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Table of Contents – ***click the page number to go to the summary and full article link.***

Racial Disparities in Differentiated Thyroid Cancer: Have We Bridged the Gap?

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*From **Thyroid**, June 2017*

Background: Racial disparities in the management of differentiated thyroid cancer (DTC) exist in the United States. There is a paucity of data examining their temporal trends. It was hypothesized that racial disparities in care provided to patients with DTC have improved over the past 15 years.

Methods: Adult patients undergoing surgery for DTC were included from the National Cancer Data Base (1998–2012). Temporal trends in appropriate extent of thyroidectomy and radioactive iodine therapy (RAI) were described for different racial groups. Multivariable logistic regression models were employed to estimate the adjusted association of receipt of appropriate extent of surgery and RAI, specifically under- and overtreatment, among different racial groups.

Results: Among 282,043 DTC patients, 80.3% were non-Hispanic white (white), 8.1% Hispanic, 7.2% non- Hispanic black (black), and 4.4% Asian. Black versus white race/ethnicity was associated with lower odds of receiving appropriate surgery (odds ratio [OR] = 0.78 [confidence interval (CI) 0.71–0.87]; $p < 0.001$). Appropriate RAI treatment was higher in blacks (OR = 1.07 [CI 1.02–1.12]; $p = 0.01$) and lower for Hispanics (OR = 0.90 [CI 0.86–0.95]; $p < 0.001$) compared with whites. There was a higher likelihood of RAI undertreatment in minority groups (Hispanic OR= 1.27, black OR= 1.26, Asian OR= 1.25; $p < 0.001$), and a lower likelihood of RAI over-treatment (Hispanic OR= 0.89, black OR= 0.83, Asian OR= 0.79; $p < 0.001$) compared with whites. Over time, an increasing proportion of black and white patients underwent appropriate extent of thyroidectomy (1998 vs. 2012: 78% vs. 88% and 81% vs. 91%, respectively). Compared with 1998, fewer patients in 2012 were under-treated with RAI: whites (48% vs. 29%, respectively), blacks (51% vs. 33%), Hispanics (51% vs. 37%), and Asians (55% vs. 39%). The extent of RAI over-treatment increased (1998 vs. 2012): whites (1% vs. 4%), blacks (2% vs. 4%), Hispanics (2% vs. 4%), and Asians (2% vs. 3%), respectively.

Conclusions: Appropriate utilization of surgery and RAI for DTC has improved over time. However, the proportion of patients receiving appropriate thyroid surgery is consistently lower for blacks compared with whites. RAI over-treatment increased for all races over the study period. Efforts are needed to standardize DTC care among minority patients.

Summary statements:

