Published in final edited form as:

Head Neck. 2016 May ; 38(5): 700–706. doi:10.1002/hed.23944.

Tobacco Use and Surgical Outcomes in Head and Neck Cancer Patients

Jeanne L. Hatcher, MD,

Department of Otolaryngology – Head and Neck Surgery, Wake Forest School of Medicine, Winston-Salem, NC

Katherine R. Sterba, PhD, MPH,

Department of Public Health Sciences, Medical University of South Carolina, Charleston, SC

Janet A. Tooze, PhD, MPH,

Department of Biostatistical Sciences, Wake Forest School of Medicine, Winston-Salem, NC

Terry A. Day, MD,

Department of Otolaryngology – Head and Neck Surgery, Medical University of South Carolina, Charleston, SC

Matthew J. Carpenter, PhD,

Department of Psychiatry and Behavioral Sciences, Medical University of South Carolina, Charleston, SC

Anthony J. Alberg, PhD, MPH,

Department of Public Health Sciences, Medical University of South Carolina, Charleston, SC

Christopher A. Sullivan, MD,

Department of Otolaryngology – Head and Neck Surgery, Wake Forest School of Medicine, Winston-Salem, NC

Nora C. Fitzgerald, MS, and

Department of Biostatistical Sciences, Wake Forest School of Medicine, Winston-Salem, NC

Kathryn E. Weaver, PhD, MPH

Department of Social Sciences and Health Policy, Wake Forest School of Medicine, Winston-Salem, NC

Abstract

Background—Tobacco use is a risk factor for head and neck cancer, but effects on postoperative outcomes are unclear.

Corresponding Author: Jeanne L. Hatcher, MD, 550 Peachtree Street, 9th Floor, Suite 4400, Atlanta, GA 30308, (404) 778-3381, jeanne.hatcher@emory.edu.

The authors have no conflicts of interest to report.

Publisher's Disclaimer: This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process which may lead to differences between this version and the Version of Record. Please cite this article as an 'Accepted Article', doi: 10.1002/hed.23944

Methods—Head and neck cancer patients (N=89) were recruited before surgery. We assessed self-reported tobacco use status (never, former current) at study entry and recent tobacco exposure via urinary cotinine on surgery day. Outcomes included length of hospital stay (LOS) and complications.

Results—Most participants reported current (32.6%) or former (52.8%) tobacco use; 43.2% were cotinine positive on surgery day. Complications occurred in 41.6%; mean LOS was 4.0 and 8.8 days in patients who received low and high acuity procedures, respectively. Current and former smokers were over six times more likely to have complications than never smokers ($p=.03$). For high acuity procedures, LOS was increased in current (by 4.4 days) and former smokers (by 2.3 days, $p=0.02$).

Conclusions—Tobacco use status is associated with postoperative complications and may distinguish at risk patients.

Keywords

Tobacco; Cotinine; Head and Neck Cancer; Length of Stay; Postoperative Complication

Introduction

Tobacco use is the primary risk factor for head and neck cancer^{1, 2}. Roughly half of patients report smoking at the time of diagnosis and one third continue to smoke during treatment³⁻⁵. Risk factors for continued smoking among head and neck cancer patients include having relatives at home who smoke, greater nicotine dependence, less severe disease, less extensive treatment, and treatment completion^{3, 5, 6}. The 2014 Surgeon General's Report highlights that smoking is related to both cancer-specific and all-cause mortality in cancer patients⁷. In addition, continued tobacco use during and after cancer treatment increases risk for cancer recurrence, second primary cancers, decreased quality of life, poor wound healing, skin and mucosal toxicities, and decreased survival time^{4, 8-15}.

In contrast to the well-documented long-term effects of tobacco use, less is known about some of the short-term consequences, particularly during and immediately following cancer treatment. Some studies have demonstrated the detrimental effects of smoking on surgical wounds¹⁶⁻¹⁹ but these have been mixed with regard to the relationship between tobacco use and post-operative outcomes, particularly within head and neck surgical patients. Tobacco use has been associated with infection, hemorrhage, fistula formation, as well as free flap necrosis in some studies²⁰⁻²¹. Other studies have reported no association with fistula formation or free flap survival^{10, 22-23}. Recently, Pattani and colleagues²⁴ observed that tobacco users undergoing head and neck reconstruction had increased medical complications and increased length of postoperative hospital stay.

