WELCOME

FALL UPDATE 2018

Head & Neck Endocrine Tumours
Thoughts On Thyroidectomy

The extirpation of the thyroid gland . . . typifies, perhaps better than any operation, the supreme triumph of the surgeon’s art. . . . A feat which today can be accomplished by any competent operator without danger of mishap and which was conceived more than one thousand years ago. . . . There are operations today more delicate and perhaps more difficult. . . . But is there any operative problem propounded so long ago and attacked by so many . . . which has yielded results as bountiful and so adequate?

Dr. William S. Halsted, 1920
Thyroidectomy & Thyroid Cancer Surgical Quality Indicators: What Should The Surgeon Know

Sam Wiseman BSc, MD, FRCSC, FACS, Associate Professor, Department of Surgery, University of British Columbia Thyroid & Parathyroid Surgery
St. Paul’s Hospital, Providence Health Care
Director of Research, Department of Surgery, Providence Health Care
Chair Endocrine Tumor Group, British Columbia Cancer Agency
Vancouver, British Columbia, Canada
Objectives

1. Review the importance of QI in thyroid & thyroid cancer surgery

2. Be aware of contemporary complication rates for thyroid/thyroid cancer operations

3. Appreciate postop RAI uptake, Tg level, and LN yield as thyroid cancer surgery QIs

4. Understand the importance of surgeon volume in thyroid surgery & thyroid cancer surgery outcomes
What Is Healthcare Quality?

The degree to which health services for individuals and populations **increase the likelihood of desired health outcomes** and are consistent with current professional knowledge.

(Lohr et al N Eng J Med 1990;322;707-712)
Current thyroid surgical technique was pioneered by Emil Theodor Kocher that led to a **reduction in mortality from 12.8% in 1883 to less than 0.5% 15 years later**
Thyroidectomy Surgical QIs: Complications

- Are important thyroid surgical quality outcomes and thyroid surgeons should be aware of their own complication rates and how they compare to current reported outcomes

- Thyroidectomy Specific Complications
  - Recurrent Laryngeal Nerve Injury (Scope)
  - Hypoparathyroidism (Measurement)

- Nonspecific Surgical Complications
  - Pneumonia
  - Myocardial Infarction
  - Renal Failure
  - Wound Infection
  - Blood Loss/Transfusion Requirement
  - Urinary Tract Infection
  - Postoperative Hemorrhage/Return to OR
Objective: **Identify operations needing more QI**

- 10 procedures evaluated in ACS NSQIP database between 2008-20015 (*1.2 million* operations)

*(Liu et al JACS 2018;226;1:30-36)*
# Thyroidectomy Current Complication Rates: Benchmarks For Thyroid Surgery QI

<table>
<thead>
<tr>
<th>Operation</th>
<th>Year</th>
<th>Cases, n</th>
<th>Mortality</th>
<th>Pneumonia</th>
<th>Renal failure</th>
<th>Surgical site infection</th>
<th>Unplanned Intubation</th>
<th>Urinary tract infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thyroidectomy</td>
<td>2008</td>
<td>7,915</td>
<td>7</td>
<td>0.09</td>
<td>17</td>
<td>0.21</td>
<td>2</td>
<td>0.03</td>
</tr>
<tr>
<td></td>
<td>2009</td>
<td>9,339</td>
<td>8</td>
<td>0.09</td>
<td>13</td>
<td>0.14</td>
<td>0</td>
<td>0.00</td>
</tr>
<tr>
<td></td>
<td>2010</td>
<td>9,774</td>
<td>4</td>
<td>0.04</td>
<td>23</td>
<td>0.24</td>
<td>4</td>
<td>0.04</td>
</tr>
<tr>
<td></td>
<td>2011</td>
<td>11,088</td>
<td>15</td>
<td>0.14</td>
<td>35</td>
<td>0.32</td>
<td>5</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
<td>2012</td>
<td>13,212</td>
<td>16</td>
<td>0.05</td>
<td>16</td>
<td>0.12</td>
<td>1</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>2013</td>
<td>14,614</td>
<td>14</td>
<td>0.10</td>
<td>31</td>
<td>0.21</td>
<td>8</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
<td>2014</td>
<td>16,043</td>
<td>9</td>
<td>0.06</td>
<td>38</td>
<td>0.24</td>
<td>8</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
<td>2015</td>
<td>17,687</td>
<td>19</td>
<td>0.11</td>
<td>52</td>
<td>0.29</td>
<td>10</td>
<td>0.06</td>
</tr>
<tr>
<td>Subtotal</td>
<td></td>
<td>99,672</td>
<td>83</td>
<td>0.08</td>
<td>225</td>
<td>0.23</td>
<td>38</td>
<td>0.04</td>
</tr>
</tbody>
</table>

