INTRODUCTION

The detrimental health effects of smoking tobacco are well known. Smoking tobacco increases the risks of postoperative complications, many of which are germane to plastic surgery and outpatient surgery populations. Smoking has a transient effect on the tissue microenvironment and a prolonged effect on the reparative cell functions leading to delayed healing and complications. Smoking cessation restores tissue oxygenation and metabolism rapidly. The minimum duration of abstinence necessary to confer benefit from smoking cessation is unknown.

Patients undergoing surgery with preoperative smoking cessation interventions have been shown to have increased rates of smoking cessation of 50–70% when combined with nicotine replacement therapy (NRT). However, the perioperative effect of NRT for abstinent smokers has been controversial, with current opinion that any adverse effects are negligible or inconsequential. Wound infection rates have been found to be no different among abstinent smokers with concurrent use of transdermal nicotine patch compared with placebo. There are no studies to our knowledge that demonstrate any type of increased perioperative complication risk with NRT.

The literature regarding nicotine replacement strategies has only recently started to include electronic cigarettes. The electronic cigarette (or e-cig, vaping) is an electronic nicotine delivery system (ENDS) that was introduced onto the market last decade and has seen rapid growth in use worldwide. ENDS aim to address the behavioral and sensory aspects of smoking, but their effect on perioperative complications is unknown.

Background: E-cigarettes, nicotine transdermal patches, and nicotine chewing gum are occasionally used as cigarette replacements by patients, but it is unknown if their use is a safe alternative to smoking in the perioperative period.

Methods: All patients undergoing major surgery at a single outpatient ambulatory surgery center for a 5-year period were tested for urine cotinine, a nicotine metabolite, the day of surgery. Patients were divided into 4 groups: never smoked (group A), quit smoking with negative urine test (group B), continued to smoke (group C), and quit smoking with positive urine test (group D). Statistical significance of complications among groups was tested using right tailed chi-square test and point biserial correlation coefficient calculations. To control for confounding factors, age and BMI of each group were compared using unequal sample size and variance t tests.

Results: Four hundred seventy patients were included in the study. Patient count in each group was group A n = 380, group B n = 48, group C n = 92, and group D n = 10. Complication frequency was as follows D > C > A > B. Statistically significant differences were observed between D + C (cotinine positive) and A + B (cotinine negative) P = 0.0001 and between D (nicotine replacement) and B (nicotine abstinence) P = 0.00026. There was neither statistical difference between groups A and B, nor C and D.

Conclusions: Nicotine replacement carries similar risks as continued smoking and is not as safe as abstinence in the perioperative period in plastic surgery patients. Importantly, patients who stopped smoking for the surgery had equivalent risk for postoperative complications as patients who had never smoked.
Studies including a recent randomized controlled trial have shown the ENDS to be at least as effective as transdermal patch in achieving smoking cessation. A recent U.S. (Texas) study shows that 17.2% of adults have tried an ENDS and the rate among smokers is over 60%. The trend of increased usage of the ENDS has also been noted among our plastic surgery patients. Evidence suggests a risk reduction with ENDS compared with tobacco cigarettes, as they contain fewer toxins. Although patients are routinely counseled to stop smoking before their operation, some are unable to quit.

As a quality improvement project, we aimed to assess our postoperative complication rates among patients using NRT, which included ENDS, nicotine gum, and patches. We hypothesized that evidence would demonstrate a decreased rate of postoperative complications when compared with tobacco smoking.

