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Predictors of Pain among Head and Neck Cancer Patients

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Abstract

Objective—Pain is a strong contributor to cancer patients' quality of life. The objective of this study was to determine predictors of pain 1 year after the diagnosis of head and neck cancer.

Design—Prospective, multi-site cohort study.

Setting—Three academically-affiliated medical centers.

Patients—Previously untreated patients with carcinoma of the upper aerodigestive tract (n=374).

Main Outcome Measures—Participants were surveyed pre-treatment and 1 year thereafter. Multivariate analyses were conducted to determine predictors of the SF-36 bodily pain score 1 year after diagnosis.

Results—The mean SF-36 bodily pain score at 1 year was 65, compared to 61 at diagnosis (p=.004), compared to 75 among population norms (lower scores indicate worse pain). Variables independently associated with pain included pre-treatment pain score (p<0.001), less education (p=0.02), neck dissection (p=0.001), feeding tube (p=0.05), xerostomia (p<0.001), depressive symptoms (p<0.001), taking more pain medication (p<0.001), less physical activity (p=.02), and poor sleep quality (p=0.006). Current smoking and problem drinking were marginally significant (p=0.07 and 0.08, respectively).

Conclusions—Aggressive pain management may be indicated for head and neck cancer patients who undergo neck dissections, complain of xerostomia, require feeding tubes, and have medical

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comorbidities. Treatment of modifiable risk factors such as depression, poor sleep quality, tobacco and alcohol abuse may also reduce pain and improve quality of life among head and neck cancer patients.

Keywords

Head and neck cancer; pain; quality of life; symptom management; analgesia

Introduction

The Institute of Medicine considers effective analgesia a moral imperative and has recently challenged medical providers to better understand, prevent and treat pain.¹ Head and neck cancer patients frequently experience pain, even long after the completion of treatment.² The prevalence of bodily pain among head and neck cancer patients has been estimated at 70%, considerably higher than what has been reported in other cancer patients.³ Pain experienced 1 year after diagnosis strongly predicts long-term quality of life,⁴ and is associated with poorer survival among head and neck patients, particularly those with advanced disease.⁵ Bodily pain is also a robust predictor of disability in head and neck cancer patients.⁶

Many studies have investigated the factors associated with bodily pain among cancer patients, which include age, underlying physical and mental health, and depression.^{7, 8} Specific to head and neck cancer, medical comorbidities, chemotherapy, and presence of a feeding tube are associated with significant bodily pain.⁹ Tumor site and stage have been correlated with pain reported by patients with oral cavity cancer.¹⁰

Tobacco use has been temporally associated with pain severity,^{11, 12} and problem drinking has been associated with pain.¹³ Diet and physical activity also influence physical pain among cancer patients.^{14, 15} While increased physical activity¹⁶ and fruit and vegetable intake¹⁴ have been shown to improve quality of life among head and neck cancer patients, no studies have shown a relationship between these factors and pain. Moreover, bodily pain predicts poor sleep quality, and is significantly associated with insomnia.^{17, 18}

While effective pain treatments exist, identifying those most at risk for pain could facilitate targeted assessment and intervention. Thus, the objective of this study was to determine the variables associated with pain among head and neck cancer patients 1 year following diagnosis.

Materials and Methods

Design

This investigation was conducted as part of a prospective cohort study involving patients enrolled in the University of Michigan Head and Neck Cancer Specialized Program of Research Excellence. This sub-study was performed to determine variables associated with pain 1 year after diagnosis among head and neck cancer patients. The dependent variable was the SF-36 bodily pain score at 1 year post-diagnosis. The independent variables included demographic characteristics, clinical factors, and health behaviors. Institutional review board approval was obtained at each study site.

Sample

Subjects were recruited from the waiting rooms in head and neck cancer clinics within three institutions: the University of Michigan Health System, the Veterans Affairs (VA) Ann Arbor Healthcare System, and the Henry Ford Health System (HFHS). Patients with squamous cell carcinoma of the upper aerodigestive tract mucosa (excluding skin and esophagus) were eligible for enrollment. Patients who were less than 18 years of age, pregnant, non-English speaking, psychologically or cognitively unable to complete the survey, or with different tumor sites and/or histologies were excluded. Research assistants recruited patients after obtaining informed consent, and administered a written survey. Clinical data were collected directly from the surveys and were confirmed and/or abstracted from the medical record. The survey was repeated 1 year post-diagnosis. Participants received \$10 compensation after the completion of each questionnaire. Of 811 patients recruited to the study, 559 had 1-year SF-36 scores, and the 374 with complete data were included in the final multivariate analysis.

Dependent Variable

The 36-item Short-Form Health Survey (SF-36) is a comprehensively validated index used to assess quality of life.^{19, 20} It has been accepted as one of the most widely used and exhaustively studied survey-based patient assessed health outcome measures.²¹ It has been successfully employed to study head and neck cancer patients, and independently predicts survival within this cohort.^{22, 23} The SF-36 bodily pain score is an independently-validated subscale that has high fidelity and reproducibility in describing patient-reported pain;²⁴ based on a scale of 0-100, the population norm (in a cohort with a mean age of 58 years) is 75 (lower scores indicate worse pain).²⁵

Independent Variables

Demographics—Demographic information included patient age at the time of diagnosis (in years), sex, race, marital status (yes/no), and education level (high school or less vs. some college or more). Since race has been shown to effect outcomes among head and neck cancer patients, respondents were asked to self-identify their ethnicity/race using the US census two-tiered question: 1) a two category question about Hispanic/Latino origins; and 2) a five category question about race (of which respondents could select multiple categories).²⁶ Since there were few respondents in many of the categories, race was collapsed into white and non-white for analysis.

