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Disparities in outcomes between Black and White patients in North America with thoracic malignancies and COVID-19 infection (TERAVOLT)

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A B S T R A C T

Background: Patients with thoracic malignancies who develop COVID-19 infection have a higher hospitalization rate compared to the general population and to those with other cancer types, but how this outcome differs by race and ethnicity is relatively understudied.
Methods: The TERAVOLT database is an international, multi-center repository of cross-sectional and longitudinal data studying the impact of COVID-19 on individuals with thoracic malignancies. Patients from North America with thoracic malignancies and confirmed COVID-19 infection were included for this analysis of racial and ethnic disparities. Patients with missing race data or races and ethnicities with fewer than 50 patients were excluded from analysis. Multivariable analyses for endpoints of hospitalization and death were performed on these 471 patients.

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Results: Of the 471 patients, 73% were White and 27% were Black. The majority (90%) were non-Hispanic ethnicity, 5% were Hispanic, and 4% were missing ethnicity data. Black patients were more likely to have an Eastern Cooperative Oncology Group (ECOG) Performance Status ≥ 2 (p-value = 0.04). On multivariable analysis, Black patients were more likely than White patients to require hospitalization (Odds Ratio (OR): 1.69, 95% CI: 1.01–2.83, p-value = 0.044). These differences remained across different waves of the pandemic. However, no statistically significant difference in mortality was found between Black and White patients (OR 1.29, 95% CI: 0.69–2.40, p-value = 0.408).
Conclusions: Black patients with thoracic malignancies who acquire COVID-19 infection are at a significantly higher risk of hospitalization compared to White patients, but there is no significant difference in mortality. The underlying drivers of racial disparity among patients with thoracic malignancies and COVID-19 infection require ongoing investigation.

1. Introduction

The coronavirus disease 2019 (COVID-19) pandemic posed unique challenges to the oncology community, which were not distributed equally across patient populations. The Thoracic Cancers International COVID-19 Collaboration (TERAVOLT) global consortium was formed specifically to characterize the impact of SARS-CoV-2 infection on patients with thoracic cancer, and in conjunction with other large registries of patients with cancer, has yielded epidemiologic and prognostic data to inform decision-making in the clinic [1–4].

Patients with thoracic malignancies specifically are more vulnerable to hospitalization and mortality from COVID-19 than those without cancer [1]. Knowledge regarding the impact of COVID-19 on patients with cancer from minoritized racial and ethnic groups remains sparse. Recently, the COVID-19 and Cancer Consortium (CCC19) reported that Black patients with cancer and COVID-19 infection experienced worse illness severity than White patients [5]. Previously, this same group observed that race and ethnicity were not correlated with increased risk of mortality [2]. Whether these same conclusions can be drawn specifically for patients with thoracic cancer is unknown, and thus the objective of this study was to determine the association between race, ethnicity, COVID-19 infection, and clinical outcomes among patients with thoracic malignancies.

2. Methods

2.1. Study design

A prospective, multicenter observational study was performed. Institutions worldwide were invited to participate, and currently 117 centers across 21 countries have activated the study, of which 100 centers have contributed data. Eligibility criteria included patients with thoracic cancer (NSCLC, small-cell lung cancer, mesothelioma, thymic epithelial tumors, and other pulmonary neuroendocrine neoplasms) of any stage and a confirmed COVID-19 infection.

2.2. Procedures

Investigators from participating institutions collected data beginning March 23, 2020. Diagnosis of COVID-19 was determined as described in prior TERAVOLT publications [1]. Demographics collected included age, sex, race, ethnicity, smoking status, stage of cancer at the time of COVID-19 infection, type of thoracic malignancy, past and current (>3 month relative to COVID-19 diagnosis) oncology treatments, comorbidities, concomitant medications, and need for hospital admission. For this examination of racial and ethnic disparities, only data from institutions in North America were included given differing definitions of racial disparity and race categories internationally. Patients with missing racial data, those in racial groups with 50 or fewer patients, and patients listed as “Other” or “More than one race” were excluded from the analysis. Primary endpoints were hospitalization and mortality.

