<td></td>
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<tr>
<td>11 year (%)</td>
<td>33</td>
<td>47</td>
<td></td>
</tr>
</tbody>
</table>
Role of Splenectomy: Italian study

- 618 Patients
- Randomized between
  - Total gastrectomy
  - Subtotal gastrectomy
- Multivariate analysis:
  - Splenectomy associated with worse survival

Splenectomy vs. preservation

- N = 207

- 5 years survival rate: 49% vs. 55%, p = 0.50

- Median no of lymph nodes dissected: 40 vs. 40, p = 0.96

- **Prophylactic splenectomy cannot be justified**
## Total vs Subtotal gastrectomy for distal gastric cancer

<table>
<thead>
<tr>
<th>Surgery</th>
<th>N</th>
<th>Mortality (%)</th>
<th>Morbidity (%)</th>
<th>5 year survival rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gouzi et al., Ann Surg 1989;\textsuperscript{209}:162-166</td>
<td></td>
<td></td>
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<tr>
<td>TG</td>
<td>93</td>
<td>3.2</td>
<td>32</td>
<td>48</td>
</tr>
<tr>
<td>SG</td>
<td>76</td>
<td>1.3</td>
<td>34</td>
<td>48</td>
</tr>
<tr>
<td>Bozetti et al., Ann Surg 1999;\textsuperscript{230}:170-180</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TG</td>
<td>303</td>
<td>2</td>
<td>13</td>
<td>62.4</td>
</tr>
<tr>
<td>SG</td>
<td>315</td>
<td>1</td>
<td>9</td>
<td>65.3</td>
</tr>
</tbody>
</table>
Conclusion on surgery

• D2 dissection should be recommended
  • No splenectomy or pancreatectomy
  • In experienced centers

• PAND does not improve survival any further
Surgical quality assurance
Hospital volumes

- 711 gastrectomies, 80 participating hospitals
- Average of 2.2 gastrectomies/hospital/year
  (registered in study)

Quality Assurance

- Instruction in operating room by Japanese surgeon
- ‘Supervising surgeons’ present with every D2 gastrectomy
- Book and video
- Teaching meetings for surgeons
The effect of improvement of surgical quality over the introduction of adjuvant therapy

Krijnen et al., EJSO 2009
Trials vs nationwide improvements

• Trials → improve outcomes by
  • Providing better treatment options
  • Training surgeons
• Most patients treated outside trials
  • → analyze outcomes on nationwide level
Centralization in the Netherlands

Esophagectomy  Gastrectomy

RED = High-volume surgery (>20/year)
- Esophagectomy: centralization effect
- Gastrectomy: decreasing number, no centralization

Dikken, vd Velde et al, EJC 2012
Outcomes esophagectomy vs gastrectomy

• 6-Month mortality:
  • Gastrectomy → non-significant decrease
  • Esophagectomy → significant decrease

• 3-Year survival:
  • Gastrectomy → no improvement
  • Esophagectomy → catch-up with gastric cancer

Dikken, vd Velde et al, EJC 2012
30-Day mortality in the Netherlands

Blue: esophagectomy ~ 4%
Green: gastrectomy ~ 8%

Higher mortality after gastrectomy for past 5 years

Dikken, vd Velde et al, EJC 2012
Conclusion

• Urgent need for improvement of gastric cancer care in the Netherlands
  • Centralization
  • Auditing
  • Use of multi-modality treatment
“Patients can often improve their chances of survival substantially, even at high volume hospitals, by selecting surgeons who perform the operations frequently”
Centralization: volume-outcome relation US

- 10 years after initial US paper
  - Decrease in postoperative mortality
  - Esophagectomy: completely due to centralization

Finks et al, NEJM 2012
## Centralization in Denmark

2003
- Gastric cancer surgery **restricted to 5 hospitals**
- Introduction national clinical guidelines
- Introduction nationwide database

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>No. of departments</td>
<td>37</td>
<td>5</td>
</tr>
<tr>
<td>No. of operations</td>
<td>537</td>
<td>416</td>
</tr>
<tr>
<td>Anastomotic leakages (%)</td>
<td>6.1</td>
<td>5.0</td>
</tr>
<tr>
<td>Hospital mortality (%)</td>
<td>8.2</td>
<td>2.4</td>
</tr>
</tbody>
</table>
Centralization in Denmark

Cases with at least 15 lymph nodes removed

2003: 19%
2008: 67%

Jensen et al, EJSO 2002
• Smaller studies: often no volume-outcome effect
• Larger studies: volume-outcome effect
Literature on Gastrectomies
Definition of ‘high volume’ in positive studies

- Definition of ‘high volume’ in most studies ~20/year
- But studies with higher volumes
Centralization: type of referral

Should centralization only be based on case volume?

Volume-based vs. Outcome-based referral

Gruen et al, CA Cancer J Clin 2009
Auditing

• Definition
  • “providers of care are monitored and their performance is benchmarked against their peers”

• Surgical Hawthorne effect

• Gastric cancer audits currently performed in several European Countries
  • United Kingdom
  • Denmark
  • Sweden
  • Netherlands
Effect of auditing
International comparison

• Compare national audits and cancer registries

• Esophageal and gastric resections 2004-2009
  • Netherlands: N = 5,791
  • Sweden: N = 653 (part of Sweden)
  • Denmark: N = 1,420
  • England: N = 12,000

• Goals
  • Compare differences between countries
  • Analyse possible volume-outcome relation
30-Day mortality

**Esophagectomies**

![Bar chart showing 30-day mortality for different countries in esophagectomies.](image)

- NL
- SW
- DK
- UK

**Gastrectomies**

![Bar chart showing 30-day mortality for different countries in gastrectomies.](image)

- NL
- SW
- DK
- UK

*P < 0.05 compared to UK

*P < 0.05 compared to NL

**Significant differences between countries**
Large differences in annual hospital volumes
- Denmark: centralization of esophagectomies and gastrectomies
Effect of hospital volume on 30-day mortality

**Esophagectomies**

- Lower 30-day mortality with increasing hospital volume
  - Esophagectomies: up to >40/jaar
  - Gastrectomies: up to >20/jaar
Conclusions

• Participating countries:
  • Considerable variation in hospital volumes and 30-day mortality

• Significant relation between volume and 30-day mortality
  • But not the only explanation for differences between countries

• Need for a uniform European Upper GI Cancer Registry: founded in Valencia sept 2012
### Possible purposes

<table>
<thead>
<tr>
<th>Possible purposes</th>
<th>Data required</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compare outcomes after surgery</td>
<td>Type of surgery, case-mix (comorbidity), complications, short-term mortality</td>
</tr>
<tr>
<td>Compare resection rates</td>
<td>All patients with a diagnosis of oesophagogastric cancer, type of surgery</td>
</tr>
<tr>
<td>Compare patterns of care</td>
<td>Type of surgery, chemotherapy, radiotherapy, etc.</td>
</tr>
<tr>
<td>Compare long term outcomes</td>
<td>Follow-up data, TNM stage</td>
</tr>
</tbody>
</table>
One European Cancer Audit

- Identify and spread Best Practice
- Research
- Outcome monitoring (feedback)
- Guidelines Development
Conclusion

• Nationwide improvements require nationwide interventions
  • Centralization
  • Auditing

‘The best care, for every cancer patient’
Multidisciplinary care: can we do better?