Management of lymph nodes in the setting of differentiated thyroid cancer

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Disclosure

Member and ATA representative, Medullary Thyroid Cancer Registry Data Monitoring Committee funded by GlaxoSmithKline, Novo Nordisk, Astra Zeneca, and Eli Lilly
Maxim

• Routine lymph node dissection that includes the central and lateral neck compartments has shown nodal metastases in up to 80% of patients with differentiated thyroid cancer.

• The incidence of clinically significant lymph nodes is only 25%.
Patterns of lymph node metastases

- 119 patients bilateral neck dissection
  - Excluded microcarcinomas
  - Mean tumor size: 3.1cm
  - 21% had clinically involved lymph nodes
- Cervical lymph node metastases identified in 61%
- Pattern of medial to lateral to contralateral

Table 1. Localization of node involvement.

<table>
<thead>
<tr>
<th>Node localization</th>
<th>No. in node-positive patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ipsilateral ( (n = 71) )</td>
</tr>
<tr>
<td>Paratracheal</td>
<td>60 (83.3%)</td>
</tr>
<tr>
<td>Midjugular</td>
<td>44 (61.1%)</td>
</tr>
<tr>
<td>Supraclavicular</td>
<td>26 (36.1%)</td>
</tr>
<tr>
<td>Subdigastric</td>
<td>20 (27.8%)</td>
</tr>
</tbody>
</table>

Mirallie E. Localization of Cervical node metastases of papillary thyroid cancer. World J Surg 1999
ATA Surgical Affairs Committee Definitions

• Central compartment
  – Level VI

• Lateral compartment:
  – Level IIa
  – Level III
  – Level IV
  – Level Vb
Skip metastases

• Lateral compartment metastases without involvement of central compartment
• Most frequently from upper pole tumors
• 5-20% of tumors

Table 1
Location of lymph node metastases at MRND in patients with DTC and positive lateral nodes

<table>
<thead>
<tr>
<th></th>
<th>I</th>
<th>la</th>
<th>lb</th>
<th>II</th>
<th>Ia</th>
<th>Ib</th>
<th>III</th>
<th>IV</th>
<th>V</th>
<th>Vai</th>
<th>Vas</th>
<th>Vb</th>
<th>VI</th>
<th>Skip Mets</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pingpank</td>
<td>38</td>
<td>—</td>
<td>—</td>
<td>49</td>
<td>43</td>
<td>21</td>
<td>76</td>
<td>59</td>
<td>28</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Roh</td>
<td>—</td>
<td>—</td>
<td>4</td>
<td>72</td>
<td>17</td>
<td>72</td>
<td>76</td>
<td>13</td>
<td>0</td>
<td>4</td>
<td>90</td>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yanir</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>54</td>
<td>—</td>
<td>—</td>
<td>68</td>
<td>57</td>
<td>20</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>95</td>
<td>5</td>
</tr>
<tr>
<td>Mirallie</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>28</td>
<td>—</td>
<td>—</td>
<td>61</td>
<td>61</td>
<td>36</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>83</td>
<td>17</td>
</tr>
<tr>
<td>Average</td>
<td>38</td>
<td>—</td>
<td>4</td>
<td>39</td>
<td>59</td>
<td>19</td>
<td>68</td>
<td>64</td>
<td>31</td>
<td>13</td>
<td>0</td>
<td>4</td>
<td>88</td>
<td>12</td>
</tr>
</tbody>
</table>

\(^a\) Values indicate the % of patients with positive lymph nodes at each level.
\(^b\) Metastases to lateral nodes without evidence of central compartment involvement.

Fritze D, Surgical management of cervical lymph nodes in differentiated thyroid cancer. Otolaryngol Clin N Am 2010
Risk factors for lymph node mets

- Age <45
- Tumor Size
- Extrathyroidal extension

- Lymphovascular invasion
- BRAF mutation
- Distant metastases

**Table 3.**
Relationship between tumor size and central lymph node metastasis

<table>
<thead>
<tr>
<th>Tumor size</th>
<th>Absent</th>
<th>Present</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1–2 cm</td>
<td>109 (40.8)</td>
<td>158 (59.2)</td>
<td>267</td>
</tr>
<tr>
<td>&gt; 4 cm</td>
<td>17 (21.0)</td>
<td>64 (79.0)</td>
<td>81</td>
</tr>
<tr>
<td>Total</td>
<td>281 (37.0)</td>
<td>478 (63.0)</td>
<td>759</td>
</tr>
</tbody>
</table>

*P < 0.0001.

