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Smoking is associated with adverse clinical outcomes after thyroidectomy: a 5-year retrospective analysis

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Abstract

Objective Tobacco use has been confirmed to be a risk factor for postoperative complications, but the impact of smoking on adverse outcomes following thyroidectomy remains largely unknown.

Methods Using data spanning 2016–2020 from the National Inpatient Sample, patients aged ≥ 18 years who underwent thyroidectomy for thyroid malignancy or other thyroid disorders were identified and classified into two groups: current smokers and non-smokers. We compared outcome variables between the two groups via univariate analysis and adjusted multivariate logistic regression.

Results The present study included 13,737 records of patients who underwent thyroidectomy, among whom 1,360 (9.90%) were identified as current smokers. After propensity score matching, logistic regression analysis suggested that smoking was associated with a heightened risk of unfavorable discharge (aOR = 1.27, 95% CI [1.05–1.54], $P = 0.012$), vocal dysfunction (aOR = 1.25, 95% CI [1.00–1.55], $P = 0.049$), hypocalcemia (aOR = 1.23, 95% CI [1.05–1.44], $P = 0.010$), hypomagnesemia (aOR = 1.58, 95% CI [1.19–2.09], $P = 0.001$), and respiratory complications (aOR = 1.39, 95% CI [1.16–1.68], $P < 0.001$). Similar results were observed in both patients who underwent thyroidectomy for thyroid malignancy and those who underwent thyroidectomy for other thyroid disorders when a stratified analysis by surgical indications was performed.

Conclusion Smoking is an independent risk factor for adverse clinical outcomes after thyroidectomy.

Keywords Thyroidectomy, Thyroid cancer, Thyroid nodule, Postoperative complications, Smoking

Introduction

Smoking is currently a major healthcare crisis that poses a great threat to public health. As recent global estimates by World Health Organization have demonstrated, approximately one-fifth of the global population used tobacco in 2020 [1]. Cigarette smoking harms nearly every organ in the body and is correlated with a wide range of cancers as well as many other major health conditions [2, 3]. Tobacco smoking has caused more than 200 million deaths and resulted in annual economic costs exceeding 1 trillion dollars over the past 30 years, imposing a great burden throughout the world both healthwise and economically [4, 5]. Despite the decrease in cigarette smoking among United States (U.S.) adults over the past five decades, tobacco product use remains the

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leading cause of preventable morbidity and mortality in the US [6].

Thyroid gland disorders, including hypothyroidism, hyperthyroidism, goiter and nodules, thyroiditis and thyroid malignancy, are so common that they afflict approximately 11.7% of the US population [7]. While thyroidectomy serves as the first choice of initial treatment for thyroid malignancy, the number of thyroidectomies performed to address benign thyroid disease is increasing [8, 9] Approximately 93,000 thyroidectomies are carried out annually in the U.S [10]. Although the incidence is minimal, relevant complications can arise after thyroid surgery, while some of them, namely, recurrent laryngeal nerve palsy and hypocalcemia, can become permanent [11, 12] Thus, identifying the potential risk factors for postthyroidectomy complications is crucial for guiding clinical decision-making and improving patient outcomes.

The associations between smoking and higher rates of postoperative complications have been established by numerous studies [13–15]. Several previous studies have explored the associations between smoking and postoperative complications in head and neck surgery [16, 17]. However, the impact of smoking on adverse outcomes following thyroidectomy remains unclear. Therefore, this study aimed to assess the effects of smoking on clinical outcomes and postoperative complications after thyroidectomy using data from a large national database.

Methods

Data source and study population

All patient data included in this study were sourced from the National Inpatient Sample (NIS) from 2016–2020. The NIS is the largest publicly accessible all-payer inpatient healthcare database providing regional and national in-hospital estimates for the U.S [18]. Compared with unweighted data from approximately 7 million hospital stays each year, the NIS is a 20% stratified sample of all discharges from US hospitals.

Beginning in 2016, the NIS reported hospitalizations utilizing the International Classification of Diseases, Tenth Revision, Clinical Modification/Procedure Coding System (ICD-10-CM/PCS) codes. We identified all admissions for patients aged ≥ 18 years with a procedural record of thyroidectomy between 2016 and 2020. Records without a diagnosis of either benign or malignant thyroid disorders were excluded, as were those records with missing key demographic information. We subsequently divided the cohort into two groups on the basis of the presence or absence of a diagnosis of current smoking status (F17.2, Z72.0). The workflow in Fig. 1 shows the selection and subdivision of patients included in this study. Details of the ICD-10-CM/PCS codes used for identification and grouping are shown in Supplemental Table 1. As the data were obtained from a deidentified publicly available database, the study was exempt from Institutional Review Board approval and informed consent.

Variables and outcomes

The patient and hospital variables assessed in this study included patient age, race/ethnicity, gender, primary expected payer, median household income national quartile for patients' ZIP (Zone Improvement Plan) codes, patient location, admission type, surgical type (total, unilateral or partial), surgical indication (thyroid malignancy or other thyroid disorders), comorbidities and hospital characteristics. Age was assessed continuously. Surgical type and indications were identified through the ICD-10 diagnostic codes listed in Table 1. The preoperative comorbidity variables included myocardial infarction, congestive heart failure, cerebrovascular disease, chronic pulmonary disease, liver disease, renal disease, diabetes mellitus and metastatic solid tumors. Hospital characteristics included hospital bed size, hospital region, hospital location and teaching status (rural, urban nonteaching or urban teaching).

The clinical outcomes evaluated were discharge status and postoperative complications, including vocal dysfunction, hypocalcemia, hypomagnesemia, hematoma/seroma, acute renal failure and respiratory complications. Details of the ICD-10 codes used for classifying postoperative complications are listed in Supplemental Table 1. Given the low mortality rate associated with thyroidectomy, we instead analyzed patients' discharge status. On the basis of the discharge status provided by the NIS, we introduced an additional clinical outcome defined as unfavorable discharge (transfer to short-term hospitals, home health care or other transfers, including skilled nursing facilities, intermediate care and other types of facilities).

Statistical analyses

Continuous variables are presented as medians and interquartile ranges due to skewed data. Categorical variables are presented as total counts and proportions. Demographic and hospital characteristics were compared between the two groups via Mann–Whitney U tests for continuous variables and Pearson's chi–square test for categorical variables with or without Yates' continuity correction. Fisher's exact tests were performed when the approximations of the chi-square tests were inadequate.

To address the substantial differences in baseline characteristics between non-smokers and current smokers, propensity score matching was conducted to minimize potential confounding and enhance