Clinical Factors—Cancer descriptors included the primary tumor site and disease stage according to the American Joint Committee on Cancer (AJCC) sixth edition.²⁷ For the purposes of statistical analysis, tumor sites were grouped in aggregate (into pharynx, larynx, and oral cavity [including other/sinus]), and stage was separated into stages I/II versus stages III/IV.

Treatment variables included whether subjects received (yes/no) radiation, chemotherapy, primary site surgery, and/or neck dissection. Also assessed was the presence (yes/no) of an indwelling feeding tube and/or tracheotomy at 1 year post-diagnosis. Neck dissections were

defined as any systematic cervical nodal extirpation regardless of level(s) dissected or additional structure(s) removed.

Xerostomia was described by a question taken verbatim from the Head and Neck Quality of Life (HNQOL), a validated, disease-specific QOL instrument for patients with head and neck cancer.²⁸ Medical comorbidities were assessed by chart abstraction using the validated Adult Comorbidity Evaluation-27 (ACE-27) index and classified into two groups: moderate to severe comorbidity versus no to mild comorbidity.²⁹ Depression was measured using the validated 5-item Geriatric Depression Scale-Short Form (GDS-SF): a score of 4 or higher on this scale indicates probable depression.³⁰ Pain medicine usage by subjects at 1 year was assessed with one question measured on a 5-point Likert scale from 1 (never) to 5 (always).

Health Behaviors—Subjects were asked about their prior and current tobacco use; respondents who reported any tobacco use within the past month were considered current smokers; those who reported use prior to 1 month ago were considered former smokers. The 10-item Alcohol Use Disorders Identification Test (AUDIT) was used to assess the amount of alcohol intake and related problems; a score of 8 or higher on this test indicates a high risk of alcohol-related disorders.³¹ Selected questions from the validated Willett food frequency questionnaire were used; respondents reported the average number of servings of fruit, vegetables and fried foods consumed over the past year.³² The validated Physical Activity Scale for the Elderly (PASE) was used to measure activity; scores ranged from 0-400 or more (higher scores indicate more activity), and the population mean for people age 65-100 was 103.³³ Sleep quality was assessed using the validated Medical Outcomes Study sleep measure (MOS-Sleep); lower scores indicate poorer sleep.^{34, 35}

Statistical Analysis

Descriptive statistics were calculated for all measures. Frequencies and percentages are presented for categorical variables, and means and standard deviation are presented for continuous measures. A correlation matrix was employed to determine the co-linearity between variables (not shown). Bivariate analyses (analysis of variance and Spearman rho) were used to test correlations between SF-36 Pain Index and each independent variable. Based upon the bivariate analyses, ordinary least squares multiple linear regression was conducted to determine independent variables associated with the dependent variable at 1 year after diagnosis. All analyses were conducted using SAS 9.3 software (Cary, NC).

Results

Description of Sample

The demographic and health characteristics of the sample are summarized in Table 1. The mean age of participants was 58 years, most were male (78%), Caucasian (91%) and married (60%) and just over half had some college education or more (56%). The majority of primary sites were pharyngeal (53%), and advanced stage disease was common (75% stages III, IV). About 84% had radiation, 62% had chemotherapy, 38% had primary site surgery, and 43% underwent neck dissection. At 1 year post-treatment, 18% of patients had an indwelling feeding tube, and 4% had a tracheotomy. Xerostomia was frequent, with 44%

complaining of “a lot” or “extreme” symptoms at 1 year. Approximately 39% screened positive for depression. Most patients (54%) never or rarely used pain medicine at 1 year. About one-quarter (22%) were current smokers, and only 12% were problem drinkers.

Bivariate Analysis

The mean SF-36 pain score was lower (worse) pre-treatment than 1 year later (61 vs. 65; $p=0.004$). Factors associated with 1 year pain on bivariate analysis are summarized in Table 2 and included marital status, educational level, cancer site, primary site surgery, neck dissection, feeding tube, tracheotomy, xerostomia, depression, smoking, problem drinking, vegetable and fruit intake, physical activity, and sleep.

Multivariate Analysis

The multivariate analysis is reported in Table 3. Multivariate analysis indicated that pre-treatment pain ($p<0.001$), less education ($p=0.02$), neck dissection ($p=0.001$), presence of a feeding tube ($p=0.05$), xerostomia ($p<0.001$), depressive symptoms ($p<0.001$), taking more pain medication ($p<0.001$), less physical activity ($p=.006$), and poor sleep quality ($p=0.02$) were independently associated with worse pain 1 year after diagnosis. Current smoking and problem drinking approached significance in the multivariate analyses ($p=.07$ and $.08$, respectively). While cancer site, primary site surgery, tracheotomy, comorbidities, and vegetable and fruit intake were significant in the bivariate analyses, they were no longer significant in the multivariate analyses.

Alternative regression models were created in order to control for potential confounders and statistical limitations (data not shown). Models that did not incorporate pre-treatment pain scores and those that excluded analgesic usage both yielded similar results to the reported data. Cancer stage re-stratified into stages I/II/III versus stage IV, inclusion of tumor N stage, inclusion of recurrent disease, and chemoradiation (as a yes/no variable) also did not change the results.