The existing research linking tobacco use to negative surgical outcomes has several methodological limitations. First, most studies define tobacco status using either self-report or abstracted medical record data, both of which are subject to systematic measurement error. Studies find that self-reported tobacco use is often discordant with objective biomarkers of smoking, such as cotinine, the major metabolite of nicotine, particularly for

recent quitters^{25, 26}. Few studies investigating tobacco use and surgical outcomes of head and neck cancer patients utilize an objective measure of tobacco use. In one study that did use both self-report and cotinine measurement, elevated cotinine was significantly associated with flap complications, but self-reported tobacco use was not²⁷. Second, most studies are based on retrospective designs. Third, the timing of the assessment of tobacco exposure has varied significantly across studies. Using historical or self-reported data with inconsistent proximity to surgery date limits ability to make conclusions concerning the relationships between smoking and surgical outcomes.

The present study addresses each of these limitations with a prospective examination of tobacco use and its relationship with head and neck cancer surgical outcomes, using two measures of tobacco use while controlling for other clinical factors. We examined the relationship between tobacco use, as assessed by both cotinine level on the day of surgery and self-reported smoking status at study entry, on postoperative length of hospital stay and surgical complications in head and neck cancer patients.

Materials and Methods

This prospective study was conducted at two academic medical centers in North and South Carolina, with Institutional Review Board approval from both centers. Patients were recruited from June 2011 to October 2012. Eligible participants were those 18 years and older with a stage I-IV squamous cell carcinoma of the upper aerodigestive tract scheduled to undergo a major surgical procedure. Procedures included any combination of tumor resection, neck dissection, and/or reconstruction. Minor surgical procedures such as endoscopy or biopsy were excluded.

Potential participants were identified through institution administrative and clinical databases and approached in outpatient clinics for recruitment. After written informed consent was obtained, participants completed a baseline questionnaire in person, by telephone or mail and received a gift card. Questionnaires assessed demographic factors including age, gender, race/ethnicity, and health insurance coverage (private versus public). Current or past tobacco use was assessed via validated questions from the Tobacco Use Supplement to the Current Population Survey²⁸ for: 1) history of smoking (smoked at least 100 cigarettes in life, yes or no), 2) current cigarette use (every day or some days versus not at all), 3) ever use of other tobacco products (smokeless, pipes, cigars, and others) and 4) current use of other tobacco products (every day or some days versus not at all). We categorized patient's self-reported smoking status at study entry as never users (smoked <100 lifetime cigarettes and no history of other tobacco products), former users (any history of cigarette or other tobacco use, but no current use), and current users (every day or some day use of cigarettes and/or other tobacco products).

On the day of surgery, recent tobacco exposure was assessed by urinary cotinine using NicAlert®, a semi-quantitative colorimetric immunoassay developed by Nymox Pharmaceutical Corporation (Hasbrouck Heights, NJ, USA). The NicAlert® test strip provided a result numbered 0-6, and a value of 3 or greater from a urine sample indicates positive tobacco use in the previous 48 hours²⁹. This cutoff was 95.0% sensitive and 94.8%

specific for detecting tobacco use relative to urinary cotinine concentration by liquid chromatography tandem mass spectrometry in prior studies³⁰. Two months after surgery, the medical record was reviewed and the following clinical factors were assessed:

1. Postoperative length of hospital stay (LOS) in days calculated using surgical and discharge dates.
2. Postoperative complications: categories included vascular, pulmonary, renal, acute blood loss anemia, ethanol withdrawal, wound, and other complications such as urinary tract infection, or delirium unrelated to ethanol withdrawal.
3. Acuity of the surgical procedure (high or low); Surgical procedure acuity was derived from an adapted rating protocol derived from that originally described by authors at MD Anderson Cancer Center^{31, 32}. High acuity procedures were considered as those which involved a surgical defect involving both skin and mucosal surfaces or a defect requiring pedicled or free flap reconstruction. Low acuity procedures included a surgical defect not including both skin and mucosal surfaces or neck dissections alone. Procedural acuity was reviewed for each case independently by two of the clinical study team members; discrepancies were discussed and resolved by consensus.
4. Type of procedure: resection, neck dissection, reconstruction, or combinations of these procedural categories.
5. American Society of Anesthesiologists (ASA) score³³: determined by the anesthesiologist, an ASA of 1 or 2 includes healthy persons or those with mild systemic disease. Severe systemic disease or that which is a constant threat to life results in an ASA of 3 or 4.
6. Duration of surgery in hours.

