Is Less More?
Thyroid Cancer Surgery in 2016

Julie Ann Sosa, MD MA FACS
Professor of Surgery and Medicine
Chief, Section of Endocrine Surgery, and
Leader, Endocrine Neoplasia Diseases Group
Duke University, Durham, NC, USA
107% increase in thyroid FNAs, 2006-2011

- Thyroid FNAs more than doubled: 16% compounded annual percentage change
- Thyroid FNAs increased as a percentage of all FNAs, from 49% to 65%.

Sosa et al 2013
2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer

The American Thyroid Association (ATA) Guidelines Taskforce on Thyroid Nodules and Differentiated Thyroid Cancer

Goals of Initial Therapy

• To improve cancer-related survival
• To minimize the risk of disease recurrence and metastatic spread
• To permit accurate long-term surveillance for disease recurrence
• To permit accurate staging of disease
• **To minimize treatment-related morbidity**

Risk stratification

Adapted from ATA Guidelines, Cooper DS, Thyroid, 2006
Updated 2009
Updated 2015
How much surgery is too much, or not enough?

Risks of misdiagnosis, long-term outcome uncertainty

Patient preferences

Medico-legal considerations

Costs to patients and payers

Avoid undertreatment of clinically significant cancer

Avoid overtreatment of indolent lesions
Surveillance bias:
Incidence of thyroid cancer by size
SEER, 1988-2009

Rate (per 100,000)

0.1-1.0 cm
1.1-2.0 cm
2.1-3.0 cm
>4.0 cm
Is the identification and eradication of all PTMCs a worthwhile goal?
Challenges

• To identify those tumors destined to become aggressive before they develop disease progression or at a point in progression at which intervention will still be very effective.

• Confirmation of appropriateness and safety of observation of PTMCs.
- Follow up 1235 patients, 1993-2011 (mean, 75 mos)
- Patients were divided by age (<40, 40-59, ≥60 yrs)
- Disease progression defined by:
  - Size enlargement
  - New lateral nodal mets
  - Progression to clinical dz (Tumor ≥12 mm or lateral mets)
Tumor enlargement

Nodal metastases
The proportion of patients with PTMC progression was lowest in the old patients and highest in the young patients.

On multivariate analysis, young age was an independent predictor of PTMC progression.
Conclusion

• Older patients with low-risk PTMC may be the best candidates for observation.

• PTMC in young patients is more progressive, but it might not be too late to perform surgery after subclinical PTMC has progressed to clinical disease, regardless of age.
Is PTMC an over-treated entity?

Probably

- More patients are undergoing total thyroidectomy (73 vs 25% lobectomy) and RAI (31%) despite a lack of evidence this translates into survival benefit.
- It is important to distinguish patients with risk factors that predispose for high risk for recurrence.

-Wang et al, WJS 2014
**Recommendation**

**If** surgery is chosen for PTMCs w/o extrathyroidal extension and cN0, initial surgery should be lobectomy unless there are clear indications to remove the contralateral lobe. Lobectomy is sufficient for small, unifocal, intrathyroidal carcinomas in the absence of prior head and neck irradiation, family history, or nodal metastases.
Extent of surgery: controversy

Total thyroidectomy:

- Eradication of possible bilateral disease
- Ability to use of radioactive iodine
- Easier detection of recurrence

Lobectomy:

- Indolent disease with excellent prognosis
- Higher risks for complications with more extensive surgery
- No survival benefit

Thyroid nodule-related surgery increased 31%, 2006-11

Total thyroidectomy is associated with more complications even in the hands of high-volume surgeons.

Figure 1. Risk of complication by surgeon volume and type of thyroidectomy

Low surgeon volume is <10 thyroidectomies/year; intermediate surgeon volume is 10-99 thyroidectomies/year; high surgeon volume is >99 thyroidectomies/year.

Hauch et al SSO 2014
Total thyroidectomy

Bilimoria et al. 2007:

52,173 PTC patients from National Cancer Database (1985-1998)
Overall survival benefit with total thyroidectomy for tumors ≥1 cm

American Thyroid Association (ATA) guidelines:
Lobectomy: tumors <1 cm
Total thyroidectomy: tumors >1 cm

Cooper DS, et al. Thyroid 2009
Total thyroidectomy was associated with improved survival for tumors $\geq 1$ cm.