Discussion

Bodily pain scores among patients with head and neck cancer are better at 1 year follow-up in comparison with the pre-treatment value. The improvement at 1 year is intuitive given the pain inherent to an untreated tumor burden at the time of diagnosis and the likelihood that the acute stigmata of cancer treatment have resolved by 1 year. Nonetheless, the mean 1 year pain score is worse than scores seen in the general population of similar age, and is predicted by pre-treatment pain.¹⁹ Our prior work with head and neck cancer patients has shown that a ten point decrement in SF-36 bodily pain scores is associated with a 20% increased risk of disability.⁶ In another study, the incidence of oral pain among 5-year head and neck cancer survivors was 43%.³⁶ Our data corroborate that head and neck cancer patients continue to experience pain 1 year after diagnosis, and that dedicated, evidence-based strategies for effective analgesia are likely to be critical in order to optimize our patients' qualities of life.

Demographics

Lower educational level was associated with more pain, corroborating data suggesting that educational level also predicts quality of life among nasopharyngeal cancer patients, and overall disability in a population of treated head and neck cancer patients.^{6, 37} Interestingly, none of the other demographic characteristics evaluated were independently associated with bodily pain scores. Our findings support the notion that physical and psychological factors influence pain to a greater extent than do demographics,³⁸ and are in accordance with a large study which found that no demographic factors predicted pain among a diverse cohort of cancer patients.³⁹

Cancer Characteristics and Treatment

While cancer site, stage, and treatment would seemingly affect pain, these were surprisingly not significant in the multivariate analyses. Instead, the adverse consequences of treatment, which were studied as independent variables as well, were more indicative of pain at 1 year. For example, xerostomia was closely associated with pain, but radiation therapy was not similarly related thus we postulate that salivary gland-sparing regimens delivered with intensity modulated radiation treatment (IMRT) might limit xerostomia and resultant pain perception.⁴⁰ Data suggesting that IMRT broadly improves quality of life when compared with conventional radiation delivery algorithms confirm this conjecture.^{41, 42} Unfortunately, specific data on radiation fields was not collected and could not be included in the analyses.

The presence of a feeding tube at 1 year strongly influences quality of life and was significantly associated with pain in the multivariate analysis.⁹ In many cases, consequences of treatment (regardless of modality) influence post-treatment function related to eating and drinking. The presence of a tracheotomy at 1 year, which also indirectly reflects tissue effects of cancer-directed treatment, was not significantly associated with pain, possibly due to the low incidence of tracheotomies at 1 year. While primary site surgery was not associated with pain, the one treatment that was significantly associated with pain was neck dissection. This finding supports prior data that highlights the tangible, long-term functional consequences of neck dissections, particularly in post-treatment settings.⁴³ Patients undergoing neck dissection were likely to also have been treated with radiation which might also contribute to pain. We did not compare pain scores for neck dissection alone to neck dissection prior to or following radiation, nor specifically control for the type of neck dissection. While the era of “radical” neck surgery has been supplanted by movements toward “selective” operations, these observations confirm that neck dissections, even those performed by experienced surgeons and that aim to limit morbidity, are not always innocuous.⁴⁴

Comorbidities and Depression

Medical comorbidities were not associated with pain, which does not corroborate findings in the general cancer patient population, however, 70% of the population had none or mild comorbidities. A relationship exists between medical comorbidities and many quality of life-related metrics in head and neck cancer patients.^{45, 46} Among head and neck cancer patients with multiple medical problems, amelioration of symptoms may require diligent titration of pharmacologic regimens and close collaboration with other clinicians.

As has been seen in other studies of cancer patients, depression is highly correlated with pain.⁴⁷ Depressed patients are more sensitive to somatic discomfort, which also engenders depressive symptoms, particularly among cancer patients.⁴⁸ Depression is also associated with health behaviors, some of which were associated with pain, and which must be considered in treating pain.^{49, 50} Smoking, alcohol abuse and depression are interrelated, and treating depression may enhance substance abuse cessation efforts. Also, depression has been shown to be correlated with sleep disturbances.⁵¹ The data suggest that clinicians should seek to diagnose and treat depression among head and neck cancer patients complaining of pain, and also that depressed patients may require aggressive analgesia in addition to treating their mood and/or sleep disorders.

Health Behaviors

Cancer patients' smoking status is closely linked with quality of life, and we identified a trend towards more pain in current tobacco users.⁵² The mechanisms by which tobacco influences head and neck cancer pain are undoubtedly multifactorial, involving central nociceptive processing mechanisms, psychological factors, and direct mucosal irritation, among others.⁵³ Maladaptive strategies in which tobacco is relied upon for pain relief are prevalent; educational and pharmaceutical initiatives in which tobacco is recast as an accomplice to pain may improve success rates in achieving abstinence.⁵⁴

Problem drinking approached significance with head and neck cancer pain. In general, patients with better function are more likely to drink alcohol socially, but alcohol may also be utilized for its analgesic properties among those in pain. Self-medication of pain with alcohol has been associated with pain frequency, depression, and use of pain medications.⁵⁵ Moreover, problem drinkers have a higher incidence of tobacco abuse, and are less likely to quit.⁵⁶ Clinicians should individualize counseling and interventional strategies for patients with problem drinking, being mindful of its complex relationship with clinical factors and other health behaviors.⁵⁷

There was an association between increased physical activity and less pain. Directed rehabilitative interventions also appear to improve somatic function in head and neck cancer patients, specifically regarding dysphagia treatment/prevention, and shoulder/neck range of motion after surgery.^{58, 59} Poor sleep was closely associated with worse pain, which is supported by prior research⁶⁰ as sleep disturbances are likely to be caused by severe pain. Our findings support the need to screen for sleep disturbances among patients with bothersome pain, and also suggest that undertreated pain may contribute to seemingly idiopathic insomnia.

