Issue #1: Premalignant Lesions

Gastric Cancer: Etiologic Factors

- H. Pylori
- diet (salt, nitrates)
- lifestyle (smoking, obesity)
- familial (~10% in West)
  - diet
  - hereditary
    - HNPCC
    - DGC
Lauren Classification of Histology

**Intestinal Type (60%)**
- grossly discrete mass
- precancerous cascade: gastritis → atrophy → intestinal metaplasia
- cohesive cells that form gland-like tubular structures
- well- or mod- diff’d adenoCa, papillary adenoCa
- incidence has declined
- H. Pylori, diet, smoking, HNPCC

**Diffuse Type (40%)**
- grossly diffuse (linnitis), microscopically multifocal
- no cell cohesion, cells infiltrate and thicken wall
- poorly diff’d signet-ring cell Ca, mucinous adenoCa
- incidence stable
- diet, smoking, obesity, HDGC
Issue #1: Premalignant Lesions

Intestinal Metaplasia

Poorly Differentiated Intestinal-Type Adenocarcinoma
Issue #1: Premalignant Lesions

Gastric Cancer Risk in Patients With Premalignant Gastric Lesions: A Nationwide Cohort Study in the Netherlands

De Vries et al., Gastroenterol 2008; 134:945
Issue #1: Premalignant Lesions

Gastric Cancer Risk in Patients With Premalignant Gastric Lesions: A Nationwide Cohort Study in the Netherlands

Figure 5. Progression rate of premalignant gastric lesions to gastric cancer in 92,250 patients with premalignant gastric lesions (90,780 censored patients).

De Vries et al., Gastroenterol 2008; 134:945
Issue #1: Premalignant Lesions

Epidemiological trends of pre-malignant gastric lesions: a long-term nationwide study in the Netherlands

De Vries et al., Gut 2007; 56:1665

Figure 2  The prevalence of atrophic gastritis, intestinal metaplasia and dysplasia (WSR) relative to total number of patients with a first gastric biopsy over time. AG: atrophic gastritis; DYS: dysplasia; IM: intestinal metaplasia; WSR: world standardised rate.
### Issue #1: Premalignant Lesions

#### The management of gastric polyps

<table>
<thead>
<tr>
<th>Polyp type</th>
<th>Usual number and size</th>
<th>Usual site</th>
<th>Malignant potential of polyp</th>
<th>Malignant potential of background mucosa</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sporadic fundic gland polyp</td>
<td>Multiple 1–5 mm</td>
<td>Upper and lower body</td>
<td>Very low</td>
<td>Very low</td>
<td>Biopsy to confirm nature of polyp</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>No follow-up needed</td>
</tr>
<tr>
<td>Familial adenomatous polyposis-associated fundic gland polyp</td>
<td>Multiple ‘carpet’ &lt;1 cm</td>
<td>Upper and lower body</td>
<td>Low</td>
<td>Low</td>
<td>Biopsy to confirm nature of polyp</td>
</tr>
<tr>
<td>Hyperplastic</td>
<td>Single 1–2 cm</td>
<td>Antrum</td>
<td>Low but significant</td>
<td>Low</td>
<td>Repeat OGD every 2 years</td>
</tr>
<tr>
<td></td>
<td>Multiple &lt;1 cm</td>
<td>Lower body</td>
<td>Low but significant</td>
<td>Low</td>
<td>Remove polyp if dysplastic</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Eradicate <em>H pylori</em></td>
</tr>
<tr>
<td>Adenoma</td>
<td>Single 1–2 cm</td>
<td>Antrum</td>
<td>High</td>
<td>Significant</td>
<td>Repeat OGD 1 year</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Eradicate <em>H pylori</em></td>
</tr>
<tr>
<td>Inflammatory fibroid polyp</td>
<td>Single 1–5 cm</td>
<td>Antrum</td>
<td>Very low</td>
<td>Very low</td>
<td>Biopsy to confirm nature of polyp</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Remove if causing obstruction</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>No follow-up</td>
</tr>
</tbody>
</table>

Andrew F Goddard, Rawya Badreldin, D Mark Pritchard, et al.

