



# American Head and Neck Society - Journal Club

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### [Location and Causation of Residual Lymph Node Metastasis After Surgical Treatment of Regionally Advanced Differentiated Thyroid Cancer](#)

*Miller JE, Al-Attar NC, Brown OH, Shaughnessy GG, Rosculet NP, Avram AM, Hughes DT*

*From **THYROID**, May, 2018*

**Background:** After initial surgical treatment of differentiated thyroid cancer (DTC), residual lymph node metastases are often found at the time of radioactive iodine (131I) therapy. Recurrence of DTC is due to persistent disease not removed at initial surgery which also did not respond to 131I treatment. This study aimed at determining locations of, and reasons for, residual nodal metastases detected by 131I scans with single-photon emission computed tomography (SPECT/CT) obtained prior to radioiodine therapy following surgical treatment of DTC.

**Methods:** This is a retrospective study of 352 patients with intermediate and high-risk DTC treated with 131I therapy at the University of Michigan from 2007 to 2014. All patients underwent total thyroidectomy with or without lymph node dissection followed by radioiodine therapy. Pre-ablation diagnostic 131I scans with SPECT/CT were used postoperatively to localize nodal metastases, which were then compared with the cervical lymph node basins dissected at the time of surgery to determine the reason for residual nodal metastases: incomplete nodal dissection versus preoperative unrecognized nodal metastases.

**Results:** Of the 352 patients in the study, 146 (41.5%) had residual nodal metastases detected on 131I scans with SPECT/CT following initial surgery but prior to 131I therapy. Among the 146 patients with residual disease, there were a total of 218 distinct nodal metastases. Relative to the primary tumor, 71.6% (n = 156) of metastases were ipsilateral, 22.0% (n = 48) were contralateral, and 6.4% (n = 14) were non-sided in the central neck (level VI/VII). Cervical lymph node levels VI, III, and II had the greatest frequencies of residual metastases (33.9%, 22.9%, 18.8%, respectively). Residual metastases occurred because of incomplete nodal dissection (49.3%), lack of preoperative identification (37.7%), or a combination of both (13%).

**Conclusion:** Residual nodal metastasis following initial surgical treatment for regionally advanced differentiated thyroid cancer is rather common on highly sensitive 131I scans with SPECT/CT and is due to both unrecognized nodal involvement preoperatively and incomplete removal of metastatic lymph nodes during compartment-orientated nodal dissection. The surgical management of high-risk DTC should include preoperative imaging to evaluate for nodal metastases in the central and lateral neck and



compartment-orientated nodal dissection of involved compartments. Attention should be given to complete dissection in levels VI, III, and II, particularly when dissecting compartments ipsilateral to the primary tumor.

### Summary Statements

- 1) The authors assume: "... recurrent DTC is persistent disease that was not removed at initial surgery and that did not respond to radioactive iodine treatment. The completeness of surgical resection is an important determinant of outcomes because residual lymph node metastases represent the most common site of disease persistence and recurrence of DTC. Additionally, persistent lymph node metastases often lose the ability to concentrate radioiodine, rendering additional RAI treatments ineffective."
- 2) The first aim of this study was to identify the most common anatomic locations of persistent lymph node metastases following initial surgical treatment of intermediate and high-risk DTC. The second aim of this study was to identify the primary reasons for residual malignant lymph nodes following initial surgical treatment of intermediate and high-risk DTC which was deemed to be either due to preoperatively unrecognized nodal involvement and omission of nodal dissection or due to incomplete surgical dissection of the involved lymph nodes.
- 3) 74/218 (33.9%) residual metastases were found in level VI, making it the level with the highest frequency of residual nodal metastases. The next most frequent regions of residual nodal metastases were found in the lateral neck: levels III [50 (22.9%)] and II [41 (18.8%)], respectively. Cervical level IV [23 (10.6%)] showed lower frequencies of residual nodal metastasis than levels II and III in the anterior lateral neck. Out of the 218 total residual metastases, 0 (0.0%) were found in level V and only 1 (0.5%) was found in level I.
- 4) Evaluation of the reasons for residual nodal metastases showed that 71 patients (48.6%) had an incomplete operation (the residual metastatic nodes were in a previously dissected compartment), 56 patients (38.4%) had preoperatively unrecognized nodal metastases (the residual nodes were in a previously undissected compartment), and 19 (13.0%) had a combination of both incomplete nodal dissection and unrecognized nodal metastases in more than one compartment.
- 5) Assessment during long-term follow-up after initial surgery (median follow-up time: 1048.5 days, range: 62–2878 days) showed that 28 of the 146 patients (19.2%) with residual nodal disease went on to have persistent disease after a single dose of radioiodine therapy. This suggests that the use of radioiodine therapy in the treatment of residual lymph node metastasis was effective in 80.8% of patients in this study's patient cohort. Of the 28 patients with persistent disease after both surgery and the initial dose of radioiodine, 20 patients underwent additional treatment for DTC, which included 18 (64.3%) who underwent a repeat surgery and 2 (7.1%) who received additional RAI therapy.

