ROLE OF RADIOTHERAPY AND CHEMOTHERAPY IN CARCINOMA ESOPHAGUS

by

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INTRODUCTION

- Third most common gastrointestinal malignancy.
- 6th leading cause of death from cancer worldwide.
- Ranks among ten most common cancers in the world.
- Incidence -10-50 per 100,000 (in India).
- Peak age: 6th to 7th decade, M:F=6:1
- Surgery may be curative in early stages
- No consensus regarding best form of therapy.
INDIAN SCENARIO

- **TUMOR FACTORS**
  - Advanced stage of presentation

- **PATIENT FACTORS**
  - Mostly disease of the elderly
  - Nutritionally deprived
  - Poor performance status
  - Marked degree of weight loss

- **SOCIAL FACTORS**
  - Poor economy to afford parenteral nutrition, antibiotics and growth factor
  - Non availability of Expertise
TREATMENT STRATEGY
TREATMENT OF CA. ESOPHAGUS

**Surgery**
- Transhiatal esophagectomy
- Ivor Lewis Procedure
- Radical Esophagectomy

**Radiation**
- External beam Radiation
- Intraluminal Brachytherapy

**Chemotherapy**
- Single agent with RT
- Combination CT(CDDP+FU/ Taxane based, Topoisomerase inhibitors, EGFR receptor inhibitors)
Treatment of ca esophagus based on multidisciplinary approach. Surgery is the treatment of choice for invasive lesion.
RADIOTHERAPY IN CA ESOPHAGUS

Pre Op Radiotherapy (INTENT)

- Reducing tumor bulk
- Sterilizing nodal areas
- Reducing the risk of dissemination at surgery.

Post Op Radiotherapy (INDICATION)

- Positive cut margins
- Nodal positivity
- Residual disease
RADIATION THERAPY TECHNIQUE

Simulation

Extent:- Assess from Barium study, Endoscopy, CT Scan, PET
Positioning:- Supine/Prone Position
In CT SIM:- 5mm slices

Treatment Planning:-
Margin: -5 cm above and 5 cm below the tumor and 2.5 cm radial margin
Reduced Portal: -2 cm margin from gross disease.
Lesion above carina: - include supraclavicular lymph nodes.
Lower Esophagus: - include Coeliac axis (T12) and gastroep. lig.
**UPPER THIRD OESOPHAGUS**

**T shaped field dimensions**
- **Length**: length of the lesion + Superior margin to include supraclavicular nodes + inferior margin of 5 cms.
- **Width**: cover medial two thirds of clavicle, 1 to 1.5 cm below it.
- Individual template is made for each patient to block lungs.

**PHASE I (AP/PA PORTALS)**
- Upper third oesophagus: T–shaped field, blocks placed to shield lungs.

**PHASE II**
- Two anterior oblique wedged fields.
- Gantry angle 45 to 60 (if >65 beam passes through the humerus) & wedge 30 to 45.

**MIDDLE THIRD OESOPHAGUS**

**PATIENTS POSITIONING**: Supine or prone (results in better coverage as esophagus shifts anteriorly by 1 to 2 cm) with arms above head to prevent obstruction of treatment beams by the arms.

**TARGET VOLUME**
- **Length**: Tumor as defined by OGD & Ba swallow + 5 cm superior & inferior margin (2-3 cm for phase II)
- **Lateral**: Extraesophageal spread defined by CT scan & Ba swallow + 2-3 cm margin
- Tumors extending up to above carina, supraclavicular LN are included in the target volume
• **PHASE I (AP/PA PORTALS)**
  • Middle third extending to carina: T-shaped field, blocks placed to shield lungs.
  • Middle third not extending to carina – lesion length + 5 cm superior and inferior margins

• **PHASE II**
  • LC above carina: anterior & two anterior oblique wedged fields.
  • LC below carina: anterior & two posterior oblique fields

**LOWER THIRD OESOPHAGUS**

**PHASE I**

**L shaped field dimensions:**
- **Length**: length of the lesion & need to cover celiac nodes (L1 lower border)
- **Width**: cover medial two thirds of the diaphragm on left, vertebral transverse process on right

**PHASE II**

- **Anterior & two posterior oblique fields.**
  - Gantry angle 115 to 120 & wedge 15 to 30
**Dose prescription protocol**

**Definitive Radiotherapy**
- Only Radiotherapy - Phase I – 40 Gy/ 20 Fr
  - Phase II – 10 Gy/ 5 Fr

Assess patient for ILRT

- **ILRT**
  - 6Gy x 2 fr.
- **NO ILRT**
  - 10 Gy/ 5 Fr -14 Gy/ 7 Fr
  - (Total dose= 60-64 Gy/30-32 Fr)
  - (200cGy/ fr)

**PALLIATIVE RADIOTHERAPY**

- **Ext RT** 20 Gy/5 Fr or 30Gy/10Fr
- Followed by ILRT 8 Gy x2 Fr
- OR
- **ILRT** 8 Gy x2 Fr
- Followed by Ext RT 20 Gy/5 Fr or 30Gy/10Fr
High dose vs standard dose concurrent chemo-RT Intergroup 0123 trial: (n=236)

- **High dose CT+RT**
  - Wk 1
  - Wk 5
  - 50.4Gy/28 fractions
  - CDDP 75mg/m² Day 1 and 5-FU 1gm/m² C.I. day 1- 4
  - Wk 9
  - Wk 13
  - 64.8Gy/36 fractions

- **Standard CT+RT**
  - Wk 1
  - Wk 5
  - Wk 9
  - Wk 13
  - 50.4Gy/28 fractions
  - CDDP 75mg/m² Day 1 and 5-FU 1gm/m² C.I. day 1- 4

High dose vs standard dose:
- Treatment deaths 10% vs 2%
- Median OS 13mo vs 18.1mo, p= NS
- 2-year survival (31% v 40%).
- Cumulative inc. of local failure AT 2Yrs(High Vs Std) :-56%Vs52 %(.71)

Minsky BD et al. JCO 2002;20:1167-1174

**STANDARD RADIATION DOSE FOR PTS TREATED WITH CONC 5 FU+CDDP=50.4 Gy**
IT IS THE FOLLOW UP OF RTOG 85-01 TRIAL.
IT IS THE COMPARISON OF 50.4 vs 64.8 G(1.8 vs 2GY0,(5 CM MARGIN IN 50.4 vs 30GY WHOLE ESO FOLLOWED BY 5CM MARGIN UP TO 50GY)
CYCLE 3 STARTED 4 WKS AFTER
CYCLE 3 AND 4 AT 4 WKS INTERVAL THAN 3 WKS.