## Table 2. Estimated Number of Adverse Events Avoided per 10,000 Operations

<table>
<thead>
<tr>
<th>Operation</th>
<th>Mortality</th>
<th>Pneumonia</th>
<th>Renal failure</th>
<th>Surgical site infection</th>
<th>Unplanned Intubation</th>
<th>Urinary tract infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colectomy</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>124</td>
<td>82</td>
</tr>
<tr>
<td>Esophagectomy</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Hepatectomy</td>
<td>76</td>
<td>—</td>
<td>24</td>
<td>—</td>
<td>—</td>
<td>98</td>
</tr>
<tr>
<td>Hysterectomy</td>
<td>5</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>9</td>
<td>—</td>
</tr>
<tr>
<td>Pancreatectomy</td>
<td>26</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>51</td>
<td>—</td>
</tr>
<tr>
<td>Proctectomy</td>
<td>16</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>49</td>
<td>—</td>
</tr>
<tr>
<td>Total hip arthroplasty</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>10</td>
<td>—</td>
</tr>
<tr>
<td>Total knee arthroplasty</td>
<td>—</td>
<td>24</td>
<td>—</td>
<td>13</td>
<td>—</td>
<td>68</td>
</tr>
<tr>
<td><strong>Thyroidectomy</strong></td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>5</td>
</tr>
<tr>
<td>Ventral hernia repair</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>44</td>
<td>—</td>
</tr>
</tbody>
</table>

Adverse events avoided = slope from Table 2 × 8 years × 10,000 operations. Events avoided are not estimated for those without significant improvements. Values presented are interpreted as number of cases avoided per 10,000 procedures in the final year, resulting from cumulative quality effects during the 8-year period.

(Liu et al JACS 2018;226;1:30-36)
Thyroidectomy For Cancer QIs: What Are Contemporary Complication Rates?

- **Objective:**
  - To determine thyroid cancer surgical complication rates and identify at risk populations

- **SEER database (1998-2011)**
  - 22,867 patients 30 day and 1 year complication rates in DTC (97.2%) & MTC (2.8%) cases

- **Complications Separated into:**
  - **General** (Fever/Infection/Hematoma/Pneumonia/Intubation/Trach/MI/PE/DVT)
  - **Thyroidectomy Specific** (Hypoparathyroidism/VC paralysis) (Starting at 31 days postop)

(Papaleontiou et al JCEM; 2017;102:2543-2551)
Thyroidectomy For Cancer QI: Complications

Overall Complication Rates:
- General (6.5%)
- Thyroidectomy Specific (12.3%)
  - 1152 cases of vocal cord paralysis
  - 2553 cases of hypoparathyroidism

Table 2. Patient Characteristics Associated With Postoperative Complications

<table>
<thead>
<tr>
<th>Clinical Factors</th>
<th>Cardiopulmonary/Thromboembolic Complications</th>
<th>Postoperative Fever/Local Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>P Value&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>General postoperative complications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (y)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤65</td>
<td>332 (2.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&gt;65</td>
<td>1119 (8.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Charlson/Deyo comorbidity score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>33 (0.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>1</td>
<td>67 (1.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≥2</td>
<td>1351 (7.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Stage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Localized</td>
<td>237 (4.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Regional</td>
<td>513 (5.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Distant</td>
<td>193 (16.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypoparathyroidism/Hypocalcemia</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>n (%)</td>
<td>P Value&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Thyroid surgery-specific complications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (y)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤65</td>
<td>743 (5.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&gt;65</td>
<td>1810 (13.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Charlson/Deyo comorbidity score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>164 (2.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>1</td>
<td>202 (5.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≥2</td>
<td>2187 (11.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Stage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Localized</td>
<td>1448 (8.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Regional</td>
<td>932 (10.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Distant</td>
<td>158 (13.5)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

<sup>a</sup>P values were calculated based on χ² test for linear trend.

(Papaleontiou et al JCEM; 2017;102:2543-2551)
Thyroidectomy QIs: What Is The Influence of Surgeon Volume On Complications?

- Retrospective review of Nationwide Inpatient Sample (2003-2009) to evaluate thyroidectomy complications and the effect of surgeon experience/volume

- **62,722** thyroidectomies evaluated
  - 57.9% Total Thyroidectomy / 42.1% Lobectomy
  - 3.3% Graves, 60.8% Benign Disease, 35.9% Cancer
  - 0.4% Neck Dissection

- **Surgeon Volume Classification**
  - Low (<10) - 50.2%
  - Intermediate (10-99) – 44.8%
  - High (>99) – 5.0%

(Hauch et al; Ann Surg Onc 2014;21:3844-3852)
Thyroidectomy QIs: Influence of Surgeon Volume On Complications

- Higher complication risk after Total Thyroidectomy (20.8%) compared to Lobectomy (10.8%) \((p<0.0001)\):  
  - Hypocalcemia (7.1% vs 16.1%, \(p<0.0001\))  
  - Respiratory Complications (0.84% vs 1.34%, \(p<0.0001\))  
  - Bleeding (0.15% vs 0.23%, \(p=0.0403\))  
  - Hematoma (1.24 vs 1.54%, \(p=0.0027\))  
  - Tracheostomy (0.004% vs 0.024%, \(p=0.0493\))  
  - Vocal Cord Paralysis (0.59 vs 1.33%, \(p<0.001\))

- Even high volume surgeons have a higher complication risk for Total Thyroidectomy compared to Lobectomy

