BRIEF REPORT

Coronavirus Disease 2019 Outcomes, Patient Vaccination Status, and Cancer-Related Delays During the Omicron Wave: A Brief Report From the TERAVOLT Analysis

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ABSTRACT

Introduction: The Thoracic Centers International coronavirus disease 2019 (COVID-19) Collaboration (TERAVOLT) registry found approximately 30% mortality in patients with thoracic malignancies during the initial COVID-19 surges. Data from South Africa suggested a decrease in severity and mortality with the Omicron wave. Our objective was to assess mortality of patients with thoracic malignancies with the Omicron-predominant wave and evaluate efficacy of vaccination.

Methods: A prospective, multicenter observational study was conducted. A total of 28 institutions contributed data from January 14, 2022, to February 4, 2022. Inclusion criteria were any thoracic cancer and a COVID-19 diagnosis on or after November 1, 2021. End points included mortality, hospitalization, symptomatic COVID-19 infection, asymptomatic COVID-19 infection, and delay in cancer therapy. Analysis was done through contingency tables and a multivariable logistic model.

Results: We enrolled a total of 346 patients. Median age was 65 years, 52.3% were female, 74.2% were current or former smokers, 86% had NSCLC, 72% had stage IV at time of COVID-19 diagnosis, and 66% were receiving cancer therapy. Variant was unknown for 70%; for those known, Omicron represented 82%. Overall mortality was 3.2%. Using multivariate analysis, COVID-19 vaccination with booster compared with no vaccination had a protective effect on hospitalization or death (OR = 0.30, confidence interval: 0.15–0.57, $p = 0.0003$), whereas vaccination without booster did not (OR = 0.64, confidence interval: 0.33–1.24, $p = 0.1864$). Cancer care was delayed in 56.4% of the patients.

Conclusions: TERAVOLT found reduced patient mortality with the most recent COVID-19 surge. COVID-19 vaccination with booster improved outcomes of hospitalization or death. Delays in cancer therapy remain an issue, which has the potential to worsen cancer-related mortality.

Keywords: COVID-19; Cancer; Thoracic; NSCLC; TERAVOLT; Registry

Introduction

The Thoracic Cancers International coronavirus disease 2019 (COVID-19) Collaboration (TERAVOLT) is a global observational study of patients with thoracic malignancies and a diagnosis of COVID-19. Prior analysis of mortality was 24.2% to 33%.[1,2]

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) B.1.529 (Omicron) variant was classified as a Variant of Concern by the WHO in November 2021.[3] Omicron was found to have the ability to evade existing SARS-CoV-2–neutralizing antibodies.[4] Nevertheless, the first Omicron-related data from South Africa had improved patient outcomes compared with earlier waves.[5]

COVID-19 vaccine efficacy seems to wane over time, with the BNT162b2 (Pfizer-BioNTech) vaccine falling from 88% effectiveness after full vaccination to 47% after five months.[6] SARS-CoV-2 antibody response in patients treated with anticancer agents was found to decrease in effectiveness at three months after the second vaccine dose, with a strong serologic response occurring after a third dose of the vaccine.[7] A prospective study of humoral responses to the SARS-CoV-2 vaccine in patients with thoracic cancer found a third vaccination resulted in an 88% seroconversion.[8]

In this study, we leveraged TERAVOLT to assess mortality and cancer treatment-related delays from the recent fourth COVID-19 wave. In addition, we analyzed the effect of vaccination with or without a booster on COVID-19-related outcomes.

Materials and Methods

A prospective, multicenter observational study was conducted. A total of 28 institutions from four continents contributed data from January 14, 2022, to February 4, 2022. Data were entered into a deidentified REDCap (Research Electronic Data Capture) database, with each institution assigned a unique number.

Main eligibility criteria were patients with any thoracic cancer (NSCLC, SCLC, mesothelioma, thymic epithelial tumors, and other pulmonary neuroendocrine neoplasms) and a laboratory-confirmed diagnosis of COVID-19 on or after November 1, 2021. Patients with any stage of cancer diagnosis were eligible, including those actively receiving anticancer treatment and those in clinical follow-up.

Data collected included the following: demographics, oncologic history, comorbidities, COVID-19 symptoms and treatment, and clinical outcomes. For this analysis, new data were collected on COVID-19 vaccination and booster status, and, if known, type of variant. Primary end points were as follows: (1) mortality; (2) hospitalization; (3) symptomatic COVID-19 defined as fever, pneumonitis, or dyspnea; (4) almost asymptomatic COVID-19 infection, defined as upper respiratory symptoms only; or (5) asymptomatic COVID-19 infection. Delay in cancer treatment due to COVID-19 was also collected.