NO DIFFERENCE IN MEDIAN SURVIVAL, 2YRS SURVIVAL RATE BUT INCREASED TREATMENT RELATED DEATHS.
acer, 07/09/2009
**BRACHY THERAPY**

**AMERICAN BRACHYTHERAPY SOCIETY RECOMMENDATION**

- Should be limited to tumor less than 10cm
- Dose: - HDR-5Gy/# X 2,1#/Week
  - LDR-20Gy single fraction
- For Palliation:-HDR-10-24 Gy in 2#
  - LDR -20-25Gy in single #
- Dose Prescription:- 1cm from midsource
- Recommended Active Length:-Visible mucosal tumor with 1-2 cm proximal and distal margin.
- Timing:- 2 to 3 weeks after completion of EBRT
- Concurrent Chemotherapy and Brachytherapy not recommended.
- Contraindication:- Tracheobronchial inv, Cervical esophagus location, stenosis that can not be bypassed.
Chemotherapeutic options

- 5FU - 20%
- CDDP - 21%
- Methotrexate - 18%

- CDDP + 5FU - 35%
- CDDP + 5FU + IFNa - 50%
- Paclitaxel + CDDP - 52%
- Irinotecan + CDDP - 57%
TREATMENT OUTCOME

• Surgical resection is the standard treatment for operable esophageal cancer ie Stages I, II and most cases of III

  • Local failure after surgery:-12% to 67%(Mei et al, Gignoux et al)
  • 5 Yrs survival with surgery:- 12-20%

• Median survival is 15 to 18 months.
• Upper & middle third, SCC - LR > Distant.
• Lower third, AC – Distant recurrences.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Tumor</th>
<th>Node</th>
<th>Metastasis</th>
<th>5-Yr Survival %</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Tis</td>
<td>N0</td>
<td>M0</td>
<td>&gt;95</td>
</tr>
<tr>
<td>I</td>
<td>T1</td>
<td>N0</td>
<td>M0</td>
<td>50–80</td>
</tr>
<tr>
<td>IIA</td>
<td>T2-3</td>
<td>N0</td>
<td>M0</td>
<td>30–40</td>
</tr>
<tr>
<td>IIB</td>
<td>T1-2</td>
<td>N1</td>
<td>M0</td>
<td>10–30</td>
</tr>
<tr>
<td>III</td>
<td>T3</td>
<td>N1</td>
<td>M0</td>
<td>10–15</td>
</tr>
<tr>
<td>IVA</td>
<td>T4</td>
<td>Any N</td>
<td>M0</td>
<td>&lt;5</td>
</tr>
<tr>
<td>IVB</td>
<td>Any T</td>
<td>Any N</td>
<td>M1a</td>
<td>&lt;1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>M1b</td>
<td></td>
</tr>
</tbody>
</table>
**IS SURGERY ENOUGH FOR OPERABLE CA ESOPHAGUS**

- STAGE I-III :- SURGERY IS THE MAIN STAY OF TREATMENT
- LOCOREGIONAL FAILURE: - 12 TO 67%

<table>
<thead>
<tr>
<th>Authors</th>
<th>Patients</th>
<th>Patient (Surg)</th>
<th>Median Survival</th>
<th>2 Yrs Survival</th>
<th>3 Yrs Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Walsh et al</td>
<td>110</td>
<td>55</td>
<td>11</td>
<td>26</td>
<td>6</td>
</tr>
<tr>
<td>Urba et al</td>
<td>100</td>
<td>50</td>
<td>18</td>
<td>NA</td>
<td>15</td>
</tr>
<tr>
<td>Bosset et al</td>
<td>282</td>
<td>139</td>
<td>19</td>
<td>40</td>
<td>35</td>
</tr>
<tr>
<td>Kelsen et al</td>
<td>440</td>
<td>227</td>
<td>16</td>
<td>37</td>
<td>23</td>
</tr>
<tr>
<td>MRC</td>
<td>802</td>
<td>402</td>
<td>13</td>
<td>34</td>
<td>NA</td>
</tr>
</tbody>
</table>

**Cause of Failure and poor survival:**-(RESECTABILITY, MICROMETASTASIS)

The proximity of vital mediastinal structures often compromises the resection. Micrometastasis at the time of initial diagnosis.
HOW TO IMPROVE THE LOCOREGIONAL CONTROL AND SURVIVAL IN OPERABLE CA. ESOPHAGUS

Radiotherapy: For locoregional control
Chemotherapy: For both local and systemic control
10(9):-1cm
10(10):-10gm
10(8):-1mm
10(12):-1Kg cross the body burden
Gross tumor surgery/rt
Surgery:-Peripheral failure,RT:-Periferal failure
acer, 07/09/2009
PREOPERATIVE RADIATION IN OPERABLE CA ESOPHAGUS

• WHY Preoperative Radiation?
  – Allows for tumor downstaging → R0 resection
  – Sterilizing nodal basin.
  – Decreases the possibility of intraoperative spillage.
  – Avoidance of surgery in rapidly progressive disease.
# Neoadjuvant Radiotherapy Randomized Trials

<table>
<thead>
<tr>
<th>Study</th>
<th>Patient</th>
<th>Dose of RT</th>
<th>Resectability</th>
<th>Local Failure</th>
<th>Median survival mo</th>
<th>5-year survival (%)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Launois (1981)</td>
<td>RT + S</td>
<td>40 Gy</td>
<td>76 NR 70 NR</td>
<td>10 12</td>
<td>9.5 11.5</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Gignoux (EORTC) (1988)</td>
<td>RT + S</td>
<td>33 Gy</td>
<td>47 58 46 67</td>
<td>48 45 10 8</td>
<td>NS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wang (1989)</td>
<td>RT + S</td>
<td>40 Gy</td>
<td>93 85 13 12</td>
<td>NA NA</td>
<td>35 30</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Arnott (1992)</td>
<td>RT + S</td>
<td>20 Gy</td>
<td>NA NR</td>
<td>8 8 9 17</td>
<td>NS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Huang</td>
<td>RT + S</td>
<td>40 Gy</td>
<td>92 90 NR NR</td>
<td>11 22</td>
<td>46 25</td>
<td>Statistical analysis was not done</td>
<td></td>
</tr>
</tbody>
</table>

