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Global Health and Cancer

Clinical Impact of the COVID-19 Pandemic in Mexican Patients with Thoracic Malignancies

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Disclosures of potential conflicts of interest may be found at the end of this article.

Key Words. Pandemic • Lung cancer • Coronavirus disease 2019 • Severe acute respiratory syndrome coronavirus 2 • Thoracic neoplasms

Abstract

Background. Accumulated evidence indicates that patients with lung cancer are a vulnerable population throughout the pandemic. Limited information is available in Latin America regarding the impact of the pandemic on medical care. The goal of this study was to describe the clinical and social effect of COVID-19 on patients with thoracic cancer and to ascertain outcomes in those with a confirmed diagnosis.

Materials and Methods. This cohort study included patients with thoracic neoplasms within a single institution between March 1, 2020, and February 28, 2021. All variables of interest were extracted from electronic medical records. During this period, the Depression Anxiety and Stress Scale 21 (DASS-2) was applied to evaluate and identify more common psychological disorders.

Results. The mean age for the total cohort ($n = 548$) was 61.5 $\pm$ 12.9 years; non-small cell lung cancer was the most frequent neoplasm (86.9%), advanced stages predominated (80%), and most patients were under active therapy (82.8%). Any change in treatment was reported in 23.9% of patients, of which 78.6% were due to the COVID-19 pandemic. Treatment delays (≥7 days) were the most frequent modifications in 41.9% of cases, followed by treatment suspension at 37.4%. Patients without treatment changes had a more prolonged progression-free survival and overall survival (hazard ratio [HR] 0.21, $p < .001$ and HR 0.28, $p < .001$, respectively). The mean DASS-21 score was 10.45 in 144 evaluated patients, with women being more affected than men (11.41 vs. 9.08, $p < .001$). Anxiety was reported in 30.5% of cases, followed by depression and distress in equal proportions (18%). Depressed and stressed patients had higher odds of experiencing delays in treatment than patients without depression (odds ratio [OR] 4.5, 95% confidence interval [CI] 1.53–13.23, $p = .006$ and OR 3.18, 95% CI 1.2–10.06, $p = .006$, respectively).

Conclusion. Treatment adjustments in patients with thoracic malignancies often occurred to avoid COVID-19 contagion with detrimental effects on survival. Psychological disorders could have a role in adherence to the original treatment regimen. ***The Oncologist*** 2021;26:1035–1043

Implications for Practice: The pandemic has placed an enormous strain on health care systems globally. Patients with thoracic cancers represent a vulnerable population, with increased morbidity and mortality rates. In Mexico, treatment modifications were common during the pandemic, and those who experienced delays had worse survival outcomes. Most treatment modifications were related to a patient decision rather than a lockdown of health care facilities in which mental health impairment plays an essential role. Moreover, the high case fatality rate highlights the importance of improving medical care access. Likewise, to develop strategies facing future threats that may compromise health care systems in non-developed countries.

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Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1] pandemic has brought significant social, health, and economic repercussions [2]. As of May 10, 2021, more than 158 million COVID-19 cases and 3.2 million deaths have been reported across the globe [3]. In Mexico, more than 2.3 million cases have been confirmed, with more than 219,000 deaths attributed to COVID-19 [4].

Patients with cancer have emerged as a vulnerable population during the pandemic because of intrinsic comorbid conditions and risk factors favoring the onset of complications, more severe and rapid symptoms, higher hospitalization rates, increased need for intensive care and invasive airway support, and higher mortality compared with individuals without cancer [5–7].

Patients with thoracic neoplasms in whom cancer symptoms might mimic those of COVID-19 may suffer from misdiagnosis or diagnostic delays, leading to detrimental effects on prognosis [8]. The Thoracic Cancers International COVID-19 Collaboration registry has confirmed an increased hospitalization rate and mortality due to COVID-19 in patients with thoracic cancers [9]. Patients with lung cancer are particularly susceptible to severe disease (62% were hospitalized and 25% died), and determinants of severity may be linked to patient-specific features, including smoking status and chronic obstructive pulmonary disease [10].

Expert panels have proposed strategies to balance cancer-related risks and benefits with the increased risk of COVID-19 [11, 12], leading some institutions to delay treatments and nonurgent interventions in order to encourage social distancing [13, 14]. Delays in cancer treatment may increase 5-year cancer-related mortality by 4.8%–16.6% (depending on cancer type) [15]; delaying cancer care has been found to be associated with increased cancer-specific mortality, which exceeds COVID-19 mortality [16]. Apart from the detrimental physical effects of cancer, the patients' mental health has been deeply affected by the pandemic [17, 18]. A particular concern is the additive negative impact of COVID-19 due to unemployment [19], economic insecurity, the death of loved ones, social isolation [20], and disruption of daily life.

