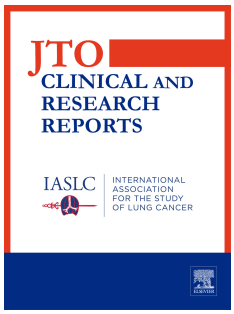

Racial, Ethnic, and Socioeconomic Characteristics Independently Predict for Cachexia Risk and Associated Survival Outcomes in Stage IV Non-Small Cell Lung Cancer: A Brief Report

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Racial, Ethnic, and Socioeconomic Characteristics Independently Predict for Cachexia Risk and Associated Survival Outcomes in Stage IV Non-Small Cell Lung Cancer: A Brief Report

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Abstract

Background: Cancer cachexia, seen in more than a third of patients with non-small cell lung cancer (NSCLC), directly leads to functional and survival detriments. As screening and interventions for cachexia and NSCLC improve, deficits in healthcare access and quality among patients disadvantaged by race and socioeconomic factors must be addressed.

Methods: We retrospectively evaluated 957 patients diagnosed with stage IV NSCLC between 2014-2020 in Dallas, Texas. Cachexia was retrospectively assessed by applying criteria for substantial unintentional weight loss in the time leading up to cancer diagnosis. Non-parametric, parametric, multivariate logistic regression, and Kaplan-Meier analyses were conducted to evaluate for variables with significant associations with cachexia incidence and survival.

Results: In multivariate analysis including age, sex, comorbidities, BMI, risk behaviors, and tumor histology, Black race and Hispanic ethnicity independently associated with more than a 70% increased risk of presenting with cachexia at the time of NSCLC diagnosis ($P<0.05$). When private insurance status was included as a covariate, this association was diminished for Hispanic patients only. Black patients presented with stage IV disease at an average of approximately 3 years younger than White patients (Kruskal-Wallis $P=0.0012$; T-test $P=0.0002$). Cachexia status at diagnosis consistently predicted for survival detriments, further highlighting the importance of addressing differential cachexia risk across race/ethnicity.

Conclusions: Fundamentally, our findings reveal elevated cachexia risk in Black and Hispanic stage IV NSCLC patients with associated survival detriments. These differences are not fully accounted for by traditional determinants of health and suggest novel avenues for addressing oncologic health inequities.

Keywords: Cachexia; Health Inequities; Palliative Care; Lung Neoplasms; Mass Screening

Introduction

Non-small cell lung cancer (NSCLC) is a leading cause of cancer-related mortality in the United States, as most patients present with late-stage disease and limited treatment options. It is estimated that 36% of patients with NSCLC suffer from cachexia,[1] a clinically challenging multifactorial syndrome characterized by significant loss of muscle and adipose stores.[2] Cancer cachexia is associated with decreased quality of life, reduced response to cancer therapies, and poor overall prognosis.[3]

Racial and socioeconomic (SES) outcome disparities are prevalent in NSCLC, as higher incidence and mortality is consistently observed in marginalized groups.[4] NSCLC patients who are Black, Hispanic, uninsured, or residing in low-income areas have been found to be less likely to receive guideline-concordant care.[5]

Although the importance of race and SES in NSCLC is well established and encourages targeted research, the relationship is poorly defined within the context of cachexia. In this study, we reviewed a 7-year dataset of patients diagnosed with stage IV NSCLC in Dallas, Texas to investigate associations between cachexia and clinical, demographic, and socioeconomic factors.

Materials and Methods

Cohort Characteristics and Cachexia Incidence at Diagnosis

Retrospective tumor data extraction and electronic medical record review were conducted through an IRB-approved study at a tertiary care center in Dallas, Texas. Demographic information, comorbid conditions, treatment information, longitudinal weight data, survival time, pertinent health behaviors, and tumor characteristics were collected for patients diagnosed with stage IV NSCLC between 2014 and 2020.

Comorbidities were quantitatively assessed by the Charlson comorbidity index. Patients were classified as not having private insurance if they were uninsured or entirely dependent on government-associated coverage (Medicare, Medicaid, and veteran programs).

The international consensus definition.[2] of cachexia was applied to determine cachexia status at diagnosis. For patients with BMI ≥ 20, unintentional weight loss exceeding 5% from baseline in the 6-month period leading to diagnosis met criteria for cachexia at cancer diagnosis. A cutoff of 2% was applied for patients with BMI < 20 per consensus definition.