Ito Y, Clinical significance of lymph node metastases of thyroid papillary carcinoma located in one lobe. World J Surg 2006
The first operation is the most important operation.

- Preoperative ultrasound (or other modalities if indicated) of the central and lateral neck compartments (with FNA biopsy when indicated) should be performed prior to initial surgery in the setting of a (+) thyroid biopsy.
- Complete compartmental resection should follow.
Do it right the first time!

Up to 57% of re-operations for thyroid cancer are preventable and a direct result of incomplete initial surgery.


Table IV. Preventability of reoperation in 72 patients with persistent or recurrent PTC

<table>
<thead>
<tr>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Group 1 (persistent PTC)</td>
</tr>
<tr>
<td>A. Reoperation preventable</td>
</tr>
<tr>
<td>1. Inadequate preoperative imaging*</td>
</tr>
<tr>
<td>a. Ultrasonography not performed before surgery</td>
</tr>
<tr>
<td>4</td>
</tr>
<tr>
<td>b. Ultrasonography of thyroid performed without assessment of levels II to V</td>
</tr>
<tr>
<td>8</td>
</tr>
<tr>
<td>2. Incomplete initial surgery</td>
</tr>
<tr>
<td>a. Known lateral neck disease not dissected</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>b. Node plucking (from lateral neck) at initial surgery with persistent disease in the same compartment</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>c. Incomplete resection of the primary thyroid neoplasm</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>d. Bulky central compartment disease not completely resected</td>
</tr>
<tr>
<td>4</td>
</tr>
<tr>
<td>B. NCCN guidelines not followed</td>
</tr>
<tr>
<td>1. Less than total or less than near-total thyroidectomy performed</td>
</tr>
<tr>
<td>8</td>
</tr>
<tr>
<td>2. Gross lymph node metastases but neck dissection not performed</td>
</tr>
<tr>
<td>6†</td>
</tr>
<tr>
<td>II. Group 2 (recurrent PTC)</td>
</tr>
<tr>
<td>A. Reoperation preventable</td>
</tr>
<tr>
<td>1. Incomplete initial operation</td>
</tr>
<tr>
<td>14 (25%)</td>
</tr>
<tr>
<td>a. Node plucking at initial surgery with recurrence in the same compartment</td>
</tr>
<tr>
<td>9</td>
</tr>
<tr>
<td>b. Gross lymph node metastases not removed</td>
</tr>
<tr>
<td>5</td>
</tr>
<tr>
<td>2. Inadequate TSH suppression (&gt;0.5 μU/mL)</td>
</tr>
<tr>
<td>17 (31%)</td>
</tr>
<tr>
<td>B. NCCN guidelines not followed</td>
</tr>
<tr>
<td>1. Less than total or near-total thyroidectomy performed</td>
</tr>
<tr>
<td>4</td>
</tr>
<tr>
<td>2. Completion total thyroidectomy not performed</td>
</tr>
<tr>
<td>14‡</td>
</tr>
<tr>
<td>3. Gross lymph node metastases but neck dissection not performed</td>
</tr>
<tr>
<td>17</td>
</tr>
</tbody>
</table>
Ultrasound-guided FNA proof of metastatic disease
Ultrasound
Normal lymph Node
Ultrasound

Lymph node with metastatic papillary thyroid cancer, demonstrating microcalcifications
Ultrasound

Heterogeneous, partially cystic lymph nodes along the jugular chain
CT with IV contrast
The role of cross-sectional imaging as an adjunct is increasing.
In 2017,

• Preop use of cross-sectional imaging with IV contrast is recommended as an adjunct to US for patients with clinical suspicion for advanced disease. (Strong recommendation, low-quality evidence)
Combined preop US/CT can enhance detection of macroscopic nodal disease resulting in change of surgical strategy in 25% of patients.

TABLE 3. Group I (primary patients): diagnostic accuracy characteristics of nodal detection tests.

<table>
<thead>
<tr>
<th></th>
<th>Evaluation of lateral neck</th>
<th>Evaluation of central neck</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PE</td>
<td>US</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>38%</td>
<td>79%</td>
</tr>
<tr>
<td>Specificity</td>
<td>93%</td>
<td>87%</td>
</tr>
<tr>
<td>95% CI</td>
<td>79–98</td>
<td>70–95</td>
</tr>
<tr>
<td>PPV</td>
<td>79%</td>
<td>80%</td>
</tr>
<tr>
<td>95% CI</td>
<td>69–89</td>
<td>70–90</td>
</tr>
<tr>
<td>NPV</td>
<td>69%</td>
<td>86%</td>
</tr>
<tr>
<td>95% CI</td>
<td>60–78</td>
<td>78–94</td>
</tr>
</tbody>
</table>

Cross sectional imaging can clarify involvement of:

- Nodal regions difficult to visualize on routine US, including the mediastinum, infraclavicular, retropharyngeal and para-pharyngeal regions.
- Larynx, trachea, esophagus, or blood vessels
When cross-sectional imaging is performed, IV contrast is a useful adjunct.