Patients with thoracic neoplasms face a triple burden: a high risk of experiencing severe clinical complications if infected with COVID-19, the risk of clinical progression because of treatment delays, and the high prevalence of anxiety, depression, and stress because of the pandemic. However, limited information is available regarding the effects of the pandemic on the outcomes of patients with thoracic neoplasms living in developing countries. Likewise, there is a lack of information regarding the impact of measures adopted to avoid overcrowding health care facilities, of resource depletion, and of psychological and emotional well-being on patient outcomes. In this study, we aimed to describe the impact of the strategies implemented to avoid high-risk exposure to COVID-19 in a Mexican cancer center on cancer-related and psychological outcomes of patients with thoracic neoplasms.

Materials and Methods

Consecutive patients with confirmed thoracic cancer (lung cancer, mesothelioma, or thymomas) were evaluated for enrollment in this prospective cohort study between March 1, 2020, and February 28, 2021. Patients were recruited from the Thoracic Oncology Unit of Instituto Nacional de Cancerología (INCan), a public cancer center located in southern Mexico City that provides care for uninsured patients with various malignancies. The study was approved by the institutional review board at INCan, and all participants provided written informed consent. All research procedures were performed in accordance with the Declaration of Helsinki and the principles of Good Clinical Practice.

Eligibility criteria for enrollment were as follows: adult patients (aged ≥18 years) with a confirmed thoracic neoplasm, regardless of disease status (surveillance vs. active therapy), clinical stage, prior lines of therapy, treatment modality (systemic therapy, radiotherapy, or surgery), and/or Eastern Cooperative Oncology Group (ECOG) performance status (PS). Only patients receiving their full treatment and follow-up at INCan were included.

During the study period, thoracic oncologists and an interdisciplinary group consisting of a nutritionist, pulmonologist, psychologist, and psychiatrist evaluated patients following international and local COVID-19–related recommendations. Demographic, clinical, and pathological variables of interest were extracted from medical records: age, gender, type of thoracic neoplasm, clinical stage (American Joint Committee on Cancer 8th edition), date of diagnosis, histology, prior lines of therapy, ECOG PS, and comorbidities. Similarly, modifications to original treatment planning, adherence to outpatient visits, and data related to COVID-19 diagnoses (imaging, diagnostic tests, and outcomes) were obtained from the medical record.

Patients receiving treatment with curative or palliative intent, irrespective of treatment modality (radiotherapy, systemic therapy, or surgery) or type of systemic therapy (target therapy, chemotherapy, or immunotherapy), were considered to be receiving active therapy.

COVID-19 Suspicion or Diagnosis

According to the local policy, every patient with radiological or clinical suspicion of COVID-19 was referred to a specialized multidisciplinary team for diagnosis and management. Treatment delivery and medical care were coordinated by an infectious disease team and a pulmonologist. All patients received a SARS-CoV-2 real-time polymerase chain reaction (RT-PCR) test or a rapid antigen test, except for those who refused undergoing testing. Admissions to hospitalization or intensive care were decided by trained health care specialists in charge of evaluating the severity of disease and treatment delivery [21].

Radiological Assessment

Most of the participants were receiving evaluation using positron emission tomography/computed tomography (PET/CT) or CT scans every 3 months to determine the efficacy of primary treatment. An additional CT scan was performed at the discretion of the multidisciplinary team for COVID-19 diagnostic purposes in patients with clinical suspicion. All imaging studies were reviewed by a thoracic radiologist and classified according to the level of suspicion based on the Dutch Radiological Society classification, COVID-19 Reporting and Data System (CO-RADS) [22]. This system stratified CT scans into

