Association of Cigarette Type and Nicotine Dependence in Patients Presenting for Lung Cancer Screening

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BACKGROUND: Over decades, there have been several alterations to cigarettes, including the addition of filters and flavoring. However, lung cancer remains the leading cause of cancer-related death in the United States.

RESEARCH QUESTION: The aim of this study was to examine the association of type of cigarette on nicotine dependence in the setting of lung cancer screening.

STUDY DESIGN AND METHODS: This study is a secondary analysis of the American College of Radiology Imaging Network arm of the National Lung Screening Trial. Tobacco dependence was evaluated by using the Fagerström Test for Nicotine Dependence, the Heaviness of Smoking Index, and time to first cigarette. Clinical outcomes, including nicotine dependence and tobacco abstinence, were assessed with descriptive statistics and χ^2 tests, stratified according to cigarette tar level, flavor, and filter. Logistic regression was used to study the influence of variables on smoking abstinence.

RESULTS: More than one-third of individuals presenting for lung cancer screening are highly addicted to nicotine and smoke within 5 min of waking up. Smokers of unfiltered cigarettes were more nicotine dependent compared with filtered cigarette smokers (OR, 1.32; $P < .01$). Although smokers of light/ultralight cigarettes had lower dependence (OR, 0.76, $P < .0001$), there was no difference in smoking abstinence compared with regular cigarette smokers. There was no difference in outcomes when comparing smokers of menthol vs unflavored cigarettes.

INTERPRETATION: In a screening population, the type of cigarette smoked is associated with different levels of dependence. Eliciting type of cigarette and time to first cigarette has the potential to allow for tailored tobacco treatment interventions within this context.

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KEY WORDS: cigarette type; lung cancer screening; nicotine dependence; tobacco cessation

ABBREVIATIONS: FTND = Fagerström Test for Nicotine Dependence; HSI = Heaviness of Smoking Index; LCS = lung cancer screening; LDCT = low-dose CT; NLST = National Lung Screening Trial; TTFC = time to first cigarette

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The 1964 US Surgeon General report heightened public awareness regarding the dangerous health effects of cigarette smoking, including lung cancer and heart disease.¹ In response to consumer concerns, tobacco manufacturers developed and marketed “lower tar” cigarettes as an alternative to quitting under the assumption that this approach would reduce risk of harms, with no true evidence to support these claims.²⁻⁵ A number of changes to the cigarette were instituted by the tobacco industry in an effort to reduce tar levels (Fig 1). Tar is a complex mixture of carcinogens and toxins delivered to the smoker, affecting health risk.³ The addition of filters was the first attempt to reduce tar delivery. Subsequent changes included using less tobacco per cigarette, increasing the burn rate of the tobacco column/rod (eg, with increased paper porosity), increasing filter efficiency (eg, ventilated or denser filters), decreasing the density of the tobacco by using reconstituted and expanded or puffed tobacco, and tobacco blending.^{4,6,7} Filter ventilation, or the process of puncturing ventilation holes into the filter to dilute smoke with air, became the optimum way to reduce tar yield in cigarettes of similar design, with larger or increased number of holes resulting in lower tar yields.^{3,6} It is well established that the tobacco industry developed filters with the intention that they might reduce harm but realized from their own internal research that the risks of mainstream smoke could not be mitigated, after which point the filters became purely a marketing tool.⁸ In 2010, the US Food and Drug Administration introduced regulation banning the use of brand descriptors such as “low tar,” “mild,” “light,” and “ultra-light” in their advertising because it was deemed to be misleading.^{9,10} However, this intervention has been partially circumvented by tobacco companies using different colors in packaging, which are readily recognized by most smokers as indicators of previously labeled light cigarettes.

