Management of Early Glottic Cancers: Role of Surgery vs Radiation Therapy

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Basic Anatomy
# Staging of Glottic Cancer

**TABLE I.**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tis</td>
<td>Tumor in situ without frank invasion of the basement membrane</td>
</tr>
<tr>
<td>T1</td>
<td>Tumor limited to the vocal cord</td>
</tr>
<tr>
<td>T1a</td>
<td>Tumor limited to one vocal cord</td>
</tr>
<tr>
<td>T1b</td>
<td>Tumor involves both vocal cords</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor extends to supraglottic and/or subglottis and/or with impaired vocal cord mobility</td>
</tr>
<tr>
<td>T3</td>
<td>Tumor limited to the larynx with vocal cord fixation and/or invades the paraglottic space and/or inner cortex of the thyroid lamina</td>
</tr>
<tr>
<td>T4a</td>
<td>Tumor invades through the thyroid cartilage and/or invades beyond the larynx</td>
</tr>
<tr>
<td>T4b</td>
<td>Tumor invades prevertebral space, encases carotid artery, or invades mediastinum</td>
</tr>
</tbody>
</table>

Excerpts from AJCC Cancer Staging Manual, May 2002
Right Glottic T₁N₀M₀ SCCa
Evolving thoughts in management
How to Assess which modality is better?

- Mendenhall et al brought up the question with three angles:
  - Local control
  - Voice Quality
  - Cost

Local Control

- **Control Rates** (assessed from meta-analyses)
  - Trans-oral Laser Resection
    - 80-90% for T1
    - 70-85% for T2
  - Open Partial Laryngectomy
    - 90-95% for T1
    - 70-90% for T2
  - Radiotherapy
    - 85-94% for T1
    - 70-80% for T2

Local Control

- Factors that influenced treatment:
  - Anterior commissure involvement hindered adequate transoral resection
  - Complications of open partial laryngectomy (subglottic stenosis, bleeding, infection, aspiration pneumonia) occurred too frequently (6-8%)
  - Significant number of T2 lesions are unfavorable for transoral laser resection due to location or size

Recommendation: Treat all T1 and T2 with XRT, T1a may be given the option of transoral laser resection

Agrawal N & Ha P:

- Improved Transoral Microsurgery techniques
- Decrease in Open procedures
- Improved rates of local control with Laser surgery and XRT
- Laryngeal Preservation following XRT failures has improved
Trending Changes in Management

- Transoral Laser Resection
  - Final Local Control Rate including salvage therapy – 97-98%
  - Laryngeal Preservation – 90-99%
  - 5 year disease-specific survival – 90-98%

- Radiotherapy
  - Final Local Control Rate including salvage therapy – 90-96%
  - Laryngeal Preservation – 83-95%
  - 5 year disease-specific survival – 95-98%

Trending Changes in Management

- Improvements in Radiation & Surgery:
  - 65 Gy is minimum total dose needed to ensure local control
  - Use of 2.25 Gy daily dose results in greater local control
  - Treatment lasting less than 40 days has better local control results than those lasting greater (95-100% vs 79-84%)
  - Early stage recurrences treated with trans-oral laser resection

Trending Changes in Management

- Local control along with laryngeal preservation rates now roughly similar
- Further work by Steiner suggests that anterior commissure is no longer a detrimental finding
- Radiation therapy results improved

Recommendation: Laser Resection and Radiation therapy may be equally effective – care should be decided based on the individual

Voice Quality
Radiation effects

- Changed mucosal fold wave
- Stiff mucosa wave dynamics
- Hyperventricular fold activity
- Chronic inflammation
- Fold tissue inelasticity
- Glottal incompetence
## Voice Quality

