Research Article

# The Smokeless Paradox: Nontobacco Nicotine Use and Complications in Anterior Cervical Discectomy and Fusion

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## ABSTRACT

**Introduction:** Cervical fusion surgeries are commonly performed to stabilize the spine and relieve pain from various conditions. Recent increases in nontobacco nicotine product use, such as electronic cigarettes, present new challenges because of their unknown effects on spinal fusion outcomes. Our study aims to explore the effect of nontobacco nicotine dependence (NTND) on the success of cervical spinal fusions.

**Methods:** We analyzed TriNetX database data for patients undergoing primary anterior cervical diskectomy and fusion, identified by specific Current Procedural Terminology codes, and categorized into cohorts based on a preoperative diagnosis of nicotine dependence, excluding those with tobacco use or dependence. Propensity matching in the ratio of 1:1 was done to control for demographics and body mass index. We analyzed 90-day medical and 2-year implant complications using chi-squared exact tests and univariate regressions within the matched cohorts.

**Results:** The NTND and control cohorts comprised 5,331 and 43,033 patients, respectively. Five thousand two hundred thirty-two matched pairs of patients were included from each cohort as shown in Table 1. Our results indicate notable disparities in complications within 90 days postoperation between the cohorts. The NTND cohort had higher risks for opioid use (85.6% vs. 80.3%, $P < 0.001$), emergency department visits (13.0% vs. 8.40%, $P < 0.001$), opioid abuse (0.4% vs. 0.2%, $P < 0.001$), inpatient hospitalizations (20.0% vs. 17.4%, $P < 0.001$), and sepsis (1.40% vs. 0.80%, $P = 0.01$). At the 2-year follow-up, increases were observed in pseudarthrosis (14.0% vs. 9.60%, $P < 0.001$), adjacent segment disease (3.70% vs. 2.20%, $P < 0.001$), dysphagia (8.90% vs. 6.3%, $P = 0.001$), and revision surgery (2.00% vs. 1.40%, $P = 0.02$).

**Conclusion:** This study highlights notable postoperative complications in patients with NTND undergoing cervical spinal fusion.

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Cervical and lumbar spinal fusion are common surgical procedures that have been performed for decades, with an increase in procedure volume over the years.[1-4] Spinal fusion procedures are effective in stabilizing the spine and alleviating pain associated with a wide range of conditions, such as degenerative disk disease, spinal stenosis, and spinal deformities.[3,4] The complexities of spinal fusion come with several risks and challenges, and there has been an effort to decrease postoperative complications, such as infection, respiratory issues, and pseudarthrosis.[3,4] Patient demographics, comorbidities, and surgical technique are few of several factors that may influence fusion success, yet nicotine dependence has emerged as a notable risk factor of interest.

Within the past decade, the use of nontobacco nicotine products, such as electronic cigarettes and nicotine pouches, has increased rapidly.[5-7] The rapid growth of e-cigarette and nicotine pouch use has largely been attributed to increased advertising and marketing avenues such as social media and the declining popularity of cigarette smoking.[6,7] The negative effect of tobacco use on bone injuries and surgical repairs has long been recognized in the literature; smoking decreases bone formation and increases bone resorption through metabolic and gene expression changes, impairing the fusion healing process.[8] Clinically, smoking has been associated with an increased risk of nonunion and revision surgery for lumbar fusion[9-11] with a dampened difference between smokers and nonsmokers undergoing cervical fusion.[12-16] Although the effect of tobacco nicotine use has been extensively studied, there exists a paucity of knowledge regarding the effect of nontobacco nicotine use on patients undergoing cervical spinal fusion.

With the increasing popularity of nontobacco nicotine products, clinicians and researchers are faced with the new challenge of analyzing the effects of nicotine delivery without the combustion of other harmful compounds present in traditional tobacco smoke. Thus, our study aims to evaluate nontobacco nicotine use on cervical spinal fusion outcomes to bridge this knowledge gap.

## Methods

This retrospective cohort study aimed to assess the risk of postoperative complications at 90 days and 1 year in patients with and without nontobacco nicotine dependence (NTND), using data from the TriNetX database. TriNetX aggregates deidentified records from 89 healthcare organizations, covering more than 100 million patients and provides real-time access to a wide range of electronic health information, including diagnoses, procedures, medications, laboratory values, and genomic data. Institutional review board approval was not required because only deidentified aggregated data were accessed. We used International Classification of Diseases, Revision 10 (ICD-10) codes to query patients who had anterior cervical diskectomy and fusion (ACDF).

