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Global Health and Cancer

Impact of COVID-19 Infection on Patients with Cancer: Experience in a Latin American Country: The ACHOCC-19 Study

Aylen Vanessa Ospina,[a] Ricardo Bruges,[b] William Mantilla,[c] Iván Triana,[a] Pedro Ramos,[d] Sandra Aruachan,[e] Alicia Quiroga,[f] Isabel Munevar,[g] Juan Ortiz,[h] Néstor Llinás,[i] Paola Pinilla,[j] Henry Vargas,[k] Henry Idrobo,[l] Andrea Russi,[j] Ray Manneh Kopp,[m] Giovanna Rivas,[n] Héctor González,[o] Daniel Santa,[p] Jesús Insuasty,[q] Laura Bernal,[d] Jorge Otero,[a] Carlos Vargas,[r] Javier Pacheco,[s] Carmen Alcalá,[t] Paola Jiménez,[u] Milton Lombana,[n] Fernando Contreras,[v] Javier Segovia,[a] Luis Pino,[a] José Lobatón,[w] Manuel González,[w] Javier Cuello,[i] Juliana Bogoya,[x] Angela Barrero,[x] Gilberto de Lima Lopes Jr[y]

[a]ICCAL Instituto de Cancer Carlos Ardila Lulle Hospital Universitario Fundación Santa Fe de Bogotá, Universidad de los Andes, Asociación Colombiana de Hematología y Oncología ACHO, Bogotá, Colombia; [b]Instituto Nacional de Cancerología. Pontificia Universidad Javeriana, Universidad El Bosque, Asociación Colombiana de Hematología y Oncología, Bogotá, Colombia; [c]Fundación Cardioinfantil, Asociación Colombiana de Hematología y Oncología, Bogotá, Colombia; [d]Clínica Universitaria Colombia, Bogotá, Colombia; [e]Clínica IMAT Oncomedica, Monteria, Colombia; [f]Hospital Pablo Tobón Uribe, Medellín, Colombia; [g]Hospital Militar Central, Bogotá, Colombia; [h]Hospital Universitario del Valle, Cali, Colombia; [i]Clínica Vida, Medellín, Colombia; [j]Hospital Universitario San Ignacio, Centro Javeriano de Oncología, Bogotá, Colombia; [k]Clínica Universitaria Colombia, Bogotá, Colombia; [l]Universidad del Valle, Christus Sinergia, Cali, Colombia; [m]Sociedad de Oncología y Hematología del Cesar, Valledupar, Colombia; [n]Clínica de Occidente, Cali, Colombia; [o]Centro de Cancerología de Colombia, CECANCOL, Ibagué, Colombia; [p]Clínica Medellín, Medellín, Colombia; [q]Hospital Universitario de Santander, Universidad Industrial de Santander, Bucaramanga, Colombia; [r]Clínica del Country, Bogotá, Colombia; [s]Fundación Universitaria de Ciencias de la Salud-Hospital San José, Bogotá, Colombia; [t]Clínica de la Costa, Barranquilla, Colombia; [u]Hematooncologos Asociados, Bogotá, Colombia; [v]Instituto Nacional de Cancerología, Universidad El Bosque, Bogotá, Colombia; [w]Clínica IMAT Oncomedica, Monteria, Colombia; [x]Instituto Nacional de Cancerología, Bogotá, Colombia; [y]Sylvester Comprehensive Cancer Center, University of Miami Health System, Miami, USA

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

Key Words. COVID-19 • Cancer • Survival • Mortality • Latin American country • Colombia

Abstract

Introduction. The ACHOCC-19 study was performed to characterize COVID-19 infection in a Colombian oncological population.

Methodology. Analytical cohort study of patients with cancer and COVID-19 infection in Colombia. From April 1 to October 31, 2020. Demographic and clinical variables related to cancer and COVID-19 infection were collected. The primary outcome was 30-day mortality from all causes. The association between the outcome and the prognostic variables was analyzed using logistic regression models and survival analysis with Cox regression.

Results. The study included 742 patients; 72% were >51 years. The most prevalent neoplasms were breast (132, 17.77%), colorectal (92, 12.34%), and prostate (81, 10.9%). Two hundred twenty (29.6%) patients were asymptomatic and 96 (26.3%) died. In the bivariate descriptive analysis, higher mortality occurred in patients who were >70 years, patients with lung cancer, ≥2 comorbidities, former smokers, receiving antibiotics, corticosteroids, and anticoagulants, residents of rural areas, low socioeconomic status, and increased acute-phase reactants. In the logistic regression analysis, higher mortality was associated with Eastern Cooperative Oncology Group performance status (ECOG PS) 3 (odds ratio [OR] 28.67; 95% confidence interval [CI], 8.2–99.6); ECOG PS 4 (OR 20.89; 95% CI, 3.36–129.7); two complications from COVID-19 (OR 5.3; 95% CI, 1.50–18.1); and cancer in progression (OR 2.08; 95% CI, 1.01–4.27). In the Cox regression analysis, the statistically significant hazard ratios (HR) were metastatic disease (HR 1.58; 95% CI, 1.16–2.16), cancer in progression (HR 1.08; 95% CI, 1.24–2.61) cancer in partial response (HR 0.31; 95% CI, 0.11–0.88), use of steroids (HR 1.44; 95% CI, 1.01–2.06), and use of antibiotics (HR 2.11; 95% CI, 1.47–2.95).

Conclusion. In our study, patients with cancer have higher mortality due to COVID-19 infection if they have active cancer, metastatic or progressive cancer, ECOG PS >2, and low socioeconomic status. ***The Oncologist*** 2021;26:e1761–e1773

Correspondence: Aylen Vanessa Ospina, M.D., Ius Constitutionale Commune en América Latina Hospital Universitario Fundación Santa Fe de Bogotá, Universidad de los Andes, Asociación Colombiana de Hematología y Oncología ACHO, Carrera 7a N.123-25 Piso 3, Bogotá, Colombia. Telephone: 57-3174270640; e-mail: avospina@hotmail.com Received February 2, 2021; accepted for publication June 1, 2021; published Online First on July 1, 2021. http://dx.doi.org/10.1002/onco.13861

Implications for Practice: This study's findings raise the need to carefully evaluate patients with metastatic cancer, in progression, and with impaired Eastern Cooperative Oncology Group status to define the relevance of cancer treatment during the pandemic, consider the risk/benefit of the interventions, and establish clear and complete communication with the patients and their families about the risk of complications. There is also the importance of offering additional support to patients with low income and residence in rural areas so that they can have more support during cancer treatment.