Statistical analysis was not done.
5 RANDOMISED TRIAL REPORTED.
NO DIFFERENCE IN RESECTION RATE.
ONLY 2 SERIES REPORTED THE LOCAL FAILURE RATE.
REPORT OF GIGNOUX ET AL MENTIONED SIGNIFICANT LOWER LOCAL FAILURE RATE IN PT WHO RECEIVED PRE OP RT.
acer, 07/09/2009

ONLY 2 STUDY REPORTED LOCAL FAILURE RATE. OUT OF WHICH ONE STUDY FAVOURS THE DECREASE IN LOCAL FAILURE (GIGNOUX) AND ANOTHER STUDY NO DIFFERENCE.
THERE WAS NO DIFFERENCE IN MEDIAN SURVIVAL.
ONE STUDY FAVOURED INCREASE IN 5 YR SURVIVAL BUT THE STATISTICAL ANALYSIS WAS NOT MENTIONED.
THE DOSE OF RADIATION USED ALSO NOT UNIFORM. ADEQUATE INTERVAL BETWEEN RT VS SURGERY WAS NOT ALLOWED (AT LEAST 4-7 WKS)
acer, 07/09/2009
Preoperative RT in potentially resectable esophageal cancer- Metaanalysis (MRC+OCCG-1995-98)

1147 patients from 5 RCTS (Pre op RT+S Vs S)

Moderate benefit to the use of preoperative RT

- At a Median follow up 9Yrs the hazard ratio 0.89 (p=0.06)
- 11% reduction in the risk of death
- At 2 years, absolute survival benefit of 4% and 5 yrs 3%

Statistically No Survival Advantages in preop RT+S Vs S alone in potentially resectable esophageal Cancer (p = 0.06)
WHAT IS THE EVIDENCE-PRE OP RADIATION

- PREOPERATIVE RADIATION DOES NOT IMPROVE RESECTABILITY, DOES NOT SIGNIFICANTLY DECREASE LOCAL FAILURE RATE OR IMPROVE SURVIVAL

ESMO RECOMMENDATION: Preoperative radiation does not add any survival benefit to surgery alone. This treatment is not recommended (II A)
<table>
<thead>
<tr>
<th>Level</th>
<th>Type of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Evidence obtained from meta-analysis of multiple, well-designed, controlled studies. Randomized trials with low false-positive and low false-negative errors (high power).</td>
</tr>
<tr>
<td>II</td>
<td>Evidence obtained from at least one well-designed experimental study. Randomized trials with high false-positive and/or-negative errors (low power).</td>
</tr>
<tr>
<td>III</td>
<td>Evidence obtained from well-designed, quasi-experimental studies such as nonrandomized, controlled, single group, pre-post, cohort, and time or matched case-control series.</td>
</tr>
<tr>
<td>IV</td>
<td>Evidence from well-designed, nonexperimental studies such as comparative and correlational descriptive and case studies.</td>
</tr>
<tr>
<td>V</td>
<td>Evidence from case reports.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Grade</th>
<th>Grade of Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>There is evidence of type I or consistent findings from multiple studies of type II, III, or IV.</td>
</tr>
<tr>
<td>B</td>
<td>There is evidence of type II, III, or IV and findings are generally consistent.</td>
</tr>
<tr>
<td>C</td>
<td>There is evidence of type II, III, or IV but findings are inconsistent.</td>
</tr>
<tr>
<td></td>
<td>There is little or no systematic empirical evidence.</td>
</tr>
</tbody>
</table>
PRE OP CT IN OPERABLE CA. ESOPHAGUS

Rationale

- Downstaging
- Eradication of micrometastasis
- Pathologic evaluation of treatment response with possible selection of adjuvant therapy

Disadvantages:

- Development of drug resistant clones.
- Delay in definitive therapy for nonresponders
- Delay in definitive treatment: Poor nutrition. (50% of patients do not respond to chemotherapy)
# Neo adjuvant Chemotherapy

Resection rate, Local Recurrence, Overall survival

<table>
<thead>
<tr>
<th>STUDY</th>
<th>NO. OF PTS.</th>
<th>RESECTION RATE</th>
<th>LOCAL / DIST RECURRENCE</th>
<th>3 YR SURVIVAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>INT 0113</td>
<td>CT+S 213 S 227</td>
<td>62% 59%</td>
<td>32% 31% 41% 50%</td>
<td>23% 26%</td>
</tr>
<tr>
<td>MRCOCWG</td>
<td>CT+S 400 S 402</td>
<td>60% 54%</td>
<td>32% 25%</td>
<td></td>
</tr>
<tr>
<td>MAGIC</td>
<td>CT+S 250 S 253</td>
<td>66% 69%</td>
<td>5 yrs 36% 23%</td>
<td></td>
</tr>
</tbody>
</table>
There is no difference in resection rate, local recurrence/distant failure and 3 yr survival. 3 randomised trial INTer group 0013 having 440 pts, Medical research council oesophageal cancer working group 802 pts and Magic trial 503 pts. In MRCOWG, curative resection could reach statistically significant. There was survival advantages in MRCOCWG and MAGIC Trial.
# Neoadjuvant chemotherapy
## Randomized Trials

