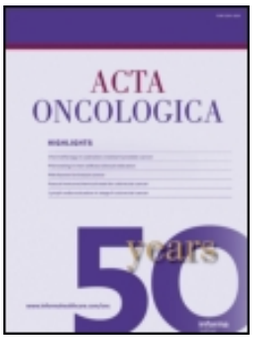

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ORIGINAL ARTICLE

Predictors of smoking cessation among cancer patients enrolled in a smoking cessation program

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Abstract

Many cancer patients continue to smoke postdiagnosis, which is associated with poorer clinical outcomes. Identifying prospective predictors of smoking cessation among patients currently receiving smoking cessation treatment can help guide the development and implementation of smoking cessation programs with this population. *Material and methods*. Data from 246 cancer patients participating in a randomized placebo-controlled smoking cessation clinical trial were used to examine baseline predictors of end-of-treatment and six-month postbaseline smoking cessation outcomes. Baseline demographic, smoking-related, disease-related, and psychological variables were examined as predictors of biochemically-confirmed point-prevalence abstinence. *Results*. Multivariate analysis indicated that, for end-of-treatment abstinence, patients were significantly more likely to have quit smoking if they were older (OR = 1.06, 95% CI: 1.03–1.10, $p < 0.05$) and were diagnosed with a non-tobacco related cancer (OR = 2.54, 95% CI: 1.24–5.20, $p < 0.05$). Likewise, for six-month abstinence, patients were significantly more likely to have quit smoking if they were older (OR = 1.04, 95% CI: 1.01–1.08, $p < 0.05$) and were significantly less likely to have quit smoking if they were female (OR = 0.47, 95% CI: 0.22–0.97, $p < 0.05$). Patients with tobacco-related cancers and female patients reported significantly higher levels of depression symptoms ($p < 0.05$), which proved predictive of smoking relapse. *Conclusions.* Patient age, gender, and cancer-type may be important factors to consider when developing and implementing smoking cessation interventions for cancer patients.

Numerous studies have documented the rate of smoking among individuals with cancer. Studies with patients that have tobacco-related cancers show very high rates of smoking; upwards of 50% of head and neck [1] and lung [2] cancer patients report current smoking. Significant rates of current smoking have also been reported among testicular (19%; [3]), prostate (16–17%; [4,5]), cervical (21%; [6]), breast (19%; [7]), bladder (18%; [8]), esophageal (39%; [9]), colorectal (22%; [10]), and lymphoma (19%; [11]) cancer patients. In addition, many studies have documented the relationship between continued smoking by cancer patients and reduced survival, increased risk for disease recurrence and a second primary tumor, and diminished quality of life (QOL; [12,13]). A recent meta-analysis of studies with lung cancer patients found that continued smoking was related to an increased risk of death, recurrence, and a second primary tumor [14]. Likewise, studies with head and neck cancer patients have demonstrated that patients who continue to smoke following their diagnosis have a lower survival rate and an increased risk for a recurrence and a second primary tumor [15–18]. Continued smoking has also been associated with reduced survival among breast [19], lymphoma [11], esophageal [9], prostate [4], cervical [20], and bladder [21] cancer patients, with an increased risk of recurrence or a second primary tumor among bladder [22], breast [7], lymphoma [23], and colorectal [24] cancer patients, and with greater treatment side effects or diminished QOL among head and neck [25,26], lung [27], prostate [28], and a heterogeneous group of [29] cancer patients.

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Consequently, the development and implementation of smoking cessation treatment programs for cancer patients has become a greater priority. This effort should be guided by an understanding of the factors related to the smoking behavior of cancer patients [13]. Prior studies have associated demographic (e.g. age, gender), disease-related (e.g. stage, cancer site), smoking-related (e.g. nicotine dependence) and psychological (e.g. depression) characteristics with cancer patient smoking behavior [29–33]. However, with very few exceptions, the existing literature is based on cross-sectional data and has used samples of patients who were not enrolled in a smoking cessation treatment program. Studies using prospective data collected from patients enrolled in a smoking cessation treatment program may better represent the population of patients for whom treatment programs would be provided.

