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Smoking Status and Pain Level Among Head and Neck Cancer Patients

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Abstract

Smoking is a risk factor for cancer of the upper aerodigestive tract with recidivism rates high even after diagnosis. Nicotine, a major product in tobacco, is a complex drug with multiple characteristics including analalgesic properties. The goal of the study was to examine pain levels in the context of smoking status among patients recently diagnosed with cancer of the upper aerodigestive tract who have not yet received any treatment including radiation, surgery, or chemotherapy. A convenience sample of 112 newly diagnosed head and neck cancer patients (78 men and 34 women) were recruited from clinics at the University of Florida. Smoking rates were: 32% never smoked, 34% former smokers, 34% current smokers. Among current smokers, 62% reported plans to quit in the next 3 months and 38% had tried to quit more than three times in the past 5 years. Current smokers reported higher general (sensory and affective) and oral pain levels (spontaneous and functional) and pain-related interference than did never and former smokers (all F's >8. and p's <.0001) even after controlling for stage of diagnosis. In addition, current smokers reported significantly greater interference from the pain ($F_{2,73}$=10.5 p<.0001).

Perspective—This study highlights the importance of understanding self-reported pain in cancer patients who continue to smoke. When pain is elevated, smokers may be motivated to use tobacco as a means of reducing pain, which in turn reinforces smoking behavior. Tobacco cessation programs should include pain management as a component of treatment.

Keywords

Cancer; Head and Neck Cancer; Smoking; Pain

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Conflict of interest

The authors declare that they have no conflict of interest with the results of this study.

Introduction

Evidence points to smoking tobacco as a risk factor for many cancers including those of the upper aerodigestive tract (oral cavity, larynx, or pharynx). In spite of this association, less than 20% of patients who smoked prior to their diagnosis quit after diagnosis; relapse rates are high.[17,46,51] Moreover, strong evidence exists that ongoing tobacco use can have a negative effect on the outcomes of primary treatment3,[14] and increase the risk of secondary primary tumors of the upper aerodigestive tract.[17]

Nicotine, a major alkaloid found in tobacco and tobacco smoke, is a complex drug with multiple pharmacologic effects ranging from addiction to initial oral irritation followed by rapid desensitization.[5,34] In addition, nicotine has analgesic properties which may be important in the maintenance of smoking even when factors such as a cancer diagnosis suggest quitting would be advisable.[10] It is plausible that in the presence of pain from any source, smoking may be playing a pain modulating role.

One of the earliest reports of the analgesic effects of nicotine in mammals was in 1932.12 While there is evidence that, under certain conditions, nicotine can produce an algogenic effect (e.g.,34,35,39), the preponderance of evidence is for an analgesic effect with the majority of the nicotinic receptor agonists being antinociceptive in humans.20 Establishing evidence of pain modulation from smoking tobacco has been somewhat more inferential. Ditre and Brandon showed that pain increased motivation to smoke, which provides additional indirect evidence of a pain-reducing effect from their smoking.[15] Still, the bioavailability of nicotine as an analgesic may be short lived and it is doubtful that smoking would render a person “pain free.”[20] A study of 4,075 subjects aged 18–64 years old adds more evidence that heavy smoking among a select group of individuals might alleviate pain and that 20 or more cigarettes per day may be the critical dose in producing pain modulation.[33]

Given previously published work,[40] we speculated that pain represents one potentially important barrier to successful quit attempts.[28] The goal of the study was to examine pain levels in the context of smoking status among patients recently diagnosed with cancer of the upper aerodigestive tract who had not yet received any treatment including radiation, surgery, or chemotherapy. Further, we speculated that smoking would be associated with pain level, but directionality did not rise to the level of hypothesis.[1,20,23]

Methods

This study was conducted according to the principles of the 1975 Declaration of Helsinki and Good Clinical Practice guidelines and was approved by the University of Florida Institutional Review Board.

Trained interviewers administered a pre-tested survey instrument to a convenience sample of patients newly diagnosed with head and neck cancer at the University of Florida Cancer Center/ Shands Hospital.[50] Subjects were approached in the examination room prior to their appointment. Information about the study was provided and if the participant agreed, informed consent was obtained. The interviews were administered prior to initiation of cancer treatment. Interviews were collected over a 20-month period.

Measures were drawn from published methodology and instruments and are described below.

Demographics

Patients were asked to report their age, race, ethnicity, and highest grade or year of school completed. Educational attainment was recoded into four categories: less than high school, high school graduation or equivalent, some college, and college graduation or greater.