In addition, we collected information from the medical record on a) diagnosis type (new, recurrent/persistent disease), b) tumor stage and location, as per American Joint Committee on Cancer (AJCC) TNM staging system³⁴, c) previous treatment (surgery, chemotherapy, or radiation), and d) medical comorbidities present prior to surgery, including cardiovascular (hypertension, coronary artery disease, congestive heart failure, cerebrovascular and peripheral vascular disease), pulmonary (chronic obstructive pulmonary disease and asthma), diabetes mellitus, chronic renal insufficiency, and other conditions noted in the preoperative assessment.

Data Analysis

We calculated descriptive statistics to describe the study population and their characteristics on the day of surgery. Because variance differed by acuity group and for ease of interpretation, we utilized general linear models stratified by procedure acuity to quantify the relationship between tobacco use and postoperative length of stay. First we fit unadjusted models for tobacco status at baseline and for cotinine status on the day of surgery. Next, to evaluate potential confounding, possible covariates (age, gender, non-Hispanic white race/ethnicity, insurance status, stage (I/II/III vs IV), tumor site, (oral cavity, oropharynx, hypopharynx/larynx, and other), recurrent or persistent disease, previous chemotherapy or

radiation, number of procedures (resection, neck dissection, reconstruction), number of comorbidities, hours of surgery, ASA score (1-2 vs. 3-4)) were individually added to the univariate models, and factors significant at the $p < 0.20$ level were retained in the final multivariable model.

Frequencies of postoperative complications by acuity, cotinine status, and tobacco use at baseline were calculated. Differences in these frequencies were assessed using chi-square tests and Fisher's exact tests. Rate ratios, the ratio of the complication rates by tobacco use, were calculated overall and by acuity group. We fit an acuity-adjusted logistic regression model to evaluate the impact of tobacco use on having any complication using the same procedure described above to introduce covariates. The final adjustment covariates were acuity, race/ethnicity, AJCC stage (1/2/3 vs 4), tumor site, number of procedures, hours of surgery, and ASA score (1/2 vs 3/4). All tests were two-sided with an alpha level of 0.05 and performed in SAS (v 9.3, Cary, NC, USA).

Results

Patient Characteristics

We approached 163 potential participants in the clinic and enrolled 129 (79% enrollment rate). Eighty-nine enrolled participants had complete data for analysis (with one participant missing cotinine). The majority of participants were male (74.2%) and either former smokers (52.8%) or current tobacco users (32.6%) at baseline (Table 1). The mean time between last tobacco use and study enrollment in the former smoker group was 9 years (SD=9.6, range .03 to 36 years). More than half (53.9%) had advanced stage disease and 42.7% had recurrent or persistent disease. At the time of enrollment in the study, the vast majority of patients had some other medical comorbidity (87.6%), the most common being vascular disease (61.8%), pulmonary disease (19.1%), and diabetes (15.7%). Seventy-two patients (80.9%) had an ASA score of 3 or 4 at the time of surgery. Over half of patients underwent a complex surgical procedure including tumor resection, neck dissection, and reconstruction. High acuity procedures were more common (71.9% vs 28.1% low acuity). There was 86% agreement between self-reported tobacco use (at study entry) and urinary cotinine (on day of surgery). The agreement amongst never smokers was 100%.

Length of Stay

The unadjusted mean LOS was 4.0 days for low acuity procedures, and 8.8 days for high acuity procedures. On average never smokers with low acuity procedures were discharged 1.5 days sooner (least square mean LOS = 2.1 days) than those who were current (least square mean LOS = 3.9 days) or former smokers (least square mean LOS = 3.6 days) in adjusted models, although this difference did not reach statistical significance. The adjusted means for those with positive and negative cotinine status were similar in unadjusted and adjusted models (Table 2).

For the high acuity procedure group, we observed significant differences in LOS by self-reported tobacco use in unadjusted models, with means of 6.1 days for never smokers, 8.4 days for former smokers, and 10.5 days for current smokers (p for trend=0.02); these

differences were not statistically significant in adjusted models (p for trend=0.13). Again, the adjusted mean LOS for those with positive and negative cotinine were similar (8.9 and 8.2 days, respectively).

Postoperative Complications

Postoperative complications were observed in 16.0% of the patients in the low acuity group and 51.6% of the patients in the high acuity group ($p = 0.002$). A general pattern of greater complications in the high acuity patients was observed, with the greatest differences in acute blood loss anemia and wound complications ($p = .02$ and $p = .03$, respectively).

