Importance: The effect of a second primary thyroid carcinoma (SPTC) on the survival of patients with previous head and neck squamous cell carcinoma (HNSCC) is not clearly defined. This study aims to analyze this relationship in an effort to guide treatment decisions and assist with patient education.

Objective: To determine whether the development of SPTC in a patient previously diagnosed with HNSCC significantly affects survival. A secondary objective is to determine whether the thyroid carcinoma that develops after HNSCC impacts overall survival more significantly than thyroid carcinoma that develops in the absence of HNSCC.

Design: A retrospective review of the Surveillance, Epidemiology, and End Results (SEER) 9 Database.

Participants: The study group consisted of three distinct populations: (1) the 117 patients diagnosed with HNSCC and SPTC; (2) the 95,556 patients diagnosed with HNSCC and no SPTC; and (3) the 62,539 patients diagnosed with thyroid carcinoma-only (TCO). Data included all patients identified between 1973 and 2010.

Interventions: Not applicable.

Main Outcomes and Measures: Length of survival from the time of diagnosis for TCO patients, as well as HNSCC patients with and without SPTC.

Results: HNSCC patients who develop SPTC can be expected to die 1.6 times sooner than those without SPTC (HR=1.58, 95% confidence interval [1.24, 2.01], p<0.001). Length of time to diagnosis of SPTC helps predict the strength of this adverse survival effect. Development of SPTC within 6-months of HNSCC does not affect survival length (HR=1.20, p=0.446), whereas patients who develop SPTC after 6-months of HNSCC are expected to die 1.8 times more quickly (HR=1.79, p<0.001). Patients who develop thyroid carcinoma and have a prior diagnosis of HNSCC die much sooner than patients with TCO (HR=3.46, 95% confidence interval [2.71, 4.41], p<0.001).

Conclusions and Relevance: This study of the SEER 9 database demonstrates that the development of SPTC in patients with HNSCC results in decreased length of survival. This difference, however, is only found in patients who develop SPTC more than 6 months after the diagnosis of HNSCC. As expected, patients with TCO live much longer than patients with HNSCC and SPTC. This may suggest that SPTC occurring greater than 6 months after diagnosis of HNSCC behaves differently than TCO. Additional studies are needed to further elucidate this finding and its treatment implications.
Objective: Intra-operative management of thyroid gland in laryngeal and hypo pharyngeal cancer is controversial. The aims of this study were to determine the incidence of thyroid gland invasion in patients undergoing surgery for laryngeal or hypo pharyngeal carcinoma, to assess predictive factors and to assess the prognosis in patients with and without thyroid gland invasion.

Subjects and Methods: One hundred and thirty-three patients who underwent surgery for carcinoma larynx and hypo pharynx from 2006 to 2010 were reviewed. Surgical specimens were examined to determine the incidence of thyroid gland invasion and predictive factors were analyzed. The recurrence rate and the survival in patients with and without thyroid gland invasion were also analyzed.

Results: Out of the 133 patients with carcinoma larynx and hypopharynx who underwent surgery, 83 (62%) were primary surgery and 50(38%) were salvage surgery after radiation failure. Excision of thyroid gland either as total thyroidectomy, hemithyroidectomy or isthmusectomy along with the laryngeal surgery was done for all patients. Histological evidence of thyroid gland invasion was observed in 28/133 (21%) patients. Most common site of carcinoma in this study was glottis. Involvement of thyroid gland in case of glottis cancer was seen in 22.37%. As compared to it the total number of subglottic carcinoma accounted for only 5% and thyroid gland involvement in these cases was seen in 28.57%. Thyroid gland invasion was found histologically in 13/43(30%) patients who had preoperative imageological evidence of thyroid cartilage erosion compared to 15/90(16.67%) without cartilage erosion (p=0.07). Histological thyroid gland invasion was detected when gross thyroid gland involvement observed during surgery 12/33 (36%) compared to 16/100 (16%) patients without gross glandular invasion (p=0.02). Pathological thyroid gland invasion was there in 26/109 (24%) of advanced clinical T stages (stage III and stage IV) of the disease compared to 2/24(8%) of early stage disease (Stages I and II) (p=0.023). All the five patients (100%) with upper oesophageal involvement had thyroid gland invasion compared to 26/128 (20.31%) without upper oesophageal involvement (p=0.03). Thyroid gland was involved in 2/7 (28.5%) patients with subglottic involvement compared to 26/126(20.6%) patients without subglottic involvement (p=0.616) There is also no association between thyroid gland invasion and age, gender, nodal stage or degree of differentiation of the tumor. In addition, no significant relationship was found between the presence of thyroid gland invasion and recurrent disease after radiotherapy. Primary or nodal recurrence was seen in 12/133 (9%) patients. There is no significant difference in the disease free survival between patients with or without thyroid gland invasion.