Cancer Staging and Tumor Site

Based on medical chart abstraction of Tumor, Node, Metastasis (TNM) summary staging, patients were classified as Stage I, Stage II, Stage III, or Stage IV. Unstaged or unknown primary tumor patients were placed in a separate category. Primary tumor site was drawn from the clinical diagnosis recorded in the medical chart. These records are based on pathology reports that conform to established standards of cancer staging.[24,25,29,55]

Tobacco and Alcohol Use

Items from previously conducted research were used to collect data relevant to tobacco and alcohol use.53 Participants were asked to self report whether they were current, former, or never smokers6 and whether they were current, past, or never alcohol drinkers.[2] Patients were also asked whether they had smoked at least 100 cigarettes in their lifetime and, if so, the frequency of current smoking (every day, some days, or not all). Participants who reported they had never smoked 100 cigarettes in their lifetime and self-identified as never smokers were classified as “never” smokers. Those who smoked at least 100 cigarettes in their lifetime but reported no smoking within the past month were classified as “former” smokers, and those who reported smoking at least 100 cigarettes in their lifetime and were now smoking every day or on some days were classified as “current” smokers.

Positive Affect and Negative Affect Schedule

The Positive and Negative Affect Schedule (PANAS) consists of 10 positive affect words and 10 negative affect words.[52] Subjects rated items on a scale from 1 to 5, based on the strength of emotion. Initial studies in development of the PANAS showed that the scales are stable at appropriate levels over a 2-month time period, highly internally consistent, and largely uncorrelated.

Pain Scales

Pain scales were selected to capture multiple dimensions including oral pain, general pain, and pain interference relevant to the study population.

The University of California San Francisco (UCSF) Oral Cancer Pain Questionnaire is scored to establish two subscales: spontaneous and function-related oral pain.[9,36] This 8-item scale showed excellent discrimination between cancer survivors and healthy matched controls on oral pain levels and includes items that tap hyperalgesia, allodynia, spontaneous, and evoked pain.40

The Short-Form McGill Pain Questionnaire has 15 pain descriptors (11 sensory, 4 affective) and subjects rate each item on a four-point intensity scale (0 = none to 3 = severe) regarding general pain during the preceding week.[43] The scales appear to be useful in evaluating pain and discomfort across a wide adult age range.22

The Brief Pain Inventory (BPI)[7,8] provides rapid assessment of the severity and impact of pain on daily functions. For purposes of this investigation, the items assessing the extent to which pain interfered with general activity, mood, walking, normal work, relations with other people, sleep, and enjoyment of life in the past 24 hours were summed and used as a pain interference

scale. The BPI has been successfully used as an outcome measure with advanced cancer patients.49

Data Reduction and Analysis

Descriptive statistics were used to characterize the sample. Chi-square analyses were conducted to compare characteristics of patients by smoking status on quit attempts, quit methods, and presence in the residence of other adults using tobacco. Analysis of variance was used to examine pain and mood levels among categories of tobacco users; follow-up tests were conducted to evaluate pairwise differences among means. To control for the number of tests that were conducted, alpha level for pairwise tests was .001. Chi square analyses were also conducted as confirmatory tests for the presence (or absence) of pain among current, past, and never smokers.

Results

Table 1 shows demographic characteristics of the study participants. One hundred twelve (78 men and 34 women) newly diagnosed head and neck cancer patients were recruited from clinics at the University of Florida. The majority of the participants were white (93%), had at least a high school diploma or equivalent (93%), were not employed (61%), and were married or had a life partner (65%). The average age of the participants was 60 years old (SD=13.4) and sixty percent of the sample self-identified as currently using alcohol (not shown).

Table 2 shows health and behavior characteristics of the study participants by smoking status. The reported tobacco use was: never smoked n=35 (32%); former smokers n=38 (34%); and current smokers n=37 (34%). Two people declined to identify smoking status. The average age at which the participants started smoking was 16.4 years of age with the current smokers having begun at 15 years and the former smokers at 18.

Forty-four percent of those who developed carcinoma of the oral cavity were never smokers compared to 19% former and 37% current smokers. Of those who developed tumors of the oropharynx, 17% were non smokers compared to 47% former smokers and 36% current smokers. All of the participants who developed tumors of the hypopharynx reported being current or former smokers. There was no statistically significant association between smoking status and tumor site, $X^2_{16}=22.9$ p=.12.

Forty-three percent of the participants diagnosed as Stage I were never smokers compared to 30% of those diagnosed as Stage IV. Thirty-one percent of the never smoked group were Stage IV compared to 42% of the current smokers. There was no statistically significant association between smoking status and tumor summary stage, $X^2_{10}=10.8$ p=.37.

