Salvage Surgery in Oropharyngeal Cancer

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Introduction

• Increasing trend in treating oropharyngeal SCC using radiation or chemoradiation protocols

• Invariably a number of patients will fail treatment and develop local and/or regional recurrences

• Represents a challenging situation
Introduction

• Surgical salvage is typically the treatment modality of choice for recurrent local and/or regional disease
• There is very limited data on long-term outcomes
• Its study is made difficult by the relatively small number of patients and the wide inclusion criteria
Introduction

- Surgery required to salvage may be associated with significant morbidity
- Long term survival for these patients is relatively poor
- QOL issues therefore become more important considerations
Salvaging the Neck
Salvaging Suspected Neck Disease

- High response rate of cervical nodes to CRT
- A neck dissection is not warranted systematically
  - Surgical complications
  - Not indicated for those with a complete response
Salvaging Suspected Neck Disease

- Post CRT imaging to
  - Evaluate response to treatment
  - Evaluate necessity of salvage surgery (and it’s feasibility)
- What imaging to use and when to use it?
  - PET
  - CT
Salvaging Suspected Neck Disease

- PET shows high sensitivity but low specificity
- Many features of nodes on CT that would predict negative path including:
  - Size
  - Absence of necrosis/calcifications/heterogeneity
  - No evidence of ECS
- Clavel et al. tried identifying CT characteristics that would more adequately predict pathological response of neck nodes to CRT
  - Reduction of $\geq 80\%$ of the max diameter of neck node post CRT was the best predictor of a negative path (NPV of 100%)
## Predictive Values of CT Characteristics

<table>
<thead>
<tr>
<th>Node characteristics</th>
<th>NPV (%)</th>
<th>PPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heterogeneity</td>
<td>91</td>
<td>27</td>
</tr>
<tr>
<td>Node $\leq 10$ mm</td>
<td>91</td>
<td>28</td>
</tr>
<tr>
<td>Node $\leq 15$ mm</td>
<td>86</td>
<td>33</td>
</tr>
<tr>
<td>$% \Delta D_{\text{max}} \geq 75%$</td>
<td>94</td>
<td>26</td>
</tr>
<tr>
<td>$% \Delta D_{\text{max}} \geq 80%$</td>
<td>100</td>
<td>26</td>
</tr>
</tbody>
</table>
Salvaging Local & Regional Disease
Salvage Surgery in Oropharyngeal Cancer

- 640 patients with tonsil ca treated with standard fractionation radiotherapy at the Princess Margaret Hospital in Toronto, Canada
- 239 (37.3%) developed local and/or regional failure with no distant metastasis
- 175 of the 239 (73%) patients were deemed candidates for surgical salvage
Salvage Surgery in Oropharyngeal Cancer

**Table 1** The percentage of patients developing local, regional, locoregional (LR) recurrence based on time

<table>
<thead>
<tr>
<th></th>
<th>Local recurrence only</th>
<th>Regional recurrence only</th>
<th>LR recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year 1</td>
<td>51 (76%)</td>
<td>33(81%)</td>
<td>60 (91%)</td>
</tr>
<tr>
<td>Year 2</td>
<td>12 (18%)</td>
<td>6 (15%)</td>
<td>5 (8%)</td>
</tr>
<tr>
<td>Year 3</td>
<td>2 (3%)</td>
<td>1(2%)</td>
<td>1(1%)</td>
</tr>
<tr>
<td>Total</td>
<td>67</td>
<td>42</td>
<td>66</td>
</tr>
</tbody>
</table>
Results

- Of the 175 patients who underwent surgical salvage, 7 (4.3%) died from complications related to surgery.
- The 2-year overall survival for patients with local, regional and locoregional recurrence was 48, 35, and 28% respectively.
- The prognosis of patients with locoregional recurrence was significantly worse ($p = 0.008$).
- Both the N-classification and T-classification were found to be significant predictors of time to death ($p = 0.0006$, and $p = 0.02$, respectively).
Survival Rates for the First 5 Years Following Salvage Surgery