1. The National Cancer Data Base (NCDB) was the data source. It is a joint program of the American Cancer Society and the Commission on Cancer (CoC) of the American College of Surgeons. The NCDB is a nationwide, facility-based, comprehensive data set containing more than 29 million cancer cases from 1500 CoC-accredited cancer programs across the United States, capturing at least 85% of all new thyroid cancer cases. A total of 282,043 patients were included in the analysis.
2. Surgical and RAI appropriateness based on ATA and NCCN guidelines.
3. Compared with other patients, black patients more often presented with larger tumors (>4 cm) and were less likely to undergo lymph node dissection. Consequently, black patients were found to have a lower rate of documented lymph node metastases.
4. Compared with white patients, black patients had reduced 5- and 10-year OS rates (94% vs. 93% and 87% vs. 84%, respectively; log-rank $p < 0.001$).
5. Appropriate extent of thyroid surgery was less likely to be performed for black compared with white patients (90.7% vs. 93.1%; $p < 0.001$ in unadjusted analyses). After adjustment, black race was associated with lower odds of receiving appropriate extent of thyroid surgery compared with white race (OR = 0.78 [CI 0.71–0.87]; $p < 0.001$).
6. In total, 47.8% of patients received RAI. The odds of receipt of appropriate RAI treatment were higher for blacks (OR = 1.07 [CI 1.02–1.12]; $p = 0.01$) and lower for Hispanics (OR = 0.90 [CI 0.86–0.95]; $p < 0.001$) compared with white patients. The likelihood of RAI under-treatment was higher for all other races compared with white patients (Hispanic OR= 1.27 [CI 1.18–1.36]; black OR= 1.269[CI 1.17–1.37]; Asian OR= 1.25 [CI 1.14–1.37]; $p < 0.001$), while whites were more likely to be over-treated with RAI when compared with all other races (Hispanic OR= 0.89 [CI 0.84–0.94]; black OR= 0.83 [CI 0.79–0.88]; Asian OR= 0.79 [CI 0.74–0.85]; $p < 0.001$).
7. Overall, the odds of receipt of appropriate thyroid surgery increased over time at a rate of 5% per year (OR= 1.05[CI 1.04–1.06], but the interaction term of year · race was not significant ($p = 0.97$), indicating that the trajectory of change over time in the adjusted odds of receiving appropriate surgery did not differ between races.
8. The adjusted proportion of patients who were under-treated with RAI decreased for all race groups over the study period. The odds of being under-treated seemed to decline at a higher rate over time for blacks compared with whites (year · race interaction $p = 0.02$), whereas Asians had a lower rate of decline over time in the odds of being under-treated.
9. Adjusted rates of RAI over-treatment increased over time for all race groups. Compared with 1998, more patients were over-treated with RAI in 2012: whites (1% in 1998 vs. 4% in 2012), blacks (2% vs. 4%), Hispanics (2% vs. 4%), and Asians (2% vs. 3%), respectively (Table 4). The overall odds of over-treatment with RAI have been marginally increasing (year of diagnosis OR= 1.01; $p < 0.001$, data not shown), but the interaction term of year · race was not significant ($p = 0.35$), again indicating that the trajectory of change over time in the adjusted odds of receipt of RAI over-treatment did not differ based on race.

Strengths

1. Large number of patients included in the study.
2. Excellent study design, use of accepted standard guidelines as the determinant of appropriateness of care.

Weaknesses

1. There are limitations to this study, including those inherent in the use of large administrative databases. Specifically, these include the possibility of coding errors and missing data.

2. The study demonstrates compromised 5- and 10-year overall survival among black patients, but in the absence of disease-specific survival data, it is difficult to attribute all of this difference to disparities in thyroid cancer treatment.

back to top

Sialadenitis without sialolithiasis: Prospective outcomes after sialendoscopy-assisted salivary duct surgery.

Delagnes EA, Aubin-Pouliot A, Zheng M, Chang JL, Ryan WR.

*From **Laryngoscope**. October 2016*

Objectives: To prospectively assess symptoms before and after sialendoscopy-assisted salivary duct surgery (SASDS) in patients with symptomatic sialadenitis without sialolithiasis. Study Design: Prospective cohort study.

Methods: Patients with chronic obstructive sialadenitis without sialolithiasis (COSWS) completed the Chronic Obstructive Sialadenitis Symptoms (COSS) questionnaire prior to SASDS and 3 months postoperatively.

Results: Of 80 consecutive patients in a 20-month period, 20 surveyed patients underwent SASDS for COSWS in 37 symptomatic glands. Major symptom improvement (> 10 COSS score reduction) was reported in 24 of 37 (65%) of all glands, including 14 of 21 (67%) of radioactive iodine (RAI)-induced cases and 10 of 13 (77%) of idiopathic sialadenitis cases. A significant reduction in postoperative mean COSS scores was seen overall (12.6 points, standard deviation [SD] 19.3, $P < 0.05$ to a post-SASDS mean score of 26.6). However, 19 of 37 (51%) glands demonstrated postoperative COSS scores above 25, denoting persistent disease. Mean COSS score reductions in RAI-induced sialadenitis (12.4 points, SD 22.7, $P < 0.05$) and idiopathic sialadenitis (16.3 points, SD 13.7, $P < 0.005$) groups were significant, with post-SASDS COSS mean scores of 30.6 (SD 19.8) and 20.8 (SD 13.8), respectively. Ducts with stenoses treated with dilation or sialodochoplasty showed significant COSS improvements of 21.1 (SD 17.9) and 12.4 points (SD 10.7), respectively ($P < 0.05$). In a multivariate analysis, both the presence of stenosis and sialodochoplasty were independent predictors of complete or partial resolution (post-COSS score < 25) and major symptom improvement ($P < 0.05$).

