Risk Adapted Strategies in the Treatment of Thyroid Cancer

Jatin P. Shah
Thyroid Cancer
Incidence & Mortality
1974 to 2017
USA

Overall Incidence
Incidence in Women
Incidence in Men
Mortality 1950

Overall 62450
Women 47230
Men 15220
Mortality 1950

Thousands
60

Misconceptions about Thyroid Cancer

- All patients need subtotal or near total Thyroidectomy
- All patients need Post Operative Radio Active Iodine ablation
- Post operative TSH should be brought down to ‘0’
- Follow up requires annual whole body radio active scans
Pathology - Biology
Cancer of the Thyroid

- Papillary: ~85%
- Follicular: ~14%
- Anaplastic: <1%

Prognosis
- Good: ~85%
- Bad: ~14%
- Ugly: <1%
Prognosis in Thyroid Cancer

A very small proportion $\sim 10\%$ of Papillary carcinomas will undergo progression to more aggressive variants.

Size, ETE, DM, Mortality
Prognosis in Thyroid Cancer

- Well Differentiated
  - Nearly All Curable

- Poorly Differentiated
  - Need Aggressive Rx
  - Majority Curable

- Anaplastic
  - Rarely Curable
## Differentiated Thyroid Cancer

### Prognostic Factors

<table>
<thead>
<tr>
<th>Mayo</th>
<th>Lahey</th>
<th>Mayo</th>
<th>Karolinska</th>
<th>MSKCC</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGES</td>
<td>AMES</td>
<td>MACIS</td>
<td>DAMES</td>
<td>GAMES</td>
</tr>
<tr>
<td>Age</td>
<td>Age</td>
<td>Metastases</td>
<td>DNA</td>
<td>Grade</td>
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<tr>
<td>Grade</td>
<td>Metastases</td>
<td>Age</td>
<td>Age</td>
<td>Age</td>
</tr>
<tr>
<td>Extension</td>
<td>Extension</td>
<td>Completeness Of resection</td>
<td>Metastases</td>
<td>Metastases</td>
</tr>
<tr>
<td>Size</td>
<td>Size</td>
<td>Invasion</td>
<td>Size</td>
<td>Size</td>
</tr>
</tbody>
</table>

![2017 International Federation of Head and Neck Oncologic Surgeons](2017.png)
Importance of Prognostic factors

- Allows Risk Group Stratification
- Permits selective surgical treatment
- Permits selective use of Radio active Iodine
- Permits appropriate follow up strategies
- Delivers cost effective evidence based treatment
- Allays anxiety on the part of the patient
- Delivers excellent outcomes
Differentiated Cancer of the Thyroid

Survival - Age

- $< 45y$, $n=845$
- $\geq 45y$, $n=915$

$P < 0.001$
Differentiated Cancer of the Thyroid

Disease Specific Survival by Age

<table>
<thead>
<tr>
<th>Age Group (y)</th>
<th>10y DSS</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30</td>
<td>100%</td>
</tr>
<tr>
<td>30-39</td>
<td>100%</td>
</tr>
<tr>
<td>40-49</td>
<td>100%</td>
</tr>
<tr>
<td>50-59</td>
<td>100%</td>
</tr>
<tr>
<td>60-69</td>
<td>90%</td>
</tr>
<tr>
<td>70+</td>
<td>70%</td>
</tr>
</tbody>
</table>
Differentiated Cancer of the Thyroid

Survival – Size – T Stage (T1,T2 vs T3,T4)

P<0.001

< 4cm
n=1584

>=4 cm
n=207
Differentiated Cancer of the Thyroid

Survival – Extra Thyroid Extension

None  n=1290
Microscopic n=317
Macroscopic n=203

P<0.001
Differentiated Cancer of the Thyroid

Survival – p N Stage

- pN0 n=1206
- pN1 n=604

5 year outcomes shown

P<0.001
Differentiated Cancer of the Thyroid

Age Distribution of N+ Patients
Differentiated Thyroid Cancer

Survival – N Status

Age < 45

Age > 45
Disease Specific Survival

Age 45 years cut off

- Stage I: 100%
- Stage II: 97%
- Stage III: 97%
- Stage IV: 80%

Age 55 years cut off

- Stage I: 100%
- Stage II: 94%
- Stage III: 94%
- Stage IV: 72%
Differentiated Cancer of the Thyroid

Survival – M Stage

M0  n=1757
M1 (Mx) n=53

P<0.001

5 year outcomes shown
Differentiated Cancer of the Thyroid

Prognostic Factors

Risk Groups (GAMES)

- Low
- Intermediate
- High

- Age
  - <45
  - >45

- Gender
  - Female
  - Male

- Size
  - < 4 cms.
  - > 4 cms.