Table 1. Patient characteristics

Characteristics	*n* (%)
Age, yr	
Mean ± SD	61.5 ± 12.9
≤60	240 (43.8)
>60	308 (56.2)
Sex	
Male	236 (43.1)
Female	312 (56.9)
Smoking status at diagnosis	
Active smoker	119 (21.7)
Former smoker	155 (28.3)
Passive smoker	39 (7.1)
Nonsmoker	235 (42.9)
Wood smoke exposure	
Yes	156 (28.5)
Thoracic neoplasm	
Non-small cell lung cancer	476 (86.9)
Small cell lung cancer	23 (4.2)
Thymoma	11 (2.0)
Mesothelioma	25 (4.6)
Others	13 (2.4)
Histology	
Adenocarcinoma	447 (81.6)
Squamous	28 (5.1)
Small cell	13 (2.4)
Neuroendocrine	13 (2.4)
Others	47 (8.6)
Clinical stage	
I	10 (1.8)
II	17 (3.1)
III	60 (10.9)
IV	442 (80.7)
Unknown	19 (3.5)
Comorbidities	
Hypertension	170 (31)
Diabetes	88 (16.1)
Obesity	38 (6.9)
Chronic obstructive pulmonary disease	30 (5.5)
Heart failure	12 (2.2)
ECOG performance status	
0–1	485 (88.5)
≥2	63 (11.5)
Type of treatment (last 60 days, $n = 454$)	
Chemotherapy	169 (30.8)
TKI	217 (39.6)
Immune checkpoint inhibitor	39 (7.1)
Chemotherapy + immune checkpoint inhibitor/TKI/radiotherapy	20 (3.7)
Surgery	5 (0.9)
Radiotherapy	4 (0.7)
Lines of therapy (metastatic disease, $n = 442$)	
1st line	273 (61.7)
2nd line	136 (30.8)
≥3rd line	33 (7.5)

Abbreviations: ECOG, Eastern Cooperative Oncology Group; TKI, tyrosine kinase inhibitors.

five categories: category 1 represents the lowest suspicion of being infected by SARS-CoV-2, with category 5 representing the highest probability of infection.

Mental Health Assessment

A mixed-method design was used to evaluate the pandemic's impact on mental health. Quantitative data were obtained using the Spanish version of the Depression Anxiety and Stress Scales (DASS-21) to screen for general distress as well as symptoms of depression, anxiety, and stress. DASS-21 is a 21-item self-applied questionnaire composed of three 7-item subscales for depression, anxiety (anxious arousal), and stress [23, 24]. Its utility has been comparable to other scales used in clinical settings, such as the Hospital Anxiety and Depression Scale [25]. The Spanish language version of DASS-21 has been validated among Hispanic individuals, of whom more than a third were of Mexican origin [26, 27]. General distress was measured with the 21-item total score, whereas two sets of variables were created for each subscale: a dichotomous variable describing the population that had depression, anxious arousal, or stress, and a categorical variable describing the severity of each symptom. Cutoffs for the dichotomous variables were ≥ 5 score for depression, ≥4 score for anxiety, and ≥ 8 scores for stress.

Statistical Analysis

Continuous variables were summarized as means, medians, ranges, and SDs. Categorical variables were summarized as proportions and 95% confidence intervals (CIs). The chi-square or Fisher's exact test was used to determine statistically significant differences among categorical variables. Statistical significance was predetermined to be present at a p value <.05 on a two-sided test.

Progression-free survival (PFS) was determined from diagnosis until disease progression, death, or loss of follow-up. Overall survival (OS) comprised the interval from diagnosis until death or censored at the last follow-up. OS and PFS were calculated using the Kaplan-Meier method; the log-rank test was used to evaluate differences among subgroups. A Cox proportional hazards model was performed for PFS and OS as a univariate analysis for each variable of interest to assess the size effect of treatment changes due to the health crisis in terms of survival.

Both continuous and categorical DASS-21 results were considered in regression models to determine its role considering the following confounding variables: age, gender, positive COVID-19 test, clinical stage, clinical progression,

Table 2. Characteristics of patients with and without treatment changes or delays

Characteristics	Patients with treatment changes/delays ($n = 131$)	Patients without treatment changes/delays ($n = 417$)	*p* value
Sex			
Male	63 (48.1)	173 (41.5)	.183
Female	68 (51.9)	244 (58.5)	
Age, yr			
≤60	66 (50.4)	174 (41.7)	.082
>60	65 (49.6)	243 (58.3)	
Type of thoracic neoplasm			
NSCLC	102 (77.9)	374 (89.7)	<.001
Others	29 (22.1)	43 (10.3)	
Histology			
Adenocarcinoma	94 (71.8)	353 (84.7)	.001
Squamous	7 (5.3)	21 (5.0)	
Others	30 (22.9)	43 (10.3)	
Clinical stage			
I–III	24 (19.5)	63 (15.5)	.295
IV	99 (80.5)	343 (84.5)	
ECOG performance status			
<2	98 (74.8)	387 (92.8)	<.001
≥2	33 (52.2)	30 (7.2)	
Lines of therapy			
1st line	63 (48.1)	217 (52)	.431
>1st line	68 (51.9)	200 (48)	
Enrolled in clinical trial			
Yes	21 (16)	124 (29.7)	.002
No	110 (84)	293(70.3)	
Comorbidities			
Yes	66 (50.4)	199 (47.7)	.595
No	65 (49.6)	218 (52.3)	
Diabetes			
Yes	34 (26)	54 (12.9)	<.001
No	97 (74)	363 (87.1)	

