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[Trends in Thyroid Cancer Incidence and Mortality in the United States, 1974-2013](#)

Lim H, Devesa SS, Sosa JA, Check D, Kitahara CM.

From JAMA, April 4, 2017

Abstract

IMPORTANCE:

Thyroid cancer incidence has increased substantially in the United States over the last 4 decades, driven largely by increases in papillary thyroid cancer. It is unclear whether the increasing incidence of papillary thyroid cancer has been related to thyroid cancer mortality trends.

OBJECTIVE:

To compare trends in thyroid cancer incidence and mortality by tumor characteristics at diagnosis.

DESIGN, SETTING, AND PARTICIPANTS:

Trends in thyroid cancer incidence and incidence-based mortality rates were evaluated using data from the Surveillance, Epidemiology, and End Results-9 (SEER-9) cancer registry program, and annual percent change in rates was calculated using log-linear regression. Annual percent changes in age-adjusted thyroid cancer incidence and incidence-based mortality rates by histologic type and SEER stage for cases diagnosed during 1974-2013.

RESULTS:

Among 77 276 patients (mean [SD] age at diagnosis, 48 [16] years; 58 213 [75%] women) diagnosed with thyroid cancer from 1974-2013, papillary thyroid cancer was the most common histologic type (64 625 cases), and 2371 deaths from thyroid cancer occurred during 1994-2013. Thyroid cancer incidence increased, on average, 3.6% per year (95% CI, 3.2%-3.9%) during 1974-2013 (from 4.56 per 100 000 person-years in 1974-1977 to 14.42 per 100 000 person-years in 2010-2013), primarily related to increases in papillary thyroid cancer (annual percent change, 4.4% [95% CI, 4.0%-4.7%]). Papillary thyroid cancer incidence increased for all SEER stages at diagnosis (4.6% per year for localized, 4.3% per year for regional, 2.4% per year for distant, 1.8% per year for unknown). During 1994-2013, incidence-



based mortality increased 1.1% per year (95% CI, 0.6%-1.6%) (from 0.40 per 100 000 person-years in 1994-1997 to 0.46 per 100 000 person-years in 2010-2013) overall and 2.9% per year (95% CI, 1.1%-4.7%) for SEER distant stage papillary thyroid cancer.

CONCLUSIONS AND RELEVANCE:

Among patients in the United States diagnosed with thyroid cancer from 1974-2013, the overall incidence of thyroid cancer increased 3% annually, with increases in the incidence rate and thyroid cancer mortality rate for advanced-stage papillary thyroid cancer. These findings are consistent with a true increase in the occurrence of thyroid cancer in the United States.

Strengths

- demonstrates an increase in advanced stage thyroid cancer among the SEER population suggesting a true increase
- Increased mortality demonstrated as well, which should help renew focus on managing these patients in a more aggressive and multidisciplinary manner
- sound statistical methodology

Limitations

- causal factors unable to be discerned due to database study
- SEER population may not be representative of the entire US population. Some changes may be due to demographic migration during the study period.
- Treatment data not available
- Changes in staging and a fair amount of missing data regarding tumor size

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Impact of Mandibular Invasion on Prognosis in Oral Squamous Cell Carcinoma Four Centimeters or Less in Size

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*From **Laryngoscope**, August 2016*

Objectives/Hypothesis: Previous studies have reported variable results for the impact of bone invasion on survival in oral cancer. It is unclear whether bone invasion in small (≤ 4 cm) squamous cell carcinomas (SCC) of the oral cavity is an independent adverse prognosticator. Our objective was to investigate impact on survival of bone invasion in SCC of floor of mouth (FOM), lower alveolus (LA), and retromolar trigone (RMT) ≤ 4 cm in size.

Study Design: Retrospective study of 96 patients with SCC of the FOM, LA, and RMT undergoing primary surgical treatment.

Methods: Original pathology reports and slides were reviewed by three pathologists. Level of bone invasion was categorized as cortical or medullary. Main outcome measures were local control (LC) and overall survival (OS).