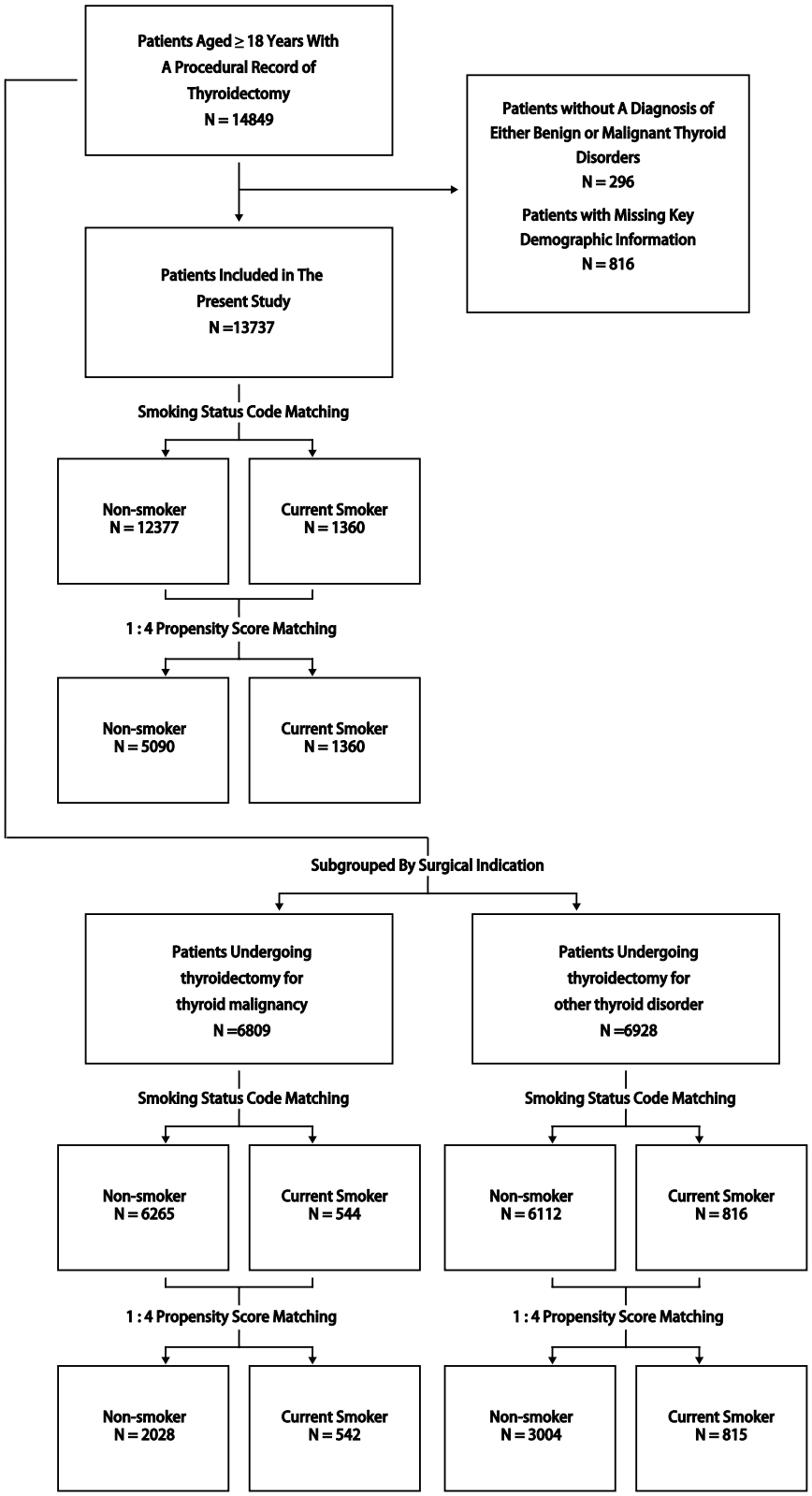

Fig. 1 Flow chart of the patient population selection and division

Table 1 ICD-10 Codes for Defining Smoking Status, Thyroid Disorder, Thyroidectomy And Surgical type

Variable	ICD-10 Codes
Current Smoker	F17.200-F17.209, F17.210-F17.219, F17.220-F17.229, F17.290-F17.299, Z72.0
Thyroid Disorder	
Thyroid Malignancy	C73, D09.3, D44.0
Benign Thyroid Disease	E01.0, E01.1, E01.2, E03.0, E04, E05, E06, E07.0, E07.1, E07.89, E07.9, E31.2, D34, D35.7, D35.9
Thyroidectomy	0GBG0ZZ, 0GBG3ZZ, 0GBG4ZZ, 0GBH0ZZ, 0GBH3ZZ, 0GBH4ZZ, 0GBJ0ZZ, 0GBJ3ZZ, 0GBJ4ZZ, 0GTG0ZZ, 0GTG4ZZ, 0GTH0ZZ, 0GTH4ZZ, 0GTJ0ZZ, 0GTJ4ZZ, 0GTK0ZZ, 0GTK4ZZ
Surgical Type	
Total Thyroidectomy	0GTK0ZZ, 0GTK4ZZ
Unilateral Thyroidectomy	0GTG0ZZ, 0GTG4ZZ, 0GTH0ZZ, 0GTH4ZZ
Partial Thyroidectomy	0GTJ0ZZ, 0GTJ4ZZ, 0GBG0ZZ, 0GBG3ZZ, 0GBG4ZZ, 0GBH0ZZ, 0GBH3ZZ, 0GBH4ZZ, 0GBJ0ZZ, 0GBJ3ZZ, 0GBJ4ZZ

comparability between the two groups when estimating the effect of smoking status. A logistic regression model incorporating all the baseline variables (including age, race/ethnicity, gender, income quartile by zip code, primary expected payer, admission type, procedure type, hospital characteristics and comorbidity) was established to calculate the propensity score. One-to-four greedy nearest neighbor matching without replacement was performed by employing calipers with a width of 0.25 of the standard deviation of the logit of the estimated propensity score. The matching process was done using the R package "MatchIt" [19]. To assess the balance achieved after matching, standardized mean differences (SMD) of covariates included in the propensity score model were calculated using the R package "cobalt" [20], with an threshold of SMD < 0.1 (10%) indicating an acceptable balance between groups [21].

To assess the impact of smoking on clinical outcomes, we applied the same statistical methods used for demographic and hospital characteristics and performed logistic regression analyses to evaluate the association between smoking status and postopertiave outcomes. The results of the logistic regression are presented as adjusted odds ratios (aOR) with 95% confidence intervals (CI).

Following the assessment of smoking status on thyrodectomy outcomes in the overall cohort, the study further stratified the population into two subgroups based on surgical indication: thyroid malignancy and other thyroid disorders. The baseline comparisons, propensity score matching, evluation of matching effectiveness, and post-matching comparisons within these subgroups were performed using the same methodology as described above.

As the association between hypocalcemia, hypomagnesemia and Vitamin D deficiency is well established, we conducted an addtional logistic regression analysis in the overall cohort, thyroid malignancy subgroup and other thyroid disorder subgroup, incoporating Vitamin D deficiency (identified by ICD-10 code: E55.9) as a covariate in the post-matching models.

The statistical analyses were performed via SAS 9.4 (SAS Institute, Cary, NC) and R software (version 4.3.3, R Foundation for Statistical Computing, Vienna, Austria). Statistical significance was set as a two-sided value of $P < 0.05$.

Results

From 2016 to 2020, a total of 13,737 records of patients undergoing thyroidectomy were included, among which 1,360 records (9.90%) were identified as current smokers. As shown in Fig. 2, the percentage of current smokers among patients who underwent thyroidectomy generally increased until 2019, before it decreased in 2020. This trend remains consistent across different surgical indications, with the percentages fluctuating within a range of 15% to 20%.

As shown in Table 2, current smokers were younger (52.5 [41–62] vs. 56 [42–67]), had a greater proportion of males (34.3% vs. 27.1%), and were more likely to be white (62.1% vs. 56.3%) or black (22.4% vs. 16.2%) in race. Moreover, current smokers had lower household income, with higher proportions falling into the first (38.3% vs. 26.4%) or second quartiles (27.5% vs. 24.5%) of the estimated median household income of residents in the patient's ZIP Code. Additionally, current smokers were more likely to be hospitalized in Midwest and rural hospitals, have Medicaid as the primary expected payer, undergo thyroidectomy for other thyroid disorders, and carry a greater comorbidity burden. Following1:4 propensity score matching, the final matched cohort comprised 6,450 patients, including 1,360 current smokers and 5,090 non-smokers. The baseline characteristics after matching are summarized in Table 2 as well and all covariates included in the propensity score model were well-balanced, with all SMD below 0.1.

