

UC Irvine

UC Irvine Previously Published Works

Title

Facility Volume as a Prognosticator of Survival in Locally Advanced Papillary Thyroid Cancer.

Permalink

<https://escholarship.org/uc/item/5wh3j3h2>

Journal

The Laryngoscope, 133(2)

Authors

Abiri, Arash

Pang, Jonathan

Roman, Kelsey

et al.

Publication Date

2023-02-01

DOI

10.1002/lary.30280

Peer reviewed



Published in final edited form as:

Laryngoscope. 2023 February ; 133(2): 443–450. doi:10.1002/lary.30280.

Facility Volume as a Prognosticator of Survival in Locally Advanced Papillary Thyroid Cancer

Arash Abiri, BS,

Jonathan C. Pang, BA,

Kelsey Roman, BS,

Khodayar Goshtasbi, MD,

Jack L. Birkenbeuel, BS,

Edward C. Kuan, MD MBA,

Tjason Tjoa, MD,

Yarah M. Haidar, MD

Department of Otolaryngology-Head and Neck Surgery, University of California, Irvine, Orange, CA, USA

Abstract

Objectives: To evaluate the influence of facility case-volume on survival in patients with locally advanced papillary thyroid cancer (PTC), and to identify prognostic case-volume thresholds for facilities managing this patient population.

Study Design: Retrospective database study.

Methods: The 2004–2017 National Cancer Database was queried for patients receiving definitive surgery for locally advanced PTC. Using K-means clustering and multivariable Cox proportional-hazards (CPH) regression, two groups with distinct spectrums of facility case-volumes were generated. Multivariable CPH regression and Kaplan-Meier analysis assessed for the influence of facility case-volume and the prognostic value of its stratification on overall survival (OS).

Results: Of 48,899 patients treated at 1,304 facilities, there were 34,312 (70.2%) females and the mean age was 48.0 ± 16.0 years. Increased facility volume was significantly associated with reduced all-cause mortality (HR 0.996; 95% CI, 0.992–0.999; $p=0.008$). Five facility clusters were generated, from which two distinct cohorts were identified: low (LVF; <27 cases/year) and high (HVF; ≥ 27 cases/year) facility case-volume. Patients at HVFs were associated with reduced mortality compared to those at LVFs (HR 0.791; 95% CI, 0.678–0.923, $p=0.003$). Kaplan-Meier analysis of propensity score-matched N0 and N1 patients demonstrated higher OS in HVF cohorts (all $p<0.001$).

Corresponding author: Yarah M. Haidar, MD, Department of Otolaryngology-Head and Neck Surgery, University of California, Irvine Medical Center, 101 The City Drive South, Orange, CA 92868, Phone: (714) 456-5753, Fax: (714) 456-5747, haidary@uci.edu. Portions of this work were submitted as a poster at the 2022 Triological Society Combined Sections Meeting, Coronado, CA.

Conflicts of Interest: ECK is a consultant for Stryker ENT (Kalamazoo, MI).

Level of Evidence: 4

Conclusions: Facility case-volume was an independent predictor of improved OS in locally advanced PTC, indicating a possible survival benefit at high-volume medical centers. Specifically, independent of a number of sociodemographic and clinical factors, facilities that treated 27 cases per year were associated with increased OS. Patients with locally advanced PTC may, therefore, benefit from referrals to higher-volume facilities.

Keywords

Papillary thyroid cancer; hospital volume; prognosis; survival; quality improvement

Introduction

Papillary thyroid carcinoma (PTC) accounts for approximately 80% of all thyroid cancers in the United States, and its incidence has been increasing over the past several decades.¹ Although non-metastatic PTC generally has an excellent prognosis, morbidity and mortality are significantly higher in patients with locally advanced disease.^{2,3} Extrathyroidal extension, in which the tumor penetrates beyond the thyroid capsule into surrounding tissues, has been reported in approximately 13% of PTC cases.⁴ The recurrent laryngeal nerves, esophagus, and trachea are common sites of invasion,⁵ and involvement of these structures places the patient at high risk of local complications like airway obstruction, hoarseness, and hemoptysis.⁶ Surgery is a critical first step in disease management; although, adjuvant therapy like radioiodine ablation is often indicated to establish local control and prevent tumor recurrence.^{6,7}

A growing body of literature suggests that high hospital case volume is associated with superior clinical outcomes and longer patient survival. This relationship has been established for a variety of malignancies, including testicular cancer,⁸ non-small cell lung cancer,⁹ and nasopharyngeal carcinoma,¹⁰ among others.^{11,12} However, the underlying mechanism for the relationship between case volume and quality of care is still under debate. Possible explanations include greater adherence to clinical guidelines, utilization of specialized multidisciplinary care teams, and greater access to advanced technologies and treatments at high volume “centers of excellence” compared to community hospitals.^{10,13–16} Since locally advanced PTC requires a high level of surgical expertise and effective coordination of care between different medical specialists, patients may benefit from treatment at high volume institutions. However, to date, no study has investigated the impact of facility case-volume on survival outcomes in this patient population. Furthermore, the current literature lacks systematically formulated case volume stratifications that could be applied to clinical decision making and assessments of facility quality of care. Therefore, in this study, we evaluated the influence of facility volume on survival in patients with locally advanced PTC and aimed to identify prognostic case volume thresholds for facilities managing this patient population.

Methods

Study Population

The 2004–2017 NCDB is a deidentified and publicly available database that reports more than 70% of newly diagnosed cancer cases nationwide from over 1500 Commission on Cancer (CoC)-accredited facilities throughout the U.S.¹⁷ Due to the anonymized nature of the NCDB, this study was exempt from University of California, Irvine Institutional Review Board approval.

We queried the database for patients with well-differentiated thyroid cancer (DTC) using the *International Classification of Disease for Oncology, 3rd Edition* (ICD-O-3) topography code for the thyroid (C73.9) and histology/behavior codes for locally advanced (T3/T4, any N, M0) papillary thyroid cancer (8050/3, 8260/3, 8340–8344/3, 8350/3). Only patients who had undergone surgery as part of their treatment course were included. Patients who received palliative care or had more than one primary malignancy were excluded. Additionally, those who had undergone chemotherapy as part of their treatment course were excluded, as less than 0.1% of patients had reportedly received chemotherapy. Finally, cases with unknown or missing treatment information were excluded.