Self-reported tobacco use at study entry was significantly associated with postoperative complications (Table 3). Compared with never smokers, former and current smokers had complication rate ratios of 6.1 and 6.3 respectively. This was primarily driven by differences among the high acuity patients, among whom current smokers had rate ratios of almost six, as compared to never smokers (58.3% vs. 10% respectively). The most prevalent complication types were pulmonary, acute blood loss anemia, and wound, but none of the rates of these individual complications were statistically significantly different by smoking history. Complication rates remained significantly higher in current or former smokers compared to never smokers after covariate adjustment (data not shown). In contrast, cotinine level was unrelated to postoperative complications (Table 4).

Discussion

It is well established that tobacco use is associated with poor cancer outcomes, including cancer recurrence, second primary cancers, decreased quality of life, poor wound healing, skin and mucosal toxicities, and decreased survival time^{4, 7-15}. This study was carried out to assess the impact of tobacco use on acute treatment outcomes: LOS following surgical treatment and rates of postoperative complications in head and neck cancer patients. We observed high rates of ever and current tobacco use in our study participants (85.4% of participants were former or current smokers and 43.2% had a positive cotinine test on the day of surgery).

Overall, we observed poorer post-surgical outcomes among both self-reported former and current smokers compared to never smokers. In particular, among patients with low acuity procedures, the adjusted mean LOS for former and current smokers were 71% and 86% longer, respectively, than never smokers; among patients with high acuity procedures, mean adjusted LOS in former and current smokers were 23% and 46% longer respectively, than never smokers. The differences were more striking and statistically significant for postoperative complications, where former and current smokers had complication rate ratios of 6.1 and 6.3 compared to never smokers, respectively.

Biochemically verified current smoking on the day of surgery was not associated with increased LOS or post-operative complication rates. The differences in complication rates and LOS when classifying smoking status by self-report as opposed to cotinine levels on the day of surgery reaffirm the importance of smoking history (and not just current smoking) when assessing risk of post-operative complications in this patient population. This is only

the second study to use cotinine to objectively measure tobacco use in this patient population in conjunction with postoperative outcomes assessment. In contrast to our findings, Marin and colleagues²⁷ observed that elevated cotinine, but not self-reported smoking history, was correlated with postoperative wound complications. Differences in findings may be due to the narrower study population and outcomes in the Marin study (wound complications following microvascular reconstruction only). We further explore issues surrounding concordance of self-report and urinary cotinine on the day of surgery in a second report from this study. Further research is necessary to assess the predictive value of cotinine for postoperative complications in a diverse sample of head and neck cancer patients. Even though cotinine level on the day of surgery was not associated with postoperative complications, this does not minimize the importance of biological verification of smoking status in this or any other patient population. Given that many patients will misreport their smoking status³⁵, and the long-standing association between smoking and outcomes of cancer treatment^{4, 7-15}, the need to accurately identify, assess, and provide cessation treatment to all smokers is critical.

The trend of increased LOS among current smokers (unadjusted mean difference of > 3 days more than never smokers) has both clinical and economic impact. Increased LOS has been linked to poor quality of life, increased risk of iatrogenic events including nosocomial infection, and delay in beginning adjuvant therapy for surgical oncology patients potentially worsening prognosis³⁶⁻³⁸. It has been estimated that similar complications to ones examined in this study may result in additional per patient costs of \$11,000, whereas reduction in complications and LOS have the potential to save hospitals over \$500,000 per year^{39, 40}. Pulmonary complications, commonly seen in this patient population and in our study, can increase overall medical costs by 71%⁴¹. Hospital and physician reimbursement will become more dependent upon quality measures and patient outcomes under U.S. healthcare reform proposals. Current diagnosis-related group (DRG) reimbursement criteria are likely to become more stringent and payers even less likely to reimburse in the setting of extended LOS. In an environment of decreasing reimbursement and unfavorable hospital margins, the cost of treating smoking-related complications will continue to create financial pressure and instability in the healthcare system.

This study is one of few to examine the effects of tobacco not only according to patient history, but also with an objective measure to provide more detailed information about the type of tobacco exposure (i.e., historical or immediate) and its impact on surgical outcomes. The prospective design and control of multiple clinical covariates in statistical analysis including the number of procedures involved, duration of surgery, presence of comorbidities, and cancer stage were strengths of the data analysis. Yet, several limitations are important to consider. 1) Given the relatively low incidence of specific types of complications, we were unable to determine if there were any differences in specific postoperative complications by tobacco status. Trends may be more apparent with more participants. 2) Due to limited sample size, we were also not able to assess differences within the former smoking group by duration of cessation. Those patients who stop using tobacco within a couple of weeks of surgery may have similar surgical outcomes as those who use tobacco on the day of surgery because medical benefits of quitting may manifest over time¹⁷⁻²⁰. In addition, we were not able to account for longitudinal changes in smoking status during the post-surgical period

