Original Article

The impact of substance use on health care utilization, treatment, and outcomes in patients with non-small cell lung cancer

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Background: Mortality from non-small cell lung cancer (NSCLC) has improved with screening and novel treatments. The substance use epidemic has threatened health outcomes in a variety of diseases, but little is known about how it is associated with NSCLC outcomes.

Methods: We performed a retrospective cohort study of 211 patients with NSCLC treated at a safety-net hospital. Sociodemographic data and clinical outcomes were extracted via review of electronic medical records. Patients were stratified based on substance use status. Comparative and multivariable analyses were performed to evaluate baseline characteristics and lung cancer outcomes including survival.

Results: Among 193 patients (91.5%) with information available on substance use, 24.9% reported substance use; specifically, alcohol, marijuana, and illicit substances. Patients with substance use were more likely to have increased health care utilization and poor social determinants of health, including safe housing, stable employment, and social support. There were no significant differences in treatment adherence. Only 6.3% of patients with substance use did not receive guideline concordant care (GCC) compared to 24.8% of patients without substance use; due to poor performance status, increased comorbidities, or loss to follow up. On univariable analysis, patients with substance use experienced inferior median overall survival (OS) if they had metastatic disease (0.40 *vs.* 1.03 years, P=0.01). However, in the multivariable analysis, substance use did not predict for survival. Independent predictors of mortality were sex (male HR, 1.67; 95% CI: 1.04–2.68; P=0.04), smoking status (current smoking HR, 2.63; 95% CI: 1.14–6.08; P=0.02), and stage (stage IV HR, 14.96; 95% CI: 6.28–35.63; P=0.008).

Conclusions: Substance use is associated with poor social determinants of health and increased health care utilization. On multivariable analysis, substance use was not independently associated with OS once guideline-concordant care was used. Future studies should focus on improving our understanding of these associations, delineating potential mechanisms, and developing evidence-based strategies to reduce health care utilization and overcome challenges related to poor social determinants of health.

Keywords: Substance use; non-small cell lung cancer (NSCLC); outcomes; healthcare utilization

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Introduction

Lung cancer is the leading cause of cancer-related deaths worldwide (1). In the United States, over 200,000 new cases were diagnosed in 2018 and non-small cell lung cancer (NSCLC) accounted for approximately 85% of these cases (2). Over the past 25 years, increased cancer screening, widespread implementation of smoking cessation programs, and improved treatment strategies have resulted in earlier diagnosis, better outcomes, and declining mortality (2). However, the rising prevalence of substance use could present unique physical and psychosocial challenges that may threaten these improving outcomes (3).

In recent years, substance use has become increasingly common and problematic throughout the United States. The estimated prevalence was 20 million individuals in 2015, thus making substance use one of the most pressing public health crises of our time (4). Recent epidemiologic studies show alarming results, including that alcohol and opioid-related fatalities remain the leading preventable cause of death in the United States, and the combined health-related costs of alcohol and opioid use disorders exceed 700 billion US dollars per year (5-7).

In patients with cancer, the prevalence of substance use is largely unknown (3). While evidence suggests an association between substance use and the risk of developing cancer, little data exists on substance use and the impact on various health outcomes in patients with cancer (8-10). One meta-analysis including 209,597 cancer survivors demonstrated worse survival and increased recurrence risk among patients with higher alcohol consumption (11). Substance use is associated with increased health care utilization, increased risk of recurrence, and worse survival (8-12). Efforts are needed to investigate the prevalence of substance use among patients with cancer and examine the relationship between substance use and cancer outcomes (8). Research into the challenges of this population may inform the development of interventions to improve outcomes for patients with cancer and substance use. In our study, we primarily sought to determine the prevalence of substance use in patients with NSCLC. We also explored the association of substance use with clinical presentation, health care utilization, treatment adherence, and overall survival (OS). We present the following article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-21-1992/rc).

