





Thyroidectomy & Thyroid Cancer Surgical Quality Indicators: What Should The Surgeon Know

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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 <u>increase the</u> <u>likelihood of desired health outcomes</u> and are consistent with current professional knowledge.







Revolutionary Thyroid Surgical Quality Improvement: Kocher's Thyroidectomy Technique



Current thyroid surgical technique was pioneered by Emil Theodor Kocher that led to a **reduction in mortality from** <u>12.8% in 1883 to less than 0.5% 15 years later</u>





EMILTHEODORKOCHER

Concerning pathological manifestations in low-grade thyroid diseases

Nobel Lecture*, December 11, 1909



Thyroidectomy Surgical QIs: Complications

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

| THYROID | |
|------------------------------|--|
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SPECIAL ARTICLE

American Thyroid Association Statement on Postoperative Hypoparathyroidism: Diagnosis, Prevention, and Management in Adults

Lisa A. Orloff¹¹ Sam M. Wiseman^{2,*} Victor J. Bernet² Thomas J. Fahey III⁴ Ashok R. Shaha² Maisie L. Shindo⁶ Samuel K. Shyder² Brendan C. Stack Jr.⁹ John B. Surwoo² and Marilene B. Wang⁹ for the American Thyroid Association Surgical Alfaire Committee Writing Task Force

Background: Hypoparathyroidism (hypoPT) is the most common complication following bilateral thyroid operations. Thyroid surgeons must employ strategies for minimizing and preventing post-thyroidectomy hypoPT. The objective of this American Thyroid Association Surgical Affairs Committee Statement is to provide an overview of its diagnosis, prevention, and treatment.

Summary: HypOPT occurs when a low inter parathytoid bermone (PTH) level is accompanied by hypocalcentia, Risk factors for post-hyporide control by hpoPT include bilateral thyroid operations, and/ordinos. Medical and surgical strategies to minimize periorative hpoPT include optimizing viamin D levels, preserving parathyroid blood supply, and autotransplanting ischemic parathyroid glands. Measurement of intraoperative or early posterative PTH level <15 pg/mL indicates increased risk for acute hypoPT. Effective management of mild to moderate potential or acuted posteparitie hypoPT can be achieved by administering either empirique PTH level <15 pg/mL indicates increased risk for acute hypoPT. Effective management of mild to moderate additional posteparitie hypoPT can be achieved by administering either empirique via metabolic and erail accluim levels as a guide. Monitoring for rebound hyperaclemia is necessary to avoid metabolic and remal completions. For more severe hypocaleemia, inpatient management my be necessary. Permanent hypoPT his Bong-term consequences for both objective wall-bilegin and should be prevented whenever possible.

Keywords: hypoparathyroidism, hypocalcemia, thyroidectomy, parathyroid hormone, central neck, paresthesia

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THYROID SURGERY

Systematic Review and Meta-Analysis of Unplanned Reoperations, Emergency Department Visits and Hospital Readmission After Thyroidectomy

Joseph Margolick,¹ Wenjia Chen,^{2,•} and Sam M. Wiseman¹

Background: Unplanned reoperation, emergency department (ED) visits, and hospital readmission following hyroid operations usually arise due to complications and are a source of frustration for both surgeons and patients. With the aim of providing insight important for the devolpment of patient quality care improvement initiatives, the primary objective of this review was to evaluate the available literature systematically in order to determine the contemporary rates of reoperation, readmission, and ED visits following thyroid operations. A secondary study objective was to determine if there were any practices that showed promise in reducing the occurrence of these undersirable postoperative events.

Methods: This systematic review was conducted in accordance with the Preferred Reporting of Items for Systematic Reviews and Meta-Analyses protocols. Twenty-two studies were included in the systematic review. Metaanalysis was performed to obtain the weighted-pooled summary estimates of rates of reoperations. ED visits, and upplanned hospital readmission. Lackknife sensitivity analyses were performed for each data set. Finally, in order to detect the risk of publication bias and the small-study effect, funnel plot analysis was performed. **Results:** The pooled rate estimate for reoperation was very low (Oxfe) (confidence interval (C1) 0.3–11/%). This

Results: The pooled rate estimate for reoperation was very low (0.6% [confidence interval (CI) 0.3–1.1%)). This was subject to publication bias because smaller studies tended to report lower rates of reoperation. The pooled rate of ED visits was 8.1% [CI 6.5–9.6%], while the pooled rate of hospital readmission from 19 studies was 2.7% [CI 2.1–3.4%]. Neck hematoma was the most common reason for reoperation, while postoperative hypocalcemia was the most common reason for hospital readmission.