<table>
<thead>
<tr>
<th>Study (year)</th>
<th>Patients</th>
<th>Chemotherapy</th>
<th>pCR (%)</th>
<th>Median Survival (mo)</th>
<th>5-year Survival (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>S 20</td>
<td>Adjuvant: C, Vin</td>
<td></td>
<td>9</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Nygaard (1992)</td>
<td>C + S0</td>
<td>C, Bleo</td>
<td>NA</td>
<td>8</td>
<td>3-y 3</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>S 41</td>
<td></td>
<td></td>
<td>8</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Ancona (2001)</td>
<td>C + S47</td>
<td>CF X 2 or 3</td>
<td>13%</td>
<td>25</td>
<td>34</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>S 47</td>
<td></td>
<td></td>
<td>24</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Schlag (1992)</td>
<td>C + S22</td>
<td>CF X 3</td>
<td>NA</td>
<td>10</td>
<td>NA</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>S 24</td>
<td></td>
<td></td>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>INT 0113 (1998)</td>
<td>C + S213</td>
<td>Neo CF X 3</td>
<td>2.5%</td>
<td>14.9</td>
<td>3 y 26</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>S 227</td>
<td>Adj CF X 2</td>
<td></td>
<td>16.1</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>MRC (2002)</td>
<td>C + S400</td>
<td>CF X 2</td>
<td>4%</td>
<td>16.8</td>
<td>2 y 43</td>
<td>P=0.004</td>
</tr>
<tr>
<td></td>
<td>S 402</td>
<td></td>
<td></td>
<td>13.3</td>
<td>34</td>
<td></td>
</tr>
</tbody>
</table>
In MRC trial though there was statistically improved overall survival but the median duration of follow up was short.

acer, 07/09/2009
Neoadjuvant chemotherapy
Meta-analysis

- There were eleven randomised trials involving 2019 patients. Eight trials (1729 patients) reported sufficient detail on survival to be included in a meta-analysis for the primary outcome.

- There was some evidence to suggest that preoperative chemotherapy improves survival, but this was inconclusive (HR 0.88; 95% CI 0.75 to 1.04).

- No difference between overall rate of resections (RR 0.96, 95% CI 0.92 to 1.01) or the rate of complete resections (R0) (RR 1.05; 95% CI 0.97 to 1.15) between the preoperative chemotherapy arm and surgery alone.

- No difference of tumour recurrence (RR 0.81, 95% CI 0.54 to 1.22) or non-fatal complication rates (RR 0.90; 95% CI 0.76 to 1.06).

- Trials reported risks of toxicity with chemotherapy that ranged from 11% to 90%.
### Review: Preoperative chemotherapy for resectable thoracic esophageal cancer

**Comparison:** 3 Tumor recurrence  
**Outcome:** 1 Local-regional recurrence

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Preop chemotherapy n/N</th>
<th>Surgery alone n/N</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Weight</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Law 1997</td>
<td>7/74</td>
<td>21/273</td>
<td>14.5%</td>
<td>0.33 [0.15, 0.73]</td>
<td></td>
</tr>
<tr>
<td>Kelsen 1998</td>
<td>31/233</td>
<td>24/234</td>
<td>21.3%</td>
<td>1.39 [0.79, 2.41]</td>
<td></td>
</tr>
<tr>
<td>Baba 2000</td>
<td>7/21</td>
<td>6/21</td>
<td>12.4%</td>
<td>1.17 [0.47, 2.89]</td>
<td></td>
</tr>
<tr>
<td>Wang 2001</td>
<td>8/50</td>
<td>16/50</td>
<td>15.3%</td>
<td>0.50 [0.24, 1.06]</td>
<td></td>
</tr>
<tr>
<td>Ancona 2001</td>
<td>9/48</td>
<td>10/48</td>
<td>14.2%</td>
<td>0.90 [0.40, 2.02]</td>
<td></td>
</tr>
<tr>
<td>MRC 2002</td>
<td>31/400</td>
<td>32/402</td>
<td>22.3%</td>
<td>0.97 [0.61, 1.56]</td>
<td></td>
</tr>
</tbody>
</table>

**Total (95% CI):** 826  
**Total events:** 93 (Preop chemotherapy), 109 (Surgery alone)  
**Heterogeneity:** $Ta^{2} = 0.14$; Chi$^{2} = 10.96$, df = 5 (P = 0.05); P = 54%  
**Test for overall effect:** Z = 1.02 (P = 0.31)

---

**Review: Preoperative chemotherapy for resectable thoracic esophageal cancer**  
**Comparison:** 2 Rate of recurrence  
**Outcome:** 2 All recurrences

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Preop chemotherapy n/N</th>
<th>Surgery alone n/N</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Weight</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nygaard 1992</td>
<td>29/250</td>
<td>28/250</td>
<td>6.1%</td>
<td>0.92 [0.65, 1.32]</td>
<td></td>
</tr>
<tr>
<td>Schlag 1992a</td>
<td>11/224</td>
<td>13/224</td>
<td>4.1%</td>
<td>0.63 [0.46, 0.90]</td>
<td></td>
</tr>
<tr>
<td>Law 1997</td>
<td>66/743</td>
<td>66/743</td>
<td>15.5%</td>
<td>0.94 [0.66, 1.34]</td>
<td></td>
</tr>
<tr>
<td>Kelsen 1998</td>
<td>17/233</td>
<td>17/234</td>
<td>16.4%</td>
<td>0.79 [0.73, 0.86]</td>
<td></td>
</tr>
<tr>
<td>Kulp 1997</td>
<td>63/800</td>
<td>63/800</td>
<td>12.5%</td>
<td>1.00 [0.85, 1.17]</td>
<td></td>
</tr>
<tr>
<td>Wang 2001</td>
<td>49/550</td>
<td>46/550</td>
<td>15.8%</td>
<td>1.04 [0.94, 1.15]</td>
<td></td>
</tr>
<tr>
<td>Ancona 2001</td>
<td>49/496</td>
<td>46/496</td>
<td>12.4%</td>
<td>0.90 [0.82, 1.15]</td>
<td></td>
</tr>
<tr>
<td>MRC 2002</td>
<td>319/4660</td>
<td>278/460</td>
<td>14.4%</td>
<td>1.10 [1.01, 1.19]</td>
<td></td>
</tr>
</tbody>
</table>

**Total (95% CI):** 963  
**Total events:** 770 (Preop chemotherapy), 745 (Surgery alone)  
**Heterogeneity:** $Ta^{2} = 0.62$; Chi$^{2} = 35.59$, df = 7 (P = 0.00006); P = 68%  
**Test for overall effect:** Z = 3.97 (P = 0.02)}
WHAT IS THE EVIDENCE:-PRE OP CHEMOTHERAPY