British Society of Gastroenterology  *Gut* 2010;59:1270–1276
The management of gastric polyps

Gastric Polyp(s)

Forceps biopsy of polyp(s) and surrounding mucosa if suspicion of non-FGP

Adenoma

Hyperplastic polyp

With dysplasia or symptoms

Eradicate H. pylori if present

Repeat endoscopy at 1 year

Polyp persists

No polyp

Polypectomy if safe to do so

Follow up endoscopy in one year

Fundic gland polyp or inflammatory fibroid polyp

Consider FAP. Consider polypectomy if symptomatic

No follow-up

Andrew F Goddard, Rawya Badreldin, D Mark Pritchard, et al.

British Society of Gastroenterology

Gut 2010;59:1270–1276
## Issue #1: Premalignant Lesions

### The management of gastric polyps

**Table 1** Management of gastric polyps associated with polyposis syndromes

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Lifetime risk of malignancy</th>
<th>Surveillance recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Familial adenomatous polyposis</td>
<td>100% (colon)</td>
<td>OGD every 2 years after age 18</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Biopsy &gt;5 polyps</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Remove polyps &gt;1 cm</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Surveillance also required for duodenal polyps</td>
</tr>
<tr>
<td>Peutz–Jeghers’</td>
<td>&gt;50% (extra-GI)</td>
<td>OGD every 2 years after age 18</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Biopsy &gt;5 polyps</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Remove polyps &gt;1 cm</td>
</tr>
<tr>
<td>Juvenile polyposis</td>
<td>&gt;50%</td>
<td>OGD every 3 years after age 18</td>
</tr>
<tr>
<td>Cowden’s</td>
<td>Rare</td>
<td>Eradicate <em>H pylori</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td>No further OGD needed</td>
</tr>
</tbody>
</table>

There is very little evidence for the following recommendations, but given the high risk of malignancy in these conditions careful surveillance is necessary.

GI, gastro-intestinal; OGD, gastroscopy.

Andrew F Goddard, Rawya Badreldin, D Mark Pritchard, et al.  

British Society of Gastroenterology  

*Gut* 2010;**59**:1270–1276
Issue #2: Early Gastric Cancer

LN Involvement depends on T Stage

Lymph nodes positive (%)
Early Gastric Cancer (EGC)

- mucosal or submucosal invasion
- ~50% of GC in Japan, 26% in Taiwan, <10% in West
- size, depth, LVI predict LN mets
- LN mets predict recurrence, DSS

Role for endoscopic mucosal resection (EMR), endoscopic submucosal dissection (ESD) or laparoscopic resection in well-defined cases
Early Gastric Cancer (EGC)

Well diff’d
< 20 mm (elevated)
< 10 mm (depressed)
Not with peptic ulcer

Fig. 1 Overall recurrence-free rate curves in endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) groups. The overall recurrence-free rate was significantly lower in the EMR group than in the ESD group (P < 0.001).

Nakamoto et al., Endoscopy 2009; 41:746
Fig. 4  Curative resection rates with EMR and ESD, according to subgroup meta-analysis for different sites in the gastrointestinal tract.

Cao et al., Endoscopy 2009; 41:751
Early Gastric Cancer (EGC)

n= 1294 EGC Japanese patients
16 centres
1994-2003
Laparoscopic gastrectomy
5 yr DFS >95%

FIGURE 2. The disease-free survival rate according to operation. The 5-year disease-free survival rate was 99.4% for LADG, 98.7% for LAPG, and 93.2% for LATG.

