

Non-Tobacco Nicotine Dependent Patients and Post-Operative Complications Following Thyroidectomy

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Abstract

Non-tobacco nicotine products, such as e-cigarettes, are often perceived as safer alternatives to tobacco, yet their impact on surgical recovery is unclear. Using the TriNetX database (2013–2023), we compared thyroidectomy patients with non-tobacco nicotine dependence (n=6,188) to matched controls without nicotine use (n=119,474). Outcomes assessed up to six months post-operatively included hypoparathyroidism, infection, thyrotoxicosis, hypocalcemia, dysphonia, laryngospasm, and mortality. After propensity matching (n=5,922), nicotine users were more likely to develop infection (RR 1.923, p<0.005), delayed wound healing (RR 2.618, p<0.05), mortality (RR 2.614, p<0.0005), and other surgical complications (RR 2.166, p<0.05). Risks for hypocalcemia, dysphonia, hypoparathyroidism, and thyrotoxicosis did not differ. These findings suggest that non-tobacco nicotine dependence confers unique risks in post-thyroidectomy recovery, underscoring the importance of perioperative counseling and updated cessation guidelines.

Introduction

Previous literature has shown that tobacco product usage increases the risk of post-operative complications and overall morbidity. Because of this, non-tobacco nicotine products have become increasingly popular and are believed to be a safer alternative to traditional tobacco products such as cigarettes. Our study aims to evaluate common post-operative complications following thyroidectomy in non-tobacco nicotine users.

Objective: to evaluate post-operative complication risks in thyroidectomy patients with non-tobacco nicotine dependence compared to non-users.

Methods

Data source: TriNetX Research Network (108 HCOs)

Cohorts:

- **Nicotine Users:** 6,188 patients ≥18 yrs, thyroidectomy + non-tobacco nicotine dependence
- **Non-nicotine Users:** 119,474 patients ≥18 yrs, thyroidectomy without nicotine/tobacco diagnoses

Outcomes:

- Hypocalcemia, dysphonia, hypoparathyroidism, thyrotoxicosis, surgical site infection, delayed wound healing, mortality, other perioperative/anesthesia complications
- All outcomes analyzed within 180 days post-operatively
- patients with outcomes prior to the time window excluded

Statistical Analyses:

- Propensity score matching (1:1, 5,922 patients per group)
- Risk ratios, odds ratios, 95% CI, p-values.

Results

A Hypocalcemia					
Cohort	Patients in Cohort	Patients with Outcome	Risk		
Nicotine	5571	323	0.058		
Non-Nicotine	5765	334	0.058		
		95% CI	z	p	
Risk Difference	0	(-0.009, 0.009)	0.01	0.992	
Risk Ratio	1.001	(0.863, 1.161)	N/A	N/A	
Odds Ratio	1.001	(0.855, 1.172)	N/A	N/A	

B Dysphonia					
Cohort	Patients in Cohort	Patients with Outcome	Risk		
Nicotine	5418	158	0.029		
Non-Nicotine	5633	195	0.035		
		95% CI	z	p	
Risk Difference	-0.005	(-0.012, 0.001)	-1.63	0.103	
Risk Ratio	0.842	(0.685, 1.036)	N/A	N/A	
Odds Ratio	0.838	(0.677, 1.037)	N/A	N/A	

C Hypoparathyroidism					
Cohort	Patients in Cohort	Patients with Outcome	Risk		
Nicotine	5826	100	0.017		
Non-Nicotine	5885	120	0.02		
		95% CI	z	p	
Risk Difference	-0.003	(-0.008, 0.002)	-1.286	0.199	
Risk Ratio	0.842	(0.647, 1.095)	N/A	N/A	
Odds Ratio	0.839	(0.642, 1.097)	N/A	N/A	