- Low volume surgeons were more likely to have complications then high volume surgeons (OR 1.53, 95% CI 1.12, 2.11, \(p=0.0083\))  
  - True for both Lobectomy and Total Thyroidectomy

(Hauch et al; Ann Surg Onc 2014;21:3844-3852)
Total Thyroidectomy Surgical QIs: Complications & Influence of Surgeon Volume

• Retrospective review of Nationwide Inpatient Sample (1998-2009) to evaluate total thyroidectomy complications and the effect of surgeon experience/volume

• **16,954** Total Thyroidectomies evaluated
  • 47% Thyroid Cancer, 53% Benign Disease
  • Median annual surgeon volume was 7 cases
  • 51% of surgeons performed 1 case/year

Total Thyroidectomy Surgical QIs: Influence of Surgeon Volume On Complications

- Likelihood of experiencing a complication decreased with increasing surgeon volume up to **26 cases/year** (p<0.01)

- Patients undergoing thyroidectomy by low compared to high volume surgeons were:
  - More likely to experience complications (OR 1.51, p=0.002)
  - Have longer hospital admissions (+12%, P=0.006)

### TABLE 2. Clinical Outcomes, Hospital Length of Stay, and Inflation-adjusted Hospital Costs by Surgeon Volume Status

<table>
<thead>
<tr>
<th>Complication</th>
<th>High-volume (&gt;25 Cases/y)</th>
<th>Low-volume (&lt;25 Cases/y)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endocrine-related</td>
<td>50 (1.6%)</td>
<td>316 (2.3%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Bleeding</td>
<td>31 (1.0%)</td>
<td>223 (1.6%)</td>
<td>0.006</td>
</tr>
<tr>
<td>Wound</td>
<td>21 (0.7%)</td>
<td>166 (1.1%)</td>
<td>0.005</td>
</tr>
<tr>
<td>Respiratory</td>
<td>18 (0.6%)</td>
<td>183 (1.3%)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Cardiac</td>
<td>9 (0.3%)</td>
<td>58 (0.4%)</td>
<td>0.35</td>
</tr>
<tr>
<td>Urologic</td>
<td>15 (0.5%)</td>
<td>66 (0.5%)</td>
<td>1</td>
</tr>
<tr>
<td>Overall</td>
<td>130 (4.1%)</td>
<td>876 (6.4%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>0</td>
<td></td>
<td>0.59</td>
</tr>
<tr>
<td>Length of stay, d (median, IQR)</td>
<td>1.5 (13)</td>
<td>2 (1.9)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Mean, SD</td>
<td>1 (1-2)</td>
<td>2 (1-2)</td>
<td></td>
</tr>
<tr>
<td>Inflated-adjusted costs†</td>
<td>$7166 (5052)</td>
<td>$7550 (5683)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Mean, SD</td>
<td>$5826 (4325, 8578)</td>
<td>$6385 (4800, 8674)</td>
<td></td>
</tr>
</tbody>
</table>

*Suppressed due small cell size, per HCUP-NIS policy.
†Cost data are reported in 2014 US dollars.
IQR indicates interquartile range; SD, standard deviation.

What is Quality Cancer Care?

“The provision of evidence-based, patient-centered services throughout the continuum of care in a timely and technically competent manner, with good communication, shared decision making, and cultural sensitivity, with the aim of improving clinical outcomes, including patient survival and health-related quality of life”

Quality Improvement For Cancer Patients Is Challenging

- Ongoing and continuous *modification* of cancer treatment plan
- Multidisciplinary treatment paradigm
- Lengthy time intervals for outcomes

(Albert et al; I J Rad Onc 2012;83:773-780)
What Are Cancer Care Quality Indicators?

• Disease specific, reliable, scientifically validated/evidence or consensus based measures that reflect quality of care and can be utilized to guide cancer patient & caregiver:

  ➢ Assessment
  ➢ Benchmarking
  ➢ Accreditation
  ➢ Credentialing
  ➢ Reimbursement
  ➢ Quality Improvement

(Albert et al; I J Rad Onc 2012;83:773-780)
Diversity in pathophysiology/prognosticators/treatments for different cancer types and so **QIs must be tailored to the cancer type**

- QI development has focused on cancer types:
  - High Mortality/Recurrence Risk
  - High Risk Operations
  - Most Common Operations
Thyroid Cancer Surgical QI: Challenges

- Thyroid Cancer tends to:
  - Have an excellent prognosis
  - Mortality is uncommon
    » Poor QI Outcome Measure
  - May recur over decades
    » Recurrence may be hard to track
    » QI Outcome Measure of interest
- Most considered ‘low risk’
  - May NOT require:
    » Total Thyroidectomy
    » Central Neck Neck Dissection
    » RAI treatment

(Mazzaferri at al. Journal Clin Endocin and Metab 2001)
Goal of the surgeon when performing a thyroidectomy for cancer is to safely remove all thyroid cancer/tissue (including primary tumor and nodal disease) on the side that is being operated upon.

Thyroid cancer surgical QIs are based on completeness of thyroid/thyroid cancer resection.