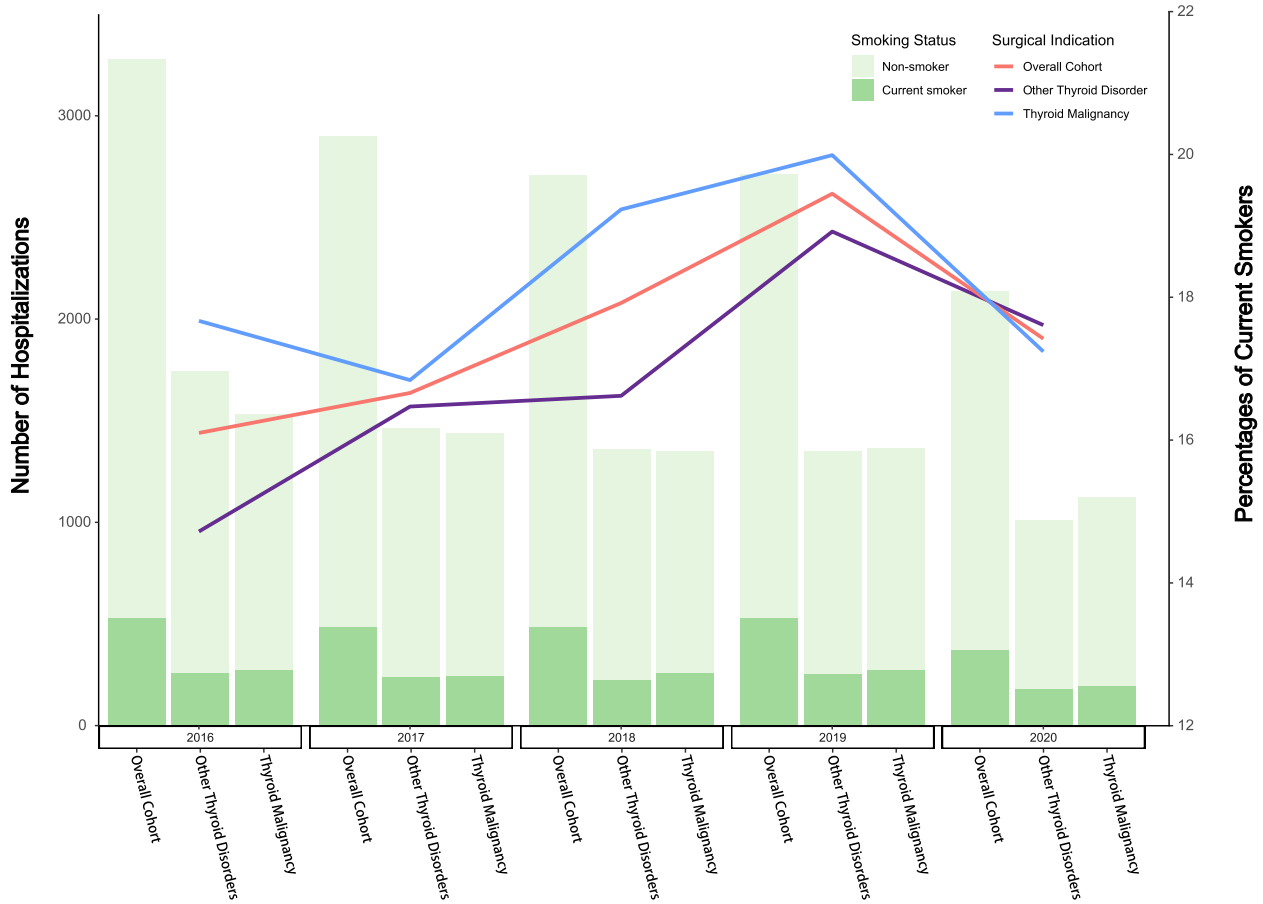

Fig. 2 Graphical presentation of trends in the number of hospitalizations and the percentages of current smokers among patients undergoing thyroidectomy within the National Inpatient Sample database from 2016–2020, stratified by surgical indications

As shown in Table 3, current smokers were more likely to have an unfavorable discharge status compared to non-smokers (12.0% vs. 9.7%, $P=0.012$). A greater incidence of postoperative complications, including any complication (35.7% vs. 29.1%, $P<0.001$), vocal dysfunction (8.5% vs. 6.9%, $P=0.048$), hypocalcemia (18.3% vs. 15.4%, $P=0.010$), hypomagnesemia (5.3% vs. 3.4%, $P=0.001$), and respiratory complications (12.7% vs. 9.5%, $P<0.001$), was also observed.

The results of the multivariate logistic regression after matching are shown in Table 4 and Fig. 3. Multivariate regression revealed that current smoking status was an independent risk factor for unfavorable discharge (OR = 1.27, 95% CI [1.05–1.54], $P=0.012$), any complication (OR = 1.36, 95% CI [1.19–1.54], $P<0.001$), vocal dysfunction (OR = 1.25, 95% CI [1.00–1.55], $P=0.049$), hypocalcemia (OR = 1.23, 95% CI [1.05–1.44], $P=0.010$), hypomagnesemia (OR = 1.58, 95% CI [1.19–2.09], $P=0.001$), and respiratory complications (OR = 1.39, 95% CI [1.16–1.68], $P<0.001$).

In the stratified analysis based on surgical indication, before matching, the thyroid maliganacy cohort included 6,265 non-smokers and 544 current smoker, while the other thyroid disorder cohort comprised 6,112 non-smokers and 816 current smokers.

After 1:4 matching, the thyroid malignancy group retained 2,028 non-smokers and 544 current smokers, while the other thyroid disorder group retained 3,004 non-smokers and 815 current smokers. All covariates achieved SMD < 0,1. Baseline characteristics are presented in Supplemental Tables 3 and 4.

As shown in Table 5, similar results were observed in both patients who underwent thyroidectomy for thyroid malignancy and those who underwent thyroidectomy for other thyroid disorders. In the thyroid malignancy group, current smokers had increased rates of unfavorable discharge (13.3% vs. 8.9%, $P=0.002$), any complication (34.1% vs. 29.3%, $P=0.031$), vocal dysfunction (11.4% vs. 8.3%, $P=0.025$), and hematoma/seroma (1.8% vs. 0.8%, P = 0.041) compared to non-smokers. In the other thyroid

Table 2 Characteristics of Hospitals And Patients Undergoing Thyroidectomy Before And After Matching, Grouped by Smoking Status, National Inpatient Sample 2016–2020