In the present study, we analyzed data collected prospectively as part of a randomized, placebo-controlled smoking cessation clinical trial with cancer patients. Based on previous studies, we expected that female and younger patients, patients with tobacco-related cancers, patients with more extensive smoking histories, and patients who reported higher levels of smoking to alleviate emotional distress would be less likely to have quit smoking. The primary results of this trial indicated that bupropion was not effective for promoting abstinence but that depression symptoms were a strong predictor of cessation outcomes [29]. For the present study, we examined demographic (e.g. age, gender), disease-related (e.g. cancer stage, cancer site), smoking-related (e.g. nicotine dependence), and psychological (i.e. smoking to alleviate psychological distress) characteristics assessed at trial entry as predictors of smoking cessation at the end-of-treatment and at a six-month follow-up assessment. These results may help future efforts to develop and implement smoking cessation treatment programs for cancer patients.

Material and methods

Patients

The sample was comprised of 246 cancer patients who were self-identified smokers and interested in quitting [29]. Interest in quitting was assessed using the following face valid yes vs. no question after hearing a description of the clinical trial: "Does this sound like something that you are interested in?". To be eligible, patients had to be ≥18 years of age, speak English, possess a telephone, smoke at least two cigarettes/day on average, and have a cancer diagnosis. The patients were free of Axis I psychiatric conditions and medical conditions that made taking bupropion or using nicotine patches unsafe. Over 7500 patients were screened for eligibility and interest by telephone, 291 attended an in-person eligibility screening session, and 246 patients were eligible and randomized. Enrolled participants resembled those who declined the trial [34].

Study design and procedures

The data for this study are from a double-blind, placebo-controlled smoking cessation clinical trial [29]. Informed consent was obtained from all patients and Institutional Review Board approval was ascertained and maintained throughout the clinical trial. In this trial, 246 patients were randomized to either: behavioral counseling and transdermal nicotine patch plus bupropion *or* behavioral counseling and transdermal nicotine patch plus placebo. Prior to the initiation of treatment, all patients completed a set of surveys, described below. Treatment was provided for 11 weeks. At week 12 (end-of-treatment) and week 27 (six-months post target quit-date), patients were assessed for the primary outcome variable which was seven-day point prevalence abstinence, confirmed with carbon monoxide (CO). The five smoking cessation counseling sessions (three in-person, two phone) were provided by a trained smoking cessation counselor. Sessions were manual-based and focused on behavioral strategies for preparing to quit smoking and avoiding relapse based on Social Cognitive theory.

Measures

Demographics. The age (years), gender, education (number of years of education), marital status (single, married, divorced), and race and ethnicity (Caucasian, Black, Asian American, Hispanic American) were recorded for patients by self-report.

Disease-related variables. Cancer type and stage was ascertained from medical records.

Smoking-related characteristics. Patients indicated their current level of smoking, the age at which they started smoking and years smoked, and completed the Fagerström Test for Nicotine Dependence (FTND; [35]).

Psychological correlates. Patients completed the Cigarette Evaluation Scale (CES; [36]), a self-report measure consisting of 11 items on which participants rate the pleasurable effects of tobacco, using a scale from 0 (not at all) to 7 (extremely). The scale was used to assess the degree to which patients experience psychological relief from smoking (e.g. "Does

it calm you down"). The CES has excellent psychometric qualities [37] and has been used in past smoking cessation trials [38]. Depression symptoms were assessed using Center for Epidemiological Studies Depression scale (CES-D; [39]), a 20-item measure of depression symptoms used previously with cancer patients [29]. The CES-D is reliable and is a valid predictor of clinical depression [39].

Smoking behavior. The primary outcome was seven-day point prevalence abstinence at weeks 12 and 27, confirmed with breath CO (abstinence = ≤10 ppm) [40]. Four participants at week 12 and four participants at week 27 self-reported to be abstinent from tobacco use but provided a CO sample that was above 10 ppm. This represents less than 2% of the overall sample or 6% of CO samples conducted at week 12 and 8% of samples conducted at week 27.

