Surgery for Squamous Cell Cancer of the Esophagus: Only for Salvage or as Part of Combined Modality Therapy?

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AATS/STS General Thoracic Surgery Symposium
Seattle, WA
April 26, 2015
Esophageal Resections

Histology - MDACC

MDACC Thoracic Surgery Database
Esophageal Cancer

Case #1

52 yo female who developed dysphagia and found to have middle SCCA esophagus.

EGD-EUS-T3N1, 25-33 cm.  CT-PET- no distant metastases.  Bronchoscopy- No tracheal mucosa involvement
Esophageal Cancer Treatments

Type of Esoph after Chemoradiation

• **Definitive Chemoradiation** → → → Salvage Esophagectomy
  - RTOG 8501
  - FFCD 9102

• **Preoperative Chemoradiation** → Planned Esophagectomy
  - CROSS - Trimodality

• **Chemoradiation** → or → → → Selective Esophagectomy
  - RTOG 0246
Definitive Chemoradiation
Definitive Chemoradiation

SCCA– RTOG 85-01 – CRT vs RT alone

- 44% Locoregional Failure
- 7% Site of Recurrence Not Known

Definitive CRT

Herskovic et al., NEJM, 2001
### Definitive Chemoradiation

**RTOG 85-01 – Long-Term Results**

<table>
<thead>
<tr>
<th>Years</th>
<th>Adenocarcinoma</th>
<th>Squamous Cell</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (% Alive)</td>
<td>No. (% Alive)</td>
</tr>
<tr>
<td>0</td>
<td>23 (100%)</td>
<td>107 (100%)</td>
</tr>
<tr>
<td>1</td>
<td>12 (52%)</td>
<td>63 (59%)</td>
</tr>
<tr>
<td>2</td>
<td>5 (22%)</td>
<td>41 (38%)</td>
</tr>
<tr>
<td>3</td>
<td>4 (17%)</td>
<td>32 (33%)</td>
</tr>
<tr>
<td>4</td>
<td>3 (13%)</td>
<td>17 (26%)</td>
</tr>
<tr>
<td>5</td>
<td>3 (13%)</td>
<td>21 (21%)</td>
</tr>
<tr>
<td>Total Deaths</td>
<td>22/23</td>
<td>91/107</td>
</tr>
<tr>
<td>MST (95% CI):</td>
<td>12.2 mos</td>
<td>16.9 mos</td>
</tr>
</tbody>
</table>

Cooper et al., *JAMA*, 1999
Preop CRT → Surg
Preoperative Chemoradiation

*CROSS Trial*

van Hagen et al., *NEJM*, 2012
Preoperative Chemoradiation

*CROSS Trial*

van Hagen et al., *NEJM*, 2012
## Preoperative Chemoradiation

**CROSS Trial**

<table>
<thead>
<tr>
<th>Path CR</th>
<th>Adeno</th>
<th>SCCA</th>
<th>p</th>
</tr>
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<tbody>
<tr>
<td>CROSS</td>
<td>28/121 (23%)</td>
<td>18/37 (47%)</td>
<td>( P &lt; 0.008 )</td>
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*van Hagen et al., NEJM, 2012*
## Preoperative Chemoradiation

**CROSS Trial**

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<td>18/37 (47%)</td>
<td>P&lt;0.008</td>
</tr>
<tr>
<td>MDACC</td>
<td>55/193 (29%)</td>
<td>13/42 (31%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

*van Hagen et al., NEJM, 2012*

*Rohatgi et al., Cancer 2005*
Definitive CRT
vs
Preop CRT → Surg
dCRT vs CRT→Planned Eso

Squam Responders– FFCD 9102

Multi-center
Eso: SCCA
T3-4,N0-3,M0
N=455

Responders N=259

46Gy
5-FU/CDDP x 2

Surgery N=129

20Gy
5FU/CDDP x 3
N=130

Bedenne et al., JCO, 2007
dCRT vs CRT → Planned Eso

**Squam Responders - FFCD 9102**

1.63 HR Locoregional Relapse CRT Alone (p=0.03)

*Bedenne et al., JCO, 2007*
Def CRT vs Preop CRT→Surg
Squam – German Trial

T1-4a N0-3 M0
SCCA Multi-Center

RANDOMIZE

Chemo FLEP N=86

Chem/RT (Cis, Etop + 50 gy HF or 60 gy HDR)

Chemo/RT (Cis, Etop + 64.8 gy)

Surgery

Stahl et al., JCO, 2005
Chemo/RT +/- Surgery: Phase III
Esophageal Cancer: German Trial

Overall Survival

\[ p = \text{ns} \]

Stahl et al., JCO, 2005
Definitive CRT and Salvage Esophagectomy
## Results

### Hospital Factors

<table>
<thead>
<tr>
<th></th>
<th>Salvage C/RT Group (n=13)</th>
<th>Preop C/RT Group (n=99)</th>
<th>$p^*$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital Factors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ventilator (days)</td>
<td>9.0 ± 13.3</td>
<td>3.3 ± 8.1</td>
<td>0.08</td>
</tr>
<tr>
<td>ICU (days)</td>
<td>11.2 ± 13.3</td>
<td>5.1 ± 9.4</td>
<td>0.06</td>
</tr>
<tr>
<td>Hospital stay (days)</td>
<td>29.4 ± 22.4</td>
<td>18.4 ± 18.3</td>
<td>0.03</td>
</tr>
<tr>
<td>Anast. Leak (yes)</td>
<td>5 (38%)</td>
<td>7 (7%)</td>
<td>0.005</td>
</tr>
<tr>
<td>Op. Mort. (30 day)</td>
<td>2 (15%)</td>
<td>6 (6%)</td>
<td>0.2</td>
</tr>
</tbody>
</table>

