Stomach (Gastric) Cancer

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ACDT & RC Bathinda
Gastric Cancer

Role of Radiation
WORKUP

- H&P
- Upper GI endoscopy and biopsy
- Chest/abdominal CT with oral and IV contrast
- Pelvic CT as clinically indicated
- PET-CT evaluation if no evidence of M1 disease
- CBC and chemistry profile
- Endoscopic ultrasound (EUS) if no evidence of M1 disease (preferred).
- Endoscopic mucosal resection (EMR) may contribute to accurate staging of early stage cancers
- Nutritional assessment and counseling
- Biopsy of metastatic disease as clinically indicated
- HER2-neu testing if metastatic adenocarcinoma is documented/suspected
- Smoking cessation advice, counseling and pharmacotherapy
Layers of the Stomach

- **Mucosa**
- **Submucosa**
- **Muscularis**
- **Serosa**
Stomach and Regional Lymph Nodes
Gastric cancer lymph node stations. Lymph node stations surrounding the stomach: 1, right cardial nodes; 2, left cardial nodes; 3, nodes along the lesser curvature; 4, nodes along the greater curvature; 5, suprapyloric nodes; 6, infrapyloric nodes; 7, nodes along the left gastric artery; 8, nodes along the common hepatic artery; 9, nodes around the celiac axis; 10, nodes at the splenic hilus; 11, nodes along the splenic artery; 12, nodes in the hepatoduodenal ligament; 13, nodes at the posterior aspect of the pancreas head; 14, nodes at the root of the mesentery; 15, nodes in the mesocolon of the transverse colon; 16, para-aortic nodes.
T (tumor) Stage

**Primary Tumor (T)**

TX  Primary tumor cannot be assessed
T0  No evidence of primary tumor
Tis  Carcinoma in situ: intraepithelial tumor without invasion of the lamina propria
T1  Tumor invades lamina propria, muscularis mucosae or submucosa
T1a Tumor invades lamina propria or muscularis mucosae
T1b Tumor invades submucosa
T2  Tumor invades muscularis propria*
T3  Tumor penetrates subserosal connective tissue without invasion of visceral peritoneum or adjacent structures**,***
T4  Tumor invades serosa (visceral peritoneum) or adjacent structures**,***
T4a Tumor invades serosa (visceral peritoneum)
T4b Tumor invades adjacent structures
Regional Lymph Nodes (N)
NX  Regional lymph node(s) cannot be assessed
N0  No regional lymph node metastasis§
N1  Metastasis in 1 - 2 regional lymph nodes
N2  Metastasis in 3 - 6 regional lymph nodes
N3  Metastasis in seven or more regional lymph nodes
N3a Metastasis in 7 - 15 regional lymph nodes
N3b Metastasis in 16 or more regional lymph nodes
## TNM Stage

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0</td>
<td>Tis</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IA</td>
<td>T1</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IB</td>
<td>T2</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T1</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIA</td>
<td>T3</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T1</td>
<td>N2</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIB</td>
<td>T4a</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>N2</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T1</td>
<td>N3</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIIA</td>
<td>T4a</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>N2</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>N3</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIIB</td>
<td>T4b</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T4b</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T4a</td>
<td>N2</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>N3</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIIC</td>
<td>T4b</td>
<td>N2</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T4b</td>
<td>N3</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T4a</td>
<td>N3</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IV</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
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# 5 Year Survival by Stage

<table>
<thead>
<tr>
<th>Stage</th>
<th>Survival Rate</th>
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<tbody>
<tr>
<td>IA</td>
<td>70.8%</td>
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<tr>
<td>IB</td>
<td>57.4%</td>
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<tr>
<td>IIA</td>
<td>45.5%</td>
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<tr>
<td>IIB</td>
<td>32.8%</td>
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<tr>
<td>IIIA</td>
<td>19.8%</td>
</tr>
<tr>
<td>IIIB</td>
<td>14.0%</td>
</tr>
<tr>
<td>IIIC</td>
<td>9.2%</td>
</tr>
<tr>
<td>IV</td>
<td>4.0%</td>
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</table>
Primary Treatment of Gastric Cancer is Surgery

Resectable tumors
- Tis or T1 tumors limited to mucosa (T1a) may be candidates for endoscopic mucosal resection (in experienced centers)
- T1b-T3: Adequate gastric resection to achieve negative microscopic margins (typically ≥ 4 cm from gross tumor).
  - Distal gastrectomy
  - Subtotal gastrectomy
  - Total gastrectomy
- T4 tumors require en bloc resection of involved structures
Operable gastric cancer-Treatment options

- NACT → Surgery → Adjuvant chemo
- Surgery → adjuvant Chemo-RT
Role for radiation in the treatment of gastric cancer