Study Variables

Independent covariates included patient age, sex, race, insurance type, Charlson/Deyo (CD) comorbidity index, facility type (non-academic, academic), facility volume (cases per year), T classification, N classification, extent of surgery, radioiodine therapy (RAI), or thyroid-stimulating hormone suppression therapy (THST). CD indices were binarized as 0 and 1 to indicate the absence or presence of comorbidities, respectively. Extent of surgery was dichotomized as lobectomy (lobectomy ± isthmectomy) and total thyroidectomy (total, near-total, or subtotal resection) per previously published studies.^{18,19} The primary measured outcomes were all-cause mortality and overall survival (OS) starting at the time of diagnosis.

Facility Volume Calculation and Threshold Determination

Mean annual facility volume was calculated based on the cases of locally advanced PTC that were treated at each facility. The number of cases per facility was summed and divided by the number of years that the NCDB reported data on the institution. These values represented actual case volume, as the NCDB collects data on all cancer cases from its contributing facilities.²⁰

After applying the exclusion criteria, K-means clustering was performed to group facilities into 1 to 10 clusters according to their case volumes. For each round of clustering, the sum of square within a cluster was calculated, which represented the variance of the values (i.e., facility case volumes) in that cluster. The elbow curve method²¹ was used to determine the optimal number of clusters to be 5, with a compactness of 90.9% (Figure 1). The clusters were sorted in order of increasing facility volume, with the ranges of the first and last cluster being 1–5 and 57–103 cases per year, respectively. Each cluster's OS was visualized on univariate Kaplan-Meier survival curves (Supplementary Figure 1) and, subsequently, mortality risk was compared with the preceding two clusters via

multivariable cox proportional hazards (CPH) regression (Supplementary Table 1). A case volume threshold was created whenever a cluster had significantly lower mortality than both of the preceding clusters. The clusters were then collapsed according to the identified thresholds to generate volume-stratified groups that could be used in further analyses. Thus, this method served as an objective way to minimize differences within volume-stratified patient cohorts and maximize differences between cohorts.

Statistical Analysis

All statistical analyses were performed via R (version 3.6.1; The R Foundation for Statistical Computing) in RStudio (version 1.2.1335). A p -value of <0.05 was considered statistically significant. Kruskal-Wallis and Chi-square tests were used to evaluate differences among continuous and categorical variables, respectively. CPH regression was performed to identify significant associations between sociodemographic or clinical factors and mortality risk. Variables that were found to be significantly associated with mortality on univariate analysis were included as covariates in multivariable CPH models. A lack of multicollinearity in multivariable CPH models was ensured by confirming that all covariates possessed variance inflation factors less than 10.²² OS was modeled with Kaplan Meier analysis and compared between patient cohorts using log-rank tests. To account for confounding factors in Kaplan-Meier analyses, propensity score matching was performed to create propensity-matched cohorts with statistically nonsignificant differences in the sociodemographic and clinical factors that were previously found to be statistically different on univariate analysis. Propensity scores were calculated using logistical regression, and 1-to-1 propensity matching without replacement was performed utilizing the nearest neighbor method. A caliper width equal to 0.2 of the standard deviation of the logit of the propensity score was utilized to eliminate at least 98% of bias.²³

Results

Overall, 48,899 patients with locally advanced PTC were treated at 1,304 facilities, with 34,312 (70.2%) being female and a mean age of 48.0 ± 16.0 years. Using the case-volume threshold identified from analyzing the five facility clusters, patients were assigned to one of two distinct cohorts according to their treatment at a low (LVF, <27 cases/year) or high (HVF, ≥ 27 cases/year) case-volume facility. Thus, HVFs ($N=16$) represented approximately the top 1.2% of facilities by case-volume. Patient demographic and clinical characteristics in each cohort were compared and summarized in Table 1.

Associations between various sociodemographic or clinical factors and all-cause mortality were evaluated using CPH regression and are listed in Table 2. On univariate CPH regression, higher facility volume (as a continuous variable) was associated with lower mortality (HR 0.988; 95% CI, 0.985–0.991; $p<0.001$). After accounting for a number of variables, multivariable CPH regression continued to reveal an association between increased facility volume and reduced all-cause mortality (HR 0.996; 95% CI, 0.992–0.999; $p=0.008$).

On univariate CPH regression, patients treated at HVFs were associated with lower mortality risk than those treated at LVFs (HR 0.617; 95% CI, 0.538–0.707; $p<0.001$). Multivariable

analysis demonstrated patients in the HVF cohort to be associated with reduced mortality (HR 0.791; 95% CI, 0.678–0.923; $p=0.003$). Since histogram analysis (Supplementary Figure 2) identified two very high-volume facilities, a sub-analysis was done excluding these two facilities to ensure that our case-volume threshold was still prognostically significant. Indeed, multivariable CPH analysis of this trimmed patient cohort continued to demonstrate an association between HVF patients and reduced mortality (HR 0.797; 95% CI, 0.673–0.944; $p=0.008$).

Further stratification according to nodal metastasis similarly demonstrated patients with N0 (HR 0.793; 95% CI, 0.634–0.993; $p=0.041$) or N1 (HR 0.785; 95% CI, 0.635–0.970; $p=0.024$) cancer to be associated with decreased mortality if they were treated at an HVF. Moreover, Kaplan Meier analysis of propensity score-matched patients demonstrated significantly greater OS among patients treated at HVFs, regardless of the presence of nodal metastasis (Figure 2, all $p<0.001$). To ensure that the effect of facility volume could be compared between the two Kaplan Meier analyses, we performed two layers of propensity score matching, first by node status and second by facility volume designation, such that the N0 and N1 sub-cohorts consisted of patients with similar characteristics. Among N0 patients, the 10-year OS rate of patients in the HVF cohort (89.9% [86.8–93.0]) was greater than that of those in the LVF cohort (82.7% [79.7–85.8]; $p<0.001$). Similarly, among N1 patients, those in the HVF cohort (90.2% [87.8–92.7]) were associated with a higher 10-year OS rate than patients in the LVF cohort (80.9% [77.6–84.5]; $p<0.001$).