**FIG. 1.** (A) The results of urinary iodide in all 25 patients collected in 24 hours (24U) at the baseline, first week, and first, second, and third month after iodinated contrast agents (ICA) (in logarithmic scale). (B) The results of urinary iodide in all 25 patients collected in spot sample (sU) at the baseline, first week, and first, second, and third month after ICA (in logarithmic scale).

-Padovani et al Thyroid 2012
Consensus Statement on the Terminology and Classification of Central Neck Dissection for Thyroid Cancer

The American Thyroid Association Surgery Working Group
with Participation from the American Association of Endocrine Surgeons,
American Academy of Otolaryngology—Head and Neck Surgery, and American Head and Neck Society

Sally E. Carty,1,2 David S. Cooper,2 Gerard M. Doherty,3 Quan-Yang Duh,4 Richard T. Kloos,5
Susan J. Mandel,6 Gregory W. Randolph,7 Brendan C. Stack, Jr.,8 David L. Steward,9 David J. Terris,10
Geoffrey B. Thompson,11 Ralph P. Tufano,12 R. Michael Tuttle,13 and Robert Udeisz14

THYROID
Volume 19, Number 11, 2009
© Mary Ann Liebert, Inc.
DOI: 10.1089/thy.2009.0159

Review Article
Initial management of the central neck

• Central neck dissection is indicated for clinically & radiographically identified lymph nodes in Level VI. This is a ‘therapeutic’ CLND.

• Contentious debate continues about the role of ‘prophylactic’ central neck dissection for low risk differentiated thyroid cancer when there is no clinical or radiographic evidence of nodal disease.
Central lymph node dissection

- Benefits
  - Decreases recurrence
  - Prevents compression/invasion of local structures
  - ? improves survival
- Possible complications (transient and permanent?)
  - RLN injury
  - SLN injury
  - Hypoparathyroidism
  - Bleeding
  - Lymphatic leak
Is prophylactic central lymph node dissection warranted?
Debate continues.

• Pro
  – May improve disease-specific survival, local recurrence, post-op Tgb levels
  – Will detect some pN1 disease (but this prognostically is not equivalent to cN1 disease)
  – Can inform use of RAI
  – Can improve risk estimates of recurrence
  – Safe in the hands of high-volume surgeons

-Chisholm 2009
-Bonnet 2009
-Laird 2012
-Moreno 2012
-Barczynski 2013
-Sancho 2014
Consensus is lacking. An RCT has not been done.

- Cons
  - No improvement in long-term outcomes, while
  - Increasing the likelihood of short-term post-op morbidity, including hypocalcemia

- Hughes 2010
- Wang 2012
- Yoo 2012
- Raffaelli 2012
Locoregional recurrence in 6 comparative studies

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>TT+pCCND Events</th>
<th>Total</th>
<th>TT alone Events</th>
<th>Total</th>
<th>Weight</th>
<th>Risk Ratio, Random, 95% CI</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sywak 2006</td>
<td>2</td>
<td>56</td>
<td>22</td>
<td>391</td>
<td>12.5%</td>
<td>0.63 [0.15, 2.63]</td>
<td>2006</td>
</tr>
<tr>
<td>Costa 2009</td>
<td>9</td>
<td>126</td>
<td>8</td>
<td>118</td>
<td>21.7%</td>
<td>1.05 [0.42, 2.64]</td>
<td>2009</td>
</tr>
<tr>
<td>Moo 2010</td>
<td>2</td>
<td>45</td>
<td>6</td>
<td>36</td>
<td>11.1%</td>
<td>0.27 [0.06, 1.24]</td>
<td>2010</td>
</tr>
<tr>
<td>Hughes 2010</td>
<td>4</td>
<td>78</td>
<td>3</td>
<td>65</td>
<td>12.0%</td>
<td>1.11 [0.26, 4.79]</td>
<td>2010</td>
</tr>
<tr>
<td>Barcynski 2012</td>
<td>15</td>
<td>358</td>
<td>37</td>
<td>282</td>
<td>32.0%</td>
<td>0.32 [0.18, 0.57]</td>
<td>2012</td>
</tr>
<tr>
<td>Lang 2012</td>
<td>3</td>
<td>82</td>
<td>3</td>
<td>103</td>
<td>10.7%</td>
<td>1.26 [0.26, 6.06]</td>
<td>2012</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>745</strong></td>
<td><strong>995</strong></td>
<td><strong>100.0%</strong></td>
<td></td>
<td>0.59</td>
<td>0.59 [0.33, 1.07]</td>
<td></td>
</tr>
</tbody>
</table>