Introduction

Since the first trimester of 2020, the world population has been facing the greatest health crisis in recent years because of the COVID-19 pandemic. This situation has generated a great public health challenge and has forced the health system to make rapid adaptations to the hospital infrastructure.

The first published reports of patients infected by COVID-19 showed that the risk of complications increased with age [1, 2]. Furthermore, predisposing factors for developing respiratory failure included smoking, diabetes, hypertension, and cancer.

The initial cohort of patients with cancer from China, described by Liang et al., included 18 patients, which limited the possibility of making global conclusions; however, it showed that patients with cancer had a higher risk of serious events including death (39% vs. 8%; $p = .0003$), mainly those who received oncological treatment during the month before the infection (75% vs. 43%) [3].

Additional studies showed an increased risk of complications in men, patients with lung cancer, and patients with advanced-stage neoplasms [4, 5].

In June 2020, the results of the TERAVOLT and CCC19 registries identified the following factors associated with mortality in patients with cancer: age, male sex, smoking, number of comorbidities, functional status, and presence of active cancer [6, 7].

The Gustave Roussy Hospital study identified that age older than 70 years, smoking, metastatic cancer, cytotoxic chemotherapy, and an Eastern Cooperative Oncology Group (ECOG) performance status ≥2 are factors that increase the risk of death and the importance of the ECOG scale as an independent predictor of death [8].

In Colombia, the first case diagnosed with COVID-19 was confirmed on March 6, 2020, and the number of infected increased exponentially as had been described in the rest of the world [9]. Based on this, the ACHOCC-19 study was proposed to characterize the behavior of COVID-19 infection in our population with cancer, given the absence of conclusive evidence at that time at the global, regional, and local levels.

Materials and Methods

Study Design

A cohort analytical ambispective study was carried out, with data collected from patients with cancer and COVID-19 infection from the National Cancer and COVID-19 registry of Colombia, ACHOCC-19. It was conducted from April 1 to October 31, 2020, to collect and analyze the clinical characteristics and outcomes of COVID-19 infection in patients with cancer. The first patient was registered on April 8, 2020.

The ACHOCC-19 handled anonymized data. The study included adults (more than 18 years of age) with a histologically confirmed diagnosis of cancer (solid tumors), who had been treated and were free of cancer in follow-up and have suspected or confirmed infection by COVID-19 (by polymerase chain reaction [PCR]) immunoglobulin G [IgG], or immunoglobulin M [IgM] type test or by clinical or suspected case by radiological criteria or who received systemic oncological or surgical treatment with curative intent between April 2020 and October 2020 and had confirmation of COVID-19 (by PCR, IgG, or IgM type test, or are considered a suspected case by radiological criteria.

Twenty-two institutions from the main cities of the country participated (Annex 1). The data recording was carried out by 38 oncologists with experience in the health care and research areas in two moments: the first corresponded to the verification of the inclusion criteria and the second to the recording of the outcomes, this way completing a follow-up period of 30 days for all patients.

Ethical Aspects

This study was approved by all the ethics committees of the participating institutions.

Procedures

The data were collected in a digital form that included 80 variables, classified as sociodemographic, related to COVID-19, related to cancer, and follow-up variables. The following variables were included as critical, and possibly associated with complications from COVID-19 infection: age, sex, type of residence, active smoking, obesity, number of comorbidities, surgery for cancer management within the last month, cancer status, performance status according to ECOG score, type of treatment for cancer and COVID-19. The type of cancer treatment was subclassified according to the use or not of cytotoxic chemotherapy and the dates of administration of the cancer treatment in relation to the date of diagnosis of the COVID-19 infection.

Outcomes

The primary outcome of this study is all-cause mortality within 30 days of COVID-19 diagnosis. Secondary outcomes included the requirement for noninvasive mechanical ventilation and the requirement for invasive mechanical ventilation.

Statistical Analysis

The sample size was calculated through two alternatives, the first with a confidence of 90% and an error of 5%, obtaining a sample of 286 patients, and the second using the information from GLOBOCAN 2018 to estimate the population with cancer in Colombia and taking the incidence information of COVID-19 infection in patients with cancer of 1% reported by Liang et al., which provided a sample size of 381 patients [3, 10]. Because some of the survey questions were optional, we anticipated a nonzero level of absence for some variables. We used mode imputation for categorical variables with an absence rate of 10% or less; variables with a missing rate of more than 10% were not included in the multivariate analysis. A standardized format was made for reporting dates related to COVID-19 diagnosis, COVID-19 death, neoplasia diagnosis, and date of application of the last dose of cancer treatment, which allowed an interaction of date differences for the creation of end-time variables, which were stipulated as measured in days.

In the first analysis using descriptive statistics, all sociodemographic variables were included, as were clinical characteristics before and during COVID-19 infection. Additionally, the χ^2 distribution was used to study correlations between different variables and the primary outcome, to determine whether there were independent relationships. Subsequently, the correlations between the study variables and the primary outcome were examined using a logistic regression model to perform an adjusted multivariate data analysis. In the multivariate model, age was defined in an interval variable, and an adjustment for multiple comparisons was made according to the covariate. The demographic risk variables were adjusted for each other and were the adjustment for cancer and COVID-19 treatment covariates.

We evaluated the goodness of model using the Hosmer and Lemeshow statistic. The prediction capacity of the model was evaluated through the Omnibus test, and, finally, a summary of the model was made, in which the -2 log-likelihood was used to determine the adjustment of the model to the data. The R squared of Cox and Snell, and the R squared of Nagelkerke were used to calculate the proportion of variance of the dependent variable (30-day mortality) explained by the predictor variables (independent). The final variables for which the model was adjusted had a classification table by blocks to calculate the global percentage correctly predicted and the correctly predicted percentage for deaths and nondeaths.

Survival Analysis

Survival analysis was performed using a Cox regression model; survival times were calculated using the date of death and the date of symptom onset, reported in days. The model was adjusted for the variables age, sex, area of residence, cancer status, obesity, smoking, number of comorbidities, cytotoxic and noncytotoxic treatment or no cancer treatment, cancer treatment during the last year, metastatic disease, number of complications due to COVID-19, and treatment for COVID-19.

Descriptive analysis was performed in Stata/SE edition 16.0 (Stat Corp., College Station, TX), and all correlation and multivariate analyzes were performed in two parallel programs: R version 4.0.3 (R Foundation, Vienna) and IBM SPSS Statistics 25 (IBM, Armonk, NY).

In a subsequent subanalysis, we developed a neural network, in which we identified the covariates that had the greatest sample weight for the predictive models, measuring them against the primary outcome of all-cause mortality within 30 days after the COVID-19 diagnosis.