Treating Pain Effectively

While one might postulate instead that efficacious medication usage should decrease pain, our data reinforce that head and neck cancer patients who use analgesics still report pain, suggesting their regimens may not be adequately effective. While we did not specifically address analgesic efficacy or regimens, data suggest that relatively simple interventions, such as prescribing medications on a schedule, rather than as needed, more effectively manage post-surgical head and neck cancer patients' pain.⁶¹ The World Health Organization

pain ladder offers a practical, stepwise approach to managing cancer pain that is readily applicable to head and neck cancer patients.⁶² Head and neck cancer patients are at risk for cancer recurrence and for second primaries; pain is a frequent harbinger of such phenomena, and clinicians must remain ever-vigilant during continued oncologic surveillance.

Limitations

The SF-36 bodily pain index does not distinguish head and neck symptoms, thus pain scores may or may not relate directly to patients' cancer and its treatment. In quality of life research in head and neck cancer, no single metric can effectively encapsulate the patient experience or perspective.⁶³ Given that quality of life among head and neck cancer patients may decline over many years, 1-year pain scores do not necessarily encompass the evolution of longer-term symptoms.⁶⁴ Despite extra efforts to recruit minorities, the study over-represented Caucasian men, potentially limiting the ability to extrapolate our findings in other populations.

Conclusion

Many head and neck cancer patients experience pain 1 year after diagnosis. Pain, more than any other symptom or disease, is the single greatest source of financial expense and patient complaints in America.⁶⁵ Reducing the potential for pain from neck dissection, minimizing xerostomia, and utilizing evidence-based strategies for effective analgesia are opportunities worth considering in order to limit pain and improve quality of life for these patients. An understanding of the complex relationships among cancer treatment, health behaviors and pain is instructive to clinicians faced with preventing, anticipating, counseling and treating bothersome symptoms in a challenging patient population.

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References

1. Institute of Medicine. *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research*. Washington DC: National Academies Press; 2011. Care, and Education Committee on Advancing Pain Research.
2. Chua KS, Reddy SK, Lee MC, Patt RB. Pain and loss of function in head and neck cancer survivors. *J Pain Symptom Manage*. Sep; 1999 18(3):193–202. [PubMed: 10517041]
3. Siegel R, Ward E, Brawley O, Jemal A. Cancer statistics, 2011: the impact of eliminating socioeconomic and racial disparities on premature cancer deaths. *CA Cancer J Clin*. Jul-Aug;2011 61(4):212–236. [PubMed: 21685461]

4. Funk GF, Karnell LH, Christensen AJ. Long-term Health-Related Quality of Life in Survivors of Head and Neck Cancer. *Arch Otolaryngol Head Neck Surg.* Feb; 2012 138(2):123–133. [PubMed: 22248560]
5. Osthus AA, Aarstad AK, Olofsson J, Aarstad HJ. Head and neck specific Health Related Quality of Life scores predict subsequent survival in successfully treated head and neck cancer patients: A prospective cohort study. *Oral Oncol.* Oct; 2011 47(10):974–979. [PubMed: 21856209]
6. Taylor JC, Terrell JE, Ronis DL, et al. Disability in patients with head and neck cancer. *Arch Otolaryngol Head Neck Surg.* Jun; 2004 130(6):764–769. [PubMed: 15210560]
7. Scharpf J, Karnell LH, Christensen AJ, Funk GF. The role of pain in head and neck cancer recurrence and survivorship. *Arch Otolaryngol Head Neck Surg.* Aug; 2009 135(8):789–794. [PubMed: 19687400]
8. McMillan SC, Tofthagen C, Morgan MA. Relationships among pain, sleep disturbances, and depressive symptoms in outpatients from a comprehensive cancer center. *Oncol Nurs Forum.* Jul; 2008 35(4):603–611. [PubMed: 18591165]
9. Terrell JE, Ronis DL, Fowler KE, et al. Clinical predictors of quality of life in patients with head and neck cancer. *Arch Otolaryngol Head Neck Surg.* Apr; 2004 130(4):401–408. [PubMed: 15096421]
10. Watson JM, Logan HL, Tomar SL, Sandow P. Factors associated with early-stage diagnosis of oral and pharyngeal cancer. *Community Dent Oral Epidemiol.* Aug; 2009 37(4):333–341. [PubMed: 19515198]
11. Duffy SA, Ronis DL, Valenstein M, et al. Depressive symptoms, smoking, drinking, and quality of life among head and neck cancer patients. *Psychosomatics.* Mar-Apr; 2007 48(2):142–148. [PubMed: 17329608]
12. Logan HL, Fillingim RB, Bartoshuk LM, et al. Smoking status and pain level among head and neck cancer patients. *J Pain.* Jun; 2010 11(6):528–534. [PubMed: 20015696]
13. Lawton J, Simpson J. Predictors of alcohol use among people experiencing chronic pain. *Psychol Health Med.* Aug; 2009 14(4):487–501. [PubMed: 19697258]
14. van Tonder E, Herselman MG, Visser J. The prevalence of dietary-related complementary and alternative therapies and their perceived usefulness among cancer patients. *J Hum Nutr Diet.* Dec; 2009 22(6):528–535. [PubMed: 19788709]
15. McTiernan A. Physical activity after cancer: physiologic outcomes. *Cancer Invest.* 2004; 22(1):68–81. [PubMed: 15069764]
16. Ronis DL, Duffy SA, Fowler KE, Khan MJ, Terrell JE. Changes in quality of life over 1 year in patients with head and neck cancer. *Arch Otolaryngol Head Neck Surg.* Mar; 2008 134(3):241–248. [PubMed: 18347247]
17. Shuman AG, Duffy SA, Ronis DL, et al. Predictors of poor sleep quality among head and neck cancer patients. *Laryngoscope.* Jun; 2010 120(6):1166–1172. [PubMed: 20513034]
18. Sateia MJ, Lang BJ. Sleep and cancer: recent developments. *Curr Oncol Rep.* Jul; 2008 10(4):309–318. [PubMed: 18778557]
19. Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care.* Jun; 1992 30(6):473–483. [PubMed: 1593914]
20. McHorney CA, Ware JE Jr, Raczek AE. The MOS 36-Item Short-Form Health Survey (SF-36): II. Psychometric and clinical tests of validity in measuring physical and mental health constructs. *Med Care.* Mar; 1993 31(3):247–263. [PubMed: 8450681]
21. Garratt A, Schmidt L, Mackintosh A, Fitzpatrick R. Quality of life measurement: bibliographic study of patient assessed health outcome measures. *BMJ.* Jun 15. 2002 324(7351):1417. [PubMed: 12065262]
22. Karvonen-Gutierrez CA, Ronis DL, Fowler KE, Terrell JE, Gruber SB, Duffy SA. Quality of life scores predict survival among patients with head and neck cancer. *J Clin Oncol.* Jun 1; 2008 26(16):2754–2760. [PubMed: 18509185]
23. Grignon LM, Jameson MJ, Karnell LH, Christensen AJ, Funk GF. General health measures and long-term survival in patients with head and neck cancer. *Arch Otolaryngol Head Neck Surg.* May; 2007 133(5):471–476. [PubMed: 17520761]