- No improvement in curative resection rate
- No Difference in Local Recurrence rate
- No difference in Overall survival

ESMO RECOMMENDATION:-Evidence for clinical benefit from preoperative chemotherapy exists for adenocarcinoma. Patients with adenocarcinomas of the lower esophagus/GE junction may be managed with pre- and postop. Chemotherapy. (I B)
Preoperative chemoradiation - rationale

- **Combination of CT + RT**
  - Downstage the disease: Enhances resectability
  - Drugs enhances radiosensitivity
  - Reduced dissemination of tumor cells during surgery: Hence reduces distant metastasis
  - Remove microscopic persistant disease after CT RT

- **Used as a planned approach in clinically resectable tumors**
  - Agents
    - 5-FU, CDDP
    - more recently, paclitaxel & docetaxel
  - Radiation
    - conventionally (30 – 50Gy @ 1.8 Gy to 2 Gy / #)
    - hyperfractionated or accelerated – 1.5Gy BID (45Gy)

- **Pathological CR rates** ~ 25% (16 – 56%)
- **Survival** – median: 12 – 25 months; 5 year: 16 – 55%
## Pre op.CT+RT+S Vs S

<table>
<thead>
<tr>
<th>AUTHOR</th>
<th>MEDIAN FOLLOW UP</th>
<th>REGIMEN</th>
<th>NO OF PTS</th>
<th>Ro resection/ Dist Met</th>
<th>PATH CR</th>
<th>LOCOREG FAILURE</th>
<th>3-Yr Survival</th>
<th>SURVIVAL DIFF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urba et al</td>
<td>8.2</td>
<td>5fu+cddp+Vbl+RT+S S</td>
<td>50</td>
<td>90</td>
<td>60%</td>
<td>19%</td>
<td>30</td>
<td>p=0.15</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>50</td>
<td>90</td>
<td>65%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Boset et al</td>
<td>4.6</td>
<td>Cddp+RT+S S</td>
<td>143</td>
<td>81</td>
<td>69</td>
<td></td>
<td>34</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>138</td>
<td></td>
<td></td>
<td></td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>Walsh et al</td>
<td>1.5</td>
<td>5fu+cddp+RT+S S</td>
<td>58</td>
<td>NR</td>
<td>NR</td>
<td>25</td>
<td>32</td>
<td>P+0.01</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>58</td>
<td></td>
<td></td>
<td></td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Burmeister et al</td>
<td>5.4</td>
<td>5fu+cddp+RT+S S</td>
<td>128</td>
<td>80</td>
<td>59</td>
<td>16</td>
<td>35</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>128</td>
<td></td>
<td></td>
<td></td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Tepper et al</td>
<td>6.0</td>
<td>5fu+cddp+RT+S S</td>
<td>30</td>
<td>NR</td>
<td>NR</td>
<td>33</td>
<td>13</td>
<td>P=0.008</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>26</td>
<td></td>
<td></td>
<td></td>
<td>15</td>
<td></td>
</tr>
</tbody>
</table>

Note: Bolded values indicate significant differences.
5 randomised trial compared crts vs s. Path Complete response was seen in 25 to 28%. 3 yr survival in treatment arm was 30-40%. Study by Urba et al revealed statistically better local control in CTRTS arm. 3 yrs Survival advantages were seen in study by Walsh and Tepper et al. The criticism for low survival in surgery arm may be due to advanced disease. The above 2 trials have small no of patients, There was no difference in resection rate except Boset study. No difference in dist failure rate.

acer, 08/09/2009
Preoperative chemo-radiation Metaanalysis - 1

- Preoperative chemo-radiation improved 2-year survival by 6.4% (nonsignificant; 95% CI, -1.2% to 14%)
- Treatment related mortality increased by 3.4% (95% CI, -0.1% to 7.3%)
- Recommendation is to use in the context of a clinical trial.

WHAT IS THE EVIDENCE - Pre op CT RT + S Vs S

- Complete pathological response: -25-28%.
- 2/3rd patients disease down staged.
- No survival advantages except study done by walsh et al and Tepper et al. (But the number is small)
- Nonsignificant trend towards increased treatment related mortality was seen in neoadj.arm.

BECAUSE OF TOXICITY AND ONGOING UNCERTAINTY ABOUT BENEFIT ASSOCIATED WITH PRE OP COMBINED CTRT, IT SHOULD BE USED CAUTIOUSLY AND PRIORITY SHOULD BE GIVEN TO ENROLLING THE PATIENT IN CLINICAL TRIAL

ESMO RECOMMENDATION:- Although meta-analyses and one recent phase III trial suggested that preoperative chemoradiation confers a survival benefit, it is not clear which patients (stage, tumor location, histology) will most benefit from this preoperative treatment [I, B]
POST OP RT

**Rationale**
Detail pathological Report available
Can treat areas of risk, sparing normal radiosensitive structure.
Pathological T1N0 or Metastatic lesion can be spared for Radiation.
Bulky Disease, Gross Residual disease, Proved microscopic residual/+ve Margin

**Disadvantages**
Limited tolerance following gastric pull up and irradiation of a devascularised tumor bed
Indications for Post-operative RT

- **Standard Indications**
  - Positive Margins
  - Gross Residual Disease
- **Less Clear**
  - + LN
  - + ECE on adenopathy
### Post operative RT after curative resection

