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Tobacco Dependence Predicts Higher Lung Cancer and Mortality Rates and Lower Rates of Smoking Cessation in the National Lung Screening Trial

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BACKGROUND: Incorporating tobacco treatment within lung cancer screening programs has the potential to influence cessation in high-risk smokers. We aimed to better understand the characteristics of smokers within a screening cohort, correlate those variables with downstream outcomes, and identify predictors of continued smoking.

METHODS: This study is a secondary analysis of the National Lung Screening Trial randomized clinical study. Tobacco dependence was evaluated by using the Fagerström Test for Nicotine Dependence, the Heaviness of Smoking Index, and time to first cigarette (TTFC); descriptive statistics were performed. Clinical outcomes (smoking cessation, lung cancer, and mortality) were assessed with descriptive statistics and χ^2 tests stratified according to nicotine dependence. Logistic and Cox regression models were used to study the influence of dependence on smoking cessation and mortality, respectively.

RESULTS: Patients with high dependence scores were less likely to quit smoking compared with low dependence smokers (TTFC OR, 0.50 [95% CI, 0.42-0.60]). Indicators of high dependence, as measured according to all three metrics, were associated with worsening clinical outcomes. TTFC showed that patients who smoked within 5 min of waking (indicating higher dependence) had higher rates of lung cancer (2.07% for $>$ 60 min after waking vs 5.92% $\leq$ 5 min after waking; hazard ratio [HR], 2.56 [95% CI, 1.49-4.41]), all-cause mortality (5.38% for $>$ 60 min vs 11.21% $\leq$ 5 min; HR, 2.19 [95% CI, 1.55-3.09]), and lung cancer-specific mortality (0.55% for $>$ 60 min vs 2.92% for $\leq$ 5 min; HR, 4.46 [95% CI, 1.63-12.21]).

CONCLUSIONS: Using TTFC, a one-question assessment of tobacco dependence, at the time of lung cancer screening has implications for personalizing tobacco treatment and improving risk assessment.

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KEY WORDS: lung cancer; nicotine dependence; smoking; smoking cessation

ABBREVIATIONS: ACRIN = American College of Radiology Imaging Network; FTND = Fagerström Test for Nicotine Dependence; HSI = Heaviness of Smoking Index; HR = hazard ratio; LDCT = low-dose CT; NLST = National Lung Screening Trial; TTFC = time to first cigarette

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Smoking contributes to 480,000 deaths annually in the United States from causes that include cardiovascular disease and cancer.[1] Lung cancer is the sixth leading cause of death in the United States, with nearly 90% of this cancer caused by cigarette smoking. Tobacco cessation is considered the single most effective primary prevention strategy for reducing the risk of lung cancer death. There is now evidence for secondary prevention, with lung cancer screening as a means to identify lung cancer at an earlier, more treatable stage in patients with extensive smoking histories. Based on the large randomized National Lung Screening Trial (NLST), which reported a 20% reduction in all-cause mortality, the US Preventable Service Task Force now recommends lung cancer screening with low-dose CT (LDCT) scanning for individuals at high risk based on age and smoking history.[2] An estimated eight million Americans are eligible for lung cancer screening.[3]

Many of those presenting for lung cancer screening will be current smokers, as 48% of the 53,454 patients enrolled in the NLST were active smokers at trial entry, and current estimates are that 16.8% of adults smoke cigarettes.[3] A joint policy statement from the American College of Chest Physicians and the American Thoracic Society identified smoking cessation as an essential component of a highly effective and comprehensive lung cancer screening program.[4] Furthermore, to be a lung cancer screening program accredited by the Centers for Medicare & Medicaid Services, smoking cessation must be included. Lung screening is believed to be a teachable moment to promote cessation, but evidence suggests that having a scan increases quit rates only slightly shortly following the scan, and long-term cessation rates are similar for those with both positive and negative lung findings.[5,6] However, detection of a major abnormality from lung cancer screening can lead to higher rates of smoking cessation.[7] It is important to note that one small but potentially troubling study showed that some smokers might view lung cancer screening as a "free pass" to keep smoking.[8] Although the integration of smoking cessation within the context of lung cancer screening has the potential to bolster cessation, little is known about how to best tailor interventions based on screening participants' smoking behaviors.

