Transoral robotic Surgery in the era of HPV epidemic

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Disclosures

- PCT PATENTS
- TECHNOLOGY DEVELOPMENT AGREEMENTS
- IN-PART BY NMRC B & B
Outline

• 1. Background of OPSCC – new epidemic

• 2. TORS in oropharyngeal cancer – new paradigm in surgical treatment

• 3. Future advances in robotic technology
Oropharyngeal squamous cell cancer (OPSCC)

- HPV associated OPSCC has reached epidemic proportion in Western countries
- Distinct biology compared with HPV negative cohort
- Portends a better prognosis -
- Role of de-escalation of treatment
# OPSCC

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<thead>
<tr>
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<td>Older (&gt;60 years)</td>
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## OPSCC

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42 year old lady
p16 IHC
# HPV induced OPSCC and Survival

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<tr>
<th>Study</th>
<th>Study design</th>
<th>HPV detection method</th>
<th>Treatment</th>
<th>HPV status</th>
<th>Tumour stage</th>
<th>Outcomes</th>
<th>Results</th>
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<tr>
<td>Fakhry et al, 2008</td>
<td>Prospective study within ECOG 2399 trial N = 96, 34 larynx 2 yr followup</td>
<td>In situ hybridisation and PCR</td>
<td>Induction chemo followed by chemoradiation</td>
<td>HPV+ - 38</td>
<td>Stage 3 - 11</td>
<td>OS - 95%</td>
<td>Stage 4 - 27 OS - 86% p = 0.02</td>
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<td>HPV- - 58</td>
<td>Stage 3 - 23</td>
<td>OS - 62%</td>
<td>Stage 4 - 35 OS - 53% p = 0.01</td>
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<td>p = 0.62</td>
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<td>Ang et al, 2010</td>
<td>Retrospective analysis within RTOG 0129 study N = 323 3 yr followup</td>
<td>In situ hybridization</td>
<td>Accelerated vs standard fractionation RT with concurrent cisplatin</td>
<td>HPV+ - 206</td>
<td>Stage 3 - 25</td>
<td>OS - 82.4%</td>
<td>Stage 4 - 181 OS - 73.7% p = 0.30</td>
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<td>HPV- - 117</td>
<td>Stage 3 - 19</td>
<td>OS - 57.1%</td>
<td>Stage 4 - 98 OS - 43.4% p &lt; 0.001</td>
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<td>Stage 4 - 98</td>
<td>p = 0.30</td>
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<td>Rischin et al, 2010</td>
<td>Retrospective analysis within TROG 02.02 trial N = 185 2 yr followup</td>
<td>p16</td>
<td>Chemoradiation with and without tirapazamine</td>
<td>HPV+ - 106</td>
<td>Stage 3 - 6</td>
<td>OS - 91%</td>
<td>Stage 4 - 100 FFS - 87% p = 0.12</td>
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<td>HPV- - 79</td>
<td>Stage 3 - 10</td>
<td>OS - 74%</td>
<td>Stage 4 - 69 FFS - 72% p = 0.003</td>
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<td>Stage 4 - 10</td>
<td>p = 0.12</td>
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<td>Posner et al, 2011</td>
<td>Retrospective analysis within TAX 324 trial N = 111 5 yr followup</td>
<td>PCR</td>
<td>Induction chemo (TPF vs PF) followed by chemoradiation</td>
<td>HPV+ - 56</td>
<td>Stage 3 - 10</td>
<td>OS - 82%</td>
<td>Stage 4 - 46 OS - 78% p = 0.27</td>
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<td>HPV- - 55</td>
<td>Stage 3 - 5</td>
<td>OS - 35%</td>
<td>Stage 4 - 50 FFS - 28% p &lt; 0.0001</td>
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<td>Stage 4 - 50</td>
<td>p = 0.27</td>
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Legend:
Low risk: HPV +ve, < 10 packs/year cigarette
Intermediate risk: HPV+ve with N0-N2; or HPV-ve with <10 pack/year, T2-T3
High risk: HPV-ve, smoker , advanced T4
High-risk HPV genotypes and P16INK4a expression in a cohort of head and neck squamous cell carcinoma patients in Singapore

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Keywords: human papillomavirus, p16 immunohistochemistry, HPV DNA, head and neck squamous cell carcinoma, oropharyngeal squamous cell carcinoma

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[Graphs showing overall survival and disease-specific survival]
Rational of surgery in HPV positive OPSCC

• 1) Small primary – amendable for transoral resection
• 2) Younger cohort- minimize long term sides effects of RT
• 3) Aids accurate pathological assessment
Emerging surgical trend in treating OPSCC