Conventional radiation

IMRT radiation
High risk of a local relapse after surgery

Patterns of failure after “curative” resection of gastric cancer

<table>
<thead>
<tr>
<th>Pattern of failure</th>
<th>Clinical (3)</th>
<th>Reoperation (2)*</th>
<th>Autopsy 4, 5, 33, 34, 35</th>
</tr>
</thead>
<tbody>
<tr>
<td>Locoregional</td>
<td>38</td>
<td>67</td>
<td>80–93</td>
</tr>
<tr>
<td>Peritoneal seeding</td>
<td>23</td>
<td>41</td>
<td>30–50</td>
</tr>
<tr>
<td>Localized</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diffuse</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distant metastases</td>
<td>52</td>
<td>22</td>
<td>49</td>
</tr>
</tbody>
</table>
Site of a local relapse after surgery

<table>
<thead>
<tr>
<th>Failure area</th>
<th>Incidence (%)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Clinical*</td>
<td>Reoperation†</td>
<td>Autopsy‡</td>
</tr>
<tr>
<td>Gastric bed</td>
<td>21</td>
<td>54</td>
<td>52–68</td>
</tr>
<tr>
<td>Anastomosis or stumps</td>
<td>25</td>
<td>26</td>
<td>54–60</td>
</tr>
<tr>
<td>Abdominal or stab wound</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymph node(s)</td>
<td>8</td>
<td>42</td>
<td>52</td>
</tr>
</tbody>
</table>
Post Operative or PreOp Radiation for Gastric Cancer

Local relapse (PostOp Trial, British Stomach Cancer Group, Lancet. 1994 May 28;343(8909):1309-12)

- surgery alone (27%)
- surgery plus radiation (10%)
- surgery plus chemotherapy (19%)


- surgery alone (20%)
- radiation then surgery (30%)
US-Intergroup trial design

- Phase III trial – 2 arms (T3, T4, N+)
  - Arm: surgery
  - Arm2: surgery + adjuvant chemo RT

Median OS: 36m vs. 26m
### TABLE 3. MAJOR TOXIC EFFECTS OF CHEMORADIOThERAPY.*

<table>
<thead>
<tr>
<th>TYPE OF TOXIC EFFECT</th>
<th>NO. OF PATIENTS (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hematologic</td>
<td>148 (54)</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>89 (33)</td>
</tr>
<tr>
<td>Influenza-like</td>
<td>25 (9)</td>
</tr>
<tr>
<td>Infection</td>
<td>16 (6)</td>
</tr>
<tr>
<td>Neurologic</td>
<td>12 (4)</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>11 (4)</td>
</tr>
<tr>
<td>Pain</td>
<td>9 (3)</td>
</tr>
<tr>
<td>Metabolic</td>
<td>5 (2)</td>
</tr>
<tr>
<td>Hepatic</td>
<td>4 (1)</td>
</tr>
<tr>
<td>Lung-related</td>
<td>3 (1)</td>
</tr>
<tr>
<td>Death†</td>
<td>3 (1)</td>
</tr>
</tbody>
</table>

*Major toxic effects were defined as those of grade 3 or higher. Data are for the 273 patients who received chemoradiotherapy.

†One patient died from a cardiac event, one from sepsis complicating myelosuppression, and one from pulmonary fibrosis.
Updated Analysis of SWOG-Directed Intergroup Study 0116: A Phase III Trial of Adjuvant Radiochemotherapy Versus Observation After Curative Gastric Cancer Resection


![Graphs showing relapse-free and overall survival rates with comparison of FU + leucovorin + RT vs Observation, showing statistical significance at P < .001 and P = .0046 respectively.](image-url)
Survival after radiotherapy in gastric cancer: systematic review and meta-analysis.

Radiotherapy had a significant impact on 5-year survival. Using an intent to treat (ITT) and a Per Protocol (PP) analysis, the overall 5-year RR was 1.26 and 1.31 respectively. (Survival improved by 26 to 31%)

This meta-analysis showed a statistically significant 5-year survival benefit with the addition of radiotherapy in patients with resectable gastric cancer.

Radiother Oncol. 2009 Aug;92(2):176-83
Impact of adjuvant radiation therapy (RT) on overall survival (OS) – meta-analysis

Hazard ratios (HR) for each trial are represented by squares, the size of each square represents the weight of that trial in the meta-analysis, and the horizontal line crossing the square represents the 95% confidence interval. Diamonds represent the estimated overall effect based on meta-analysis. *Included intraoperative radiation therapy.
NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Gastric Cancer
(Including cancer in the proximal 5cm of the stomach)

NCCN.org
Surgery or PreOp Chemo or Chemo-RT then Surgery

- Medically fit
  - Tis or T1af → Surgery
  - T1bf → Surgery
- Medically fit, potentially resectable
  - T2 or higher, Any N
  - Preoperative chemotherapy\textsuperscript{m} (category 1)
  - Preoperative chemoradiation\textsuperscript{m,n} (category 2B)
    → Surgery
- Locoregional disease (M0)
  - Medically fit,\textsuperscript{g} unresectable
    - Concurrent fluoropyrimidine- or taxane-based chemoradiation\textsuperscript{m,n} (category 1)
    - Chemotherapy\textsuperscript{m}
  - Medically unfit
    - Concurrent fluoropyrimidine- or taxane-based chemoradiation\textsuperscript{m,n} (category 1) (Definitive)
    - Palliative Therapy (see GAST-7)
Surgery or PreOp Chemo or Chemo-RT then Surgery