There was a statistically significant association between smoking status and alcohol use, $X^2_4=18.3$ p=.001. Of the current alcohol users, the pattern of current users of alcohol was similar across smoking categories: 36% were current, 33% former, and 31% never; however, never smokers were more likely to be never users of alcohol (77%).

Most current smokers reported daily smoking and over half indicated that they planned to quit in the next 3 months. The median number of prior quit attempts by current smokers during the past 5 years was one to two, though a substantial proportion had made more quit attempts. Twenty-five percent of those who never tried to quit before indicated they plan to quit in the next 3 months. Sixteen of current smokers do not plan to quit. The most common quit method was “cold turkey,” and 10% used nicotine replacement therapy.

Results of Analysis of Variance (ANOVA) in Table 3 showed that current smokers had significantly higher pain levels on the UCSF oral cancer-specific subscales (spontaneous, $F_{2,108}$ =14.14 p<.0001 and functional, $F_{2,108}$ =11.54 p<.0001) than never or former smokers. ANOVA also showed that current smokers had higher pain scores on the sensory and affective pain subscales of the short form McGill Pain Index ($F_{2,78}$=16.84 p<.0001; $F_{2,78}$=8.95 p<.0001, respectively). In addition, current smokers reported significantly greater interference from the pain ($F_{2,73}$ =10.5 p<.0001). Follow-up post hoc pairwise tests (Bonferonni) confirmed that current smokers' scores were significantly higher than never or former smokers' scores on all pain indices (p<.0001).

The ANOVA testing smoking status (Table 3) and negative affect (PANAS) was statistically significant (F_{108} =3.27 p<.05) but the post hoc pairwise comparison did not rise to the significance level (p=.001). Because negative affect could be associated with increased pain, we repeated these analyses comparing pain across smoking groups while controlling for negative affect. This analysis continued to show significantly higher pain among current smokers compared to the other two groups with all effect sizes .2 or greater. It is of note that the pain scales showed good reliability with Cronbach α's for this sample as high or higher than those reported in the literature (McGill Sensory Pain Rating Cronbach α=.90; McGill Affective Pain Rating. Cronbach α=.85; Positive Affect PANAS Cronbach α= .88; Negative Affect PANAS. Cronbach α=.88; UCSF Spontaneous Pain Scale. Cronbach α=.93; UCSF Functional Pain Scale. Cronbach α=.92; Pain Interference Brief Pain Inventory Cronbach α=. 93).

To test whether effects we were observing associating pain and smoking were related to stage of diagnosis, we re-analyzed our data using ANCOVA comparing pain levels by smoking status with early (I and II) versus late stage[25] (III and IV) of diagnosis serving as the covariate. Missing data reduced power as shown by the change in degrees of freedom below. The covariate was not significant in the analyses but pain levels remained significantly different based on smoking status with current smokers reporting significantly greater pain than the other two groups. The exception was that the level of affective pain subscale of the McGill no longer reached the level of significance: spontaneous pain adjusted for early vs. late stage of tumor, $F_{2,62}$ =8.08 p<.001; functional pain adjusted for early vs. late stage of tumor, $F_{2,62}$ =7.38 p<.001. Current smokers reported significantly greater interference from the pain after adjusting for early vs. late stage of diagnosis ($F_{2,39}$ =8.69 p<.001). ANCOVA also showed a trend toward current smokers having higher pain scores on the sensory and affective pain subscales of the short form McGill Pain Index after adjusting for early vs. late stage of tumor at diagnosis, but only sensory pain was statistically significant ($F_{2,39}$=4.29 p<.05; $F_{2,39}$=2.11 p≥.1, respectively).

We attempted to identify the source of the pain using the Brief Pain Inventory. The first question asks "if patients have had pain other than minor everyday pain today." For those who say yes, they are asked to shade the painful areas on a figure of a human being and then place an X on the area that hurts most. Of the 70 who stated they have had such pain today, 69 shaded in a location as the source of their pain. Of those 69, 59 patients listed the facial and neck regions as one of the sources of their pain (86%). It should be noted that of the 59 identifying a site, 21 shaded the facial and neck region plus other parts of their body as sites of pain (36%), leaving 64% identifying the facial and neck region as the sole source of pain.

Discussion

Key findings from this study are these: Current smokers have higher pain levels (all scales) and pain-related interference than never or former smokers. This association was observed even after statistically adjusting for whether participants were diagnosed in early (I and II) vs.

late (III and IV) stage with the exception of affective pain. The majority of the current smokers have tried to quit in the past 5 years.