Conclusions: ED visits and hospital readmission after thyroidectomy are common, and here are several practices that can robust their occurrence. Routine postporentive calcium and visunin D supplementation may robust rates of postporative hypoxelacemia, and avoiding postporarist hyportension may decrease the risk of next hematoma development and the need for reoperation. Older age, thyroid cancer, deependent functional status, higher ASA score, diabetes, chronic obstructive pulmonary disease, steroid use, hemodialpyis, and recent weight loss increase the risk of hospital readmission after thyroid surgery. By further identifying risk factors for reoperation. ED visis, and readmission, this review may assist practitioners in optimizing perioperative care and therefore reducing patient morbidily and mortality after thyroid operations.

Keywords: thyroidectomy, reoperation, readmission, emergency department visits, neck hematoma, hypocalcemia



Thyroidectomy QIs: What Are Contemporary Complication Rates?

- Objective: Identify operations needing more QI
- 10 procedures evaluated in ACS NSQIP database between 2008-20015 (1.2 million operations)





Thyroidectomy Current Complication Rates: Benchmarks For Thyroid Surgery QI

| | | | Mort | ality | Pneun | nonia | Renal f | ailure | Surgica infec | al site tion | Unpla intuba | nned ation | Urinary infec | tract tion |
|---------------|------|----------|-----------|---------|-----------|---------|-----------|---------|------------------|-----------------|-----------------|---------------|------------------|---------------|
| Operation | Year | Cases, n | Events, n | Rate, % | Events, n | Rate, % | Events, n | Rate, % | Events, n | Rate, % | Events, n | Rate, % | Events, n | Rate, % |
| Thyroidectomy | 2008 | 7,915 | 7 | 0.09 | 17 | 0.21 | 2 | 0.03 | 29 | 0.37 | 40 | 0.51 | 31 | 0.39 |
| | 2009 | 9,339 | 8 | 0.09 | 13 | 0.14 | 0 | 0.00 | 26 | 0.28 | 45 | 0.48 | 28 | 0.30 |
| | 2010 | 9,774 | 4 | 0.04 | 23 | 0.24 | 4 | 0.04 | 28 | 0.29 | 34 | 0.35 | 30 | 0.31 |
| | 2011 | 11,088 | 15 | 0.14 | 35 | 0.32 | 5 | 0.05 | 53 | 0.48 | 46 | 0.41 | 42 | 0.38 |
| | 2012 | 13,212 | 7 | 0.05 | 16 | 0.12 | 1 | 0.01 | 38 | 0.29 | 38 | 0.29 | 41 | 0.31 |
| | 2013 | 14,614 | 14 | 0.10 | 31 | 0.21 | 8 | 0.05 | 80 | 0.55 | 63 | 0.43 | 36 | 0.25 |
| | 2014 | 16,043 | 9 | 0.06 | 38 | 0.24 | 8 | 0.05 | 68 | 0.42 | 65 | 0.41 | 41 | 0.26 |
| | 2015 | 17,687 | 19 | 0.11 | 52 | 0.29 | 10 | 0.06 | 72 | 0.41 | 60 | 0.34 | 43 | 0.24 |
| Subtotal | _ | 99,672 | 83 | 0.08 | 225 | 0.23 | 38 | 0.04 | 394 | 0.40 | 391 | 0.39 | 292 | 0.29 |

| Table 2. Estimated Number of Adverse Events Avoided per 10,000 Oper | rations |
|--|---------|
|--|---------|

