Treatment of Oropharyngeal Cancer
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Head & Neck Oncologic Surgery
True confessions: Catherine Zeta-Jones admitted she was a 'mess' when her husband Michael Douglas was diagnosed with stage four tongue cancer in 2010
Objectives

• Treatment of HNSCC

• Oral vs Oropharyngeal Cancer

• Surgery for OPSCC
Take This Home

• Oral \neq Oropharyngeal
• White/Neck Mass/Unknown Primary=BOT or Tonsil
• TORS for Finding Unknown Primary

• CRT or SRT for Advanced T Stage OPSCC
• TORS or CRT for Early T Stage
Objectives

- Treatment of HNSCC
- Oral vs Oropharyngeal Cancer
- Surgery for OPSCC
Treatment of HNSCC
Oral, OP, Larynx, Hypopharynx
NCCN Guidelines

• Stage 1 or 2 HNSCC (ie, T1 or T2)
  – Radiation or Surgery
    • Although rarely used/indicated first line oral cavity

• Stage 3 or 4 HNSCC (ie, T3 or T4 or any N)
  – CRT or SRT
<table>
<thead>
<tr>
<th>Tumor Site</th>
<th>Stage 1-2</th>
<th>Stage 3-4</th>
<th>Recurrent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral Cavity</td>
<td>S &gt; RT</td>
<td>S + Adjuvant</td>
<td>S/RT/C/E</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>S = RT</td>
<td>S/Adj = CRT</td>
<td>S/RT/C/E</td>
</tr>
</tbody>
</table>

Surgical Therapy may redirect the use, type, and dosage of adjuvant therapy.
The Role of Surgery in HN Cancer

**All** cases of:
- Oral Cavity Cancer
- Sinus Cancer
- Thyroid Cancer
- Salivary Gland Cancer
- Melanoma
- Merkel Cell Cancer

**Some** cases of:
- Oropharyngeal Cancer
- Laryngeal Cancer
- Hypopharyngeal Cancer
- Nasopharyngeal Cancer
- Sarcoma
- Skin Cancer

*Non-metastatic*
Objectives

• Treatment of HNSCC

• Oral vs Oropharyngeal Cancer

• Surgery for OPSCC
Diagnosis
Oral Cavity vs Oropharyngeal

Oral
Etiology = Tobacco

Oropharyngeal
Etiology = HPV
“Early” Diagnosis

Oral Cavity

“Soreness or Red and white spots”

Oropharynx

“Sore throat or neck mass”
“Classic” Oropharyngeal Cancer
Demographics of Oropharyngeal Cancer Patients

HPV (-)
- Older
- African American
- Less Oral Sex/Partners
- Cigarette/Alcohol Use
- Lower SES

HPV (+)
- Younger
- European American
- More Oral Sex/Partners
- Non-smoker
- Higher SES

Oral vs OP Cancer Incidence

• Oropharynx - GREEN

• Oral - RED

• 70-80% of new OPSCC are HPV+
Human Papillomavirus and Rising Oropharyngeal Cancer Incidence in the United States


- HPV (-)
- HPV (+)

![Graph showing incidence rates for oropharynx overall, HPV-positive oropharynx, and HPV-negative oropharynx over calendar years.]
Survival - Oropharynx
Fakhry, et al, J NCI, 2008

• Overall Survival (1 and 2 Year)
  – HPV + = 97% and 95%
  – HPV - = 90% and 62%

• DFS
  – HPV + = 91% and 86%
  – HPV - = 69% and 53%

![Graph showing survival probability over time with HPV status]

**P-value = 0.004**
Diagnosis of Oropharyngeal Cancer

• Initial Presenting Symptoms
• Initial Presenting Signs
• Biopsy
  – Primary Site (Office vs Tonsillectomy)
  – Neck
  – Unknown Primary of the Head & Neck!?
    • Transoral Robotic Base of Tongue Resection/Biopsy with Tonsillectomy
50-60yo Caucasian Businessman
Lump in Neck While Shaving
Discussions about HPV with the Oropharyngeal Cancer Patient

- Etiology
- Acquisition
- Timing of Exposure
- Vaccine
- Spousal Concerns
"So you say to treat my cancer, I will need surgery and radiation or chemo and radiation treatments?"
“My wife thinks I have a sexually-transmitted cancer and wants to know where I got it!?”
Objectives

• Treatment of HNSCC

• Oral(OSCC) vs Oropharyngeal Cancer(OPSCC)