Cigarette smoking is widely accepted as a dependence disorder,[9] and an individual's level of dependence is predictive of his or her ability to quit smoking.[10,11] The FagerstrÖm Test for Nicotine Dependence (FTND) is a six-item self-report scale commonly used for the measurement of severity of dependence on cigarettes.[12] The Heaviness of Smoking Index (HSI) constitutes two items from the FTND: amount smoked and time to first cigarette (TTFC).[13] All three measures (FTND, HSI, and TTFC) have been shown to predict smoking cessation outcomes, with higher dependence scores corresponding to lower quit rates.[10,11] Greater nicotine dependence may also contribute to lung cancer risk. For example, higher scores on the FTND[14] and, more specifically, the TTFC[15-17] are associated with an increased lung cancer risk, independent of smoking history. Of note, it has recently been shown that assessing nicotine dependence with TTFC can help to classify lung cancer screening patients with regard to their lung cancer risk, which may be helpful in shared decision-making visits and establishing better risk-predictive eligibility criteria for screening.[18]

The present study was conducted to better understand how level of nicotine dependence affects the cessation rates of those undergoing lung cancer screening and to assess its impact on lung cancer diagnosis, all-cause mortality, and lung cancer-specific mortality. By identifying predictors of continued smoking, we aim to inform effective cessation efforts as they are integrated and implemented into lung cancer screening programs.

Subjects and Methods

This study was approved by the Medical University of South Carolina Institutional Review Board (No. 00054733). It is a secondary analysis of subjects from the American College of Radiology Imaging Network (ACRIN) arm of the NLST randomized controlled trial.

Participants

The NLST enrolled 53,452 current and former (quit within 15 years) smokers ages 55 to 74 years with a minimum of a 30 pack-year cigarette smoking history.[3] Participants were randomized to three rounds of annual screening with LDCT or chest radiography. The ACRIN arm of the NLST (n = 14,125) was selected for analysis because this subset completed more detailed smoking questionnaires on variables of interest (eg, nicotine dependence) than the other NLST participants. Because the focus of this endeavor was on how current nicotine dependence related to medical outcomes, the

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present analyses include only the current smokers in the ACRIN subset (n = 7,057).[19]

Variables

Self-reported data were used to assess the participants' age, sex, race, smoking history (number of pack-years), marital status, and educational background. Self-reported smoking status questionnaires also assessed other items regarding smoking behavior, including the FTND, HSI, and TTFC. Total scores on the FTND range from 0 to 10, on the HSI from 0 to 6, and on the TTFC from 0 to 3; higher scores reflect greater severity of nicotine dependence. All three metrics have been shown to predict both behavioral and biochemical indices of smoking.[10,12,13,20,21] Clinical outcome data assessed included smoking cessation, lung cancer diagnosis, overall deaths, and lung cancer deaths.

Statistical Analysis

Nicotine dependence, as assessed by using the FTND, HSI, and TTFC, was evaluated with descriptive statistics. FTND scores were grouped to reflect level of severity of nicotine dependence: very low (0-2), low (3-4), moderate (5), high (6-7), and very high (8-10) dependence.[22] Similarly, HSI scores were grouped to reflect severity of nicotine dependence: very low (0-2), low (3), moderate (4), high (5), and very high (6) nicotine dependence. TTFC is scored as > 60 min (0; lowest dependence), 31 to 60 min (1), 6 to 30 min (2), and within 5 min (3; highest dependence).

Four primary clinical outcomes were evaluated: (1) smoking cessation following LDCT; (2) lung cancer rates; (3) all-cause mortality rates; and (4) lung cancer-specific mortality. Participants were coded as abstinent from smoking if they answered "No" to the following smoking status question at any point in the 6 years following their lung screening: "In the past 6 months, have you smoked any cigarettes?"