### Cohort Selection

Patients who underwent primary ACDF were identified using specific Current Procedural Terminology codes CPT-22551. These patients were further categorized into two cohorts based on their preoperative diagnosis of NTND with no restrictions and all indications ACDF. The NTND cohort was defined as patients with a preoperative diagnosis of nicotine depednence (ICD-10: F17), excluding those specifically dependent to cigarettes (ICD-10: F17.21), chewing tobacco (ICD-10: F17.22), or other tobacco products (ICD-10: F17.29). This group was cmpared to patients who underwent ACDF but had no history of nicotine dependence or a personal history of nicotine use (ICD-10 Z87.981 and F17).

### Statistics

For all outcomes of interest, risk ratios (RRs) and 95% confidence intervals (CIs) were computed using the TriNetX system, with $P$ values less than 0.05 deemed statistically significant. Categorical variables were analyzed using the chi-squared test, whereas continuous variables were evaluated with Student $t$-tests.

### Unmatched Cohort

Overall, the study assessed 5,331 patients in the NTND cohort with a mean age of 53.3 ± 11.1 years, and 43,033 in patients without a preoperative diagnosis of nicotine dependence with a mean age of 56.5 ± 12.8 years ($P < 0.001$). Notable differences were observed across various factors between these two cohorts, including age, sex, and ethnicity, as depicted in Table 1. The nonnicotine dependence group had a higher mean age compared with the control group, along with differences in sex distribution, ethnicity (including White, African American, Asian, and other races), and more patients in the 25 to 30 kg/m$^2$ category; 1:1 propensity matching was employed for demographics (age, sex, race, ethnicity), comorbid previous medical conditions, including diabetes mellitus, hypertension, heart failure, chronic obstructive pulmonary disease,

**Table 1.** Demographic Comparison of Pre and Post 1:1 Propensity Match

| Factor or Variable | Unmatched Cohort | | | | Matched Cohort | | |
|---|---|---|---|---|---|---|---|
| | Cohort | Patients, Mean (SD) | % of Cohort | *P* | Patients, Mean (SD) | % of Cohort | *P* |
| Age at index | NTND | 5,331, 53.3 (11.1) | 100% | <0.001 | 5,232, 53.3 (11.2) | 100% | 0.982 |
| | Control | 43,033, 56.5 (12.8) | 100% | — | 5,232, 53.3 (12.0) | 100% | — |
| Male | NTND | 2,721 | 51.00% | <0.001 | 2,656 | 50.80% | 0.544 |
| | Control | 19,939 | 46.30% | — | 2,625 | 50.20% | — |
| Female | NTND | 2,417 | 45.30% | <0.001 | 2,384 | 45.60% | 0.492 |
| | Control | 21,091 | 49.00% | — | 2,419 | 46.20% | — |
| White | NTND | 3,980 | 74.70% | 0.003 | 3,901 | 74.60% | 0.039 |
| | Control | 31,290 | 72.70% | — | 3,992 | 76.30% | — |
| Black | NTND | 745 | 14.00% | <0.001 | 728 | 13.90% | 0.777 |
| | Control | 4,643 | 10.80% | — | 718 | 13.70% | — |
| Asian | NTND | 48 | 0.90% | <0.001 | 48 | 0.90% | 0.189 |
| | Control | 935 | 2.20% | — | 36 | 0.70% | — |
| Other race | NTND | 98 | 1.80% | <0.001 | 98 | 1.90% | 0.024 |
| | Control | 1,329 | 3.10% | — | 69 | 1.30% | — |
| Not Hispanic | NTND | 4,313 | 80.90% | <0.001 | 4,220 | 80.70% | 0.251 |
| | Control | 31,813 | 73.90% | — | 4,266 | 81.50% | — |
| Hispanic | NTND | 203 | 3.80% | <0.001 | 203 | 3.90% | 0.538 |
| | Control | 2,220 | 5.20% | — | 191 | 3.70% | — |
| Comorbidities | | | | | | | |
| Diabetes mellitus | NTND | 995 | 18.70% | 0.012 | 963 | 18.40% | 0.113 |
| | Control | 7,435 | 17.30% | — | 901 | 17.20% | — |
| Hypertensive diseases | NTND | 2,652 | 49.70% | <0.001 | 2,567 | 49.10% | 0.681 |
| | Control | 18,007 | 41.80% | — | 2,588 | 49.50% | — |
| Heart failure | NTND | 195 | 3.70% | <0.001 | 182 | 3.50% | 0.832 |
| | Control | 1,058 | 2.50% | — | 186 | 3.60% | — |
| COPD | NTND | 744 | 14.00% | <0.001 | 645 | 12.30% | 0.654 |
| | Control | 1,004 | 2.30% | — | 630 | 12.00% | — |
| Diseases of liver | NTND | 265 | 5.00% | <0.001 | 249 | 4.80% | 0.016 |
| | Control | 1,309 | 3.00% | — | 199 | 3.80% | — |
| Chronic kidney disease (CKD) | NTND | 263 | 4.90% | 0.648 | 257 | 4.90% | 0.163 |
| | Control | 2,062 | 4.80% | — | 227 | 4.30% | — |
| Overweight | NTND | 1,197 | 22.50% | 0.015 | 1,172 | 22.40% | 0.163 |
| | Control | 9,042 | 21.00% | — | 1,113 | 21.30% | — |
| OPIOID | NTND | 4,992 | 93.60% | <0.001 | 4,900 | 93.70% | 0.062 |
| | Control | 39,461 | 91.70% | — | 4,852 | 92.70% | — |