Data analysis. The first step was to use χ^2 test and ANOVA to evaluate individual predictors of week 12 and week 27 abstinence (e.g. age, nicotine dependence). Next, variables that were associated with either outcome ($p < 0.05$) in these analyses were included in subsequent separate multivariate logistic regression analyses, one for week 12 and one for week 27 abstinence. Baseline level of smoking (cigarettes per day) and treatment arm (bupropion vs. placebo) were included as covariates to control for these variables in the logistic regression models. Finally, follow-up ANOVAs and Pearson correlations were conducted for additional interpretation of significant predictors of abstinence.

Results

Sample characteristics

To summarize, half of the sample was female and close to one third of the sample was made up of ethnic/racial minorities, including 29% African American. Almost half the sample had a college degree or higher. The average patient age was 54.8 years and the average cigarettes/day was 17.5 (S.D. = 9.3). The average FTND score was 3.2 (S.D. = 1.2; Range = 1–5) and the average cigarettes/day was 17.5 (S.D. = 9.3). Close to one third of the sample had stage 3 or 4 cancer and close to one third of the sample had tobacco-related cancers (head and neck or lung) vs. non-tobacco-related cancers (breast, prostate, lymphoma, colorectal, kidney, pancreas, liver, genitourinary, or esophageal). There were no significant differences across the treatment arms in terms of sample baseline characteristics [29]. The quit rate at week 12 was 26% and the quit rate at week 27 was 18%.

Univariate predictors of week 12 and week 27 abstinence

As shown in Table I, patients who were abstinent at week 12 were significantly more likely to be older ($F[1,244] = 12.64$, $p < 0.001$), less likely to report that they smoke to alleviate psychological distress ($F[1,244] = 3.88$, $p = 0.05$), and more likely to have a non-tobacco-related cancers ($\chi^2[1] = 5.12$, $p = 0.03$). As shown in Table II, patients who were abstinent at week 27 were significantly more likely to be older ($F[1,244) = 9.92$, $p = 0.002$), more likely to be male ($\chi^2[1] = 5.73$, $p = 0.02$), and more likely to have started smoking at a later age ($F[1,244] = 3.93$, $p = 0.05$).

Multivariate predictors of week 12 and week 27 abstinence

As shown in Table III, the multivariate regression model for week 12 abstinence indicated that patients were significantly more likely to have been abstinent at this time-point if they were older and had a non-tobacco-related cancer. Likewise, the multivariate regression model for week 27 abstinence indicated that patients were significantly more likely to have been abstinent at this time-point if they were older and male. To help interpret these results, we examined if cancer type, sex, and age were related to depression symptoms, since depression symptoms were identified previously as a strong predictor of abstinence outcomes [29]. Specifically, we compared baseline depression symptoms between: 1) patients with non-tobacco-related cancers vs. tobacco-related cancers; 2) male vs. female patients; and 3) younger vs. older patients. While patient age was not related to level of depression symptoms ($r = -0.04$, $p > 0.05$), patients with non-tobacco-related cancers reported a significantly lower level of depression symptoms ($F[1,240] = 4.03$, $p < 0.05$), compared to patients with tobacco-related cancers (Means = 8.87 vs. 11.51). Likewise, male patients reported a significantly lower level of depression symptoms ($F[1,240] = 6.71$, $p = 0.01$), compared to female patients (Means = 8.24 vs. 11.36).

Discussion

The aim of this study was to identify prospective predictors of smoking behavior in a sample of cancer patients participating in a smoking cessation treatment program. In addition to the main results of this study published previously that identified depression symptoms as an important predictor of cessation outcomes [29], the current analyses identify patient age, cancer type, and gender as additional important variables to consider in developing and implementing

Table I. Univariate analysis of predictors of abstinence at week 12.