<table>
<thead>
<tr>
<th>Therapy</th>
<th>n/stage</th>
<th>Moment of assessment</th>
<th>Voice outcome</th>
<th>Quality of life</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hirano, 1985 [9]</td>
<td>ES 17 T1a</td>
<td>3 m</td>
<td>Yes*</td>
<td>No</td>
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<tr>
<td>RT 14 T1a</td>
<td>3 m</td>
<td></td>
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<tr>
<td>Elner, 1988 [5]</td>
<td>ES 10 T1a</td>
<td>12 m</td>
<td>Yes*</td>
<td>No</td>
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<tr>
<td>RT 15 T1a</td>
<td>12 m</td>
<td></td>
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<tr>
<td>Epstein, 1990 [6]</td>
<td>ES 13 T1a</td>
<td>31 m</td>
<td>Yes*</td>
<td>No</td>
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<tr>
<td>RT 42 T1a</td>
<td>59 m</td>
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<td></td>
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<tr>
<td>Ott, 1992 [18]</td>
<td>ES 15 T1</td>
<td>1 to 8 yrs</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>RT 13 T1/T2</td>
<td>1 to 8 yrs</td>
<td></td>
<td></td>
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<tr>
<td>Cragle, 1993 [3]</td>
<td>ES 11 T1</td>
<td>5 to 58 m</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>RT 20 T1</td>
<td>1 to 7 yrs</td>
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<tr>
<td>McGuirt, 1994 [16]</td>
<td>ES 11 T1a</td>
<td>&gt;6 m</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>RT 13 T1a</td>
<td>&gt;6 m</td>
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<td></td>
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<tr>
<td>Rydell, 1995 [21]</td>
<td>ES 18 T1a</td>
<td>3 and 24 m</td>
<td>Yes*</td>
<td>No</td>
</tr>
<tr>
<td>RT 18 T1a</td>
<td>3 and 24 m</td>
<td></td>
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<tr>
<td>Rosier, 1998 [20]</td>
<td>ES 6 T1a</td>
<td>&gt;4 yrs</td>
<td>Yes</td>
<td>No</td>
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<tr>
<td>RT 7 T1a</td>
<td>&gt;4 yrs</td>
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<tr>
<td>Delsupehe, 1999 [4]</td>
<td>ES 30 T1/T2</td>
<td>6 and 24 m</td>
<td>Yes</td>
<td>No</td>
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<tr>
<td>RT 12 T1/T2</td>
<td>6 and 24 m</td>
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<tr>
<td>Wedman, 2002 [27]</td>
<td>ES 15 T1a</td>
<td>2 to 15 yrs</td>
<td>Yes*</td>
<td>No</td>
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<tr>
<td>RT 9 T1a</td>
<td>2 to 15 yrs</td>
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<tr>
<td>Stoeckli, 2001 [24]</td>
<td>ES 40 T1/T2</td>
<td>&gt;4 yrs</td>
<td>No</td>
<td>No</td>
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<tr>
<td>RT 16 T1/T2</td>
<td>&gt;4 yrs</td>
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<tr>
<td>Smith, 2003 [23]</td>
<td>ES 30 Tis/T1</td>
<td>n.i.</td>
<td>No</td>
<td>Yes</td>
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<tr>
<td>RT 11 Tis/T1</td>
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</tbody>
</table>
# Voice Quality Evaluation Tools

## Voice Handicap Index (VHI)
*(Jacobson, Johnson, Grywalski, et al.)*

Instructions: These are statements that many people have used to describe their voices and the effects of their voices on their lives. Check the responses that indicate how frequently you have the same experience.

(Never = 0 points; Almost Never = 1 point; Sometimes = 2 points; Almost Always = 3 points; Always = 4 points)

<table>
<thead>
<tr>
<th></th>
<th>Never</th>
<th>Almost Never</th>
<th>Sometimes</th>
<th>Almost Always</th>
<th>Always</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1. My <strong>voice</strong> makes it difficult for people to hear me.</td>
<td></td>
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<tr>
<td>F2. I ran out of air when I talk</td>
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<td>F3. People have difficulty understanding me in a noisy room</td>
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<td>F4. The sound of my voice varies throughout the day.</td>
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<td>F5. My family has difficulty hearing me when I call them throughout the house.</td>
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<td>F6. I use the phone less often than I would like.</td>
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<tr>
<td>F7. I'm tense when talking with others because of my voice.</td>
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<td>F8. I tend to avoid groups of people because of my voice.</td>
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<tr>
<td>F9. People seem irritated with my voice.</td>
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<tr>
<td>P10. People ask, &quot;What's wrong with your voice?&quot;</td>
<td></td>
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<tr>
<td>F11. I speak with friends, neighbors, or relatives less often because of my voice.</td>
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<tr>
<td>F12. People ask me to repeat myself when speaking face-to-face.</td>
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<td>F13. My voice sounds creaky and strained.</td>
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<td>P14. I feel as though I have to strain to produce voice</td>
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<tr>
<td>E15. I find other people don't understand my voice problem.</td>
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<td>F16. My voice difficulties restrict my personal and social life.</td>
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<tr>
<td>P17. The clarity of my voice is unpredictable.</td>
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<tr>
<td>P18. I try to change my voice to sound different.</td>
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<tr>
<td>F19. I feel left out of conversations because of my voice.</td>
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<td>P20. I use a great deal of effort to speak.</td>
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<tr>
<td>P21. My voice is worse in the evening.</td>
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<tr>
<td>P22. My voice problem causes me to lose income.</td>
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<tr>
<td>E23. My voice problem upsets me.</td>
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<tr>
<td>E24. I am less outgoing because of my voice problem.</td>
<td></td>
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<tr>
<td>E25. My voice makes me feel handicapped.</td>
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<tr>
<td>P26. My voice &quot;gives out&quot; on me in the middle of speaking.</td>
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</tr>
<tr>
<td>E27. I feel annoyed when people ask me to repeat.</td>
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<tr>
<td>E28. I feel embarrassed when people ask me to repeat.</td>
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<tr>
<td>E29. My voice makes me feel incompetent.</td>
<td></td>
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<tr>
<td>E30. I'm ashamed of my voice problem.</td>
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</tbody>
</table>
Voice Quality Evaluation Tools