None of these oncological QIs are considered standard of care currently.
Not All Thyroidectomies Are Total

• The remnant of thyroid tissue that is intentionally left by the surgeon in the thyroid bed in order to reduce the risk of RLN and Parathyroid injury is influenced by multiple factors:

  ➢ Surgical Indication
  ➢ Clinical Setting
  ➢ Surgical Anatomy
  ➢ Surgeon
    – Training
    – Comfort
    – Experience
    – Judgment

• **Near-total** thyroidectomy (<1-2g)
The Reality Regarding Thyroid Remnants

• Incomplete thyroid/cancer resection predicts a worse outcome (reduced survival and increased recurrence risk)

  Score = 3.1 (age <40) or 0.8 × age (age >40) + 0.3 × tumour size (cm) + 1 if incompletely resected + 1 if locally invasive + 3 if distant spread

  20-year survival by MACIS score
  - <6 = 99%
  - 6-6.99 = 80%
  - 7-7.99 = 56%
  - ≥8.00 = 24%

• Larger thyroid remnants may not adequately be ablated by postop RAI
  - Stimulated WBS (5 mCi iodine-131) 6-12 months postop predicted success of remnant ablation by 100 mCi iodine-131

(Rosario et al Clin Nuc Med;2004;6;358-361)
Proposed Thyroid Cancer Surgical QIs

1. Remnant Thyroid Uptake of RAI
2. Postoperative Thyroglobulin Level
3. Metastatic Lymph Node Ratio
Remnant Thyroid RAI Uptake

• Post-radioactive iodine ablation treatment a whole body scan is carried out 3-7 days later to evaluate for remnant thyroid tissue & the presence of regional/distant metastases

• Remnant thyroid radioiodine uptake (RTRU) is calculated as a % of the total radioisotope given that is detected in the thyroid bed after adjusting for decay
Remnant Thyroid RAI Uptake

- RTRU correlates with volume of residual thyroid tissue present when evaluated by neck US

- 66 thyroidectomy patients (benign) had remnant volume and uptake evaluated by US, TSH, and RAI scan 1 month postop

(Erbil et al JLO;2008;122;615-622)
Remnant Thyroid Tissue RAI Uptake

• Retrospective review of cases undergoing TT and postop RAI for thyroid cancer treatment

• Remnant uptake analyzed as ratio of the % uptake of dose received (UDR) and evaluated for association with recurrence

• 21/223 patients recurred (FU 25 mo)

• Patients with recurrence had a 10x higher UDR then those that didn’t recur

• The higher UDR, the higher the recurrence risk

(Schneider et al Thyroid;2013;23;1269-76)
Is There An Influence Of Surgeon Volume On RTRU?

- Surgeons classified as **high** (3) or **low** (5) volume (defined by 20 thyroid operations/year)

- **UDRs of high volume surgeons were significantly lower than low volume surgeons**

- Overall **33 complications** (24 temporary/9 permanent)

- High volume surgeons had significantly lower permanent complications, even at high UDR

- Low volume surgeons, had a **stepwise increase** in complications as UDR rises

(Schneider et al Thyroid;2013;23;1269-76)
Growing Literature Evaluating Remnant Thyroid Tissue RAI Uptake As A Thyroidectomy QI

<table>
<thead>
<tr>
<th>Study (year)</th>
<th>N</th>
<th>Variables Studied</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rosario et al. (2004)</td>
<td>142</td>
<td>RAI uptake post TT</td>
<td>- Inverse correlation between RAI uptake and ablation efficiency ($r^2 = 0.92$, $p &lt; 0.05$)</td>
</tr>
<tr>
<td>Lim et al. (2012)</td>
<td>173</td>
<td>Quantified postoperative cervical uptake</td>
<td>- Quantified cervical uptake &gt;10% after thyroidectomy is a significant predictor for ablation failure (OR = 4.95 [1.07 – 22.88]; $p = 0.041$) and disease-free status (OR = 0.87 [0.76 – 0.98]; $p = 0.024$)</td>
</tr>
<tr>
<td>Schneider et al. (2013)</td>
<td>223</td>
<td>Post-TT RAI UDR Surgeon volume</td>
<td>- Odds ratio for UDR independently predicting disease recurrence is 3.71 [1.5-13.10]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- The post-TT UDRs of high-volume surgeons were significantly smaller than low-volume surgeons (0.003 vs 0.025; $p = 0.002$)</td>
</tr>
<tr>
<td>Holsinger et al. (2014)</td>
<td>245</td>
<td>RAI uptake post TT</td>
<td>- 65% of patients with RAI uptake &gt;0.2% had measurable stimulated Tg levels compared with 25% of patients with RAI uptake ≤0.2% ($p &lt; 0.001$)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Rates of local and/or regional recurrence were low regardless of RAI uptake</td>
</tr>
<tr>
<td>Oltmann et al. (2014)</td>
<td>45</td>
<td>CT vs TT Surgeon volume</td>
<td>- CT patients had higher UDR than those undergoing TT (0.0008 vs 0.0004; $p = 0.04$)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- CT patients managed by high-volume surgeons had lower UDR than those managed by low-volume surgeons (0.005 vs 0.006; $p = 0.03$)</td>
</tr>
</tbody>
</table>