The clinical outcomes were evaluated with descriptive statistics and χ^2 tests stratified according to nicotine dependence. The Cochran-Armitage test for trend was used to assess trend in outcomes. Logistic regression was used to study the influence of nicotine dependence on smoking cessation, and Cox regression was used to study its association with clinical outcomes (lung cancer diagnosis, all-cause mortality, and lung cancer-specific mortality), controlling for sex, age, race, pack-years, treatment arm, and presence of lung nodule (yes/no). We also checked differences in the association between the outcomes and nicotine dependence according to treatment arm by including interactions in the respective models. Estimates of ORs, hazard ratios (HRs), 95% CIs, and likelihood ratio tests for trend are displayed. Assumptions pertaining to both the logistic and Cox regression models were assessed via residual plots. All statistical analyses were performed by using SAS version 9.4 (SAS Institute, Inc).[23]

Results

Participant Demographic Characteristics

Of the 7,057 current smokers, 3,504 underwent spiral CT imaging, and 3,553 underwent radiography. Participant demographic characteristics are presented in Table 1. Approximately one half of the current smokers were female (45.9%), and the majority were white (89.8%), with a mean 55.2 ± 22.0 pack-year history of smoking. Lung nodules were detected in 19.5% of the current smokers (across 3 years of annual screening). The mean FTND score was 6.1 ± 2.3, and the mean HSI score was 4.2 ± 1.4, indicating moderate to high nicotine dependence, and 34.0% of participants reported that they smoked within 5 min of waking (TTFC).

TABLE 1] Demographic Characteristics of Current Smokers

Characteristic	Current Smokers (N = 7,057)
Randomized to CT imaging arm	3,504 (49.7%)
Age, mean ± SD, y	61.0 ± 4.9
Female	3,240 (45.9%)
White	6,336 (89.8%)
Married	4,130 (58.5%)
Education > 12 y	2,300 (32.6%)
Pack-years, mean ± SD	55.2 ± 22.0
Age began smoking, mean ± SD, y	16.8 ± 4.0
Lung nodule detected	1,377 (19.5%)
FTND, mean ± SD	6.1 ± 2.3
HSI, mean ± SD	4.2 ± 1.4
TTFC < 5 min	2,399 (34.0%)

FTND = Fagerström Test for Nicotine Dependence; HSI = Heaviness of Smoking Index; TTFC = time to first cigarette.

Smoking Cessation Outcomes

The outcomes evaluating the relationship between level of dependence and quitting smoking after undergoing lung cancer screening show an effect of dependence on quitting behavior. Indeed, compared with those with very low levels of dependence, with each incremental increase in the severity of dependence, the likelihood of quitting smoking decreased. For example, Table 2 shows that compared with very low dependence smokers as assessed on the HSI, very high dependence smokers were less likely to quit (OR, 0.59 [95% CI, 0.49-0.72]). As shown in Table 3, this finding was observed for TTFC as well, with those who smoked within 5 min of waking showing a reduced likelihood of quitting smoking compared with those who smoked after > 60 min (OR, 0.50 [95% CI, 0.42-0.60]). Over the course of the 6-year follow-up period, 34.2% of participants reported abstinence from cigarettes.

Clinical Outcomes

The clinical outcomes according to level of dependence as assessed by using the FTND, HSI, and TTFC are presented in Tables 4 and 5. Patients who had higher FTND scores had higher rates of lung cancer (2.34% for

TABLE 2] Likelihood of Quitting Smoking by Level of Dependence According to FTND and HSI

	FTND		HSI	
Variable	OR	95% CI	OR	95% CI
Low dependence	0.94	0.76-1.16	0.95	0.80-1.14
Medium dependence	0.67	0.54-0.84	0.75	0.63-0.89
High dependence	0.71	0.58-0.87	0.72	0.60-0.85
Very high dependence	0.59	0.48-0.73	0.59	0.49-0.72