<table>
<thead>
<tr>
<th># Years following surgery</th>
<th>Survival (%)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>58</td>
<td>(51–65)</td>
</tr>
<tr>
<td>2</td>
<td>40</td>
<td>(33–47)</td>
</tr>
<tr>
<td>3</td>
<td>30</td>
<td>(23–37)</td>
</tr>
<tr>
<td>4</td>
<td>26</td>
<td>(20–33)</td>
</tr>
<tr>
<td>5</td>
<td>23</td>
<td>(17–30)</td>
</tr>
</tbody>
</table>
Overall survival following salvage surgery

At the time of the last follow-up only 13 patients were alive and 162 patients had died, the majority of which died with disease.
Discussion

- Surgery remains the mainstay of salvage treatment
  - The use of re-irradiation with or without chemotherapy for salvage appears feasible and has been reported in the literature
  - Recent RTOG trial (2008)
    - Grade 4 or higher acute toxicity in over 25% of patients receiving concurrent chemo/radiation
    - Treatment related deaths in 8% of patients
Discussion

• Speech and swallowing are significantly affected after salvage surgery
• Knowing that long term prognosis is relatively poor, these QOL issues become more important considerations
Discussion

• Pacheco-Ojeda & al. and Nichols & al. described the importance of negative margins and their significant effect on prognosis and OS.
• Tumor margins be based on pre-treatment evaluation
• Selecting a surgical approach that allows adequate exposure is essential
• Second recurrence after salvage surgery in seen in 2/3 of cases
• Usually local recurrences followed by regional and distant mets
Discussion

- Zafereo & al. reported a higher second recurrence rate in those with
  - Absence of a disease-free interval
  - Recurrent neck disease
  - Positive surgical margins

- The presence of a disease free interval does not seem to affect overall survival but higher 3 year overall survivals have been reported
Discussion

- Long term follow-up demonstrates the high mortality rate in patients with recurrent disease despite undergoing salvage surgery
- Median disease free survival 7.8 months (Goodwin)
- The median time to death following salvage surgery is short at 1.3 years
- Median expected survival of 4 months for those with non treated recurrences
Conclusion

- The high recurrence rate and the short interval to these recurrences coupled with the high associated cost of treatment warrants realistic discussion on expectations.
- The best way to manage recurrences is to prevent it from occurring.
- Treatment protocols have been developed to try and improve locoregional control as well as survival.
Conclusion

- Despite the poor prognosis, 20%-25% of patients will be alive at 5 years
- Should be considered when possible
- Favorable candidates are younger, have small local recurrent tumors, no recurrent neck disease, negative margins and possibly have had a disease free interval
Thank you
## PET and regional disease

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>NPV (%)</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kim et al. 2011</td>
<td>39</td>
<td>92</td>
<td>91</td>
<td>65</td>
</tr>
<tr>
<td>Loo et al. 2011</td>
<td>27</td>
<td>100</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Mori et al. 2011</td>
<td>65</td>
<td>-</td>
<td>98</td>
<td>40</td>
</tr>
<tr>
<td>Hoshikawa et al. 2011</td>
<td>35</td>
<td>93</td>
<td>88</td>
<td>-</td>
</tr>
</tbody>
</table>
Discussion

- These results are in keeping with those from the MDACC experience in that 22% of patients were not able to communicate orally and that 32% were able to tolerate a soft or regular diet after salvage surgery.
- The majority of patients (51%) undergoing salvage surgeries for H&N cancer altogether achieves their baseline status or surpasses it within an average of 4.8 months.
- The likelihood of successful outcomes correlated with recurrent stage and patients operated on stage IV recurrences had only 39% chance of achieving or exceeding their baseline FLIC (functional living index for cancer) scores. (Goodwin)