Conclusion: SASDS provides short-term symptom reduction in patients with COSWS; particularly in RAI-induced and idiopathic sialadenitis, and in duct stenosis amenable to dilation or sialodochoplasty. However, approximately half of the glands did not achieve meaningful symptom resolution.

Summary

- A case series of 20 patients with chronic obstructive sialadenitis without sialolithiasis (COSWS) treated by sialoendoscopy with mechanical dilation. Sialadenitis-specific symptoms before and after the procedure were measured with the previously validated COSS questionnaire. A higher score means worse symptoms.
- Three months after SASDS, the mean COSS scores improved by a mean of 12.6 points (15.8 for parotid gland and 7.0 for submaxillary gland). 65% of patients had a major improvement (75% for parotid and 46% for submaxillary). Partial or complete resolution of symptoms occurred in

49% of patients, similar for both glands. Patients with idiopathic origin had greater symptom resolution.
- Treatment was not feasible for 10% of patients.

Strengths
- Selected group of patients with homogeneous salivary condition
- Experienced group of operators able to make diverse maneuvers to surpass the stenosis
- Measurement of outcomes with a specific instrument.
- Prospective assessment of symptoms.

Weaknesses
- Small sample size
- Short term (3 months) follow up period.
- Small decrease in scores that could not represent minimal clinically significant improvements
- Symptom scores were calculated by gland and not by patient. It is possible that patients with multiglandular disease over or underscore in the questionnaire.

back to top

Does resident involvement in thyroid surgery lead to increased postoperative complications?

Kshirsagar RS, Chandy Z, Mahboubi H, Verma SP.

*From **Laryngoscope**. May, 2017*

Objectives/Hypothesis: To evaluate the impact of resident involvement during thyroid surgery on 30-day postoperative complications. Study Design: Retrospective cohort study.

Methods: All patients who underwent thyroid surgery in 2011 were identified from the American College of Surgeons National Surgical Quality Improvement Program database. Patient demographics, perioperative details, resident involvement in surgery, and 30-day postoperative complications were extracted. Propensity score analysis was used to match resident and nonresident cases. Univariate and multivariate analysis were performed to determine the relationship between resident involvement in thyroid surgery and postoperative outcomes.

Results: 1,747 patients with and 1,747 patients without resident involvement were case-matched for patient demographics, perioperative variables, and surgical case type. There was no significant difference (P < .19) in 30-day postoperative complication rates of surgeries with and without resident involvement, which were 1.4% and 2%, respectively. Operative time was longer in surgeries with residents than those without residents (119± 67 minutes vs. 102 ±55 minutes, P < .001). Cases with resident involvement had an unplanned reoperation rate of 0.9%, which was significantly lower than the 2.3% rate of surgeries without residents (P< .001). Multivariate analysis revealed no significant association between resident involvement and overall complications (odds ratio 5 0.70; P 5 .18).

Conclusions: Resident participation in thyroid surgery was not associated with an increased 30-day postoperative complication rate. These findings demonstrate that patient safety is not adversely affected by resident participation in thyroid surgery.