• Treatment for OPSCC
Oropharyngeal Cancer Treatment

• Stage I/II = Surgery or Radiation

• Stage III/IV = CCRT vs SRT (No Studies.....yet!)
  • CCRT
    – Post Treatment Scans +/- Neck Dissection
  • SRT
    – Pathology dictates adjuvant treatment
    – Upstaging vs Downstaging
    – 2 Modalities vs 3 Modalities
ECOG 3311 and RTOG 1016

ECOG 3311

Transoral Surgery Followed By Low-Dose or Standard-Dose Radiation Therapy With or Without Chemotherapy in Treating Patients With HPV Positive Stage III-IVA Oropharyngeal Cancer

RTOG 1016

PHASE III TRIAL OF RADIOTHERAPY PLUS CETUXIMAB VERSUS CHEMORADIOTHERAPY IN HPV-ASSOCIATED OROPHARYNX CANCER
Oropharyngeal Cancer

GORTEC Concomitant Chemo/XRT Trial


GORTEC Trial (J Natl Cancer Inst 91:2081-2086, 1999)
Final Results

Final Results of the 94-01 French Head and Neck Oncology and Radiotherapy Group Randomized Trial Comparing Radiotherapy Alone With Concomitant Radiochemotherapy in Advanced-Stage Oropharynx Carcinoma

Febrice Denis, Pascal Gersaud, Etienne Baudet, Marc Alfonsi, Christian Sere, Thierry Gemain, Philippe Bergerov, Beatrice Rhein, Jacques Tertohouse, and Gilles Calais

• Pattern of failure
  – Local 58% vs 41%
  – Regional 33% vs 19%

• Grade 3/4 Complications
  – 56% vs 30%
Fakhry, et al, J NCI, 2008
Survival by Smoking Status
RTOG 0129

Tobacco Smoking and Increased Risk of Death and Progression for Patients With p16-Positive and p16-Negative Oropharyngeal Cancer
Maura L. Gillison, Qiang Zhang, Richard Jordan, Weihong Xiao, William H. Westra, Andy Trotti, Sharon Spencer, Jonathan Harris, Christine H. Chung, and K. Kian Ang
Trans-Oral Robotic Surgery (TORS)
TORS Oncologic Efficacy

<table>
<thead>
<tr>
<th>Study</th>
<th># Pts</th>
<th>Stage</th>
<th>N+</th>
<th>F/U</th>
<th>Survival</th>
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<tbody>
<tr>
<td>Cohen 2010</td>
<td>50</td>
<td>T1-3</td>
<td>82%</td>
<td>24mos</td>
<td>1Yr=95.7% 2 Yr=80.6%</td>
</tr>
<tr>
<td>Weinstein 2010</td>
<td>47</td>
<td>T1-4</td>
<td>98%</td>
<td>26mos</td>
<td>OS 1 Yr=96% OS 2 Yr=82% DFS 1 Yr=96% DFS 2 Yr=79%</td>
</tr>
<tr>
<td>White 2010</td>
<td>89</td>
<td>T1-4</td>
<td>68%</td>
<td>26 mos</td>
<td>DFS All 86.3% DFS TORS 89.3%</td>
</tr>
<tr>
<td>Genden 2011</td>
<td>30</td>
<td>T1/2</td>
<td>80%</td>
<td>20.4mos</td>
<td>18mos DFS78% OS 90%</td>
</tr>
<tr>
<td>Weinstein 2012</td>
<td>30</td>
<td>T1-4</td>
<td>33%</td>
<td>18mos</td>
<td>OS 100% 1 LR, 3 RR</td>
</tr>
</tbody>
</table>
TORS vs RT
Swallowing Outcomes

Median MDADI Scores Primary XRT v. TORS

- Median PXRT
- Median TORS

40 Patients
Transoral Laser Microsurgery (TLM) for OPSCC
Haughey, et al, 2011

• 204 pts, T1-4
• Overall Survival =
  – 89%(2yr) and 78%(5yr)
• Disease Specific Survival =
  – 91%(2yr) and 84%(5yr)
• Gtube Dependency =
  – (1 Yr=18.8%, 2 Yr=9.3%, 5 yr=3.8%)
  – 39/89 Gtube at some point
• Tracheotomy (18% temporary)
TLM
Swallowing Outcomes (FOSS)

FIGURE 7. Distribution of FOSS (Functional Outcome Swallow-
Chemoradiotherapy

Machtay 2002

Pignon 2000

Dennis 2004

VS.

TORS + adjuvant

White 2010

Weinstein 2010

Genden 2011
Chemoradiotherapy

3 YR OS 82%
Ang 2010

2 YR OS 88%
Gillison 2000

2 YR OS 88%
Gillison 2000

VS.