Data optimization was performed weekly in the registry to avoid loss of follow-up, alteration, or failures in data collection. Data with p values less than .05 were considered statistically significant, both in the logistic regression model and in the survival analysis.

Role of the Funding Source

The sponsors of the study had no role in study design, data collection, analysis, interpretation of data, or writing of the article.

Results

Of the 783 patients collected in the ACHOCC-19, 41 patients were excluded because of duplication of information. All records were started during the COVID-19 pandemic and 100% had a 30-day follow-up report (interquartile range, 0–30 days).

Regarding the demographic, clinical, tumor, and socioeconomic characteristics of the population (Table 1), 534 (72%) patients were older than 51 years and 200 (27%) older than 70 years. Four hundred three (54%) were women. As risk factors for complications from COVID-19, 18 (2.42%) had active smoking, 87 (11.7%) had more than two comorbidities, 37 (14%) had an ECOG performance status >2, and 295 (38.7%) had metastatic neoplasia.

The area of residence was urban for 677 (91%) patients and 354 (47.7%) belonged to the low-income socioeconomic level. The most prevalent neoplasms were breast cancer ($n = 132$, 17.77%), colorectal cancer ($n = 92$, 12.34%), and prostate cancer ($n = 81$, 10.9%).

Regarding cancer treatment, 352 (63.9%) patients were in active treatment, of whom 213 (28.67%) received systemic treatment with palliative intention. Eighty-one patients (10.98%) had undergone surgical treatment in the month prior to COVID-19 infection.

Of those who were receiving active cancer treatment, 205 (27.6%) had a partial response or stable disease and 147 (36.38%) had progressing cancer. A total of 454 (61.18%) patients had received cancer therapy within the previous 12 months. According to the type of treatment, 209 (28.18%) were receiving cytotoxic therapy and 144 (19.5%) were under noncytotoxic treatment.

Regarding the clinical presentation of COVID-19 infection, 220 (29.6%) patients were asymptomatic throughout the course of the disease, 229 (36.58%) had mild disease, 242 (38.66%) had moderate disease with hospitalization, and 126 (20.6%) had severe disease requiring mechanical ventilation. At diagnosis, 720 (97%) had positive PCR for COVID-19 and 201 (51.4%) patients were followed during

Table 1. Description of the population characteristics

Characteristics	$n = 742$, *n* (%)
Age, yr	
18–30	38 (5.2)
31–40	56 (7.55)
41–50	93 (12.53)
51–60	188 (23.34)
61–70	165 (22.24)
>70	202 (27.22)
Sex	
Male	339 (45.69)
Female	403 (54.31)
City ($n = 10$)	
Bogotá	473 (63.8)
Medellín	106 (14.27)
Montería	86 (11.71)
Cali	45 (6.06)
Valledupar	10 (1.35)
Ibagué	8 (1.08)
Bucaramanga	7 (0.94)
Popayan	3 (0.40)
Guajira	2 (0.26)
Barranquilla	1 (0.13)
Smoking status	
Yes	18 (2.42)
No	723 (97.58)
BMI	
<18.5	46 (6.49)
18.5–24.9	380 (53.74)
24.9–29.9	205 (28.91)
>30	76 (10.72)
>40	1 (0.14)
Number of comorbidities	
0	340 (45.8)
1	201 (27)
2	115 (12.4)
>2	87 (11.7)
Types of malignancies	
Breast	132 (17.77)
Colorectal	92 (12.34)
Prostate	81 (10.90)
Head and neck	39 (5.25)
Gastric	38 (5.11)
Lung	37 (4.98)
Cervix	36 (4.85)
Sarcoma	33 (4.44)
Renal	25 (3.36)
Ovary	22 (2.96)
Melanoma	21 (2.86)
CNS	20 (2.69)
Hepatocarcinoma	20 (2.69)
Thyroid	19 (2.67)
Bladder	18 (2.42)
Uterus	16 (2.15)
Germ	15 (2.02)
Pancreas	11 (1.48)
Nonmelanoma skin	11 (1.48)
Neuroendocrine	8 (1.08)
Unknown primary	8 (1.08)
Anal	7 (0.94)
Vesicle	6 (0.81)
Esophagus	5 (0.67)
Osteosarcoma	4 (0.54)
Thymus	4 (0.54)
GIST	3 (0.40)
Cholangiocarcinoma	3 (0.40)
Penis	3 (0.40)
(Appendix, small intestine, mesothelioma, adrenal gland, giant cells)	1 (0.12)
Clinical presentation at diagnosis	
Mild	229 (36.58)
Moderate without hospitalization	28 (4.47)
Moderate with hospitalization	242 (38.66)
Severe with mechanical ventilation	127 (20.26)
Asymptomatic all the course of the disease	220 (29.6)
Cancer status	
Present, stable, responding to treatment	205 (27.6)
Progressive disease	147 (36.38)
Remission or no evidence of disease	107 (20.33)
Unknown	263 (36.38)
Missing	19 (2.56)
ECOG performance status	
0	159 (22.73)
1	282 (40.06)
2	162 (23.01)
3	78 (11.08)
4	22 (3.13)
Missing	37 (4.98)
Treatment status	
Recent diagnosis—treatment has not started	133 (17.9)
Neoadjuvant/adjuvant	141 (18.98)
On follow-up without treatment	181 (25.50)
Supportive treatment	65 (8.75)
Systemic palliative therapy[a]	213 (28.67)
Missing	9 (1.21)
Type of anticancer therapy	
Radiation therapy with curative intent	42 (5.65)
Radiation therapy with palliative intention	32 (4.315)
Cytotoxic systemic therapy	208 (28.16)
Chemotherapy	167 (22.48)
Chemotherapy immunotherapy	13 (1.75)
Monoclonal antibody chemotherapy	29 (3.90)
Noncytotoxic therapy	144 (19.5)
Duplex immunotherapy	1 (0.13)
Immunotherapy	18 (2.24)
ITK	17 (2.29)
Monoclonal antibody	15 (2.02)
Endocrine therapy	82 (11.04)
Endocrine therapy cyclin inhibitor	8 (1.08)
High-dose steroids	4 (0.54)
Nontreatment	360 (49.2)

(continued)

Table 1. (continued)