Variables were compared with very low dependence smokers. See Table 1 legend for expansion of abbreviations.

very low dependence smokers vs 6.12% for very high dependence smokers; HR, 2.44 [95% CI, 1.32-4.51]; $P < .01$) and higher rates of all-cause mortality (5.85% very low dependence vs 11.03% very high dependence; HR, 2.09 [95% CI, 1.40-3.12]; $P < .01$). Furthermore, this pattern of findings was also observed with HSI scores; patients who had higher HSI scores showed higher rates of lung cancer (2.60% for very low dependence smokers vs 6.45% for very high dependence smokers; HR, 2.18 [95% CI, 1.34-3.56]; $P < .01$), higher rates of all-cause mortality (6.34% very low dependence vs 12.31% very high dependence; HR, 2.15 [95% CI, 1.55-2.98]; $P < .01$), and higher rates of lung cancer-specific mortality (1.02% very low dependence vs 3.52% very high dependence; HR, 2.87 [95% CI, 1.37-5.98]; $P < .01$).

The same pattern was observed for TTFC; patients who smoked within 5 min of waking (indicating higher dependence) had higher rates of lung cancer (2.07% for $>$ 60 min of waking vs 5.92% $\leq$ 5 min of waking; HR, 2.56 [95% CI, 1.49-4.41]; $P < .01$), all-cause mortality (5.38% for $>$ 60 min of waking vs 11.21% $\leq$ 5 min of waking; HR, 2.19 [95% CI, 1.55-3.09]; $P < .01$), and lung cancer-specific mortality (0.55% for $>$ 60 min of waking vs 2.92% $\leq$ 5 min of waking; HR, 4.46 [95% CI, 1.63-12.21]; $P < .01$). Importantly, this trend was not observed for the other question that constitutes the HSI (number of cigarettes smoked per day), highlighting the unique contribution of TTFC in evaluating dependence on cigarettes that contain nicotine.

TABLE 3] Likelihood of Quitting Smoking by Level of Dependence According to TTFC

	TTFC	
Variable	OR	95% CI
31-60 min	0.75	0.61-0.91
6-30 min	0.66	0.56-0.78
$\leq$ 5 min	0.50	0.42-0.60

Variables were compared with $>$ 60 min TTFC. See Table 1 legend for expansion of abbreviation.

Discussion

Successful tobacco cessation is critical within the context of lung cancer screening, but how best to implement tobacco treatment has yet to be determined. To our knowledge, our study is the first to investigate the relationship between degree of nicotine dependence and both likelihood to quit smoking and clinical cancer and mortality outcomes in a cohort of screened patients. It found that current smokers participating in lung cancer screening are more dependent on tobacco compared with the average US smoker (FTND of 6.1 vs 4.4-4.6, respectively).[24] This finding is further highlighted by two other important outcomes of this study that should inform lung cancer screening tobacco cessation efforts moving forward. First, those with high nicotine dependence are less likely to quit smoking after lung screening. This finding is independent of pack-years and supports the need for an assessment of tobacco dependence to identify those at high risk who are likely to have more difficulty making a quit attempt following screening. Second, people presenting for lung cancer screening with high levels of nicotine dependence are more likely to die of lung cancer and all other causes compared with those who are less dependent. This finding is consistent with the literature showing that greater nicotine dependence may contribute to lung cancer risk and mortality.[14-18]

Several hypotheses have been suggested to explain the independent relationship between nicotine dependence and lung cancer risk and mortality. For example, the relationship between nicotine dependence and lung cancer risk and lung cancer-specific morality could be a reflection of greater toxicant exposure. Previous research has shown a dose-dependent relationship between TTFC and cotinine, a marker of nicotine uptake,[21] as well as TTFC and biochemical levels of 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol, a tobacco smoke carcinogen.[25] Alternatively, dependence could reflect differences in nicotine metabolism. The literature on the nicotine metabolite ratio shows that normal nicotine