Kitano et al., Ann Surg 2007, 245:68
Issue #3: Hereditary DGC

HDGC Criteria

I. 2 or more path documented cases of DGC in 1st- or 2nd-degree relatives, with at least one Dx’d before age 50

II. 3 or more path documented cases of DGC in 1st- or 2nd-degree relatives, of any age

* ~30% of such families have a truncating mutation in CDH1
E-cadherin (CDH1) Mutations and HDGC

- Tumour suppressor gene
- Chromosome 16q22.1
- 1998 – 3 Maori families with DGC
- Germline truncating mutations
- Lifetime GC risk ~70% (AD, high pen)
- Lifetime lobular breast Ca risk ~40%

**E-cadherin (CDH1) Mutations and HDGC**

Normal endoscopy + random Bx
Normal chromoendoscopy + random Bx
Normal EUS, CT, PET

6/6 had multiple foci of T1 cancer

---

**FIGURE 1.** Family pedigree showing autosomal dominant inheritance of gastric cancer (GC). Individual mutation testing results for the codon 1003 CDH1 mutation are indicated by a + or −. Individuals affected with GC are shaded. The 6 who underwent prophylactic gastrectomy on the current study are numbered 1 to 6. Five other individuals who have had prophylactic gastrectomies are labeled a to e. Individual c had the procedure prior to the availability of genetic testing but was ultimately found not to have inherited a CDH1 mutation.

E-cadherin (CDH1) Mutations and HDGC

Recommendation: TG in CDH1 mutation carriers @ 5 yrs younger than youngest family member at GC presentation

**Table 4. Criteria for CDH1 mutation testing modified to reflect current data**

<table>
<thead>
<tr>
<th>Modified testing criteria</th>
<th>Potential additional criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Family with two or more cases of gastric cancer, with at least one DGC diagnosed before the age of 50. (&gt;30%) *&lt;br&gt;2. Family with multiple LBC with or without DGC in first-degree relatives (unknown) *&lt;br&gt;3. Isolated individual diagnosed with DGC at &lt;35 y from a low-incidence population (&gt;10%) *&lt;br&gt;4. Isolated personal history of both DGC and LBC (unknown) *</td>
<td>5. Family with three or more cases of gastric cancer diagnosed at any age one or more of which is a documented case of DGC; no other criteria met (such families are extremely rare)&lt;br&gt;6. Family with one or more cases of both DGC and signet ring colon cancer (this association is unproven)</td>
</tr>
</tbody>
</table>

* Percentage of expected positive results.
Surveillance by Chromoendoscopy in HDG

Shaw, Blair et al., Gut 2005, 54: 461
Surveillance by Chromoendoscopy in HDG

Shaw, Blair et al., Gut 2005, 54: 461

Figure 3  Outcome of 99 chromoendoscopies: five years’ annual surveillance in 33 E-cadherin mutation carriers.
Decision-Making and Impact of Prophylactic Gastrectomy in Individuals with Hereditary Diffuse Gastric Cancer Syndrome

Muir, Aronosn, Swallow, Esplen. Department of Surgery and Psychiatry, University of Toronto

Study population:
- English-speaking patients with known CDH-1 mutation considering prophylactic gastrectomy at Mt. Sinai Hospital
- current N = 7, expected N = approx 20

First study to examine the health-related quality of life and psychological impact of surgery in this patient population

Questionnaires assessing:
- quality of life (EORTC QLQ 30 & EORTC STO 22)
- body image
- regret
- decisional conflict
- psychological wellbeing (BSI: brief symptom inventory)
- satisfaction with hospital services
- interest in support resources
- current health, diet, medications

Questionnaires distributed to patients at 5 time points:
- 1 month pre-op
- 2-4 weeks post-op
- 6 months post-op
- 1 year post-op
- 2 years post-op

Goal: Improved understanding of unique patient needs allowing tailoring of services to provide optimum care & decision-making support
Issue #4: Quality of Resection

Outcomes of Resection for Gastric Cancer

% alive at 5 years

North America: 7%
Japan: 2%

1993
The Question of Quality: What is the Secret of Japan?

- younger, less CV disease
- less obese
- stage migration 2° to better N staging
- TECHNIQUE
1997 AJCC, 5th Ed.