RAI: Radioactive iodine; TT: Total thyroidectomy; US: Ultrasound; TSH: Thyroid stimulating hormone; rhTSH: Recombinant human TSH; L-T4: L-thyroxine; UDR: Uptake dose ratio; Tg: Thyroglobulin; CT: Completion thyroidectomy

(Liu & Wiseman; Exp Rev Anticancer Ther; 2016;16;919-928)
Remnant Thyroid RAI Uptake As A QI

• RTRU may serve as a QI for thyroid cancer surgery because it correlates with ‘completeness of thyroidectomy’ and recurrence risk

• Thoughts & Limitations
  – Cannot be utilized in lobectomy (Low Risk) patients
  – Utility limited in RAI non-avid recurrence
  – Not appropriate for locally advanced/completely resectable cases
  – Not accurate in the presence of significant metastatic disease
  – Influence of other concurrent thyroid disease (ie. Graves)
  – What is an “acceptable” RTRU?
  – Should RTRU influence postoperative surveillance and follow up?
  – Is there a RTRU that mandates reoperation or repeat RAI treatment?

Do you know your patient’s RTRU?
Postoperative Thyroglobulin Level

- Tg is a glycoprotein, a prohormone, only synthesized by thyrocytes stored in colloid, that’s production is stimulated by TSH

- Stimulated and unstimulated Tg measurement is used for postop surveillance of all thyroid cancer patients

- Tg measurement after Total Thyroidectomy correlates with volume of remnant thyroid tissue &/or cancer and may serve as a thyroid cancer surgical QI
Postoperative Thyroglobulin Level

No mention of early postoperative serum Tg measurement

(C5) What is the role of serum Tg measurement in the follow-up of DTC?

RECOMMENDATION 62

(A) Serum Tg should be measured by an assay that is calibrated against the CRM457 standard. Thyroglobulin antibodies should be quantitatively assessed with every measurement of serum Tg. Ideally, serum Tg and anti-Tg antibodies should be assessed longitudinally in the same laboratory and using the same assay for a given patient.

(Strong recommendation, High-quality evidence)

(B) During initial follow-up, serum Tg on thyroxine therapy should be measured every 6–12 months. More frequent Tg measurements may be appropriate for ATA high-risk patients.

(Strong recommendation, Moderate-quality evidence)

(C) In ATA low- and intermediate-risk patients that achieve an excellent response to therapy, the utility of subsequent Tg testing is not established. The time interval between serum Tg measurements can be lengthened to at least 12–24 months.

(Weak recommendation, Low-quality evidence)

(D) Serum TSH should be measured at least every 12 months in all patients on thyroid hormone therapy.

(Weak recommendation, Low-quality evidence)

RECOMMENDATION 63

(A) In ATA low-risk and intermediate-risk patients who have had remnant ablation or adjuvant therapy and negative cervical US, serum Tg should be measured at 6–18 months on thyroxine therapy with a sensitive Tg assay (<0.2 ng/mL) or after TSH stimulation to verify absence of disease (excellent response).

(Strong recommendation, Moderate-quality evidence)

(B) Repeat TSH-stimulated Tg testing is not recommended for low- and intermediate-risk patients with an excellent response to therapy.

(Weak recommendation, Low-quality evidence)

(C) Subsequent TSH-stimulated Tg testing may be considered in patients with an indeterminate, biochemical incomplete, or structural incomplete response following either additional therapies or a spontaneous decline in Tg values on thyroid hormone therapy over time in order to reassess response to therapy.

(Weak recommendation, Low-quality evidence)

(ATA Guidelines 2015)
Is There An Influence Of Surgeon Volume On Postoperative Thyroglobulin Level?

- Retrospective review of all thyroid operations (DTC ≥ 1 cm) during 2011 in a regional health system (U Pitt)

- 42 surgeons/volume evaluated for:
  - Extent of initial operation
  - % uptake on $^{123}$I pre-RAI TSH stimulated uptake scan
  - Pre-ablation TSH-stimulated Tg level
  - Dose of $^{131}$I administered

(Adkisson et al; Surgery; 2014;156;1453-60)
Surgeon Volume & Thyroid Cancer Surgical QIs

Higher Surgeon Volume

>30 Thyroid ORs/Year
- Total Thyroidectomy
- More ‘complete’ % uptake on $^{123}$I
- Stimulated Tg
- Administered $^{131}$I dose
- Fewer complications

>50 Thyroid ORs/Year
For Stage 3 & 4 Disease
- More ‘complete’ % uptake on $^{123}$I