Table 1. Demographic and Clinical Characteristics

Patient Characteristics	All Patients (N = 346)
Continent	
Europe	181/346 (52%)
North America	150/346 (43%)
South America	9/346 (3%)
Asia	6/346 (2%)
Age, y (median)	
≥65	185/346 (53%)
<65	161/346 (46%)
BMI	
Median	25.0
Sex	
Female	181/346 (52%)
Male	165/346 (48%)
Race	
White	221/304 (73%)
Black or African American	46/304 (15%)
Asian	15/304 (5%)
Other	22/304 (7%)
Smoking status	
Current	70/340 (20%)
Former	186/340 (55%)
Never	84/340 (25%)
ECOG	
0, 1	271/336 (81%)
≥2	65/336 (19%)
Comorbidity	
None	112/346 (32%)
Any	234/346 (68%)
COPD	96/346 (28%)
Diabetes	13/346 (4%)
Hypertension	139/346 (40%)
Baseline steroid use (>10 mg of prednisone or equivalent)	
Yes	41/346 (12%)
No	305/346 (88%)
Time since cancer diagnosis	
≤12 mo	143/346 (41%)
>12 mo	203/346 (59%)
Diagnosis	
NSCLCs	296/346 (85%)
SCLC	32/346 (9%)
Mesothelioma	9/346 (3%)
Thymic carcinoma	2/346 (0.6%)
Thymoma	3/346 (0.9%)
Carcinoid/neuroendocrine	4/346 (1.2%)
Cancer stage at COVID-19 diagnosis	
I, II, or III	98/345 (28%)
IV	247/345 (72%)
Cancer treatment at time of COVID-19 diagnosis (multiple allowed)	
None	100 (29%)
Cytotoxic chemotherapy	107 (31%)
Immunotherapy	96 (28%)
Targeted therapy	69 (20%)
Radiotherapy	14 (4%)
Other	16 (5%)
COVID-19 variant	
Unknown/not reported	267/346 (77%)
Of Known	
Omicron	65/79 (82%)
Delta	14/79 (18%)
Vaccination status	
Unvaccinated	48/337 (14%)
Vaccinated without booster	133/337 (40%)
Vaccinated with booster	156/337 (46%)

BMI, body mass index; COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; ECOG, Eastern Cooperative Oncology Group.

Statistical Analysis

Descriptive statistics of patient demographics (e.g., age, sex) and clinical characteristics (e.g., comorbidities, anticancer therapy) were reported as frequencies (proportions) for categorical variables and median (interquartile range) for continuous variables. Summary measures for association between demographic and clinical characteristics, vaccination, and outcomes were assessed by univariable logistic models; the association with risk of hospitalization or death was also assessed with multivariable logistic models. Results are given as ORs with 95% confidence intervals (CIs). In multivariable analysis of factors associated with risk of death, we included all factors known to be associated with COVID-19 outcomes in general patient populations.[9] The study analysis was based on a convenience sample; no power analysis was done to calculate sample size.

Results

We enrolled 346 patients, with 182 (53.3%) from Europe, 150 (43.1%) from North America, 10 (2.9%) from South America, and 6 (1.7%) from Asia (Table 1). Almost all patients (98.0%) had at least 14 days of follow-up after their COVID-19 diagnosis. Median age was 65 years, 52.3% were female, and 74.2% were current or former smokers. At least one comorbidity was present in 234 patients (67.6%).

Regarding cancer characteristics, 143 (41.3%) had been diagnosed within 1 year of COVID-19 infection. NSCLC was the predominant diagnosis (85.6%), and 71.4% had stage IV disease at time of COVID-19 diagnosis. Most (71.1%) were receiving cancer treatment at the time of COVID-19 diagnosis, which included cytotoxic chemotherapy (30.9%), immunotherapy (27.7%), targeted therapy (19.9%), and radiation (4.0%).

COVID-19 variant was unknown for 69.7%; for those known, omicron was present in 82.3% (65 of 79) and

Table 2. COVID-19–Related Outcomes

Outcome Measures	All Patients (N = 346)
≥14 d of follow-up from COVID-19 diagnosis	
Yes	339/346 (98%)
No	7/346 (2%)
Delay in cancer treatment due to COVID-19 diagnosis	
Yes	195/343 (57%)
No	148/343 (43%)
Worst COVID-19 outcome patient encountered	
Asymptomatic	60/342 (18%)
Almost asymptomatic (upper respiratory symptoms only)	131/342 (38%)
Fever, pneumonitis, or dyspnea	71/342 (21%)
Admission to hospital	69/342 (20%)
Death	11/342 (3%)

COVID-19, coronavirus disease 2019.

delta in 18% (14 of 29). Most patients were vaccinated for COVID-19 (289 of 346, 83.5%) at the time of COVID-19 diagnosis, with 133 (38%) receiving a vaccine without booster, 156 (45.1%) receiving vaccine with a booster, and 48 patients (14%) being unvaccinated. Most patients received no therapy for COVID-19 (59.2%), such as steroid, antiviral, or antibody infusion.

Overall mortality was 3.2% (Table 2). Other COVID-19 outcomes included asymptomatic infection (17.3%), mild symptoms of upper respiratory symptoms only (37.9%), moderate symptoms of fever, pneumonitis, or shortness of breath (20.5%), or admission to hospital (19.9%). A delay in cancer care was experienced in 56.4% of the patients.