### Strengths

- Large study
- Use of a very sensitive test (SPECT/CT) to detect residual nodal disease.
- Robust data regarding nodal levels involved, single versus multifocal tumors and relationship this had to nodal disease, impact of residual nodal disease on disease recurrence and need for additional treatment.



## Weaknesses

- Retrospective
- Only intermediate and high-risk DTC patients who were referred for RAI treatment were included in this study, which introduces an inherent selection bias. The conclusions of this study can only be applied to this cohort of patients with intermediate and high-risk DTC and not to patients with low risk DTC who were excluded from this study, but who make up the majority of patients with thyroid cancer.
- An additional limitation is the use of 131I SPECT/CT as the primary outcome measure for residual lymph node metastasis which may not be typical in other institutions. SPECT/CT is likely more sensitive than ultrasound or CT imaging and therefore may detect higher rates of lymph node micrometastases, some of which may not have comparable clinical relevance to lymph node macrometastasis noted on lower sensitivity imaging studies such as ultrasound or CT.
- Additionally, FNA was not utilized to confirm the presence of PTC in every suspicious lymph node detected on SPECT/CT, so there is possibility that false positives on 131I SPECT/CT may skew the rates of residual lymph node metastasis toward higher than actual rates.
- Lack of a standardized preoperative imaging protocol.

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## [Safety of outpatient thyroidectomy: Review of the American College of Surgeons National Surgical Quality Improvement Program](#)

McLaughlin EJ, Brant JA, Bur AM, Fischer JP, Chen J, Cannady SB, Chalian AA, Newman JG.

from *Laryngoscope*, May 2018

**Objectives/Hypothesis:** To investigate national trends in admission status after thyroidectomy in the United States and to evaluate the factors associated with 30-day unplanned readmission and reoperation.

**Study Design:** Retrospective review of American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP)

**Methods:** The ACS-NSQIP database was queried for patients who underwent a partial or total thyroidectomy between 2005 and 2014. Outpatient surgery was defined as discharge on the day of surgery. Patient demographic information, unplanned hospital readmission, and reoperation were reviewed. Risk factors were identified using logistic regression modeling.

**Results:** A total of 76,604 cases met inclusion criteria as described above. There were 1,473 (1.9%) patients who underwent reoperation and 477 unplanned 30-day readmissions (1.4%) for procedures performed since 2012. There was a significant positive trend in the percentage of thyroidectomy (partial and total) patients who underwent outpatient procedures by year of operation ( $P < .001$ ). Outpatient procedures were not more likely to have unplanned readmissions or reoperations. Independent patient risk factors for unplanned readmission and reoperation included current dialysis, chronic steroid use, unintentional weight loss, American Society of Anesthesiologists class 3 to 4, and active bleeding disorders.

**Conclusions:** Over the past decade there has been a clear trend toward increasing outpatient thyroid surgery. Thyroidectomy performed as an outpatient was not found to be an independent risk factor for readmission or reoperation. Patients with serious medical comorbidities and active bleeding disorders are



at increased risk of unplanned readmission or reoperation and should have their surgery performed on an inpatient basis.