### TABLE 2. Cox Proportional Hazards Analysis Stratified by Tumor Size Demonstrating the Risk of Recurrence and Death for Patients Who Underwent Lobectomy Compared to Total Thyroidectomy for PTC

<table>
<thead>
<tr>
<th></th>
<th>Hazard Ratio (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All Patients</td>
</tr>
<tr>
<td><strong>Recurrence</strong></td>
<td></td>
</tr>
<tr>
<td>Total thyroidectomy</td>
<td>1.00 (Referent)</td>
</tr>
<tr>
<td>Lobectomy</td>
<td>1.57 (1.20–2.06)</td>
</tr>
<tr>
<td></td>
<td>$P = 0.001$</td>
</tr>
<tr>
<td><strong>Survival</strong></td>
<td></td>
</tr>
<tr>
<td>Total thyroidectomy</td>
<td>1.00 (Referent)</td>
</tr>
<tr>
<td>Lobectomy</td>
<td>1.21 (1.02–1.44)</td>
</tr>
<tr>
<td></td>
<td>$P = 0.027$</td>
</tr>
</tbody>
</table>

Hazard Ratios greater than 1.0 indicate increased risk of recurrence or death.

*Adjusted for gender, age, race, nodal status, distant metastases, socioeconomic factors, RAI administration, year of diagnosis, and hospital volume.
Thyroid lobectomy

Thyroid lobectomy for treatment of well differentiated intrathyroidal malignancy

Iain J. Nixon, MD, a Ian Ganly, MD, PhD, a Snehal G. Patel, MD, a Frank L. Palmer, BA, a
Monica M. Whitcher, BA, a Robert M. Tuttle, MD, b Ashok Shaha, MD, a and
Jatin P. Shah, MD, a New York, NY

• 889 pts with pT1 and T2 intra-thyroidal WDTCs treated 1986-95 at MSKCC
• 59% had total thyroidectomy, 41% lobectomy
• Median follow up: 99 mos
• OS, DSS, and RFS were measured
There was no difference in locoregional recurrence or DSS between total thyroidectomy and lobectomy.

Table III. Patient characteristics, tumor characteristics, and outcomes stratified by surgical group

<table>
<thead>
<tr>
<th>Variable</th>
<th>Lobectomy n = 361</th>
<th>Total thyroidectomy n = 528</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;45 yr</td>
<td>195 (54)</td>
<td>230 (44)</td>
<td>.002</td>
</tr>
<tr>
<td>&gt;45 yr</td>
<td>166 (46)</td>
<td>298 (56)</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td>.345</td>
</tr>
<tr>
<td>Male</td>
<td>82 (23)</td>
<td>106 (20)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>279 (77)</td>
<td>422 (80)</td>
<td></td>
</tr>
<tr>
<td>pT stage</td>
<td></td>
<td></td>
<td>.143</td>
</tr>
<tr>
<td>pT1</td>
<td>249 (69)</td>
<td>388 (73)</td>
<td></td>
</tr>
<tr>
<td>pT2</td>
<td>112 (31)</td>
<td>140 (27)</td>
<td></td>
</tr>
<tr>
<td>RAI</td>
<td></td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>No</td>
<td>360 (99.7)</td>
<td>333 (63)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1 (0.3)</td>
<td>195 (37)</td>
<td></td>
</tr>
<tr>
<td>Pathology</td>
<td></td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Papillary Ca</td>
<td>310 (86)</td>
<td>490 (93)</td>
<td></td>
</tr>
<tr>
<td>Follicular Ca</td>
<td>36 (10)</td>
<td>16 (3)</td>
<td></td>
</tr>
<tr>
<td>Hürthle cell Ca</td>
<td>15 (4)</td>
<td>22 (4)</td>
<td></td>
</tr>
<tr>
<td>10-yr local recurrence</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>10-yr neck recurrence</td>
<td>0 (0)</td>
<td>5 (0.8)</td>
<td>.96</td>
</tr>
<tr>
<td>10-yr distant recurrence</td>
<td>0 (0)</td>
<td>5 (3)</td>
<td>.05</td>
</tr>
<tr>
<td>10-yr deaths of any cause</td>
<td>18 (7)</td>
<td>27 (9)</td>
<td>.64</td>
</tr>
<tr>
<td>10-yr disease-specific deaths</td>
<td>0 (0)</td>
<td>1 (1.5)</td>
<td>.246</td>
</tr>
</tbody>
</table>