- Extent
  - Intraglandular
  - Extraglandular

- Grade
  - Low
  - High

- Dist. Mets.
  - Absent
  - Present
Risk Group Stratification

Based on Prognostic Factors

Risk Group Stratification is the most important clinical parameter for selection of the extent of initial surgery, the need for adjuvant therapy, the degree of rigorous follow up, and for the assessment of over all prognosis, for local, regional, or distant failure and Survival.
Differentiated Cancer of the Thyroid

Disease specific Survival – Risk Groups (GAMES)

5 year outcomes shown

Low n=576
Intermediate n=817
High n=417

P<0.001
Extent of Thyroidectomy for Cancer

• All thyroid operations done for proven or suspected Cancer should be “Extra capsular”

• “Subtotal Thyroidectomy” and “Near Total Thyroidectomy” transgress thyroid tissue, and therefore are not Cancer operations, and should not be done

• There are only two Oncologic operations:
  “Lobectomy” or “Total Thyroidectomy”
Extent of Thyroidectomy for Cancer

• “Extra capsular” operations leave no residual thyroid tissue behind, and thus avoid the need for RAI ablation
• Pay special attention to the upper pole, pyramidal lobe and the region of the cricothyroid membrane
• Following an “extracapsular total thyroidectomy”, TGb is not measurable at 6 weeks, and thus it allows biochemical follow up
Lobectomy
Total Thyroidectomy
Extra Thyroid Extension

Most important factor impacting on the extent of Surgery
Differentiated Cancer of the Thyroid

Extra Thyroid Extension

Microscopic: Not Staged (No impact)

Minor: T3
- Strap muscles
- Soft tissues

Major: T4A
- Trachea
- Larynx
- Esophagus
- Recurrent laryngeal nerve
Extra Thyroid Extension – T4a
Disease specific Survival
by completeness of Resection (R Stage)

R0 – Gross Clearance
R1 – Micro. Residual
R2 – Gross Residual

P<0.001
Extrathyroid Extension

Principles of Surgery

- All gross tumor should be removed
- Preserve functioning structures
- Preserve vital structures
- Balance between tumor control and best functional results
- Use adjuvant treatments - RAI, and/or RT
Cervical Lymph Nodes

- Micro metastases are common >50%
- Occult metastases have no impact on prognosis in low risk patients
- Elective node dissection is not recommended in low risk patients
- Therapeutic neck dissection is indicated for metastatic nodes identified clinically, on imaging studies or intra-operatively
- "Berry picking" is not recommended
- Lymph node dissection should be compartmental and comprehensive
**Patterns of Neck Metastases**
For differentiated cancer of
the Thyroid gland

**AJCC/UICC 2009 Staging**

Nodal Staging for Thyroid Cancer

\[ N_x \] – regional lymph nodes cannot be assessed
\[ N_0 \] – No regional lymph node metastases
\[ N_1 \] – Regional lymph node metastases

\[ N_{1a} \]
Metastases to Level VI
pretracheal,
paratracheal,
prelaryngeal,
delphian

\[ N_{1b} \]
Metastases to unilateral, bilateral or contralateral cervical or superior mediastinal lymph nodes

**Central Compartment Node Dissection Level VI & VII**

**Modified Neck Dissection – Type III**

Lymph node dissection
- Level I – not usually
- Level II - V

*Structures preserved*
- Submandibular gland
- Internal jugular vein
- Sternocleidomastoid
- Spinal Accessory
Central Compartment
Node Dissection
Lateral Neck Dissection
Distant Metastases

- Radio active Iodine
- External Radiotherapy (selected cases)
- Surgery (Palliative)
- Chemotherapy ??
- Targeted Therapy (Investigational)
- Agents under study: Sorafenib, Lenvatinib, Selumetinib, Pazopanib, Vandetinib, Cabozantinib, other...
Differentiated Cancer of the Thyroid Mortality

- 1810 patients (1985-2005)
- Excluded M1 and unresectable
- N=1752
- Median f/u = 100 months
- 165 deaths
  - 17 died of disease
  - 6 died from unknown causes with disease
- Disease specific mortality 1.3%
**Differentiated Cancer of the Thyroid**

**Trends in Mortality**

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Death Rate</th>
<th>Central Neck Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Tollefsen</em></td>
<td>1964</td>
<td>10%</td>
<td>&gt;40%*</td>
</tr>
<tr>
<td>Smith</td>
<td>1988</td>
<td>7%</td>
<td>36%</td>
</tr>
<tr>
<td>Shaha</td>
<td>1996</td>
<td>9%</td>
<td>10%</td>
</tr>
<tr>
<td>Kobayashi</td>
<td>1996</td>
<td>5%</td>
<td>&lt;28%</td>
</tr>
<tr>
<td>Ronga</td>
<td>2002</td>
<td>4%</td>
<td>12%</td>
</tr>
<tr>
<td><strong>Nixon</strong></td>
<td>2012</td>
<td>1%</td>
<td>0% **</td>
</tr>
</tbody>
</table>

* Locoregional recurrence was a common cause of death

** Locoregional recurrence is a rare cause of death
Thank You