Characteristics	$n = 742$, *n* (%)
None in the 1 year before COVID-19	266 (35.8)
Recent surgery (1 month)	
Yes	81 (10.98)
No	657 (89.02)
Missing	4 (0.4)
Metastatic disease	
Yes	295 (39.7)
No	436 (58.7)
Missing	11 (0.14)
Type of residence	
Urban	677 (91.2)
Rural	65 (8.2)
Socioeconomic status	
1–2	354 (47.77)
3–4	179 (24.1)
5–6	28 (3.78)
Missing	180 (24.29)
Treatment for COVID-19	
Hydroxychloroquine alone	15 (2.0)
Antibiotic therapy	272 (37.2)
Steroids	268 (36.6)
Ivermectin	21 (2.9)
Neither	335 (45.8)
Tocilizumab	1 (0.1)
Ritonavir/Lopinavir	7 (1)
Remdesivir	2 (0.3)
Anticoagulation	163 (22.3)
Positive COVID test	
Yes	720 (97.04)
No	22 (2.96)
Antibodies IgG elevation	
Yes	12 (1.62)
No	12 (1.62)
Missing	719 (98.3)
Negative COVID-19 test	
14 days	144 (19.4)
28 days	30 (4)
>28 days	27 (3.6)
Missing	355 (47.8)
Improving symptoms	
14 days	257(34.6)
28 days	72 (9.7)
>28 days	46 (6.1)
Missing	365 (49.1)
Complication due to COVID-19 (excluding primary and secondary outcomes)	
Hemophagocytic syndrome	2 (0.27)
Concomitant bacterial infection	101 (13.59)
Cardiogenic shock	8 (1.08)
Hypovolemic shock	1 (0.13)
Distributive shock	22 (2.96)
SARS	58 (7.81)

[a]Includes cytotoxic and noncytotoxic treatment.
Abbreviations: BMI, body mass index; CNS, central nervous system; ECOG, Eastern Cooperative Oncology Group; GIST, gastrointestinal stromal tumor; IgG, immunoglobulin G; ITK, inhibitor tirosine kinasa; SARS, severe acute respiratory syndrome.

the course of the disease with this test. As treatment for COVID-19 infection, antibiotics were administered to 272 (37.2%) patients, steroids to 268 (36.6%) patients, and anticoagulation to 163 (22.3%) patients. Finally, 101 (13.59%) patients presented bacterial concomitant infection. Table 1 summarizes the sociodemographic and clinical variables, as well as the patients' outcomes.

On November 30, 2020, 196 (26.3%) patients had died within 30 days (Table 2). In the bivariate descriptive analysis, higher mortality was observed in patients with more than 70 years of age, residence in a rural area, low socioeconomic status, lung cancer, presence of more than two comorbidities, history of smoking, high acute-phase reactants at the time of diagnosis of infection, and treatment for COVID-19 infection with antibiotics, corticosteroids, or anticoagulants.

In a descriptive analysis between the use of antibiotics, corticosteroids, and anticoagulation compared with the clinical presentation of the disease at diagnosis, it was evidenced these three drugs were administered to patients with the worst prognosis. One hundred two (37.78%) patients with severe disease with mechanical ventilation and 129 (47.78%) patients with moderate illness with hospitalization received antibiotics, whereas anticoagulation was administered to 58 (35.58%) patients with severe disease with mechanical ventilation and to 78 (47.85%) patients with moderate disease with hospitalization. Ninety-two (34.33%) patients with severe disease with mechanical ventilation and 145 (54.10%) patients with moderate disease with hospitalization received corticosteroids. The use of these three types of drugs in patients with mild disease or without hospitalization was significatively lower (<15%).

Some possible prognostic variables had a failure rate of more than 10% and, therefore, were not included in the multivariate model. The associations between prognostic variables and 30-day all-cause mortality are shown in Table 3. The goodness of adjustment reported in our models had a statistical value of 10.3 with a significance of 0.24, which indicates that the model has a good adjustment. The accuracy of the model to classify patients who died in 30 days was 92.7%.

Several clinically relevant prognostic variables associated with an increase in 30-day all-cause mortality were identified after partial adjustment in our multivariate model: cancer status (disease progressing vs. stable disease, in partial response, remission or without evidence of disease), ECOG performance status (2 vs. 0; 3 or 4 vs. 0), and the presence of two complications from COVID-19 infection. Variables that behaved as protective factors were also identified, including residence in an urban area and absence of complications from COVID-19.

Age, nutritional status, smoking, sex, type and time of administration of cancer treatment, and recent surgery did not reach statistically significant values to associate them with 30-day mortality in the multivariate logistic regression analysis.

In a descriptive analysis of the variables "Hospital admission" and "Use of cancer treatment," 369 (58.9%) patients required hospital admission, of whom 44% were actively receiving cancer therapy.

Table 2. Primary and secondary outcomes versus possible prognostic variables

Variables	Outcomes, *n* (%)			χ^2
	Died	Required mechanical ventilation	Noninvasive mechanical ventilation	
All	196 (26.3)	106 (14.27)	23 (3.1)	
Age, yr				0.000
18–30, $n = 38$	5 (13.16)	1 (2.63)	0	
31–40, $n = 56$	10 (17.86)	9 (16.07)	1 (1.79)	
41–50, $n = 93$	13 (13.98)	7 (7.53)	1 (1.08)	
51–60, $n = 188$	45 (23.94)	22 (11.70)	5 (2.66)	
61–70, $n = 165$	46 (27.88)	32 (19.39)	5 (3.03)	
>70, $n = 202$	76 (37.62)	34 (16.83)	11 (5.45)	
Sex				0.000
Male, $n = 339$	113 (33.33)	57 (16.81)	18 (5.31)	
Female, $n = 403$	83 (20.6)	49 (12.16)	5 (1.24)	
Type of malignancies				0.02
Breast, $n = 132$	25 (18.94)	15 (11.36)	1 (0.76)	
Colorectal, $n = 92$	28 (30.4)	19 (2.5)	0	
Prostate, $n = 81$	30 (37.4)	17 (20.9)	6 (7.41)	
Head and neck, $n = 39$	8 (20.5)	9 (23)	1 (2.56)	
Gastric, $n = 38$	13 (34.2)	5 (13.1)	1 (2.63)	
Lung, $n = 37$	20 (54)	6 (16.2)	1 (2.7)	
Cervix, $n = 36$	6 (16.7)	4 (11.11)	1 (2.78)	
Smoking status				0.00
Yes	10 (55.56)	2 (11.11)	1 (5.56)	
No	186 (25.66)	104 (14.34)	22 (3.03)	
BMI				0.24
<18.5, $n = 46$	16 (34.78)	3 (6.52)	1 (2.17)	
18.5–24.9, $n = 381$	101 (26.61)	46 (12.07)	12 (3.15)	
24.9–29.9, $n = 205$	48 (23.41)	38 (18.54)	7 (3.41)	
>30, $n = 76$	19 (25)	14 (18.42)	3 (3.95)	
>40, $n = 1$	1	0	0	
Number of comorbidities				0.001
0, $n = 340$	66 (19.41)	36 (10.59)	9 (2.65)	
1, $n = 201$	63 (31.34)	24 (11.94)	4 (1.99)	
2, $n = 115$	37 (32.17)	23 (20)	9 (7.83)	
>2, $n = 87$	30 (34.48)	23 (26.44)	1 (1.15)	
Metastatic disease				0.00
Yes, $n = 295$	101 (34.24)	40 (13.56)	14 (4.75)	
No, $n = 437$	92 (21)	63 (14.42)	9 (2.06)	
Cancer status				0.00
Present, stable, $n = 166$	31 (18.67)	27 (16.27)	1 (0.06)	
Progressive disease, $n = 147$	66 (44.9)	17 (11.56)	5 (3.4)	
Remission or no evidence of disease, $n = 107$	15 (14.02)	14 (13.08)	2 (1.87)	
Responding to treatment, $n = 40$	4 (10)	6 (15)	1 (2.5)	
ECOG performance status				0.00
0, $n = 160$	8 (5)	12 (7.5)	0	
1, $n = 282$	47 (16.67)	48 (17)	5 (1.77)	
2, $n = 162$	63 (38.89)	24 (14.81)	6 (3.7)	
3, $n = 78$	50 (64.1)	12 (15.38)	5 (6.41)	
4, $n = 22$	19 (86.36)	4 (18.18)	3 (13.64)	