Methods

Study design and patients

We retrospectively identified 211 patients diagnosed with NSCLC at a safety-net hospital in Boston, Massachusetts between January 1st 2014 and December 30th 2017. The number of cases available during the study time period determined sample size. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the institutional review board of Boston University/Boston Medical Center (No. H-37619) and individual consent for this retrospective analysis was waived. Baseline demographics, co-morbidities, information on social determinants of health, details on cancer type and stage, substance use status, and information on treatment were extracted by review of electronic medical records. Information extracted on social determinants of health included presence of stable housing, stable employment, and relationship status. We chose specific social determinants based on their known association with access to healthcare and health outcomes as well as their availability in the medical record. Treatment information included type of treatment (surgery, radiation, systemic therapy, or any combination thereof) and treatment adherence (number of missed appointments to surgery, medical oncology, and radiation oncology clinics *vs.* the total number of appointments scheduled). Study data was managed using Research Electronic Data Capture (REDCap) electronic data capture tools hosted at Boston University, CTSI 1UL1TR001430 (13). REDCap is a secure, web- based application designed to support data capture for research studies, providing (I) an intuitive interface for validated data entry; (II) audit trails for tracking data manipulation and export procedures; (III) automated export procedures for seamless data downloads to common statistical packages; and (IV) procedures for importing data from external sources.

Guideline concordant care (GCC) was defined as treatment in accordance with National Comprehensive Cancer Network (NCCN) guidelines at the time of treatment decision making (initial treatment plan visit) for each individual patient. Health care utilization was determined based on frequency of emergency department (ED) visits and all urgent and elective hospital admissions at our institution from the time of diagnosis until the end of the follow up period. Patient adherence to treatment was assessed by evaluating, for each patient, the proportion of missed treatment-related appointments in medical oncology,

radiation oncology, and thoracic surgery. Survival status was documented at the study cut-off date on December 31st, 2020. OS was defined as the time from diagnosis to death from any cause. Patients were censored at time of death, loss to follow-up, or study cut-off date.

Substance use occurs along a continuum, specifically, use, abuse, and dependence (14). Substance use (without abuse or dependence) can cause or exacerbate physical and psychological problems: symptoms related to substance use or worsened comorbidities, and the consequences of decreased treatment adherence, being under the influence, or undermining one's social support system (15-17). Thus, our study focused on substance use, and we did not capture data separately on abuse or dependence. Substance use was obtained through electronic medical record review and defined as any consumption of illicit drugs, inhalants or solvents, marijuana, and/or use of prescription drugs outside of their intended purpose. Alcohol and tobacco use were defined separately. All parameters were compared between patients with current and/or former substance use and those without substance use. In our analysis, we did not separate substances given the main purpose of the study was not to determine causality of NSCLC incidence but rather to describe the possible effects of substance use on outcomes as seen with other medical conditions.

Statistical analysis

All subjects in the study were included in the evaluation of baseline demographics, co-morbidities and details on cancer type and stage. Descriptive statistics including medians, percentile ranges, and percentages were used to summarize characteristics since the data had an asymmetrical distribution. Subjects whose substance use status was unknown were omitted from the final statistical analysis. The remaining patients were separated into two groups: patients with no substance use (Group 1) and patients with current and/or former substance use (Group 2). Relative risk was calculated to determine the probability of characteristics occurring in Group 1 as compared to Group 2. Chi-squared tests were used to compare qualitative differences between groups. An independent (unpaired) *t*-test with unequal variance and a 95% confidence interval was used to calculate the two-tailed P values. A multivariable analysis was done including possible and known predictors of OS (age, sex, race/ethnicity, stage). In our multivariable analysis, we also adjusted for major confounders such as smoking status and Charlson Comorbidity Index (CCI). The median follow-up was determined based on the median time between diagnosis and the time of death, loss to follow up, or the end of the study. GraphPad Prism 8 was used to determine the OS between groups and generate Kaplan-Meier survival curves. Hazard ratios (HRs) between the groups were calculated using the log-rank method.