| Operation | Mortality | Pneumonia | Renal failure | Surgical site infection | Unplanned intubation | Urinary tract infection |
|-------------------------|-----------|-----------|---------------|-------------------------|----------------------|-------------------------|
| Colectomy | _ | _ | _ | 124 | 82 | 128 |
| Esophagectomy | _ | _ | _ | _ | _ | 95 |
| Hepatectomy | 76 | _ | 24 | — | 98 | 164 |
| Hysterectomy | 5 | _ | _ | _ | 9 | _ |
| Pancreatectomy | 26 | _ | _ | — | 51 | 265 |
| Proctectomy | 16 | _ | _ | 49 | _ | 186 |
| Total hip arthroplasty | _ | _ | _ | _ | 10 | 78 |
| Total knee arthroplasty | — | 24 | — | 13 | — | 68 |
| Thyroidectomy | - | _ | _ | _ | _ | 5 |
| Ventral hernia repair | | | | 44 | _ | _ |

Adverse events avoided = slope from Table 2×8 years $\times 10,000$ 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.



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)



Thyroidectomy For Cancer QI: Complications



^cP-values were calculated based on chi-square test for linear trend.





^c P-values were calculated based on chi-square test for linear trend

Figure 1. (a) Postoperative complications according to SEER thyroid cancer stage. (b) Postoperative complications according to patient age (years). (c) Postoperative complications according to the Charlson/Deyo comorbidity score. - Overall Complication Rates:

• General (6.5%)

Table 2. Patient Characteristics Associated With Postoperative Complications

- Thyroidectomy Specific (12.3%)
 - 1152 cases of vocal cord paralysis
 - 2553 cases of hypoparathyroidism

| | Cardiopulmonary/ Complie | Thromboembolic cations | Postoperative Fever/Local Complications | | |
|--|-----------------------------|------------------------|--|----------------------|--|
| Clinical Factors | n (%) | P Value ^a | n (%) | P Value ^a | |
| General postoperative complications | | | | | |
| Age (y) | | | | | |
| ≤65 | 332 (2.3) | | 192 (1.3) | | |
| >65 | 1119 (8.4) | < 0.001 | 444 (3.3) | < 0.001 | |
| Charlson/Deyo comorbidity score | | | | | |
| 0 | 33 (0.6) | | 25 (0.4) | | |
| 1 | 67 (1.9) | | 25 (0.7) | | |
| ≥2 | 1351(7.2) | < 0.001 | 586 (3.1) | < 0.001 | |
| Stage | | | | | |
| Localized | 737 (4.1) | | 373 (2.1) | | |
| Regional | 513 (5.9) | | 195 (2.2) | | |
| Distant | 193 (16.5) | < 0.001 | 63 (5.4) | < 0.001 | |
| | Hypoparathyroidis | m/Hypocalcemia | Vocal Cord/Fold Paralysis | | |
| | n (%) | P Value ^a | n (%) | P Value ^a | |
| Thyroid surgery-specific complications | | | | | |
| Age (y) | | | | | |
| ≤65 | 743 (5.1) | | 204 (1.4) | | |
| >65 | 1810 (13.6) | < 0.001 | 948 (7.1) | < 0.001 | |
| Charlson/Deyo comorbidity score | | | | | |
| 0 | 164 (2.9) | | 55 (1.0) | | |
| 1 | 202 (5.8) | | 51 (1.5) | | |
| ≥2 | 2187 (11.7) | < 0.001 | 1046 (5.6) | < 0.001 | |
| Stage | | | | | |
| Localized | 1448 (8.1) | | 420 (2.4) | | |
| Regional | 932 (10.7) | | 568 (6.5) | | |
| Distant | 158 (13.5) | < 0.001 | 150 (12.8) | < 0.001 | |

 ^{a}P values were calculated based on χ^{2} 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%





Thyroidectomy QIs:

Influence of Surgeon Volume On Complications

- <u>Higher complication risk after Total Thyroidectomy (20.8%) compared to</u> <u>Lobectomy (10.8%) (p<0.0001):</u>
 - 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% Cl 1.12,2.11,p=0.0083)
 - True for both Lobectomy and Total Thyroidectomy