Results: Bone invasion was present in 31 cases (32%). On review of pathology slides, all cases of bone invasion demonstrated medullary involvement. Median follow-up was 36 months for all patients, and 53 months for patients not dying from cancer. Among tumors ≤ 4 cm, bone invasion was associated with significantly worse LC ($P = .04$) and OS ($P = .0005$). Medullary invasion (hazard ratio: 2.2, 95% confidence interval: 1.1-4.4, $P = .03$), postoperative radiotherapy (hazard ratio: 0.3, 95% confidence interval: 0.1-0.5, $P < .001$), and positive pathologic nodal status (hazard ratio: 4.1, 95% confidence interval: 1.9-8.6, $P < .001$) were independent predictors of worse OS among the entire cohort.

Conclusions: Mandibular medullary bone invasion is a poor prognosticator in oral cancers, irrespective of small size of primary tumor. Such cases should be considered for postoperative radiotherapy.

Summary: Demonstrates the significance of mandibular invasion in oral cavity SCC in primaries ≤ 4 cm.

Strengths:

- Clearly defined study population of specific subsites of the oral cavity at increased risk for bony invasion.
- Statistically significant differences were reported
- Clearly differentiated between cortical and medullary bone invasion in all cases.
- Provides evidence for recommending post op radiation in patients with mandibular invasion.
- Acceptable follow up at >3 years.

Weaknesses:

- Retrospective study
- Small sample size, 26 patients with tumors ≤ 4 cm with bony invasion (the focus group for this study)
- 5/72 patients (14.4%) undergoing surgery including mandibulectomy died within one month of surgery. High post operative mortality rate in this cohort.
- Some complexities of pathologic management of the bony specimens as outlined by the authors that may have led to underestimation of cases with cortical bony involvement. Note: This would not necessarily have affected the results of this study conclusion which focused on medullary involvement.

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Oncologic Outcomes of Selective Neck Dissection in HPV-Related Oropharyngeal Squamous Cell Carcinoma

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*From **Laryngoscope**, March 2017*

Objectives: To examine outcomes of selective neck dissection (SND) in patients with human papillomavirus (HPV)-related oropharyngeal squamous cell carcinoma (OPSCC) who present with clinical neck disease.



Study Design: Multi-institutional retrospective review.

Methods: Two institutional databases of patients with HPV-related OPSCC were reviewed to identify patients with clinical (c) N1-N3 neck disease who underwent SND \pm adjuvant therapy.

Results: Three hundred and twenty-four patients were identified with a median follow-up of 49 months (range 3–199 months). All patients underwent transoral resection of the primary tumor and SND, including levels II–IV and \pm levels I or V, with resection of additional nonlymphatic tissue (extended SND) as indicated by extent of disease, including the spinal accessory nerve (7%), the internal jugular vein (13%), and the sternocleidomastoid muscle (8%). Two hundred and seventy (83%) patients underwent adjuvant radiation. There were 13 (4%) regional recurrences and 19 (6%) distant recurrences. Regional control following salvage was 98%. On univariable analysis, absence of radiation was associated with regional recurrence (odds ratio [OR] 9.2, 95% confidence interval [CI] 2.9–29.4). On multivariable analysis, adjuvant radiation was associated with improved disease-free survival (DFS) (OR 0.27, 95% CI 0.14–0.53) but lost significance for overall (OS) and disease specific survival (DSS) ($P > 0.05$). Five-year Kaplan-Meier estimates for OS, DSS, and DFS were 88% (95% CI 84%–92%), 93% (95% CI 89%–96%), and 83% (95% CI 78%–87%), respectively.

Conclusion: In HPV-related OPSCC presenting with clinical neck disease, a SND \pm additional tissue resection and adjuvant therapy, when indicated, provides excellent long-term regional control. Omission of radiotherapy increases the risk of regional recurrence, although it may not significantly impact OS or DSS. It appears unnecessary to routinely perform a comprehensive neck dissection.