Predictor	Abstinent (N = 63)	Smoking (N = 183)	p
Age (Mean Years)	60.2	54.8	<0.001
Sex			0.15
Female (%)	21.2	78.8	
Male (%)	29.7	70.3	
Race			
European Ancestry (%)	25.9	74.1	1.0
Non-European Ancestry (%)	25.0	75.0	
Marital Status			
Married (%)	25.0	75.0	0.88
Un-married (%)	26.4	73.6	
Education			
High School or Less	21.0	79.0	0.08
Bachelor's Degree or More	31.8	68.2	
Baseline Cigarettes Per Day (Mean)	16.0	18.1	0.13
Age Started Smoking (Mean Years)	17.7	16.5	0.07
Years Smoked (Mean Years)	40.9	37.7	0.06
FTND (Mean)	3.1	3.2	0.39
Smoke to Alleviate Psychological Distress (Mean)*	21.2	23.1	0.05
Cancer Type			
Tobacco-related (%)	16.7	83.3	0.03
Non-tobacco-related (%)	29.9	70.1	
Cancer Stage			
Stage 1 or 2 (%)	26.0	74.0	0.50
Stage 3 or 4 (%)	31.1	68.9	

FTND, Fagerström Test for Nicotine Dependence; p, probability; chi-square test of significance was used for categorical predictors (e.g. age) and ANOVA was used for continuous predictors (e.g. age); * the range = 30 (10–40).

a smoking cessation treatment program. The present analysis represents one of the few prospective studies with a relatively large sample of cancer patients undergoing smoking cessation treatment in this area of research.

In this sample of cancer patients enrolled in a smoking cessation treatment program, older patients were significantly more likely to quit smoking than younger patients. This result converges with large epidemiological surveys of the general population of smokers [41], large epidemiological surveys of individuals with a history of cancer [42], and smaller cohort studies of cancer patients [2,43]. While age was not inversely related to depression symptoms, older patients may be more likely to quit smoking since they are more likely to have comorbid physical problems which either make smoking more difficult or underscored the health risks of smoking, thereby enhancing motivation to quit. As such, younger cancer patients who smoke may need to be targeted with more intensive interventions to promote cessation.

In addition, we found that patients with non-tobacco-related cancers were more likely to quit smoking, compared to patients with tobacco-related cancers. This result diverges from a previous finding [33] and suggests that the relationship between cancer site and smoking behavior may be somewhat more complex. To explore a potential explanation for this finding, we assessed if cancer site was associated with depression symptoms, which we previously identified as a strong predictor of abstinence in this trial [29]. Consistent with our suspicion, patients with non-tobacco-related cancers reported significantly lower levels of depression symptoms than patients with tobacco-related cancers. Parenthetically, cancer site was not associated with smoking history, including initial level of smoking, age at initiation, years smoked, and level of nicotine dependence. As such, in the present study, the increased risk for smoking relapse seen among patients with tobacco-related cancers may be due to significantly high levels of depression symptoms among these patients. These patients may require additional counseling or pharmacotherapy to address psychological distress to improve their chances for successful smoking cessation.

Lastly, we found that male patients were more likely to quit smoking than female patients. This result converges with data collected from the general population of smokers which shows that the rate of decline in smoking over the past several decades among women has been significantly slower than among men and that women have shown less responsiveness to treatments for nicotine dependence [44]. One previously proffered explanation for this relationship between sex and the ability to quit smoking has been higher rates of depression symptoms among women [45]. This potential explanation garnered

Table II. Univariate analysis of predictors of abstinence at week 27.

Predictor	Abstinent (N = 44)	Smoking (N = 202)	p
Age (Mean Years)	60.7	55.2	0.002
Sex			
Female (%)	11.9	88.1	0.02
Male (%)	23.4	76.6	
Race			
European Ancestry (%)	16.7	83.3	0.49
Non-European Ancestry (%)	20.2	79.8	
Marital Status			
Married (%)	16.9	83.1	0.74
Un-married (%)	19.1	80.9	
Education			
High School or Less	15.2	84.8	0.24
Bachelor's Degree or More	21.5	78.5	
Baseline Cigarettes Per Day (Mean)	15.5	18.0	0.10
Age Started Smoking (Mean Years)	18.1	16.5	0.05
Years Smoked (Mean Years)	41.3	38.0	0.08
FTND (Mean)	2.9	3.2	0.11
Smoke to Alleviate Psychological Distress (Mean)*	21.6	22.8	0.26
Cancer Type			
Tobacco-related (%)	12.8	87.2	0.16
Non-tobacco-related (%)	20.7	79.3	
Cancer Stage			
Stage 1 or 2 (%)	20.7	79.3	0.71
Stage 3 or 4 (%)	18.0	82.0	

FTND, Fagerström Test for Nicotine Dependence; p, probability; χ^2 test of significance was used for categorical predictors (e.g. age) and ANOVA was used for continuous predictors (e.g. age); * the range = 30 (10–40).