Conclusions:

We recommend limited indications for hemithyroidectomy or total thyroidectomy in laryngeal and hypopharyngeal surgery which include advanced stage disease with thyroid cartilage invasion and gross thyroid gland involvement, or disease with upper oesophageal or subglottic involvement. The whole thyroid gland should be preserved when the laryngeal tumour is confined to the supraglottic and glottic regions without clinical evidence of thyroid gland involvement.
Background: Medullary thyroid cancer (MTC) is a distinct form of thyroid carcinoma that originates in the para-follicular ‘C’ cells of the thyroid gland and accounts for nearly 5-10% of all thyroid cancers. Sporadic MTC accounts for nearly 75% of cases and inherited MTC constitutes the rest. The factors affecting the prognosis of patients with MTC have been less studied and we have attempted to do the same in our cohort of patients.

Materials and Methods: A comprehensive retrospective review of the database of the 53 patients with histologically proven, sporadic MTC, who presented to our cancer centre over a period of 28 years from 1985 to 2012, was performed. All fit and non-metastatic patients were considered for Definitive surgery which included a Total Thyroidectomy and a central compartment lymph node dissection. Lateral neck node dissections were done when clinic-radiologically /histologically positive cases. Adjuvant external beam radiotherapy was considered for patients with R plus resections and/or in patients with moderate to high lateral lymph node positivity. All the patients were followed up for a median duration of 90 months. Statistical analysis was carried out with the SPSS (SPSS Inc., IL, USA) software package version 17 and survivals were calculated with the help of life tables. A formal analysis of the prognostic factors influencing survival was performed which additionally included the effect of Metastatic Lymph node ratio, postoperative persistent hypercalcitonemia and the effect of adjuvant radiotherapy in moderate to high lateral neck node positivity.

Results: Of the total 53 patients, 27(50.9%) were males and 26(49.1%) were females. The mean age of the patients at presentation was 42.6 ± 13.9 years. Nearly 3/4ths of the patients presented in Stage IVa.(AJCC-TNM) The 5 year and 10 year disease free survival of the patient cohort was 56% and 34% respectively, the 5 year and 10 year overall survival was 93% and 80% respectively. Analysis of the prognostic factors failed to reveal a statistical significance to age, sex, invasive characteristics of the tumour, lymph nodal status and metastatic lymph node ratio. The median survival of patients who were given adjuvant EBRT following moderate to high lateral neck node positivity was statistically significant when compared of the patients who did receive the same. Patients with persistent post-operative hypercalcitonemia had a poorer overall survival compared to patients who did not.

Conclusion: Our study clearly shows the indolent biologic progression of sporadic MTC, despite the fact that nearly 3/4ths of our patients presented with Stage IVa disease.

Contrary to the popular belief, our study shows MTC to be a radiosensitive tumour. A consideration for adjuvant radiotherapy must be given to patients with moderate to high lateral neck nodal disease. Our study, despite being retrospective, does throw some newer insights into some of the less studied prognostic factors in the management of MTC.
NATIONAL TRENDS AND DRIVERS OF COST IN THYROID SURGERY

Objective:

To identify national trends and factors driving changes in hospital costs following thyroid surgery using the Nationwide Inpatient Dataset (NIS).

Methods:

Discharge data from the Nationwide Inpatient Sample (NIS) for 47,035 patients who underwent total thyroidectomy or thyroid lobectomy in 2003, 2005, 2007, 2009, 2011 were analyzed. Total hospital charges for thyroid surgery were converted to 2011 inflation-adjusted hospital and group-specific costs. Generalized linear regression was used to assess drivers of hospital specific costs. Factors and covariates that were significantly associated with cost were then trended over time.

Results:

Mean 2011 inflation-adjusted group and hospital specific costs associated with thyroid surgery significantly increased between each of the studied years. Generalized linear regression identified a covariate and several factors that were independently highly associated with increased hospital costs. These included increasing length of stay, male sex, total thyroidectomy (versus lobectomy), a diagnosis of thyroid malignancy, undergoing surgery at a teaching hospital, a higher all patient diagnosis related group (DRG) risk of mortality and severity score, and a more recent year of surgery. Of these, significant temporal increases were noted in the proportion of patients undergoing total thyroidectomy, the proportion of patients undergoing surgery at a teaching hospital, and the proportion of patients with higher DRG severity of illness classification scores. The mean length of stay, proportion of male patients, and proportion of patients undergoing surgery for a thyroid malignancy were all relatively unchanged over the studied time period.

