NEOADJUVANT THERAPY FOR
LOCALLY ADVANCED RECTAL CANCER: THE SENSIBLE CHOICE

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Themes of the Day

- Staging
- Survival Benefit
- Improved Local Control
- Pre-op Downstaging
- Toxicity Profile & Complications
Staging of Rectal Cancer

- Locally advanced rectal cancer
- Treatment: Chemoradiotherapy
- The question: Adjuvant vs. Neoadjuvant

**Box 1**
Tumor-node-metastasis (TNM) staging system for rectal cancer

- Primary tumor (T)
  - Tx: Primary tumor cannot be assessed
  - Tis: Tumor invades submucosa
  - T1: Tumor invades muscularis propria
  - T2: Tumor invades through the muscularis propria into the subserosa
  - T3: Tumor invades other organs or structures, or perforates visceral peritoneum

- Regional lymph nodes
  - Nx: Regional lymph nodes cannot be assessed
  - N0: No regional lymph node metastases
  - N1: Metastases in one to three regional lymph nodes
  - N2: Metastases in four or more regional lymph nodes

- Distant metastasis
  - Mx: Presence or absence of distant disease cannot be determined
  - M0: No distant metastases detected
  - M1: Distant metastases detected


**Table 1**
Stage-specific survival

<table>
<thead>
<tr>
<th>Stage</th>
<th>Grouping</th>
<th>Five-Year Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>T1-2, N0, M0</td>
<td>&gt;90%</td>
</tr>
<tr>
<td>IIA</td>
<td>T3, N0, M0</td>
<td>60%-85%</td>
</tr>
<tr>
<td>IIIB</td>
<td>T4, N0, M0</td>
<td>60%-85%</td>
</tr>
<tr>
<td>IIA</td>
<td>T1-2, N1, M0</td>
<td>55%-60%</td>
</tr>
<tr>
<td>IIIB</td>
<td>T3-4, N1, M0</td>
<td>35%-42%</td>
</tr>
<tr>
<td>IIIC</td>
<td>T1-4, N2, M0</td>
<td>25%-27%</td>
</tr>
<tr>
<td>IV</td>
<td>T1-4, N0-2, M1</td>
<td>5%-7%</td>
</tr>
</tbody>
</table>

Swedish Rectal Cancer Trial, NEJM 1997

- 1168 pts, Pre-op RT v OR
- Incr 5yr OS- 58% v 48%
  p=0.004
- Decr LR- 11% v 27%
  p<0.001, no TME
- Similar OR mortality- 4% v 3%
Meta Analysis

- Camma, et al, JAMA 2000
- 14 RCT, Pre-op RT v OR
  - Incr OS (OR 0.84 p=0.03) and DSS (OR 0.74 p<0.001)
  - Decr LR (OR 0.49 p<0.001)
  - Incr Comps
TME Effect, Kapiteijn, et al, NEJM 2001

- 1805 pts, pre-op RT v OR only
- All pts had TME
- No diff OS
- Decr LR- 2.4% v 8.2% (p<0.001)

- Incr blood loss (p<0.001)
  - 1000 v 900 cc
- Incr Perineal comp
- Other M&M similar
Adjuvant vs. Neoadjuvant

- Sauer, et al, NEJM 2004
- 823 pts, pre vs post-op
- ChemoRT, all TME
- No Diff in OS, DFS
- Decr LR, 6% vs 13% p=0.006
- Less Gr III/IV and long-term toxicity, p=0.01, only 54% completed post-op
- APR- 39% vs 19% salvage of sphincter, p=0.004
- No Diff-Mortality, Leak, WH, Bleed

- 1350 pts, pre-op RT v selective post-op RT for CRM+
- All CRM+, LN+: adj 5FU
- Incr DFS (OR 0.76 p=0.01), Similar OS
- Decr LR, OR 0.39 p<0.0001
- M&M similar
Roh, et al, JCO, 2009

- 255, T3-4 or N1, pre vs post op ChRT
- Improved 5yr DFS, 64.7% v 53.4%, p=0.01
- Trend OS, 74.5% v 65.6%, p=0.065
- Incr RFI
- Similar comps, toxicity
Prognostic Indicator
Chan, et al, Int J Rad Onc Biol Phys, 2005

- 128 pts, T3, T4 fixed or tethered, preop CRT
- 25% complete response (pCR Stg 0)
- 66% decr in T
- MV-post tx TNM, T ↓stg, T4 strongest predictors of RFS, DSS
- 23% sphincters saved <5cm tumors
Neoadjuvant

100 pts

ChemoRT

90 pts

10% - Toxicity Not Tolerate

OR

81 pts

10% - Met Dz Unresectable

Adjuvant

100 pts

OR

90 pts

10% - Met Dz Unresectable

ChemoRT

54 pts

40% - Toxicity Not Tolerate Pt Dropout
Conclusions

- Neoadj Tx reduces local recurrence
- Safe, less toxic, more effective
- Possible survival benefit
- More patients treated appropriately
References