Nicotine and Pain

Our findings that current smokers report higher pain levels are similar to those reported by Weingarten and colleagues.[54] Chronic pain patients who smoked had greater pain intensity and pain interference than non-smokers. Cooley and colleagues provide additional evidence that cancer patients who continue to smoke after diagnosis may be self medicating through smoking.[10] They found that among patients diagnosed with lung cancer, the majority made an attempt to quit smoking, and those who were unsuccessful in the months that followed surgery had post operative pain rated as more severe than those who quit. It follows that smoking produces an analgesic effect, which enhances its reinforcing qualities and increases the difficulty of quitting.

A recent study by Ditre and Brandon shows a direct influence of laboratory-induced pain on motivation to smoke and a shorter latency to smoke.[15] This direct causal relationship was only partially mediated by negative affect. Thus, we conjecture, based on Ditre and Brandon's work, that the pain experienced by our patients probably increases urges to continue smoking. However, the effect of smoking on pain thresholds and perception in humans is complex.31, 48 Interestingly, Jamner et al.32 found that a nicotine patch increased pain thresholds in men but not in women. Girdler et al.[23] reported that female smokers have decreased pain sensitivity to ischemic pain, whereas male smokers have decreased pain sensitivity to cold pressor pain. Smoking status did not appear to influence pain perception for either gender in response to thermal heat pain. Damaj found evidence of greater analgesic efficacy when nicotine was administered to male (versus female) mice.[11] From these extant reports, it appears both genetic and non-genetics may influence the analgesic properties of nicotine.

Arguing that some patients smoke to self-medicate for pain (current smokers) raises the question of why these individuals experience more pain than do others. We can only speculate regarding the reasons. Pain is a complex syndrome and deriving the exact cause of pain among cancer patients is problematic. In our study, nearly 2/3 (61%) indicated they had pain other than minor everyday pain on that day. The fact that of those identifying a pain site, the head and neck region was the most common but not the only site identified is not surprising, given the site of the cancer and age of the patients. Another possibility is that enhanced pain sensitivity may be a factor in our findings. One could speculate that inter-individual differences in pain sensitivity, based on both genetic and non-genetic factors, may contribute not only to more severe clinical pain, but also to reduced success of smoking cessation, given that the analgesic effects of nicotine would be more reinforcing in these individuals.[18,19,21]

Some have conjectured that smoking is linked to the production as well as the amelioration of pain. That is, the nicotinic agonist effects and the effect of smoking as such may be opposite to each other. Although this represents an intriguing perspective, the effects would be difficult to observe as they would cancel each other out and we would see no difference in pain levels between current smokers and nonsmokers. This explanation seems unlikely as we see significantly greater pain levels in the current smokers than nonsmokers. In addition, the research on nicotine as an oral irritant shows that while nicotine contacting mucous membranes produces irritation initially, repeated exposure decreases the irritation which persists for at least 24 hours.5 In addition in human studies, the oral irritant properties of nicotine were significantly reduced in the presence of menthol, suggesting that additives in cigarettes may further reduce the "oral irritation" phenomena.[13] Thus we conclude that it is more probable that the well characterized analgesic properties of nicotine are influencing the maintenance of smoking behavior through pain modulation but the short-term effects are not sufficient to totally eliminate the pain. It should be noted, however, that data from John and colleagues

(2009) show that the level of nicotine dependence influences the analgesic effect, with heavy smokers with lower levels of nicotine dependence achieving greater analgesic effects than nicotine-dependent smokers. This point is interesting and the measurement of "dependence" in our population warrants further study. The first documentation that smoking damages taste dates back to 1961.[37] More recent studies show that taste inhibits oral pain47 and may inhibit pain at other body sites as well.4,38,[44,46,56] Thus, damage to taste might be expected to intensify pain via disinhibition and is a plausible explanation for the observed increase in pain among current smokers. In light of our findings and those of others,[10,15,33] we believe that there is a strong indication that patients are using smoking as a means to manage pain.

Implications for Smoking Cessation Trials

There is a growing understanding that smoking cessation programs need to be included in cancer treatment programs and should to be tailored to the individual.[45] In spite of the need, few such programs exist and, regardless of the best efforts, the results of such programs are mixed.[26,27,41] We believe results of this study provide guidance in designing and testing cessation trials. In particular, if pain increases urges to smoke and if smoking confers analgesic benefits, then the success of smoking cessation efforts could be enhanced through the inclusion of pain management. Given the trend toward higher levels of negative affect among smokers, treatments that provide both pain reduction and mood enhancement may be particularly beneficial. For example, cognitive-behavioral pain management approaches have been effective for improving both pain and psychological status and may therefore be useful adjuncts to smoking cessation.[16,30] Current smokers in this study had made multiple, unsuccessful efforts to quit during the past 5 years, which highlights, as supported by Cooley and colleagues, [10] the importance of enhancing approaches to smoking cessation in this population. Based on our findings, incorporating pain management approaches may improve smoking cessation outcomes, though this hypothesis awaits empirical support.