Discussion

Prognostic associations between facility volume and various outcome measures of head and neck malignancies have been previously reported.^{10,12,24–26} However, to our knowledge, this study is the first to determine a systematic, data-driven facility case-volume threshold informed by population-based patient survival data for locally advanced PTC. Using LVF (<27 cases/year) and HVF (≥27 cases/year) as prognostic case-volume designations, our analysis demonstrated that high facility case-volume, representing approximately the top 1.2% of facilities in our cohort, was an independent predictor of overall survival in locally advanced PTC. This was an association that remained statistically significant after adjusting for an array of potentially confounding demographic, socioeconomic, and clinical variables in a multivariable regression model. Specifically, rates of both 5- and 10-year OS were significantly higher for patients treated at HVFs compared to those receiving care at LVFs. Further validating this observation, a Kaplan-Meier analysis of propensity score-matched N0 and N1 patients demonstrated that, regardless of the presence of nodal metastasis, treatment at higher case-volume centers was significantly associated with improved survival.

The persistence of the observed benefit of HVF treatment on patient outcomes across a spectrum of non-thyroidal malignancies has drawn a number of probable explanations.^{8–12} High case volumes at the facility level may translate into high case volumes at the provider level, which has been demonstrated to be a significant predictor of high-quality oncologic management, sensitive and specific radiologic detection and diagnoses, improved surgical tumor control and post-operative outcomes, as well as lower complication and recurrence rates post-radiation therapy—all effects that have been established to, in turn, directly

influence patient outcomes in numerous cancers.^{13,14,27–32} In addition to experience via ample case volume, physicians at HVFs may also be more likely to be subspecialized, more extensively trained, and better resourced to comply with the most recent evidence-based clinical guidelines.^{33–36} Of course, this does not imply that all physicians at high-volume facilities are necessarily better trained than their colleagues at lower-volume facilities, but rather that the higher surgeon case-volume that inherently results from working at a high-volume facility may produce an “average” effect that contributes to a positive correlation between facility volume and patient outcomes. Studies suggest that patients treated at HVFs are also more likely to access a diverse array of ancillary services such as dietitians, social services, palliative care, and oncologic psychiatry, all of which have the potential to improve patient outcomes and quality of life.^{37–40} As such, facility volume emerged as an increasingly useful prognostic variable and marker of treatment quality. To further that end, this study derived a specific and statistically meaningful case-volume threshold that can be used to prognosticate locally advanced PTC and inform improvement of care.

Mechanisms offered in previous studies to explain their findings of improved thyroid cancer outcomes in relation to facility case volume were similarly varied in nature. Many studies examined extent of surgery as a potentially expounding factor and demonstrated a positive association between rates of total thyroidectomies and facility volume. In 2009, a multicenter study in France that categorized facilities into three groups by case volume found that the odds of receiving a unilateral thyroid lobectomy, as opposed to total thyroidectomy, for thyroid cancer increased by a factor of 2.85 in low-volume and 2.03 in medium-volume centers relative to high-volume centers.⁴¹ A more recent study examining the proportion of medullary thyroid patients receiving neck dissections found a positive relationship between the incidence of neck dissection and hospital volume (low-volume: 23.8%, low-medium-volume: 47.7%, medium-volume: 60.3%, high-volume: 65.9%) to accompany their findings of a positive relationship between 5-year OS rate and hospital volume.²⁵ The authors went on to hypothesize that high-volume centers have a greater capacity to update their practices and comply with changing care guidelines, thus contributing to their superior patient outcomes.²⁵ Not surprisingly then, in an effort to develop a composite measure of quality of hospital management of thyroid cancers, Megwalu *et al.* included a case volume threshold (10 thyroid cancer cases per year) as one of their two combined criteria.²⁴ Using these criteria, they identified high quality centers where patients with DTC experienced significantly improved OS and disease-specific survival.²⁴

While our study focused on the association between facility volume and patient survival, other investigations have previously also evaluated the relationship between avoidable readmissions and hospital volume. In a retrospective study, Mitchell *et al.* derived a set of criteria from 2006 thyroid disease management guidelines categorizing thyroid surgeries as avoidable or unavoidable, and found that 50% of all thyroid surgeries at low-volume centers were avoidable compared to 14% at high-volume centers.⁴² Operations for thyroid cancers specifically led to avoidable reoperations significantly more often when performed at a low-volume center. These conclusions, however, may have been limited by the study not accounting for patient election for surgery and availability of services. In a 2013 study, Youngwirth *et al.* found that pediatric thyroid cancer patients treated at LVFs were more

likely to be readmitted after thyroid surgery than patients treated at HVFs.⁴³ The authors based their analysis on a case-volume threshold (<39 vs. 39 cases over the study period), revealing a significantly higher percentage of patients receiving total thyroidectomy (as opposed to lobectomy or no surgery) at HVFs compared to LVFs (90.8% vs. 86.3%). However, the authors noted that this case-volume threshold was, in of itself, fairly low and was likely expounded by the fact that the analyzed high-volume facilities treating pediatric thyroid cancer were also frequently high-volume facilities treating adult thyroid cancer.⁴³

Differences in facility volume have also been previously associated with varying postoperative complication rates. Pieracci et al. found increasing hospital volume of substernal thyroidectomies in the treatment of substernal thyroid goiters, to be a significant predictor of decreased risk of overall complications, postoperative bleeding, blood transfusion, respiratory failure, and mortality.²⁶ Similar trends have also been demonstrated at the provider level. A study of the Nationwide Inpatient Sample found that thyroidectomies, when performed by low-volume surgeons, were associated with an elevated risk of complications compared with high-volume surgeons (15.8% vs 7.7%).⁴⁴ Similarly, recent meta-analyses found that care provided by higher volume thyroid surgeons resulted in decreased surgical and medical complications, fewer recurrences, and shorter length of hospital stay when compared to care under lower volume surgeons, especially for patients with advanced stage disease.^{45,46} Granted, associating outcomes with surgeon volume as opposed to hospital volume provides a distinct analysis by nature. Indeed, one study of 2002 New York and Florida discharge data on endocrine surgeries found that, while high surgeon volume was associated with decreased risk of complications and reduced length of hospital stay, hospital volume had a negligible influence on patient outcomes.⁴⁷ Nonetheless, the theme remains relatively consistent—a positive relationship between patient outcomes and case volume, at both provider and hospital levels.