Statistical Evaluation

With the classification of cachexia incidence at cancer diagnosis as the binary dependent variable, multivariate logistic regression was conducted including the covariates: age at diagnosis, sex, pretreatment BMI, alcohol history, tobacco history, Charlson comorbidity value, tumor histology, and race.

Independent-samples Kruskal-Wallis testing was conducted with pairwise comparisons to determine whether any statistically significant difference existed based on age at cancer diagnosis across race/ethnicity groups of the cohort. Statistically significant comparison groups were further evaluated with independent-samples T-testing.

Survival was evaluated through Kaplan-Meier estimators and cox regression analysis for non-Hispanic (NH) White and Black patients stratified by cachexia status at diagnosis, as these groups

had sufficient (N>100) representation within the overall cohort. Survival was evaluated as time in days from cancer diagnosis date to the date of death or last contact, with appropriate censoring.

All statistical analyses, tables, and figures were created or carried out on IBM SPSS Statistics for Macintosh, Version 28.0. (Armonk, NY). Tests were conducted at the 5% significance level.

Results

Cachexia Incidence at Diagnosis

The total cohort was comprised of 957 patients, with 42.95% (N=411) meeting criteria for cachexia at diagnosis. Table 1 displays frequencies of patient and tumor characteristics within our cohort along with cachexia incidence by category. More specific payor information for patients without private insurance can be found in Supplementary Table 1.

Table 1: Population Characteristics and Cachexia Incidence

Category	Characteristic	N	Cachexia incidence (%)
Patient information	**Median age at diagnosis (years), IQR**	65, 57-72	
	Sex		
	Male	524	252 (48.09%)
	Female	432	158 (36.57%)
	Race		
	Non-Hispanic White	579	228 (39.38%)
	Black	216	118 (54.63%)
	Asian	72	23 (31.94%)
	Hispanic	90	42 (46.67%)
	Insurance		
	No private insurance	437	223 (51.03%)
	Any private insurance	475	175 (36.84%)
Risk factors	**Median Charlson comorbidity score, IQR**	11, 9-13	
	Median pretreatment BMI (kg/m^2), IQR	24.80, 21.98-28.62	
	Alcohol history		
	None	575	250 (43.48%)
	Current or prior	334	141 (42.22%)
	Tobacco history		
	None	211	70 (33.18%)
	Current or prior	698	321 (45.99%)
Tumor characteristics	**Histology**		
	Adenocarcinoma	705	283 (40.14%)
	Squamous	137	71 (51.82%)
	Large cell	16	8 (50%)
	Mixed/NOS	99	49 (49.49%)
	Total	957	411 (42.95%)

Multivariate Analyses

In multivariate analysis including private insurance as a binary covariate, Black patients demonstrated an odds ratio of 1.558 (95% CI: 1.051-2.309; *P=0.0272*) towards cachexia at diagnosis. Hispanic ethnicity was not associated with an elevated risk of cachexia incidence at

diagnosis (*P=0.03937*). Private insurance demonstrated a protective association towards cachexia incidence, with an odds ratio of .692 (95% CI: 0.496-0.964; *P=0.0298*; Table 2).

Table 2: Multivariate Analysis of Cachexia Incidence at Cancer Diagnosis

Category	Parameter	Odds ratio (95% CI)	P-value
Patient information	**Age at diagnosis (years)**	1.005 (0.989-1.021)	*0.5618*
	Female sex	0.719 (0.520-0.994)	***0.0457***
	Race		
	Non-Hispanic White	-	*0.1575*
	Black	1.558 (1.051-2.309)	***0.0272***
	Asian	0.982 (0.470-2.050)	*0.9606*
	Hispanic	1.285 (0.722-2.288)	*0.3937*
	Private insurance	0.692 (0.496-0.964)	***0.0298***
Risk factors	**Charlson comorbidity score**	1.005 (0.954-1.058)	*0.8620*
	Pretreatment BMI	0.981 (0.954-1.008)	*0.1641*
	Alcohol history	1.045 (0.751-1.453)	*0.7948*
	Tobacco history	1.606 (1.027-2.510)	***0.0377***
Tumor characteristics	**Histology**		
	Adenocarcinoma	-	*0.4141*
	Squamous cell	1.326 (0.867-2.027)	*0.1929*
	Large cell	1.117 (0.373-3.345)	*0.8427*
	Mixed/NOS	1.414 (0.834-2.399)	*0.1983*

Repeated analysis excluding the private insurance covariate demonstrated significant elevations of cachexia risk at diagnosis greater than 70% for Black (OR: 1.748; 95% CI: 1.205-2.535; *P=0.0033*) and Hispanic (OR: 1.717; 95% CI: 1.005-2.932; *P=0.0477*; Supplementary Table 2) patients.