2.3. Statistical analysis

Descriptive statistics of patients’ demographics and clinical characteristics were reported as frequencies (proportions) for categorical variables. The pre-determined multivariable data analysis plan is described here. First, we applied multiple imputations (with 10 imputations) for missing values of covariates using additive regression, bootstrapping, and predictive mean matching. Then, we applied the multivariable logistic regression method with clinically and biologically pre-determined covariates in each of the 10 imputed datasets. The pandemic was defined in three waves, which included Wave 1 from March 2020 through December 2020 (initial variant wave), Wave 2 from January 2021 through December 2021 (Delta variant-dominated), and Wave 3 from January 2022 through March 2022 (Omicron variant-dominated) [6]. For the mortality analysis, only patients who died as a complication of COVID-19, as reported in the TERAVOLT database, were included. After the 10-run analyses, the average of the adjusted odds ratios (ORs) was reported. All statistical analyses were performed using R 4.0.3 (The R Foundation for Statistical Computing, Vienna, Austria) and the R packages Hmisc 4.5.0 and survey 4.0.

3. Results

A total of 597 patients with COVID-19 infection and thoracic cancers from North America were identified from the TERAVOLT registry. Of these, 65 patients were missing data on race or declined to report race and therefore were not included in the race analysis (Supplemental Fig. 1). Due to low numbers of patients identifying as Asian/Pacific Islander or Native American, these 39 patients were also not included in the race analysis. An additional 22 patients were excluded due to “Other” or “More than one race” entered into the database. Of the remaining 471 patients, 343 (73%) were White and 128 (27%) were Black. Ethnically, 90% of patients were non-Hispanic, 5% were Hispanic, and ethnic data were missing for 4% of patients. A separate multivariable analysis comparing Hispanic and non-Hispanic patients was not performed given the low number of Hispanic patients (n = 25). Characteristics were similar between Black and White patients, including similar median age (68.5 years for White vs 67.0 for Black), smoking history (78% vs 80% current/former smoking rates), BMI (30% vs 28% with BMI ≥ 30), cancer stage (78% with ≥ stage III disease in both groups), and similar rates of active treatment (57% vs 52%). Eastern Cooperative Oncology Group performance status (ECOG PS) was significantly worse among Black patients (28% with ECOG ≥ 2) compared to White patients (19% with ECOG ≥ 2, p = 0.04), with higher ECOG numbers indicating worse functional status. Additional baseline characteristics stratified by race are displayed in Table 1.

When examining COVID-19 infection-related complications on multivariable analysis, Black patients were more likely to require hospitalization compared to White patients (OR: 1.69, 95% CI: 1.01–2.83, p-value = 0.044). However, the difference in mortality was not statistically significant (OR 1.29, 95% CI: 0.69–2.40, p-value = 0.408). Hispanic ethnicity was not associated with an increase in hospitalization or mortality compared to non-Hispanic ethnicity (hospitalization OR 0.72, 95% CI: 0.30–1.69; mortality OR 1.39, 95% CI: 0.54–3.55). ECOG ≥ 2 and number of comorbidities ≥ 3 were associated with increased risk of hospitalization (Fig. 1; Supplemental Table 2). ECOG ≥ 2, older age, cancer stage ≥ III, and the development of pneumonia were each associated with increased risk of mortality (Fig. 2; Supplement Table 1).

Table 1
Baseline Characteristics of White and Black Patients with Thoracic Malignancies and COVID-19 Infection.

Race	Combined (N = 471)[a]	White (N = 343)	Black(N = 128)
Hospitalization	58 % (275)	54 % (186)	70 % (89)
Death	19 % (91)	18 % (62)	23 % (29)
Age (IQR)	67.0 (60–75)	68.5 (61.0–76.0)	67.0 (58.8–76)
Sex			
Male	46 % (219)	50 % (170)	38 % (49)
Female	54 % (252)	50 % (173)	62 % (79)
Ethnicity			
Non-Hispanic	90 % (426)	91 % (311)	90 % (115)
Hispanic	5 % (25)	6 % (20)	4 % (5)
Missing	4 % (20)	3 % (12)	6 % (8)
Number of Comorbidities			
0	10 % (50)	11 % (38)	9 % (12)
1–2	48 % (228)	51 % (174)	42 % (54)
3+	41 % (192)	38 % (130)	48 % (62)
Missing	0 % (1)	0 % (1)	0 % (0)
Smoking Status			
Never	21 % (97)	21 % (72)	20 % (25)
Former/Current	79 % (372)	78 % (269)	80 % (103)
Missing	0 % (2)	1 % (2)	0 % (0)
BMI			
< 30	70 % (329)	69 % (238)	71 % (91)
≥ 30	29 % (138)	30 % (102)	28 % (36)
Missing	1 % (4)	1 % (3)	1 % (1)
ECOG PS			
0	21 % (101)	22 % (75)	20 % (26)
1	35 % (167)	37 % (126)	32 % (41)
2+	21 % (101)	19 % (65)	28 % (36)
Missing	22 % (102)	22 % (77)	20 % (25)
Cancer Stage			
I	11 % (56)	10 % (35)	16 % (21)
II	4 % (18)	4 % (13)	4 % (5)
III	18 % (86)	17 % (57)	23 % (29)
IV	59 % (280)	61 % (209)	55 % (71)
Missing	7 % (31)	8 % (29)	2 % (2)
On Active Cancer Tx			
No	44 % (206)	42 % (145)	48 % (61)
Yes	56 % (263)	57 % (196)	52 % (67)
Missing	0 % (2)	1 % (2)	0 % (0)
Cytotoxic Chemotherapy	33 % (157)	32 % (109)	38 % (48)
Immunotherapy	28 % (134)	31 % (105)	23 % (29)
Targeted Therapy	15 % (71)	16 % (56)	12 % (15)
Radiotherapy	12 % (56)	10 % (35)	16 % (21)
Required O2 prior to Covid-19 Infection			
No	78 % (368)	77 % (265)	80 % (103)
Yes	14 % (68)	14 % (47)	16 % (21)
Missing	7 % (35)	9 % (31)	3 % (4)
Developed Pneumonia			
No	28 % (136)	25 % (87)	38 % (49)
Yes	23 % (106)	20 % (69)	29 % (37)
Missing	49 % (229)	55 % (187)	33 % (42)