---

**Table II.** Analysis of surgeon volume and quantitative measures of adequate initial surgery

<table>
<thead>
<tr>
<th>Thyroid cases per year</th>
<th>No. surgeons (DTC patients)</th>
<th>$^{123}$I prescan uptake, % HVS (LVS)</th>
<th>P value</th>
<th>Serum Tg, ng/mL</th>
<th>Serum Tg, HVS (LVS)</th>
<th>P value</th>
<th>Mean dose $^{131}$I given, mCi HVS (LVS)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥10</td>
<td>16 (331)</td>
<td>3.1 (6.0)</td>
<td>.135</td>
<td>3.9 (7.4)</td>
<td>.115</td>
<td>94.9 (92.5)</td>
<td>.85</td>
<td></td>
</tr>
<tr>
<td>≥20</td>
<td>13 (326)</td>
<td>2.5 (2.5)</td>
<td>.9</td>
<td>3.7 (6.1)</td>
<td>.16</td>
<td>95.0 (96.7)</td>
<td>.85</td>
<td></td>
</tr>
<tr>
<td>≥25</td>
<td>11 (302)</td>
<td>2.3 (3.1)</td>
<td>.2</td>
<td>3.8 (5.0)</td>
<td>.86</td>
<td>91 (108)</td>
<td>.03</td>
<td></td>
</tr>
<tr>
<td>≥30</td>
<td>8 (275)</td>
<td>2.2 (4.4)</td>
<td>.01</td>
<td>3.8 (8.4)</td>
<td>.02</td>
<td>90 (107)</td>
<td>.03</td>
<td></td>
</tr>
<tr>
<td>≥50</td>
<td>6 (239)</td>
<td>2.2 (4.2)</td>
<td>.005</td>
<td>3.5 (8.8)</td>
<td>.007</td>
<td>88 (108)</td>
<td>.002</td>
<td></td>
</tr>
<tr>
<td>≥100</td>
<td>5 (224)</td>
<td>2.0 (3.9)</td>
<td>.001</td>
<td>3.7 (6.6)</td>
<td>.04</td>
<td>92 (105)</td>
<td>.02</td>
<td></td>
</tr>
</tbody>
</table>

*Bold type represents $P < .05$.

DTC, Differentiated thyroid cancer; HVS, high-volume surgeons; LVS, low-volume surgeons.

---

**Table IV.** Analysis of surgeon volume and quantitative measures of adequate initial surgery for patients with AJCC TNM stage III/IV disease

<table>
<thead>
<tr>
<th>No. of Tx/y*</th>
<th>$^{123}$I prescan uptake, % HVS (LVS)</th>
<th>P value</th>
<th>Serum Tg, ng/mL</th>
<th>Serum Tg, HVS (LVS)</th>
<th>P value</th>
<th>Mean dose $^{131}$I given, mCi HVS (LVS)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>2.4 (3.0)</td>
<td>.7</td>
<td>5.5 (6.5)</td>
<td>.8</td>
<td>104 (192)</td>
<td>.3</td>
<td></td>
</tr>
<tr>
<td>30</td>
<td>2.8 (4.8)</td>
<td>.2</td>
<td>5.3 (7.7)</td>
<td>.5</td>
<td>105 (117)</td>
<td>.5</td>
<td></td>
</tr>
<tr>
<td>50</td>
<td>2.2 (5.2)</td>
<td>.004</td>
<td>5.0 (8.2)</td>
<td>.3</td>
<td>105 (121)</td>
<td>.2</td>
<td></td>
</tr>
<tr>
<td>100</td>
<td>1.9 (3.9)</td>
<td>.001</td>
<td>3.5 (6.8)</td>
<td>.03</td>
<td>93.5 (115)</td>
<td>.05</td>
<td></td>
</tr>
</tbody>
</table>

*At thresholds of 10 and 20 cases per year, the number of patients with stage III/IV disease was too small for analysis.

Bold type represents $P < .05$.

AJCC, American Joint Committee on Cancer; HVS, high-volume surgeon; LVS, low-volume surgeon; Tx, thyroidectomy.

(Adkisson et al; Surgery; 2014;156;1453-60)
## Growing Literature Evaluating Postoperative Thyroglobulin Level As A QI