that may have impacted complications. Some participants had recently quit smoking resulting in a negative cotinine, though the detrimental effects of tobacco use on pulmonary function may still be present. More pulmonary complications were seen in those with a positive cotinine, although this difference was not statistically significant; a larger sample size would be needed to detect a statistically significant difference of this magnitude. Importantly, the duration of cessation needed to reduce post-operative risk is not known in this patient population and may vary by specific complication. 3) Another consideration not addressed in this study was human papilloma virus (HPV) status of the tumor. Potential interactions between HPV status and smoking status should be examined in future studies.

Conclusions

In this study, self-reported tobacco use history was strongly associated with poorer surgical outcomes after head and neck surgery. This report adds to the growing evidence about the negative effects of tobacco on clinical outcomes in head and neck cancer and emphasizes the continued importance of history of tobacco use. Further research is needed to assess whether smoking cessation interventions improve surgical outcomes among head and neck cancer patients and the duration of cessation needed to derive benefit. Knowledge of past or current tobacco use and the risk for complication in this population may provide an opportunity to implement risk reduction strategies.

Acknowledgments

This research was supported by a joint pilot grant from the Comprehensive Cancer Center of Wake Forest University (CCCWFU) and the Hollings Cancer Center of the Medical University of South Carolina and by the Biostatistics Core of the CCCWFU (P30 CA012197). Data management support (REDCap) provided by the Wake Forest School of Medicine Translational Sciences Institute NCRR/NIH grant M01RR007122. The authors also acknowledge support from the South Carolina Clinical and Translational Research (SCTR) Institute at the Medical University of South Carolina through NIH Grant Number UL1 TR000062.

We thank the following individuals for their assistance with patient recruitment and data collection: Kathryn Josephs-Finlay, Mitch Worley, Martin Piazza, Rebecca Patten, Lee Anne Tetrick, Isaac Dingle, Brendan O'Connell, and Conor McLaughlin.

References

1. Vokes EE, Weichelbaum RR, Lippman SM, Hong WK. Head and neck cancer. *N Engl J Med*. 1993; 328:184–94. [PubMed: 8417385]
2. Argiris A, Karamouzis MV, Raben D, Ferris RL. Head and Neck Cancer. *Lancet*. 2008; 371:1695–709. [PubMed: 18486742]
3. Ostroff JS, Jacobsen PB, Moadel AB, et al. Prevalence and Predictors of Continued Tobacco Use after Treatment of Patients with Head and Neck Cancer. *Cancer*. 1995; 75:569–76. [PubMed: 7812925]
4. Stevens MH, Gardner JW, Parkin JL, Johnson LP. Head and neck cancer survival and lifestyle change. *Arch Otolaryngol*. 1983; 109:746–9. [PubMed: 6639443]
5. Cooley ME, Wang Q, Johnson BE, et al. Factors associated with smoking abstinence among smokers and recent-quitters with lung and head and neck cancer. *Lung Cancer*. 2012; 76:144–49. [PubMed: 22093155]
6. Schnoll RA, Maelstrom M, James C, et al. Correlates of tobacco use among smokers and recent quitters diagnosed with cancer. *Patient Educ Couns*. 2002; 46:137–45. [PubMed: 11867244]
7. U.S. Department of Health and Human Services. The Health Consequences of Smoking - 50 Years of Progress: A Report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human

Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2014.