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)

| Complication | High-volume (>25 Cases/y) | Low-volume (≤25 Cases/y) | Р |
|---------------------------------|---------------------------|--------------------------|----------|
| Endocrine-related | 50 (1.6%) | 316 (2.3%) | 0.01 |
| Bleeding | 31 (1.0%) | 223 (1.6%) | 0.006 |
| Wound | 21 (0.7%) | 146 (1.1%) | 0.05 |
| Respiratory | 18 (0.6%) | 183 (1.3%) | 0.0002 |
| Cardiac | 9 (0.3%) | 58 (0.4%) | 0.35 |
| Urologic | 15 (0.5%) | 66 (0.5%) | 1 |
| Overall | 130 (4.1%) | 876 (6.4%) | < 0.0001 |
| In-hospital mortality | 0 | * | 0.59 |
| Length of stay, d (median, IQR) | | | < 0.0001 |
| Mean, SD | 1.5 (1.3) | 2.0 (1.9) | |
| Median, IQR | 1 (1-2) | 2 (1-2) | |
| Inflated-adjusted costs† | | | < 0.0001 |
| Mean, SD | \$7166 (5052) | \$7550 (5683) | |
| Median, IQR | \$5826 (4325, 8578) | \$6385 (4800, 8674) | |



(Abdelgadir et al; Ann Surg 2017;265:402-407)



What is Quality Cancer Care?

"The provision of evidence-based, patient-centered services throughout the continuum of care in a **timely** and <u>technically competent</u> 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**"





(NIH Publication No. 03e4373. Bethesda: U.S. Department of Health and Human Services, National Institutes of Health; 2002)

Quality Improvement For Cancer Patients Is Challenging

 Ongoing and continuous modification of cancer treatment plan



- Multidisciplinary treatment paradigm
- Lengthy time intervals for outcomes



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





Surgical Quality Indicators In Cancer Patients

- 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

| ical practice. This task has been | | | | | | | Ose in Montoring | opulation-based Treatment |
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Journal of Survical Oncolory 2013;108:348-35

Quality Indicators for Ductal Carcinoma In Situ (DCIS) of the Breast

Development Using a Multidisciplinary Delphi Process and Its

Indicators for Advanced Ovarian Cancer Surgery Davis Querles, MD.⁹ Parayoin Plancham, MS¹. Valis Chin, AD1 (distribute Fostporolog, MD2 Dormond Barros, MD3, David Chind, MD1 (Ginomet Adverse), MM2 Shorest Constant, MO2 Guries Creatherg, MD4 Ben Drakton, MD, PMA: Philip Harres, MA1 + Lose Landvall, MD4 Christian Merrik, MD5; Philipp Merice, MD, PBAJ), Annh Raft, MD (PD5) Inabelle Roy-Cognard, MD, PhD1B: Andrea Rockall, MD1 C Cristiana Sossa, MD1 ++ Are via ad rez. MD1 + H gance Strips, MD1 + and Andreas ab Balo, MD1 + Are via ad rez. MD1 + H gance Strips, MD1 + and Andreas ab Balo, MD1 +

ORIGINAL STUDY

European Society of Gynaecologic Oncology Quality

tives: The surgical management of advanced ovarian cancer involves complete y. Implementation of a quality management program has a major impact on survival and of this work was to develop a list of quality indicates (Qi) for advanced ovarian surgery that can be used to audit and improve the clinical practical production of the out surder the augits of the European Society of Cynaetologic Obcology (ESCO) team and preoperative workup. Quali

ORIGINAL STUDY

Lymph Node Ratio as a Quality and Stage III Colon Car

ven L Chen, MD, MBA^{*}, Scott R. Steele, MD[†], John Eber Anton Bilchik, MD, PhD§¶, and Alexander St



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)