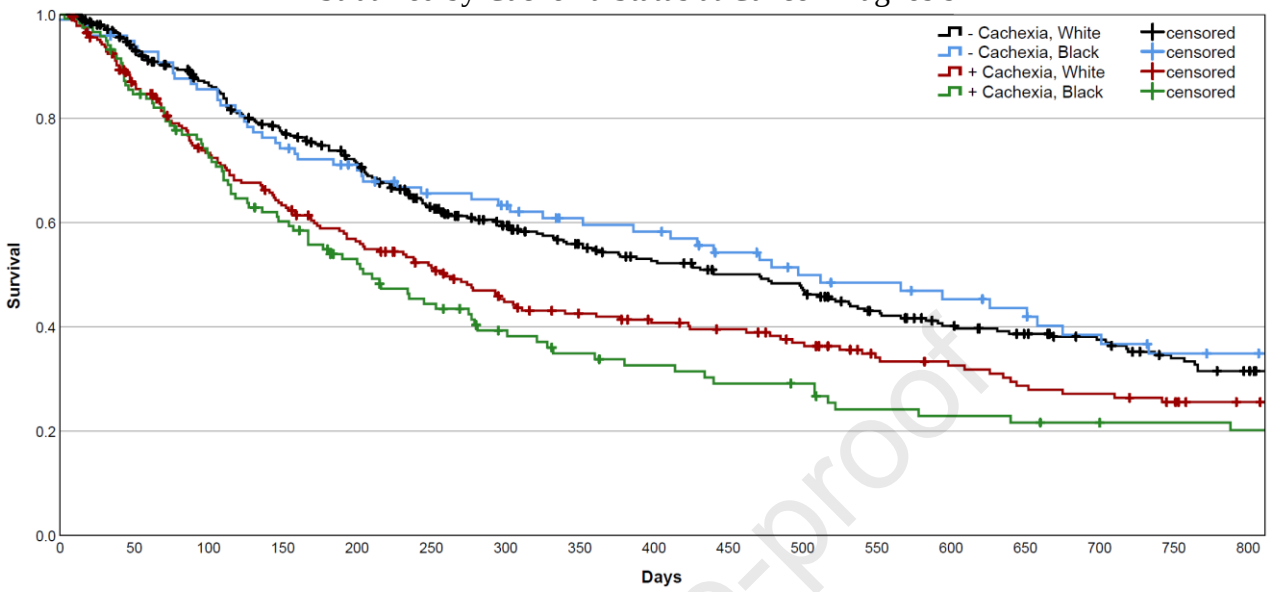
Comparing Age at Diagnosis

Pairwise comparisons between race/ethnicity groups on Kruskal-Wallis testing detected a significant difference in age at diagnosis solely between NH White and Black patients (*P=0.0012*; Supplementary Table 3). Independent-samples T-testing between these groups again demonstrated a significant difference of age at diagnosis (*P=0.0002*; Supplementary Table 4). NH White and Black patients presented with mean ages of 65.64 and 62.60 years at diagnosis, respectively.

Survival

Figure 1 demonstrates Kaplan-Meier curves for NH White and Black patients stratified by cachexia status at diagnosis. Within the cohort of patients who did not present with cachexia at diagnosis, there was no significant difference between survival time between NH White and Black patients detected on log-rank testing (*P=0.5121*). Similar analysis within the cohort of patients with cachexia at diagnosis also found no significant difference between NH White and Black patients (*P=0.2744*). Significant survival differences were found for all groups with opposing cachexia status at diagnosis (*P<0.05*). Supplementary Tables 5 and 6 display median survival times and log-rank comparisons.

Figure 1: Two-Year Kaplan-Meier Survival Curves for Non-Hispanic White and Black Patients Stratified by Cachexia Status at Cancer Diagnosis



Simultaneous interpretation of survival influence of Black race – compared to NH White patients – and cachexia status was performed via cox regression. Black race was associated with a hazard ratio of 1.044 (95% CI: 0.860-1.268; *P=0.6633*), while cachexia status was associated with a hazard ratio of 1.416 (95% CI: 1.187-1.690; *P=0.0001*).