Results

Patient characteristics

Of the 211 patients diagnosed with NSCLC during the specified timeframe, 18 patients (8.5%) were excluded due to lack of data on substance use. Of the 193 patients included in the final analysis, 50.3% (n=97) were male and 49.7% (n=96) were female, with almost half being White (47.2%, n=91) followed by Black (38.9%, n=75), Asian (6.7%, n=13), Hispanic (6.2%, n=12), and other races and ethnicities (1.0%, n=2). There were significant differences in the distribution of sex and race/ethnicity among patients with and without substance use. Patients with substance use were more likely to be male and non-Hispanic Black [male *vs.* female: 60.4% (29/48) *vs.* 39.6% (19/48), P=0.04; Black *vs.* White *vs.* Asian *vs.* other: 56.3% (27/48) *vs.* 41.7% (20/48) *vs.* 0% *vs.* 0%, P=0.02]. Patients with substance use were less likely to have metastatic disease at diagnosis [substance use *vs.* no substance use: 22.9% (11/48) *vs.* 34.5% (50/145), P=0.03]. Baseline patient characteristics are shown in *Table 1*. In the final cohort assessed, 24.9% (n=48) of patients had current and/or former substance use. Among the 48 patients identified with current and/or former substance use, 10.4% (5/48) reported intravenous substance use and 83.3% (40/48) reported non-intravenous substance use. Data on route of substance use was missing on 6.3% (3/48) of patients. Cocaine and marijuana use were the most prevalent with 45.8% (22/48) and 52% (25/48) of patients reporting cocaine and marijuana use, respectively. Intravenous heroin use was reported in 10.4% (5/48) and methamphetamine use in 0% (0/48). Polysubstance use was noted in 27.1% (13/48) of patients. Additionally, only 4.2% (2/48) of patients reported receiving supportive services or undergoing treatment for substance use.

There was a statistically significant difference in median age at diagnosis among the groups. Patients with substance use were 10 years younger at diagnosis than those without substance use (median, 58 *vs.* 68; range, 36–78 *vs.* 47–91; P<0.01). Current smoking status was also significantly different amongst the groups. Those with substance use

Table 1 Patient demographic and clinical characteristics

Characteristics	All patients (n=193)	Never substance use (n=145)	Current and/or former substance use (n=48)	P value[†]
Sex, n (%)				0.04
Female	96 (49.7)	77 (53.1)	19 (39.6)	
Male	97 (50.3)	68 (46.9)	29 (60.4)	
Age at diagnosis, median [range]	65 [36–91]	68 [47–91]	58 [36–78]	<0.01
Race/ethnicity, n (%)				0.02
Asian	13 (6.7)	13 (9.0)	0 (0.0)	
Black	75 (38.9)	48 (33.1)	27 (56.3)	
Hispanic/Latino	12 (6.2)	11 (7.6)	1 (2.1)	
White	91 (47.2)	71 (49.0)	20 (41.7)	
Other	2 (1.0)	2 (1.4)	0 (0.0)	
Cancer stage[‡], n (%)				0.03
I	75 (38.9)	59 (40.7)	16 (33.4)	
II	18 (9.3)	9 (6.2)	9 (18.8)	
III	37 (19.2)	25 (17.2)	12 (25.0)	
IV	61 (31.6)	50 (34.5)	11 (22.9)	
Unknown	2 (1.0)	2 (1.4)	0 (0.0)	
Cancer treatment, n (%)				
Surgery	72 (37.3)			
Concurrent chemoradiation	43 (22.2)			
Radiation only	33 (17.1)			
Chemotherapy only	45 (23.3)			
Adjuvant chemotherapy	19 (9.8)			
Targeted therapy	10 (5.2)			
NSCLC histologic type, n (%)				0.75
Adenocarcinoma	132 (68.4)	101 (69.7)	31 (64.6)	
Large cell carcinoma	8 (4.2)	6 (4.1)	2 (4.2)	
Squamous cell carcinoma	52 (26.9)	37 (25.5)	15 (31.3)	
Other	1 (0.5)	1 (0.7)	0 (0.0)	
ECOG performance status at diagnosis[§], n (%)				
0–1	66 (34.2)	50 (34.5)	16 (33.3)	
2–3	26 (13.5)	22 (15.2)	4 (8.3)	
4	7 (3.6)	6 (4.1)	1 (2.1)	
Unknown	94 (48.7)	67 (46.2)	27 (56.3)	

Table 1 (*continued*)

Table 1 (*continued*)