8. Day GL, Blot WJ, Shore RE, et al. Second cancers following oral and pharyngeal cancers: role of tobacco and alcohol. *JNCI*. 1994; 86:131–7. [PubMed: 8271296]
9. Hiyama T, Sato T, Yoshino K, Tsukuma H, Hanai A, Fujimoto I. Second primary cancer following laryngeal cancer with special reference to smoking habits. *Jpn J Cancer Res*. 1992; 83:334–9. [PubMed: 1506266]
10. Kim AJ, Suh JD, Sercarz JA, et al. Salvage Surgery with Free flap Reconstruction: Factors Affecting Outcome After Treatment of Recurrent Head and Neck Squamous Carcinoma. *Laryngoscope*. 2007; 117:1019–1023. [PubMed: 17545864]
11. Des Rochers C, Dische S, Saunders MI. The problem of cigarette smoking in radiotherapy for cancer in the head and neck. *Clin Oncol*. 1992; 4:214–6.
12. Karim AB, Snow GB, Siek HT, Njo KH. The quality of voice in patients irradiated for laryngeal carcinoma. *Cancer*. 1983; 51:47–9. [PubMed: 6821807]
13. Rugg T, Saunders ML, Dische S. Smoking and mucosal reactions to radiotherapy. *Br J Rad*. 1990; 63:554–6.
14. Porock D, Nikoleeti S, Cameron F. The Relationship Between Factors That Impair Wound Healing and the Severity of Acute Radiation Skin and Mucosal Toxicities in Head and Neck Cancer. *Cancer Nurs*. 2004; 27:71–8. [PubMed: 15108954]
15. Chen AM, Chen LM, Vaughan A, et al. Tobacco smoking during radiation therapy for head-and-neck cancer is associated with unfavorable outcome. *Int J Radiat Oncol Biol Phys*. 2011; 79:414–19. [PubMed: 20399030]
16. Lind J, Kramhoft M, Bodtker S. The influence of smoking on complications after primary amputations of the lower extremity. *Clin Orthop*. 1991; 267:211–217. [PubMed: 2044281]
17. Sorensen LT, Horby J, Friis E, et al. Risk factors for impaired wound healing and infection in breast cancer surgery. *Eur J Surg Oncol*. 2002; 28:815–820. [PubMed: 12477471]
18. Moller AM, Villebro N, Pedersen T, et al. Effect of preoperative smoking intervention on postoperative complications: a randomized clinical trial. *Lancet*. 2002; 359:114–117. [PubMed: 11809253]
19. Sorensen LT, Karlsmark T, Gottrup F. Abstinence from smoking reduces incisional wound infection: a randomized controlled trial. *Ann Surg*. 2003; 238:1–5. [PubMed: 12832959]
20. Haughey BH, Wilson E, Kluwe L, et al. Free flap reconstruction of the head and neck: Analysis of 241 cases. *Otolaryngol Head Neck Surg*. 2001; 125:10–7. [PubMed: 11458207]
21. Nahabedian MY, Singh N, Deune EG, Silverman R, Tufaro AP. Recipient Vessel Analysis for Microvascular Reconstruction of the Head and Neck. *Ann Plast Surg*. 2004; 52:148–55. [PubMed: 14745264]
22. Khouri RK, Colley BC, Kunselman AR, et al. A Prospective Study of Microvascular Free-Flap Surgery and Outcome. *Plast Reconstr Surg*. 1998; 102:711–21. [PubMed: 9727436]
23. Redaelli de Zinis LO, Ferrari L, Tomenzoli D, Premoli G, Parrinello G, Nicolai P. Postlaryngectomy Pharyngocutaneous Fistula: Incidence, Predisposing Factors, and Therapy. *Head Neck*. 1999; 21:131–8. [PubMed: 10091981]
24. Pattani KM, Byrne PB, Boahene K, Richmon J. What Makes a Good Flap Go Bad?: A Critical Analysis of the Literature of Intraoperative Factors Related to Free Flap Failure. *Laryngoscope*. 2010; 120:717–23. [PubMed: 20205243]
25. Hald J, Overgaard J, Grau C. Evaluation of objective measures of smoking status: a prospective clinical study in a group of head and neck cancer patients treated with radiotherapy. *Acta Oncol*. 2003; 42:154–159. [PubMed: 12801134]
26. Morales NA, Romano MA, Michael Cummings K, et al. Accuracy of self-reported tobacco use in newly diagnosed cancer patients. *Cancers Causes Control*. 2013 Jun 24.:1223–30.
27. Marin VP, Pytynia KB, Langstein HN, Dahlstrom KR, Wei Q, Sturgis EM. Serum cotinine concentration and wound complications in head and neck reconstruction. *Plast Reconstr Surg*. 2008; 121:451–7. [PubMed: 18300961]
28. Tobacco Use Supplement to the Current Population Survey. From National Cancer Institute; website: <http://appliedresearch.cancer.gov/studies/tus-cps/>