(continued)

Table 2. (continued)

Variables	Outcomes, *n* (%)			χ^2
	Died	Required mechanical ventilation	Noninvasive mechanical ventilation	
Treatment state				0.00
Recent diagnosis—treatment has not started, $n = 133$	37 (27.82)	17 (12.78)	7 (5.26)	
Neoadjuvant/adjuvant, $n = 141$	23 (16.31)	18 (12.77)	2 (1.42)	
On follow-up without treatment, $n = 182$	36 (19.78)	30 (16.48)	7 (3.85)	
Supportive treatment, $n = 65$	34 (52.31)	6 (9.23)	3 (4.62)	
Systemic palliative therapy, $n = 212$	64 (30)	33 (15.49)	4 (1.88)	
Type of anticancer therapy				0.1
Radiation therapy with curative intent, $n = 42$	2 (4.7)	3 (7.14)	0	
Radiation therapy with palliative intention, $n = 32$	8 (25)	1 (3.1)	0	
Cytotoxic systemic therapy, $n = 208$	52 (25)	27 (12.9)	19 (3.5)	0.5
Cytotoxic chemotherapy, $n = 208$	42 (20)	19 (9.13)	4 (1.92)	
Chemotherapy + immunotherapy, $n = 208$	3 (1.4)	2 (1.28)	0	
Monoclonal antibody chemotherapy, $n = 208$	7 (3.34)	5 (2.4)	0	
Noncytotoxic therapy, $n = 144$	1 (0.06)	0	0	
Duplex immunotherapy, $n = 144$	2 (1.38)	2 (1.28)	0	
Immunotherapy, $n = 144$	6 (4.16)	3 (2)	1 (0.06)	
ITK, $n = 144$	2 (1.28)	0	0	
Monoclonal antibody, $n = 144$	23 (15.97)	15 (10.4)	3 (2)	
Endocrine therapy, $n = 144$	2 (1.28)	2 (1.28)	0	
Endocrine therapy cyclin inhibitor, $n = 144$	3 (2)	2 (1.28)	0	
High-dose steroids, $n = 144$	95 (26.3)	52 (14.4)	15 (4.17)	
Nontreatment, $n = 360$				
Surgery within the last month				0.08
Yes, $n = 657$	181 (27.5)	86 (13)	22 (3.3)	
No, $n = 81$	15 (18.5)	20 (24)	1 (1.3)	
Treatment for COVID-19				
Hydroxychloroquine alone, $n = 15$	4 (26.37)	6 (40)	1 (6.6)	0.9
Antibiotic therapy, $n = 272$	126 (46.3)	81 (29.78)	20 (7.35)	0.00
Steroids, $n = 269$	125 (46.47)	78 (29)	15 (5.58)	0.00
Ivermectin, $n = 21$	6 (28.57)	6 (28.57)	1 (4.76)	0.8
Neither, $n = 345$	37 (10.7)	8 (2.32)	0	0.00
Tocilizumab, $n = 1$	0	1	0	
Ritonavir/Lopinavir, $n = 7$	4 (57.14)	2 (28.57)	1 (14.2)	0.06
Remdesivir, $n = 2$	0	2 (100)	0	
Anticoagulation, $n = 164$	75 (45.7)	50 (30.4)	14 (8.5)	0.00
Type of residence				0.02
Urban, $n = 59$	170 (25.11)	95 (14)	18 (2.66)	
Rural, $n = 170$	23 (38.9)	10 (16,95)	4 (6.78)	
Socioeconomic status				0.1
1–2, $n = 354$	102 (28.8)	44 (12.43)	6 (1.69)	
3–4, $n = 179$	37 (20.67)	25 (13.97)	4 (2.23)	
5–6, $n = 28$	6 (21.43)	4 (14.29)	1 (3.57)	
Missing, $n = 182$				
LDH				0.00
Normal, $n = 180$	37 (20.5)	26 (14.4)	3 (1.67)	
Increased 1×, $n = 157$	55 (35)	30 (19.11)	9 /5.73)	
Increased 2×, $n = 108$	64 (59.26)	31 (28.7)	9 (8.33)	
Unknown, $n = 295$	39 (13.2)	19 (6.4)	1 (0.34)	

(continued)

Table 2. (continued)

Variables	Outcomes, *n* (%)			χ^2
	Died	Required mechanical ventilation	Noninvasive mechanical ventilation	
D Dimer				0.00
Normal, $n = 44$	11 (25)	9 (20.4)	3 (6.82)	
Increased, $n = 266$	95 (35.7)	66 (24.8)	18 (6.77)	
Unknown, $n = 428$	87 (20.33)	30 (7)	2 (0.47)	
Procalcitonin				0.03
Normal, $n = 32$	3 (9.38)	5 (15.3)	2 (6.25)	
Increased, $n = 23$	9 (39.13)	10 (43.8)	1 (4.35)	
Unknown, $n = 683$	183 (26.79)	90 (13.18)	20 (2.93)	
PCR				0.00
Normal, $n = 41$	4 (9.76)	2 (4.88)	2 (4.88)	
Increased, $n = 399$	150 (37.59)	87 (21.8)	18 (4.5)	
Unknown, $n = 300$	42 (14)	16 (5.33)	3 (1)	
Reticulocyte				0.02
Normal, $n = 77$	31 (40.2)	11 (14.29)	1 (1.3)	
Increased, $n = 9$	1 (11.11)	3 (33.33)	0	
Unknown, $n = 655$	163 (25)	92 (14.5)	22 (3.36)	
Ferritin				0.00
Normal, $n = 44$	7 (15.9)	4 (9.0)	2 (4.55)	
Increased, $n = 166$	72 (38.3)	49 (26)	15 (7.96)	
Unknown, $n = 511$	117 (22.9)	53 (10.37)	6 (1.17)	
Troponin				0.00
Normal, $n = 173$	28 (27.7)	35 (20.2)	10 (5.78)	
Increased, $n = 73$	34 (46.58)	26 (35.6)	8 (10.96)	
Unknown, $n = 497$	114 (22.9)	45 (9)	5 (1)	

Abbreviations: BMI, body mass index; ECOG, Eastern Cooperative Oncology Group; ITK, inhibitor tirosine kinasa; LDH, lactate dehydrogenase; PCR, C reactive protein.