| | | Projected inciden | ce . | , | 5-year net survival | | |
|-------------------------|------|-------------------|-------|------|------------------------|-------|----|
| Both sexes combined | Rank | Cases | ASIR* | Rank | Deaths | ASMR* | % |
| All cancers | - | 206,200 | 515.9 | - | 80,800 | 198.1 | 60 |
| Lung and bronchus | 1 | 28,600 | 69.9 | 1 | 21,100 | 51.4 | 17 |
| Colorectal | 2 | 26,800 | 66.3 | 2 | 9,400 | 23.1 | 64 |
| Breast | 3 | 26,500 | 68.1 | 3 | 5,000 | 12.6 | 87 |
| Prostate | 4 | 21,300 | 110.4 | 5 | 4,100 | 23.8 | 95 |
| Bladder | 5 | 8,900 | 21.8 | 8 | 2,400 | 5.7 | 73 |
| Non-Hodgkin lymphoma | 6 | 8,300 | 20.8 | 7 | 2,700 | 6.7 | 66 |
| Uterus (body, NOS) | 7 | 7,300 | 35.7 | 18 | 1,150 | 5.3 | 84 |
| Melanoma | 8 | 7.200 | 18.5 | 15 | 1.250 | 3.1 | 88 |
| Thyroid | 9 | 7,100 | 19.0 | 21 | 220 | 0.5 | 98 |
| Kidney and renal pelvis | 10 | 6,600 | 16.5 | 12 | 1,900 | 4.6 | 67 |
| Leukemia | 11 | 6,200 | 15.5 | 6 | 2,900 | 7.2 | 58 |
| Pancreas | 12 | 5,500 | 13.5 | 4 | 4,800 | 11.9 | 8 |
| Oral | 13 | 4,700 | 11.9 | 16 | 1,250 | 3.1 | 63 |
| Stomach | 14 | 3,500 | 8.6 | 11 | 2,100 | 5.1 | 25 |
| Brain/CNS | 15 | 3,000 | 7.8 | 9 | 2,400 | 6.0 | 24 |
| Multiple myeloma | 16 | 2,900 | 7.1 | 14 | 1,450 | 3.5 | 42 |
| Ovary | 17 | 2,800 | 13.7 | 13 | 1,800 | 8.2 | 44 |
| Liver | 18 | 2,500 | 6.1 | 17 | 1,200 | 3.0 | 19 |
| Esophagus | 19 | 2,300 | 5.7 | 10 | 2,200 | 5.3 | 14 |
| Cervix | 20 | 1,550 | 8.3 | 20 | 400 | 2.0 | 73 |
| Larynx | 21 | 1,150 | 2.8 | 19 | 440 | 1.1 | 63 |
| Testis | 22 | 1,100 | 6.1 | 23 | 45 | 0.2 | 96 |
| Hodgkin lymphoma | 23 | 990 | 2.7 | 7 | 140 | 0.4 | 85 |
| All other cancers | _ | 19,500 | 48.5 | _ | 10,400 | 25.5 | - |





Thyroid Cancer Surgical QIs



- Goal of the surgeon when performing a thyroidectomy for cancer is to <u>safely remove all</u> <u>thyroid cancer/tissue</u> (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



• Near-total thyroidectomy (<1g)



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 × timour size (cm) + 1 if incompletely reserved + 1 if locally invasive

- 3 if distant spread

<6 = 99% 6-6.99 = 89% 7-7.99 = 56% >8.00 = 24%

20-year survival by MACIS score

- 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





MACIS

SCORE

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





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







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 then 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







Growing Literature Evaluating Remnant Thyroid Tissue RAI Uptake As A Thyroidectomy QI

| Study (year) | N | Variables Studied | Outcome |
|------------------------------------|-----|--|--|
| Rosario e <i>t al.</i> (2004) | 142 | RAI uptake post TT | - Inverse correlation between RAI uptake and ablation efficiency (r^2 = 0.92, p < 0.05) |
| Lim <i>et al.</i> (2012) | 173 | Quantified postoperative cervical uptake | Quantified cervical uptake >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) |
| Schneider <i>et al.</i> (2013) | 223 | Post-TT RAI UDR Surgeon volume | Odds ratio for UDR independently predicting disease recurrence is 3.71 [1.5-13.10] The post-TT UDRs of high-volume surgeons were significantly smaller than low-volume surgeons (0.003 vs 0.025; p = 0.002) |
| Holsinger e <i>t al.</i> (2014) | 245 | RAI uptake post TT | - 65% of patients with RAI uptake >0.2% had measurable stimulated Tg levels compared with 25% of patients with RAI uptake ≤0.2% (p < 0.001) - Rates of local and/or regional recurrence were low regardless of RAI uptake |
| Oltmann e <i>t al.</i> (2014) | 45 | CT vs TT Surgeon volume | CT patients had higher UDR than those undergoing TT (0.0008 vs 0.0004; p = 0.04) 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) |

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



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

 <u>Tg measurement after Total</u> <u>Thyroidectomy correlates with</u> <u>volume of remnant thyroid tissue &/</u> <u>or cancer</u> 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.