- Increased HPV induced OPSCC

- 1) Small primary – amendable for transoral resection
Emerging surgical trend in treating OPSCC

- 2) Younger cohort - minimize long term sides effects of RT
6 weeks post CRT for p16 +ve Rt Tonsillar Cancer
Emerging surgical trend in treating HPV positive OPSCC

• Aids accurate pathological assessment for possible De-escalation
Phase II Randomized Trial of Transoral Surgical Resection followed by Low-dose or Standard-dose IMRT in Resectable p16+ Locally Advanced Oropharynx Cancer (E3311)

- p16+, Stage III/IV (cT1-2N1-N2b) OPSCC
- Credentialing of surgeon required as part of site participation in the trial
- Stratify by stage and smoking status
ECOG 3311 p16+ trial schema

Assess Eligibility:
- HPV (p16)+
- SCC oropharynx
- Stage III-IV: cT1-2, N1-2b
- Baseline Functional/QOL Assessment

LOW RISK:
- T1-T2N0-N1 negative margins
  - Observation
  - Radiation Therapy IMRT 50Gy/25 Fx

INTERMEDIATE:
- Clear/close margins < 1mm ECS
- 2-4 metastatic LN PNI, LVI
  - Evaluate 2-year PFS Local-Regional Recurrence, Functional Outcomes/QOL

HIGH RISK:
- Positive Margins > 1mm ECS or ≥5 metastatic LN
  - Radiation Therapy IMRT 60 Gy/30 Fx +
    - Radiation Therapy IMRT 66 Gy/33 Fx + CDDP 40 mg/m² weekly
  - Accrual goal = 377
Traditional approach vs TORS in OPSCC

1980s to 2009

2009 till present
Starting a robotic head and neck surgery program

• 1) Re-learning anatomy - ”inside-out”
• 2) Building a team
• 3) Credentialing
• 4) Appropriate patient selection
• 5) Continuous education/ training and credentialing
• Anatomy is the road map for surgeons

• Re-learning the “inside-out” or “medial to lateral” approach
Transoral Anatomy of the Tonsillar Fossa and Lateral Pharyngeal Wall: Anatomic Dissection With Radiographic and Clinical Correlation

Chwee Ming Lim, MD; Vikas Mehta, MD; Raymond Chai, MD; Carlos-Neto D. Pinheiro, MD; Tanya Rath, MD; Carl Snyderman, MD, MBA; Umamahewswar Duvvuri, MD, PhD

Objectives/Hypothesis: To evaluate the transoral anatomy of the tonsillar fossa and lateral pharyngeal wall and to correlate these findings with radiographic measurements and transoral robotic surgery (TORS) of patients with early tonsillar tumor.

Study Design: Preclinical cadaveric study and patient cohort.

Methods: Six complete cadaveric dissections were performed to identify key anatomic landmarks, and these landmarks were validated in two consecutive patients with T1 human papillomavirus-positive squamous cell carcinoma of the tonsil treated by TORS. For radiographic landmark analysis, 25 patients who underwent contrast-enhanced computed tomography (CT) of the neck for a variety of endoscopic skull base procedures were selected. Measurements were taken from the lateral pharyngeal wall at C2-C3 interspace and greater horn of hyoid (C6) to the external carotid artery (ECA).

Results: The glossopharyngeal (IX) nerve was consistently identified deep to the superior constrictor musculature and at the intersection of the posterior tonsillar pillar with the base of tongue. The styloglossus muscle forms the deep plane medial to the ECA. The mean measurements for left C2-C3 interspace to the ECA and right C2-C3 interspace to ECA were 17.6 ± 0.8 mm and 18.4 ± 0.8 mm, respectively. Similarly, the mean measurements for left hyoid to ECA and right hyoid to ECA were 3.4 ± 0.8 mm and 4.3 ± 0.6 mm, respectively.

Conclusions: A systematic approach to dissect the tonsillar fossa and lateral pharyngeal wall can be performed using key anatomic landmarks. CT measurements taken at the C2-C3 interspace and greater horn of hyoid bone (C6 level) to the ECA are consistently and reliably achieved.