Data are shown as *n* (%).
Abbreviations: ECOG, Eastern Cooperative Oncology Group; NSCLC, non-small cell lung cancer.

line of treatment, changes in the type of treatment, and delays in primary treatment.

All statistical analyses were carried out using Statistical Package for the Social Sciences version 26.0 (SPSS Inc, Chicago, IL).

Results

Study Population

A total of 549 patients with confirmed thoracic cancer were included. Mean age was 61.5 ± 12.9 years, 56.9% of participants were women, 88.5% had an ECOG PS of 0–1, and 50% were current or former smokers. Most patients had non-small cell lung cancer (86.7%), with adenocarcinoma being the most common histological subtype (81.6%), and the majority had clinical stage IV disease (80.7%). Almost half of the patients (48.4%) had at least one comorbidity, hypertension (31%), diabetes mellitus (16%), and obesity (6.9%) being the most common. Other baseline characteristics of interest are described in Table 1.

Of the total cohort, 536 (97.8%) patients received at least one treatment modality (systemic therapy, radiotherapy, or surgery) as initial therapy; of these, 454 (82.8%) were still receiving some form of treatment at the last visit. Around 26.5% of treated patients were participating in various research protocols and remained enrolled throughout the pandemic. The most common initial systemic treatment among patients receiving active therapy was tyrosine kinase inhibitors (TKIs) (37%), followed by chemotherapy (35.6%) and immune checkpoint inhibitors (ICIs) (2.2%). At the time of last contact, TKIs were still the most common systemic treatment (39.6%), with an increase seen in the number of patients receiving ICIs (7.1%) and a

Table 3. Treatment changes during the COVID-19 pandemic

Treatment changes	$n = 131$, *n* (%)
Type of treatment modification	
Delay ≥7 days	55 (42)
Dose modifications	14 (10.7)
Treatment interruptions	49 (37.4)
Treatment not started	11 (8.4)
Other	2 (1.5)
Type of treatment modified	
Chemotherapy	54 (45.4)
TKI	33 (27.7)
Immune checkpoint inhibitor	23 (19.3)
Chemotherapy + immune checkpoint inhibitor	7 (5.9)
Chemotherapy + radiotherapy	1 (0.8)
Chemotherapy + TKI	1 (0.8)
Surgery	5 (3.8)
Reasons for treatment modification	
Avoiding SARS-CoV-2 exposure	46 (35.1)
Medical indication	25 (19.1)
Suspicion of COVID-19 infection	18 (13.7)
Medication shortage	16 (12.2)
Confirmed COVID-19 infection	14 (10.7)
Functional status deteriorated	12 (9.2)
Disease status after treatment modification	
With disease progression	65 (49.6)
Without disease progression	58 (44.3)
Unknown	8 (6.1)

Abbreviations: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; TKI, tyrosine kinase inhibitors.

decline in chemotherapy usage (30.8%) ($p < .01$). In the palliative setting, systemic therapy was delivered as first, second, or further lines of therapy in 273 (61.6%), 136 (30.7%), and 34 (7.7%) patients, respectively.

Treatment Modifications

One hundred thirty-one (23.9%) patients had at least one treatment adjustment during the pandemic, most of which were a direct consequence of COVID-19–related measures (90.8%). Compared with patients who did not have treatment adjustments, patients with at least one adjustment were less likely to have non-small cell lung cancer, had a worse performance status, and were less likely to be enrolled in a clinical trial (Table 2). Chemotherapy was the most often modified treatment (45.4%), followed by TKIs (27.7%) and ICIs (19.3%). The most common treatment modifications were treatment delays in 55 (41.9%) patients, of whom 14.5% represented delays prolonged more than 30 days. Treatment discontinuation and dose reductions occurred in 37.4% and 10.7%, respectively. The main reason for treatment delays (35.1% of patients) was missed outpatient visits because of fear of experiencing a high-risk COVID-19 exposure. In comparison, only 19.1% of patients underwent treatment modifications because of treating physician's or multidisciplinary team's choices. Approximately 12% of patients were unable to receive some form of treatment because of a national shortage of medications during the pandemic (Table 3). Twenty-seven patients underwent a surgical procedure during the studied period, of which five had to be delayed because of the absence of a negative confirmatory PCR test to rule out COVID-19. Seventy-one patients received radiotherapy, of which none had delays or interruptions.