Wave of pandemic was not significantly associated with hospitalization rates, though later wave of pandemic (2 and 3 vs 1) was associated with lower risk of mortality (OR 0.43, CI: 0.20–0.91, p-value = 0.028) (Supplemental Table 3). These associations are independent of the other covariates.

4. Discussion

We investigated the presence of any racial disparities in hospitalization or mortality from COVID-19 infection related complications for patients with thoracic cancer in North America. Given well-described worse outcomes of patients with thoracic malignancy with COVID-19 infection relative to both patients without cancer and those with non-thoracic malignancies [1,7], along with known disparities in cancer care between Black and White patients [8,9], concern has been raised that Black patients with thoracic malignancies may experience poorer clinical outcomes. To the best of our knowledge, this study is the only large cohort examination of racial disparities in hospitalization and survival for patients with thoracic malignancies and COVID-19.

We identified that Black patients in North America with thoracic malignancies and COVID-19 were at greater odds for hospitalization compared to White patients despite mostly similar baseline population characteristics. Our finding that Black patients with COVID-19 and thoracic cancer have greater odds for hospitalization but not mortality aligns with and provides additional detail to the findings of Fu et al. that Black patients have a higher risk of hospitalization but not mortality in the general cancer population. The increased risk for mortality in patients with ECOG ≥ 2, older age, cancer stage $\geq$ III, the development of pneumonia, and earlier wave of pandemic aligns with our prior published analysis which included the full international TERAVOLT registry [3]. This study did have inherent limitations. For example, the patients identified in this study do not represent a clearly defined pool of COVID-positive outpatients of whom a proportion became ill, and thus the total number of patients at risk cannot be clearly known. In addition, most patients in this analysis were infected with COVID-19 during Wave 1 of the pandemic, before the widespread availability of vaccinations; this limited our ability to analyze the contribution of differences in vaccine uptake among patients of different groups.