<table>
<thead>
<tr>
<th>Trial</th>
<th>No</th>
<th>RT dose/#</th>
<th>Local recc % PORT vs SX</th>
<th>Median Surv PORT VS Sx</th>
<th>Overall Surv. PORT vs Sx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Teniere '91 (French)</td>
<td>221</td>
<td>45-55Gy/25-30#</td>
<td>15% vs 30% overall</td>
<td>18 vs 18 mo</td>
<td>21% vs 19% at 5 years</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zieren '95 (German)</td>
<td>68</td>
<td>55.8Gy/31#</td>
<td>48.5% vs 65%</td>
<td>14 vs 13 mo</td>
<td>22% vs 20% at 3 years</td>
</tr>
<tr>
<td>Xiao ZF '03 (Chinese)</td>
<td>495</td>
<td>50-60Gy/25-30#</td>
<td>16.2% vs 25.9% (P&lt;0.05)</td>
<td>-</td>
<td>34.1 vs 17.6 for N+ (p=0.06)</td>
</tr>
<tr>
<td>Fok '91 (Hong Kong)</td>
<td>60 (C) 60 (P)</td>
<td>49-52.5Gy/14-15#</td>
<td>15% vs 36% (scc) (p=0.02)</td>
<td>8.7 Vs 15.2 mo (p=0.02)</td>
<td>10% vs 13%, p=NS</td>
</tr>
</tbody>
</table>
In the study by F0k the dose per fraction was 3.5 Gy. Study by Tenier, Xiao et al., Fok et al. there was decrease local recurrence in PORT. There was no change in overall survival.
Adjuvant Radiation Vs chemotherapy

Randomize Post Surgery N=258

Radiation

Cis/Vindesinex2

5 yr survival : 44%

5 yr survival: 42%
No difference in time to recurrence or sites of recurrence

Radiotherapy (50 Gy)
2 courses of chemotherapy consisting of cisplatin (50 mg/m2) and vindesine (3 mg/m2) following curative resection

Chest 1993 Jul;104(1):203-7
WHAT IS THE EVIDENCE

Post operative RT

- PORT after **curative resections decreases local recurrence**
- Do not improve over all survival
- Therefore PORT may be offered for **positive surgical margins**, **N+ disease** or perhaps after **non-curative resections**
What about post-op chemotherapy alone?

- 2 randomized Japanese trials
  - **Ando N** et al. *J of Thoracic and Cardiovascular Surgery*. 1997; 114:204-205
    - Randomized study; 205 patients
    - S + C vs. S 2 cycles alone
    - Chemo – of Cisplatin (70 mg + Vindesine /m2)
    - **5 y OS S + C 48.1% vs. S 44.9% (p = NS)**

  - **Ando N** et al. *JCO*. Dec 2003; 21(24): 4592-4596
    - Randomized study; 242 patients
    - Thoracic SCCA
    - S+C vs. S alone
    - Chemo – 2 cycles of Cisplatin (80 mg/m2) + 5 FU (800mg/m2/5 day infusion)
    - 5 y OS S+ CT 61 vs. 51 % (p=0.3)
    - **5 y DFS 55% vs. 45% (p=0.04);**
      - 5 Yrs DFS in N–VE patients (S Vs S+CT) 77% vs. 82% (p=0.3)
      - 5 Yrs DFS in N + patients 35% vs. 53% (p=0.06)
    - Adjuvant CT may benefit in node +ve Pts
2 randomized study by japanese group by same author Ando N et al. In all the study post op 2 cycles were given. In 1st study cddp+vindesin and in 2nd study cddp+5 fu was tried. In both the study there was no difference in OS. But in cddp+5fu group, there is improved 5 yrs DFS in post op CT group. The 5 yr DFS was better in node +ve group not node _ve pts.
WHAT IS THE EVIDENCE S vs S+ POST OP CT in operable Ca Esophagus)

POST OP CT DOES NOT IMPROVE OVERALL SURVIVAL EXCEPT DFS IN RO & N1 PT.
# Post operative CT+RT Vs S alone

<table>
<thead>
<tr>
<th>Trial</th>
<th>No</th>
<th>RT dose/# CT PROT</th>
<th>Loco reg recc % POCTRT vs SX</th>
<th>Median Surv PORT CT VS Sx</th>
<th>Overall Surv. POCTRT vs Sx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mc Donalad Trial</td>
<td>556</td>
<td>45Gy/25# 5 FU+LV</td>
<td>19 Vs 29%</td>
<td>36 vs 27 mo</td>
<td>50% vs 41% at 3 years p=0.005</td>
</tr>
<tr>
<td></td>
<td>20% GE JN. Adeno</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Taiwan Study</td>
<td>60</td>
<td>40Gy+15 to 20Gy boost Conc Cddp-4 Cycle Cddp+5 FU</td>
<td>40% vs 60%</td>
<td></td>
<td>70% vs 33.7% at 3 years</td>
</tr>
<tr>
<td></td>
<td>Th.Eso S.C.C</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Canadian Study</td>
<td>n=70</td>
<td>50(36+14) Gy CT-ConcCT RT Cddp+5 FU</td>
<td>13% vs 35. %</td>
<td>DFS10.2 Vs 10.6 mo O.S 47.5 vs 14.1 mo</td>
<td>48% Vs 0% at 5 Yrs</td>
</tr>
<tr>
<td></td>
<td>N1 Adeno/SCC</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Incidence of Gr IV toxicity(41 % Vs 32%).in Mc Donald Trial.
A randomised trial has evaluated the role of post rt vs s alone. The goal of the Mc Donald study was to evaluate the effect of post op rt ct in Ca esophagus. However, 20% of patients had Ca of the lower end of the esophagus. There was a decrease in local recurrence, increased median survival, and overall survival. In the Mc Donald study, there was increased Gr IV toxicity.

acer, 08/09/2009
Macdonald Trial – Overall Survival

Macdonald Trial – Relapse Free Survival

Taiwan Study - Results

Canadian Study – Overall Survival

Figure 1. Overall Survival among All Eligible Patients, According to Treatment-Group Assignment.

Figure 2. Relapse-free Survival among All Eligible Patients, According to Treatment-Group Assignments.