**YOUR VOICE-RELATED QUALITY OF LIFE QUIZ**

**Because of my voice....**

I have trouble speaking loudly or being heard in noisy situations.

I run out of air and need to take frequent breaths when talking.

I do not know what will come out when I begin speaking.

I am anxious or frustrated.

I get depressed.

I have trouble using the telephone.

I have trouble doing my job or practicing my profession.

I avoid going out socially.

I have to repeat myself to be understood.

I have become less outgoing.

**How much of a problem is this?**

1 2 3 4 5

**Your Quiz Score** | **Your Voice-Related Quality of Life (V-RQOL) Score**
---|---
10 | 100 (excellent)
20 | 75 (fair to good)
30 | 50 (poor to fair)
40 | 25 (poor)
50 | 0 (worst possible)
Voice Quality

- McGuirt et al:
  - 24 patients with T1a Glottic SCC
    - 11 patients in surgical arm (all with resection of less than half of cordal depth)
    - 13 patients in XRT arm (~63 Gy)
  - Only male patients
  - Evaluations performed 6 months post-treatment
  - No recurrence encountered in any patient

Voice Quality

Voice Quality

- The following aspects measured:
  - Maximum Phonation Time
  - Intensity
  - Fundamental Frequency (pre-op vs post-op)
  - Perturbation scores
  - Voicing Percentage

Voice Quality

- Results:
  - Radiation and Surgery showed benefits in different categories

Recommendation:
Treatment of early glottic carcinoma by laser resection is more expedient and cost-effective than irradiation.

Krengli et al: 57 Patients with T1a SCC
- 30 treated with CO2 laser cordectomy
- 20 treated with radiation therapy

Voice Quality

• Evaluations performed 2 yrs post-treatment completion

• Results:
  • 25% of XRT arm demonstrated severe glottic inadequacy
  • 65% of surgical arm showed insufficient ventricular compensation or arytenoid hyperadduction
  • Patients whose surgery did not include resection of vocalis muscle did better than those whose did
  • Severe dysphonia noted in 25% of XRT arm vs 70% of surgical arm

• Recommendation: Radiation Therapy

Voice Quality

- Peeters et al:
  - 102 pts T1a subepithelial or subligamental glottic SCC
  - 56 pts in surgical arm
  - 46 pts in XRT arm
  - Pts with mucosal wave treated with CO₂ laser
  - Pts with absent mucosal wave treated with XRT

Voice Quality

- VHI
  - 60% of surgical arm with normal scores
  - 42% of XRT arm with normal scores
  - Greater Problems with intelligibility on XRT than Surgery (60% vs 39%)
  - Vocal deterioration by nighttime greater in XRT than Surgery (70% vs 49%)

Voice Quality

• Conclusions:
  • T1a Glottic Cancer patients should undergo routine videostroboscopy
  • T1a Glottic Cancer treated with radiation noted more voice-related problems than surgery
  • Treatment should be guided by depth of invasion

Recommendation: Superficial tumors, where a wave is still present, should be treated with surgery

Voice-Related Quality of Life

- Meta-Analysis
  - 6 studies
  - 208 patients treated with Trans-oral Laser Excision
  - 91 treated with External Beam Radiation Therapy
  - All with T1 Glottic SCC
  - All patients completed pre- and post-op Voice Handicap Index (VHI) questionnaires