Discussion

Development of cachexia is common among cancer patients, associated with reduced function, decreased response to anticancer therapy, and increased mortality.[3] Despite the prevalence and impact of cancer cachexia, weight loss in cancer patients is rarely actively monitored.[2] While cachexia research has progressed over the past decade, our understanding of racial/ethnic disparities in cachexia is limited. One study found that an increased risk of cachexia among Black patients contributed to outcome disparities in pancreatic cancer.[6] To our knowledge, this is the first study assessing the relationship between race/ethnicity and cachexia risk in patients with NSCLC.

Health Inequity in Stage IV NSCLC Cachexia

Prior studies have demonstrated that Black NSCLC patients consistently present with more advanced disease at diagnosis, undergo prolonged diagnosis-to-treatment times, and are less likely to receive recommended care.[7,8] Hispanic ethnicity, lower household income, and a lack of private insurance have similarly been observed to associate with worsened outcomes and survival.[9] Development of cachexia is clinically important in NSCLC care, especially in advanced stages, where pre-treatment weight loss independently predicts for survival outcomes.[10] In this study, we further characterize associations between cachexia with race, ethnicity, and private insurance in NSCLC.

Multivariate analysis without a private insurance covariate found a significantly increased risk of cachexia at diagnosis exceeding 70% for Black and Hispanic patients. This indicates an oncologic outcome inequity independent of underlying patient and tumor characteristics including prior comorbidities and risk behaviors – representing generally conceived determinants of health. Cachexia risk in multivariate analysis was attenuated for Hispanic patients after adjusting for

access to private insurance. This suggests a contributory role of increased dependence on public insurance towards cachexia burden in Hispanic populations. Despite the consideration of this measure, Black patients demonstrated a 55.8% greater cachexia risk, revealing racial inequities persisting beyond this surrogate measure of healthcare access.

In survival analysis of NH White and Black patients, race was not found to significantly predict for survival within groups of equivalent cachexia status at diagnosis. Cachexia incidence, however, consistently associated with pronounced survival detriment. This observation, in conjunction with the differential cachexia incidence we observed, suggests that the decreased survival observed in Black and Hispanic NSCLC patients may depend on cachexia and/or factors contributing to its progression. This was further substantiated in our cox regression analysis, which found no association between Black race and survival risk when considered simultaneously with cachexia status at diagnosis.

Advanced disease is an important risk factor for development of cancer cachexia.[2] The increased frequency of late-stage NSCLC presentation for Black patients has been supported to result from delayed detection and inadequate quality and consistency of screening.[7,11] Although all patients in this study presented with stage IV NSCLC, the elevated incidence of cachexia in Black patients at time of diagnosis suggests a within-stage delay in cancer detection compared to NH White patients. Important factors contributing to delayed detection in Black patients are inadequacies of lung cancer screening protocols and utilization. Current United States Preventive Services Task Force (USPSTF) recommendations are predominantly based on the National Lung Screening Trial (NLST),[12] whose participants were disproportionately White and of higher SES compared to the general population, and the Nederlands-Leuvens Longkanker Screenings Onderzoek (NELSON),[13] which did not report on participant race, ethnicity, or SES. In our cohort, we found that Black patients presented significantly younger than NH White patients at diagnosis, by about 3 years. This finding is consistent with prior literature demonstrating that race-specific adjustment of age requirements in USPSTF guidelines would result in more equitable lung cancer screening.[7,14] Importantly, of the individuals eligible under current guidelines, Black patients and those with low SES are still less likely to obtain recommended screening.[7] Early detection is crucial in preventing and palliating cachexia.[3] This highlights the necessity for efforts in health policy to mitigate further barriers in healthcare access in parallel to the revision of screening criteria.

The greater cachexia risk observed in minority or socioeconomically disadvantaged groups might also depend on environmental or pathophysiological mechanisms not evaluated in this study. A key risk factor for cachexia development is poor nutrition status,[2] which is well-known to correlate with race and SES. Our cohort received care in Texas, which has consistently demonstrated poor health equity measures and ranks in the bottom quartile nationally when assessed by access to, quality of, and utilization of healthcare services among minority populations.[15]

Conclusion

Significant disparities persist in cachexia risk at time of stage IV NSCLC diagnosis, even after controlling for several demographic and clinical characteristics. Hispanic patients demonstrate an increase in cachexia risk that is at least partially attributable to decreased access to private insurance. Black patients demonstrate increased cachexia risk irrespective of insurance status. As the field of cancer cachexia sees improvements in diagnostic and interventional strategy, future research must simultaneously expand to further characterize the specific mechanisms behind outcome disparities to substantiate targeted and equitable reform to health policy.

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Supplemental data 1.pdf (Supplementary Tables 1-6)

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