(*continued*)

**Table 1.** (*continued*)

| Factor or Variable | Unmatched Cohort | | | | Matched Cohort | | |
|---|---|---|---|---|---|---|---|
| | Cohort | Patients, Mean (SD) | % of Cohort | *P* | Patients, Mean (SD) | % of Cohort | *P* |
| BMI | | | | | | | |
| 25–30 kg/m$^2$ | NTND | 1,746 | 32.80% | <0.001 | 1,698 | 32.50% | 0.285 |
| | Control | 12,850 | 29.90% | — | 1,647 | 31.50% | — |
| 30–35 kg/m$^2$ | NTND | 1,350 | 25.30% | 0.283 | 1,315 | 25.10% | 0.297 |
| | Control | 10,608 | 24.70% | — | 1,269 | 24.30% | — |
| 35–40 kg/m$^2$ | NTND | 711 | 13.30% | 0.171 | 698 | 13.30% | 1 |
| | Control | 5,454 | 12.70% | — | 698 | 13.30% | — |

BMI = body mass index, COPD = chronic obstructive disease, NTND = nontobacco nicotine dependence
Obesity BMI >30.

chronic kidney disease, and obesity, body mass index, and opioid use.

### 1:1 Propensity Matched Cohort

The TriNetX platform was used to conduct 1:1 propensity score matching employing logistic regression. The platform integrates the nearest-neighbor matching with a tolerance level of 0.01 and ensures that the difference between propensity scores is $P \leq 0.01$. After propensity score matching, no notable differences were observed between the two groups in terms of demographic characteristics (age, sex, ethnicity) or comorbidities, including diabetes mellitus, hypertension, heart failure, chronic obstructive pulmonary disease, liver disease, chronic kidney disease, and overweight status.

### Outcomes

We detail the medical complications observed within 90 days postoperatively, which include opioid prescriptions, surgical site infection, pulmonary embolism (PE), deep vein thrombosis (DVT), emergency department visits, opioid abuse, inpatient hospitalizations, wound complications, postoperative infections, and sepsis. In addition, the primary implant-related outcomes measured at 2 years postoperatively include pseudarthrosis, adjacent segment disease, implant failure, dysphagia, and revision cervical spine surgery with codes depicted in supplemental table 1, http://links.lww.com/JAAOS/B263.

## Results

In evaluating medical complications within 90 days postoperation, our analysis revealed notable disparities between the cohort with NTND and the control group. The RR for opioid use was markedly higher in the NTND cohort (RR 1.07, 95% CI, 1.05 to 1.08), with 85.6% experiencing this outcome compared with 80.3% of the control group. Patients in the NTND cohort also experienced higher rates of postoperative opioid abuse with 0.40% of patients developing this dependence compared with 0.20% of the control patients (RR 2.1, 95% CI, 0.99 to 4.46).

Moreover, the NTND ACDF cohort exhibited a higher average number of outcomes (mean of 4.05, median 2) compared with the control group (mean of 2.94, median 2; $P < 0.001$). Emergency department visits were markedly more prevalent in the nontobacco nicotine–dependent cohort with an RR of 1.55 (95% CI, 1.38 to 1.74). Increased occurrences of inpatient hospitalizations within this period were also noted in the nontobacco nicotine–dependent cohort, with a RR of 1.15 (95% CI, 1.06 to 1.24). Other notable findings included higher incidences of wound complications, postoperative infections, and sepsis in the nontobacco nicotine–dependent cohort as shown in Table 2.