## Voice-Related Quality of Life

### TABLE 2. VHI ACCORDING TO TREATMENT

<table>
<thead>
<tr>
<th>Authors</th>
<th>Mean</th>
<th>95% CI</th>
<th>Group</th>
<th>Extent of Resection*</th>
<th>Radiation Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loughran et al\textsuperscript{8}</td>
<td>25.3</td>
<td>11.1-39.5</td>
<td>CLE</td>
<td>Superficial lamina propria, ligament, medial vocalis</td>
<td></td>
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<tr>
<td>Peretti et al\textsuperscript{15}</td>
<td>25.4</td>
<td>13.2-37.7</td>
<td>EBRT</td>
<td>Superficial vocalis, total and extended cordectomy</td>
<td>55 Gy in 6 weeks</td>
</tr>
<tr>
<td>Brondbo and Benninger\textsuperscript{17}</td>
<td>13.2</td>
<td>9.6-16.8</td>
<td>CLE</td>
<td>Superficial lamina propria</td>
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<tr>
<td>Peeters et al\textsuperscript{18}</td>
<td>12.2</td>
<td>3.8-20.8</td>
<td>CLE</td>
<td>Superficial lamina propria, medial vocalis</td>
<td></td>
</tr>
<tr>
<td>Brondbo and Benninger\textsuperscript{17}</td>
<td>18.2</td>
<td>10-26.3</td>
<td>EBRT</td>
<td></td>
<td>50-70 Gy in 20-35 fractions</td>
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<tr>
<td>Behrman et al\textsuperscript{19}</td>
<td>28.5</td>
<td>21.1-35.9</td>
<td>EBRT</td>
<td></td>
<td>66 Gy in 33 fractions</td>
</tr>
<tr>
<td>Fung et al\textsuperscript{20}</td>
<td>12.6</td>
<td>7.2-17.9</td>
<td>EBRT</td>
<td></td>
<td>61 Gy in 25 fractions</td>
</tr>
</tbody>
</table>

*Types of resections included in study.
Voice-Related Quality of Life

- Meta-Analysis – Discussion
  - TLE with CO2 – VHI 12.9
  - XRT – VHI 18.5
- Reasons for difference in outcome:
  - Tumors treated by XRT may have been understaged
  - Decreased vibration in contralateral vocal fold
  - Altered microcirculation of vocal folds
  - Loss of salivary glands in larynx

Cost analysis
Cost Analysis

- Laser Treatment
  - Operating Room cost
  - Professional Fees (surgeon, anesthesia, pathology)
  - CO₂ laser
  - Operating Microscope

~ Total Cost - $1836.92/case

Cost Analysis

• Radiation Treatment
  • Radiation center staffing and material cost
  • LINAC estimated annual cost
  • Professional Fees (radiation oncologists and nurses)

~ Total Cost - $2454.74/case

Cost analysis

- Surgical Treatment for Treatment failures
  - Partial Laryngectomy with local flap - $7675.82
  - Total Laryngectomy - $8062.80
  - Partial Laryngectomy with free flap - $13201.89

* Assumes 10 day hospital stay, home health nursing visits for 4 weeks in addition to surgical costs alone

Cost Analysis

- **Best Case Scenario** – Patient cured by primary treatment with no long-term sequelae
  - CO$_2$ laser for therapy - $1836.86
  - XRT for therapy - $2386.95

- **Scenarios factoring in local control rates** – (recurrences treated with surgical intervention)
  - CO$_2$ laser for initial treatment - $2407.32
  - XRT for initial treatment - $4828.79

Surgical Intervention
Subepithelial Cordectomy

Subepithelial Cordectomy

Fig. 2a, b  Subligamental cordectomy (type II)

Subepithelial Cordectomy

Fig. 3a, b Transmucosal cordectomy (type III). In order to expose the entire vocal fold, partial resection of the ventricular fold may be necessary (hatched area).

Subepithelial Cordectomy

Subepithelial Cordectomy

---

Subepithelial Cordectomy

Fig. 7 Extended cordectomy encompassing the ventricular fold (type Vc). The inferior resection of the vocal fold is maximum.

Fig. 8 Extended cordectomy encompassing the subglottis to a distance of 1 cm (type Vd).

Extent of Resection and Voice Outcome

- Hillel AT et al:
  - Theory: Voice outcomes are better in following subligamentous resection versus subepithelial resection
  - 17 patients
    - 13 (1 Cis, 11 T1, 1 T2) undergoing subligamentous resection
    - 4 (1 Cis, 3 T1) undergoing subepithelial resection
Extent of Resection and Voice Outcome

• Results:
  • Subligamentous group showed excellent glottic closure
  • Mild decrease in mucosal wave of subligamentous group versus moderate decrease in subepithelial group

Extent of Resection and Voice Outcome

- Discussion:
  - Traditional Thought: Greater preservation leads to better voice outcomes
  - Loss of SLP leaves a vocal ligament that is poorly pliable → glottic insufficiency & dysphonia
  - Removal of ligament also leads to exposed vocalis muscle → responds with hypertrophy and/or hyperplasia

Right Glottic T₁N₀M₀ SCCa
Videostroboscopy of T1NoMo Right Glottic SCCa
Post-Laser Resection of Right Glottic T1NoMo SCCa
Bibliography

- AJCC Cancer Staging Manual 2002
- Peeters AJGE et al. Health Status and voice outcome after treatment for T1a glottic carcinoma. Eur Arch Otorhinolaryngol 2004; 261: 534-540