24. Wittink H, Turk DC, Carr DB, Sukiennik A, Rogers W. Comparison of the redundancy, reliability, and responsiveness to change among SF-36, Oswestry Disability Index, and Multidimensional Pain Inventory. *Clin J Pain*. May-Jun;2004 20(3):133–142. [PubMed: 15100588]
25. Ware, JE.; Kosinski, M.; Keller, SD. SF-36 physical and mental health summary scales: a users manual. Boston: The Health Institute, New England Medical Centre; 1994.
26. Wallman KK, Evinger S, Schechter S. Measuring our nation's diversity: developing a common language for data on race/ethnicity. *Am J Public Health*. Nov; 2000 90(11):1704–1708. [PubMed: 11076235]
27. Greene, FL. American Joint Committee on Cancer., American Cancer Society. AJCC cancer staging handbook : from the AJCC cancer staging manual. 6th. New York: Springer; 2002.
28. Terrell JE, Nanavati KA, Esclamado RM, Bishop JK, Bradford CR, Wolf GT. Head and neck cancer-specific quality of life: instrument validation. *Arch Otolaryngol Head Neck Surg*. Oct; 1997 123(10):1125–1132. [PubMed: 9339991]
29. Piccirillo JF. Importance of comorbidity in head and neck cancer. *Laryngoscope*. Apr; 2000 110(4):593–602. [PubMed: 10764003]
30. Lewinsohn PM, Seeley JR, Roberts RE, Allen NB. Center for Epidemiologic Studies Depression Scale (CES-D) as a screening instrument for depression among community-residing older adults. *Psychol Aging*. Jun; 1997 12(2):277–287. [PubMed: 9189988]
31. Saunders JB, Aasland OG, Babor TF, de la Fuente JR, Grant M. Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO Collaborative Project on Early Detection of Persons with Harmful Alcohol Consumption--II. *Addiction*. Jun; 1993 88(6):791–804. [PubMed: 8329970]
32. Willett WC, Sampson L, Stampfer MJ, et al. Reproducibility and validity of a semiquantitative food frequency questionnaire. *American Journal of Epidemiology*. 1985; 122(1):51–65. [PubMed: 4014201]
33. Washburn RA, Smith KW, Jette AM, Janney CA. The Physical Activity Scale for the Elderly (PASE): development and evaluation. *J Clin Epidemiol*. Feb; 1993 46(2):153–162. [PubMed: 8437031]
34. Hays RD, Martin SA, Sesti AM, Spritzer KL. Psychometric properties of the Medical Outcomes Study Sleep measure. *Sleep Med*. Jan; 2005 6(1):41–44. [PubMed: 15680294]
35. Viala-Danten M, Martin S, Guillemin I, Hays RD. Evaluation of the reliability and validity of the Medical Outcomes Study sleep scale in patients with painful diabetic peripheral neuropathy during an international clinical trial. *Health Qual Life Outcomes*. 2008; 6:113. [PubMed: 19091084]
36. 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*. Nov 30; 2008 140(2):323–331. [PubMed: 18845396]
37. Fang FM, Tsai WL, Lee TF, Liao KC, Chen HC, Hsu HC. Multivariate analysis of quality of life outcome for nasopharyngeal carcinoma patients after treatment. *Radiother Oncol*. Nov; 2010 97(2):263–269. [PubMed: 20817290]
38. Turk DC, Okifuji A. Does sex make a difference in the prescription of treatments and the adaptation to chronic pain by cancer and non-cancer patients? *Pain*. Aug; 1999 82(2):139–148. [PubMed: 10467919]
39. Rustoen T, Fossa SD, Skarstein J, Moum T. The impact of demographic and disease-specific variables on pain in cancer patients. *J Pain Symptom Manage*. Aug; 2003 26(2):696–704. [PubMed: 12906954]
40. Lin A, Kim HM, Terrell JE, Dawson LA, Ship JA, Eisbruch A. Quality of life after parotid-sparing IMRT for head-and-neck cancer: a prospective longitudinal study. *Int J Radiat Oncol Biol Phys*. Sep 1; 2003 57(1):61–70. [PubMed: 12909216]
41. Graff P, Lapeyre M, Desandes E, et al. Impact of intensity-modulated radiotherapy on health-related quality of life for head and neck cancer patients: matched-pair comparison with conventional radiotherapy. *Int J Radiat Oncol Biol Phys*. Apr 1; 2007 67(5):1309–1317. [PubMed: 17289292]
42. Pow EH, Kwong DL, McMillan AS, et al. Xerostomia and quality of life after intensity-modulated radiotherapy vs. conventional radiotherapy for early-stage nasopharyngeal carcinoma: initial report