(Strong recommendation, Low-quality evidence)

(E) ATA high-risk patients (regardless of response to therapy) and all patients with biochemical incomplete, structural incomplete, or indeterminate response should continue to have Tg measured at least every 6–12 months for several years.

(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)



Is There An Influence Of Surgeon Volume On Postoperative Thyroglobulin Level?

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

• 42 surgeons/volume evaluated for:



- Extent of initial operation
- % uptake on I¹²³ pre-RAI TSH stimulated uptake scan
- Pre-ablation TSH-stimulated Tg level
- Dose of I¹³¹ 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'

<u>% uptake on I¹²³</u> <u>Stimulated Tg</u> <u>Administered I¹³¹dose</u>

- Fewer complications

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

| Thyroid cases per year | No. surgeons (DTC patients) | I ¹²³ prescan uptake, % HVS (LVS) | P value | Serum Tg, ng/mL HVS (LVS) | P value | Mean dose I ¹³¹ given, mCi HVS (LVS) | P valu |
|---------------------------|--------------------------------|---|---------|------------------------------|---------|---|--------|
| ≥10 | 16 (331) | 3.1 (6.0) | .135 | 3.9 (7.4) | .115 | 94.9 (92.5) | .85 |
| ≥20 | 13 (326) | 2.5 (2.5) | .9 | 3.7 (6.1) | .16 | 95.0 (96.7) | .85 |
| ≥25 | 11 (302) | 2.3 (3.1) | .2 | 3.8 (5.0) | .36 | 91 (108) | .03 |
| ≥30 | 8 (275) | 2.2 (4.4) | .01 | 3.8 (8.4) | .02 | 90 (107) | .03 |
| ≥50 | 6 (239) | 2.2 (4.2) | .005 | 3.5 (8.8) | .007 | 88 (108) | .002 |
| ≥100 | 5 (224) | 2.0 (3.9) | .001 | 3.7 (6.6) | .04 | 92 (105) | .02 |

Bold type represents P < .05.

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

 I^{123} prescan uptake, Mean dose I^{131} given, Serum Tg, ng/mL % HVS (LVS) P value mCi, HVS (LVS) P value No. of Tx/y* HVS (LVS) P value 25 2.4(3.0).7 5.5(6.5).8 104(132).3 30 2.8(4.8).2 5.3(7.7).5 105(117).5 .3 50 .004 .2 2.2(5.2)5.0(8.2)105(121)100 1.9 (3.9) .001 3.5 (6.8) .03 93.5 (115) .05

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

*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.