Cancer-Related Clinical Outcomes

Among patients who had at least one treatment adjustment during the studied period, the median PFS was of 10.9 (10.2–11.6) months. In contrast, median PFS was not reached (NR; HR 0.21, 95% CI 0.14–0.30, $p < .001$) among those without treatment modifications (Fig. 1).

Sixty-one patients (11.1%) had died at the time of the analysis. Although median OS was not reached in both groups because of a short follow-up, differences between groups were significant, favoring patients without modifications (HR 0.28, 95% CI 0.16–0.46, $p < .001$) (Fig. 1). In the multivariate analysis, the presence of any treatment modification remained a significantly increased risk factor for death (HR 2.3, 95% CI 1.4–4.0, $p < .001$) and progression (HR 4.2, 95% CI 2.9–6.1, $p < .0001$) after the adjustment for confounding variables. Other major adverse factors were a poor ECOG performance status and the start of treatment after pandemic onset (supplemental online Tables 1, 2). The only protective factor for survival was to be part of a clinical trial (HR 0.4, 95% CI 0.2–0.8, $p = .016$).

Clinical Presentation of Patients with Suspected or Confirmed COVID-19

Sixty-six patients had a suspicion of COVID-19. Most (84.8%) had clinical manifestations compatible with SARS-CoV-2 infection. Compared with patients who never had a suspicion of COVID-19, those with a suspicion of COVID-19 were more likely to have an ECOG PS ≥2 (22.7 vs. 10%; $p = .002$). Five patients presented with suggestive radiological findings without symptoms, and five were detected incidentally through preoperative imaging. COVID-19 diagnostic tests were performed in 60 (90.9%) patients, with PCR performed in 58 (96.7%), whereas six patients refused testing and medical care. A positive COVID-19 test was confirmed in 32 (52.5%) patients. There were no significant baseline clinical differences between patients who had a positive COVID-19 test and the rest of the patient population. The most common COVID-19 symptoms were dyspnea (59%), cough (52.5%), fatigue (36.1%), fever (31.1%), and sore throat (12.9%).

Forty-three imaging studies were performed in patients with a suspicion of COVID-19: 42 CT scans or PET/CT studies and 1 chest x-ray. According to the CO-RADS classification, nine (20.9%) patients had a very high suspicion of COVID-19 (category 5), six patients an indeterminate study (category 3), and 17 cases were confirmed with a positive PCR test (category 6) (Table 4). All confirmed PCR cases were categorized as very high and/or high suspicion based on imaging studies.

Median PFS was significantly worse among patients with suspected COVID-19 compared with those who never had a suspicion of COVID-19 (11.7 vs. NR, HR 0.51, 95% CI 0.32–