N0- No regional LN metastases

N1- Metastasis in 1-6 regional LN

N2- Metastasis in 7-15 regional LN

N3- Metastasis in > 15 regional LN

“…it is suggested that at least 15 regional nodes be assessed…”
Significant Regional Variation in Staging and Survival of Gastric Cancer-An Analysis of the SEER Database

Natalie G. Coburn, MD, MPH
Carol J. Swallow, MD, PhD
Calvin Law, MD, MPH

ASCO, 2005
Defining the Study Population

SEER 1973-2001
Other Digestive Cancer
N = 216,830

Gastric Malignancy
N = 58,371

Adenocarcinoma Only
N=49,218

Gastric Surgery
(Excludes wedge, bx, endoscopy)
N=12,990

1988-2001
N=24,651

Age 18+
N = 49,208

Invasive Disease
N = 12,902

Lymph Node Assessment Done
N = 11,713

Non-M1
N = 10,129

Final Study Population
N = 10,129
Overall Results

- 10,129 cases
- Male: 64%
- Age
  - Median: 70 years
  - Mean: 68.3 ± 12.5 years
- Median # of LN assessed: 9
- Overall percentage of patients with Adequate LN assessment = 28.6%
  - Improved to 32.7% 1998-2001 (p<0.05)
Adequate LN Assessment - SEER Database

Minimum # LN recommended by AJCC, 1997: 15
Median # LN evaluated, since 1997: 10

Adequate LN Assessment - by SEER Region

![Bar chart showing % ALNA by SEER Region. The chart indicates that SEER Region 1 has a significantly higher ALNA compared to other regions. The Reference Group is indicated by an asterisk.]
Factors Predictive of Survival - SEER Region

Survival Functions

P<0.001

Region 1

Region 9
How can we improve?

Mount Sinai Hospital, Toronto

Trends in Adequacy of LN Assessment

Gupta, Haddad, Bacani, O’Brien, Pollett, Gallinger, Swallow, CSSO 2005
Extent of LND reported by Ontario general surgeons

Helyer, Coburn, O'Brien, Swallow, ASCO 2006
Helyer et al, Gastric Cancer 2007: 10 (4): pp 205-14
The Question of Quality:
What do Ontario surgeons strive for?

- n=206 who perform gastric surgery
- # nodes desired
  - mean = 11
  - median = 10 (2-30)

Helyer, Coburn, O’Brien, Swallow, ASCO 2006
Helyer et al, Gastric Cancer 2007: 10 (4): pp 205-14
Improving gastric cancer survival: Development and measurement of quality indicators using the RAND/UCLA Appropriateness Method and population-based data analysis

(Coburn et al., Toronto Gastric Cancer Study Group)

1) Extensive literature review

2) Expert Panel
   a) paper questionnaire regarding appropriateness (2009)
   b) panel meets in Toronto to discuss disagreements (2010)

3) Provincial chart review of 2000 cases to determine how often 'appropriate' care was given, and did this affect outcome?
Laparoscopic vs Open Gastrectomy: RCT