Summary

- Analysis of the prospective surgical cohort of the American College of Surgeons National Quality Improvement Program for thyroidectomy made with or without resident participation. Authors used specific statistical methods in order to avoid selection bias and a multivariate analysis.
- There was not difference in covariates between cohorts with or without participation of residents. 30 –day complication rate was not statistically different . The operative time increased 17 min in the group with resident participation but this group had a lower rate of unplanned reoperation (2.3% to 0.9%)

Strengths

- Use of the e American College of Surgeons National Quality Improvement Program (ACS-NSQIP) database
- Big sample size
- Propensity score matching that decrease the risk of selection bias
- Prospective registration of variables and outcomes
- Using unplanned reoperation as a proxy for acute hematoma, it is possible to suggest a lower rate in the group with resident participation.

Weaknesses

- It is impossible to know the role of the resident and the participation in critical steps during the procedure. If the resident is not participating actively in the procedure, outcomes will only represent the complication rate of graduated surgeons.
- Outcomes reported are not specific for thyroid surgery. Critical outcomes as laryngeal nerve paralysis or hypocalcemia were not evaluated, so the conclusions must be interpreted with caution.

back to top

Elective Neck Dissection for Head and Neck Cutaneous Squamous Cell Carcinoma with Skull Base Invasion

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*From **Otolaryngology – Head & Neck Surgery**. April, 2017*

Objectives. Skull base invasion from cutaneous squamous cell carcinoma (cSCC) via perineural spread affects survival and the rate of regional metastasis. Our objective is to investigate the factors associated with elective neck dissection (END) in this population and the survival difference with END compared with observation for patients with a cN0 neck.

Study Design. Case series with chart review.

Setting. Academic.

Subjects and Methods. Patients were treated surgically for head and neck cSCC with skull base invasion via perineural spread with a cN0 neck from 2004 to 2014. Clinicopathologic data were collected and analyzed. Primary outcomes were diseasefree survival (DFS) and overall survival (OS).

Results. Fifty-nine patients met inclusion criteria: 28 underwent an END and 31 underwent neck observation. Free tissue transfer reconstruction was significantly associated with END (P \.001). Patients treated with an END had significantly improved 5-year DFS (57% and 32%, P = .042) and OS (60% and 37%, P = .036) compared with those who were observed and a significantly reduced rate of regional recurrence (9% and 37%, P = .024). The rate of occult nodal metastasis identified with END was 36% and is approximately equal to the regional failure rate of the neck observation group (37%).

Conclusion. END was more commonly used in cases requiring free tissue transfer. The use of END for head and neck cSCCs that have invaded the skull base is not routinely performed but was found to be associated with a survival advantage and reduced regional recurrence rate.

Summary. This paper attempts to better define rates of regional metastasis, survival outcomes and use of elective neck dissection in cSCC with skull base invasion and cN0 neck. Exclusion criteria included patients who underwent therapeutic neck dissection or definitive chemoradiation.

The most common END performed was levels 1 to 3 (n = 16), which was performed for any anterior lesion that did not involve the parotid. For a posterior lesion that did not involve the parotid, an END levels 1 to 4 was performed (n = 7). If the parotid was involved with the primary tumor, then a parotidectomy was performed as well as an END levels 1 to 4 (n = 5). Elective parotidectomy was not performed.

The rate of occult nodal metastasis identified with END was 36% and is approximately equal to the regional failure rate of the neck observation group (37%). END was performed more frequently with patients who underwent 1) free tissue transfer, 2) orbital exenteration, 3) adjuvant chemotherapy and adjuvant radiation, however, in multivariate analysis, END remained an independent predictor of improved survival and reduced regional recurrence rate.