Demographic Characteristics	Unmatched cohort				Matched cohort		
	Non-smoker *n* = 12,377 (%)	Current Smoker *n* = 1360 (%)	P-value	SMD	Non-smoker *n* = 5090 (%)	Current Smoker *n* = 1360 (%)	SMD
Age (y, median, IQR)	56 (42–67)	52.5 (41–62)	**< 0.001**	0.190	52 (39–65)	52.5 (41–62)	0.024
Race/Ethnicity			**< 0.001**				
White	56.3	62.1		0.120	61.6	62.1	0.012
Black	16.2	22.4		0.157	22.0	22.4	0.010
Hispanic	16.1	8.8		0.224	9.5	8.8	0.028
Other[a]	11.4	6.7		0.165	6.9	6.7	0.008
Gender			**< 0.001**	0.157			0.012
Female	72.9	65.7			66.3	65.7	
Male	27.1	34.3			33.7	34.3	
Income Quartile by Zip Code			**< 0.001**				
1st	26.4	38.3		0.256	37.1	38.3	0.026
2nd	24.5	27.5		0.069	27.8	27.5	0.006
3rd	24.8	19.7		0.123	20.1	19.7	0.009
4th	24.3	14.5		0.249	15.1	14.5	0.016
Primary Expected Payer			**< 0.001**				
Medicare	33.4	27.6		0.126	28.7	27.6	0.024
Medicaid	15.7	29.5		0.333	25.3	29.5	0.094
Private	45	35.7		0.189	38.8	35.7	0.064
Other[b]	5.9	7.1		0.052	7.1	7.1	0.000
Admission Type			0.132	0.043			
Elective	82.4	80.7			82.0	80.7	
Non-elective	17.6	19.3			18.0	19.3	
Procedure Type			0.067				
Total Thyroidectomy	55.5	57.2		0.035	57.1	57.2	0.003
Unilateral Thyroidectomy	35.9	33.0		0.061	33.3	33.0	0.007
Partial Thyroidectomy	8.6	9.8		0.040	9.6	9.8	0.006
Surgical Indication			**< 0.001**	0.215			0.142
Thyroid Malignancy	50.6	40.0			53.0	60.0	
Other Thyroid Disorders	49.4	60.0			47.0	40.0	
Hospital Bed Size			0.176				
Small	13.0	14.0		0.032	14.4	14.0	0.010
Medium	22.2	23.6		0.034	23.4	23.6	0.004
Large	64.9	62.4		0.053	62.2	62.4	0.004
Hospital Location/Teaching Status			**< 0.001**				
Rural	2.9	4.7		0.097	4.4	4.7	0.015
Urban Non-teaching	13.1	11.5		0.046	10.7	11.5	0.027
Urban Teaching	84.1	83.8		0.009	84.9	83.8	0.032
Hospital Region			**< 0.001**				
Northeast	23.0	18.0		0.123	19.0	18.0	0.024
Midwest	16.3	24.8		0.212	23.3	24.8	0.034
South	34.3	38.5		0.087	38.6	38.5	0.001
West	26.4	18.7		0.186	19.1	18.7	0.012
Comorbidity							
Myocardial Infarction	2.6	3.8	**0.014**	0.067	3.5	3.8	0.012
Congestive Heart Failure	5.4	7.3	**0.006**	0.076	6.8	7.3	0.019
Cerebrovascular Disease	1.6	2.1	0.220	0.036	2.0	2.1	0.007

Table 2 (continued)

Demographic Characteristics	Unmatched cohort				Matched cohort		
	Non-smoker *n* = 12,377 (%)	Current Smoker *n* = 1360 (%)	P-value	SMD	Non-smoker *n* = 5090 (%)	Current Smoker *n* = 1360 (%)	SMD
Chronic Pulmonary Disease	13.8	26.1	**< 0.001**	0.313	23.5	26.1	0.060
Liver Disease	1.7	3.1	**< 0.001**	0.091	2.7	3.1	0.026
Renal Disease	6.7	6.0	0.371	0.028	6.2	6.0	0.007
Diabetes Mellitus	20.5	19.8	0.570	0.017	19.9	19.8	0.004
Metastatic Solid Tumor	22.5	20.0	**0.035**	0.062	20.7	20.0	0.018

[a] Includes Asian or Pacific Islander, Native American, and other

[b] Includes self−pay, no charge and others

Mann–Whitney U test was performed for age

SMD standardized mean difference

Table 3 Post-matching Clinical Outcomes of Patients Undergoing Thyroidectomy Grouped by Smoking Status, National Inpatient Sample 2016–2020

Clinical Outcomes	Non-smoker *n* = 5090 (%)	Current Smoker *n* = 1360 (%)	*P*-value
Unfavorable Discharge	9.7	12.0	**0.012**
Any Complication	29.1	35.7	**< 0.001**
Vocal Dysfunction	6.9	8.5	**0.048**
Hypocalcemia	15.4	18.3	**0.010**
Hypomagnesemia	3.4	5.3	**0.001**
Hematoma/Seroma	1.1	1.7	0.105
Acute Renal Failure	3.3	3.5	0.805
Respiratory	9.5	12.7	**< 0.001**

Pearson's chi−square tests were performed [for postoperative complications]

Table 4 Post-matching Logistic Regression Analysis of Clinical Outcomes in Patients Undergoing Thyroidectomy, Grouped by Smoking Status, National Inpatient Sample 2016–2020

Clinical Outcomes	Odds Ratio	95%CI	*P*-value
Unfavorable Discharge	1.27	1.05–1.54	**0.012**
Any Complication	1.36	1.19–1.54	**<0.001**
Vocal Dysfunction	1.25	1.00–1.55	**0.049**
Hypocalcemia	1.23	1.05–1.44	**0.010**
Hypomagnesemia	1.58	1.19–2.09	**0.001**
Hematoma/Seroma	1.49	0.92–2.43	0.107
Acute Renal Failure	1.04	0.75–1.45	0.805
Respiratory	1.39	1.16–1.68	**<0.001**

disorder group, current smokers had higher rates of any complication (36.7% vs. 27.7%, $P < 0.001$), hypocalcemia (16.7% vs. 13.2%, $P = 0.011$), hypomagnesemia (5.8% vs. 3.6%, $P = 0.006$), and respiratory complications (14.6% vs. 9.8%, $P < 0.001$). Logistic regression analyses further confirmed these associations, with detailed results presented in Supplemental 4.. Further visualization of the association between smoking status and postoperative outcomes across the overall cohort, thyroid malignancy subgroup, and other thyroid disorder subgroup is presented in Fig. 4.

To evaluate the confounding effect of Vitamin D deficiency, we performed a sensitivity analysis by adding it to the post-matching logistic regression models. The prevalence of Vitamin D deficiency across the overall cohort and subgroups is summarized in Supplemental Table 5. As shown in Table 6, adjusting for Vitamin D deficiency did not substantially alter the associations between smoking and postoperative hypocalcemia or hypomagnesemia, particularly in the overall cohort (Hypocalcemia: aOR = 1.23, 95% CI [1.05–1.44], $P = 0.010$; Hypomagnesemia: aOR = 1.57, 95% CI [1.19–2.09], $P = 0.002$) and the subgroup undergoing thyroidectomy for benign thyroid disorders (Hypocalcemia: aOR = 1.31, 95% CI [1.06–1.63], $P = 0.012$; Hypomagnesemia: aOR = 1.62, 95% CI [1.14–2.31], $P = 0.007$). These findings indicate that despite the influence of Vitamin D deficiency, smoking remains an independent risk factor for postoperative electrolyte imbalances.

Discussion

Tobacco use is a severe global health issue that imposes both health and economic burdens on human society. Despite the global decline in smoking prevalence, the total number of smokers continues to rise due to population growth. In 2019, an estimated 1.14 billion individuals worldwide were current smokers [22]. In the present study, we observed a statistically significant correlation between current smoking status and adverse clinical outcomes after thyroidectomy.