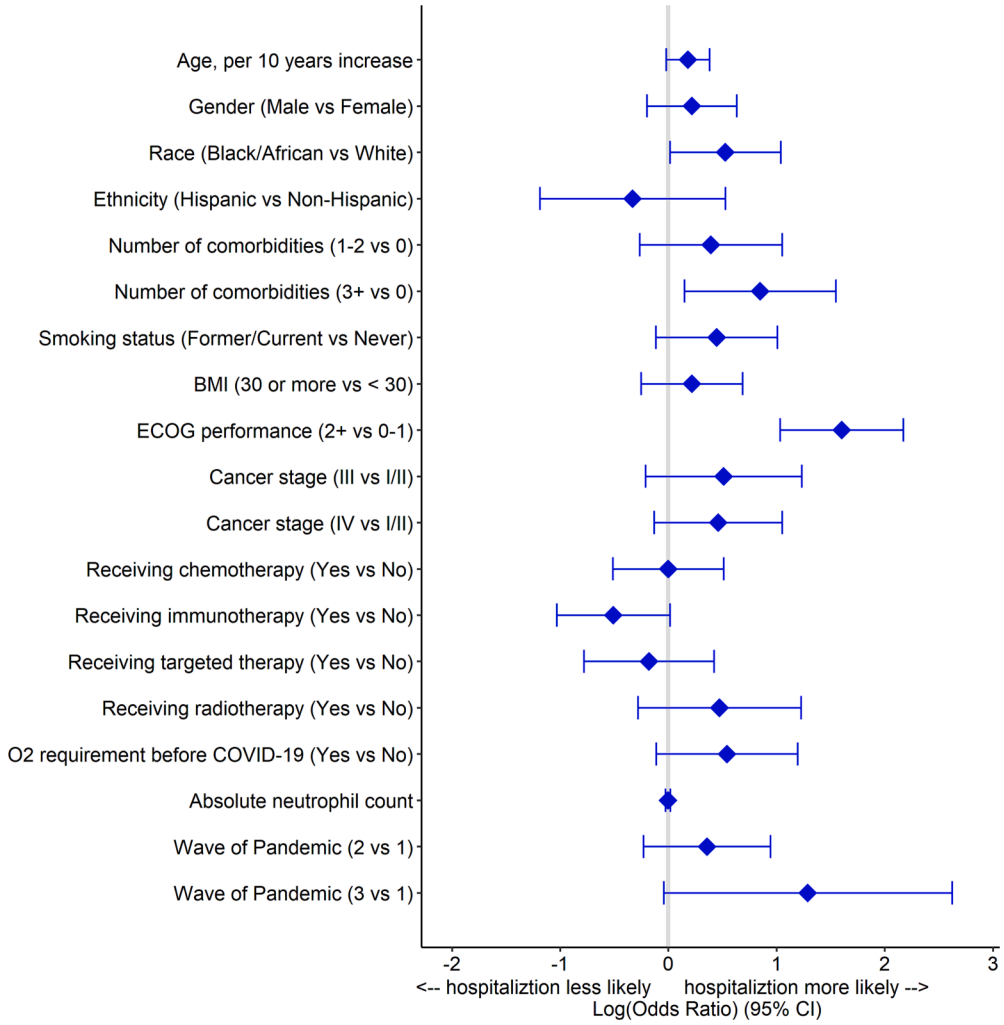

Fig. 1. Forest Plot of Association of Baseline Characteristics with COVID-19-related Hospitalization. Results of multivariable logistic regression analysis for hospitalization, where the covariates in the regression model were pre-determined. Data shown include 471 patients. Odds ratios greater than 1 suggest higher risk of hospitalization for COVID-19. Pre-determined covariates for hospitalization analysis were age, gender, race, ethnicity, number of comorbidities, smoking status, body mass index, ECOG performance, cancer stage, cytotoxic chemotherapy, immunotherapy, targeted therapy, radiotherapy, O2 use prior to COVID-19 infection, absolute neutrophil count, and wave of pandemic. Black race, 3+ comorbidities, and ECOG PS $\geq$ 2 were each associated with increased risk for hospitalization.