Characteristics	All patients (n=193)	Never substance use (n=145)	Current and/or former substance use (n=48)	P value[†]
Smoking status[¶], n (%)				<0.01
Current	64 (33.2)	35 (24.1)	29 (60.4)	
Former	103 (53.4)	86 (59.3)	17 (35.4)	
Never	25 (13.0)	23 (15.9)	2 (4.2)	
Unknown	1 (0.5)	1 (0.7)	0 (0.0)	
Alcohol use[$], n (%)				0.30
Current	56 (29.0)	30 (20.7)	26 (54.2)	
Former	113 (58.5)	76 (52.4)	11 (22.9)	
Never	22 (11.4)	38 (26.2)	0 (0.0)	
Unknown	2 (1.0)	1 (0.7)	1 (2.1)	
Pack years of smoking				0.08
Patients with data on pack years, n (%)	162 (83.9)	119 (82.1)	43 (89.6)	
Number of pack years, mean ± SD	43.0±26.7	50.0±28.0	37.5±21.8	
Frequency of alcohol use of current and/or former alcohol users, n (%)				
Occasional (less than once/week)	9 (4.7)	8 (5.5)	1 (2.1)	
Weekly	12 (6.2)	9 (6.2)	3 (6.3)	
2–6 days/week	17 (8.8)	10 (6.9)	7 (14.6)	
Daily	34 (17.6)	21 (14.5)	13 (27.1)	

[†], all calculations were made using a two-tailed P value and unequal variance; [‡], two patients with missing data; [§], 94 patients with missing data (67 in never substance use and 27 in current and/or former substance use); [¶], 1 patient with missing data in never substance use group; [$], 2 patients with missing data (one patient in never substance use group and one patient in current and/or former substance use). NSCLC, non-small cell lung cancer; ECOG, Eastern Cooperative Oncology Group; SD, standard deviation.

were more likely to be current smokers [60.4% (29/48) *vs.* 24.1% (35/145), P<0.01]. All patients with substance use reported current or prior alcohol use (*Table 1*).

Social determinants of health

A higher proportion of patients with substance use were unemployed and on disability than those without substance use [unemployed: 29.2% (14/48) *vs.* 13.1% (19/145); disability: 14.6% (7/48) *vs.* 5.5% (8/145); P=0.01]. Additionally, a higher proportion of patients with substance use had housing insecurity [8.3% (4/48) *vs.* 3.4% (5/145), P<0.01] compared to those without substance use. Interestingly, relationship status was significantly different among the groups. Those with substance use were more likely to be single or divorced [75.0% (36/48) *vs.* 43.4% (63/145), P<0.01] (*Table 2*).

Health care utilization

Our analysis showed that patients with substance use had higher health care utilization compared to patients without substance use (*Table 2*). A significantly higher percentage of patients with substance use had ED visits [60.4% (29/48) *vs.* 41.4% (60/145), P=0.02]. Although a higher percentage of patients with substance use had hospital admissions, this did not reach statistical significance [85.4% (41/48) *vs.* 73.1% (106/145), P=0.16].

Patient adherence to treatment

The mean percentage of thoracic surgery, medical oncology,

Table 2 Social determinants of health and healthcare utilization among non-substance users (Group 1) and substance users (Group 2)