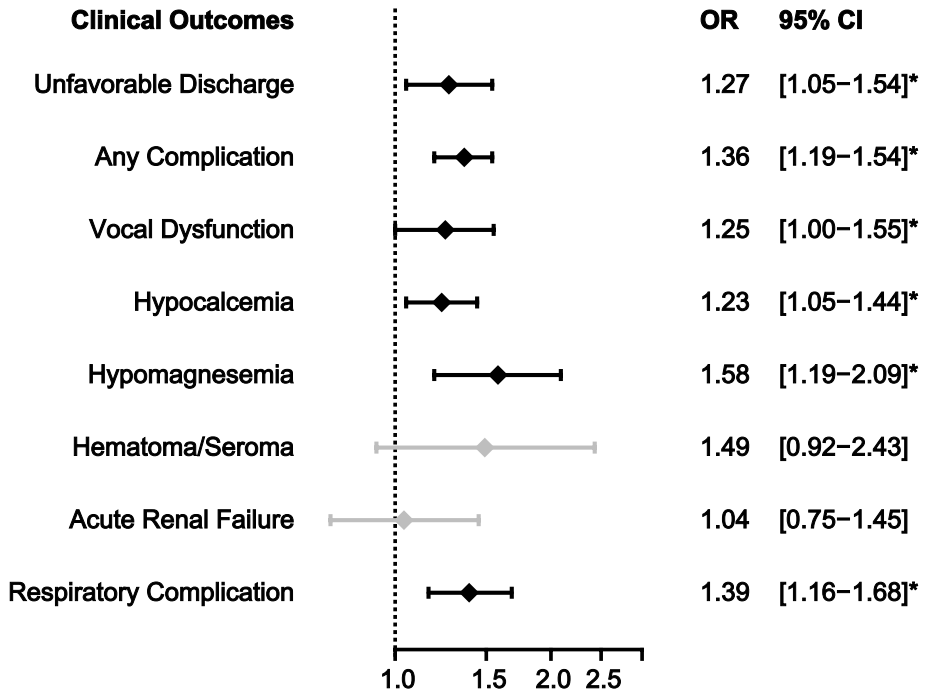

Fig. 3 Forest plot displaying post-matching odds ratios from logistic regression analysis of clinical outcomes among current smokers compared with non-smokers undergoing thyroidectomy. * $P < 0.05$

Table 5 Post-matching Clinical Outcomes of Patients Undergoing Thyroidectomy Grouped by Smoking Status, Stratified by Smoking Status and Surgical Indication, National Inpatient Sample 2016–2020

Clinical Outcomes	Thyroid Malignancy ($n = 2570$)			Other Thyroid Disorder ($n = 3819$)		
	Non-smoker $n = 2028$ (%)	Current Smoker $n = 542$ (%)	*P*-value	Non-smoker $n = 3004$ (%)	Current Smoker $n = 815$ (%)	*P*-value
Unfavorable Discharge	8.9	13.3	**0.002**	10.4	11.0	0.588
Any Complication	29.3	34.1	**0.031**	27.7	36.7	**< 0.001**
Vocal Dysfunction	8.3	11.4	**0.025**	4.8	6.4	0.062
Hypocalcemia	18.0	20.7	0.164	13.2	16.7	**0.011**
Hypomagnesemia	3.3	4.6	0.129	3.6	5.8	**0.006**
Hematoma/Seroma	0.8	1.8	**0.041**	1.3	1.6	0.517
Acute Renal Failure	2.0	2.6	0.131	4.6	4.0	0.480
Respiratory	7.9	10.0	0.423	9.8	14.6	**< 0.001**

Pearson's chi−square tests were performed for postoperative complications

Compared with non-smokers, current smokers experienced a greater risk of unfavorable discharge status (OR = 1.27, 95% CI [1.05–1.54], $P = 0.012$) and postoperative complications, including any complication, vocal dysfunction, hypocalcemia, hypomagnesemia, and respiratory complications. Similar results were observed in both patients who underwent thyroidectomy for thyroid malignancy and those who underwent thyroidectomy for other thyroid disorders when a stratified analysis by surgical indications was performed.

Tobacco use has long been confirmed as a risk factor for poor postoperative complications. A retrospective study analyzing data from over 500,000 noncardiac surgical patients revealed that current smokers had significantly greater odds of 30-day mortality and various serious postoperative complications than never smokers

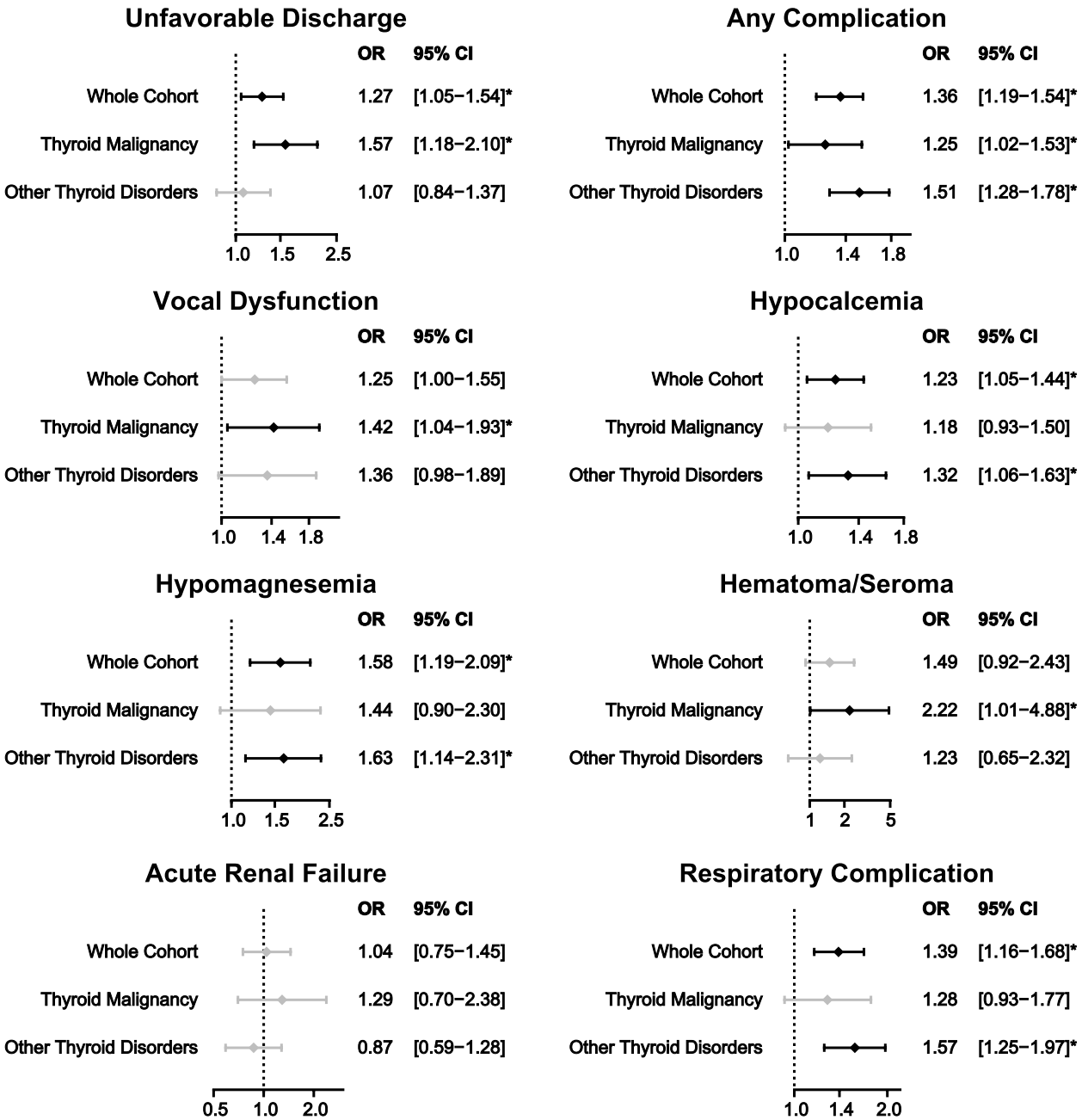

Fig. 4 Forest plots displaying odds ratios from logistic regression analysis of clinical outcomes among current smokers compared with non-smokers undergoing thyroidectomy in three post-matching cohorts stratified by surgical indications. * $P < 0.05$

did [23]. Another retrospective study of 393,794 patients revealed that current smokers had significantly higher rates of postoperative pneumonia, surgical-site infections and deaths than did prior smokers and never smokers [24] Studies focusing on individual surgical specialties have reached the same conclusion [25, 26]. However, the impact of smoking on postoperative complications after thyroidectomy remains underexplored. A cohort study of 154,895 patients revealed several frailty-related factors significantly associated with major postoperative adverse events within 30 days of thyroid or parathyroid surgery, with current smoking status (OR, 1.25; 95% CI [1.05–1.48]) being one of the identified factors but not thoroughly assessed [27]. To date, the present study is the first to investigate the impact of smoking on various postoperative complications following thyroidectomy.