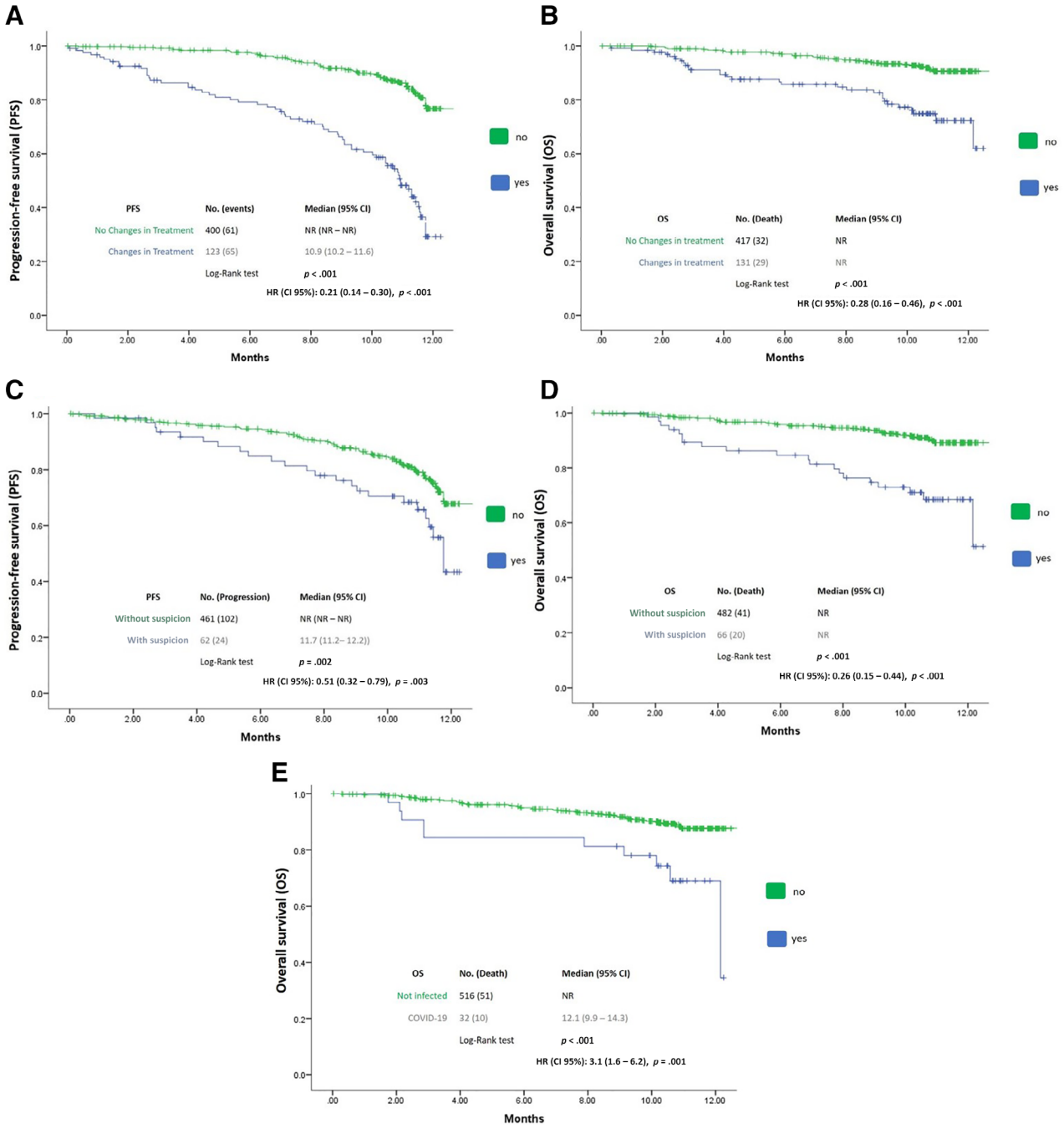

Figure 1. Survival outcomes during the COVID-19 pandemic. Progression-free survival **(A)** and overall survival **(B)** according to the presence or absence of treatment modifications due to health crisis. Progression-free survival **(C)** and overall survival **(D)** in patients with and without suspicion of COVID-19. **(E):** Overall survival in patients with and without confirmed COVID-19 diagnosis.
Abbreviations: CI, confidence interval; HR, hazard ratio; NR, not reached; OS, overall survival; PFS, progression-free survival.

0.79, $p = .003$; Fig. 1). Similarly, although the median was not reached in both groups, OS was significantly worse in the subgroup of patients with a suspected case (HR 0.26, 95% CI 0.15–0.44, $p < .001$; Fig. 1).

COVID-19-Related Clinical Outcomes

The 1-year cumulative incidence of COVID-19 among patients with thoracic neoplasms was 5.8%. Of the 32 patients with a confirmed COVID-19 test, 19 (59.3%) had a moderate/severe clinical course and needed hospitalization. Seven patients required medical management in the intensive care unit (ICU). The mean time within an inpatient facility was 4.1 days (1–30) for hospitalized patients and 14.4 (3–42) days for patients in the ICU. Twenty patients (62.5%) with a confirmed diagnosis required oxygen supplementation; five received mechanical ventilation, and two noninvasive ventilation. Face masks were the most commonly used device to provide supplementary oxygen ($n = 8$).