% with complication

Mortality

LAP, n=30
OPEN, n=29

Morbidity

STG for distal cancer

Laparoscopic vs Open Gastrectomy: RCT

STG for distal cancer

Laparoscopic vs Open Gastrectomy: RCT


STG for distal cancer

% alive at 5 years

OS

DFS
## Laparoscopic vs Open Gastrectomy: Meta-analysis of 4 RCTs

STG for distal cancer

### Mean of lymph nodes harvested (standard deviation)

<table>
<thead>
<tr>
<th>Authors</th>
<th>Pt</th>
<th>LADG</th>
<th>Pt</th>
<th>ODG</th>
<th>MD (95% c.i.)</th>
<th>weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kitano et al</td>
<td>14</td>
<td>20.2(3.6)</td>
<td>14</td>
<td>24.9 (3.5)</td>
<td>-4.7(-7.33, -2.07)</td>
<td>0.78</td>
</tr>
<tr>
<td>Lee et al</td>
<td>24</td>
<td>31.8(13.5)</td>
<td>23</td>
<td>38.1(15.9)</td>
<td>-6.3(-14.75,2.15)</td>
<td>0.08</td>
</tr>
<tr>
<td>Hayashi et al</td>
<td>14</td>
<td>28(14)</td>
<td>14</td>
<td>27(10)</td>
<td>1(-8.01,10.01)</td>
<td>0.07</td>
</tr>
<tr>
<td>Huscher et al</td>
<td>30</td>
<td>30(14.9)</td>
<td>29</td>
<td>33.4(17.4)</td>
<td>-3.4(-11.68,4.88)</td>
<td>0.08</td>
</tr>
<tr>
<td><strong>Pooled</strong></td>
<td>82</td>
<td>28.51(171.11)</td>
<td>80</td>
<td>32.14 (203.93)</td>
<td>-4.3(-6.66, -2.02)*</td>
<td>1</td>
</tr>
</tbody>
</table>

Memon et al., Surgical Endoscopy 2008, 22:1781
Issue #5: Management of Advanced GC

“Palliative” Gastrectomy

- Conventional wisdom: better quality of life with resection
- Institutional series: longer survival in patients who underwent resection vs. those who did not

**NB**: alternative modalities of palliation
• 211 consecutive patients with gastric adenocarcinoma, 2001-2004, Leeds, UK
• 208 had CT; 57 had laparoscopy
• 67 synchronous M1 disease; 45 on CT, 16 at laparoscopy, 6 other
• 63 treated nonoperatively; info avail on 55

Figure 2. Palliative interventions for symptoms related to an unresected primary tumor in patients with M1 gastric adenocarcinoma.

Sarela et al., Arch Surg 2007; 142:143-9
Noncurative gastrectomy was associated with:
mortality of 6%,
morbidity of 50% benefit in <50%
(Miner et al, JACS 2004; 198:1013)

Figure 3. Kaplan-Meier analysis of survival for 55 patients with synchronously metastatic adenocarcinoma of the stomach or gastroesophageal junction and an unresected primary tumor (median survival, 7 months; 1-year actuarial survival, 35%).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Category</th>
<th>1-Year Survival, %</th>
<th>Median Survival, mo</th>
<th>Univariate Analysis</th>
<th>Multivariate Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>1.0 (0.9-1.0)</td>
<td>NA</td>
</tr>
<tr>
<td>ECOG FPS</td>
<td>0 or 1 vs 2 or 3</td>
<td>46 vs 11</td>
<td>9 vs 2</td>
<td>2.8 (1.5-5.4)</td>
<td>0.7 (0.3-1.8)</td>
</tr>
<tr>
<td>Histologic grade</td>
<td>Other vs poor</td>
<td>48 vs 26</td>
<td>9 vs 4</td>
<td>2.0 (1.0-3.9)</td>
<td>1.2 (0.6-2.4)</td>
</tr>
<tr>
<td>Pattern of metastasis</td>
<td>Nonperitoneal vs peritoneal</td>
<td>58 vs 28</td>
<td>16 vs 4</td>
<td>3.1 (1.2-8.0)</td>
<td>2.3 (0.9-6.3)</td>
</tr>
<tr>
<td>Stomach-related intervention</td>
<td>No vs yes</td>
<td>49 vs 30</td>
<td>9 vs 4</td>
<td>0.9 (0.5-1.8)</td>
<td>NA</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>Yes vs no</td>
<td>52 vs 0</td>
<td>13 vs 1</td>
<td>15.7 (6.5-38.0)</td>
<td>15.6 (6.5-38.0)</td>
</tr>
</tbody>
</table>

Sarela et al., Arch Surg 2007; 142:143-9
• ≈1/3 known to have cancer prior to presentation with perf
• ≈50% in antrum
• ≈50% have obvious distant mets at laparotomy

Perf’d Gastric Ulcers: Words to the Wise

- ≈ 10% grossly c/w benign were malignant on final path
- just think about it
- biopsy
- Follow-up endoscopy!