3 YR OS 82%
Ang 2010

2 YR OS 95%
Fakhry 2002

Genden 2011

Chemoradiotherapy + TORS + adjuvant

Weinstein 2010
Surgical Approaches to Oropharyngeal Cancer

BEFORE!
AFTER!
TORS Base of Tongue Resection
TORS Video

• Base of tongue video:
Algorithm - Oral Cancer

Stage I-IVA

Tumor Board

Surgery

Contraindication?

ND

Radiation

Adjuvant Therapy?
Algorithm - Early Stage OPSCC

Stage I-II

Tumor Board

Radiation

Surgery

TORSTM

TTS

ND

Adjuvant Therapy?
Algorithm-Late Stage OPSCC

Stage III-IV OPSCC

Tumor Board

Chemotherapy
Radiation

Surgery

TORS  TLM  TTS  TOTC

ND

Adjuvant Therapy?
Current TORS OPSCC treatment algorithm

Any T Any N OPSCC

TORS + SND

T1-3 N0

- PNI, - LVI, - margins → observation

+ PNI or + LVI, or + margins → adjuvant XRT*

Any T N2+ or T4 N0

- ECS & - margins → adjuvant XRT*

+ ECS or + margins → adjuvant Chemo + XRT

*adjuvant XRT to 60 Gy
**MUSC Protocol for OPSCC**

### Stage I/II OPSCC

<table>
<thead>
<tr>
<th>Surgery recommended for most</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radiation recommended for:</td>
</tr>
<tr>
<td>- Soft Palate involvement</td>
</tr>
<tr>
<td>- High risk perioperative morbidity</td>
</tr>
</tbody>
</table>

### Stage III/IV OPSCC

<table>
<thead>
<tr>
<th>Surgery recommended for:</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Early T stage</td>
</tr>
<tr>
<td>- Potential for downstaging</td>
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<table>
<thead>
<tr>
<th>Chemoradiation recommended for</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Extensive soft palate involvement</td>
</tr>
<tr>
<td>- Bilateral base of tongue or involving contralateral neurovascular bundle</td>
</tr>
<tr>
<td>- Carotid involvement</td>
</tr>
<tr>
<td>- High risk perioperative morbidity</td>
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Surgery or No Surgery?
Summary

• Head and neck cancer treatment should follow NCCN guidelines of surgery or radiation for early stage and combined chemoradiation or surgery/(c)radiation for advanced stage

• The terms “Oral” and “Oropharyngeal” cancer are often used synonymously but they represent different diseases with dramatically different etiopathogenesis, treatment and outcomes

• Oropharyngeal Cancer treatment should be tailored to the patient’s desires and resultant side effects and toxicities that may affect quality of life
Thank You!
Case 1

- **CC:** 43 yo male presents to his primary care physician with a painless right neck mass

- **Social hx:** married and positive for alcohol use (12 beers/day) and smoking (30 pack year)
Exam
PET/CT

• Hyper-metabolic activity along right tonsilar pillar

• Hyper-metabolic lymphadnopathy (right neck)
Staging

- Tonsil biopsy – SCCA, p16 +

- T2N1M0 SCCA right tonsil
  – (mild extension to BOT)

- “Doc, tell me what you think we should do?”
Panel Questions

- Single modality treatment vs. multimodality treatment
- Surgical excision +/- adjuvant treatment OR Radiation therapy +/- chemotherapy
- Management of the neck disease
Outcome

- Trans-oral robotic resection (TORS) and right neck dissection

- Negative margins, +LVI, +PNI

- 2/33 lymph nodes (<3cm) positive for SCCA, no ECE
Panel Questions

• Radiation?

• Radiation and chemotherapy?
Post-Treatment Exam 12 weeks

- Patient underwent adjuvant treatment with chemotherapy and radiation therapy
- No functional swallowing deficits
Case 2

- 50 y/o M presents with large right neck mass x 4 months

- Occasional right sided sore throat

- Non-smoker, rare Etoh

- No significant past surgical history

- Pmh: htn, hld, GERD
Exam

- Right sided 4 cm neck mass which is firm but mobile
- OC clear
- Flexible laryngoscopy
Imaging

• R BOT mass

• Cystic Right neck mass measuring 3.5 cm

• Biopsy of base of tongue mass reveals SCCA, p16+
Treatment

• Staged as a T2N2a of the right BOT (extension to right tonsillar fossa and vallecula)

• Surgery + adjuvant treatment?

• Concurrent Chemoradiation?
Questions

• With such large lymphadenopathy, would you expect ECE thereby calling for chemotherapy?

• Is there potential for de-escalation of adjuvant therapy in this patient if surgery is performed with clear margins?
Outcome

• The patient was given a surgical and non-surgical option

• Patient chose CRT, currently in treatment