TABLE 4] Clinical Outcomes According to Level of Dependence

Variable	All		Lung Cancer		All-Cause Mortality		Lung Cancer-Specific Mortality	
	No.	%	No.	%	No.	%	No.	%
Overall	7,057	100	348	4.93	637	9.03	159	2.25
FTND								
Very low dependence	513	7.27	12	2.34	30	5.85	5	0.97
Low dependence	1,216	17.23	54	4.44	107	8.80	24	1.97
Medium dependence	957	13.56	44	4.60	78	8.15	17	1.78
High dependence	2,231	31.61	107	4.80	186	8.34	52	2.33
Very high dependence	2,140	30.32	131	6.12	236	11.03	61	2.85
Trend test				< .001		< .001		< .001
HSI								
Very low dependence	883	12.51	23	2.60	56	6.34	9	1.02
Low dependence	1,222	17.32	52	4.26	110	9.00	23	1.88
Medium dependence	1,511	21.41	73	4.83	113	7.48	33	2.18
High dependence	1,906	27.01	101	5.30	169	8.87	40	2.1
Very high dependence	1,535	21.75	99	6.45	189	12.31	54	3.52
Trend test				< .001		< .001		< .001
TTFC[a]								
> 60 min	725	10.27	15	2.07	39	5.38	4	0.55
31-60 min	927	13.14	42	4.53	78	8.41	19	2.05
6-30 min	3,003	42.55	149	4.96	251	8.36	66	2.20
≤ 5 min	2,399	33.99	142	5.92	269	11.21	70	2.92
Trend test				< .001		< .001		< .001

See Table 1 legend for expansion of abbreviations.
[a]Three values were missing from the TTFC analyses (final TTFC n = 7,054); trend test = Cochran-Armitage trend test.

metabolizers are more likely to have high nicotine dependence as measured by using the HSI than slow nicotine metabolizers.[26] Furthermore, slow metabolizers have a greater likelihood of quitting smoking than normal metabolizers.[27] These differences in amount or duration of exposure to cigarette smoke could affect the risk for lung cancer. Indeed, a case-control study in the Singapore Chinese Health Study showed that the ORs of developing lung cancer for intermediate, slow, and poor metabolizers determined according to cytochrome P450 2A6 genotypes were 0.85, 0.55, and 0.32, respectively, compared with normal metabolizers.[28]

Our findings show that TTFC, which is a brief single-item measure, was somewhat better at predicting lung cancer mortality. Thus, inserting one additional question into standard intake forms for lung cancer screening programs would not be time-consuming or difficult, and would aid in the identification of high-risk, high-dependence smokers. Although previous research has shown that undergoing multiple LDCT scans for lung cancer screening promotes cessation,[29] a single session LDCT screening does not.[5,30,31] Likewise, referral to a physician for an abnormal scan result may increase initial quit attempts, but this behavior is not always sustained.[29,32] Regardless of the outcome of the scan, our study confirms that continued smoking leads to worse clinical outcomes and highlights the importance of identifying those less likely to quit smoking. The present dataset followed up participants for 6 years following their lung screening. Thus, the significant increases in incidence and mortality were observed in a relatively short time span. Quantitatively assessing the level of nicotine dependence through the use of simple tools such as TTFC as part of a lung cancer screening program would identify those most dependent on cigarettes who will have more difficulty quitting smoking. It is crucial for lung cancer screening programs to provide assistance to these patients as soon as possible. A more rigorous treatment program for these individuals or novel interventions that could be delivered at the time of the first screening may better