29. NicAlert® by Nymox product insert. <http://www.nymox.com/default.action?itemid=47>
30. Lee A, Gin T, Chui PT, et al. The accuracy of urinary cotinine immunoassay test strip as an add-on test to self-reported smoking before major elective surgery. *Nicotine Tob Res.* 2013; 15:1690–5. [PubMed: 23516325]
31. Weber RS, Lewis CM, Eastman SD, et al. Quality and performance indicators in an academic department of head and neck surgery. *Arch Otolaryngol Head Neck Surg.* 2010; 136:1212–18. [PubMed: 21173370]
32. Shellenberger TD, Madero-Visbal R, Weber RS. Quality indicators in head and neck operations. *Arch Otolaryngol Head Neck Surg.* 2011; 137:1086–93. [PubMed: 22106231]
33. American Society of Anesthesiologists Score definition: American Society of Anesthesiologists. website: <http://www.asahq.org/Home/For-Members/Clinical-Information/ASA-Physical-Status-Classification-System>
34. American Joint Commission on Cancer staging: AJCC. website: <https://cancerstaging.org/Pages/default.aspx>
35. Warren GW, Arnold SM, Valentino JP, et al. Accuracy of self-reported tobacco assessments in a head and neck cancer treatment population. *Radiother Oncol.* 2012; 103:45–48. [PubMed: 22119370]
36. Bonnema J, VanWersh AMEA, Van Geel AN, et al. Cost of care in a randomized trial of early hospital discharge after surgery for breast cancer. *Eur J Cancer.* 1998; 34:2015–20. [PubMed: 10070303]
37. Penel N, Fournier C, Lefebvre D, et al. Multivariate analysis of risk factors for wound infection in head and neck squamous cell carcinoma surgery with opening mucosa. Study of 260 surgical procedures. *Oral Oncol.* 2005; 41:294–303. [PubMed: 15743692]
38. Wedgwood KR, Benson EA. Non-tumour morbidity and mortality after modified radical mastectomy. *Am R Coll Surg Engl.* 1992; 79:314–317.
39. Genther DJ, Gourin CG. The effect of alcohol abuse and alcohol withdrawal on short-term outcomes and cost of healthcare after head and neck cancer surgery. *Laryngoscope.* 2012; 122:1739–47. [PubMed: 22566069]
40. Chan JY, Sememov YR, Gourin CG. Postoperative urinary tract infection and short-term outcomes and costs in head and neck cancer surgery. *Otolaryngol Head Neck Surg.* 2013; 148:602–10. [PubMed: 23348871]
41. Jones NF, Jarrahy R, Song JI, Kaufman MR, Markowitz B. Postoperative medical complications - not microsurgical complications - negatively influence the morbidity, mortality, and true costs after microsurgical reconstruction for head and neck cancer. *Plast Reconstr Surg.* 2007; 119:2053–60. [PubMed: 17519700]

Table 1

Characteristics of Head and Neck Cancer Patients Undergoing Surgical Treatment

	Patients (N=89)	
	N or Mean	% or SD
Demographics and Clinical Factors		
Age - Mean (SD)	58.8	10.5
Gender - % Male	66	74.2
Non-Hispanic White (%)	73	82.0
Insurance Status (%)		
Private	47	52.8
Public	30	33.7
None	12	13.5
Recurrent disease (%)	29	32.6
Persistent disease (%)	11	12.4
AJCC TNM stage (%)		
• I	19	21.4
• II	7	7.9
• III	15	16.9
• IV	48	53.9
Primary Tumor Site (%)		
• oral cavity	34	38.2
• oropharynx	22	24.7
• hypopharynx or larynx	27	30.3
• other	6	6.7
Previous Treatment with chemotherapy or radiation	30	33.7
Medical Comorbidities		
Any comorbidity	78	87.6
• vascular disease	55	61.8
• pulmonary disease	17	19.1
• diabetes (I or II)	14	15.7
• renal disease (CRI)	1	1.1
Other	65	73.0
Number of comorbidities - Mean (SD)	1.7	1.0
Tobacco Use		
Self-reported Tobacco use at Baseline (%)		
Never	13	14.6
Former	47	52.8
Current	29	32.6
Positive cotinine on day of surgery ^a (%)	38	43.2

	Patients (N=89)	
	N or Mean	% or SD
Surgical Characteristics		
Preoperative Hemoglobin	13.5	1.8
Surgical Procedure Acuity		
Low	25	28.1
High	64	71.9
Type of Surgical Procedure		
Resection only	9	10.1
Neck Dissection only	4	4.5
Resection/Reconstruction	4	4.5
Resection/Neck Dissection	21	23.6
Resection/Neck Dissection/Reconstruction	51	57.3
ASA Score		
1 or 2	17	19.1
3 or 4	72	80.9
Hours of Surgery - Mean (SD)	8.4	3.9
LOS (days, mean (SD))		
Low Acuity	4.0	2.4
High Acuity	8.8	4.9

^aN=88; positive cotinine was result 3 using NicAlert® test kit;