Figure 1. Overall survival Kaplan–Meier plot stratified by treatment received. CRT: adjuvant chemoradiation therapy.
Post operative CT+RT Vs S alone

Macdonald Trial - Conclusions

- Add chemoRT for GE junction adenoCA
  - T3 or higher
  - + LN
  - + margins, + residual disease
  - ? Selected T2 cases

Taiwan Study - Conclusions

- ChemoRT showed improved OS compared to RT alone in T3 or higher patients

Canadian Trial - Conclusion

- Benefit of ChemoRT in node + patients
<table>
<thead>
<tr>
<th></th>
<th>No of Randomised Trial</th>
<th>Metaanalysis</th>
<th>Local Control</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre op RT</td>
<td>5</td>
<td>1</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Pre op CT</td>
<td>6</td>
<td>1</td>
<td>No</td>
<td>No except MRC Trial(G.E.Junction)</td>
</tr>
<tr>
<td>Preop CT RT</td>
<td>7</td>
<td>2</td>
<td>YES</td>
<td>Modest Improve in survival</td>
</tr>
<tr>
<td>Post op RT</td>
<td>4</td>
<td>0</td>
<td>YES</td>
<td>No</td>
</tr>
<tr>
<td>Post op CT</td>
<td>2</td>
<td>0</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Post op CT RT</td>
<td>3</td>
<td>0</td>
<td>Yes</td>
<td>YES</td>
</tr>
</tbody>
</table>
INOPERABLE NON METASTATIC CA ESOPHAGUS

Radiation alone

Combination chemoradiation
# RADIATION ALONE

<table>
<thead>
<tr>
<th>AUTHOR</th>
<th>NO OF PTS</th>
<th>DOSE</th>
<th>2 YRS SURVIVAL</th>
<th>5 YRS SURVIVAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pearson</td>
<td>208</td>
<td>50Gy/4Wks</td>
<td>NA</td>
<td>17%</td>
</tr>
<tr>
<td>Beatty et al</td>
<td>344</td>
<td>&gt;40Gy to &gt; 50Gy</td>
<td>21%</td>
<td>0%</td>
</tr>
<tr>
<td>Schuchmann et al</td>
<td>127</td>
<td>&lt;45Gy &gt;45 Gy</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Newaishy et al</td>
<td>444</td>
<td>50-55Gy/4 Wks</td>
<td>19%</td>
<td>9%</td>
</tr>
<tr>
<td>Okawa et al</td>
<td>96</td>
<td>NR</td>
<td>9%(I-20%,II-10%,III-3%,IV-0%)</td>
<td></td>
</tr>
<tr>
<td>Lederman et al</td>
<td>263</td>
<td>11%(yrs)</td>
<td>7%</td>
<td></td>
</tr>
</tbody>
</table>
Radiation Therapy Alone
Inoperable Ca Esophagus

- Patients receiving radiation alone for inoperable esophageal cancer is palliative in vast majority of the cases having

  MEDIAN SURVIVAL:-6 to 12 Months & 5 YRS SURVIVAL RATE < 10%
Concurrent chemoradiation – Intergroup trial (RTOG 85-01) : n = 121 Landmark trial

RTOG 8501 provided a convincing evidence of the superiority of chemoradiation. Established chemoradiation as the conventional nonsurgical treatment for esophageal cancer.
This is the RTOG 85-01 study, which is a landmark trial where pts were treated with concurrent ct rt followed by ct vs rt alone. In this study there was improvement in local failure rate, median survival as well as 5 yrs survival.
Concurrent chemoradiation – further intensification

Add brachytherapy

Wk 1

Wk 5

Wk 6.5

Wk 8

Wk 11

50Gy/25 fractions

CDDP 75mg/m² Day 1 and 5-FU 1gm/m² C.I. day 1- 4

Add chemotherapy + Add further EBRT
External beam RT, concurrent CT and brachytherapy (RTOG 92-07) n=75(RTOG 85-01+Brachy)

Wk 1  Wk 5  Wk 8  Wk 9  Wk 10  Wk 11

50Gy/25 fractions

HDR brachy 5Gy x 3 #

CDDP 75mg/m² Day 1 and 5-FU 1gm/m² C.I. day 1- 4

<table>
<thead>
<tr>
<th>Grade III</th>
<th>Grade IV</th>
<th>Grade V</th>
<th>Fistula</th>
<th>comp.resp</th>
</tr>
</thead>
<tbody>
<tr>
<td>58%</td>
<td>26%</td>
<td>8%</td>
<td>18%per Yr</td>
<td>73%</td>
</tr>
</tbody>
</table>

Due to toxicity it should be used with caution, BENEFIT IS UNCERTAIN

High dose vs standard dose concurrent chemo-RT Intergroup 0123 trial: (n=218)

High dose vs standard dose:
- Treatment deaths 10% vs 2%
- Median OS 13mo vs 18.1mo, p= NS
- 2-year survival (31% v 40%).
- Cumulative incidence of local failure (High Vs Std): -56% vs 52%

Minsky BD et al. JCO 2002;20:1167-1174
Neoadjuvant + concurrent chemo-RT
Intergroup 0122 trial: (n=45)

<table>
<thead>
<tr>
<th>Neoadjuvant segment</th>
<th>WEEK</th>
<th>CT + RT segment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>13</td>
<td>17</td>
<td></td>
</tr>
</tbody>
</table>

5-FU 1000mg/m²/24hr x 5days
CDDP 100mg/m² x 1
75mg/m² x 1
RT 64.8Gy/36#

Toxicity and survival

<table>
<thead>
<tr>
<th>Grade III</th>
<th>Grade IV</th>
<th>Grade V</th>
<th>compliance</th>
<th>median OS</th>
</tr>
</thead>
<tbody>
<tr>
<td>39%</td>
<td>23%</td>
<td>13%</td>
<td>66%</td>
<td>20 months</td>
</tr>
</tbody>
</table>

Concurrent CT+RT- meta analysis - 11RCT

- With eleven concomitant RTCT studies.
- Concomitant RTCT provided significant reduction in mortality with a harms ratio (HR) of 0.73 (95% confidence interval (CI) 0.64 to 0.84).
- The absolute survival benefit for RTCT at 1yr and 2 yr was 9% (95% CI 5 to 12%) and 4% (95% CI 3 to 6%) respectively.
- There was an absolute reduction of local recurrence rate of 12% (95% CI 3 to 22%)
- This was associated with a significant risk of severe and life-threatening toxicities

Cochrane Database of Systematic Reviews, Issue 3, 2009
Based on the available data, when a non-operative approach is selected then concomitant RTCT is superior to RT alone for patients with localized esophageal cancer but with significant toxicities. In patients who are in good general condition, and the risk benefit has been thoroughly discussed with the patient, concomitant RTCT should be considered for the management of esophageal cancer compared with radiotherapy alone.