So et al., Br J Surg 2000; 87:1702.
Kasakura et al., Am Surg 2002; 68:434
Gertsch et al., Arch Surg 1995; 130:177.
Now, Later or Never?

The Surgeon’s Dilemma

- diagnosis unproven
- stage unknown
- survival from perf/peritonitis uncertain
- delayed relap (2 stage): adhesions, delay
Gastrectomy for Perf’d Gastric Cancer: Mortality and Morbidity

Management of perforated gastric carcinoma: A report of 16 cases and review... Yuichi Kasakra; Jaffer A Ajani; Masashi Fujii; Fumiro Mochizuki; Tadatoshi T...
The American Surgeon; May 2002; 68, 5; Research Library pg. 434

Review of Japanese literature of perf’d GC

- Total n=128
- R0 n=62
- 5 yr OS R0 74%
- 5 yr OS R1/R2 7.5%

Adachi et al. 1997
Perforated Gastric Ulcers: Is there a “standard” management?

**Historical Perspective**

- **pre 1950s** - Oversew/Patch/Excise ± V&P
  - High postop M&M
  - High recurrence rate

- **1950s to 1980s** - RESECT
  - 20% mortality
  - Functional sequelae

- **present** - Oversew/Patch/Excise
Quality in Management of Gastric Cancer

Summary

Goals in the resection of localized disease

- R0 resection
- accurate staging
- STG > TG
- D1+ dissection
- consider adjuvant treatment stage 1B – IV, M0

Goals in the treatment of incurable disease

- symptom control
- strongly consider non-operative approaches
THE HOT QUESTION OF TODAY:
What is the role of postoperative adjuvant chemoradiation with D2 dissection?

Korean Protocol: D2

- 5 cycles 5-FU and leucovorin
- 45 Gy RT concurrent from 2nd cycle
- n=291, median f/u 48 mos.
- in-field recurrence rate= 16% (1/3 of all recurrences)   Br J Cancer 2004; 91: 11
Gastric Cancer in Canada

New Cases and Deaths, 2008

![Graph showing new cases and deaths of gastric cancer in Canada, 2008.]

Epidemiology

Stomach cancer was the fourth most common malignancy in the world in 2000, with an estimated 870,000 new cases and 650,000 deaths per year. [1] Approximately 90% of stomach cancers occur in the distal stomach, and most cases are adenocarcinomas. The risk factors for stomach cancer include a family history of the disease, a high intake of salt, and a diet high in processed meat and smoked fish. In addition, chronic atrophic gastritis and a history of Helicobacter pylori infection are also associated with an increased risk of stomach cancer.

Summary

Gastric cancer is the third most common cancer worldwide, with higher incidence rates in Eastern Asia and South Eastern Europe. Advanced disease at the time of diagnosis is the main cause of death. Early detection and treatment are crucial in improving survival rates.

Etiology

The main etiologic factors for stomach cancer include a high intake of salt, a diet high in processed meats, and a history of chronic atrophic gastritis. Other factors include a history of Helicobacter pylori infection, cigarette smoking, and a family history of stomach cancer.

Prevention

Reducing the intake of salt, processed meats, and smoking can help in reducing the risk of stomach cancer. Early detection through regular gastroscopy and endoscopic biopsy can improve survival rates.
Gastric Cancer
Trends in Incidence and Mortality

Cancer 1998; 83:2049-53
U.S.A. figures from SEER

Susan S. Devesa, m.d.¹
William J. Blot, m.d.²
Joseph F. Fraumeni, Jr., m.d.¹

¹ Division of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, Maryland.
² International Epidemiology Institute, Rockville, Maryland.
GE Junction Cancers