TABLE 5] HRs With 95% CIs According to Level of Dependence

Variable	Lung Cancer			All-Cause Mortality			Lung Cancer-Specific Mortality		
	HR	95% CI	*P* Value	HR	95% CI	*P* Value	HR	95% CI	*P* Value
FTND									
Low dependence	1.96	1.05-3.66	.04	1.55	1.03-2.33	.03	2.02	0.77-5.32	.15
Medium dependence	1.88	0.99-3.58	.05	1.45	0.95-2.22	.09	1.73	0.63-4.74	.29
High dependence	1.95	1.06-3.56	.03	1.50	1.02-2.22	.04	2.14	0.85-5.43	.11
Very high dependence	2.44	1.32-4.51	< .01	2.09	1.40-3.12	< .01	2.51	0.98-6.44	.06
Likelihood trend			.02			< .01			.08
HSI									
Low dependence	1.64	1.00-2.68	.05	1.51	1.10-2.10	.01	1.83	0.84-3.96	.13
Medium dependence	1.79	1.12-2.87	.02	1.25	0.91-1.73	.18	2.07	0.99-4.33	.05
High dependence	1.85	1.16-2.95	.01	1.51	1.11-2.07	.01	1.84	0.88-3.83	.10
Very high dependence	2.18	1.34-3.56	< .01	2.15	1.55-2.98	< .01	2.87	1.37-5.98	< .01
Likelihood trend			< .01			< .01			.01
TTFC									
31-60 min	2.05	1.14-3.70	.02	1.51	1.03-2.22	.04	3.43	1.17-10.10	.03
6-30 min	2.19	1.29-3.74	< .01	1.55	1.11-2.18	.01	3.51	1.28-9.65	.01
≤ 5 min	2.56	1.49-4.41	< .01	2.19	1.55-3.09	< .01	4.46	1.63-12.21	< .01
Likelihood trend			< .01			< .01			< .01

Reference group: very low dependence for FTND and HSI, and > 60 min for TTFC; likelihood ratio test for trend. HR = hazard ratio. See Table 1 legend for expansion of other abbreviations.

facilitate smoking cessation. For example, TTFC is currently used to guide dosing for nicotine replacement gum and lozenges.[9]

Tobacco cessation in lung cancer screening is a nascent field, and thus data are emerging presently. This situation is highlighted by the National Cancer Institute's 2016 Smoking Cessation at Lung Examination (SCALE) collaboration, which funded eight centers to assess tobacco treatment in the context of lung cancer screening.[33] It is crucial that lung cancer screening is not seen as a "free pass" for very-high-risk patients to smoke[8] and that tobacco treatment interventions are provided. Notably, a preliminary study of a telephone counseling program for lung cancer screening patients (N = 92) was conducted in which participants in the telephone counseling arm received six counseling calls vs no calls in the usual care arm.[34] Quit rates at 3 months in this pilot study were 17.4% in the telephone counseling arm and 4.3% in the usual care arm. Although preliminary, this outcome shows that participation in a smoking cessation program leads to higher quit rates than usual care. Given the findings regarding clinical outcomes in the present study, it would seem that following National Comprehensive Cancer Network guidelines and providing a first-line strong course of medication (ie, nicotine patch combined with a short-acting nicotine medication [such as a nicotine lozenge] or varenicline) for high dependence smokers combined with behavioral counseling sessions are warranted.[35]

Similarly, engaging primary care providers in tobacco treatment interventions is essential. One study within a subset of NLST participants (n = 3,336) analyzed provider delivery of the 5As (Ask, Advise, Assess, Assist, and Arrange) for tobacco screening and treatment 1 year following screening.[36] The following rates of delivery of the 5 As were found: Ask, 77.2%; Advise, 75.6%; Assess, 63.4%; Assist, 56.4%; and Arrange follow-up, 10.4%. Assist was associated with a 40% increase in the odds of quitting (OR, 1.40 [95% CI, 1.21-1.63]), and Arrange was associated with a 46% increase in the odds of quitting (OR, 1.46 [95% CI, 1.19-1.79]). These findings highlight the importance of providing tobacco treatment from all avenues available.