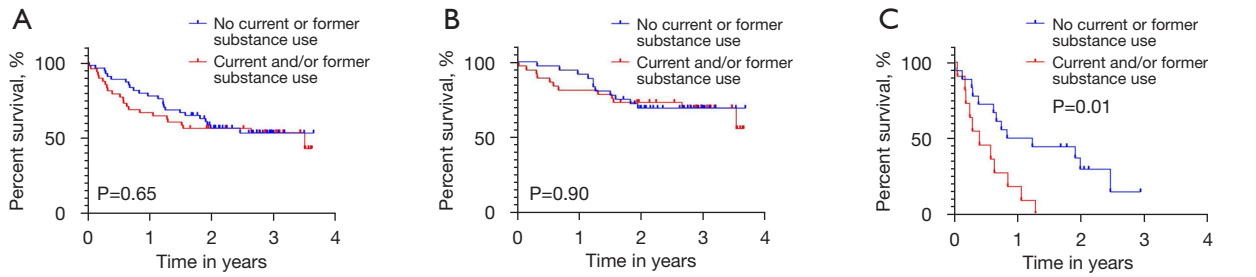
Characteristics	All patients (n=193)	Group 1: never substance use (n=145)	Group 2: current and/or former substance use (n=48)	P value[#] (Group 1 *vs.* Group 2)
Work status, n (%)				0.01
Employed	29 (15.0)	21 (14.5)	8 (16.7)	
Disability	15 (7.8)	8 (5.5)	7 (14.6)	
Retired	55 (28.5)	47 (32.4)	8 (16.7)	
Unemployed	33 (17.1)	19 (13.1)	14 (29.2)	
Unknown	61 (31.6)	50 (34.5)	11 (22.9)	
Housing status, n (%)				<0.01
Domiciled	179 (92.8)	138 (95.2)	41 (85.4)	
Not domiciled	9 (4.7)	5 (3.4)	4 (8.3)	
Unknown	5 (2.6)	2 (1.4)	3 (6.3)	
Relationship status, n (%)				<0.01
Divorced	34 (17.6)	29 (20.0)	5 (10.4)	
Married	58 (30.1)	54 (37.2)	4 (8.3)	
Single	65 (33.7)	34 (23.4)	31 (64.6)	
Widow	20 (10.4)	16 (11.0)	4 (8.3)	
Unknown	16 (8.3)	12 (8.3)	4 (8.3)	
Hospital admissions				0.16
Patients who were admitted to the hospital, n (%)	147 (76.2)	106 (73.1)	41 (85.4)	
Number of hospital admissions per patient, median [range]	3 [1–14]	2 [1–14]	3 [1–12]	
Number of hospital admissions per patient, mean ± SD	3.4±2.7	3.3±2.6	3.6±2.8	
ED visits				0.02
Patients who visited the ED, n (%)	89 (46.1)	60 (41.4)	29 (60.4)	
Number of ED visits per patient, median [range]	2 [1–24]	2 [1–24]	2 [1–18]	
Number of ED visits per patient, mean ± SD	3.0±3.6	2.5±3.3	4.0±4.0	

[#], all calculations were made using a two-tailed P value and unequal variance. ED, emergency department; SD, standard deviation.

and radiation oncology appointments missed per patient was higher in patients with substance use but was not statistically significant (9.1% *vs.* 6.1%, P=0.31; 19.8% *vs.* 11.1%, P=0.17; 11.1% *vs.* 3.3%, P=0.18, respectively).

Substance use and GCC

We determined whether patients received GCC based on NCCN guidelines at the time of each patient's treatment. Of the entire cohort, 79.8% (n=154) of patients received GCC. Among the 20.2% (n=39) of patients who did not receive GCC, 38.5% (n=15) had metastatic disease and 7.7% (n=3) reported substance use. Overall, 6.3% (3 of 48) of patients with substance use did not receive GCC compared to 24.8% (36 of 145) of patients without substance use. For both groups poor performance status (69.2%, n=27), increased comorbidities (15.4%, n=6), and loss to follow up (15.4%, n=6) were the reasons for patients not receiving GCC.



Year	0	1	2	3
Number at risk				
Never substance use	145	134	116	85
Current and/or former substance use	48	32	24	14

Figure 1A	Median overall survival, years	Number of deaths
Never substance use	Not reached	24
Current and/or former substance use	3.51	23
Hazard ratio (95% CI) 1.14 (0.64–2.04)		

Year	0	1	2	3
Number at risk				
Never substance use	95	92	80	64
Current and/or former substance use	37	31	24	14

Figure 1B	Median overall survival, years	Number of deaths
Never substance use	Not reached	11
Current and/or former substance use	Not reached	12
Hazard ratio (95% CI) 1.05 (0.46–2.30)		

Year	0	1	2	3
Number at risk				
Never substance use	50	42	36	33
Current and/or former substance use	11	2	0	0

Figure 1C	Median overall survival, years	Number of deaths
Never substance use	1.03	13
Current and/or former substance use	0.40	11
Hazard ratio (95% CI) 2.60 (1.16-5.80)		

Figure 1 Kaplan-Meier survival estimates for patients with NSCLC stratified by never *vs.* current and/or former substance use. (A) All stages of NSCLC; (B) patients with stage I–III NSCLC; (C) patients with stage IV NSCLC only. Median OS and HRs with 95% CIs are listed below each figure. CI, confidence interval; NSCLC, non-small cell lung cancer; OS, overall survival; HR, hazard ratio.