Besides facility case volume, our multivariable analysis revealed other factors, both oncologic and non-clinical, that independently predicted mortality. These have the potential to further widen the survival differences between HVF and LVF locally advanced PTC patients, whether in complementation or opposition to the influences of facility case-volume. Indeed, a significantly lower proportion of patients aged 55 years comprised our HVF cohort compared to our LVF cohort, a notable observation as the 55 age group was found to be at particularly higher risk for mortality than the younger patient population. This observation would be consistent with the well-reported phenomenon of regionalization of health services as living at a distance from HVFs presents logistical, socioeconomic, and psychosocial barriers to patients seeking their care, particularly those vulnerable due to elderly age.^{48,49} A significantly lower proportion of patients enrolled in government insurance programs were treated at HVFs, which may explain this group's higher associated risk for mortality relative to patients with private health insurance. Assuming HVFs do indeed provide higher quality care through their specialized and experienced providers, compliance to the latest clinical guidelines, and access to greater ancillary resources, the higher mortality experienced by these nonprivate insurance holders may be partly attributed to their lack of access to HVFs. Our analysis also showed that HVFs treated a significantly higher ratio of T3 to T4 diseases compared to LVFs, suggesting that HVFs may potentially be detecting disease earlier and/or pursuing more aggressive treatment compared to LVFs.

An alternative explanation would be the sizable body of evidence that demonstrates more advanced disease upon presentation for patients from low socioeconomic backgrounds, corroborating with higher rates of T4 disease at facilities that care for a higher proportion of these populations.^{50,51} Additionally, HVFs treated a significantly lower proportion of their patients with RAI compared to LVFs, a finding that builds upon past literature demonstrating the associations between surgeon case-volume and RAI decision making as well as between specialized surgical training and lower proportions of well-differentiated thyroid cancer patients receiving RAI after total thyroidectomy.^{52,53} Thus, our analysis suggests that some attribution of favorable survival outcomes at HVFs to various demographic, social, and clinical factors is plausible and warrants further investigation.

While the present study offers evidence for a novel prognostic quality threshold for facilities treating locally advanced PTC, certain considerations should be made when interpreting these results. Since patients were extracted from a de-identified national database, selection and information bias is possible. Moreover, due to NCDB limitations, we were restricted to using OS as our primary outcome measure and could not evaluate recurrence-free or disease-free survival. Additionally, T classification was not based on the recent 8th edition of the American Joint Committee on Cancer (AJCC) staging guidelines, which removed microscopic extrathyroidal extension from the definition of T3 disease.⁵⁴ Lastly, while we accounted for a wide variety of clinical and sociodemographic variables via multivariable regression and propensity score matching, certain variables (e.g., family support, adequate follow-up, treatment regimen adherence, etc.) were not captured by the NCDB and could not be controlled for in our analyses.

Conclusion

Our analysis of 48,899 patients with locally advanced PTC demonstrated facility case-volume to be independently associated with reduced mortality. Furthermore, using a systematic and data-driven approach, we identified a novel prognostic facility case-volume threshold. Specifically, independent of a number of sociodemographic and clinical factors, we found centers that treated more than 26 cases per year to be associated with increased overall survival. Our findings, therefore, appear to support regionalization of care to higher-volume facilities where patients may have improved outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Financial Disclosure:

Research reported in this publication was supported in part by the National Institute of General Medical Sciences of the National Institutes of Health under award number T32GM008620. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

References

1. Lim H, Devesa SS, Sosa JA, Check D, Kitahara CM. Trends in Thyroid Cancer Incidence and Mortality in the United States, 1974–2013. *JAMA*. 2017;317(13):1338–1348. doi:10.1001/jama.2017.2719 [PubMed: 28362912]
2. Bortz MD, Kuchta K, Winchester DJ, Prinz RA, Moo-Young TA. Extrathyroidal extension predicts negative clinical outcomes in papillary thyroid cancer. *Surgery*. 2021;169(1):2–6. doi:10.1016/j.surg.2020.04.003 [PubMed: 32682508]
3. McConahey WM, Hay ID, Woolner LB, van Heerden JA, Taylor WF. Papillary thyroid cancer treated at the Mayo Clinic, 1946 through 1970: initial manifestations, pathologic findings, therapy, and outcome. *Mayo Clin Proc*. 1986;61(12):978–996. doi:10.1016/s0025-6196(12)62641-x [PubMed: 3773569]
4. Hay ID, Thompson GB, Grant CS, et al. Papillary thyroid carcinoma managed at the Mayo Clinic during six decades (1940–1999): temporal trends in initial therapy and long-term outcome in 2444 consecutively treated patients. *World J Surg*. 2002;26(8):879–885. doi:10.1007/s00268-002-6612-1 [PubMed: 12016468]
5. Wang LY, Nixon IJ, Patel SG, et al. Operative management of locally advanced, differentiated thyroid cancer. *Surgery*. 2016;160(3):738–746. doi:10.1016/j.surg.2016.04.027 [PubMed: 27302105]
6. McCaffrey JC. Evaluation and treatment of aerodigestive tract invasion by well-differentiated thyroid carcinoma. *Cancer Control*. 2000;7(3):246–252. doi:10.1177/107327480000700304 [PubMed: 10832111]
7. Shindo ML, Caruana SM, Kandil E, et al. Management of invasive well-differentiated thyroid cancer: an American Head and Neck Society consensus statement. *AHNS consensus statement. Head Neck*. 2014;36(10):1379–1390. doi:10.1002/hed.23619 [PubMed: 24470171]
8. Wolde SL, Matulay JT, Clinton TN, et al. Impact of hospital case volume on testicular cancer outcomes and practice patterns. *Urol Oncol*. 2018;36(1):14.e7–14.e15. doi:10.1016/j.urolonc.2017.08.024
9. Goyal G, Kommalapati A, Bartley AC, Gunderson TM, Adjei AA, Go RS. Association between hospital volume and mortality of patients with metastatic non-small cell lung cancer. *Lung cancer*. 2018;122:214–219. doi:10.1016/j.lungcan.2018.06.025 [PubMed: 30032834]
10. Goshtasbi K, Abiri A, Lehigh BM, Haidar YM, Tjoa T, Kuan EC. The influence of facility volume on patient treatments and survival outcomes in nasopharyngeal carcinoma. *Head Neck*. 2021;43(9):2755–2763. doi:10.1002/hed.26739 [PubMed: 33998094]
11. Lee B, Kim K, Park Y, Lim MC, Bristow RE. Impact of hospital care volume on clinical outcomes of laparoscopic radical hysterectomy for cervical cancer: A systematic review and meta-analysis. *Medicine (Baltimore)*. 2018;97(49):e13445. doi:10.1097/MD.00000000000013445
12. Torabi SJ, Benchetrit L, Kuo Yu P, et al. Prognostic Case Volume Thresholds in Patients With Head and Neck Squamous Cell Carcinoma. *JAMA Otolaryngol Head Neck Surg*. 2019;145(8):708–715. doi:10.1001/jamaoto.2019.1187 [PubMed: 31194229]
13. Chowdhury MM, Dagash H, Pierro A. A systematic review of the impact of volume of surgery and specialization on patient outcome. *Br J Surg*. 2007;94(2):145–161. doi:10.1002/bjs.5714 [PubMed: 17256810]
14. Birkmeyer JD, Sun Y, Goldfaden A, Birkmeyer NJO, Stukel TA. Volume and process of care in high-risk cancer surgery. *Cancer*. 2006;106(11):2476–2481. doi:10.1002/cncr.21888 [PubMed: 16634089]
15. Bozic KJ, Maselli J, Pekow PS, Lindenauer PK, Vail TP, Auerbach AD. The influence of procedure volumes and standardization of care on quality and efficiency in total joint replacement surgery. *J bone Jt Surg*. 2010;92(16):2643–2652. doi:10.2106/JBJS.I.01477
16. Mesman R, Westert GP, Berden BJMM, Faber MJ. Why do high-volume hospitals achieve better outcomes? A systematic review about intermediate factors in volume-outcome relationships. *Health Policy (New York)*. 2015;119(8):1055–1067. doi:10.1016/j.healthpol.2015.04.005
17. National Cancer Database. American College of Surgeons. Published 2020. <https://www.facs.org/Quality-Programs/Cancer/NCDB>