RAI, Radioiodine ablation.
Thyroid Lobectomy for Papillary Thyroid Cancer: Long-term Follow-up Study of 1,088 Cases

Kenichi Matsuzu · Kiminori Sugino · Katsuhiko Masudo · Mitsuji Nagahama · Wataru Kitagawa · Hiroshi Shibuya · Keiko Ohkuwa · Takashi Uruno · Akifumi Suzuki · Syunsuke Magoshi · Junko Akaishi · Chie Masaki · Michikazu Kawano · Nobuyasu Suganuma · Yasushi Rino · Munetaka Masuda · Kaori Kameyama · Hiroshi Takami · Koichi Ito

- Retrospective study of 1088 pts with PTC who underwent lobectomy, 1986-95
- No patients received RAI.
- Median follow-up was 17.6 yrs.
Cause-specific survival

- **CSS rate**
  - CSS rates:
    - 10-Year: 99.4%
    - 15-Year: 98.5%
    - 20-Year: 97.8%
    - 25-Year: 95.2%

- **Age**
  - < 45 years old (n = 483)
  - ≥ 45 years old (n = 605)

- **Primary tumor size**
  - ≤ 40 mm (n = 979)
  - > 40 mm (n = 109)

- **Extrathyroidal invasion**

- **Clinical lymph node metastasis**

- **Lymph node dissection**
  - none (n = 130)
  - central (n = 60)
  - central and lateral (n = 898)
And more concern...

Concerns regarding Bilimoria et al; exclusion of possible confounders:
- Patient comorbidities
- Multifocality
- Extrathyroidal extension
- Adequacy of resection

Mendelsohn et al 2010
- 22,724 patients with PTC
- No difference in survival between lobectomy and total thyroidectomy

To examine the association between extent of surgery and overall survival among patients with papillary thyroid carcinoma 1-4 cm.
Study variables

National Cancer Data Base
>1500 hospitals
85% of all incident thyroid cancer cases in the U.S.

Independent variables
Demographics: Age, gender, race, income
Patient comorbidities: Charlson Deyo scores
Pathology: Tumor size, multifocality, extrathyroidal extension, nodal/ distant metastases

**Extent of surgery:** Lobectomy, total thyroidectomy

Dependent variable/Outcome
Overall survival
## Patient characteristics (N=61775)

<table>
<thead>
<tr>
<th></th>
<th>Lobectomy (N=6849)</th>
<th>Total Thyroidectomy (N=54926)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Female</strong></td>
<td>81%</td>
<td>79%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>&lt;45</td>
<td>51%</td>
<td>53%</td>
<td></td>
</tr>
<tr>
<td>45-64</td>
<td>37%</td>
<td>37%</td>
<td></td>
</tr>
<tr>
<td>≥65</td>
<td>12%</td>
<td>10%</td>
<td></td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>White</td>
<td>88%</td>
<td>88%</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>7%</td>
<td>6%</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>4%</td>
<td>4%</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>1%</td>
<td>2%</td>
<td></td>
</tr>
<tr>
<td><strong>Comorbidity</strong></td>
<td></td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>0</td>
<td>88%</td>
<td>89%</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>10%</td>
<td>9%</td>
<td></td>
</tr>
<tr>
<td>≥2</td>
<td>2%</td>
<td>1%</td>
<td></td>
</tr>
</tbody>
</table>
# Tumor/treatment characteristics