The frequency of mechanical ventilation was higher as the decade of age increased from 50 years, with a slight decrease after 70 years; a high frequency of invasive ventilatory support was found in the group aged 31–40. Adjusted for the gender variable, a higher frequency of invasive ventilation was evidenced in men.

Survival Analysis

The result of the Cox regression as a 30-day survival analysis had the following statistically significant hazard ratios: cancer status, metastatic disease, and use of antibiotics and corticosteroids (Table 4).

The survival plots for the statistically significant variables in the Cox model are found in Figures 1–4. Figure 5 shows the variables adjusted in the logistic regression model with adjusted odds ratios (ORs) and 95% confidence intervals.

In a deep learning analysis using a neural network, it was found that the variables with the highest predictive weight for 30-day mortality from all causes after the diagnosis of COVID-19 were ECOG status 3–4, number of complications due to COVID-19, and cancer in progression. On the other hand, variables such as living in an urban area and cancer in partial response showed little prediction of mortality, congruent with an OR lower than 1. The other variables did not have an important predictive weight in the neural network.

Discussion

Given the absence of epidemiologically significant data on the impact of COVID-19 infection in patients with cancer, the ACHOCC-19 study was generated from the Asociación Colombiana de Hematología y Oncología. The objective of this project was to collect local information on the behavior of the infection to generate recommendations applicable to our population. The participation of 38 researchers was obtained from 21 hospital institutions nationwide in 10 cities.

The information collection was based on prognostic factors associated with mortality in patients with cancer that were reported in the initial series from China [3].

In addition, characteristics such as the area of residence and socioeconomic level were included, considering that in developing countries, these factors influence access to the health system and clinical outcomes.

In Colombia, the first peak of the pandemic occurred between July and August 2020. During the previous months, the health system generated a gradual increase in intensive care unit beds and adaptation of hospitalization areas [11]. During the highest phase of infections, there

Table 3. Multivariable partially adjusted odds ratios

Variable	Odds ratio (95% CI)
Age, yr	
18–30	1 (ref)
31–40	1.04 (0.15–6.93)
41–50	2.00 (0.32–12.40)
51–60	2.32 (0.44–12.09)
61–70	2.21 (0.41–11.74)
>70	3.57 (0.69–18.37)
Sex	
Female	1 (ref)
Male	1.29 (0.74–2.26)
Current smoking	
No	1 (ref)
Yes	1.75 (0.36–8.33)
Obesity	
No	1 (ref)
Yes	1.13 (0.36–3.52)
Number of comorbidities	
0	1 (ref)
1	1.52 (0.77–2.97)
2	0.96 (0.40–2.26)
>2	0.80 (0.30–2.12)
Metastatic disease	
No	1 (ref)
Yes	1.16 (0.65–2.07)
Type of residence	
Rural	1 (ref)
Urban	0.43 (0.18–1.01)
Cancer status	
Unknown	1 (ref)
Present, stable	0.85 (0.36–2.02)
Responding to treatment	0.30 (0.06–1.51)
Progressive disease	2.08 (1.01–4.27)
Remission or no evidence of disease	0.86 (0.31–2.38)
ECOG performance status	
0	1 (ref)
1	2.74 (0.90–8.31)
2	7.84 (2.52–24.3)
3	28.67 (8.25–80.61)
4	20.89 (3.36–90.89)
In cytotoxic treatment	
No	1 (ref)
Yes	0.78 (0.35–1.40)
Treatment in the year before COVID-19	
No	1 (ref)
Yes	0.91 (0.34–2.41)
Active cancer treatment	
Yes	1 (ref)
No	0.51 (0.11–2.45)
Surgery in the previous month	
No	1 (ref)
Yes	0.44 (0.16–1.23)
Treatment for COVID-19	
Other	1 (ref)
Hydroxychloroquine alone	0.41 (0.01–1.24)
Antibiotic therapy	1.29 (0.56–2.53)
Steroids	2.16 (0.97–4.78)
Ivermectin	0.88 (0.16–4.88)
Anticoagulation	1.62 (0.82–3.12)
Neither	1.93 (0.64–5.88)
Number of complications due to COVID-19	
0	1 (ref)
1	1.32 (0.49–3.61)
2	5.3 (1.55–18.17)

Abbreviations: CI, confidence interval; ECOG, Eastern Cooperative Oncology Group.

Table 4. Adjusted hazard ratio

Variable	HR (95% CI)
Cancer status	
Unknown	1 (ref)
Present, stable	0.65 (0.41–1.05)
Responding to treatment	0.31 (0.11–0.88)
Progressive disease	1.80 (1.24–2.61)
Remission or no evidence of disease	0.66 (0.37–1.20)
Metastatic disease	
No	1 (ref)
Yes	1.58 (1.16–2.16)
Treatment for COVID-19	
Antibiotic therapy	2.11 (1.47–2.95)
No use	1 (ref)
Steroids	1.44 (1.01–2.06)
No use	1 (ref)

Cox regression as survival analysis. Hazard ratio adjusted to all-cause mortality in 30 days after COVID-19 diagnosis. Only variables with clinically significant outcome p value < .05 are described.
Abbreviations: CI, confidence interval; HR, hazard ratio.

was no collapse of the health system or a shortage of resources and supplies that impeded patient care.

At the time of our cohort analysis, we did not find any series of patients with cancer and COVID-19 infection published in Latin America. The available results of the CCC19 cohort were reviewed, which shows important similarities to ours [7].

In our study, we detected that patients with cancer are at higher risk of mortality due to COVID-19 infection if they have active cancer, present metastatic or progressive neoplasia, and/or impaired functional status with an ECOG status higher than 2.