18. Bilimoria KY, Bentrem DJ, Linn JG, et al. Utilization of total thyroidectomy for papillary thyroid cancer in the United States. *Surgery*. 2007;142(6):902–906. doi:10.1016/j.surg.2007.09.002
19. Adam MA, Pura J, Goffredo P, et al. Impact of extent of surgery on survival for papillary thyroid cancer patients younger than 45 years. *J Clin Endocrinol Metab*. 2015;100(1):115–121. doi:10.1210/jc.2014-3039 [PubMed: 25337927]
20. Bilimoria KY, Stewart AK, Winchester DP, Ko CY. The National Cancer Data Base: a powerful initiative to improve cancer care in the United States. *Ann Surg Oncol*. 2008;15(3):683–690. doi:10.1245/s10434-007-9747-3 [PubMed: 18183467]
21. Omar T, Zohdy M, Rushi J. Clustering Application for Data-Driven Prediction of Health Insurance Premiums for People of Different Ages. In: 2021 IEEE International Conference on Consumer Electronics (ICCE). ; 2021:1–6. doi:10.1109/ICCE50685.2021.9427598
22. Yoo W, Mayberry R, Bae S, Singh K, Peter He Q, Lillard JW Jr. A Study of Effects of MultiCollinearity in the Multivariable Analysis. *Int J Appl Sci Technol*. 2014;4(5):9–19. <https://pubmed.ncbi.nlm.nih.gov/25664257> [PubMed: 25664257]
23. Austin PC. Optimal caliper widths for propensity-score matching when estimating differences in means and differences in proportions in observational studies. *Pharm Stat*. 2011;10(2):150–161. doi:10.1002/pst.433 [PubMed: 20925139]
24. Megwalu UC, Ma Y, Hernandez-Boussard T, Divi V, Gomez SL. The Impact of Hospital Quality on Thyroid Cancer Survival. *Otolaryngol neck Surg*. 2020;162(3):269–276. doi:10.1177/0194599819900760
25. Al-Qurayshi Z, Khadra H, Chang K, Pagedar N, Randolph GW, Kandil E. Risk and survival of patients with medullary thyroid cancer: National perspective. *Oral Oncol*. 2018;83:59–63. doi:10.1016/j.oraloncology.2018.06.002 [PubMed: 30098780]
26. Pieracci FM, Fahey TJ 3rd. Effect of hospital volume of thyroidectomies on outcomes following substernal thyroidectomy. *World J Surg*. 2008;32(5):740–746. doi:10.1007/s00268-007-9347-1 [PubMed: 18200430]
27. Abrams TA, Meyer G, Meyerhardt JA, Wolpin BM, Schrag D, Fuchs CS. Patterns of Chemotherapy Use in a U.S.-Based Cohort of Patients with Metastatic Pancreatic Cancer. *Oncologist*. 2017;22(8):925–933. doi:10.1634/theoncologist.2016-0447 [PubMed: 28476943]
28. Huntington SF, Hoag JR, Zhu W, et al. Oncologist volume and outcomes in older adults diagnosed with diffuse large B cell lymphoma. *Cancer*. 2018;124(21):4211–4220. doi:10.1002/cncr.31688 [PubMed: 30216436]
29. Bagaria SP, Neville M, Gray RJ, et al. The Volume-Outcome Relationship in Retroperitoneal Soft Tissue Sarcoma: Evidence of Improved Short- and Long-Term Outcomes at High-Volume Institutions. *Sarcoma*. 2018;2018:3056562. doi:10.1155/2018/3056562
30. Enestvedt CK, Perry KA, Kim C, et al. Trends in the management of esophageal carcinoma based on provider volume: treatment practices of 618 esophageal surgeons. *Dis esophagus*. 2010;23(2):136–144. doi:10.1111/j.1442-2050.2009.00985.x [PubMed: 19515189]
31. Boero IJ, Paravati AJ, Xu B, et al. Importance of Radiation Oncologist Experience Among Patients With Head-and-Neck Cancer Treated With Intensity-Modulated Radiation Therapy. *J Clin Oncol*. 2016;34(7):684–690. doi:10.1200/JCO.2015.63.9898 [PubMed: 26729432]
32. Jeldres C, Suardi N, Saad F, et al. High provider volume is associated with lower rate of secondary therapies after definitive radiotherapy for localized prostate cancer. *Eur Urol*. 2008;54(1):97–105. doi:10.1016/j.eururo.2007.10.070 [PubMed: 17997022]
33. Newman EA, Guest AB, Helvie MA, et al. Changes in surgical management resulting from case review at a breast cancer multidisciplinary tumor board. *Cancer*. 2006;107(10):2346–2351. doi:10.1002/cncr.22266 [PubMed: 16998942]
34. Wuthrick EJ, Zhang Q, Machtay M, et al. Institutional clinical trial accrual volume and survival of patients with head and neck cancer. *J Clin Oncol*. 2015;33(2):156–164. doi:10.1200/JCO.2014.56.5218 [PubMed: 25488965]
35. Bilimoria KY, Bentrem DJ, Feinglass JM, et al. Directing surgical quality improvement initiatives: comparison of perioperative mortality and long-term survival for cancer surgery. *J Clin Oncol*. 2008;26(28):4626–4633. doi:10.1200/JCO.2007.15.6356 [PubMed: 18574159]