Summary:

Over 300 patients with oropharyngeal cancer with N1-N3 neck disease from 2 institutions were studied retrospectively and demonstrated that a SND with post operative radiation with indicated provides excellent long term regional control. Overall survival for all study patients was 88%, and for patients with pathological N3 disease the estimated 5-year overall survival was 91% (subset analysis on 23 patients with N3 disease).

Strengths:

- Clearly organized data from 2 high volume centers.
- Excellent review of the history of radical neck dissections through more SND.
- Significant thought in analyzing data around characteristics that have already been shown to significantly affect prognosis (smoking >10 pack years, early vs late stage nodal ds, >5 positive nodes, etc) thus building on information already known to the literature.
- Excellent outcomes including patients with N3 disease.

Weaknesses:

- Retrospective study
- Variations in adjuvant radiotherapy between institutions that could affect survival outcomes.
- Lack of comparison groups including those treated by a standard MRND and those with HPV negative disease.



The Role of Adjuvant Chemotherapy in Surgically Managed, p16-Positive Oropharyngeal Squamous Cell Carcinoma.

Skillington SA, Kallogjeri D, Lewis JS Jr, Piccirillo JF.

From JAMA Otolaryngology Head Neck Surgery, March 1, 2017

IMPORTANCE:

Human papillomavirus (HPV)-related oropharyngeal squamous cell carcinoma (OPSCC) has a favorable prognosis, and p16 immunohistochemistry is a surrogate marker of high-risk HPV infection and strong prognosticator. Given this favorable prognosis, treatment de-escalation for p16-positive OPSCC is now being considered with the goal of decreasing treatment-associated morbidity without compromising tumor control. The role of adjuvant chemotherapy in this setting is becoming increasingly unclear.

OBJECTIVE:

To compare survival between surgically managed patients with p16-positive OPSCC who received adjuvant chemoradiotherapy and patients who received adjuvant radiotherapy alone.

DESIGN, SETTING, AND PARTICIPANTS:

This was a cohort study of patients with OPSCC diagnosed from June 1996 to June 2010, with follow-up through December 2014, at a single tertiary referral center. One hundred ninety-five surgically managed, p16-positive patients without a history of head and neck cancer or distant metastasis at time of diagnosis were included.

EXPOSURES:

Patients were dichotomized into adjuvant radiotherapy and adjuvant chemoradiotherapy groups.

MAIN OUTCOMES AND MEASURES:

Overall survival was the primary outcome, and disease-free survival was the secondary outcome. Propensity-weighted multivariate Cox proportional hazards analysis was conducted to quantify the effect of adjuvant chemotherapy on survival.

RESULTS:

The study included 195 patients with p16-positive, surgically managed OPSCC. Median duration of follow-up was 87 months (interquartile range, 68-116 months). Ninety patients received adjunct chemoradiotherapy (mean age, 54.3 years), 88 patients received adjuvant radiotherapy (mean age, 56.4 years), and 17 patients received surgery alone. The 5-year overall survival rate for patients who received adjuvant chemoradiotherapy was 82% (95% CI, 73%-90%) and 84% (95% CI, 76%-91%) for patients who received adjuvant radiotherapy alone. The 5-year disease-free survival rate for patients who received adjuvant chemoradiotherapy was 79% (95% CI, 71%-88%) and 79% (95% CI, 70%-88%) for patients who received radiotherapy alone. After weighting cases by the inverse probability of receiving adjuvant chemotherapy and controlling for age, comorbidity, smoking, pathological T stage, and pathological N stage, the receipt of adjuvant chemotherapy was not significantly associated with disease-free survival (adjusted hazard ratio, 0.91; 95% CI, 0.59-1.42) but was associated with a statistically insignificant yet clinically meaningful increase in all-cause mortality (adjusted hazard ratio, 1.46; 95% CI, 0.91-2.33).