In addition, menthol flavoring was added to improve tolerance of cigarettes by reducing the burning

sensation, thereby promoting continued use. The menthol flavor provides an analgesic, anesthetizing, and cooling sensation. Due to these characteristics, tobacco companies used targeted marketing to enhance the appeal of menthol cigarettes to specific populations, including young, female, and black smokers.^{11,12}

In an effort to standardize and regulate the measurement of tar levels, the Federal Trade Commission used a smoking machine simulating smoking behavior. This machine produces a 35 mL inhalation (puff) over 2 s at a rate of one puff per minute, burning each cigarette to a fixed butt length, and measures the amount of tar produced.³ Using these measurements, the Federal Trade Commission defined “ultralight” cigarettes as 1 to 6 mg of tar yield per cigarette, “light” cigarettes as 7 to 15 mg of tar yield per cigarette, and “regular” cigarettes as > 15 mg of tar yield per cigarette.^{3,6} However, internal industry research shows that this method of measurement does not adequately reflect varying human behaviors in smoking cigarettes and revealed that, when smokers switched to light cigarettes, they increased their puff volume to maintain similar levels of smoke delivery.¹³

Regardless of categorization and changes made, cigarette smoking is still responsible for 80% of lung cancer diagnoses, which is the leading cause of cancer death worldwide.¹⁴ Despite improvements in cancer treatment, the 5-year lung cancer survival rate remains low at 18%, highlighting the importance of primary and secondary prevention.¹⁴ Lung cancer screening (LCS) with low-dose CT (LDCT) imaging has been shown to improve mortality, and tobacco treatment is an integral part of effective screening.¹⁵⁻¹⁷

Previous research has shown that within a screening setting, 7 years of smoking abstinence resulted in a reduction in lung cancer-specific mortality (20%) equivalent to LDCT screening, and the reduction was even greater (38%) when combined with LCS.¹⁸

Figure 1 – A-C, Anatomy of a cigarette depicting different methods to reduce tar yield. A, Reduced density of tobacco with reconstituted or expanded tobacco, additives and flavorings, tobacco blending (with barley, Oriental, or burley tobaccos), or use of lower nicotine yield tobacco and reduced circumference of cigarette rod allows for less tobacco per cigarette. B, Increased porosity and additives to paper allow for increased burn rate and air dilution. C, Filter ventilation allows air dilution of smoke delivered to user.

At least 60% of LCS participants express motivation to quit smoking, including interest in tobacco treatment counseling and interventions.¹⁷ It has also been shown that within a screening program, dependence predicts worse clinical outcomes, including higher incidence of lung cancer, all-cause mortality, and lung cancer-specific mortality.¹⁹ Lung

cancer mortality is also increased when smoking unfiltered cigarettes.^{20,21}

Using data from the National Lung Screening Trial (NLST), we sought to investigate the association of different cigarette types, as defined by filter status, tar level, and menthol flavor, on tobacco dependence and abstinence.

Subjects and Methods

This study is a secondary data analysis of a subset of participants of the NLST from the American College of Radiology Imaging Network centers. This study was approved by the Institutional Review Board of the Medical University of South Carolina (Pro 00054733).

Participants

The NLST design has been previously described.¹⁵ The American College of Radiology Imaging Network arm of the trial included 14,123 participants who completed more detailed smoking questionnaires on variables of interest (eg, cigarette tar level, flavor, filter, nicotine dependence).²² Both former and current smokers completed the detailed smoking questionnaires at study entry (e-Fig 1), with former smokers asked to recall their smoking habits. This initial questionnaire included questions to determine nicotine dependence using the tools described in the following section. Participants were sent smoking habit questionnaires (e-Fig 2) every 6 months for the duration of follow-up to determine cessation or recidivism during the trial.¹⁵

Variables

The primary exposures, cigarette tar level (regular, light, or ultralight), flavor (unflavored or menthol), and filter status (filtered or unfiltered), were collected at baseline from both current and former smokers. The clinical outcomes evaluated were smoking abstinence and nicotine dependence. Participants were defined as abstinent from smoking when they answered “no” to the smoking status question, “In the past 6 months, have you smoked any cigarettes?” in their final questionnaire response. Nicotine dependence was assessed at baseline in the initial questionnaire using the Fagerström Test for Nicotine Dependence (FTND), the Heaviness of Smoking Index (HSI), and the time to first cigarette (TTFC). The FTND is a well-validated, six-

item, self-report scale commonly used for the measurement of severity of dependence.²³ The HSI constitutes two higher yield items from the FTND: number of cigarettes smoked per day and TTFC.^{24,25} Higher scores represent higher levels of dependence, with the FTND ranging from 0 to 10, HSI 0 to 6, and TTFC 0 to 3. All three scales have been validated and predict both biochemical and behavioral indexes of smoking.^{25,26} The FTND, HSI, and TTFC scores were grouped to reflect level of severity of nicotine dependence.^{24,27}