Dexamethasone was administered to 12 (37.5%) patients, most of whom had a severe disease. Other medications like azithromycin and antiviral medications

Table 4. Characteristics of patients with a suspicion of COVID-19 infection

Characteristics	*n* (%)
Reason for suspicion	
Clinic	56 (84.8)
Imaging study	5 (7.6)
Preoperative study	5 (7.6)
Symptoms	
Symptomatic	59 (89.4)
Asymptomatic	7 (10.6)
Underwent imaging studies	
Yes	43 (65.2)
No	23 (34.8)
Type of diagnostic imaging	
Radiography	1 (2.3)
CT/PET-CT	42 (97.7)
Imaging findings	
Very high suspicion	12 (27.9)
High suspicion	9 (20.9)
Moderate suspicion	11 (25.6)
Low suspicion	11 (25.6)
CO-RADS classification	
Negative	2 (4.7)
Low suspicion	2 (4.7)
Indeterminate	6 (14)
Very high suspicion	9 (20.9)
Confirmed (PCR)	17 (39.5)
Not valuable	7 (16.3)
Confirmatory COVID-19 testing performed	
Yes	60 (90.9)
No	6 (9.1)
Type of confirmatory test	
PCR	58 (96.7)
Antigens	2 (3.3)
COVID-19 diagnosis confirmed	
Yes	32 (48.5)
No	34 (51.5)
Cause of suspicious symptoms	
COVID-19	28 (47.5)
Disease progression	8 (13.6)
Other infection	9 (15.3)
Treatment-induced pneumonitis	3 (5.1)
Another cause	11 (18.6)

Abbreviations: CO-RADS, COVID-19 Reporting and Data System; CT, computed tomography; PCR, polymerase chain reaction; PET-CT, positron emission tomography/computed tomography.

(lopinavir/ritonavir) were administered in three patients and one patient, respectively. One patient received tocilizumab within a clinical trial, and convalescent plasma transfusion was administered in one single case with a severe clinical presentation and a rapidly fatal course. Of all affected patients, 16 recovered fully from the disease (50%), and 7 more recovered with long-term symptoms. The case fatality rate (CFR) was 28.1%. The main causes of death were severe respiratory distress syndrome ($n = 6$) and refractory septic shock ($n = 3$). Median OS was significantly shorter among patients with confirmed COVID-19 than among those who never had COVID-19 (12.1 months vs. NR, HR 3.1, 95% CI 1.6–6.2, $p = .001$; Fig. 1).

Impact of Delays on Mental Health

One hundred forty-four (26.2%) patients underwent psychological assessment. Mean DASS-21 score was 10.45, with women showing significantly worse scores than men (mean 11.41 vs. 9.08, $p < .001$). At least 35.4% of patients had one positive symptom: anxiety was present in 30.5%, whereas depression and distress were both present in 18.0%. Women had a higher prevalence of positive symptoms for all subscales in comparison to men. Severe and extremely severe cases of anxiety and depression were identified in 44.2% and 60% of patients, respectively. Age, gender, and treatment modifications were not associated with stress in the DASS-21. However, having stage IV disease was significantly associated with both stress (odds ratio [OR] 0.046, $p = .032$) and anxiety (OR 0.02, $p = .023$). After adjusting for age and sex, participants reporting anxiety (OR 7.5, $p < .01$) or stress (OR 17.33, $p < .001$) were at a significantly higher risk of depression. Depressed and stressed patients had higher odds of experiencing delays in treatment than patients without depression (OR 4.5, 95% CI 1.53–13.23, $p = .006$ and OR 3.18, 95% CI 1.2–10.06, $p = .006$).

Discussion

The COVID-19 pandemic led to therapeutic modifications in a quarter of patients with thoracic malignancies treated at a public cancer center in Mexico. Patients who had treatment modifications had shorter survival than those who did not. Of note, treatment modifications remained of clinical relevance after the adjustment for predefined variables. A significant proportion of patients had a suspicion of COVID-19, although in some cases this was due to the underlying malignancy, with confirmation of infection occurring in half of them. Patients who had a suspicion of COVID-19 also had worse survival than those who did not.

The pandemic has placed an enormous strain on health care systems globally, generating unmeasurable economic and social consequences. Patients with cancer have been affected greatly because of the high risk of COVID-19–related morbidity and mortality, and as a consequence of restrictions in access to care caused by policies aimed at flattening the transmission curve [11]. In a recent systematic review that encompassed 62 studies, delays and disruptions of treatment, diagnosis, and general health service occurred frequently during the pandemic; most of them were provider or system related because of a reduction in service availability [28]. In contrast, the main reason for treatment delays in our study was rescheduling or cancellation of outpatient visits because of patient preferences rather than institutional policy. This is explained by the fact that INCan remained open as a referral cancer center throughout the pandemic without interruption of most clinical activities. Like in our study, a recent meta-analysis of 34 studies demonstrated an increased mortality rate for each 4-week delay across surgical,

systemic, and radiotherapy indications among patients with various types of cancer [29]. Patients with a worse performance status were more likely to have treatment delays, which could be a reason for the worse overall survival in this subset of patients. Interestingly, patients enrolled in clinical trials were less likely to have treatment delays, which could be explained by shortages in medications for patients outside clinical trials.