D Thyrotoxicosis					
Cohort	Patients in Cohort	Patients with Outcome	Risk		
Nicotine	4327	42	0.01		
Non-Nicotine	4830	53	0.011		
		95% CI	z	p	
Risk Difference	-0.001	(-0.005, 0.003)	-0.597	0.55	
Risk Ratio	0.885	(0.591, 1.323)	N/A	N/A	
Odds Ratio	0.883	(0.588, 1.327)	N/A	N/A	

Figure 1. Measure of association of select post-operative complications following thyroidectomy in nicotine-dependent non-tobacco using patients versus non-nicotine using controls. Propensity score matched cohorts were analyzed for incidence of (A) hypocalcemia, (B) dysphonia, (C) hypoparathyroidism, and (D) thyrotoxicosis within 6 months of surgery. Outcomes are reported as risk proportions, risk differences with 95% confidence intervals, and risk/odds ratios.

A Infection					
Cohort	Patients in Cohort	Patients with Outcome	Risk		
Nicotine	5041	113	0.022		
Non-Nicotine	5490	64	0.012		
		95% CI	z	p*	
Risk Difference	0.011	(0.006, 0.016)	4.29	0	
Risk Ratio	1.923	(1.418, 2.607)	N/A	N/A	
Odds Ratio	1.944	(1.427, 2.648)	N/A	N/A	

B Delayed Wound Healing					
Cohort	Patients in Cohort	Patients with Outcome	Risk		
Nicotine	5839	26	0.004		
Non-Nicotine	5880	10	0.002		
		95% CI	z	p*	
Risk Difference	0.003	(0.001, 0.005)	2.692	0.007	
Risk Ratio	2.618	(1.264, 5.425)	N/A	N/A	
Odds Ratio	2.625	(1.265, 5.449)	N/A	N/A	

C Mortality					
Cohort	Patients in Cohort	Patients with Outcome	Risk		
Nicotine	5907	47	0.008		
Non-Nicotine	5914	18	0.003		
		95% CI	z	p*	
Risk Difference	0.005	(0.002, 0.008)	3.612	0	
Risk Ratio	2.614	(1.520, 4.495)	N/A	N/A	
Odds Ratio	2.627	(1.524, 4.528)	N/A	N/A	

D Other Complications of Surgery and Anesthesia					
Cohort	Patients in Cohort	Patients with Outcome	Risk		
Nicotine	5842	28	0.005		
Non-Nicotine	5876	13	0.002		
		95% CI	z	p*	
Risk Difference	0.003	(0.000, 0.005)	2.365	0.018	
Risk Ratio	2.166	(1.123, 4.178)	N/A	N/A	
Odds Ratio	2.172	(1.124, 4.197)	N/A	N/A	

Figure 2. Measure of association of select post-operative complications following thyroidectomy in nicotine-dependent non-tobacco using patients versus non-nicotine using controls. Propensity score matched cohorts were analyzed for incidence of (A) infection, (B) delayed wound healing, (C) mortality, and (D) other complications of surgery and anesthesia within 6 months of surgery. Outcomes are reported as risk proportions, risk differences with 95% confidence intervals, and risk/odds ratios.