<table>
<thead>
<tr>
<th>Study (year)</th>
<th>N</th>
<th>Variables</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ruiz-García et al.</td>
<td>98</td>
<td>Type of surgery</td>
<td>- 10-year disease free survival was 100% in patients with Tg ≤23 ng/mL and 68.4% in patients with Tg &gt;23 ng/mL</td>
</tr>
<tr>
<td>(1991)</td>
<td></td>
<td>unspecified</td>
<td></td>
</tr>
<tr>
<td>Lin et al.</td>
<td>847</td>
<td>1 month after TT</td>
<td>- 1-month post-operative Tg level &gt;10ug/L is a significant prognostic factor for patients with DTC</td>
</tr>
<tr>
<td>(2002)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bernier et al.</td>
<td>407</td>
<td>TT</td>
<td>- Tg during T4 withdrawal of ≥5ng/mL is predictive of unsuccessful ablation (RR = 1.02 [1.00 – 1.03]; p &lt; 0.05)</td>
</tr>
<tr>
<td>(2005)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Makarewicz et al.</td>
<td>178</td>
<td>TT</td>
<td>- Tg during T4 withdrawal was significantly higher in patients who later developed recurrence compared to those who did not (97.4 ng/mL vs. 4.3 ng/mL; p = 0.000001)</td>
</tr>
<tr>
<td>(2006)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heemstra et al.</td>
<td>366</td>
<td>Near TT</td>
<td>- Tg during T4 withdrawal of &lt;27.5ug/L had a positive predictive value of 97.8% for disease-free remission and is an independent prognostic marker for disease-free remission (likelihood ratio = 43.2; p &lt; 0.001)</td>
</tr>
<tr>
<td>(2007)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hall et al.</td>
<td>213</td>
<td>3 months after TT</td>
<td>- Patients with Tg during T3 withdrawal of &gt;20pmol/L had a significantly increased risk of disease recurrence (p = 0.001)</td>
</tr>
<tr>
<td>(2003)</td>
<td></td>
<td></td>
<td>- Tg during T3 withdrawal of &gt;20pmol/L is a significant predictor of recurrence (RR = 5.1 [2.0 – 13.1]; p = 0.001)</td>
</tr>
<tr>
<td>Alagic-Smailbegovic et</td>
<td>116</td>
<td>1 month after TT</td>
<td>- Mean Tg was 190.8 ng/mL in patients who later developed recurrent disease and 9.3 ng/mL in those who had no evidence of recurrence (p = 0.023)</td>
</tr>
<tr>
<td>al. (2012)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kendler et al.</td>
<td>96</td>
<td>1 month after TT</td>
<td>- Tg ≥18 ng/mL in thyroid hormone withdrawal is an independent predictor of unsuccessful ablation (RR = 5.89, p &lt; 0.0001)</td>
</tr>
<tr>
<td>(2012)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lee et al.</td>
<td>218</td>
<td>3 months after TT</td>
<td>- Tg &lt;2ng/mL in thyroid hormone withdrawal had a negative predictive value of 94.9% for disease free status</td>
</tr>
<tr>
<td>(2013)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moon et al.</td>
<td>253</td>
<td>TT with CND</td>
<td>- rhTSH-stimulated Tg of &lt;1.79 ng/mL has a negative predictive value of 99.5% for persistent or recurrent disease at 1 year post-ablation</td>
</tr>
</tbody>
</table>

RAI: Radioactive Iodine; Tg: Thyroglobulin; TT: Total thyroidectomy; RR: Relative risk; T4: Thyroxine; T3: OR: Odds ratio; rhTSH: Recombinant human thyroid stimulating hormone; Anti-Tg Ab: Anti- thyroglobulin antibody. * Prospective study.

(Liu & Wiseman; Exp Rev Anticancer Ther; 2016;16;919-928)
Postoperative Thyroglobulin Level As A QI

- Postop Tg may serve as a QI for thyroid cancer surgery because it correlates with ‘completeness of thyroidectomy’ and recurrence risk

- Thoughts & Limitations
  - Utility in lobectomy (Low Risk) patients unknown
  - Not useful for tumors that don’t synthesize Tg
  - Not appropriate in locally advanced/not completely resectable cancers
  - Not accurate in the presence of bulky metastatic disease
  - Influence of other concurrent thyroid disease (ie. Hashimoto’s)?
  - What is the optimal timing of Tg measurement relative to surgery and RAI?
  - What is an acceptable postoperative Tg level?
  - Should Tg influence postoperative surveillance and follow up?
  - Is there a Tg level that mandates reoperation or repeat RAI treatment?

Do you know your patient’s postoperative Tg level?
Central Neck Dissection For Thyroid Cancer

- **Variation in surgical practice** regarding CND for thyroid cancer treatment
- Central neck lymph node metastases can be detected **in 20-50% of cases**
- Lymph node metastases **increase risk of cancer recurrence**
- The AHNS defines a central neck dissection as a comprehensive removal of:
  - **NECK NODE LEVEL VI**
    - Prelaryngeal (Delphian) Lymph Nodes
    - Pretracheal Lymph Node
  - Left +/- Right **Paratracheal** Lymph Nodes

(Agrawal et al; Head Neck;2017;39;1269-1279)
RECOMMENDATION 36

(A) Therapeutic central-compartment (level VI) neck dissection for patients with clinically involved central nodes should accompany total thyroidectomy to provide clearance of disease from the central neck.

(Strong recommendation, Moderate-quality evidence)

(B) Prophylactic central-compartment neck dissection (ipsilateral or bilateral) should be considered in patients with papillary thyroid carcinoma with clinically uninvolved central neck lymph nodes (cN0) who have advanced primary tumors (T3 or T4) or clinically involved lateral neck nodes (cN1b), or if the information will be used to plan further steps in therapy.

(Weak recommendation, Low-quality evidence)

(C) Thyroidectomy without prophylactic central neck dissection is appropriate for small (T1 or T2), noninvasive, clinically node-negative PTC (cN0) and for most follicular cancers.

(Strong recommendation, Moderate-quality evidence)
What Is Metastatic Lymph Node Ratio?