Substance use and OS

After a median follow up of 0.78 years (range, 0.02–3.64 years), the median OS for patients with substance use was 3.51 years and was not reached for patients without substance use (*Figure 1A*). A trend toward worse OS was notable in the first 6 months of diagnosis in patients with substance use and localized or locally advanced NSCLC (*Figure 1B*). Patients with substance use and stage IV NSCLC had a significantly decreased OS (HR, 2.60; 95% CI: 1.16–5.80; P=0.01) with 65% of patients dying in the first 6 months of diagnosis (*Figure 1C*). In contrast, only about 30% of patients with stage IV NSCLC and without substance use died in the first 6 months of diagnosis.

Multivariable analysis for prognostic factors

A multivariable analysis was done including possible predictors of OS (*Table 3*). Sex, smoking status, and disease stage were statistically significant independent predictors of OS. CCI was a suggestive predictor of OS in our cohort (HR, 1.15; 95% CI: 1.00–1.32; P=0.05). Substance use was not independently associated with OS (HR, 0.68; 95% CI: 0.34–1.40; P=0.30).

Discussion

Mortality rates in NSCLC are declining due to widespread screening protocols and advances in treatment modalities (2). However, psychosocial factors, such as substance use, could influence health care utilization, treatment adherence, and survival. Limited data is available regarding the prevalence of substance use in cancer patients and its effect on the aforementioned outcomes. In our study, we found that the prevalence of substance use was 24.9% among patients with NSCLC which is significantly higher than reported for the US population (11.2%) but comparable to that previously reported in the literature for cancer patients (3,7,18,19). We also noted increased health care utilization and poor social determinants of health in NSCLC patients with current or former substance use.

We further studied demographics and clinical characteristics of patients with and without substance use in our NSCLC population. There were significant differences in sex and race/ethnicity between those with and without substance use. This is a noteworthy observation as several ongoing studies seek to explore the relationship between psychosocial factors and racial disparities in cancer and potential interventions (NCT03407417, NCT04030130,

Table 3 Multivariable analysis of demographic and clinical characteristics and their association with OS (n=190: n=80 died, n=110 censored)

Demographic/clinical characteristic	HR	95% CI	P value
Age (years)	1.00	0.98–1.03	0.81
Sex (male *vs.* female)	1.67	1.04–2.68	0.04
Race/ethnicity (*vs.* Black)			
White	1.06	0.63–1.77	0.83
Asian	0.55	0.16–1.94	0.35
Other	0.88	0.11–7.14	0.91
Hispanic/Latino	1.47	0.54–3.97	0.45
Smoking status (*vs.* never)			
Current	2.63	1.14–6.08	0.02
Past	2.66	1.23–5.76	0.01
Current substance use (*vs.* no)			
Use	0.68	0.34–1.40	0.30
Stage (*vs.* I)			
II	4.04	1.45–11.24	0.008
III	5.92	2.64–13.28	<0.0001
IV	14.96	6.28–35.63	<0.0001
CCI	1.15	1.00–1.32	0.05

OS, overall survival; CCI, Charlson comorbidity index; HR, hazard ratio; CI, confidence interval.

NCT04314752, NCT04410302, and NCT05034289). We also found that patients with substance use were 10 years younger at diagnosis of NSCLC than those without substance use. The reason for the association is unclear. However, studies in the general population suggest that substance use is most often initiated in adolescence and has both early and long-term negative effects on physical health including the development of cancer in adulthood (20-23). Therefore, patients with substance use may be more susceptible to developing cancer at a younger age due to initiation of substance use early in life. Several studies have highlighted that smokers are more likely to use substances than non-smokers (24-26). In our cohort, those with substance use were more likely to be current smokers. Since smoking is a known risk factor for the development of lung cancer, direct causation between substance use and lung cancer development cannot be inferred from this study. The role of substance use in lung cancer pathogenesis should be studied separately while accounting for individual smoking status.

As social and economic conditions can significantly influence access to health care received by an individual patient, we also evaluated baseline social determinants of health in our cohort (27-29). Despite patients with substance use being more likely to have poorer social support and social determinants of health (financial instability, housing instability, etc.), they received comparable treatment to patients without substance use. At our safety-net hospital, we universally screen for social determinants of health and address socioeconomic barriers in parallel with cancer treatment through cancer care navigators who connect patients to available resources (30). Addressing socioeconomic barriers to care likely minimizes their effect on cancer outcomes as suggested in the literature (28,30).