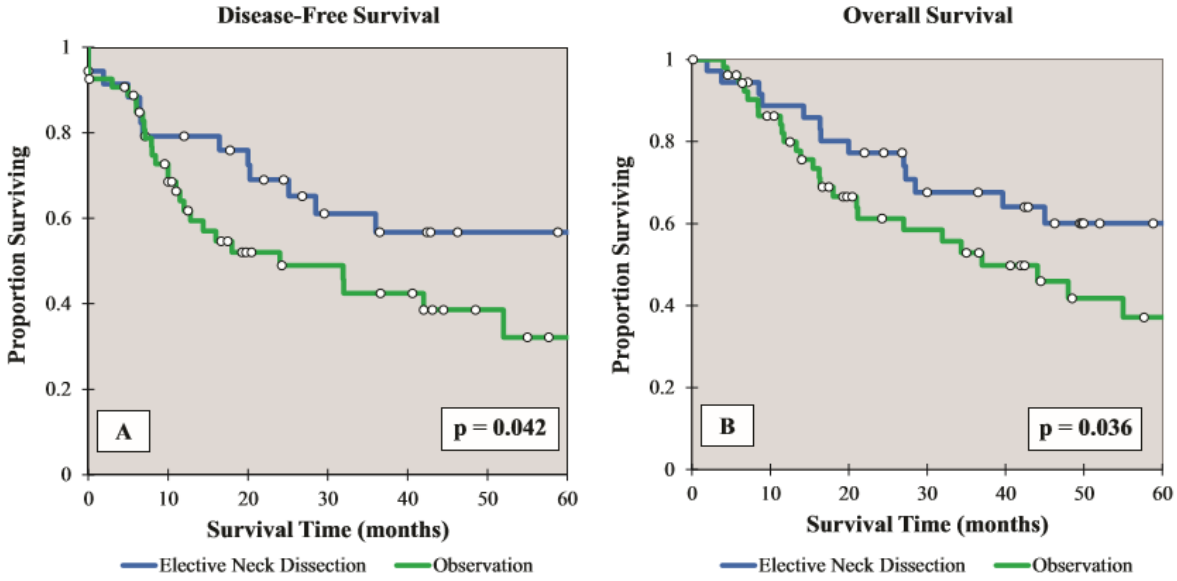

Figure 1. (A) Disease-free and (B) overall survival for cutaneous squamous cell carcinoma (cSCC) with skull base invasion with a cN0 neck, comparing patients treated with an elective neck dissection (n = 28) to those who were observed (n = 31).

Table 3. Multivariate Analysis of Factors Affecting Disease-Free Survival and Overall Survival Reported as Proportional Hazard Ratios with 95% Confidence Intervals.[a]

	Disease-Free Survival		Overall Survival	
Variable	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value
Age at diagnosis	1.311 (1.005-1.570)	**.039**	1.290 (1.020-1.065)	**.013**
Active immunosuppression	1.795 (1.026-2.324)	**.025**	1.434 (1.130-1.987)	**.041**
Orbital invasion	1.401 (1.292-1.798)	**.040**	1.677 (1.399-1.819)	**.036**
Skull base invasion zonal classification	2.113 (1.818-2.516)	**.013**	2.210 (1.191-3.012)	**.012**
Neck dissection	1.859 (1.059-3.604)	**.026**	1.936 (1.160-2.767)	**.015**

Abbreviations: CI, confidence interval; HR, hazard ratio.
[a]*P* < .05 in bold.

Strengths

- Relatively large series evaluating this understudied patient population
- Critical use of multivariate analysis to adjust for confounding factors and identify independent predictors of survival.
- Demonstrates significantly improved survival over extensive followup period of 5 years in END group: DFS (57% vs. 32%) and OS (60% vs. 37%)

Weaknesses

- Retrospective, not randomized
- No standardized treatment or surgeon
- Varied patient comorbid conditions not taken into consideration.

back to top

Staged Surgery for Advanced Thyroid Cancers: Safety and Oncologic Outcomes of Neural Monitored Surgery

Behzad Salari, MD, Rebecca J. Hammon, MD, Dipti Kamani, MD, and Gregory W. Randolph, MD

From ***Otolaryngology – Head & Neck Surgery****. May, 2017*

Objective. Thyroidectomy with extensive multicompartment bilateral neck dissections for advanced-stage thyroid cancer may lead to increased risk of complications, including bilateral recurrent laryngeal nerve (RLN) paralysis and hypoparathyroidism. A planned staged approach derived from a detailed preoperative radiographic map is associated with a low complication profile. This study evaluates oncologic results and safety of neural monitored, staged thyroid cancer surgery for management of advanced thyroid cancer.