>50 Thyroid ORs/Year For Stage 3 & 4 Disease

More 'complete'
 % uptake on I¹²³

Growing Literature Evaluating Postoperative Thyroglobulin Level As A QI

| Study (year) | N | Variables | Outcome | |
|----------------------------|-----|-----------------|---|---|
| Ruiz-Garcia et al. | 98 | Type of surgery | - 10-year disease free survival was 100% in patients with Tg ≤23 ng/mL and | |
| (1991) | | unspecified | 68.4% in patients with Tg >23 ng/mL | |
| Lin et al. | 847 | 1 month after | - 1-month post-operative Tg level >10ug/L is a significant prognostic factor for | |
| (2002) | 047 | TT | patients with DTC | |
| Bernier et al. | 407 | тт | - Tg during T4 withdrawal of \geq 5ng/mL is predictive of unsuccessful ablation (PR = 1.02 [1.00 - 1.03]; p < 0.05) | |
| (2005) | | | (RR = 1.02 [1.00 = 1.03], p < 0.03) | |
| Makarewicz et al. | | | - Tg during T4 withdrawal was significantly higher in patients who later | |
| (2006) | 178 | TT | developed recurrence compared to those who did not | |
| () | | | (97.4 ng/mL vs. 4.3 ng/mL; p = 0.000001) | |
| Hoomstra of al | | | - Tg during T4 withdrawal of <27.5ug/L had a positive predictive value of 97.8% | |
| (2007) | 366 | Near TT | for disease-free remission and is an independent prognostic marker for | |
| (2007) | | | | disease-free remission (likelihood ratio = 43.2; p < 0.001) |
| | | | - Patients with Tg during T3 withdrawal of >20pmol/L had a significantly | |
| Hall et al. | 212 | 3 months after | increased risk of disease recurrence (p = 0.001) | |
| (2003) | 213 | TT | - Tg during T3 withdrawal of >20pmol/L is a significant predictor of recurrence | |
| | | | (RR = 5.1 [2.0 – 13.1]; p = 0.001) | |
| Alagic-Smailbegovic et al. | 110 | 1 month after | - Mean Tg was 190.8 ng/mL in patients who later developed recurrent disease | |
| (2012) | 110 | TT | and 9.3 ng/mL in those who had no evidence of recurrence (p = 0.023) | |
| Kendler et al. | 06 | 1 month after | - Tg ≥18 ng/mL in thyroid hormone withdrawal is an independent predictor of | |
| (2012) | 90 | TT | unsuccessful ablation (RR = 5.89, p < 0.0001) | |
| Lee et al. | 040 | 3 months after | - Tg <2ng/mL in thyroid hormone withdrawal had a negative predictive value of | |
| (2013) | 210 | тт | 94.9% for disease free status | |
| Moon et al. | 252 | TT with CND | - rhTSH-stimulated Tg of < 1.79 ng/mL has a negative predictive value of | |
| (2016) | 200 | | 99.5% for persistent or recurrent disease at 1 year post-ablation | |
| | | | | |

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



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 a comprehensive removal of :

NECK NODE LEVEL VI

- **Prelaryngeal** (Delphian) Lymph Nodes
- Pretracheal Lymph Node
 and
- Left +/or Right Paratracheal Lymph Nodes

+/-

NECK NODE LEVEL VII



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

Central Neck Dissection: ATA Guidelines







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 Yield)





Metastatic Lymph Node Ratio

- Evaluation of MLNR in 10,955 DTC patients with >3 LN removed in the SEER database (1988-2007) (median follow up 25 month
- MLNR was strongly associated with DSM (HR 4.33, 95%CI 1.68-11.18, p<0.01)
- MLNR ≥ 0.42 separated cases based on disease specific mortality LNR = 0.42



FIG. 2 Kaplan-Meier estimates of disease-free survival according to

the threshold lymph node ratio

.012 1.72% Probability of Death 5 0.65% .008 900 004 0.2 0.4 0.6 0.8 1.0 Lymph Node Ratio (LNR)



FIG. 3 Probability of thyroid cancer-specific death by lymph node (Schneider et al; Ann Sug Onc:2013:20:1906-1911) ratio. The dashed line indicates the threshold lymph node ratio

Growing Literature Evaluating Metastatic Lymph Node Ratio As A QI

| Study (year) | N | Variables | Outcome |
|----------------------------|-------|-------------------|---|
| 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



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?





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Final Thoughts: Should Guideline Adherence Be Considered A Thyroid Surgical QI?

- Could address difficulty with finding thyroid cancer surgery QIs for Low Risk patients
- <u>Guidelines are Guidelines</u> and constantly changing based upon new evidence
- Should not following guidelines be an indicator of poor oncological surgical quality?



Frequency of High-Risk Characteristics Requiring Total Thyroidectomy for 1–4 cm Well-Differentiated Thyroid Cancer

| | - |
|----------|--|
| | Surgery 163 (2018) 81-87 |
| | Contents lists available at ScienceDirect |
| | Surgery |
| ELSEVIER | journal homepage: www.elsevier.com/locate/yn |
| Thyroid | |

Correct extent of thyroidectomy is poorly predicted preoperatively by the guidelines of the American Thyroid Association for low and intermediate risk thyroid cancers

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 = <u>6,000</u>



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
 - ≻ <u>MLNR</u>
 - ➢ <u>Other?</u>
 - Own thyroidectomy surgical volumes



 This information is <u>readily available, quantifiable, is associated with surgical</u> <u>and oncological outcomes, and allows for quality</u> <u>improvement</u> (NOW HOW <u>DO WE APPLY THESE QIS IN THE REAL WORLD???</u>)