We also examined the association between substance use and health care utilization. Notably, there was increased health care utilization in patients with current and/ or former substance use as compared to those without substance use. The observed trend coincides with that of the general population. In a recent meta-analysis of 92 studies assessing the frequency of health- care utilization in substance users, compared to the general population, patients with substance use had on average 4.8 and 7.1 times more ED visits and hospital admissions, respectively (12). The magnitude of the difference (1.47 *vs.* 4.8 times and 1.17 *vs.* 7.1 times) is likely to be less in our cohort compared to the general population because we did not capture ED visits and hospital admissions outside of our institution. Interestingly, in the study noted above, opioid substitution therapy was associated with reduced ED presentation and hospital admissions. This underscores the role of targeted interventions for patients with substance use during cancer treatment (12).

Another crucial observation in our study was that substance use predicted for several patient characteristics that portend worse OS: male sex, current tobacco smoking, current alcohol consumption, and poor social determinants of health. Although univariable analysis showed that substance use portended worse survival in patients with metastatic NSCLC, this was lost in the multivariable analysis. Additionally, majority of the patients 79.8% (n=154) received GCC suggesting that current and novel treatment strategies are effective across populations. In our study, only 4.2% of patients with current and/or former substance use were receiving supportive services or undergoing treatment for substance use. However, substance use is likely a clinical characteristic that should trigger

interventions targeted at reducing healthcare utilization and overcoming the challenges of poor social determinants of health. Interventions could include counseling programs, establishing social support, and networking relationships, patient navigation services, and substance use treatment if indicated (28,30-32).

Since patients with substance use were more likely to be smokers and current smoking is likely a risk factor for inferior OS in lung cancer, we sought to control for possible confounding (33). On multivariable analysis, current or former smoking was an independent prognostic factor for OS, however, current, or former substance use was not. Substance use may, however, compound the negative effects of smoking on OS.

Strengths and limitations

To our knowledge, this is the first study to evaluate the effect of substance use on NSCLC outcomes. The present study highlights important potential differences in clinical and sociodemographic characteristics between NSCLC patients with and without substance use. Additionally, our study was conducted at a safety-net hospital with a diverse cohort of patients from various racial and ethnic groups. The diversity of the cohort increases the external validity of our study and gives us the unique opportunity to evaluate for racial and ethnic differences. Therefore, the study results have implications for future studies and interventions. We were able to obtain a sample size that allowed for precision in assessing clinical and sociodemographic characteristics, health care utilization, and treatment patterns (34). Importantly, the relationships observed between substance use and specific characteristics are consistent with current available evidence on substance use in other cancers. This consistency makes our findings more reliable.

Our study also has some limitations. We only looked at patients diagnosed with NSCLC for which a major risk factor and potential confounder is smoking. As previously stated, smokers are more likely to use substances, so our population was enriched for patients with substance use. Although univariable analysis showed inferior OS in patients with advanced lung cancer and substance use, our sample size was likely too small to determine if there is an independent association on multivariable analysis. Additionally, we relied on self-report for substance use history which is dependent on providers soliciting the information and patients responding accurately. Given that our study involves the investigation of a socially unacceptable behavior such as substance use, reliance on self-report could lead to both ascertainment and responder bias. Toxicology screening is not a routine part of cancer care and thus, was not available for all. Therefore, toxicology was not assessed. Moreover, health care utilization parameters may have been underreported as our study did not capture emergency room visits or hospital admissions outside of our institution. Treatment adherence was not directly assessed. Attending appointments was thought to indirectly indicate treatment compliance. Finally, the results of our study will need to be interpreted with caution given that they are derived from a single institution.

Conclusions

Our study shows an increased prevalence of substance use among patients with NSCLC compared to the general population, which is possibly linked to the increased prevalence of smoking in this population. Moreover, a history of substance use is associated with poor social determinants of health and increased healthcare utilization suggesting that these are targets for future interventions. Future prospective studies should focus on improving our understanding of the aforementioned associations, delineating potential mechanisms, and developing evidence-based strategies to reduce health care utilization and overcome challenges related to poor social determinants of health.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-21-1992/rc

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the institutional review board of Boston University/Boston Medical Center (No. H-37619) and individual consent for this retrospective analysis was waived because all research information was recorded in a way that there is less than a very small risk that subjects can be identified (per category 9 of the Human Research Protection Policies and Procedures of Boston University/Boston Medical Center).

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