- on a randomized controlled clinical trial. *Int J Radiat Oncol Biol Phys*. Nov 15; 2006 66(4):981–991. [PubMed: 17145528]
43. Terrell JE, Welsh DE, Bradford CR, et al. Pain, quality of life, and spinal accessory nerve status after neck dissection. *Laryngoscope*. Apr; 2000 110(4):620–626. [PubMed: 10764008]
 44. Nibu K, Ebihara Y, Ebihara M, et al. Quality of life after neck dissection: a multicenter longitudinal study by the Japanese Clinical Study Group on Standardization of Treatment for Lymph Node Metastasis of Head and Neck Cancer. *Int J Clin Oncol*. Feb; 2010 15(1):33–38. [PubMed: 20101430]
 45. Piccirillo JF, Tierney RM, Costas I, Grove L, Spitznagel EL Jr. Prognostic importance of comorbidity in a hospital-based cancer registry. *Jama*. May 26; 2004 291(20):2441–2447. [PubMed: 15161894]
 46. Piccirillo JF, Vlahiotis A. Comorbidity in patients with cancer of the head and neck: prevalence and impact on treatment and prognosis. *Curr Oncol Rep*. Mar; 2006 8(2):123–129. [PubMed: 16507222]
 47. Massie MJ. Prevalence of depression in patients with cancer. *J Natl Cancer Inst Monogr*. 2004(32):57–71. [PubMed: 15263042]
 48. Tesch RS, Denardin OV, Baptista CA, Dias FL. Depression levels in chronic orofacial pain patients: a pilot study. *J Oral Rehabil*. Oct; 2004 31(10):926–932. [PubMed: 15387830]
 49. Duffy SA, Ronis DL, Valenstein M, et al. A tailored smoking, alcohol, and depression intervention for head and neck cancer patients. *Cancer Epidemiol Biomarkers Prev*. Nov; 2006 15(11):2203–2208. [PubMed: 17119047]
 50. Lydiatt WM, Moran J, Burke WJ. A review of depression in the head and neck cancer patient. *Clin Adv Hematol Oncol*. Jun; 2009 7(6):397–403. [PubMed: 19606075]
 51. Shuman AG, Duffy SA, Ronis DL, et al. Predictors of poor sleep quality among head and neck cancer patients. *Laryngoscope*. Jun; 2010 120(6):1166–1172. [PubMed: 20513034]
 52. Ditre JW, Gonzalez BD, Simmons VN, Faul LA, Brandon TH, Jacobsen PB. Associations between pain and current smoking status among cancer patients. *Pain*. Jan; 2011 152(1):60–65. [PubMed: 21168758]
 53. Logan HL, Fillingim RB, Bartoshuk LM, et al. Smoking status and pain level among head and neck cancer patients. *J Pain*. Jun; 2010 11(6):528–534. [PubMed: 20015696]
 54. 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*. Apr; 2005 114(3):372–385. [PubMed: 15777863]
 55. Riley JL 3rd, King C. Self-report of alcohol use for pain in a multi-ethnic community sample. *J Pain*. Sep; 2009 10(9):944–952. [PubMed: 19712901]
 56. Leeman RF, McKee SA, Toll BA, et al. Risk factors for treatment failure in smokers: relationship to alcohol use and to lifetime history of an alcohol use disorder. *Nicotine Tob Res*. Dec; 2008 10(12):1793–1809. [PubMed: 19023831]
 57. Miller PM, Day TA, Ravenel MC. Clinical implications of continued alcohol consumption after diagnosis of upper aerodigestive tract cancer. *Alcohol Alcohol*. Mar-Apr; 2006 41(2):140–142. [PubMed: 16308354]
 58. van der Molen L, van Rossum MA, Burkhead LM, Smeele LE, Rasch CR, Hilgers FJ. A randomized preventive rehabilitation trial in advanced head and neck cancer patients treated with chemoradiotherapy: feasibility, compliance, and short-term effects. *Dysphagia*. Jun; 2011 26(2):155–170. [PubMed: 20623305]
 59. McNeely ML, Parliament MB, Seikaly H, et al. Effect of exercise on upper extremity pain and dysfunction in head and neck cancer survivors: a randomized controlled trial. *Cancer*. Jul 1; 2008 113(1):214–222. [PubMed: 18457329]
 60. Rogers LQ, Courneya KS, Robbins KT, et al. Factors associated with fatigue, sleep, and cognitive function among patients with head and neck cancer. *Head Neck*. Oct; 2008 30(10):1310–1317. [PubMed: 18642320]
 61. Gil Z, Smith DB, Marouani N, Khafif A, Fliss DM. Treatment of pain after head and neck surgeries: control of acute pain after head and neck oncological surgeries. *Otolaryngol Head Neck Surg*. Aug; 2006 135(2):182–188. [PubMed: 16890065]