Study Design. Case series with chart review.

Setting. Tertiary care center.

Subjects and Methods. With institutional review board approval, 35 consecutive patients with advanced thyroid malignancy and extensive nodal disease managed with staged surgery between January 2004 and May 2013 by the senior author (G.W.R.) were identified, and the oncologic and surgical outcomes were reviewed.

Results. In total, 37.2% of patients had stage III or IV disease, with extrathyroidal extension in 71.4%, vascular invasion in 51.4%, and RLN invasion in 17% of patients. A total of 34% patients had positive lymph nodes in more than 5 nodal compartments; the average positive lymph node yield was 17, and extranodal extension was present in 51%. Three patients had RLN sacrifice, and there were no other cases of temporary or permanent RLN paralysis; permanent hypoparathyroidism and chyle leak occurred in one patient each. Locoregional recurrence occurred in 5.7% of patients after a 147-week mean follow-up. In patients with papillary thyroid carcinoma, median postoperative nonstimulated and stimulated thyroglobulin levels were 0.2 and 0.75 ng/mL, respectively.

Conclusion. A neural monitored, staged surgical approach was conducted without significant adverse events in this small sample and represents and effective alternative strategy option to simultaneous bilateral surgery in the management of thyroid cancer with extensive neck metastases.

Summary. This study evaluates oncologic outcome and safety of neural monitored staged thyroidectomy for advanced thyroid disease (PTC and MTC) with extensive bilateral central and lateral neck nodes.
- In the current study, patients with extensive bilateral central and lateral neck nodes on preoperative imaging are staged surgically with (1) the dominant lateral neck, ipsilateral thyroid, and ipsilateral central neck along with the pretracheal and prelaryngeal compartments performed first and (2) the contralateral, less dominant lateral neck, thyroid, and central neck completed after a recovery interval. If thyroid primaries were bilateral, the largest dominant tumor side (which also was typically the side of dominant largest nodal disease) was done first.

- The staged approach was a planned preoperative surgical strategy; none were staged as an intraoperative decision based on the occurrence of intraoperative complications.
- The authors waited 8-10 weeks between surgeries.
- Oncologic markers included TG (PTC), calcitonin and CEA (MTC), serum calcium and albumin levels.

- RLN injury and hypoparathyroidism was described as temporary (<6mo) or permanent (>6mo).
- All cases were performed with RLN monitoring.
- Outcomes
    - Surgical: The average stage of cancer in this series is significantly more advanced than any other series in the literature. Nonetheless, in comparing this series to the literature a it relates to all thyroid cancer operations, there were
        - 0% RLN injury compared to 3.6%
        - 2.9% permanent hypoparathyroidism compared to 2-16%.
    - Oncologic: In this series where 37.5% of patients were stage III-IV, there was a 5.7% recurrence rate compared to historical risk of recurrence of 10% in stage I PTC and 20-30% in stage II-III PTC.

Strengths

- Clear and defined treatment strategy outlined for staged surgery in advanced thyroid cancer with extensive neck node involvement
- Excellent outcomes both surgical and oncologic (median followup only 28 months) for this surgical feasibility study.
- Incorporation of IONM findings into surgical planning for bilateral thyroid procedures is a relatively new application of IONM. Routine RLN monitoring allows for intraoperative flexibility in surgical strategy by providing feedback on LOS on the initial side of resection. The decision can be made intraoperatively to pursue 2-stage surgery following LOS to avoid bilateral RLN paralysis, a highly morbid complication of thyroid surgery. This surgical feasibility study supports this concept offered by referenced authors Goretski et al and Melin et al.

Weaknesses

- single-institution, single-cohort, retrospective, nonrandomized study with a small sample size with relatively short follow-up
- 2 biologically different diseases and short followup – success of disease control should be asserted cautiously
- No cost-benefit analysis

back to top