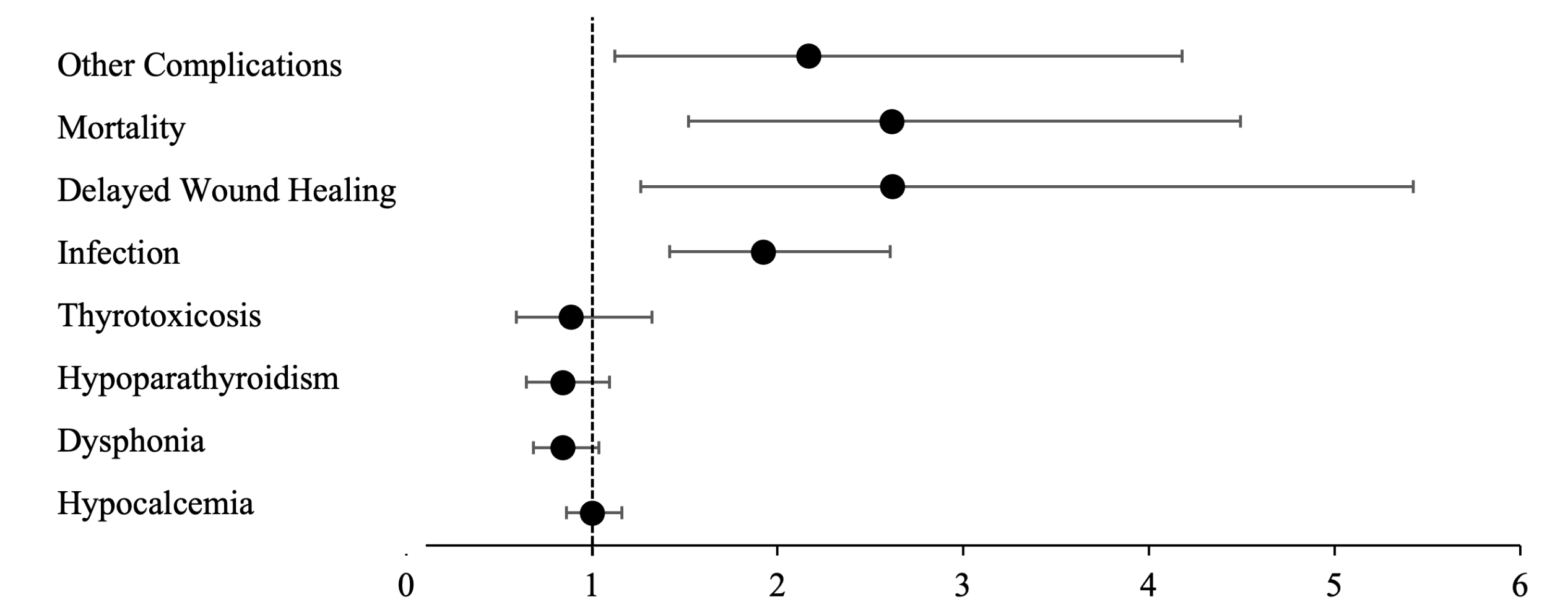


Figure 3. Forest plot of post-operative complications in nicotine-dependent non-tobacco using patients versus non-nicotine using patient controls. Odds ratios with 95% confidence intervals are shown for eight outcomes within 6 months post-operatively. Forest plots display relative risk (RR) with 95% confidence intervals for seasonal cohort comparisons of postoperative outcomes including hypocalcemia, dysphonia, hypoparathyroidism, thyrotoxicosis, infection, delayed wound healing, mortality, and other surgical and anesthesia complications. Relative risks > 1 indicate a higher risk for each postoperative complication of interest in the non-tobacco nicotine-user cohort compared to controls. Dashed vertical line indicates the null value (RR = 1).

Discussion

- Non-tobacco nicotine use was linked to higher risks of infection, delayed wound healing, mortality, and other perioperative and anesthesia related complications after thyroidectomy
- No significant differences were found regarding post-operative hypocalcemia, dysphonia, hypoparathyroidism, or thyrotoxicosis in non-tobacco nicotine users compared to non-nicotine using controls
- A higher mortality rate in non-tobacco nicotine users highlights potential systemic risks of nicotine use separate from tobacco smoking
- Findings align with previous evidence that nicotine, regardless of delivery method, may negatively impact surgical recovery

Conclusions

- Non-tobacco nicotine use confers quantifiable risk of post-operative complications post-thyroidectomy
- Surgical consenting process should include counseling regarding the use of all nicotine products rather than tobacco alone
- Further patient education can help dispel the misconception that e-cigarette and other non-tobacco nicotine products are “risk-free” before undergoing surgery

Future Directions

- Stratify outcomes by type of nicotine product (e-cigarettes, nicotine pouches)
- Explore dose-dependent relationships between nicotine use intensity and postoperative complications
- Develop proper perioperative guidelines for patient counseling specific to non-tobacco nicotine users

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