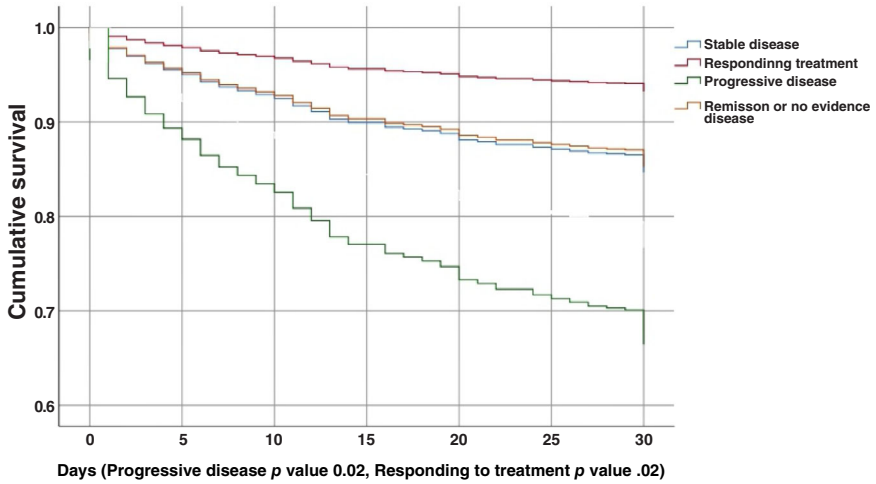

Figure 1. Survival analysis by cancer status.

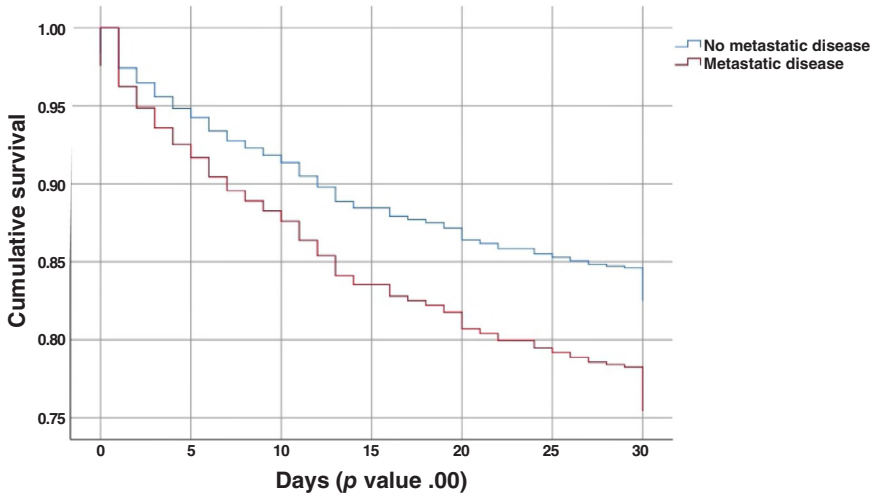

Figure 2. Survival analysis by metastatic disease.

Diagnostic PCR was performed in 97% of those infected, and only half of the patients had a follow-up test because of the emergence of evidence that did not support this requirement [12].

The outcome of acute-phase reactants was available in a small percentage of the population, and although it was associated with worse outcomes, this cannot be adequately interpreted. Our patients had a higher 30-day mortality rate (26%) when compared with the information available from the CCC19 cohort (13%) [7] and from a cohort of similar size from China (1.4%) [13].

These data also differ from those of the New York region, where the Mount Sinai Hospital analysis reported a mortality of 11% [14]. A series of 218 patients from the Montefiore health system showed a similar case fatality rate of 28%, although the authors recognized a selection bias toward more severe cases [15].

We consider that the high mortality in our cohort is related to the higher frequency of patients with progressive metastatic disease (36.38%) who were under palliative systemic cancer treatment (28.67%).

Patients with progressing cancer died at a numerically higher rate; however, the frequency of mechanical ventilation for this group was not proportional, because many of these patients were not candidates for advanced respiratory support because of their oncological condition. On the contrary, patients with stable or responding neoplasia were the ones who received the most mechanical ventilation, which we interpreted as having their underlying oncological disease controlled.

When comparing with the available series, we conclude that the geographical location does not generate differences in the clinical outcomes of COVID-19 infection, because the results of our cohort in Latin America are similar to the North American and European cohorts [6–8, 16].

For our population, it was evidenced that socioeconomic factors such as residing in rural areas and having a low level of economic income are associated with higher mortality, which we relate to difficulties in accessing the health system, presenting advanced neoplasms in progression, and presenting uncontrolled comorbidities, all generating a synergistic effect (syndemic).

The absence of an association of 30-day mortality with recent surgery and administration of systemic cancer treatment during the last year suggests that approaches with

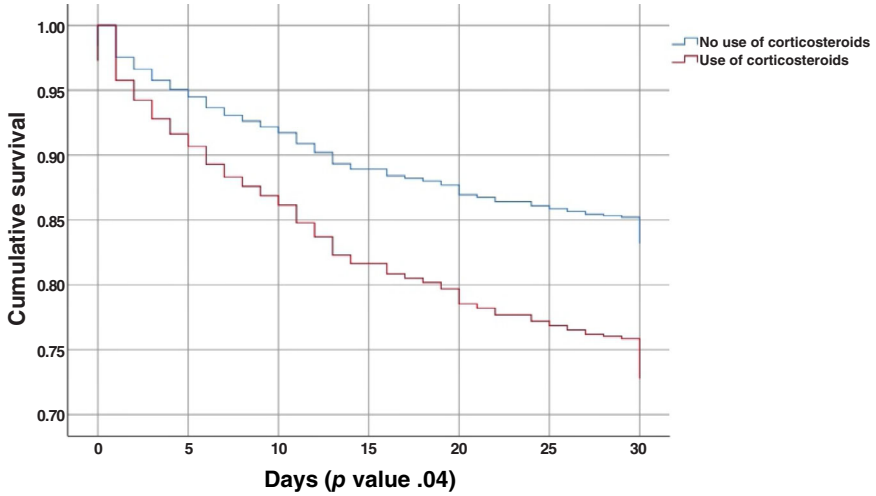

Figure 3. Survival analysis by use of corticosteroids in the COVID-19 treatment.