Limitations

These results should be considered in the context of study limitations. First, the data used were drawn from a convenience sample. We fully acknowledge that clinic-based recruitment influenced the sample selected. While over 90% of the patients we approached for interviews agreed to be interviewed, scheduling factors may have influenced patient enrollment. It is of note that the percentages of early versus late stage of diagnosis of our sample compared to overall clinic data showed that our sample had slightly more early stages (Stage I and Stage II, 45%) than those included in overall hospital data (33%).[50] Readers should also be aware that we did not biochemically verify patients' self-reported smoking status. Nevertheless, prior research suggests that current smokers status is accurate and few misrepresentations occur between never smokers and former smokers.42 In addition, we asked when the smoker quit, and if it was less than a month previous we categorized the person as a current smoker rather a former smoker. Therefore, even though biochemical verification was not used to verify smoking status, we feel confident in the accuracy of our results.

Conclusion

Levels of pain and pain interference were higher among current smokers, even after controlling for stage of diagnosis. Because nicotine is known to have analgesic properties, cancer patients may be less willing to quit smoking without reassurance that their pain needs will be addressed. Based on our data and others, smoking cessation programs integrated into oncologic clinical settings should address pain management as a routine part of the program.[3,28] These data provide new information on pain and tobacco use to guide the development and implementation of smoking cessation clinical trials into the oncologic context.

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References

1. al'Absi M, Wittmers LE, Hatsukami D, Westra R. Blunted opiate modulation of hypothalamic-pituitary-adrenocortical activity in men and women who smoke. Psychosom Med 2008;70:928–935. [PubMed: 18799426]
2. Babor, TF.; Higgins-Biddle, JC.; Saunders, JB.; Monteiro, MG. The Alcohol Use Disorders Identification Test: guidelines for use in primary care. Second Edition. World Health Organization Department of Mental Health and Substance Dependance; 2001.
3. Baile WF. Alcohol and nicotine dependency in patients with head and neck cancer. J Support Oncol 2008;6:165–166. [PubMed: 18491684]
4. Blass EM, Shah A. Pain-reducing properties of sucrose in human newborns. Chem Senses 1995;20:29–35. [PubMed: 7796057]
5. Carstens E, Albin KC, Simons CT, Carstens MI. Time course of self-desensitization of oral irritation by nicotine and capsaicin. Chem Senses 2007;32:811–816. [PubMed: 17641107]
6. Centers for Disease Control and Prevention. Smoking and tobacco use: Survey question design resource. [Accessed December 8, 2008]. Available at: http://apps.nccd.cdc.gov/sqdr/SurveyDirectory.aspx
7. Cleeland CS, Ryan KM. Pain assessment: global use of the Brief Pain Inventory. Ann Acad Med Singapore 1994;23:129–138. [PubMed: 8080219]
8. Cleeland CS, Mendoza TR, Wang XS, Chou C, Harle MT, Morrissey M, Engstrom MC. Assessing symptom distress in cancer patients: the M.D. Anderson Symptom Inventory. Cancer 2000;89:1634–1646. [PubMed: 11013380]
9. Connelly ST, Schmidt BL. Evaluation of pain in patients with oral squamous cell carcinoma. J Pain 2004;5:505–510. [PubMed: 15556829]
10. Cooley ME, Sarna L, Kotlerman J, Lukanich JM, Jaklitsch M, Green SB, Bueno R. Smoking cessation is challenging even for patients recovering from lung cancer surgery with curative intent. Lung Cancer Mar 2009;23
11. Damaj MI. Behavioral modulation of neuronal calcium/calmodulin-dependent protein kinase II activity: differential effects on nicotine-induced spinal and supraspinal antinociception in mice. Biochem Pharmacol 2007;74:1247–1252. [PubMed: 17850767]
12. Davis L, Pollock LJ, Stone TT. Visceral pain. Surg Gynecol Obstet 1932;55:418–426.
13. Dessirier JM, O'Mahony M, Carstens E. Oral irritant properties of menthol: sensitizing and desensitizing effects of repeated application and cross-desensitization to nicotine. Physiol Behav 2001;73:25–36. [PubMed: 11399291]
14. Devlin JG, Langer CJ. Combined modality treatment of laryngeal squamous cell carcinoma. Expert Rev Anticancer Ther 2007;7:331–350. [PubMed: 17338653]
15. Ditre JW, Brandon TH. Pain as a motivator of smoking: effects of pain induction on smoking urge and behavior. J Abnorm Psychol 2008;117:467–472. [PubMed: 18489224]
16. Dixon KE, Keefe FJ, Scipio CD, Perri LM, Abernethy AP. Psychological interventions for arthritis pain management in adults: a meta-analysis. Health Psychol 2007;26:241–250. [PubMed: 17500610]
17. Do KA, Johnson MM, Lee JJ, Wu XF, Dong Q, Hong WK, Khuri FR, Spitz MR. Longitudinal study of smoking patterns in relation to the development of smoking-related secondary primary tumors in patients with upper aerodigestive tract malignancies. Cancer 2004;101:2837–2842. [PubMed: 15536619]
18. Fillingim RB, Kaplan L, Staud R, Ness TJ, Glover TL, Campbell CM, Mogil JS, Wallace MR. The A118G single nucleotide polymorphism of the mu-opioid receptor gene (OPRM1) is associated with pressure pain sensitivity in humans. J Pain 2005;6:159–167. [PubMed: 15772909]
19. Fillingim RB, Wallace MR, Herbstman DM, Ribeiro-Dasilva M, Staud R. Genetic contributions to pain: a review of findings in humans. Oral Dis 2008;14:673–682. [PubMed: 19193196]