Total events: 35 TT+pCCND, 79 TT alone

Heterogeneity: Tau² = 0.19; Chi² = 8.03, df = 5 (P = 0.15); I² = 38%
Test for overall effect: Z = 1.74 (P = 0.08)

- Recurrence rate of TT: 7.9%
- Recurrence rate of TT/pCCND: 4.7%
- Relative risk of recurrent PTC after TT/pCCND: 0.59 (NS)
- Number needed to treat to prevent one recurrence: 31

(Wang et al)
Prophylactic central neck dissection *(changed from 2009)*

- pCLND *should be considered* for cN0 PTC patients and:
  - Advanced primary tumors (T3 or T4)
  - Clinically involved lateral neck nodes (cN1b)
  - If the information will be used to plan further steps in therapy.
  - *(Weak Recommendation, Low-quality evidence)*
Prophylactic central neck dissection (unchanged from 2009)

• Thyroidectomy \textit{w/o} pCLND \textit{may be appropriate} for patients who are cN0 with:
  – Small (T1 or T2) PTCs,
  – Non-invasive PTCs, and
  – Most follicular cancer.

  (Strong Recommendation, Moderate-quality evidence)
Prophylactic lateral dissection is not indicated for DTC.
American Thyroid Association
Consensus Review and Statement
Regarding the Anatomy, Terminology, and Rationale
for Lateral Neck Dissection in Differentiated Thyroid Cancer

Brendan C. Stack, Jr. (Chair),1 Robert L. Ferris,2 David Goldenberg,3 Megan Haymart,4
Ashok Shaha,5 Sheila Sheth,6 Julie Ann Sosa,7 and Ralph P. Tufano,6,9
for the American Thyroid Association Surgical Affairs Committee
ATA Surgical Affairs Committee Recommendation

• “A prophylactic lateral neck dissection alone for thyroid cancer has **NOT** been proven effective to improve survival. There are significant risks to lateral neck dissection .... that render prophylactic lateral neck dissection **unwarranted**.”

Stack...Sosa...et al 2012
ATA RECOMMENDATION 37

- Therapeutic lateral neck compartmental lymph node dissection should be performed for patients with biopsy-proven metastatic lateral cervical lymphadenopathy.
  (Strong recommendation, Moderate-quality evidence)
Potential Injuries (up to 50% risk)

- Greater auricular nerve
- Spinal accessory nerve
- Phrenic nerve
- Hypoglossal nerve
- Vagus nerve
- Brachial plexus
- Sympathetic trunk
- Thoracic duct (13% chyle leak)
- Internal jugular vein
- Carotid artery
- 11% chronic neck pain/numbness
- Double the risk of hypoparathyroidism

Cheah et al WJS 2002
Important tenets

• A prophylactic lateral neck dissection has not been proven effective to improve survival!

• The reported rate of recurrence in the lateral neck is just 5-15%.
  – Treating the neck when metastases become apparent does not affect overall outcome.

• Preoperative US is an excellent outcome predictor for DFS and DSS. It can find high-risk disease without a scalpel!

• A sonographically-based surgical approach provides excellent long-term regional control.
Neck mapping for the surgeon, often by the surgeon
Kaplan-Meier estimate for lateral neck disease-free interval, stratified by sonographic status of the ipsilateral neck

Kaplan-Meier estimate for disease-specific survival, stratified by presence of sonographic abnormalities in the lateral neck compartments

Kaplan-Meier estimate for recurrence-free survival (years to recurrence or death for any reason), stratified by sonographic status of the lateral neck compartments

Moreno et al, Arch OTO 2011
What is the importance of lymph nodes in PTC?

What is the meaning of lymph nodes?