Conclusions:

Hospital costs attributable to thyroid surgery increased significantly from 2003 – 2011. Our results suggest that this increase is at least in part due to an increasing proportion of sicker patients undergoing thyroid surgery, an increasing proportion of patients receiving total thyroidectomy rather than lobectomy and an increasing proportion of thyroid surgeries being performed at teaching hospitals. The independent association of year with increasing costs suggests additional unidentified contributing factors.
DIAGNOSTIC THYROIDECTOMY MAY BE PREFERRED IN PATIENTS WITH SUSPICIOUS ULTRASONOGRAPHIC FEATURES DESPITE A CYTOPATHOLOGIC DIAGNOSIS OF AUS/FLUS USING THE BETHESDA SYSTEM

Seok-Mo Kim, MD, Bup-Woo Kim, MD, Hyeung Kyoo Kim, MD, Ho Jin Chang, MD, Kuk Jin Kim, MD, Yong Sang Lee, MD, Hang-Seok Chang, MD, PhD, FACS, Cheong Soo Park, MD, PhD, FACS; Thyroid Cancer Center, Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Korea

Background: Atypia/follicular lesion of undetermined significance (AUS/FLUS) is a new category in the Bethesda System for Reporting Thyroid Cytopathology (BSRTC). Patients with this condition are recommended to undergo repeat fine-needle aspiration cytology (FNAC). This study assessed the clinical factors suggesting diagnostic lobectomy in patients with atypia.

Materials and Methods: Of the 5,440 patients who underwent thyroid surgery in our hospital between January 2011 and December 2012, 213 were diagnosed preoperatively with atypia. The frequency of FNAC and ultrasonographic images were compared between patients with final pathologic diagnoses of cancer and benign conditions.

Results: Of the 213 patients, 158 (74.2%) were diagnosed with thyroid carcinoma on final pathology reports. Univariate and multivariate analyses showed that frequency of FNAC did not correlate significantly with a diagnosis of cancer. Hypoechochogenicity (odds ratio [OR] 2.521, p=0.007) and microcalcification (OR 3.247; p=0.005) showed significant correlations with cancer risk.

Conclusion: Although patients cytopathologically diagnosed with AUS/FLUS are recommended to undergo repeat FNAC, microcalcification and hypoechochogenicity on ultrasonography are significantly associated with cancer risk, suggesting the need for diagnostic lobectomy.
PERFORMANCE OF THE AFIRMA GENE EXPRESSION CLASSIFIER AT A THYROID CANCER REFERRAL CENTER

Allen S Ho, MD, Luke A Donatelli, MD, Sayani Niyogi, DO, Stephanie A Fish, MD, James A Fagin, MD, Ashok R Shaha, MD, Jatin P Shah, MD, Richard J Wong, MD, Ronald A Ghossein, MD, Oscar Lin, MD, Luc GT Morris, MD, MSc; Memorial Sloan-Kettering Cancer Center

BACKGROUND: The Afirma Gene Expression Classifier (AGEC) is an RNA-based assay used to assess risk of malignancy in cytologically indeterminate thyroid nodules. Initial results of a prospective AGEC trial have been published, but the generalizability of these results remains unclear, as AGEC performance characteristics are dependent on the institutional prevalence of malignancy. Our objective was to examine performance of the AGEC at our center, and to estimate negative and positive predictive values (NPV and PPV) of the assay.

METHODS: Retrospective cohort analysis of all patients treated at Memorial Sloan-Kettering Cancer Center (MSKCC) with thyroid nodules classified as Bethesda category III or IV and evaluated with the AGEC assay. The estimated prevalence of malignancy in indeterminate nodules at MSKCC was 35%. All nondiagnostic Afirma results were excluded. Surgical pathology when available was correlated with the preoperative Afirma findings. PPV, NPV, and prevalence of malignancy were estimated using Bayes Theorem.

RESULTS: From February 2013 through November 2013, 96 patients with Bethesda III and IV thyroid nodules underwent AGEC testing (47 external, 49 internal patients). Median age was 49.0 years, 67.7% of patients were female, median nodule size was 1.7 cm (range, 0.5-6.1cm), and mean followup was 1.7 months. Amongst internal patients, the benign call rate was 42.9% (21/49). Amongst both internal and external patients, 37.5% (36/96) have undergone surgery: 58.3% (21/36) had a total thyroidectomy, and 41.7% (15/36) had a hemithyroidectomy. Of those undergoing surgery, 55.9% (19/34) of AGEC-suspicious and 0.0% (0/2) of AGEC-benign nodules harbored cancer in the biopsied nodule. Most malignancies were subtypes of papillary thyroid cancer (follicular variant, 63.2%; classical variant, 26.3%). Of external patients, MSKCC cytopathology analysis was concordant 69.6% (16/23) of the time, with 26.1% (6/23) upstaged and 4.3% (1/23) downstaged after re-review. In our cohort, the estimated NPV of AGEC was 86-92%, while the PPV was 55.9%. AGEC significantly affected clinical decision making, with 49.3% (34/69) of AGEC-suspicious patients undergoing surgery compared to 7.4% (2/27) of AGEC-benign patients.