<table>
<thead>
<tr>
<th></th>
<th>Lobectomy (N=6849)</th>
<th>Total Thyroidectomy (N=54926)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tumor size</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.0-2.0 cm</td>
<td>60%</td>
<td>59%</td>
<td>NS</td>
</tr>
<tr>
<td>2.1-4.0 cm</td>
<td>40%</td>
<td>41%</td>
<td></td>
</tr>
<tr>
<td><strong>Multifocality</strong></td>
<td>29%</td>
<td>44%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Extrathyroidal extension</strong></td>
<td>5%</td>
<td>16%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Nodal metastases</strong></td>
<td>7%</td>
<td>27%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Distant metastases</strong></td>
<td>0.4%</td>
<td>1.0%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Positive surgical margin</strong></td>
<td>7%</td>
<td>27%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>RAI administration</strong></td>
<td>33%</td>
<td>65%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
## Adjusted survival analysis

<table>
<thead>
<tr>
<th>Tumor size</th>
<th>Total thyroidectomy vs. lobectomy</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0-4.0 cm</td>
<td>Adjusted hazard ratio* (95% CI)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.95 (0.83-1.04)</td>
<td>0.40</td>
</tr>
</tbody>
</table>

*Adjusted for: age, gender, race, annual income, insurance status, hospital volume, patient comorbidities, tumor multifocality, extrathyroidal extension, lymph node involvement, distant metastases, surgical margins, and radioactive iodine (RAI) treatment.
Total thyroidectomy (2009)

• ‘For thyroid cancer >1 cm, initial surgery should be total thyroidectomy unless there are contraindications. Lobectomy may be sufficient for <1 cm, low-risk, unifocal, intrathyroidal PTCs w/o prior head/neck irradiation or nodal metastases.’

(Recommendation rating: A) -ATA Guidelines 2009
Total thyroidectomy or lobectomy (2015)

- ‘For patients with thyroid cancer >1 cm and <4 cm w/o extrathyroidal extension, and cN0, the initial surgery can be *either* total thyroidectomy (high-risk tumors with nodal mets, requiring RAI), *or* thyroid lobectomy *(low and medium-risk tumors).*’

-ATA Guidelines 2015
The operation should be selected in the setting of the larger overall treatment strategy formulated by the care team. Patient preference is critical when evaluating relative risks and benefits.
Communication is essential.

- Important intra-op findings and details of postop care should be communicated by the surgeon to the patient and other physicians who are important in the patient’s postop care. (Strong recommendation, Low-quality evidence)
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</th>
<th>TT alone</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Events</td>
<td>Total</td>
<td>Events</td>
<td>Total</td>
</tr>
<tr>
<td>Sywak 2006</td>
<td>2</td>
<td>56</td>
<td>22</td>
</tr>
<tr>
<td>Costa 2009</td>
<td>9</td>
<td>126</td>
<td>8</td>
</tr>
<tr>
<td>Moo 2010</td>
<td>2</td>
<td>45</td>
<td>6</td>
</tr>
<tr>
<td>Hughes 2010</td>
<td>4</td>
<td>78</td>
<td>3</td>
</tr>
<tr>
<td>Barcynski 2012</td>
<td>15</td>
<td>358</td>
<td>37</td>
</tr>
<tr>
<td>Lang 2012</td>
<td>3</td>
<td>82</td>
<td>3</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>745</td>
<td>995</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

- 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 *w/o* pCLND *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)*
Surgeon experience and patient outcomes

When less ISN’T more.

<>
Annual surgeon volume (range 1-157 cases)
Adjusted association of surgeon volume and patient outcomes

Threshold
25 cases/yr
Definition of high-volume surgeons

Cohort
(Total thyroidectomy)

Low-volume
<25 cases/yr

High-volume
≥25 cases/yr
Adjusted* outcomes in low- vs. high-volume groups

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Effect</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall complications</td>
<td>OR 1.55</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LOS</td>
<td>↑ 23%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Inflation-adjusted costs</td>
<td>↑ 7%</td>
<td>0.002</td>
</tr>
</tbody>
</table>

*Adjusted for effect of age, gender, race, comorbidities, thyroid diagnosis
Conclusions

• Surgeon volume is significantly associated with improved outcomes, shorter hospitalization, and lower costs.

• The threshold number of total thyroidectomy cases for improved outcomes is 25/yr.

• The majority of patients underwent surgery by low-volume surgeons.