At the 2-year follow-up, primary implant-related outcomes showed notable differences. Pseudarthrosis (RR 1.46, 95% CI, 1.31 to 1.63), adjacent segment disease (RR 1.69, 95% CI, 1.34 to 2.14), and implant failure (RR 1.30, 95% CI, 0.8 to 2.09) were notably higher in nontobacco nicotine–dependent cohort. Dysphagia also presented more frequently in this cohort (RR 1.21, 95% CI, 1.09 to 1.36), and rate of revision cervical spine surgery was statistically significant (RR 1.42, 95% CI, 1.06 to 1.91) as shown in Table 3.

## Discussion

We conducted a retrospective cohort analysis of 10,464 matched patients comparing cervical spinal surgery

**Table 2.** Ninety Medical Complications in 1:1 Propensity Matched Nontobacco Nicotine Dependence versus Control

| Complication | % of Outcomes NTND | % of Outcomes Control | Risk Ratio (RR) | 95% Confidence Interval (CI) | *P* |
|---|---|---|---|---|---|
| SSI | 0.50% | 0.30% | 1.71 | 0.89-3.31 | 0.10 |
| PE | 0.80% | 0.80% | 1.08 | 0.70-1.65 | 0.74 |
| DVT | 1.10% | 1.00% | 1.08 | 0.74-1.58 | 0.39 |
| ED visits | 13.00% | 8.40% | 1.55 | 1.38-1.74 | **<0.001** |
| Inpatient hospitalizations | 20.00% | 17.40% | 1.15 | 1.06-1.24 | **<0.001** |
| Wound complication | 0.54% | 0.52% | 1.04 | 0.61-1.76 | **<0.001** |
| Postoperative infection | 0.19% | 0.19% | 1.00 | 0.42-2.40 | 1 |
| Sepsis | 1.40% | 0.80% | 1.61 | 1.11-2.35 | **0.01** |
| Dysphagia | 6.90% | 5.80% | 1.22 | 1.04-1.43 | **0.014** |

DVT = deep vein thrombosis, ED = emergency department, MI = myocardial infarction, NTND = non-tobacco nicotine dependence, PE = pulmonary embolism, SSI = surgical site infection
Notable values are in bold.

outcomes in NTND and nonnicotine–dependent patients to determine the incidence and risk of postsurgical complications. The effects of nicotine dependence, independent of tobacco use, on surgical outcomes are not well characterized, making this research important for understanding the risks and informing clinical practices for this growing patient population. At the 3-month follow-up, we found higher rates of dysphagia, postoperative wound complications and infections, and sepsis in the nontobacco nicotine–dependent group. At the 2-year postoperative follow-up, certain complications, including pseudarthrosis, adjacent segment disease, and need for revision, were more common in the nontobacco nicotine–dependent cohort.

Our study is the first to evaluate nontobacco nicotine use and cervical spinal outcomes. Historically, tobacco use and cervical spinal outcomes were well described, and tobacco use and poor patient outcomes after c-spine surgery is well documented in the literature. Smoking before cervical spinal surgery is associated with negative patient-reported outcomes, higher reported pain scores, increases in overall complication rate, slower healing time, higher rate of wound infection, and higher rates of future revision surgery.[8,10,14,17-22] Jackson and Devine, in 2016, evaluated the previous literature on lumbar and cervical spinal surgical outcomes in smoking patients. In surgical lumbar spine patients, studies have shown markedly higher rates of nonunion and pseudarthrosis.[9,10,23,24] For surgical cervical spine patients, nonsignificance or no association was found in all studies that examined postoperative nonunion and fusion rates for ACDF.[12–15,25,26] Smoking cessation was found to decrease negative outcomes, even in studies with nonsignificance. Even chewing tobacco has been correlated with increased likelihood of pseudarthrosis and postoperative complications, including DVT,

**Table 3.** Two-Year Outcomes in 1:1 Propensity Matched Analysis in Nontobacco Nicotine Dependence Versus Control Patients

| Condition | % of Outcomes NTND Cohort | % of Outcomes Control | Risk Ratio (RR) | 95% Confidence Interval (CI) | *P* |
|---|---|---|---|---|---|
| Pseudarthrosis | 14.00% | 9.60% | 1.46 | 1.31-1.63 | **<0.001** |
| Adjacent segment disease | 3.70% | 2.20% | 1.69 | 1.34-2.14 | **<0.001** |
| Implant failure | 0.70% | 0.60% | 1.3 | 0.81-2.09 | 0.277 |
| Revision ACDF | 2.00% | 1.40% | 1.42 | 1.06-1.91 | **0.02** |

ACDF = anterior cervical diskectomy and fusion, NTND = nontobacco nicotine dependence
Notable values are in bold.

pulmonary emboli, and myocardial infarction after spine surgery.[27]