20. Flores CM. The promise and pitfalls of a nicotinic cholinergic approach to pain management. Pain 2000;88:1–6. [PubMed: 11098093]
21. Foulkes T, Wood JN. Pain genes. PLoS Genet 2008;4:e1000086. [PubMed: 18654615]
22. Gagliese L, Melzack R. Chronic pain in elderly people. Pain 1997;70:3–14. [PubMed: 9106804]
23. Girdler SS, Maixner W, Naftel HA, Stewart PW, Moretz RL, Light KC. Cigarette smoking, stress-induced analgesia and pain perception in men and women. Pain 2005;114:372–385. [PubMed: 15777863]
24. Greene, FL.; Page, DL.; Fleming, ID.; Fritz, AG.; Balch, CM.; Haller, DG.; Morrow, M. American Joint Committee on Cancer(AJCC) Staging Manual. 6th Edition. New York: Springer; 2002.
25. Greene, FL.; Comptom, CC.; Fritz, AG.; Shah, JP.; Winchester, DP., editors. AJCC Cancer Staging Atlas. Chicago: Springer; 2006.
26. Gritz ER, Fingeret MC, Vidrine DJ, Lazev AB, Mehta NV, Reece GP. Successes and failures of the teachable moment: smoking cessation in cancer patients. Cancer 2006;106:17–27. [PubMed: 16311986]
27. Gritz ER, Vidrine DJ, Fingeret MC. Smoking cessation a critical component of medical management in chronic disease populations. Am J Prev Med 2007;33:S414–S422. [PubMed: 18021917]
28. Haman KL. Psychologic distress and head and neck cancer: part 1--review of the literature. J Support Oncol 2008;6:155–163. [PubMed: 18491682]
29. Harrison, LB.; Sessions, RB.; Hong, WK., editors. Head and Neck Cancer A Multidiciplinary Approach. Second Edition. Philidelphia: Lippincott Williams & Wilkins; 2004.
30. Hoffman BM, Papas RK, Chatkoff DK, Kerns RD. Meta-analysis of psychological interventions for chronic low back pain. Health Psychol 2007;26:1–9. [PubMed: 17209691]
31. Hong D, Conell-Price J, Cheng S, Flood P. Transdermal nicotine patch for postoperative pain management: a pilot dose-ranging study. Anesth Analg 2008;107:1005–1010. [PubMed: 18713921]
32. Jamner LD, Girdler SS, Shapiro D, Jarvik ME. Pain inhibition, nicotine, and gender. Exp Clin Psychopharmacol 1998;6:96–106. [PubMed: 9526150]
33. John U, Meyer C, Rumpf HJ, Hapke U. Nicotine dependence criteria and nicotine withdrawal symptoms in relation to pain among an adult general population sample. Eur J Pain 2009;13:82–88. [PubMed: 18436459]
34. Keele, CA.; Armstrong, D. Substances Producing Pain and Itch. London: Arnold; 1964.
35. Khan IM, Buerkle H, Taylor P, Yaksh TL. Nociceptive and antinociceptive responses to intrathecally administered nicotinic agonists. Neuropharmacology 1998;37:1515–1525. [PubMed: 9886674]
36. Kolokythas A, Connelly ST, Schmidt BL. Validation of the University of California San Francisco Oral Cancer Pain Questionnaire. J Pain 2007;8:950–953. [PubMed: 17686656]
37. Krut LH, Perrin MJ, Bronte-Stewart B. Taste perception in smokers and non-smokers. Br Med J 1961;1:384–387. [PubMed: 13754660]
38. Lewkowski MD, Young SN, Ghosh S, Ditto B. Effects of opioid blockade on the modulation of pain and mood by sweet taste and blood pressure in young adults. Pain 2008;135:75–81. [PubMed: 17560720]
39. Liu L, Zhu W, Zhang ZS, Yang T, Grant A, Oxford G, Simon SA. Nicotine inhibits voltage-dependent sodium channels and sensitizes vanilloid receptors. J Neurophysiol 2004;91:1482–1491. [PubMed: 14657192]
40. Logan HL, Bartoshuk LM, Fillingim RB, Tomar SL, Mendenhall WM. Metallic taste phantom predicts oral pain among 5-year survivors of head and neck cancer. Pain 2008;140:323–331. [PubMed: 18845396]
41. Martinez E, Tatum KL, Weber DM, Kuzla N, Pendley A, Campbell K, Ridge JA, Langer C, Miyamoto C, Schnoll RA. Issues related to implementing a smoking cessation clinical trial for cancer patients. Cancer Causes Control 2009;20:97–104. [PubMed: 18758971]
42. Martinez ME, Reid M, Jiang R, Einspahr J, Alberts DS. Accuracy of self-reported smoking status among participants in a chemoprevention trial. Prev Med 2004;38:492–497. [PubMed: 15020184]
43. Melzack R. The short-form McGill Pain Questionnaire. Pain 1987;30:191–197. [PubMed: 3670870]
44. Mercer ME, Holder MD. Antinociceptive effects of palatable sweet ingesta on human responsivity to pressure pain. Physiol Behav 1997;61:311–318. [PubMed: 9035263]