Statistical Analysis

Each outcome was evaluated with descriptive statistics and χ^2 tests, each stratified according to cigarette tar level, flavor, and filter. Logistic regression was used to study the influence of cigarette tar level, flavor, and filter on smoking abstinence. This model controlled for smoking status at baseline (current or former smoker). Partial proportional odds models were used to examine the influence of cigarette tar level, flavor, and filter on nicotine dependence outcomes (FTND, HSI, and TTFC). In each model, we controlled for sex, age, race, pack years, and treatment arm (LDCT imaging vs chest radiograph). We also assessed multicollinearity using the variance inflation factor to mitigate the influence of highly correlated covariates. We also checked differences in the association between the outcomes and the primary exposures according to receipt of LDCT scan by including interactions in the respective models. Estimates of ORs and 95% CIs were determined. Estimates of predictive performance were based on C-statistics for logistic regression models. Logistic regression model fit was assessed by using the Akaike information criterion. Assumptions pertaining to the logistic regression model were assessed via residual plots. All statistical analyses were performed by using SAS 9.4 software (SAS Institute, Inc.).

Results

Participant Characteristics

Of the 14,123 participants included in the analysis, the majority were white (92.3%) with a level of education > 12 years (70.4%) (Table 1). The average total pack year history was 55.9 ± 23.7 , and average age of smoking initiation was 17.3 ± 4.6 years. Most smoked filtered cigarettes ($n = 12,488$ [88.4%]), and nearly one-half smoked light or ultralight cigarettes ($n = 6,222$ [44%]). Less than one-quarter ($n = 3,210$ [22.7%]) smoked menthol cigarettes. However,

among black participants, more than one-half (54%) smoked menthol cigarettes, compared with only 20.8% of white participants ($P < .0001$). At enrollment, 7,056 (50%) participants were current smokers. At the end of the follow-up period, 1,949 of the current smokers in the study (27.6%) achieved self-reported abstinence. Based on the FTND and HSI, the average person was moderately addicted to nicotine. However, approximately one-third were highly dependent, reporting smoking a cigarette within 5 min of waking up.

TABLE 1] Demographic Characteristics and Smoking History of Study Population (N = 14,123)

Characteristic	Value
Age, mean $\pm$ SD, y	61.6 $\pm$ 5.1
Women	6,354 (45.0)
White	13,038 (92.3)
Married	8,923 (63.2)
Education > 12 y	9,941 (70.4)
Pack years, mean $\pm$ SD	55.9 $\pm$ 23.7
Age began smoking, mean $\pm$ SD	17.3 $\pm$ 4.6
Randomized to CT arm	7,084 (50.2)
Smoking status	
Current smoker throughout study	5,107 (36.2)
Current smoker quit during study	1,949 (13.8)
Re-started smoking during study	486 (3.4)
Former smoker throughout study	6,581 (46.6)
Cigarette type	
Regular	7,869 (55.7)
Lights	4,660 (33.0)
Ultralights	1,562 (11.1)
Flavor	
Regular	10,888 (77.1)
Menthol	3,210 (22.7)
Filter	
Filtered	12,488 (88.4)
Unfiltered	1,611 (11.4)
FTND score, mean $\pm$ SD (range, 0-10)	3.6 $\pm$ 1.3
HSI score, mean $\pm$ SD (range, 0-6)	3.3 $\pm$ 1.4
Time to first cigarette	
Within 5 min	4,771 (33.8)
Within 6 to 14 min	5,470 (38.8)
From 15 to < 60 min	2,042 (14.5)
$\geq$ 60 min	1,833 (13.0)

Data are presented as No. (%) unless otherwise indicated. FTND = Fagerström Test for Nicotine Dependence; HSI = Heaviness of Smoking Index.