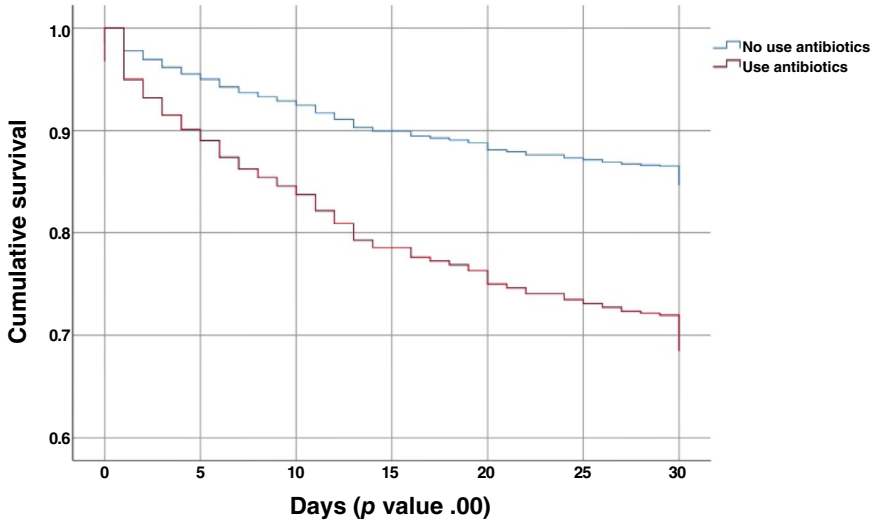

Figure 4. Survival analysis by use of antibiotics in COVID-19 treatment.

curative intent, including surgical resection, and neo/adjuvant and maintenance systemic treatments, do not seem to increase the risk and do not justify stopping treatment for these patients during the pandemic. Similar findings were reported in the CCC19 cohort [7].

In the survival analysis, the administration of corticosteroids, antibiotics, and anticoagulants behaved as a risk factor for mortality; however, in the analysis stratified by severity of the COVID-19 infection, it was evidenced that the patients who received them had the worst prognosis because they had more severe clinical conditions with a higher risk of mortality and the risk cannot be associated only with the administration of the medications by itself. However, it cannot be ruled out that in patients with poor functional status and/or progressing neoplasia with severe COVID 19 disease the use of corticosteroids may behave as a factor that makes it difficult to control another associated infectious process. For this reason, we consider that this variable should be studied in greater depth. On the other hand, it is possible that the group of patients who were asymptomatic or had mild disease who did not receive any of these treatments will be responsible for the best prognosis of the patients without in-hospital treatment for COVID-19 infection.

Most of the patients included were symptomatic (70%); therefore, selection bias cannot be ruled out. However, a significant percentage of asymptomatic patients (29.6%) was included, because screening had started in some institutions in the country. This sample will allow us to perform a subsequent analysis and define the characteristics of patients with cancer who remained asymptomatic and without complications during COVID-19 infection, for which there are no published data.

Conclusion

Our findings raise the need to carefully evaluate patients with metastatic cancer, in progression, and with impaired ECOG status to define the relevance of cancer treatment during the pandemic, consider the risk/benefit of the interventions, and establish clear and complete communication with the patients and their families about the risk of

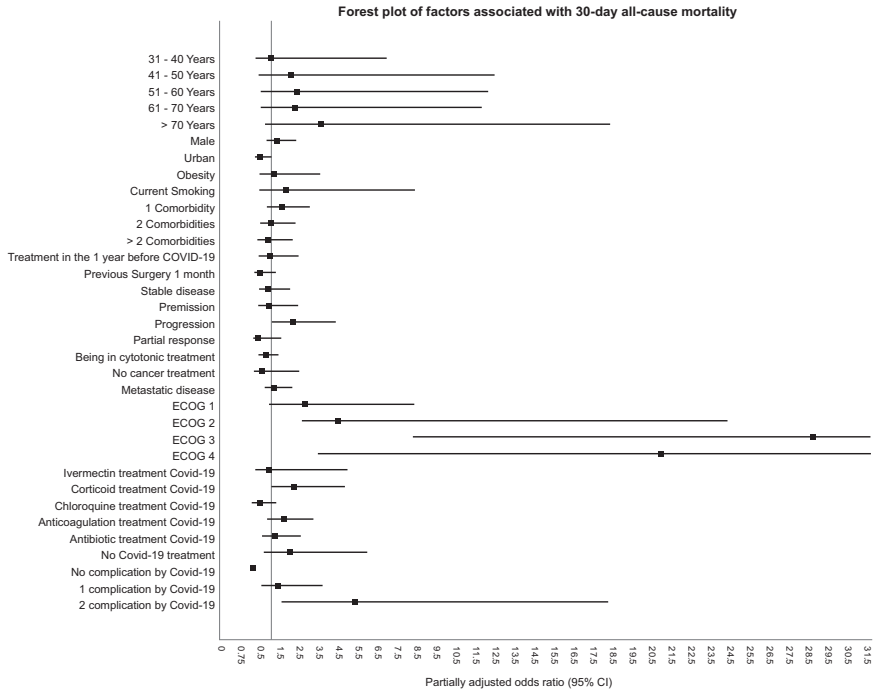

Figure 5. Forest plot of variables adjusted in the multivariate model for 30-day mortality from all causes after infection by COVID-19. Abbreviation: CI, confidence interval; ECOG, Eastern Cooperative Oncology Group.

complications. There is also the importance of offering additional support to patients with low income and residence in rural areas so that they can have more support during cancer treatment.

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Author Contributions

Conception/design: Aylen Vanessa Ospina, Ricardo Bruges, William Mantilla, Iván Triana, Pedro Ramos, Sandra Aruachan, Alicia Quiroga, Isabel Munevar, Juan Ortiz, Néstor Llinás, Paola Pinilla, Henry Vargas, Henry Idrobo, Andrea Russi, Ray Manneh, Giovanna Rivas, Héctor González, Daniel Santa, Jesús Insuasty, Laura Bernal, Jorge Otero, Carlos Vargas, Javier Pacheco, Carmen Alcalá, Paola Jiménez, Milton Lombana, Fernando Contreras, Javier Segovia, Luis Pino, José Lobatón, Manuel González, Javier Cuello, Juliana Bogoya, Angela Barrero, Gilberto de Lima Lopes Jr.

Provision of study material or patients: Aylen Vanessa Ospina, Ricardo Bruges, William Mantilla, Iván Triana, Pedro Ramos, Sandra Aruachan, Alicia Quiroga, Isabel Munevar, Juan Ortiz, Néstor Llinás, Paola Pinilla, Henry Vargas, Henry Idrobo, Andrea Russi, Ray Manneh, Giovanna Rivas, Héctor González, Daniel Santa, Jesús Insuasty, Laura Bernal, Jorge Otero, Carlos Vargas, Javier Pacheco, Carmen Alcalá, Paola Jiménez, Milton Lombana, Fernando Contreras, Javier Segovia, Luis Pino, José Lobatón, Manuel González, Javier Cuello, