Gastric cancer: How strong can curative intent treatment be in the elderly?

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Gastric cancer: epidemiology

- Fourth most commonly diagnosed cancer worldwide
- Still the second most common cause of cancer-related death globally
- Global incidence rates
  - Almost 1,000,000 cases
  - Nearly 700,000 deaths

Gastrectomy and the Elderly

- More than 50% of the patients are diagnosed at the age of 65 or older.
  - > 500,000 pts/year worldwide
- More than 70% of deaths from gastric cancer occur at the age of 65 or older.
  - Approximately 500,000 deaths/year worldwide
# Gastric Cancer Characteristics in the Elderly

<table>
<thead>
<tr>
<th></th>
<th>Younger</th>
<th>Elderly (70 or older)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender ratio: M/F</td>
<td>1.6/1</td>
<td>2.45/1</td>
</tr>
<tr>
<td>Family History</td>
<td>Presence</td>
<td>Absence</td>
</tr>
<tr>
<td>Location</td>
<td>Proximal or GE junction</td>
<td>Lower or Distal Third</td>
</tr>
<tr>
<td>Synchronous Cancer</td>
<td></td>
<td>Increased frequency</td>
</tr>
<tr>
<td>Pattern metastasis</td>
<td>Peritoneum</td>
<td>Liver</td>
</tr>
</tbody>
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4-Cancer 1990;65:2086–90.
Surgery In the Elderly

• R0 resection is the only curable modality
  – The overall 5-year survival rate after curative resection in octogenarian patients varies between 44% to 65% while disease-specific 5-year survival rates vary from 53% to 62.5%.

Hepatogastroenterology 1998;45:268–75.
Surgical Risks and the Elderly

- Surgical risk, evaluated preoperatively with the ASA score, is higher in elderly
  - Higher rate of concomitant diseases.

- Total gastrectomy and D2 lymphadenectomy is less often performed in the elderly.
  - However 90-day postoperative mortality rate is not higher even in octogenarian patients with pre-existing comorbidities

Gastric Cancer 2007;10:39–44.
State of the art

- 5-year survival rates with surgery alone are below 25%
- Multimodal strategies result in 10–14% improvement of OS in stage II and III
- Surgical resection alone is no longer standard!

<table>
<thead>
<tr>
<th>Region</th>
<th>Procedure</th>
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<tbody>
<tr>
<td>Europe</td>
<td>D2 resection†</td>
</tr>
<tr>
<td></td>
<td>± perioperative chemotherapy</td>
</tr>
<tr>
<td>USA</td>
<td>D1 or D0 resection</td>
</tr>
<tr>
<td></td>
<td>± adjuvant chemoradiotherapy</td>
</tr>
<tr>
<td>Japan</td>
<td>D2 resection</td>
</tr>
<tr>
<td></td>
<td>± adjuvant chemotherapy</td>
</tr>
</tbody>
</table>
GASTRIC CANCER MAGIC CLINICAL TRIAL DESIGN

Gastric and Lower Third of the Esophagus

RANDOMIZE

CSC Arm
Preoperative ECF
Surgery
Postoperative ECF

S Arm
Surgery alone

Cunningham et al NEJM, 355, 12, 2006
MAGIC Trial

- **S arm (N=253)**
  - 95% proceed to surgery
- **CSC arm (N=250)**
  - 20% of patients at the perioperative chemotherapy arm were over 70 years old.
    - 88% completed preop CT
    - 55% began postop CT
    - 42% (104 pts) completed all 6 cycles
- **Postop complications (46%) and 30d mortality similar (6%) in both arms**
  - Median Duration of post-operative hospital stay = 30 days in both arms.

Cunningham et al NEJM, 355, 12, 2006
MAGIC SURVIVAL

MS: CSC 24 monts x S 20 Months
5 year survival: CSC 36% x C23%

Logrank p-value = 0.009
Hazard Ratio = 0.75 (95% CI 0.63 – 0.93)

Cunningham et al NEJM, 355, 12, 2006
Conclusions 1

- Perioperative chemotherapy + surgery improves survival compared to surgery alone.
  - 20% of patients at the perioperative chemotherapy arm were over 70 years old.
Surgery Followed by ChemoXRT
INT-0116

RESECTED
STAGE IB-IV (MO)
GASTRIC/GE JUNCTION
ADENOCARCINOMA

OBSERVATION

5FU/LV X2 4,500 cGy
RADIATION

5FU/LV

5FU/LV

(Macdonald, N Engl J Med, 2001)
## Adjuvant Trial: Intergroup 0116

### Patient Characteristics

<table>
<thead>
<tr>
<th>T stage</th>
<th>(556 pts)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T 1/2</td>
<td>31.1%</td>
</tr>
<tr>
<td>T 3/4</td>
<td>68.8%</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Nodal status</th>
<th></th>
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<tbody>
<tr>
<td>Negative</td>
<td>14.2%</td>
</tr>
<tr>
<td>Positive</td>
<td>85.7%</td>
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<table>
<thead>
<tr>
<th>Dissection</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>D0</td>
<td>54%</td>
</tr>
<tr>
<td>D1 (Removal all N1 Nodes)</td>
<td>36%</td>
</tr>
<tr>
<td>D≥2 perigastric, celiac, splenic or splenic-hilar, hepaticartery, and cardial lymph nodes,</td>
<td>10%</td>
</tr>
</tbody>
</table>

Overall Survival by Treatment Arm

3-yr survival difference: 40% vs 50%
Conclusion INT-0116

• Adjuvant chemoxrt improves survival after surgery compared to observation
  – Age as a potential covariate yielded no significant differences to the effects of treatment.

(Macdonald, N Engl J Med, 2001)
Adjuvant Chemotherapy
Adjuvant S1 Trial

1059 Gastric Ca pts
stage II and III
Gastrectomy + D2 dissection

RANDOMIZED

S1 x 1 year
Observation

Adjuvant S1 in Gastric Cancer

• S-1 adjuvant chemotherapy for 1 year led to improvement in overall and relapse-free survival chemotherapy and the trial was discontinued early.
  – 3-year overall survival: 80% vs 70% in the S-1 and surgery-only groups, respectively.

• Adjuvant S-1 after curative surgery has become a standard treatment in Japan.

Neo Adjuvant and Adjuvant Therapy

- Adjuvant chemoradiotherapy and perioperative or chemotherapy are recommended by the ESMO Guidelines in high-risk gastric cancer.

Gastric Cancer and the Elderly

Conclusions

• Age should not dictate the patients who should be submitted to curative treatment.
  – Performance status and organ function are paramount.

• T3 tumors or higher or N positive tumors that are not metastatic should be considered for surgery plus neo-adjuvant or adjuvant therapy
Strategies

- Surgery – Your hospital standard of total or partial gastrectomy with either D1 or D2 Ln dissection.

- Perioperative chemotherapy (Preferred)
  - Magic Trial (503 pts, 26% esophageal/GE Junction). – Positive

- Adjuvant
  - Chemotherapy alone (S1 trial)
  - Chemotherapy and chemoradiotherapy (intergroup 0016)
Thanks For Your Attention!