Cigarette Characteristics, Nicotine Dependence, and Abstinence

There was no difference in abstinence rates between unfiltered and filtered cigarette smokers (Table 2). The group that smoked unfiltered cigarettes was 30% more likely to be very highly dependent compared with smokers of filtered cigarettes ($P < .01$) (e-Table 1, Fig 2). Unadjusted and adjusted dependence outcomes are presented in e-Tables 1 and 2.

There was no significant difference in abstinence rates in patients who smoked light or ultralight cigarettes compared with those who smoked regular cigarettes

(Table 2), even though this group was less nicotine dependent. Those who smoked light/ultralight cigarettes had lower cumulative odds of being “very highly dependent” compared with lower dependence levels ($P < 0.01$) (e-Table 1, Fig 2). There was no difference in adjusted smoking abstinence or dependence for menthol cigarette smokers compared with those who smoked unflavored cigarettes.

Discussion

Individuals are selected for LCS based on their smoking history. It has been previously shown that a higher level of nicotine dependence is associated with worse lung cancer incidence and mortality.¹⁹ This study extends that work by examining the relationship between cigarette type and nicotine dependence and has three important observations. First, those smoking unfiltered cigarettes are more nicotine dependent. Second, although light/ultralight smokers were less dependent, they were not more likely to quit smoking. Finally, there was no difference in smoking abstinence rates or dependence between those smoking menthol cigarettes compared with those smoking unflavored cigarettes.

To our knowledge, this study is the first to describe the impact of filters on smoking behavior and dependence in an LCS population. Individuals presenting for LCS are highly dependent on nicotine, with 34% smoking within 5 min and 73% smoking within 14 min of waking, respectively. These rates are significantly higher than the average current smoker in the United States (24% and 65%, respectively), as measured by the Tobacco Use Supplement of the Current Population Survey conducted by the American Cancer Institute and the Centers for Disease Control and Prevention.²⁸ This level of dependence warrants multimodal and aggressive tobacco treatment. Of the participants, 14% report abstinence, which is similar to cessation rates from other large LCS trials, which report 11% to 13% quit rates.²⁹ Furthermore, we found that people who smoked unfiltered cigarettes are the most highly addicted according to any measure. This is the same population who has the highest all-cause and lung cancer-related mortality. These findings indicate the importance of identifying these individuals who stand to benefit most from aggressive tobacco treatment.

Tobacco companies marketed low-tar cigarettes to consumers as an alternative to quitting, suggesting that this improved health risks by adding labels such as “light” or “ultralight” to their cigarettes. Previous work

TABLE 2] Smoking Abstinence Stratified According to Cigarette Type

Cigarette Type	OR	95% CI	P Value	C-Statistic
Unfiltered vs filtered	0.91	0.78-1.06	.21	0.86
Light/ultralight vs regular	0.97	0.88-1.06	.46	0.86
Menthol vs unflavored	1.07	0.97-1.20	.17	0.86

established there was no difference in lung cancer or all-cause mortality for those who smoked light/ultralight cigarettes compared with those who smoked regular cigarettes.²⁰ In this study, light/ultralight smokers were not more successful at smoking cessation despite being less dependent on nicotine compared with regular tar cigarette smokers. Unfortunately, most smokers believe light/ultralight cigarettes deliver less tar and impart a reduction in risk, and this misconception may dissuade them from quitting.³⁰ In one study, < 10% of smokers of light/ultralight cigarettes were aware that they deliver similar amounts of tar and nicotine as a regular cigarette.³¹

In addition, compensatory smoking allows smokers of light/ultralight cigarettes to achieve a higher nicotine level by increasing puff volume, number of puffs per cigarette, and time length of puff. It also involves smoking more cigarettes per day, smoking cigarettes to a shorter butt length, or obstructing filter ventilation holes with their fingers to deliver more nicotine and, consequently, tar into their lungs.^{32,33} Studies have shown that smokers who switch from higher tar yield cigarettes to lower tar yield cigarettes maintain the same plasma concentration of nicotine and tobacco smoke toxins.³²