36. Solomon D, DeNicola N, Feferman Y, et al. Assessing the Implementation of American College of Surgeons Quality Indicators for Pancreatic Cancer Across an Integrated Health System. *J Oncol Pract.* 2019;15(8):e739–e745. doi:10.1200/JOP.18.00587 [PubMed: 31260384]
37. Isenring EA, Capra S, Bauer JD. Nutrition intervention is beneficial in oncology outpatients receiving radiotherapy to the gastrointestinal or head and neck area. *Br J Cancer.* 2004;91(3):447–452. doi:10.1038/sj.bjc.6601962 [PubMed: 15226773]
38. Moffatt S, Noble E, White M. Addressing the financial consequences of cancer: qualitative evaluation of a welfare rights advice service. *PLoS One.* 2012;7(8):e42979. doi:10.1371/journal.pone.0042979
39. Roland KB, Milliken EL, Rohan EA, et al. Use of Community Health Workers and Patient Navigators to Improve Cancer Outcomes Among Patients Served by Federally Qualified Health Centers: A Systematic Literature Review. *Heal equity.* 2017;1(1):61–76. doi:10.1089/heq.2017.0001
40. David JM, Ho AS, Luu M, et al. Treatment at high-volume facilities and academic centers is independently associated with improved survival in patients with locally advanced head and neck cancer. *Cancer.* 2017;123(20):3933–3942. doi:10.1002/ncr.30843 [PubMed: 28640546]
41. Lifante JC, Duclos A, Couray-Targe S, Colin C, Peix JL, Schott AM. Hospital volume influences the choice of operation for thyroid cancer. *Br J Surg.* 2009;96(11):1284–1288. doi:10.1002/bjs.6741 [PubMed: 19847866]
42. Mitchell J, Milas M, Barbosa G, Sutton J, Berber E, Siperstein A. Avoidable reoperations for thyroid and parathyroid surgery: effect of hospital volume. *Surgery.* 2008;144(6):897–899. doi:10.1016/j.surg.2008.07.022
43. Youngwirth LM, Adam MA, Thomas SM, Roman SA, Sosa JA, Scheri RP. Pediatric thyroid cancer patients referred to high-volume facilities have improved short-term outcomes. *Surgery.* 2018;163(2):361–366. doi:10.1016/j.surg.2017.09.042 [PubMed: 29174431]
44. Al-Qurayshi Z, Robins R, Hauch A, Randolph GW, Kandil E. Association of Surgeon Volume With Outcomes and Cost Savings Following Thyroidectomy: A National Forecast. *JAMA Otolaryngol Head Neck Surg.* 2016;142(1):32–39. doi:10.1001/jamaoto.2015.2503 [PubMed: 26561736]
45. Liang T-J, Liu S-I, Mok K-T, Shi H-Y. Associations of Volume and Thyroidectomy Outcomes: A Nationwide Study with Systematic Review and Meta-Analysis. *Otolaryngol neck Surg.* 2016;155(1):65–75. doi:10.1177/0194599816634627
46. Bedi HK, Jedrzejko N, Nguyen A, Aspinall SR, Wiseman SM. Thyroid and parathyroid surgeon case volume influences patient outcomes: A systematic review. *Surg Oncol.* 2021;38:101550. doi:10.1016/j.suronc.2021.101550
47. Stavrakis AI, Ituarte PHG, Ko CY, Yeh MW. Surgeon volume as a predictor of outcomes in inpatient and outpatient endocrine surgery. *Surgery.* 2007;142(6):887–899. doi:10.1016/j.surg.2007.09.003 [PubMed: 18063073]
48. Finlayson SR, Birkmeyer JD, Tosteson AN, Nease RFJ. Patient preferences for location of care: implications for regionalization. *Med Care.* 1999;37(2):204–209. doi:10.1097/00005650-199902000-00010 [PubMed: 10024124]
49. Bhattacharyya N, Abemayor E. Patterns of hospital utilization for head and neck cancer care: changing demographics. *JAMA Otolaryngol Head Neck Surg.* 2015;141(4):307–312; quiz 400. doi:10.1001/jamaoto.2014.3603 [PubMed: 25634082]
50. Harari A, Li N, Yeh MW. Racial and Socioeconomic Disparities in Presentation and Outcomes of Well-Differentiated Thyroid Cancer. *J Clin Endocrinol Metab.* 2014;99(1):133–141. doi:10.1210/jc.2013-2781 [PubMed: 24243631]
51. Lim IIP, Hochman T, Blumberg SN, Patel KN, Heller KS, Ogilvie JB. Disparities in the initial presentation of differentiated thyroid cancer in a large public hospital and adjoining university teaching hospital. *Thyroid.* 2012;22(3):269–274. doi:10.1089/thy.2010.0385 [PubMed: 22233131]
52. Papaleontiou M, Banerjee M, Yang D, Sisson JC, Koenig RJ, Haymart MR. Factors that influence radioactive iodine use for thyroid cancer. *Thyroid.* 2013;23(2):219–224. doi:10.1089/thy.2012.0380 [PubMed: 23134514]

53. Schuessler KM, Banerjee M, Yang D, Stewart AK, Doherty GM, Haymart MR. Surgeon training and use of radioactive iodine in stage I thyroid cancer patients. *Ann Surg Oncol*. 2013;20(3):733–738. doi:10.1245/s10434-012-2745-0 [PubMed: 23224826]
54. Tuttle RM, Haugen B, Perrier ND. Updated American Joint Committee on Cancer/Tumor-Node-Metastasis Staging System for Differentiated and Anaplastic Thyroid Cancer (Eighth Edition): What Changed and Why? *Thyroid*. 2017;27(6):751–756. doi:10.1089/thy.2017.0102 [PubMed: 28463585]