At multivariate analysis, COVID-19 vaccination with booster had a protective effect on hospitalization or death compared with no vaccination (OR = 0.30, CI: 0.15–0.57, $p = 0.01$; Table 3). Vaccination without booster had an OR of 0.64 (CI: 0.33–1.24, $p = 0.19$). Eastern Cooperative Oncology Group performance status more than 1 was associated with an increased risk of hospitalization or death (OR = 1.78, CI: 1.04–3.05, $p = 0.04$). A delay in cancer care was experienced in 56.4% of the patients.

Discussion

In this analysis of the fourth COVID-19 wave, overall mortality of patients with thoracic malignancies in the TERAVOLT database was notably lower at 3.2% compared with 24.2% to 33% in prior surges.[1,2] This improvement in mortality is similar to that reported for the general population, with an analysis of patients hospitalized in South Africa with COVID-19 revealing a mortality of 2.7% in wave 4 compared with 19.7% in wave 1 (ancestral variant) and 29.1% in wave 3 (delta).[5]

Our analysis reveals the importance of a booster vaccination to achieve the maximum protective effect from severe COVID-19 outcomes, including hospitalization or death (relative risk = 0.30) in patients with thoracic cancer. In our analysis, vaccination without booster versus unvaccinated trended toward a protective effect with relative risk of 0.64, though it did not meet statistical significance (CI: 0.33–1.24, $p = 0.19$). The protective effect of a booster observed in this analysis is reflective of the humoral response found to two or three vaccine doses in both the thoracic malignancy population and a broader population receiving anticancer therapy.[7,8,10] In the general population, the adjusted OR of symptomatic COVID-19 for three doses of Pfizer-BioNTech BNT162b2 or Moderna mRNA-1273 versus unvaccinated was 0.33 (95% CI: 0.31–0.35) for Omicron and 0.065 (95% CI: 0.059–0.071) for Delta.[11] With this knowledge, we should continue to advocate for our patients to receive booster vaccinations to protect this vulnerable population.

Despite COVID-19–related mortality being lower with this wave, more than half (56.4%) of the patients included in this analysis experienced a delay in their cancer care which may lead to a future increase in cancer mortality. The data obtained from this study may suggest that there is no need to delay oncology treatments in patients who have been vaccinated and have also had the booster. New trials are warranted to confirm this hypothesis.

The variant type was unknown for almost two-thirds of the patients in this analysis, which limits the ability to generalize the results specifically toward the Omicron

Table 3. Multivariable Logistic Analysis of Effect on Composite Outcome of Hospitalization, or Death

Variables	Effect	95% Confidence Interval	Chi-Square Test	*p* Value	Global *p*
Vaccinated with booster vs. not vaccinated	0.30	0.15-0.57	13.02	0.01	0.0007
Vaccinated without booster vs. not vaccinated	0.64	0.33-1.24	1.74	0.19	–
Age 65 y or higher	0.87	0.55-1.36	0.39	0.53	–
At least 1 comorbidity	0.98	0.60-1.57	0.01	0.92	–
Active or history of smoking	1.02	0.62-1.66	0.01	0.95	–
ECOG ≥2	1.78	1.04-3.05	4.43	0.04	–

ECOG, Eastern Cooperative Oncology Group.

wave. Nevertheless, given the time frame of the diagnosis (on or after November 1, 2021) and the virulence of Omicron, we assumed that most of the infections were Omicron, consistent with the general variant predominance at the time.[12] In the patients where the variant type was known (n = 79), 82% had Omicron compared with 14% who had Delta suggesting Omicron was the dominant variant during this time frame.

Another limitation of this study is that further characterization of the delay of cancer care is unknown. The severity of delay may range from a delay in long-term surveillance imaging to initiation of curative intent therapy. Further studies are needed to characterize the impact on therapy delays on cancer-related mortality for patients. An additional limitation of this study is that the primary reason for hospitalization was not further characterized. Many patients in the Omicron wave were found on admission to have an asymptomatic COVID-19 infection, and this was not reflected in our analysis. Furthermore, given the sample size and low mortality, we were not powered to look at risk factors for death alone.

Our analysis suggests that vaccination with booster is protective against severe outcomes of COVID-19 infection, highlighting the importance of continued efforts to improve vaccination and booster rates in patients with thoracic malignancies while ensuring continuity of cancer care. Further research to characterize the effect on cancer-related mortality related to COVID-19 infection is necessary to minimize the impact of the pandemic on our patients.

CRediT Authorship Contribution Statement

Marina Chiara Garassino, Valter Torri, Jennifer G. Whisenant, Christine M. Bestvina, Alessio Cortellini: Conceptualization, Methodology.

Valter Torri: Software Validation, Visualization.

Valter Torri, Jennifer G. Whisenant: Formal analysis.

Valter Torri, Jennifer G. Whisenant, Marina Chiara Garassino, Baena, Christine M. Bestvina: Investigation, Resources.

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