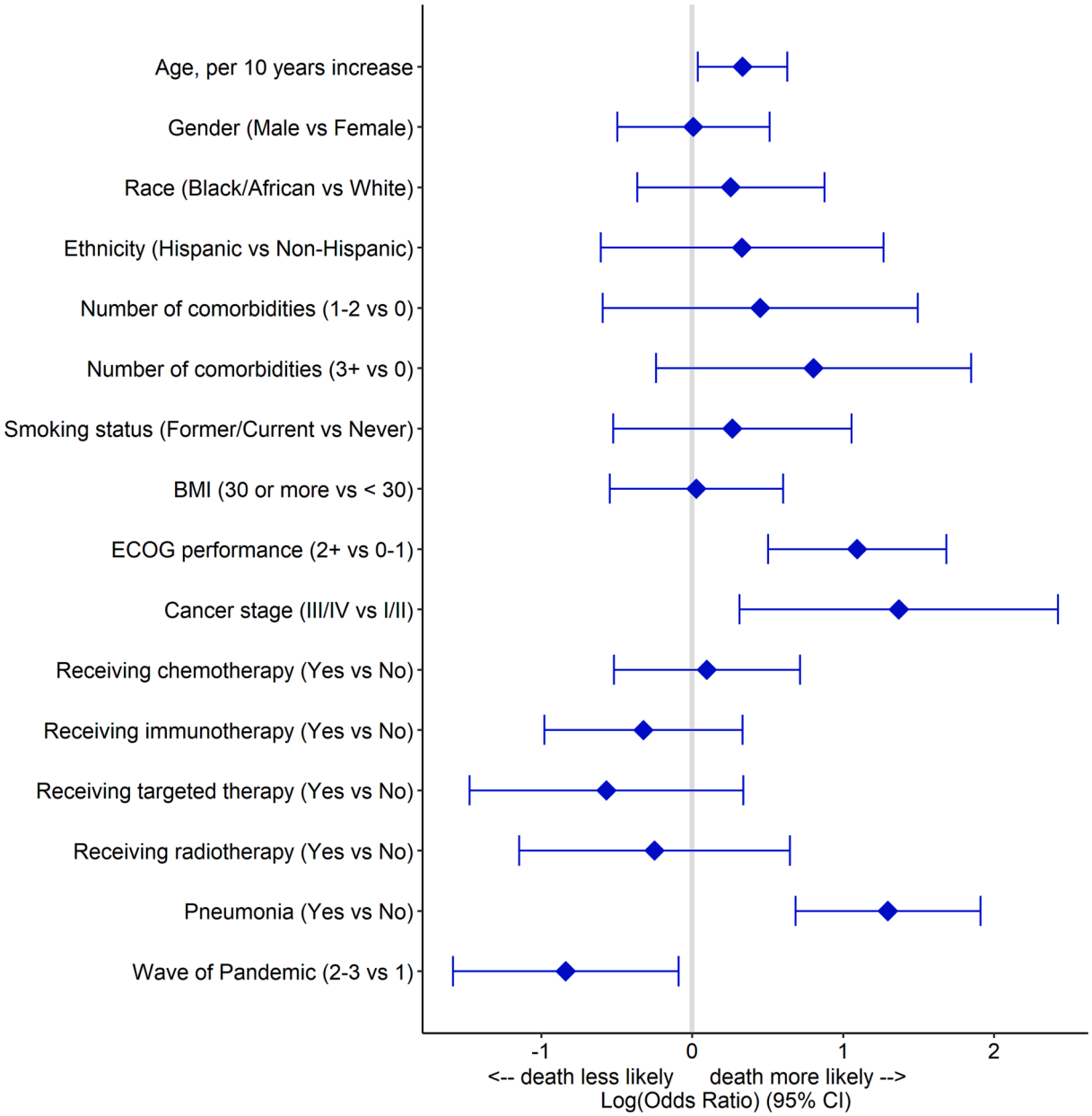

Fig. 2. Forest Plot of Association of Baseline Characteristics with COVID-19-related Mortality. Results of multivariable logistic regression analysis for mortality, where the covariates in the regression model were pre-determined. Data shown include 471 patients. Odds ratios greater than 1 suggest higher risk of mortality from COVID-19-related complication. Pre-determined covariates for mortality analysis were age, gender, race, ethnicity, number of comorbidities, smoking status, body mass index, ECOG performance, cancer stage, cytotoxic chemotherapy, immunotherapy, targeted therapy, radiotherapy, pneumonia, and wave of pandemic. Older age, ECOG PS $\geq$ 2, cancer stage $\geq$ III, and development of pneumonia were associated with increased risk for mortality. Wave 2–3 of the pandemic was associated with lower risk of mortality compared to Wave 1. Waves 2 and 3 were combined for mortality analysis due to no mortality events in Wave 3.

The factors underlying the observed disparity in hospitalization rates between Black and White patients with thoracic malignancies and COVID-19 infections remain to be elucidated, although several warrant consideration. While the baseline characteristics of Black and White patients in this study were largely similar, there were more Black patients with multiple comorbid conditions and an ECOG PS $\geq$ 2 as compared to White patients, which could contribute to the increased likelihood of requiring hospitalization. In addition to these factors, there is a growing body of literature examining the contribution of structural racism to observed differences in both cancer and COVID-19 outcomes by race. The impact of structural racism on health is due to the "totality" of multiple systems (housing, health care, education, etc) resulting in health inequities and disproportionately poor outcomes experienced by Black Americans [10–12]. To begin to address these poor outcomes, some studies have demonstrated that when access to health care is equitable, via decreasing barriers to insurance access, racial disparities between Black and White patients are ameliorated [13]. In lung cancer care specifically, targeted multi-level antiracism interventions have been shown capable of eliminating racial disparities in receipt of treatment and in timely care [14,15]. Perhaps most likely, the observed increased odds of COVID-19 related hospitalizations among Black patients is attributable to a combination of pre-existing clinical factors and structural racism. Additional investigation will be required to inform these considerations.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.lungcan.2023.107423.

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