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

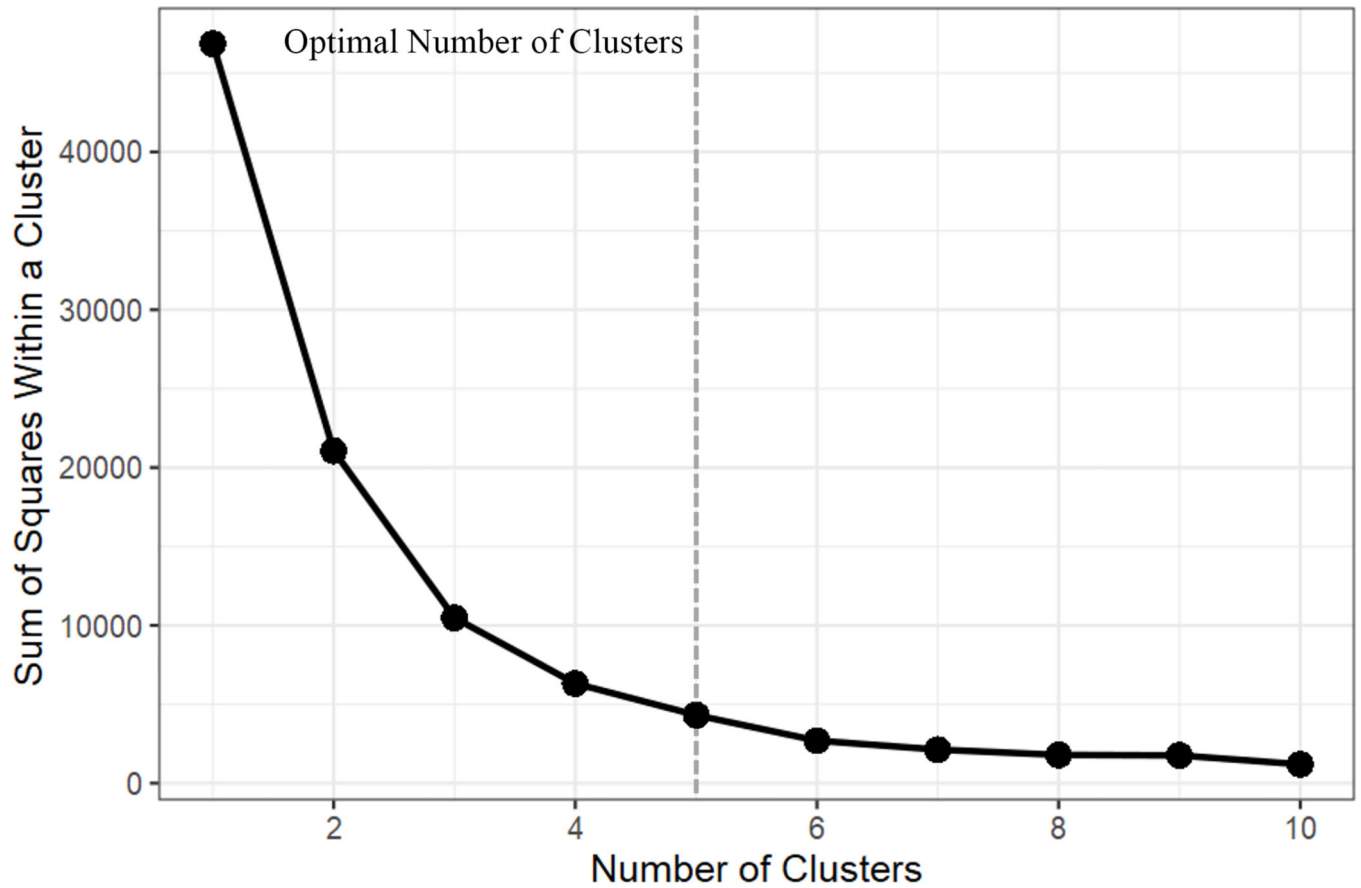


Figure 1: Plot of the sum of squares within a cluster versus the number of clusters generated from K-means clustering, demonstrating five to be an appropriate number of clusters.

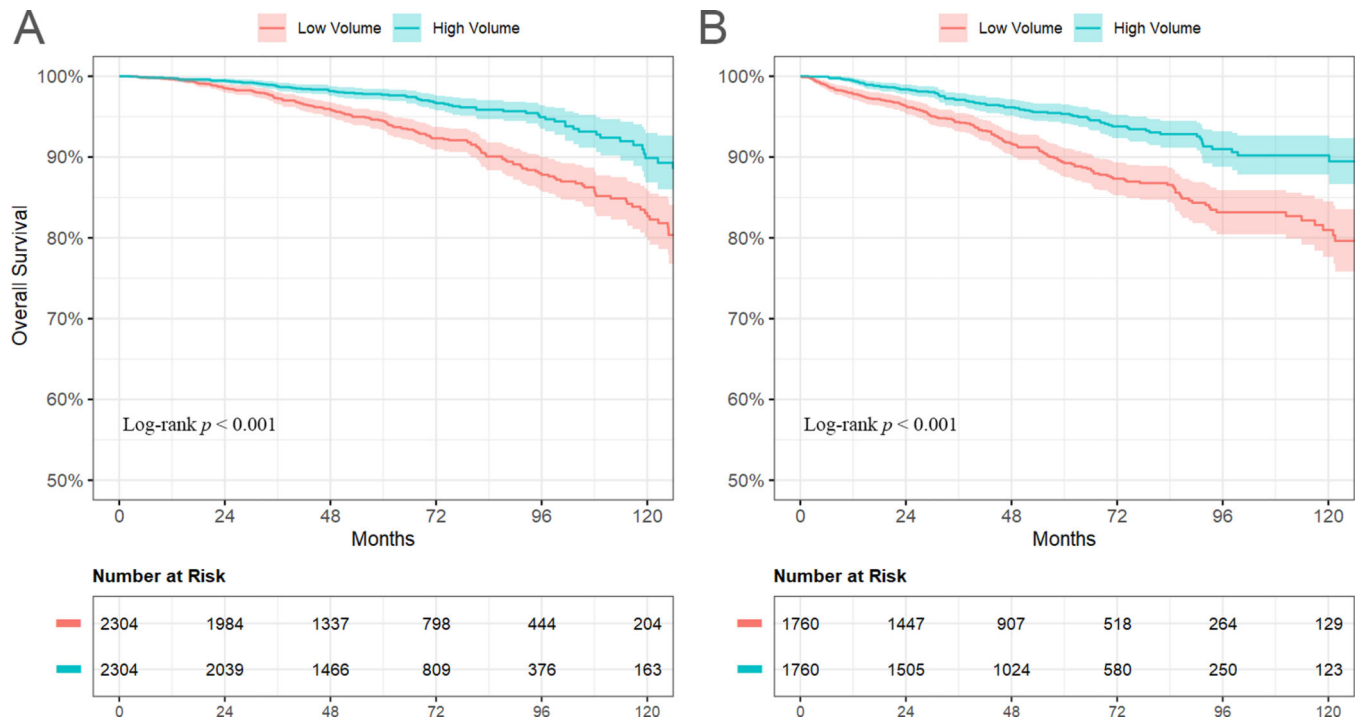


Figure 2: Kaplan-Meier curves of overall survival in propensity score-matched (A) N0 patients (N=4,608) and (B) N1 patients (N=3,520) with locally advanced papillary thyroid cancer, demonstrating significantly improved survival in high volume facilities, regardless of the presence of nodal metastasis. Shaded areas represent 95% confidence intervals.