### Summary

- Use of the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) prospective database with coverage of community and academic centers and quality control with more than 76000 cases.
- Outpatient defined as those with less than 23 hours of admission
- Multivariate analysis to predict inpatient surgery and unplanned readmission.
- 14187 procedures made in outpatient basis with an unplanned 30-day readmission rate of 1.4%.
- The rate of outpatient surgery increased in recent years.
- Variables related with inpatient surgery and unplanned readmissions were: total thyroidectomy, dyspnea, dialysis, bleeding disorders, African American race, and 3-4 ASA class.

### Strengths

- Prospectively recorded big database information with quality control measures
- A strong statistical multivariate analysis
- Follow-up with a lower risk of losses.

### Weaknesses

- Definition of outpatient surgery includes a wide time period. It is impossible to discriminate if the patient leaves the hospital the same day or the next one before 24 hours of admission.
- Causes of readmission are not clear. This data help to optimize measures to prevent specific causes for readmission
- Observational studies with administrative registries have an intrinsic selection bias. In this case, it is impossible to know it rate of outpatient surgery is due to surgeons decision or clinical factors.

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## [Development and external validation of a risk-prediction model to predict 5-year overall survival in advanced larynx cancer](#)

*Petersen JF, Stuiver MM, Timmermans AJ, Chen A, Zhang H, O'Neill JP, Deady S, Vander Poorten V, Meulemans J, Wennerberg J, Skroder C, Day AT, Koch W, van den Brekel MWM*

*from Laryngoscope, May 2018*

**Objectives/Hypothesis:** TNM-classification inadequately estimates patient-specific overall survival (OS). We aimed to improve this by developing a risk-prediction model for patients with advanced larynx cancer.

**Study Design:** Cohort study.

**Methods:** We developed a risk prediction model to estimate the 5-year OS rate based on a cohort of 3,442 patients with T3T4N0N1M0 larynx cancer. The model was internally validated using bootstrapping samples and externally validated on patient data from five external centers (n 5 770). The main outcome was performance of the model as tested by discrimination, calibration, and the ability to distinguish risk groups based on tertiles from the derivation dataset. The model performance was compared to a model based on T and N classification only.



**Results:** We included age, gender, T and N classification, and subsite as prognostic variables in the standard model. After external validation, the standard model had a significantly better fit than a model based on T and N classification alone (C statistic, 0.59 vs. 0.55,  $P < .001$ ). The model was able to distinguish well among three risk groups based on tertiles of the risk score. Adding treatment modality to the model did not decrease the predictive power. As a post hoc analysis, we tested the added value of comorbidity as scored by American Society of Anesthesiologists score in a subsample, which increased the C statistic to 0.68.

**Conclusions:** A risk prediction model for patients with advanced larynx cancer, consisting of readily available clinical variables, gives more accurate estimations of the estimated 5-year survival rate when compared to a model based on T and N classification alone.

### Summary

- A derivation of the clinical prediction rule from the Netherlands Cancer Registry covering 3442 registries, with external validation in other datasets with 770 patients. .
- Patients with T3-T4/N0N1 M0 squamous cell carcinoma of the larynx who were treated with a primary TL, CRT, or primary RT
- Outcomes were 5 year overall survival
- Five year overall survival was 44% for radiotherapy, 45% for CRT and 49% for laryngectomy.
- Characteristics of the derivation model were: age 62 y-o, 78% male, 56% T3N0/N+, 63% supraglottic and 58% were treated by RT.
- Addition of age, gender, subsite and comorbidity to TN improved the discriminative power of the model. Calibration was similar between models.

### Strengths

- Big database information with long term follow-up
- A strong statistical analysis
- An external validation of the model with large sample size.

### Weaknesses

- Data about comorbidity used only ASA score. Other specific scores as ACE-27 were not used
- The derivation dataset had a higher percentage of patients treated exclusively with RT, which represent the long time span for collection of patients.
- The addition of more variables increased calibration, without any change in discrimination, but with a risk of lower compliance.

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