45. Schnoll RA, Malstrom M, James C, Rothman RL, Miller SM, Ridge JA, Movsas B, Unger M, Langer C, Goldberg M. Correlates of tobacco use among smokers and recent quitters diagnosed with cancer. Patient Educ Couns 2002;46:137–145. [PubMed: 11867244]
46. Schnoll RA, James C, Malstrom M, Rothman RL, Wang H, Babb J, Miller SM, Ridge JA, Movsas B, Langer C, Unger M, Goldberg M. Longitudinal predictors of continued tobacco use among patients diagnosed with cancer. Ann Behav Med 2003;25:214–222. [PubMed: 12763716]
47. Tie K, Fast K, Kveton J, Cohen Z, Duffy VB, Green B, Prutkin JM, Bartoshuk LM. Anesthesia of chorda tympani nerve and effect on oral pain. Chem Senses 1999;24:609.
48. Turan A, White PF, Koyuncu O, Karamanliodlu B, Kaya G, Apfel CC. Transdermal nicotine patch failed to improve postoperative pain management. Anesth Analg 2008;107:1011–1017. [PubMed: 18713922]
49. Twycross R, Harcourt J, Bergl S. A survey of pain in patients with advanced cancer. J Pain Symptom Manage 1996;12:273–282. [PubMed: 8942122]
50. University of Florida Shands Cancer Center. 2007 Annual Report for Shands at the University of Florida. [Accessed December 12, 2008]. Available at: http://www.shands.org/hospitals/UF/service/Cancer/81300annualreport.pdf
51. Walker MS, Vidrine DJ, Gritz ER, Larsen RJ, Yan Y, Govindan R, Fisher EB. Smoking relapse during the first year after treatment for early-stage non-small-cell lung cancer. Cancer Epidemiol Biomarkers Prev 2006;15:2370–2377. [PubMed: 17132767]
52. Watson D, Clark LA, Carey G. Positive and Negative Affectivity and Their Relation to Anxiety and Depressive-Disorders. J Abnorm Psychol 1988;97:346–353. [PubMed: 3192830]
53. Watson JM, Logan HL, Tomar SL, Sandow P. Factors associated with early-stage diagnosis of oral and pharyngeal cancer. Community Dent Oral Epidemiol Jun 4 Epub ahead of print. 2009
54. Weingarten TN, Moeschler SM, Ptaszynski AE, Hooten WM, Beebe TJ, Warner DO. An assessment of the association between smoking status, pain intensity, and functional interference in patients with chronic pain. Pain Physician 2008;11:643–653. [PubMed: 18850028]
55. Werning, JW. Oral Cancer: Diagnosis, Management, and Rehabilitation. 1st Edition. New York: Thieme Medical Publishers, Inc; 2007.
56. Zmarzty SA, Wells AS, Read NW. The influence of food on pain perception in healthy human volunteers. Physiol Behav 1997;62:185–191. [PubMed: 9226361]