62. Grond S, Zech D, Lynch J, Diefenbach C, Schug SA, Lehmann KA. Validation of World Health Organization guidelines for pain relief in head and neck cancer. A prospective study. *Ann Otol Rhinol Laryngol.* May; 1993 102(5):342–348. [PubMed: 7683853]
63. Rogers SN, Lowe D, Brown JS, Vaughan ED. A comparison between the University of Washington Head and Neck Disease-Specific measure and the Medical Short Form 36, EORTC QOQ-C33 and EORTC Head and Neck 35. *Oral Oncol.* Sep; 1998 34(5):361–372. [PubMed: 9861341]
64. Mehanna HM, Morton RP. Deterioration in quality-of-life of late (10-year) survivors of head and neck cancer. *Clin Otolaryngol.* Jun; 2006 31(3):204–211. [PubMed: 16759240]
65. Pizzo PA, Clark NM. Alleviating suffering 101--pain relief in the United States. *N Engl J Med.* Jan 19; 2012 366(3):197–199. [PubMed: 22256802]

Table 1
Patient Characteristics (N=559)^a

Characteristics	N	Mean or %	SD
SF-36 Pain Index			
Baseline	537	60.5	27.1
1 Year follow up	559	65.1	26.2
Demographics			
Age	559	58.4	10.7
Sex			
Male	433	77.5	
Female	126	22.5	
Race			
Caucasian	506	90.5	
Non-Caucasian	53	9.5	
Marital Status (at one year)			
Married	304	60.0	
Single	203	40.0	
Education			
High school or less	245	43.9	
Some college or more	313	56.1	
Clinical Characteristics			
Cancer Site			
Pharynx	296	53.0	
Larynx	129	24.0	
Oral cavity	134	23.1	
Cancer Stage			
I,II	140	25.0	
III, IV	419	75.0	
Primary Site Surgery			
Yes	211	37.8	
No	347	62.2	
Neck Dissection			
Yes	239	42.8	
No	319	57.2	
Radiation			
Yes	472	84.4	
No	87	15.6	
Chemotherapy			
Yes	346	61.9	
No	213	38.1	
Feeding tube at one year			
Yes	102	18.3	

Characteristics	N	Mean or %	SD
No	455	81.7	
Tracheotomy at one year			
Yes	21	3.8	
No	536	96.2	
Xerostomia at one year			
Not at all	113	20.8	
Slightly	93	17.1	
Moderately	100	18.4	
A lot	145	26.7	
Extremely	92	16.9	
Medical Comorbidity			
None or mild comorbidity	391	70.0	
Moderate or severe comorbidity	168	30.0	
Depressive Symptoms at one year^b			
Yes	214	39.3	
No	330	60.7	
Health Behaviors			
Use of pain medicine at one year			
Never	207	37.3	
Rarely	95	17.1	
Sometimes	91	16.4	
Frequently	71	12.8	
Always	91	16.4	
Smoking status at one year			
Current smoker (population norm 19.3%)	125	22.4	
Former smoker	346	61.9	
Never smoker	88	15.7	
Problem Drinking at one year^c			
Yes (population norm 7-13%)	65	11.9	
No	481	88.1	
Vegetable intake			
None to 1 per week	225	53.6	
2-4 per week to 5-6 per week	56	13.3	
1 per day or more	139	33.1	
Fruit intake			
None to 1-3 per month	172	40.9	
1 per week to 2-4 per week	131	31.1	
5-6 per week or more	118	28.0	
Physical Activity at one year (population norm 103) ^d	558	131.7	87.6
Sleep at one year (population norm 72) ^e	557	68.5	20.8

^a 559 patients had SF-36 pain index reported at one year after diagnosis; numbers may not add to total for other variables due to missing data.

^b Geriatric Depressive Scale Short Form 4

^c Alcohol Use Disorders Identification Test (AUDIT) 8

^d Physical Activity Scale for the Elderly (PASE); scores ranged from 0-400 or more; higher scores indicate more activity.

^e Medical Outcomes Study sleep measure (MOS-Sleep); lower scores indicate poorer sleep.

Table 2
Bivariate Association with SF-36 pain score at one year post-treatment (N=559)^a

Characteristics	N	Mean SF-36 Pain Score*	SD	P-value
<i>Demographics</i>				
Age				
58	301	62.9	26.5	0.10
> 58	258	67.8	25.7	
Sex				
Male	433	65.2	26.1	0.89
Female	126	64.9	26.8	
Race				
Caucasian	506	65.5	25.9	0.32
Non-Caucasian	53	61.7	29.3	
Marital Status (at one year)				
Married	304	68.0	25.0	0.003
Single	203	60.9	27.4	
Education				
High school or less	245	62.7	27.5	0.05
Some college or more	313	67.1	25.1	
<i>Clinical Characteristics</i>				
Cancer Site				
Pharynx	296	68.3	25.0	(Reference)
Oral cavity	134	63.2	26.5	0.04
Larynx	129	61.4	27.6	0.01
Cancer Stage				
I,II	140	65.3	26.8	0.94
III,IV	419	65.1	26.1	
Primary Site Surgery				
Yes	211	61.8	27.0	0.02
No	347	67.2	25.6	
Neck Dissection				
Yes	239	61.0	26.7	0.001
No	319	68.2	25.5	
Radiation				
Yes	472	65.0	25.7	0.84
No	87	65.7	26.4	
Chemotherapy				
Yes	346	65.3	26.1	0.85
No	213	64.9	26.5	
Feeding tube at one year				
Yes	102	53.3	25.3	<0.001
No	455	67.9	25.7	