Systemic treatment changes during the pandemic at our center were similar to those found in other international studies. Importantly, we showed a decrease in the number of patients receiving cytotoxic chemotherapy and an increase in the use of ICIs and TKIs. In contrast with chemotherapy, it was unusual for TKI to be suspended by patients or physicians during the pandemic, even in selected cases of active infections. Moreover, TKIs were administered beyond radiological progression in clinically stable subjects to avoid more frequent visits and shorter intervals of administration with alternative therapies. In general, TKIs were prescribed every 2 months rather than monthly in order to decrease hospital visits, as was suggested in a Latin American expert consensus of thoracic malignancies [11]. The low proportion of patients receiving ICIs in our cohort illustrates the lack of availability of these treatments in most developing countries. In patients receiving ICIs, the longest possible interval between cycles (based on U.S. Food and Drug Administration recommendations) was used.

The cumulative incidence of COVID-19 infections in our cohort was of around 6%, with most patients requiring hospitalization and more than 20% being admitted to the ICU. This mirrors the results of a Chinese cohort that reported similar ICU admission rates (27.2%) and mechanical ventilation requirements (18.1%). In an extensive retrospective epidemiological study in Italy, the mortality rate was almost 24%, and the hospitalization rate was 64% among patients with lung cancer compared with 14.7% and 56.6% in patients with other tumors, demonstrating the increased morbidity in this subset of patients [30, 31].

The CFR in our cohort was 28.1%. Importantly, a third of included patients were current smokers, and half had received radiotherapy previously, both of which are determinants of COVID-19 severity [32, 33]. In addition, patients with a suspicion of COVID-19 had worse overall survival, which could be potentially related with a worse performance status among this subset of patients. In a recent systematic review and pooled analysis of 52 studies, including 18,650 patients with cancer and COVID-19, the CFR was 25.6% [34]. Another study, conducted among patients with lung cancer, found a need for hospitalization of 60%, and a CFR of 25% [10]. Importantly, a significant proportion of our patients had long-term effects after infection, which highlights the relevance of rehabilitation and post–COVID-19 pulmonary functional therapy [35]. Another important aspect of our study is the impact of the pandemic and of treatment delays on the patients' mental health. Depression, stress, and anxiety, although not related directly with treatment delays, were identified in a significant proportion of patients, particularly those with advanced disease.

This study has limitations. We were unable to register outpatient visits or hospitalizations at other health care facilities, so it is likely that the incidence of COVID-19, as well as the CFR, may be underestimated. Also, we could not evaluate delays from starting symptoms to first medical contact or diagnosis, which may provide valuable information. Owing to the low number of patients undergoing surgical procedures and/or radiotherapy, it is difficult to evaluate the impact of delays or treatment modifications of these therapeutic strategies. Furthermore, we did not explore the efficacy of COVID-19 therapies in our patient population because of the heterogeneity and the small number of patients.

Our study also has several strengths. To our knowledge, this represents the first and largest cohort of patients with thoracic malignancies treated in a developing country in Latin America during the COVID-19 pandemic. As such, it highlights some of the most pressing issues facing the health care systems of developing nations, including a generalized lack of access to health care and a low availability of innovative treatments such as immunotherapy. Our results show that physicians and patients took several measures to decrease the risk of contagion, causing treatment delays in a significant proportion of patients. Although it is important to avoid treatment modifications that may negatively impact survival outcomes, it is also important to highlight that in many cases treatment delays or interruptions might have been acceptable, particularly in patients with poor performance status. A potential solution to unwanted delays is the creation of predictive models to guide oncologists in the approach, diagnosis, and treatment of patients during times of limited access to care. Another important issue highlighted by our results is that access to clinical trials may be a way to avoid treatment delays in developing countries, since this ensures the availability of treatments and resources for patients. Finally, our results emphasize the relevance of integrating mental health evaluations into the care of patients with thoracic malignancies during the pandemic in order to identify emotional disorders that may contribute to even higher rates of social isolation.

Conclusion

Patients with thoracic cancer represent a particularly vulnerable population to COVID-19, with increased morbidity and mortality rates. In developing countries like Mexico, treatment modifications were very common during the pandemic, and patients who underwent delays or interruptions had worse cancer-related outcomes. Furthermore, patients with thoracic cancers and a suspicion of COVID-19 had a high CFR, which highlights the importance of improving the care of this vulnerable subset of patients.

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Disclosures

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