- Proposed as a QI for thyroid cancer surgery
- Reflects the success of the surgeon in central neck compartment lymphadenectomy

# Metastatic Lymph Nodes
Total # of Lymph Nodes (Lymph Node Node Yield)
Evaluation of MLNR in 10,955 DTC patients with >3 LN removed in the SEER database (1988-2007) (median follow up 25 months)

- MLNR was strongly associated with DSM (HR 4.33, 95%CI 1.68-11.18, p<0.01)

- MLNR $\geq 0.42$ separated cases based on disease specific mortality

(Schneider et al; Ann Sug Onc;2013;20;1906-1911)
Growing Literature Evaluating Metastatic Lymph Node Ratio As A QI

<table>
<thead>
<tr>
<th>Study (year)</th>
<th>N</th>
<th>Variables</th>
<th>Outcome</th>
</tr>
</thead>
</table>
| Wada et al. (2007)   | 134 | % of LNM  | - % of LNM was significantly higher in patients with local disease recurrence than in those without local disease recurrence (54.8% vs. 23.9%, p < 0.0005)  
- % of LNM was significantly higher in patients with distant metastasis than in those without distant metastasis (49.1% vs. 25.5%, p < 0.01)  
- % of LNM is unrelated to death from disease |
| Beal et al. (2010)   | 9926| MLNR      | - There is significant decrease in overall survival with increased MLNR (univariate analysis p < 0.001; multivariate analysis: p = 0.01) |
| Vas Nunes et al. (2013) | 198 | LNR, LNY  | - Patients with LNR ≥ 0.30 had a 3.4 times higher risk of persistent or recurrent disease compared with patients with LNR of 0.00 (p = 0.031)  
- Patients with LNR ≤ 0.11 had an 80% chance of remaining disease free during 5 years of follow-up |
| Schneider et al. (2013) | 6,103 | LNR      | - Higher rate of DSM experienced by those with a LNR ≥ 0.42 compared to those with LNR < 0.42 (1.72% vs. 0.65%; p < 0.01) when three or more lymph nodes were harvested |
| Schneider et al. (2013) | 217 | LNR, cLNR | - Significantly higher rate of recurrence in patients with LNR ≥ 0.7 (p < 0.01) or cLNR ≥ 0.86 (p < 0.01)  
- Odds ratio for LNR predicting disease recurrence is 19.5 [4.1 – 22.9]; p < 0.01 |
| Ryu et al. (2014)    | 283 | LNR after pCND | - Patients with recurrence had a mean LNR of 0.77 +/- 0.22; patients without recurrence had a mean LNR of 0.39 +/- 0.27, when three or more lymph nodes were dissected (p < 0.001)  
- LNR > 0.65 is significantly associated with recurrence (<0.001) |

LNM: Lymph node metastasis; MLNR: Metastatic lymph node ratio; LNR: Lymph node ratio; LNY: Lymph node yield; DSM: Disease-specific mortality; cLNR: Central lymph node ratio; pCND: Prophylactic central neck dissection

(Liu & Wiseman; Exp Rev Anticancer Ther; 2016;16;919-928)
Metastatic Lymph Node Ratio As A QI

- MLNR may serve as a QI for thyroid cancer surgery because it correlates with ‘completeness of lymphadenectomy’ and recurrence risk

- Thoughts & Limitations
  - Utility in the setting of bulky disease is poor (cannot achieve a low ratio)
  - Surgical intention: Therapeutic vs Prophylactic must be considered
  - Impact of nodal metastases size/extranodal extension unknown
  - Influence of other concurrent thyroid disease (ie. Hashimoto’s)
  - What is an “acceptable” MLNR?
  - Should MLNR influence postoperative surveillance and follow up?

Do you know your patient’s MLNR?
Final Thoughts: Should Guideline Adherence Be Considered A Thyroid Surgical QI?

• Could address difficulty with finding thyroid cancer surgery QIs for Low Risk patients

• Guidelines are Guidelines and constantly changing based upon new evidence

• Should not following guidelines be an indicator of poor oncological surgical quality?
Final Thoughts:
How Many High Volume Surgeons Would It Take To Perform All The Thyroidectomies In The USA Annually? Realistic?

Estimate: Total # Thyroidectomies In US/Year = 150,000

High Volume Surgeon >99 Thyroidectomies/Year
Total # High Volume Thyroid Surgeons Needed = 1,500

High Volume Surgeon >24 Thyroidectomies/Year
Total # High Volume Thyroid Surgeons Needed = 6,000

Conclusions

• Thyroid surgical QIs are focused on surgical complications

• Thyroid cancer surgical QIs allow for evaluation of the completeness of:
  
  • Thyroidectomy
    – Remnant Thyroid Uptake of RAI
    – Postoperative Thyroglobulin Level
  
  • Central Neck Lymphadenectomy
    – Metastatic Lymph Node Ratio

• Application of these QIs is largely limited to patients who have undergone a total thyroidectomy +/- RAI (primarily High Risk)
Conclusions

• Despite no specific QI currently considered standard, and further study being needed, surgeons who perform thyroid operations should be aware of their:

  - Patient’s thyroid surgical QIs
    - Morbidity & Mortality
    - Recurrence Risk

  - Patient’s thyroid cancer surgical QIs
    - Postop RAI uptake
    - Postop TG
    - MLNR
    - Other?

  - Own thyroidectomy surgical volumes

• This information is readily available, quantifiable, is associated with surgical and oncological outcomes, and allows for quality improvement (NOW HOW DO WE APPLY THESE QIs IN THE REAL WORLD???)
Thank You

Questions?

I AM USUALLY HERE