AJCC: American Joint Committee on Cancer

ASA: American Society of Anesthesiologists

LOS: length of hospital stay

Least Squares Means of Length of Hospital Stay (LOS) following Head and Neck Cancer Surgical Procedure by Acuity, Cotinine, and Tobacco Status

Table 2

	N	LOS unadjusted		p-value	LOS adjusted*		p-value
		Mean	SE		Mean	SE	
Low Acuity	25						
Self-Reported Tobacco use				0.58 (trend test)			0.30
Current	5	4.1	0.8	0.81	3.9	0.9	0.27
Former	11	4.4	0.7	0.51	3.6	0.9	0.30
Never	9	3.2	1.1	ref	2.1	1.5	ref
Cotinine Status							
Positive	11	4.2	0.7	0.80	3.8	0.9	0.97
Negative ^a	14	3.9	0.6		3.8	0.6	
High Acuity	64						
Self-reported Tobacco use				0.02			0.13
Current	8	10.5	1.1	0.03	9.8	1.4	0.15
Former	36	8.4	0.8	0.23	8.3	0.9	0.40
Never	20	6.1	1.7	Ref	6.7	1.7	ref
Cotinine Status							
Positive	27	9.6	0.9	0.26	8.9	0.9	0.56
Negative	36	8.2	0.8		8.2	0.8	

* Adjusted for Number of Procedures, Number of Comorbidities, Hours of Surgery, Surgery for Persistent or Recurrent Disease, and AJCC Stage (I/II/III vs IV).

^a Negative cotinine was considered test result <3 using NicAlert®.

Table 3
Incidence of Postoperative Complications among Head and Neck Cancer Surgical Patients by Self-Reported Tobacco Use Status

	All Participants N=89 (%)	Never (N=13)		Former (N=47)		Current (N=29)		p- value ^d
		N	%	N	%	N	%	
Any complication	37 (41.6%)	1	7.7	22	46.8	14	48.3	0.03
Low acuity (N=25)	4 (16.0%)	0	0.0	3	23.1 (3/13)	1	10.0 (1/10)	0.50
High acuity (N=64)	33 (51.6%)	1	10.0 (1/10)	23	52.3 (23/44)	14	58.3 (14/24)	0.03
Vascular	3 (3.4%)	1	7.7	2	4.3	0	0.0	0.26
Pulmonary	11 (12.4%)	0	0.0	5	10.6	6	20.7	0.21
Acute blood loss anemia	12 (13.5%)	0	0.0	6	12.8	6	20.7	0.22
Wound	16 (18.0%)	0	0.0	10	21.3	6	20.7	0.20
Low acuity (N=25)	1 (4.0%)	0	0.0	1	9.1(1/11)	0	0.0	1.00
High acuity (N=64)	15 (23.4%)	0	0.0	9	25.0 (9/36)	6	30.0 (6/20)	0.26
Ethanol withdrawal	4 (4.5%)	0	0.0	2	4.3	2	6.9	0.81
Other complications	7 (7.9%)	0	0.0	4	8.5	3	10.3	0.75

^dFrom Fisher's exact test

Table 4
Incidence of Postoperative Complications among Head and Neck Cancer Surgical Patients by Urinary Cotinine Level

	All Participants (N=88)		Negative Cotinine ^b (N=50)		Positive Cotinine (N=38)		p- value ^a
			N	%	N	%	
Any complication		37 (42.1%)	19	38.0	18	47.4	0.39
Low acuity (N=25)		4 (16.0%)	3	21.4 (3/14)	1	9.1 (1/11)	0.60
High acuity (N=63)		33 (52.4%)	16	44.4 (16/36)	17	63.0 (17/27)	0.20
Vascular		3 (3.4%)	3	6.0	0	0.0	0.26
Pulmonary		11 (12.5%)	4	8.0	7	18.4	0.20
Acute blood loss anemia		12 (13.6%)	4	8.0	8	21.1	0.12
Wound		16 (18.2%)	9	18.0	7	18.4	1.00
Low acuity (N=25)		1 (4.0%)	1	7.1 (1/14)	0	0.0	1.00
High acuity (N=63)		15 (23.8%)	8	22.2 (8/36)	7	25.9 (7/27)	0.77
Ethanol withdrawal		4 (4.6%)	1	2.0	3	7.9	0.31
Other complications		7 (8.0%)	4	8.0	3	7.9	1.00

^aFrom Fisher's exact test;

^bNegative cotinine was considered test result <3 using NicAlert®