CONCLUSION: Given our center’s higher prevalence of malignancy for indeterminate nodules, slightly higher PPV and slightly lower NPV were observed compared to previously published rates. The prevalence of malignancy among indeterminate nodules varies from center to center. Ideally, physicians utilizing the AGEC assay should assess their center’s pre-test probability of malignancy, as this factor affects the performance characteristics of the AGEC.
HOW IMPORTANT IS RADIOACTIVE IODINE IN TREATMENT OF DIFFERENTIATED THYROID CARCINOMA?
Kumar Alok Pathak, MD, FRCS, William D Leslie, MD, FRCP, Richard W Nason, MD, FRCS, Thomas Klonisch, MD, PhD; University of Manitoba, CancerCare Manitoba

Background: Radioactive iodine (RAI) has been traditionally used as an adjuvant treatment for differentiated thyroid cancers. The present study assesses whether it actually improves disease specific survival in these patients.

Methods: 1472 patients with differentiated thyroid cancer more than 1 cm in size or with extra-thyroidal extension or lymph nodal/distant metastasis, were selected from a population based cohort of 2306 thyroid cancers diagnosed during 1970-2010. Their oncological outcome of these patients in terms of overall, disease specific (DSS and disease free survival (DFS) was calculated by Kaplan Meir method and inter-group comparisons were made by log rank test. Cox proportional hazard and competing risk analysis models was used for multivariable analysis.

Results: Mean age at diagnosis was 46.7+ 17.5 years and 59.8% of them had total thyroidectomy. In all 41.6% received therapeutic dose RAI treatment (>1.5 Giga Becquerel) and 58.4% of them were managed only by TSH suppression or had a lower dose RAI (>1.5 Giga Becquerel). 27.3% of those who had therapeutic dose of RAI had recurrent disease and 17.5% died of their disease as compared to only 10.1% recurrences and 6.1% death due to disease in those who did not receive it. On multivariable analysis DSS was independently by age at diagnosis, gender, T4/T4 tumor, distant metastasis and completeness of resection were the only factors which had significant influence on DSS. Use of adjuvant RAI did not have significant impact on DSS. Only in patients with distant metastases RAI provided a survival advantage (p<0.001).

Conclusion: Radioactive iodine offers survival advantage over TSH suppression only in metastatic differentiated thyroid cancer. In view of the higher risk of developing post RAI second primary cancer, RAI should be used very judiciously.
BACKGROUND: Surgeon performed ultrasound-guided fine needle aspirate (US-FNA) allows patients convenient access to a diagnostic test that has become the standard of care in the work up of thyroid nodules. Wait times are invariably reduced as referral delays between multiple providers are avoided, which further reduces delay in time to diagnosis. There is scant data reporting adequacy and accuracy of surgeon performed US-FNA. Furthermore, while in Canada this service is offered almost exclusively in academic centres, the learning curve as well as impact of head and neck surgical trainees on adequacy rates are largely unknown.

OBJECTIVES: 1) To examine the adequacy and accuracy of all surgeon performed US-FNA biopsies of the thyroid gland at a single institution from the adoption of the procedure into practice.

2) To report the learning curve for a surgeon adopting US-FNA in their practice, and impact of trainees on adequacy.

METHODS: Surgeon performed US-FNA biopsies between 2009-2013 without on-site cytological specimen assessment were reviewed retrospectively. Biopsy was performed by primary surgeon or senior trainee under direct supervision of the primary surgeon. Specimen adequacy, cytologic diagnosis according to Bethesda criteria, and surgical pathology were used to calculate adequacy and accuracy.

RESULTS: In total, 1067 separate biopsies were examined in 723 individuals. The adequacy rate for the first hundred patients following adoption into practice was 71%, followed by 78% for the next hundred, and 85% for the third hundred. When FNAB was subsequently taught to trainees, adequacy rate significantly differed by trainee involved (p<0.04), and higher inadequacy rates were noted in July and January during the adoption of new trainees (p=0.04). Of inadequate samples, 11% went on to have surgery with 32% of those bearing malignancy on final pathology. Neither nodule size nor palpability impacted adequacy, but cystic lesions on ultrasound were more likely to yield inadequate specimens (p<0.001). Of nodules with Bethesda 3, 4, 5, and 6 cytology, 62% went on to have surgery, with malignancy rates of 52%, 63%, 93% and 95% respectively.

CONCLUSIONS: Surgeon performed US-FNA biopsy is a useful tool that can be performed adequately in an outpatient setting, and the Bethesda system appropriately stratified lesions for risk of malignancy. While trainee involvement impacts adequacy rates, inadequate sampling decreases with experience.