Table 6 Post-matching Logistic Regression Analysis of Postoperative Calcium and Magnesium Imbalances in Patients Undergoing Thyroidectomy, Adjusted for Vitamin D deficiency and Stratified by Smoking Status (Overall Cohort, Thyroid Malignancy Subgroup, and Other Benign Thyroid Disorder Subgroup), National Inpatient Sample 2016–2020

Postoperative Calcium and Magnesium Imbalances	Adjusted Odds Ratio[a]	95%CI	P-value
Patients Undergoing Thyroidectomy			
Hypocalcemia	1.23	1.05–1.44	**0.010**
Hypomagnesemia	1.57	1.19–2.09	**0.002**
Patients Undergoing Thyroidectomy For Thyroid Malignancy			
Hypocalcemia	1.18	0.93–1.50	0.165
Hypomagnesemia	1.44	0.90–2.30	0.131
Patients Undergoing Thyroidectomy For Other Thyroid Disorders			
Hypocalcemia	1.31	1.06–1.63	**0.012**
Hypomagnesemia	1.62	1.14–2.31	**0.007**

[a] Adjusted for Vitamin D deficiency

Previous studies on the epidemiology of smoking have confirmed that current smokers are more likely to be male, younger, less educated, have lower income levels, and live in urban areas [28–31]. Consistent with these studies, our analysis revealed that among patients undergoing thyroidectomy, current smokers were younger, included a greater proportion of males, and had lower income levels than non-smokers did. In addition, racial and ethnic disparities were noted among current smokers, with higher proportions of whites and blacks. Studies have indicated that non-Hispanic white smokers are more likely to develop nicotine dependence [31–33], whereas black individuals find it harder to quit smoking, probably because of higher nicotine blood levels per given volume of nicotine intake and slower clearance of its metabolite [32, 34, 35].

Hypocalcemia is a well-recognized postoperative complication after thyroidectomy, primarily stemming from the impact of surgery on the parathyroid gland, and calcitonin release and hypoalbuminemia are also involved in this mechanism [36]. In the present study, we found that a higher rate of hypocalcemia in current smokers (18.3% vs. 15.4%, $P=0.010$) with current smoking status was an independent risk factor for postoperative hypocalcemia (aOR = 1.23, 95% CI [1.05–1.44], $P=0.010$). Most studies concerning the associations between smoking and parathyroid hormone (PTH) or calcitonin reported increased calcitonin and decreased PTH levels in smokers, providing a potential explanation for our findings [37]. Although the underlying mechanism is not fully understood, smoking-triggered PTH-D axis dysfunction, increased calcitonin release from lung neuroendocrine cells and the direct toxic effect of smoking on parathyroid cells are considered potential contributors [38, 39]. A similar increased risk was observed for postoperative hypomagnesemia in current smokers (5.3% vs. 3.4%, $P=0.001$; aOR = 1.58, 95% CI [1.19–2.09], $P=0.001$). Identifying possible risk factors for hypomagnesemia and timely recognition and rectification of the serum magnesium level are crucial. Hypomagnesemia is associated with postoperative hypocalcemia and may serve as a risk factor for the development of both short- and long-term hypocalcemia [40, 41].

Vocal dysfunction, encompassing dysphonia and hoarseness, is one of the most significant and worrisome postoperative complications following thyroidectomy, as it can become permanent. This condition can be attributed mainly to iatrogenic recurrent laryngeal nerve injury or compression by edema or hematoma [42]. In a prospective study involving 139 patients who underwent thyroid and parathyroid surgery, smoking was found to have no effect on postoperative vocal fold function or changes in the highest pitch of the singing voice [43]. Another nonrandomized prospective study including 100 patients suggested that smoking was not associated with the occurrence of vocal fold immobility but did alter larynx function after thyroidectomy [44]. In the present study, we observed a greater incidence (8.5% vs. 6.9%, $P=0.048$) and an increased risk of vocal dysfunction (aOR = 1.25, 95% CI [1.00–1.55], $P=0.049$) in current smokers. Tobacco use has been associated with perioperative peripheral nerve injuries and delayed healing, which could be explained by a smoking-induced altered inflammatory response, vasoconstriction and relative hypoxia [45, 46]. However, the outcomes we examined reflect early postoperative status rather than long-term status. These results could also be due to compression from postoperative tissue swelling and hematoma, which are known risks associated with smoking [47, 48].

Smoking increases inflammation and oxidative stress, damages vessel walls and makes them more fragile and prone to rupture [49, 50]. Additionally, smoking decreases alveolar oxygen pressure and subcutaneous wound tissue oxygen, and nicotine-induced vasoconstriction further increases the risk of hematoma in smokers [51].

Smoking has long been confirmed as a significant variable related to postoperative respiratory complications [52, 53]. Our results revealed a higher rate (12.7% vs. 9.5%, $P<0.001$) and an increased risk of postoperative respiratory complications (aOR = 1.39, 95% CI [1.16–1.68], $P<0.001$) in current smokers. Smoking negatively affects lung function by reducing mucociliary clearance and impairing small airway function [53]. Smokers' compromised local protective mechanism of the respiratory tract, narrowed small airways, goblet cell hyperplasia and mucus hypersecretion lead to their vulnerability to respiratory complications [54, 55].

There are several limitations in this study, most of which are inherent to the NIS and the retrospective methodology. First, the NIS cannot trace patients with recurrent hospitalizations or capture outpatient encounters, while the number of people recommended for ambulatory operations is increasing because of decreased turnover time and increased efficiency. Besides, as ICD-10 coding system lacks histopathological details, this study fails to differentiate thyroid cancer subtypes, which may impact the occurence of postoperative complications. In addition, a smoking-related diagnosis might be absent from the patient's medical record or misclassified as no tobacco use, given their perceived lower significance compared with the primary diagnosis, reasons for admission or common comorbidity. This may contribute to the underestimation of the smoking population. Moreover, as this was a retrospective study, we could not obtain information about whether any tobacco cessation intervention or replacement therapy was implemented. Furthermore, despite adjusting for key confounders, residual confounding from unmeasured factors like surgeon volume and healthcare accessibility may exist, potentially influencing the observed association between smoking and adverse outcomes. While our findings suggest a potential association, this should be interpreted with caution. Future studies with more granular data are needed to validate our findings. The NIS database lacks smoking-related data, such as smoking duration or pack-years, so we were not able to quantify the amount of smoking at the individual level. Future research incorporating more detailed smoking metrics is needed to better understand the impact of smoking on postthyroidectomy complications. Despite these limitations, the current study is the first to thoroughly evaluate the impact of smoking on several postoperative complications following thyroidectomy. Our analysis revealed greater risks for adverse clinical outcomes in the smoking population than in those who did not smoke on the basis of data from a large nationwide database. The national representativeness of the NIS, the inclusion of large cohorts with more than 13,000 hospitalizations, the use of propensity score matching minimized potential confounding effects, and the consistent results of subset analysis make our analysis solid, reliable and generalizable.