CONCLUSIONS AND RELEVANCE:

Among patients with p16-positive OPSCC managed surgically with adjuvant radiotherapy, the addition of adjuvant chemotherapy provided no additional disease-free survival benefit and was associated with



worse overall survival. These results should help inform future clinical trials aiming to deescalate treatment for p16-positive patients. United States.

Strengths

- Well-designed study with advanced statistical methodology (i.e. propensity matching) that can account for many of the biases inherent within retrospective analyses.
- Answers an important question regarding adjuvant therapy showing no difference in OS or DFS in surgically managed p16 patients treated with adjuvant XRT vs CRT.
- Largest study to date looking into this question with minimal differences between the two populations

Limitations

- Utilization of the AJCC 7th staging which is known to not delineate the survival between the stages as robustly as the new staging
- Surgical margin status not included
- Granular data regarding the adjuvant therapy (i.e. exact chemotherapy used, dosages received, completion of adjuvant treatment, radiation dosing,) not included
- The suggestion of increase in all-cause mortality with the use of chemotherapy should be interpreted with caution due to the large confidence interval
- Retrospective data

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[Optimal Perioperative Care in Major Head and Neck Cancer Surgery with Free Flap Reconstruction: A Consensus Review and Recommendations from the Enhanced Recovery After Surgery Society](#)

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From JAMA Otolaryngology Head Neck Surgery, March 1, 2017

Abstract

IMPORTANCE Head and neck cancers often require complex, labor-intensive surgeries, especially when free flap reconstruction is required. Enhanced recovery is important in this patient population but evidence-based protocols on perioperative care for this population are lacking.

OBJECTIVE To provide a consensus-based protocol for optimal perioperative care of patients undergoing head and neck cancer surgery with free flap reconstruction.

EVIDENCE REVIEW Following endorsement by the Enhanced Recovery After Surgery (ERAS) Society to develop this protocol, a systematic review was conducted for each topic. The PubMed and Cochrane databases were initially searched to identify relevant publications on head and neck cancer surgery from 1965 through April 2015. Consistent key words for each topic included “head and neck surgery,” “pharyngectomy,” “laryngectomy,” “laryngopharyngectomy,” “neck dissection,” “parotid lymphadenectomy,” “thyroidectomy,” “oral cavity resection,” “glossectomy,” and “head and neck.” The final selection of literature included meta-analyses and systematic reviews as well as randomized



controlled trials where available. In the absence of high-level data, case series and nonrandomized studies in head and neck cancer surgery patients or randomized controlled trials and systematic reviews in non-head and neck cancer surgery patients, were considered. An international panel of experts in major head and neck cancer surgery and enhanced recovery after surgery reviewed and assessed the literature for quality and developed recommendations for each topic based on the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) system. All recommendations were graded following a consensus discussion among the expert panel.

FINDINGS The literature search, including a hand search of reference lists, identified 215 relevant publications that were considered to be the best evidence for the topic areas. A total of 17 topic areas were identified for inclusion in the protocol for the perioperative care of patients undergoing major head and neck cancer surgery with free flap reconstruction. Best practice includes several elements of perioperative care. Among these elements are the provision of preoperative carbohydrate treatment, pharmacologic thromboprophylaxis, perioperative antibiotics in clean-contaminated procedures, corticosteroid and antiemetic medications, short acting anxiolytics, goal-directed fluid management, opioid-sparing multimodal analgesia, frequent flap monitoring, early mobilization, and the avoidance of preoperative fasting.

CONCLUSIONS AND RELEVANCE The evidence base for specific perioperative care elements in head and neck cancer surgery is variable and in many cases information from different surgical procedures form the basis for these recommendations. Clinical evaluation of these recommendations is a logical next step and further research in this patient population is warranted.

SUMMARY

- Describes the Enhanced Recovery After Surgery approach to patient care used in other specialties
- Reviews current evidence for 17 topics of perioperative care
- The evidence base for perioperative care elements in head and neck cancer surgery is variable and certain recommendations from other procedures can be adapted in this patient population

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