Menthol cigarettes represent another method tobacco companies used to reduce the harshness of cigarette smoke. It has been hypothesized that menthol cigarettes could cause increased lung cancer incidence due to the ability to take larger puffs with increased delivery of carcinogens to peripheral lung zones. It was also postulated that this contributed to the disparity in lung cancer-related mortality for black subjects, 84% of whom admit to smoking menthol cigarettes compared with only 24% of white subjects.³⁴ This preference for menthol cigarettes in the black community was confirmed in our study, with more than twice as many black smokers of menthol cigarettes compared with

white smokers. Another study showed that menthol cigarettes were associated with poorer smoking cessation success,³⁴ although this was not confirmed here as both smoking abstinence rates and dependence measures between menthol and unflavored cigarette smokers were the same.

The current investigation highlights that clinicians should ask their patients about cigarette brand and dependence as an integral part of smoking cessation counseling during the LCS visit. This information not only serves as an opportunity to educate patients on their smoking behaviors but can also help tailor nonpharmacologic and pharmacologic smoking treatment. For example, smokers of unfiltered cigarettes with TTFC < 5 min may benefit from upfront dual pharmacologic therapy with more frequent follow-up. How dependence scores and brand of cigarette can direct appropriate tobacco treatment is an essential area for further research. Furthermore, the findings from this study reinforce the need for the US Food and Drug Administration and government regulators to implement product standards to reduce the risks from smoking conventional combusted cigarettes regardless of whether they are filtered. For example, reducing the amount of nicotine in the tobacco rod has been shown in multiple studies to reduce biomarkers of smoke exposure and consumption and to promote quitting.^{35,36} Furthermore, engineering cigarettes to reduce the toxins smokers are exposed to should be considered.

There were several limitations to this study. First, given the self-report nature of the data collection instrument, there is a risk of recall bias. In addition, abstinence is self-reported, which may not represent true abstinence. Second, the results do not account for those who switched cigarette type or brands. In a study of > 3,000 patients exploring brand switching of adult smokers from 2006 to 2011, the authors found that only 12% to

Figure 2 – Forest plot illustrating nicotine dependence scores comparing types of cigarette. Smokers of unfiltered cigarettes score higher in nicotine dependence, whereas smokers of light cigarettes score lower. There is no difference in dependence for smokers of menthol cigarettes vs smokers of regular cigarettes. FTND = Fagerström Test for Nicotine Dependence; HSI = Heaviness of Smoking Index; TTFC = time to first cigarette.

15% of smokers report switching strength of cigarette and only 3% to 6% report switching flavors.³⁷ Third, the results were adjusted for pack year history, which, although necessary to eliminate confounding, could also mask the potential association of smoking light/ultralight cigarettes with compensatory smoking, especially if light/ultralight cigarette smokers increased the number of cigarettes per day to compensate for lower nicotine levels. The NLST study enrolled patients from 2002 to 2004, prior to regulations prohibiting the use of “light,” “ultra-light,” “mild,” or “low tar” from cigarette labels. How the new labels affect these specific outcomes has not yet been studied. Finally, black smokers, who account for the majority of menthol cigarette smokers, accounted for only 4% of NLST participants.¹⁵

Conclusions

Although LCS is considered a “teachable moment” for tobacco cessation, and a mandated component for LCS, little is known about how to incorporate and optimize tobacco treatment in this group of long-term, highly addicted smokers. Providers should not underestimate the level of tobacco dependence in those who are eligible for screening and should suspect that they will have difficulty quitting, especially depending on the type of cigarette that is smoked. There are trials underway investigating various strategies for implementing tobacco treatment into LCS.³⁸ Until the results of these trials are available, routinely collecting type of cigarette smoked and TTFC could help providers in tailoring patient-centered tobacco treatment.

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Additional information: The e-Figures and e-Tables can be found in the Supplemental Materials section of the online article.

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