Characteristics	N	Mean SF-36 Pain Score*	SD	P-value
Tracheotomy at one year				
Yes	21	53.4	29.5	0.04
No	536	65.7	26.0	
Xerostomia at one year				
Not at all	113	71.5	27.2	<0.001
Slightly	93	70.2	23.7	
Moderately	100	71.1	23.3	
A lot	145	63.3	24.6	
Extremely	92	49.4	25.6	
Comorbidity				
None or mild comorbidity	391	67.8	25.9	<0.001
Moderate or Severe comorbidity	168	59.0	26.1	
Depressive Symptoms at one year^c				
Yes	214	50.5	25.0	<0.001
No	330	74.9	22.1	
Health Behaviors				
Use of pain medicine at one year				
Never	207	83.7	18.3	<0.001
Rarely	95	68.1	22.6	
Sometimes	91	57.3	17.9	
Frequently	71	48.0	23.0	
Always	91	41.6	23.1	
Smoking status at one year				
Current smoker	88	50.9	25.0	<0.001
Former smoker	346	65.6	26.0	
Never smoker	125	73.8	23.6	
Problem Drinking at one year^d				
Yes	65	48.8	25.9	<0.001
No	481	67.2	25.6	
Vegetable intake				
None to 1 per week	225	62.9	25.7	<0.001
2-4 per week to 5-6 per week	56	64.8	21.9	
1 per day or more	139	74.0	23.6	
Fruit intake				
None to 1-3 per month	172	62.6	25.7	0.002
1 per week to 2-4 per week	131	66.9	23.6	
5-6 per week or more	118	73.2	24.4	
Physical Activity Score at one year				
121	283	58.3	27.1	<0.001
>121	275	72.0	23.3	
Sleep Score at one year				
73	276	52.2	24.8	<0.001

Characteristics	N	Mean SF-36 Pain Score*	SD	P-value
>73	281	77.9	21.0	

* Lower scores signify worse pain

^a 559 patients had SF-36 pain index at one year after diagnosis; numbers may not add to 559 for other variables due to missing data.

^b p-values derived from ANOVA methods (categorical variables) or Spearman test (continuous variables). Continuous variables are dichotomized by median for purpose of summarizing the means in this table.

^c Geriatric Depressive Scale Short Form 4

^d Alcohol Use Disorders Identification Test (AUDIT) 8

Table 3
Multivariate predictors of SF-36 pain score at one year post-treatment (N=374)^a

	Parameter Estimate	95% CI Interval	P-value
Baseline SF-36 pain score	0.20	(0.13, 0.27)	<0.001
<i>Demographics</i>			
Age (10 year increase)	0.50	(-1.37, 2.38)	0.60
Sex (female vs. male)	2.93	(-1.25, 7.10)	0.17
White	1.15	(-5.39, 7.69)	0.73
Marital Status (married vs. single)	-0.74	(-4.40, 2.92)	0.69
Education (High school or less vs. some college or more)	4.19	(0.64, 7.75)	0.02
<i>Clinical Characteristics</i>			
Cancer Site			
Oral cavity (vs. Pharynx)	4.13	(-0.72, 8.97)	0.10
Larynx (vs. Pharynx)	-2.26	(-7.27, 2.74)	0.38
Cancer Stage (III, IV vs. I, II)	1.69	(-3.37, 6.75)	0.51
Primary Site Surgery	2.69	(-2.52, 7.90)	0.31
Neck Dissection	-6.83	(-10.94, -2.72)	0.001
Radiation	5.29	(-1.04, 11.62)	0.10
Chemotherapy	3.14	(-1.91, 8.19)	0.22
Feeding tube at one year	-5.11	(-10.24, 0.01)	0.05
Tracheotomy at one year	4.00	(-7.21, 15.20)	0.49
Xerostomia at one year Extremely/A lot (vs. Moderate/Slightly/Not at all)	-6.69	(-10.58, -2.81)	<0.001
Comorbidity (moderate/severe vs. mild/none)	-2.79	(-6.67, 1.09)	0.16
Depressive symptoms at one year^b	-9.95	(-14.23, -5.67)	<0.001
<i>Health Behaviors</i>			
Use of pain medicine at one year			
Never	19.75	(14.09, 25.42)	<0.001
Rarely	9.42	(3.01, 15.83)	0.004
Sometimes	3.72	(-2.68, 10.12)	0.26
Frequently	-0.06	(-6.50, 6.38)	0.99
Always (Reference)			
Current smoker (vs. never) at one year	-5.94	(-12.33, 0.44)	0.07
Former smoker (vs. never) at one year	-1.55	(-5.83, 2.72)	0.49
Problem Drinking at one year^c	-5.54	(-11.77, 0.68)	0.08
Vegetable intake			
1 per day or more	0.98	(-3.13, 5.09)	0.64
2-4 per week to 5-6 per week	-3.37	(-8.77, 2.02)	0.22
None to 1 per week (reference)			
Fruit intake			
5-6 per week or more	-3.38	(-8.12, 1.36)	0.16
1 per week to 2-4 per week	-2.71	(-6.83, 1.40)	0.20
None to 1-3 per month (reference)			

	Parameter Estimate	95% CI Interval	P-value
Sleep Score at one year^d	0.15	(0.03, 0.26)	0.02
Physical Activity Score at one year^e	0.03	(0.01, 0.06)	0.006

Note: Bold values have $p < 0.05$

CI: confidence interval

^a 374 patients had complete data on all variables.

^b Geriatric Depressive Scale Short Form = 4

^c Alcohol Use Disorders Identification Test (AUDIT) = 8

^d Physical Activity Scale for the Elderly (PASE); scores ranged from 0-400 or more; higher scores indicate more activity; reference is one unit increase.

^e Medical Outcomes Study sleep measure (MOS-Sleep); lower scores indicate poorer sleep; reference is one unit increase.