*Swisher et al., JTCVS, 123:175-83, 2002*
## Salvage Esophagectomy

### Literature Review

<table>
<thead>
<tr>
<th>Reference</th>
<th>Hospital stay (days)</th>
<th>Anastomotic leakage or fistula (%)</th>
<th>Conduit necrosis (%)</th>
<th>Pneumonia (%)</th>
<th>In-hospital death (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meunier et al. 21</td>
<td>47*</td>
<td>33</td>
<td>16</td>
<td>16</td>
<td>33</td>
</tr>
<tr>
<td>Murakami et al. 11</td>
<td>n.r.</td>
<td>n.r.</td>
<td>25</td>
<td>0</td>
<td>25</td>
</tr>
<tr>
<td>Wilson et al. 5</td>
<td>14*</td>
<td>6</td>
<td>0</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Swisher et al. 22</td>
<td>29.4†</td>
<td>38</td>
<td>8</td>
<td>38</td>
<td>15</td>
</tr>
<tr>
<td>Nakamura et al. 3</td>
<td>39.9†</td>
<td>22</td>
<td>0</td>
<td>11</td>
<td>8</td>
</tr>
<tr>
<td>Tomimaru et al. 24</td>
<td>n.r.</td>
<td>20</td>
<td>0</td>
<td>20</td>
<td>12</td>
</tr>
</tbody>
</table>

Thorpe et al., Br J Surg, 2007
Salvage Esophagectomy in Modern Era
Salvage Esophagectomy
2 Stage Procedure

First Stage

Second Stage

27 High Risk Pts (7 Salvage)
No Increased Morbidity vs 118 Low Risk Pts

Salvage Esophagectomy

Free Jejunal Interposition

Jejunal Free Graft

Ascioti et al, Ann Thor Surg, 2005
Salvage Esophagectomy

Omental Transposition

Courtesy of David Rice MD
Salvage Esophagectomy

Omental Transposition

Courtesy of David Rice MD
MDACC: Omental Transpostion

Salvage Esophageal Anastomotic Leak

Sepesi et al., JTCVS,144:1146-51; 2012
## Salvage Esophagectomy

**Op Mortality – Modern Era**

<table>
<thead>
<tr>
<th></th>
<th>Salvage  n=65</th>
<th>Planned  n=521</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOS (days)</td>
<td>12 (4-153)</td>
<td>11 (0-88)</td>
<td>NS</td>
</tr>
<tr>
<td>30d Mortality</td>
<td>2 (3.1%)</td>
<td>15 (2.9%)</td>
<td>NS</td>
</tr>
<tr>
<td>90d Mortality</td>
<td>3 (4.6%)</td>
<td>27 (5.2%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

*Marks et al., AATS, 2012*
CRT and Selective Esophagectomy
RTOG 0246 Study Design

ELIGIBLE

Chemo
5-FU
Cisplatin
Paclitaxel

ChemoRT
5-FU
Cisplatin (50.4 Gy)

if Local Disease and no Mets

Selective Surgery

Residual

Recurrent

- SCCA/Adeno Eso/GEJ
- Clinical Stage > T1N0
- No Metastases
## Long-Term Outcome
(ChemoRT ± S Trials in Adeno/SCCA Eso/GEJ)

<table>
<thead>
<tr>
<th>Trial</th>
<th>3 yr OS</th>
<th>5 yr OS</th>
</tr>
</thead>
<tbody>
<tr>
<td>CROSS (CRTS)</td>
<td>60%</td>
<td>---</td>
</tr>
<tr>
<td>CALGB 9781 (CRTS)</td>
<td>63%</td>
<td>39%</td>
</tr>
<tr>
<td>RTOG 0246 (C→CRT Selective S)</td>
<td>44%</td>
<td>37%</td>
</tr>
<tr>
<td>SCOPE 1 (Def CRT)</td>
<td>27%</td>
<td>---</td>
</tr>
<tr>
<td>RTOG 8501 (Def CRT)</td>
<td>17%</td>
<td>13%</td>
</tr>
</tbody>
</table>
Esophageal Cancer

Case #1

Treated with Definitive Chemoradiation: Oxaliplatin and 5-fluorouracil and RT to 54.4 Gy.

EGD – ulcer, NED – refused surgery.
Esophageal Cancer

Case #1

16 months later dysphagia  CT-PET –Increase FDG (SUV 17) circum middle eso; EGD revealed necrotic SCCA in middle eso **Bronch:** Necrotic ulcer R BI with fragments of Squamous Cell Carinoma
Esophageal Cancer

Case #2

**EUS:** 16-19 cm, recurrent squamous cell carcinoma

**CT-PET:** proximal eso FDG avid lesion (SUV-8.9), no distant metastases

**Bronchoscopy:** fistulous communication 8 cm proximal to carina
SCCA Esophageal Cancer
MDACC Combined Modality Approach

Loco-Regionally SCCA Eso Cancer

Low Risk Surgery and Mid/Dist Location ➔ ChemoRT (50.4 Gy) ➔ Planned Esophagectomy

High Risk Surgery Or Cerv Location ➔ ChemoRT (50.4 Gy)

Selective Esophagectomy
Summary

SCCA Eso Cancer-Combined Modality Approach

- **Upper Eso Location** – laryngopharyngectomy
  - Definitive Chemoradation
  - Salvage Esophagectomy for Recurrent Local Disease

- **Middle/Lower Eso Location** – Good Risk
  - Preop CRT → Planned Esophagectomy

- **Middle/Lower Eso Location** – Poor Risk
  - CRT → Clin CR → Selective Esophagectomy for Recurrent Local Disease
  - CRT → Clin non-CR → Consider Selective Esophagectom