I don't know. The computers are down.
### Papillary or Follicular Ca staging

<table>
<thead>
<tr>
<th></th>
<th>&lt; 45 years</th>
<th>&gt; 45 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>Any T, N &amp; M0</td>
<td>pT1, N0, M0</td>
</tr>
<tr>
<td>Stage II</td>
<td>Any T, N &amp; M1</td>
<td>pT2, N0, M0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>pT3, N0, M0</td>
</tr>
<tr>
<td>Stage III</td>
<td></td>
<td>pT4, N0, M0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Any pT, N1, M0</td>
</tr>
<tr>
<td>Stage IV</td>
<td></td>
<td>Any pT, N, M1</td>
</tr>
</tbody>
</table>

Undifferentiated or anaplastic carcinomas are ALL stage IV
The impact of lymph node involvement on survival in patients with papillary and follicular thyroid carcinoma

Victor Zaydfudim, MD, a Irene D. Feurer, PhD, a,b Marie R. Griffin, MD, MPH, c and John E. Phay, MD, a
Nashville, Tenn

Zaydfudim et al. 2008:

1. 15,497 PTC patients from SEER

2. Lymph node metastases:

   ≥45 yrs: associated with survival (HR 1.46, p<0.01)

   <45 yrs: NOT associated with survival (HR 1.11, p=0.54)

A critical analysis of the American Joint Committee on Cancer (AJCC) staging system for differentiated thyroid carcinoma in young patients on the basis of the Surveillance, Epidemiology, and End Results (SEER) registry

Tran Cao et al. 2012:

1. 49,240 pts with DTC in SEER
2. For pts <45 yrs: Lymph node metastases were associated with compromised survival (HR 2.09, p<0.01)
3. Potential limitations:
   - Extent of surgery
   - Radioactive iodine therapy

Cao, et al. Surgery 2012
Presence and Number of Lymph Node Metastases Are Associated With Compromised Survival for Patients Younger Than Age 45 Years With Papillary Thyroid Cancer

Mohamed Abdelgadir Adam, John Para, Paolo Goffredo, Michaela A. Ditman, Shelby D. Reed, Randall P. Scher, Terry Hyslop, Sanziana A. Roman, and Julie A. Sosa
Hypotheses

1. Presence of lymph node metastases and number of metastatic lymph nodes are associated with compromised survival for patients <45 yrs with Stage I PTC.

2. It is possible to stratify patients’ risk of death based on the number of metastatic lymph nodes.
Methods

Data sets
National Cancer Data Base (NCDB)
Validation: Surveillance Epidemiology End Results (SEER)

Inclusion criteria
PTC: ICD-O-3 codes: 8050; 8260; 8340; 8341; 8342; 8343
Age ≥18 yrs with Stage 1 PTC who underwent surgery
Study period: 1998-2006

Exclusion criteria
Aggressive variants (tall, diffuse sclerosing, insular)
Multiple cancer diagnoses
Unknown extent of surgery, removal of less than a lobe
Study variables

Independent variables
- Demographics: Age, gender, race, income
- Pathologic: Tumor size, multifocality, extrathyroidal extension, number of metastatic lymph nodes, distant metastases
- Treatment: Extent of surgery, RAI

Dependent variable/Outcome
- Overall survival
Study design

PTC patients:
- 18-44 yrs.
- Stage I
  - Known extent of surgery
  - Excluded aggressive variants

No LN metastases:
(Negative on pathological exam or when LN not examined)

LN metastases:
(Pathologically confirmed)
Statistical analysis

1. Unadjusted analysis:
   - Chi-square; Wilcoxon

2. Adjusted survival analysis:
   - Adjusted Kaplan-Meier
   - Cox proportional hazards

3. Number of lymph nodes on survival
   - Restrictive Cubic Splines
Adjusted survival analysis: NCDB

Lymph node metastases are associated with compromised survival (p<0.05)
Adjusted survival analysis: SEER
Lymph node metastases are associated with compromised survival (p<0.05)
Restrictive Cubic Splines

1. Piecewise polynomial functions
2. Relax the linearity assumption in multivariable regression analyses
3. Examine a relationship between a continuous predictor and an outcome in the setting of a non-linear relationship

Metastatic lymph nodes are associated with survival.
Adjusted association of the number of metastatic lymph nodes and survival

<table>
<thead>
<tr>
<th>Effect</th>
<th>HR (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of metastatic LNs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤6</td>
<td>1.12 (1.01 – 1.25)</td>
<td>0.03</td>
</tr>
<tr>
<td>&gt;6</td>
<td>0.99 (0.92 – 1.05)</td>
<td>0.75</td>
</tr>
</tbody>
</table>
Implications