ESMO RECOMMENDATION:- For patients unable or unwilling to undergo surgery, combined chemoradiation is superior to radiotherapy alone [I, A].
LOCAL FAILURE & SURVIVAL APPEAR SIMILAR IN CHEMORADIATION VS SURGERY ARM IN INOPERABLE CA ESOPHAGUS

<table>
<thead>
<tr>
<th></th>
<th>RTOG 8501</th>
<th>MRC</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOCAL FAILURE</td>
<td>39-45%</td>
<td>31%</td>
</tr>
<tr>
<td>MEDIAN SURVIVAL</td>
<td>14-20 MO</td>
<td>13-16 MO</td>
</tr>
<tr>
<td>5 YR SURVIVAL</td>
<td>20-30%</td>
<td>20%</td>
</tr>
</tbody>
</table>
PREDICTOR OF RESPONSE TO CHEMORADIATION

• Radiation dose, 5FU/CDDP based regimen (Geh et al)
• Patient who achieved a pCR had improved survival (Borger et al)
• % decrease SVU in 18-FDG-PET-better response and survival (Blackstock et al)
• Absence of p53 and week bcl-X1- Higher response to Chemotherapy (Sarbia M et al)
• Pt with HIGH MVD (Micro vascular density) had better survival (Kishi et al)
• Lymphocyte infiltration around the tumor – better survival (Morita et al).
Newer regimens

<table>
<thead>
<tr>
<th>Reference</th>
<th>Number of patients</th>
<th>Radiotherapy dose</th>
<th>Induction chemotherapy</th>
<th>Chemotherapy with radiation</th>
<th>Resection rate</th>
<th>Complete response rate</th>
<th>Pathological complete remission ± minimal residual disease</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wright et al. [16]</td>
<td>40</td>
<td>58.5 Gy (tumour), 45 Gy to mediastinum</td>
<td>None</td>
<td>Cisplatin, 5-FU, paclitaxel</td>
<td>90%</td>
<td>39%</td>
<td>61% at 2 years</td>
<td></td>
</tr>
<tr>
<td>Adelstein et al. [17]</td>
<td>40</td>
<td>45 Gy (preoperative) + 24 Gy (post-op) if T3–4 or N1</td>
<td>None</td>
<td>Cisplatin, paclitaxel</td>
<td>95%</td>
<td>23%</td>
<td>30% at 3 years (projected)</td>
<td></td>
</tr>
<tr>
<td>Schnirer et al. [18]</td>
<td>10</td>
<td>45–50.4 Gy</td>
<td>NO</td>
<td>5-FU, paclitaxel</td>
<td>50%</td>
<td>20%</td>
<td>60% of patients undergoing surgery 71%</td>
<td></td>
</tr>
<tr>
<td>Ajani et al. [19]</td>
<td>38</td>
<td>45 Gy</td>
<td>TCF</td>
<td>5-FU, cisplatin</td>
<td>92%</td>
<td>30%</td>
<td>DFS and OS 72% and 63% at 3 years, 51% and 39% at 5 years DFS and OS 40% and 42% at 2 years</td>
<td></td>
</tr>
<tr>
<td>Safran et al. [20]</td>
<td>41</td>
<td>39.6 Gy</td>
<td>None</td>
<td>Cisplatin, paclitaxel weekly</td>
<td>50%</td>
<td>29%</td>
<td>2 year 47%, 3 year 41%, Median survival 22 months DFS and OS 56% and 59% at 2 years, 45% and 45% at 4 years OS at 1, 2, 3 and 4 years are 75%, 56%, 50%, 50%, respectively, median survival 40 months</td>
<td></td>
</tr>
<tr>
<td>Bains et al. [21]</td>
<td>41</td>
<td>50.4 Gy</td>
<td>Cisplatin, paclitaxel</td>
<td>Cisplatin, paclitaxel</td>
<td>92%</td>
<td>22% of resected specimen (26% of patients with R0 resection) 36%</td>
<td>Not stated</td>
<td></td>
</tr>
<tr>
<td>Meluch et al. [22]</td>
<td>129</td>
<td>45 Gy</td>
<td>None</td>
<td>5-FU, carboplatin, paclitaxel</td>
<td>74%</td>
<td>38%</td>
<td>62%</td>
<td></td>
</tr>
<tr>
<td>Goldberg et al. [23]</td>
<td>29</td>
<td>60 Gy</td>
<td>Cisplatin, paclitaxel</td>
<td>5-FU, cisplatin, paclitaxel</td>
<td>75%</td>
<td>18%</td>
<td>18.6% (25% of patients undergoing resection) 37.5%</td>
<td></td>
</tr>
<tr>
<td>Current 2004</td>
<td>16</td>
<td>45 Gy</td>
<td>TCF</td>
<td>TCF</td>
<td>75%</td>
<td>18.6% (25% of patients undergoing resection) 37.5%</td>
<td>Not stated</td>
<td></td>
</tr>
</tbody>
</table>

DFS, disease-free survival; 5-FU, 5-fluorouracil; OS, overall survival; TCF, paclitaxel, cisplatin and 5-fluorouracil.
TAKE HOME MESSAGE

OPERABLE NON METASTATIC

• SURGERY:- Mainstay of treatment for operable Ca.Esophagus
  • NEOADJUVANT RT :- Does not improve local control or survival
  • NEOADJUVANT CT:- No improve resection rate, local control and survival
  • NEOADJUVANT CHEMORADIATION:- Improves local control and modest improvement in survival.

NACT RT may be restricted to patients achieving significant response or pCR and non-responders may have worse outcome compared with patients treated with surgery only

• POST OP ADJUVANT CT:- Currently undefined. No improvement in locoregional control or overall survival (except R0,N1)
• POST OP ADJUVANT RT:- Improves local control, but not survival.
• POST OP ADJUVANT CT RT:- Improves local control and survival
In inoperable non metastatic Ca. Esophagus, the role of radiation is only palliative having median survival 6-12 mos. and 5 yrs survival rate is less than 10%.

Definitive chemoradiation improves local control and overall survival in comparison to radiation alone. (If patient medically unfit for surgery, lack of facility (experienced surgeon), cervical disease.)
THANK YOU