- Increasingly common in North America
- Extensive preop staging required (including PET)
- Consider preop chemo ±RT (T3/T4)
- Tailored procedure based on level and T stage
Siewert Classification of GE Junction Cancers

- **Type I:** adenocarcinoma of the distal esophagus, which usually arises from an area with specialized intestinal metaplasia of the esophagus (i.e., Barrett esophagus) and may infiltrate the esophagogastric junction from above;
- **Type II:** true carcinoma of the cardia arising immediately at the esophagogastric junction;
- **Type III:** subcardial gastric carcinoma that infiltrates the esophagogastric junction and distal esophagus from below.

*Figure 2.* The 10-year survival rates of patients with R0-resected (no residual macroscopic or microscopic tumor) adenocarcinoma of the distal esophagus (type I tumors), true carcinoma of the cardia (type II tumors), and subcardial gastric cancer infiltrating the esophagogastric junction (type III tumors). Type I vs. type III, $P < .01$; type II vs. type III, $P < .05$; type I vs. type II, not significant.
GE Junction Cancers

Incidence of Lower Mediastinal Nodal Involvement

N = 50 specimens
N = 1730 nodes

Honi et al., Hepatogastroenterology 2002; 49: 419
GE Junction Cancers

- **Type I:** adenocarcinoma of the distal esophagus, which usually arises from an area with specialized intestinal metaplasia of the esophagus (i.e., Barrett esophagus) and may infiltrate the esophagogastric junction from above;
- **Type II:** true carcinoma of the cardia arising immediately at the esophagogastric junction;
- **Type III:** subcardial gastric carcinoma that infiltrates the esophagogastric junction and distal esophagus from below.

<table>
<thead>
<tr>
<th>Level</th>
<th>In Germany</th>
<th>In Japan</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Transmed esophagectomy, Lower med LND, celiac axis LND</td>
<td>Upper med LND, resection of cardia and lower esophagus, D2</td>
</tr>
<tr>
<td>II, T1</td>
<td>Extended TG + transhiatal resection distal esophagus, D2</td>
<td>resection of cardia and lower esophagus, D2</td>
</tr>
<tr>
<td>II, T2,3,4</td>
<td>Extended TG + transhiatal resection distal esophagus, D2</td>
<td>Extended TG, D2</td>
</tr>
<tr>
<td>III</td>
<td>Extended TG + transhiatal resection distal esophagus, D2</td>
<td>Extended TG, D2</td>
</tr>
</tbody>
</table>
Table 3. Phase III trials of chemotherapy and surgery for resectable esophageal and gastric carcinomas including gastroesophageal junction cancers

<table>
<thead>
<tr>
<th>Trial</th>
<th>N</th>
<th>Site</th>
<th>Histology</th>
<th>GEJ</th>
<th>CT regimen</th>
<th>Curative resection</th>
<th>OS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>S</td>
<td>CS</td>
</tr>
<tr>
<td>Intergroup O113\textsuperscript{22}</td>
<td>440</td>
<td>E</td>
<td>SCC 46% ADC 54%</td>
<td>NR</td>
<td>CF: preop × 3, postop × 2</td>
<td>59%</td>
<td>62%</td>
</tr>
<tr>
<td>MRC\textsuperscript{23,24}</td>
<td>802</td>
<td>E</td>
<td>SCC 31% ADC 66%</td>
<td>10%*</td>
<td>CF: preop × 2</td>
<td>54%</td>
<td></td>
</tr>
<tr>
<td>FFCD 9703\textsuperscript{25}</td>
<td>224</td>
<td>E/G</td>
<td>ADC 100%</td>
<td>64%*</td>
<td>CF: preop × 2-3</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>MAGIC\textsuperscript{28}</td>
<td>503</td>
<td>G</td>
<td>ADC 100%</td>
<td>12%</td>
<td>ECF: preop × 3, postop × 3</td>
<td>66%</td>
<td>69%</td>
</tr>
</tbody>
</table>