- Medically fit → Tis or T1af
  - or Surgery
  - or T1bf → Surgery

- Medically fit, potentially resectable
  - T2 or higher, Any N → Preoperative chemotherapym (category 1)
    - or Preoperative chemoradiationm,n (category 2B) → Surgery

- Locoregional disease (M0)
  - Medically fit, unresectable
    - Medically unfit → Concurrent fluoropyrimidine- or taxane-based chemoradiationm,n (category 1) (Definitive)
      - or Chemotherapym

- Palliative Therapy (see GAST-7)
Surgery or **PreOp** Chemo or Chemo-RT then Surgery

- **Medically fit** → Tis or T1af → or
  - Surgery
  - Surgery

- T1bj → Surgery

- **Medically fit**, potentially resectable
  - T2 or higher, Any N

- **Locoregional disease (M0)**
  - Medically fit, potentially resectable
    - Medically unfit
      - Medically unfit

  - Unresectable
    - Concurrent fluoropyrimidine- or taxane-based chemoradiation m,n (category 1) (Definitive)
    - Palliative Therapy (see GAST-7)
Surgery or PreOp Chemo or Chemo-RT then Surgery

- Medically fit
  - Tis or T1af: Surgery
  - T1bj: Surgery
- Medically fit, potentially resectable
- T2 or higher, Any N
- Locoregional disease (M0)
  - Medically fit, g
    - unrectestable
  - Medically unfit
- Concurrent fluoropyrimidine- or taxane-based chemoradiationm,n (category 1) (Definitive)
  - or
  - Palliative Therapy (see GAST-7)
Surgery or **PostOp** Chemo or Chemo-RT then Surgery
Surgery or **PostOp** Chemo or Chemo-RT then Surgery

R0 = complete resection with negative margins
Surgery or **PostOp** Chemo or Chemo-RT then Surgery

**High Risk Features:** poor diff or high grade, lymphovascular or perineural invasion or age <50y
Surgery or **PostOp** Chemo or Chemo-RT then Surgery

**SURGICAL OUTCOMES/CLINICAL PATHOLOGIC FINDINGS**
(Patients Have Not Received Preoperative Chemotherapy or Chemoradiation)

**R0 resection**
- Tis or T1, N0
  - Observe

- T2, N0
  - Observe or
    - 5-FU ± leucovorin or capecitabine, then fluoropyrimidine-based chemoradiation, then 5-FU ± leucovorin or capecitabine for selected patients

- T3, T4, Any N or Any T, N+
  - Chemo or 5-FU ± leucovorin or capecitabine, then fluoropyrimidine-based chemoradiation, then 5-FU ± leucovorin or capecitabine for selected patients

**R1 resection**
- Chemoradiation (fluoropyrimidine-based)

**R2 resection**

R1 = resection with + microscopic margins
R2 = resection with macroscopic (visible) cancer left behind
Radiation Technique for Gastric Cancer
Radiation Guidelines

Dose
- 45-50.4 Gy (1.8 Gy/day)

Blocking
- Custom blocking is necessary to reduce unnecessary dose to normal structures including liver (60% of liver < 30 Gy), kidneys (at least 2/3 of one kidney < 20 Gy), spinal cord (< 45 Gy), heart (1/3 of heart < 50 Gy, effort should be made to keep the left ventricle doses to a minimum) and lungs.
Clinical benefit of palliative radiation therapy in advanced gastric cancer.
Department of Radiation Oncology, The University of Texas M.D. Anderson Cancer Center, Houston, Texas 77030, USA.

The rates of control for bleeding, (70%) dysphagia/obstruction (81%) and pain (86%)

These symptoms were controlled without additional interventions for a median of 70%, 81%, and 49% of the patient's remaining life, respectively.

Patients receiving CRT had a trend towards better median overall survival than those receiving RT alone (6.7 vs. 2.4 months,).

Lower radiation dose (<41 Gy predicted for poorer local control (6-month local control 70% vs. 100%,

The role of palliative radiation therapy in symptomatic locally advanced gastric cancer.

Department of Radiation Oncology, The Cancer Institute, National University Hospital, Singapore.

The majority of patients received 30 Gy/10 fractions. Median survival was 145 days, actuarial 12-month survival 8%.

A total of 54.3% with bleeding responded (median duration of response of 140 days), 25% with obstruction responded (median duration of response of 102 days), and 25% with pain responded (median duration of response of 105 days)

Conclusion

- Adjuvant Chemo-Radiation has improved outcome after surgery.
- The normal tissues need to be spared using modern techniques like 3D-CRT / IMRT / IGRT.
- Multidisciplinary approach to be adopted.
- Extent of resection and performance status – key to success.

Thank you