Table 1:

Demographics of patients with locally advanced papillary thyroid cancer (N=48,899).

Variables	Low Volume (N=42,048)	High Volume (N=6,851)	P-Value
Age, yr			
< 55	27,259 (64.8)	4,633 (67.6)	<0.001 *
55	14,789 (35.2)	2,218 (32.4)	
Sex			
Male	12,573 (29.9)	2,014 (29.4)	0.397
Female	29,475 (70.1)	4,837 (70.6)	
Race			
White	34,869 (86.4)	5,324 (83.9)	<0.001 *
Black	2,905 (7.2)	349 (5.5)	
Asian	2,565 (6.4)	669 (10.5)	
Insurance			
Private	28,333 (71.2)	5,182 (78.7)	<0.001 *
Government	11,458 (28.8)	1,404 (21.3)	
CD Score			
0	35,390 (84.2)	5,741 (83.8)	0.440
1	6,658 (15.8)	1,110 (16.2)	
Facility Type			
Non-Academic	25,194 (60.0)	373 (5.4)	<0.001 *
Academic	16,799 (40.0)	6,478 (94.6)	
Facility Volume, cases/yr[†]	5 (1–26)	35 (27–103)	<0.001 *
T Classification			
T3	37,027 (88.1)	6,407 (93.5)	<0.001 *
T4	5,021 (11.9)	444 (6.5)	
N Classification			
N0	21,129 (51.4)	3,195 (47.3)	<0.001 *
N1	19,985 (48.6)	3,562 (52.7)	
Extent of Surgery			
Lobectomy	2,141 (5.2)	416 (6.1)	0.001 *
Total Thyroidectomy	39,332 (94.8)	6,386 (93.9)	
RAI Therapy			
No	10,565 (25.1)	2,033 (29.7)	<0.001 *
Yes	31,483 (74.9)	4,818 (70.3)	
THST			
No	14,537 (35.2)	854 (12.6)	<0.001 *
Yes	26,797 (64.8)	5,898 (87.4)	

Variables	Low Volume (N=42,048)	High Volume (N=6,851)	P-Value
5-Year OS Rate (%)	94.0 (93.3–94.7)	97.3 (96.9–97.8)	<0.001 *
10-Year OS Rate (%)	85.4 (83.7–87.2)	92.0 (90.5–93.6)	<0.001 *

CD: Charleson/Deyo; RAI: Radioactive Iodine; THST: Thyroid-Stimulating Hormone Suppression Therapy; OS: Overall Survival

Not all cases reported values for the collected variables, thus the percentages reflect the number of cases with available data.

[†]Reported as median (range)

* Statistically significant, $p < 0.05$

Table 2:

Univariate and multivariable Cox proportional-hazards regression of patients with locally advanced papillary thyroid cancer, demonstrating reduced mortality risk with higher facility volume.

Covariates	Univariate		Multivariable	
	HR (95% CI)	P-Value	HR (95% CI)	P-Value
Age, yr				
< 55	1 [Reference]		1 [Reference]	
55	9.012 (8.196–9.908)	<0.001 *	5.262 (4.698–5.894)	<0.001 *
Sex				
Male	1 [Reference]		1 [Reference]	
Female	0.537 (0.498–0.578)	<0.001 *	0.648 (0.597–0.703)	<0.001 *
Race				
White	1 [Reference]		1 [Reference]	
Black	1.147 (0.997–1.319)	0.055	1.274 (1.090–1.489)	0.039 *
Asian	0.667 (0.552–0.807)	<0.001 *	0.717 (0.586–0.879)	<0.001 *
Insurance				
Private	1 [Reference]		1 [Reference]	
Government	6.501 (5.995–7.051)	<0.001 *	3.087 (2.816–3.383)	<0.001 *
Facility Type				
Non-Academic	1 [Reference]		1 [Reference]	
Academic	0.846 (0.785–0.912)	<0.001 *	1.022 (0.934–1.119)	0.633
Facility Volume	0.988 (0.985–0.991)	<0.001 *	0.996 (0.992–0.999)	0.008 *
CD Score				
0	1 [Reference]		1 [Reference]	
1	2.785 (2.572–3.015)	<0.001 *	1.710 (1.568–1.864)	<0.001 *
T Classification				
T3	1 [Reference]		1 [Reference]	
T4	3.139 (2.899–3.400)	<0.001 *	2.232 (2.042–2.440)	<0.001 *
N Classification				
N0	1 [Reference]		1 [Reference]	
N1	1.163 (1.079–1.254)	<0.001 *	1.452 (1.335–1.580)	<0.001 *
Extent of Surgery				
Lobectomy	1 [Reference]		1 [Reference]	
Total Thyroidectomy	0.746 (0.643–0.866)	<0.001 *	0.875 (0.741–1.032)	0.113
RAI Therapy				
No	1 [Reference]		1 [Reference]	
Yes	0.524 (0.486–0.566)	<0.001 *	0.563 (0.515–0.614)	<0.001 *
THST				

Covariates	Univariate		Multivariable	
	HR (95% CI)	P-Value	HR (95% CI)	P-Value
No	1 [Reference]		1 [Reference]	
Yes	0.726 (0.673–0.783)	<0.001 *	0.958 (0.879–1.045)	0.334

HR: Hazard Ratio; CI: Confidence Interval; CD: Charlson/Deyo; RAI: Radioactive Iodine; THST: Thyroid-Stimulating Hormone Suppression Therapy

* Statistically significant, $p < 0.05$