**METHODS**

The study was a 5-year prospective study that included patients undergoing surgery by either of 2 surgeons at an outpatient surgery center between (1/1/2012-12/2016). Data were compiled in 2017; hence, no selection bias or practice patterns were changed during the study. Patients were informed that they should not smoke for four weeks before and six weeks after their surgery date. Each patient consented to taking part in the study and allowed their urine to be tested the day of surgery. The patients were encouraged to stop all nicotine use, but if necessary, nonsmoked nicotine (ie, transdermal patch, chewing gum, ENDS) would be tolerated. Cotinine is the predominant metabolite of nicotine and is commonly used as a biomarker to monitor nicotine exposure. The simple urine stick test cost $3.80 and was performed at the same time as urine pregnancy tests if appropriate. The urine cotinine level was measured in patients undergoing major flap surgery or having general anesthesia. It was explained that if their urine was found to contain evidence of nicotine, their surgery may be canceled. Patients were followed by the surgeons for 6 weeks to monitor for postoperative complications. Postoperative complications included any unplanned outcome requiring medical attention or return to the operating room. The complications found were wound dehiscence, flap loss (both major and minor), capsule formation (Baker 3 or 4), hematoma, and seroma. We then divided the patients into 4 groups: non-nicotine users (group A), smokers remaining abstinent with a negative urine test (group B), smokers with positive urine test (group C), and nonsmoked nicotine users (group D). Any patient that had not used tobacco in at least 12 months was designated as a non-nicotine user.

Statistical analysis comparing the groups was performed using right-tailed chi-square test and point biserial correlation coefficient calculation. To control for confounding factors, age, and BMI of each group was compared using unequal sample size and variance t test. All statistical conclusions were supported using the power calculation for right-tailed chi-square tests. Power in this context is mathematically defined as 1 - P[A] where A is the area of the chi-square distribution outside of the confidence interval, “alpha” (0.05 for this study), and P[A] is the probability of observing activity in that area.

An institutional review board at Berkshire Medical Center, Pittsfield, Mass., reviewed and approved the study protocol.

**RESULTS**

A total of 470 patients were included in the study (Figs. 1, 2). There were 428 patients who tested negative for cotinine and 42 positive for cotinine, with a complication rate of 9% (n = 38) and 31% (n = 13), respectively. This demonstrated a significantly higher complication rate ($P = 0.0001$, power = 0.99) among patients testing positive for cotinine in their urine (Tables 1, 2). Of the

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**Study Layout**

![Study Layout Diagram](image)

**Fig. 1.** A graphic of the number of the patients involved in the study. Diagram includes patients testing positive/negative for cotinine (a nicotine metabolite). Four subgroups were analyzed including nonsmokers, previous smokers, tobacco smokers, and nonsmoked nicotine users.
patients testing negative for cotinine, 380 were non-nicotine users (group A) and 48 were previous smokers that had remained abstinent from tobacco use (group B). The complication rate in group A was 9% and group B was 6%, not a statistically significant difference ($P = 0.496$, power = 0.90). Of the 42 patients positive for cotinine, 32 patients were tobacco smokers (group C) and 10 patients reported using nonsmoked nicotine sources (group D). The complication rate in group C was 25% and group D was 50%, also not a statistically significant difference ($P = 0.431$, power = 0.32). Regarding the safety of nonsmoked nicotine sources, group B complication rate was significantly lower than that of group D, 6% and 50%, respectively ($P = 0.00026$, power = 0.95). There was no significant difference in patient age and BMI among the 4 groups. Average age and BMI, respectively, non-nicotine users (48.5, 25.2), smokers remaining abstinent (48.5, 25.2), smokers (49.2, 25.8), and nonsmoked nicotine users (44.2, 26.38). All complications are listed in Table 2. Surgery performed in each group are listed in Table 3.

**DISCUSSION**

Results of this study demonstrate that the impact of NRT including the ENDSs as part of a smoking cessation strategy does not appear to reduce the risk of perioperative complications compared with smoking in plastic surgery patients. This is the first study to include ENDS in NRT among plastic surgery patients. This suggests that although ENDS users are not exposed to cigarette smoke, similar nicotine delivery efficacy and toxin exposure related to ENDS usage carries an increased risk of perioperative complications compared with patients with no nicotine usage.