Although these studies provide promising results, the exact type of tobacco intervention and when, how, and where in the screening continuum it should be introduced is not clear. What is definitely known is that combining smoking abstinence with screening improves outcomes. We previously showed that within the NLST,

7 years of abstinence alone is equivalent to the mortality reduction seen with screening (20%) but that the combination of smoking abstinence and LDCT screening resulted in a 38% reduction in death from lung cancer.[37] In addition, a study evaluating patients undergoing repeated LDCT screening found that compared with current smokers, former smokers had a 39% reduction in overall mortality.[38] Of note, our findings reveal a stronger association with all-cause mortality than lung cancer and lung cancer-specific mortality. We see a greater percentage of very high dependence patients lost to all-cause mortality (HSI: 12.31%) compared with lung cancer-specific mortality (HSI: 3.52%). However, the HRs are very similar (2.15 vs 2.87, respectively). This outcome likely reflects a greater number of patients lost to all-cause mortality (eg, due to coronary heart disease) than lung cancer in general, yet the risk of mortality is similar.

Strategies to assist with tobacco treatment in the context of lung screening are of vital importance not for the health benefit but the cost to the health care system. For example, the cost per quality-adjusted life year for lung cancer screening with LDCT is approximately $81,000[39] vs the cost per quality-adjusted life year for smoking cessation, which is exponentially less at $1,100 per quality-adjusted life year.[40]

The present study has several limitations. First, it was a secondary analysis of a randomized trial, and the smoking status questionnaire was not collected for the entire NLST sample. Thus, we were only able to examine data from 7,057 of the 25,762 current smokers; however, this group is the largest cohort of screened patients thus far with detailed nicotine dependence information. Second, the data are based on self-reported smoking behavior. Some patients may not accurately represent their smoking (eg, due to embarrassment or recall bias). However, studies examining the validity of smokers' self-reports have noted that differences between self-report and biochemical validation have been relatively small in absolute terms.[41,42] Third, both the HSI and TTFC are a subset of the FTND. Thus, these measures are highly related, explaining the similar pattern of findings with the three measures. Of note, this is also a strength of using the TTFC, in that our findings hold up for this brief, easy to administer single-item measure. Finally, the associations between the clinical outcomes and the levels of dependence reflect a generally increasing trend from very low dependence to very high dependence, with the very high dependence group demonstrating the strongest, most consistent, and most impressive outcomes. Within the other dependence categories, there are some inconsistencies, either with between-group differences not reaching statistical significance (eg, Table 5) or the trend not showing a linear pattern (eg, the association between HSI dependence categories and all-cause mortality in Table 5). These inconsistencies are likely explained by the small range of possible scores for the FTND (0-10), HSI (0-6), and TTFC (0-3), which may only identify statistically significant relationships for those scoring at the extreme ends of the scale and homogeneity of dependence for those who score in the middle of the range.

The findings from the present study contribute to the literature showing that smoking is a crucial variable to consider in the context of lung cancer screening, and they indicate that level of nicotine dependence contributes to ability to quit smoking and clinical cancer and mortality outcomes. We suggest adding TTFC, which is a single-question assessment of dependence, at the time of screening to identify high-risk smokers who are less likely to quit and are at higher risk for lung cancer, all-cause mortality, and lung cancer-specific mortality. Identifying high-risk and high dependence smokers may result in improved downstream tobacco treatment if a referral is made to treatment services, as well as improving risk assessment of patients undergoing screening.

Conclusions

Current smokers presenting for lung cancer screening have varying levels of tobacco dependence that predicts both ability to quit and clinical outcomes of lung cancer diagnosis, all-cause mortality, and lung cancer-specific mortality. Identifying individuals with higher levels of nicotine dependence through the use of the TTFC, which is a single-question assessment, at the time of screening has the potential to influence tobacco treatment efforts and increase cessation success within the context of lung cancer screening programs. Given the extensive smoking histories of lung cancer screening patients and their risk for poor clinical outcomes, using this information to develop tailored tobacco treatment and improve risk assessment for lung cancer may lead to better individual and health system outcomes.

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