Table 1

Selected Characteristics Of Study Participants*

	Newly Diagnosed Head and Neck Cancer (N=112)	
	n or mean	**% or sd**
SEX		
Male	78	70%
Female	34	30%
RACE		
White[a]	103	93%
Black	3	3%
Other racial groups[b]	4	4%
EDUCATION		
Less than high school diploma	6	7%
High school diploma or GED[c]	26	31%
Some college	21	25%
Bachelor's degree or higher	30	37%
EMPLOYMENT STATUS		
Employed	43	39%
Not employed	68	61%
MARITAL STATUS		
Single	16	14%
Married/life partner	72	65%
Divorced/separated	12	11%
Widowed	11	9%

*Categories may not sum to 112 due to missing data

[a]White was composed of 2 Hispanic and 101 Non Hispanic Whites

[b]Other category was composed of 4 Asians, Pacific Islanders

[c]GED = general educational development diploma

Table 2

Health and Behavior Characteristics by Smoking Status[+]

	Smoking Status[*]		
	Current	**Former**	**Never**
	n=37	**n=38**	**n=35**
PRIMARY TUMOR SITE			
Oral Cavity	37%	19%	44%
Oropharynx	36%	47%	17%
Hypopharynx	80%	20%	0%
Nasopharynx	38%	12%	50%
Larynx	22%	67%	11%
Other (Nasal Cavity, Salivary Glands, Thyroid)	29%	57%	14%
Primary site not identified or not available	28%	29%	43%
Misc. HNC (Skin, Nerve, Carotid)	9%	36%	55%
TUMOR STAGE			
Stage I n=14	9%	36%	43%
Stage II n=27	30%	39%	23%
Stage III n=19	27%	32%	21%
Stage IV n=26	33%	27%	30%
Unstaged or recurrent or unknown primary n=26	20%	80%	0%
ALCOHOL USE STATUS			
Current n=64	36%	33%	31%
Former n=32	41%	47%	13%
Never n=13	8%	15%	77%
AGE STARTED SMOKING REGULARLY (years)	15 (4.2)	18 (3.8)	--
CURRENT AGE	54 (13.5)	64 (11.2)	61 (13.0)

[*] Two people declined to identify their smoking status

[+] Categories may not sum to total due to missing data or rounding error

Table 3

Means and Standard Deviations ( ) of Psychosocial Characteristics by Smoking Status: Results of Analysis of Variance and post-hoc tests

	Current Smoker	Former Smoker	Never Smoked		Post hoc test (p=0.001)
Spontaneous Oral Pain Scale	100.5(101.4)[a]	33.9(52.2)[b]	20.0(33.2)[b]	$F_{2,108}$=14.14 p<.0001	*[a] is significantly different than [b]*
Function-related Oral Pain Scale	126.4(109.4)[a]	59.9(70.6)[b]	37.3(56.8)[b]	$F_{2,108}$=11.54 p<.0001	*[a] is significantly different than [b]*
Sensory Pain Rating Index (McGill)	14.1(9.1)[a]	5.2(5.6)[b]	4.4(4.7)[b]	$F_{2,78}$=16.84 p<.0001	*[a] is significantly different than [b]*
Affective Pain Rating Index (McGill)	4.5(3.8)[a]	1.4(1.7)[b]	1.7(2.8)[b]	$F_{2,78}$=8.95 p<.0001	*[a]is significantly different than[b]*
Pain Interference (Brief Pain Inventory)	37.4(19.7)[a]	18.5(15.2)[b]	17.9(17.0)[b]	$F_{2,73}$=10.5 p<.0001	*[a] is significantly different than [b]*
Negative Affect (PANAS)[+]	26.5(9.4)[b]	21.4(8.1)[b]	21.8(7.1)[b]	$F_{2,78}$=3.27 p=.04	*No significant difference among the three subgroups*
Positive Affect (PANAS)[+]	27.6(8.6)	30.3(8.0)	32.3(8.0)	$F_{2,78}$=2.09 p=.13	n/a

[+]PANAS= (Positive Affect and Negative Affect Schedule)