Key Words: Transoral robotic surgery, tonsillar fossa, lateral pharyngeal wall, anatomic dissection.
Consistent identification of main trunk of IX nerve

- a) IX nerve
- b) Superior constrictor
- c) Styloglossus

IX nerve identified at intersection point of posterior tonsillar pillar and base of tongue after superior constrictor musculature transected and reflected medially
Branches of IX nerve

a) Styloglossus
b) Branch of IX nerve running towards lateral pharyngeal wall
c) Main IX nerve

Branches of IX nerve (after robotic radical tonsillectomy)

Head
Clinical correlation

- Main trunk of IX preserved following TORS for T1 tonsil cancer
• Prof Wang Cheng Yuan
• Visting Scholar UPMC
• 2012-2013
TORS Set up

Figure 1: Operating Room Setup for da Vinci TORS
TORS set up
Transoral exposure
T1No SCC left tonsil
T1N1M0 CA BOT
P16 Positive
TORS for oropharyngeal cancer
TORS for salvage
Oncologic results

• Primary Aim is negative margin resection
Pathology report

Margins:
Left aryepiglottic margin: 0.7 cm (J2)
Left base of tongue: 0.9 cm (J4)
Right base of tongue: 1.0 cm (J7)
Deep margin: 0.4 cm (J4)

DIAGNOSIS

(A) Right tongue base, (B) left tongue base, (C) right false cord, (D) left false cord, (E) Left pyiform, (F) Left arytenoid, (G) deep margin, and (H) pre-epiglottic tissue:
- Negative for malignancy.

(J) Tumour of the epiglottis, supraglottic laryngectomy:
- Squamous cell carcinoma, moderately differentiated, involving the epiglottis and extending to the left base of tongue,
- Margins are free of tumour.

Ordering Doctor: LIM CHWEE MING (06438G)

Results:
- There is no evidence of malignancy.

DIAGNOSIS
- (A) Left hypopharynx margin; biopsy: Negative for malignancy.
- (B) Medial pharyngeal wall margin; biopsy: Negative for malignancy.
- (C) Deep margin; biopsy: Negative for malignancy.
- (D) Superior margin; biopsy: Negative for malignancy.
- (E) Left tongue base margin; biopsy: Negative for malignancy.
- (F) Left pharyngeal wall tumour, partial oropharyngectomy:
  - Squamous cell carcinoma, moderately differentiated.
  - Tumour invades into superficial layers of skeletal muscle tissue.
- All margins are free of tumour.
Appropriate selection
PET CT
Managing bleeding complications in TORS

• Scenarios
  1) Primary intraoperative bleed
  2) Secondary postoperative bleed
HEMORRHAGE DURING TORS
TORS T1 BOT SCC
Transoral clipping of vessel during TORS
Pre-emptive clipping of vessels transorally
Analysis of post–transoral robotic-assisted surgery hemorrhage: Frequency, outcomes, and prevention

Rajarsi Mandal, MD, Umamaheswar Duvvuri, MD, PhD, Robert L. Ferris, MD, PhD, Thomas M. Kaffenberger, BS, Garret W. Choby, MD, Seungwon Kim, MD

1Department of Otolaryngology, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania, 2Veterans Affairs Pittsburgh Health System, Pittsburgh, Pennsylvania, 3University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania.

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ABSTRACT: Background. Transoral robotic-assisted surgery (TORS) carries a small, but not insignificant, risk of life-threatening postsurgical hemorrhage. The purpose of this study was to analyze all post-TORS hemorrhagic events at our institution to establish preventative recommendations.

Methods. We conducted a retrospective review of 224 consecutive patients who underwent TORS for any indication at a single tertiary care institution.

Results. Twenty-two patients (n = 22; 9.82%) had varying degrees of postoperative bleeding. An impaired ability to protect the airway at the time of hemorrhage increased the rate of severe complications. Prophylactic transcervical arterial ligation did not significantly decrease overall postoperative bleeding rates (9.1% vs 9.9%; p = 1.00); however, there was a trend toward decreased hemorrhage severity in prophylactically ligated patients (3.0% vs 7.3%; p = .7040).

Conclusion. Prophylactic transcervical arterial ligation may reduce the incidence of severe bleeding following TORS. Post-TORS patients displaying an inability to protect the airway should be strongly considered for prophylactic tracheostomy to assist airway protection. © 2015 Wiley Periodicals, Inc. Head Neck 00: 000–000, 2015

KEY WORDS: transoral robotic-assisted surgery (TORS), TORS hemorrhage, TORS bleeding, TORS complications, prophylactic arterial ligation
Summary

• Pre-emptive ligation of vessels in the neck appeared to decrease the severity of bleeding in patients undergoing TORS

• Airway control management is the utmost importance in minimizing mortality in patients who developed bleeding post TORS
Sagittal anatomy of lingual artery
Beware of anatomical variants
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*da Vinci SP Surgical System is still in development, not 510(k) cleared and the safety or effectiveness of the product has not been established. The product is not currently for sale in the US.*

da Vinci X and da Vinci SP are not currently registered or available for sale in Singapore.
Future directions

1) Flexible and adaptive robotic system

2) New platforms
   - ultrasound
   - Intraoperative margins evaluation – eg Raman spectroscopy
   - laser

Vessel identification (real time)