The specific findings of this study largely correspond to the previous literature. Smoking before cervical spine surgery is a well-known risk factor for developing dysphagia.[28,29] The pathophysiologic cause of this complication is not understood, but we theorize that a restrictive airway caused by chronic irritation increases postoperative inflammation and symptoms of dysphagia. More research is necessitated to characterize the underlying cause. Wound complications are also known complications of chronic smokers after orthopaedic procedures.[30,31] Our study indicated sepsis as a notable complication for NTND, and although severe soft-tissue infections have been reported, we believe that more research on sepsis is necessitated as it is not well characterized in the literature.[32]

Whether nontobacco nicotine use has better outcomes than tobacco use is still not well described, and research on nontobacco nicotine use is sparse. Recently studies, including one by DeShazo et al on total knee arthroplasty, have shown that patients with NTND are at a higher risk of postoperative complications such as DVT, PE, and sepsis, while another study investigating shoulder arthroplasty reported higher risks of prosthetic dislocation, prosthetic joint infection, and mechancial loosening in NTND cohort.[33,34] In addition, although previous studies have shown that the negative effects of cigarette use on cervical fusion have failed to reach statistical significance, our study shows that the cohort with nonnicotine tobacco use have statistically significant diminished clinical outcomes in several areas. More research on NTND patients needs to be conducted to fully elucidate its effects on surgical outcomes.

However, smoking cessation has been evaluated as a protective preoperative factor. Ninety days before lumbar spinal fusion smoking cessation decreases all-cause postoperative complications when compared with those who actively smoked up until the day of surgery.[35] Other research has found that patients with painful spinal syndromes, including postoperative pain, who ceased smoking, regardless of smoking history, experienced clinically notable improvement in pain scores. Those who continued to smoke during treatment had no improvement in reported pain.[36] Important to note that this was in geriatric patients, however, so responses may vary by patient population and age. Smoking cessation for at least 6 months after spinal fusion surgery is associated with lower nonunion rates and higher return-to-work rates.[9] As previously mentioned, Jackson and Devine, in 2016, reported that smoking cessation reduced their cervical spine fusion surgical complications in a dose-dependent manner by duration of abstinence.

Although nontobacco nicotine products have been helpful for smoking cessation and are mainly used by smokers,[37–39] orthopaedic surgeons should encourage their patients to stop all nicotine products, especially before undergoing a major operation like cervical spine surgery. Currently, the American Academy of Orthopaedic Surgeons urges patients to quit smoking before surgery, and the American College of Surgeons recommends to end all tobacco use before elective surgery.[40,41] E-cigarettes have similar rates of wound healing and reduction in angiogenesis as cigarette smoke, and clinicians are encouraged to treat both products similarly.[42,43] We believe that with the results of this study, and the abundance of research on smoking as a proxy for nicotine, that guidelines should be updated to include nontobacco nicotine cessation as part of its general preoperative criteria.

Although our study provides valuable contributions to the literature regarding nontobacco nicotine use and spinal fusion outcomes, there are inherent limitations to this retrospective study. To start, although our study examines the effects of nontobacco nicotine on patients undergoing cervical spinal fusion, it is important to recognize that the nicotine in nontobacco products is chemically identical to that in tobacco products. Therefore, any differences observed in this study may be attributed to variations in nicotine concentration, as well as differences in the delivery methods, which may increase the risk of surgical complications. This aspect warrants further investigation in future studies. In addition, patient selection was largely based on medical history indicated with ICD-10 codes. This process is vulnerable to several factors such as ICD-10 code inaccuracies and heterogeneity, resulting in potential missed cases or misclassification of patients. This potentially contributed to the markedly different demographic characteristics between the two cohorts. Opioid abuse was also defined using the ICD-10 code F11.1 to categorize patients with new-onset opioid abuse postoperatively, which is different from opioid dependence, which is F11.2. We recognize that providers may have different interpretations of the criteria used in these ICD-10 codes and may limit the ability to properly interpret the opioid use data in the study. Moreover, our study is limited by the variability of nicotine use among patients, specifically the method of nicotine delivery, dose, duration of use, and accuracy of reporting within the database. Finally, a potential limitation of this study is the

inherently present selection bias in using large databases like TriNetX, as it relies on data from large contributing healthcare institutions, which may not fully represent the broader population, potentially affecting the generalizability of the results.

## Conclusion

The use of nontobacco nicotine is increasing at a notable rate. At present, the amount of research on nontobacco nicotine use dependence and its effects on surgical outcomes is minimal. Our study of 10,644 patients found that nontobacco nicotine–dependent patients had a higher incidence of sepsis, inpatient hospitalizations and opioid use at the 3-month follow-up, and higher rates of implant failure and pseudarthrosis at 2 years postoperation.

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