Conclusions

Our study revealed that current smoking is associated with heightened risks of worse clinical outcomes, including higher incidence of unfavorable discharge, any complication, vocal dysfunction, hypocalcemia, hypomagnesemia, and respiratory complications. Our results emphasize the importance of considering smoking history, help foresee potential adverse surgical outcomes, and offer guidance for surgeons in providing appropriate informed consent and postoperative care instructions to patients.

Abbreviations

US	United States
NIS	National Inpatient Sample
ICD-10-CM/PCS	International Classification of Diseases, Tenth Revision, Clinical Modification/Procedure Coding System
ZIP	Zone Improvement Plan
SMD	Standardized mean difference
aOR	Adjusted odds ratio
CI	Confidence interval

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12902-025-01901-8.

Supplementary Material 1

Acknowledgements
Not applicable.

Clinical trial number
Not applicable.

Authors' contributions
Yue Chen and Junxin Chen conceived the study, data analysis, interpretation of the findings, and manuscript preparation. Yanrui Huang, Weijian Ke, Shuang Yu, and Weiwei Liang contributed to data curation, investigation, and methodology. Haipeng Xiao gave constructive comments to increase the quality of the study. Yanbing Li and Hongyu Guan conceptualized the study, managed the project, and contributed to reviewing and revising the manuscript. All authors reviewed and approved the final manuscript.

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Data availability
The data utilized and analyzed in this study was obtained from the NIS database, accessible online at https://hcup-us.ahrq.gov/db/nation/nis/nisdbdocumentation.jsp.

Declarations

Ethics approval and consent to participate
As the data were obtained from a deidentified publicly available database, the study was exempt from Institutional Review Board (IRB) approval and informed consent.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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References

1. WHO. Tobacco. [cited 2023 May 24]. Available from: https://www.who.int/news-room/fact-sheets/detail/tobacco
2. United States Surgeon General. The Health Consequences of Smoking -- 50 Years of progress: A Report of the Surgeon General: (510072014–001). 2014 [cited 2023 May 25]. Available from: http://doi.apa.org/get-pe-doi.cfm?doi=https://doi.org/10.1037/e510072014-001
3. Zuo L, He F, Sergakis GG, Koozehchian MS, Stimpfl JN, Rong Y, et al. Interrelated role of cigarette smoking, oxidative stress, and immune response

in COPD and corresponding treatments. Am J Physiol Lung Cell Mol Physiol. 2014Aug 1;307(3):L205–218.
4. Murray CJL, Aravkin AY, Zheng P, Abbafati C, Abbas KM, Abbasi-Kangevari M, et al. Global burden of 87 risk factors in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. The Lancet. 2020Oct 17;396(10258):1223–49.
5. Goodchild M, Nargis N, d'Espaignet ET. Global economic cost of smoking-attributable diseases. Tob Control. 2018Jan 1;27(1):58–64.
6. Cornelius ME, Loretan CG, Jamal A, Davis Lynn BC, Mayer M, Alcantara IC, et al. Tobacco Product Use Among Adults - United States, 2021. MMWR Morb Mortal Wkly Rep. 2023May 5;72(18):475–83.
7. Canaris GJ, Manowitz NR, Mayor G, Ridgway EC. The Colorado thyroid disease prevalence study. Arch Intern Med. 2000Feb 28;160(4):526–34.
8. American Thyroid Association (ATA) Guidelines Taskforce on Thyroid Nodules and Differentiated Thyroid Cancer, Cooper DS, Doherty GM, Haugen BR, Kloos RT, Lee SL, et al. Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer. Thyroid. 2009;19(11):1167–214.
9. L D. Symposium on evidence-based endocrine surgery (2): benign thyroid disease. World journal of surgery. 2008 Jul [cited 2023 May 29];32(7). Available from: https://pubmed.ncbi.nlm.nih.gov/18408964/
10. Sun GH, DeMonner S, Davis MM. Epidemiological and Economic Trends in Inpatient and Outpatient Thyroidectomy in the United States, 1996–2006. Thyroid®. 2013;23(6):727–33.
11. Sebastian A, Radu M, Robin K, Peter W. Sixth National Audit Report 2021. The The British association of endocrine & thyroid surgeon. Available from: https://e-dendrite.com/Publishing/Reports/BAETS/Sixth_Audit_Report.pdf. [cited 2025 Mar 15].
12. Thomusch O, Machens A, Sekulla C, Ukkat J, Lippert H, Gastinger I, et al. Multivariate analysis of risk factors for postoperative complications in benign goiter surgery: prospective multicenter study in Germany. World J Surg. 2000Nov;24(11):1335–41.
13. Delgado-Rodríguez M, Medina-Cuadros M, Martínez-Gallego G, Gómez-Ortega A, Mariscal-Ortiz M, Palma-Pérez S, et al. A Prospective Study of Tobacco Smoking as a Predictor of Complications in General Surgery. Infect Control Hosp Epidemiol. 2003Jan;24(1):37–43.
14. Grønkjær M, Eliasen M, Skov-Ettrup LS, Tolstrup JS, Christiansen AH, Mikkelsen SS, et al. Preoperative smoking status and postoperative complications: a systematic review and meta-analysis. Ann Surg. 2014Jan;259(1):52–71.
15. Jm C, Sf B, Bc W. Tobacco use is associated with increased rates of infection and revision surgery after primary superior labrum anterior and posterior repair. Journal of shoulder and elbow surgery [Internet]. 2016 Nov [cited 2023 Nov 21];25(11). Available from: https://pubmed.ncbi.nlm.nih.gov/27262413/
16. Lassig AAD, Yueh B, Joseph AM. The effect of smoking on perioperative complications in head and neck oncologic surgery. Laryngoscope. 2012;122(8):1800–8.
17. Fiorini FR, Deganello A, Larotonda G, Mannelli G, Gallo O. Tobacco Exposure and Complications in Conservative Laryngeal Surgery. Cancers. 2014Sep;6(3):1727–35.
18. HCUP-US NIS Overview [Internet]. [cited 2023 Apr 21]. Available from: https://hcup-us.ahrq.gov/nisoverview.jsp
19. Stuart EA, King G, Imai K, Ho D. MatchIt: Nonparametric Preprocessing for Parametric Causal Inference. Journal of Statistical Software [Internet]. 2011 [cited 2023 Nov 29]; Available from: https://dash.harvard.edu/handle/1/11130519
20. Covariate Balance Tables and Plots [Internet]. [cited 2025 Feb 15]. Available from: https://ngreifer.github.io/cobalt/
21. Austin PC. Using the Standardized Difference to Compare the Prevalence of a Binary Variable Between Two Groups in Observational Research. Communications in Statistics - Simulation and Computation. 2009May 14;38(6):1228–34.
22. GBD 2019 Tobacco Collaborators. Spatial, temporal, and demographic patterns in prevalence of smoking tobacco use and attributable disease burden in 204 countries and territories, 1990–2019: a systematic analysis from the Global Burden of Disease Study 2019. Lancet. 2021;397(10292):2337–60.
23. Turan A, Mascha EJ, Roberman D, Turner PL, You J, Kurz A, et al. Smoking and perioperative outcomes. Anesthesiology. 2011Apr;114(4):837–46.
24. Hawn MT, Houston TK, Campagna EJ, Graham LA, Singh J, Bishop M, et al. The attributable risk of smoking on surgical complications. Ann Surg. 2011Dec;254(6):914–20.
25. Sharma A, Deeb AP, Iannuzzi JC, Rickles AS, Monson JRT, Fleming FJ. Tobacco Smoking and Postoperative Outcomes After Colorectal Surgery. Ann Surg. 2013Aug;258(2):296–300.
26. Althoff AD, Reeves RA, Traven SA, Wilson JM, Woolf SK, Slone HS. Smoking is associated with increased surgical complications following total shoulder arthroplasty: an analysis of 14,465 patients. J Shoulder Elbow Surg. 2020Mar 1;29(3):491–6.
27. Mascarella MA, Milad D, Richardson K, Mlynarek A, Payne RJ, Forest VI, et al. Preoperative Risk Index Among Patients Undergoing Thyroid or Parathyroid Surgery. JAMA Otolaryngology-Head & Neck Surgery. 2020Jan 1;146(1):7–12.
28. Mahdaviazad H, Foroutan R, Masoompour SM. Prevalence of tobacco smoking and its socioeconomic determinants. Clin Respir J. 2022;16(3):208–15.
29. Cornish D, Brookman A, Horton M, Scanlon S. Adult smoking habits in the UK: 2018. Office For National Statistics: Office For National Satistics. 2019;1–14.
30. Grant BF, Shmulewitz D, Compton WM. Nicotine Use and DSM-IV Nicotine Dependence in the United States, 2001–2002 and 2012–2013. AJP. 2020Nov;177(11):1082–90.
31. Han B, Einstein EB, Compton WM. Patterns and Characteristics of Nicotine Dependence Among Adults With Cigarette Use in the US, 2006–2019. JAMA Netw Open. 2023Jun 23;6(6): e2319602.
32. American Psychiatric Association. Diagnostic and statistical manual of mental disorders: DSM-5. 5th ed. Washington, D.C: American Psychiatric Association; 2013.
33. Strong DR, Pearson J, Ehlke S, Kirchner T, Abrams D, Taylor K, et al. Indicators of dependence for different types of tobacco product users: Descriptive findings from Wave 1 (2013–2014) of the Population Assessment of Tobacco and Health (PATH) study. Drug Alcohol Depend. 2017Sep;1(178):257–66.
34. Pérez-Stable EJ, Herrera B, Jacob P III, Benowitz NL. Nicotine Metabolism and Intake in Black and White Smokers. JAMA. 1998Jul 8;280(2):152–6.
35. Caraballo RS, Giovino GA, Pechacek TF, Mowery PD, Richter PA, Strauss WJ, et al. Racial and Ethnic Differences in Serum Cotinine Levels of Cigarette SmokersThird National Health and Nutrition Examination Survey, 1988–1991. JAMA. 1998Jul 8;280(2):135–9.
36. Chisthi MM, Nair RS, Kuttanchettiyar KG, Yadev I. Mechanisms behind Post-Thyroidectomy Hypocalcemia: Interplay of Calcitonin, Parathormone, and Albumin—A Prospective Study. J Invest Surg. 2017Jul 4;30(4):217–25.
37. Babić Leko M, Pleić N, Gunjača I, Zemunik T. Environmental Factors That Affect Parathyroid Hormone and Calcitonin Levels. Int J Mol Sci. 2021Dec 21;23(1):44.
38. Mousavi SE, Amini H, Heydarpour P, Amini Chermahini F, Godderis L. Air pollution, environmental chemicals, and smoking may trigger vitamin D deficiency: Evidence and potential mechanisms. Environ Int. 2019Jan;1(122):67–90.
39. Tabassian AR, Nylen ES, Giron AE, Snider RH, Cassidy MM, Becker KL. Evidence for cigarette smoke-induced calcitonin secretion from lungs of man and hamster. Life Sci. 1988Jan 1;42(23):2323–9.
40. Brophy C, Woods R, Murphy MS, Sheahan P. Perioperative magnesium levels in total thyroidectomy and relationship to hypocalcemia. Head Neck. 2019Jun;41(6):1713–8.
41. Liu RH, Razavi CR, Chang HY, Tufano RP, Eisele DW, Gourin CG, et al. Association of Hypocalcemia and Magnesium Disorders With Thyroidectomy in Commercially Insured Patients. JAMA Otolaryngology-Head & Neck Surgery. 2020Mar 1;146(3):237–46.
42. Steurer M, Passler C, Denk DM, Schneider B, Niederle B, Bigenzahn W. Advantages of Recurrent Laryngeal Nerve Identification in Thyroidectomy and Parathyroidectomy and the Importance of Preoperative and Postoperative Laryngoscopic Examination in More Than 1000 Nerves at Risk. Laryngoscope. 2002;112(1):124–33.
43. Musholt TJ, Musholt PB, Garm J, Napiontek U, Keilmann A. Changes of the speaking and singing voice after thyroid or parathyroid surgery. Surgery. 2006;140(6):978–88 discussion 988–989.
44. de Pedro NI, Fae A, Vartanian JG, Barros APB, Correia LM, Toledo RN, et al. Voice and vocal self-assessment after thyroidectomy. Head Neck. 2006;28(12):1106–14.