Table III. Logistic regression of week 12 (top) and week 27 (bottom) abstinence.

Predictor of Week 12	OR	95% CI	p
Baseline cigarettes per day	0.98	0.94–1.02	0.25
Treatment Arm (Reference = Placebo)	0.83	0.45–1.55	0.57
Age	1.06	1.03–1.10	<0.001
Smoke to Alleviate Psychological Distress	0.99	0.94–1.04	0.67
Cancer Type (Reference = Tobacco-related)	2.54	1.24–5.20	0.01
Predictor of Week 27	**OR**	**95% CI**	**p**
Baseline cigarettes per day	0.97	0.93–1.01	0.14
Treatment Arm (Reference = Placebo)	0.95	0.48–1.89	0.88
Age	1.04	1.01–1.08	0.03
Age Started Smoking	1.05	0.98–1.12	0.14
Sex (Reference = Male)	0.47	0.24–0.97	0.04

OR, Odds ratio; CI, confidence interval; p, probability; each model included baseline cigarettes per day and treatment arm as covariates.

further support in the present study with our finding that female cancer patients reported greater depression symptoms than men. As such, female patients may also require additional counseling or pharmacotherapy to address psychological distress to improve their chances for successful smoking cessation.

These findings should be viewed in the context of study limitations. First, the present study examined a relatively narrow range of predictors of abstinence and, thus, future studies may be needed to explore additional determinants of smoking outcomes among cancer patients undergoing smoking cessation treatment. Second, although the prospective nature of the data is a study strength, relative to most studies in this area, the analyses are correlational, and causal interpretations should not be made. Third, the present study was based on a sample of patients currently undergoing treatment for nicotine dependence. As such, the present findings can be generalized to patients willing to enroll in a formal smoking cessation clinical trial, not to all cancer patients. Indeed, the present sample may differ from the general population of cancer patients who smoke in terms of characteristics that influence smoking behavior such as quit motivation and depressive symptoms. Indeed, the present sample's FTND scores were relatively low, indicating that the present sample had lower nicotine dependence than is typical of smokers participating in smoking cessation clinical trials and lower than the population of cancer patients who smoke. Lower FTND scores may have been the result of cancer patients reducing the amount smoked and refraining from smoking when they are feeling ill, both of which would lower FTND scores. It is possible that including patients with higher levels of nicotine dependence would alter the results reported here. Furthermore, the generalizability of the results may be additionally limited by the exclusion criteria that were necessary to reduce the risk of adverse side effects from nicotine replacement therapy and bupropion, the treatments provided to patients in this clinical trial.

Nevertheless, the study findings identify three potentially important factors to consider when developing and implementing a smoking cessation treatment program with cancer patients – patient age, sex, and cancer type – and underscore the potential effect of depression symptoms that may link patient sex and cancer type to smoking cessation outcomes. Younger patients, female patients, and patients with tobacco-related cancers may need to be targeted with more intensive smoking cessation interventions which specifically address symptoms of psychological distress such as interventions described by Dy et al. [46]. Indeed, cancer patients are at heightened risk for developing clinically relevant symptoms of depression [47] which significantly predict smoking relapses [29]. Cancer patients, therefore, may require targeted treatments to address their use of tobacco to self-medicate to alleviate symptoms of depression. Future studies are needed to further elucidate predictors of

smoking behavior among cancer patients, including additional measures of psychological distress (e.g. anxiety, guilt, shame, fatalism), indicators of cognitive impairment, and the unique time-course of relapse among patients [48]. In turn, an important direction for future research is to test innovative treatments that address these predictors in order to reduce the high rates of continued smoking in this population and improve patient clinical outcomes.

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