1. Cervical lymph node metastases are associated with compromised survival among patients <45 yrs.

2. In the current AJCC staging, young patients with nodal metastases may be under-staged.

3. Rigorous preoperative screening for lymph node metastases is warranted for patients <45 yrs.
Exploring the Relationship Between Patient Age and Cancer-Specific Survival in Papillary Thyroid Cancer: Rethinking Current Staging Systems

Mohamed Abdelgadir Adam, Samantha Thomas, Terry Hyslop, Randall P. Scher, Sanziana A. Roman, and Julie A. Sosa
Cancer-specific survival estimate by patient age

<table>
<thead>
<tr>
<th>Age Groups, years</th>
<th>Survival Estimate, %</th>
<th>95% CI</th>
<th>Events*</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-19</td>
<td>99.8</td>
<td>98.7 to 100.0</td>
<td>&lt; 10</td>
</tr>
<tr>
<td>20-29</td>
<td>99.9</td>
<td>99.5 to 100.0</td>
<td>&lt; 10</td>
</tr>
<tr>
<td>30-39</td>
<td>99.8</td>
<td>99.5 to 99.9</td>
<td>&lt; 10</td>
</tr>
<tr>
<td>40-49</td>
<td>99.5</td>
<td>99.2 to 99.7</td>
<td></td>
</tr>
<tr>
<td>50-59</td>
<td>98.1</td>
<td>97.6 to 98.5</td>
<td>75</td>
</tr>
<tr>
<td>60-69</td>
<td>94.8</td>
<td>93.4 to 95.8</td>
<td>91</td>
</tr>
<tr>
<td>70-79</td>
<td>91.5</td>
<td>89.0 to 93.4</td>
<td>70</td>
</tr>
<tr>
<td>80-89</td>
<td>79.2</td>
<td>72.5 to 84.5</td>
<td>50</td>
</tr>
<tr>
<td>≥ 90</td>
<td>73.9</td>
<td>50.9 to 87.3</td>
<td>&lt; 10</td>
</tr>
</tbody>
</table>

*SEER Data Use Agreement precludes reporting of statistics for small groups.³⁰
Linear association between patient age and risk of death

- Restricted cubic splines
- Thin plate splines
- Adaptive smoothers
Conclusions and implications

• Age is associated with an increased risk of disease-specific mortality in a continuous, linear fashion, without an apparent age cut-point demarcating survival difference.

• These results challenge the appropriateness of using a patient age cut-point in current (<45 yrs) and imminent (<55 yrs) AJCC staging systems.

• We might be under-staging young patients with intermediate- and high-risk tumors, and they might be under-treated, as a result.
In 2009
Thyroid cancer staging

• All current staging systems for thyroid cancer incorporate age:
  – AJCC
  – European Organization for Research and Treatment of Cancer (EORTC)
  – National Thyroid Cancer Treatment Cooperative Study
  – AGES
  – AMES
  – MACIS

• Is age an appropriate criterion for thyroid cancer staging? If so, is 45 years the right cut-point?
Setting Limits: Lymph Node Removal & Thyroid Cancer

BY KELLY HORVATH | JAN 2017

A new study seeks to establish a clinical guideline to quantify the risk of metastatic lymph nodes in thyroid cancer patients. The findings should go a long way to help ease the mind of the patients...and the physicians.

With thyroid cancer incidence on the rise, especially papillary thyroid cancer, surgical tumor resection is a critical component of the overall treatment plan, which might also include one or more of several adjuvant treatment options such as concomitant lymph node (LN) dissection.

The American Cancer Society notes that although metastatic (M1) disease occurs.
How Many Lymph Nodes Are Enough? Assessing the Adequacy of Lymph Node Yield for Papillary Thyroid Cancer

Timothy J. Robinson, Samantha Thomas, Michaela A. Dinan, Sanziana Roman, Julie Ann Sosa, and Terry Hyslop

Fig 2. Probability of a false-negative lymphadenectomy as a function of number of lymph nodes examined in a patient with truly lymph node-positive disease.

Fig 3. Probability of occult nodal disease on the basis of American Joint Committee on Cancer tumor stage.
What is an adequate lymphadenectomy?
- We estimate that 6, 9, and 18 LN need to be removed to ensure a reasonably adequate LN evaluation for patients with T1b, T2, and T3 disease.
- As few as 3, 4 and 8 LN are needed for patients with T1b, T2, and T3 disease undergoing true pCLND.
Acknowledgments

www.dcri.org/our-research/endocrine-neoplasia-research-group