There were 470 patients in the study, 90 of which were nicotine users at the start. Forty-eight of those nicotine users were able to stop using nicotine without replacement. These abstinent smokers decreased their complication rate in our study to levels comparable to nonsmokers. Those patients who continued to use nicotine, either smoked or not smoked, had significantly increased risk of postoperative complications. Although we observed a trend that nonsmoked nicotine was associated with more postoperative complications than smoked nicotine (50% versus 25%) due to small numbers, we were unable to demonstrate statistical significance. Assuming the same distribution of results, 106 additional patients with positive cotinine (148 total) would be needed to obtain a statistical power of 0.80 for this test and a statistical power of 0.90 would require 158 additional patients with positive cotinine (200 total).

Early studies evaluating the efficacy of nicotine delivery among different ENDS brands demonstrated that ENDS achieved lower levels of serum nicotine than tobacco cigarette smoking or NRT. However, a more recent study evaluating the cotinine levels among experienced ENDS users in a real-life setting more representative of actual ENDS usage, which suggests similar nicotine delivery efficacy, Saliva cotinine levels in ENDS users reached similar levels previously observed in smokers and higher than levels previously found in NRT users differs and is not consistent among the different products sold by individual companies. Of concern is that newer generana.  

**Table 1. Statistical Analysis**

| Comparison          | Result          | $P$   | Correlation Coefficient |
|---------------------|-----------------|-------|-------------------------|
| A + B versus C + D  | $C + D > A + B$ | 0.0001| $r = 0.354$             |
| A versus B          | No difference   | 0.497 | $r = -0.04$             |
| C versus D          | No difference   | 0.135 | $r = -0.264$            |
| B versus D          | $D > B$         | 0.0003| $r = 0.56$              |

Comparisons of groups complication rates and corresponding statistical analysis demonstrating significantly more complications in cotinine positive urine compared with negative urine ($A + B$ versus $C + D$). Also significantly more complications in nonsmoked nicotine users compared with abstinent smokers ($D > B$).
tion devices are much more efficient at nicotine delivery compared with first-generation devices. Improvements in technology of the devices may help explain the similar nicotine levels observed among tobacco smokers and ENDS users. The usage of electronic cigarettes has been shown to cause a significant reduction in cutaneous blood flow, which could negatively impact wound healing. This fact provides further evidence of the significant physiological changes that result from electronic cigarette usage leading to increased postoperative complications.

The ENDS utilizes a combination of the following 6 constituents: propylene glycol, glycerin, nicotine, ethanol, acetol, and propylene oxide. Propylene glycol or glycerin is commonly used as a medium that is heated until aerosolized resulting in emission of toxin/carcinogens of more than 31 toxic compounds that have been clearly documented to be harmful. Perhaps, the presence of these carcinogens place patients at a higher risk of perioperative complications when used as part of NRT strategy.

Limitations of this study include that tobacco usage and nicotine replacement methods were self-reported and individual usage habits and doses of the patients were not captured. Self-reporting data collection would not eliminate the possibility of concurrent tobacco smoking and nicotine replacement strategy. Future studies could better monitor nicotine usage and modality used with the addition of abansine testing, a metabolite produced during tobacco smoking. Abansine testing would allow investigators to differentiate between tobacco smoking or ENDS as source of nicotine.

**CONCLUSIONS**

Results of this study demonstrate that usage of NRT in the perioperative period is not associated with a reduced risk of perioperative complications when compared with tobacco smoking. This suggest that although patients using nicotine replacement including ENDS are not exposed to cigarette smoke, there is still detrimental nicotine and toxin delivery. As ENDS become more commonplace in nicotine replacement therapies and increasingly perceived by patients as a safe alternative to tobacco smoking, plastic surgeons must take care in recommending ENDS usage or any other NRT in smoking cessation efforts, given the amount of uncertainty that still remains regarding its safety. Policies and practice should still advocate for smoking cessation in the plastic surgery patient population. Further research is needed to determine the safety of nicotine replacement therapies as part of smoking cessation in the perioperative period to reduce tobacco-related surgical complications in plastic surgery patients.

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