45. Welch MB, Brummett CM, Welch TD, Tremper KK, Shanks AM, Guglani P, et al. Perioperative peripheral nerve injuries: a retrospective study of 380,680 cases during a 10-year period at a single institution. Anesthesiology. 2009Sep;111(3):490–7.
46. Rodriguez-Fontan F, Reeves B, Tuaño K, Colakoglu S, D' Agostino L, Banegas R. Tobacco use and neurogenesis: A theoretical review of pathophysiological mechanism affecting the outcome of peripheral nerve regeneration. Journal of Orthopaedics. 2020;22:59–63.
47. Garip M, Van Dessel J, Grosjean L, Politis C, Bila M. The impact of smoking on surgical complications after head and neck reconstructive surgery with a free vascularised tissue flap: a systematic review and meta-analysis. Br J Oral Maxillofac Surg. 2021Apr 1;59(3):e79–98.
48. Al-Delayme RM. The effect of cigarette smoking on the severity of pain, swelling and trismus after the surgical extraction of impacted mandibular third molar. J Clin Exp Dent. 2013Jul 1;5(3):e117–21.
49. Powell JT. Vascular damage from smoking: disease mechanisms at the arterial wall. Vasc Med. 1998Feb 1;3(1):21–8.
50. Sørensen LT. Wound Healing and Infection in Surgery: The Pathophysiological Impact of Smoking, Smoking Cessation, and Nicotine Replacement Therapy: A Systematic Review. Ann Surg. 2012Jun;255(6):1069.
51. Hwang K, Son JS, Ryu WK. Smoking and Flap Survival. Plast Surg (Oakv). 2018Nov 1;26(4):280–5.
52. McCulloch TM, Jensen NF, Girod DA, Tsue TT, Weymuller EA Jr. Risk factors for pulmonary complications in the postoperative head and neck surgery patient. Head Neck. 1997;19(5):372–7.
53. Moores LK. Smoking and postoperative pulmonary complications An evidence-based review of the recent literature. Clin Chest Med. 2000;21(1):139-46 ix-x.
54. Drannik AG, Pouladi MA, Robbins CS, Goncharova SI, Kianpour S, Stämpfli MR. Impact of Cigarette Smoke on Clearance and Inflammation after Pseudomonas aeruginosa Infection. Am J Respir Crit Care Med. 2004Dec;170(11):1164–71.
55. Bosken CH, Wiggs BR, Paré PD, Hogg JC. Small Airway Dimensions in Smokers with Obstruction to Airflow. American Review of Respiratory Disease [Internet]. 2012 Dec 17 [cited 2023 Dec 21]; Available from: https://www.atsjournals.org/doi/epdf/https://doi.org/10.1164/ajrccm/142.3.563?role=tab

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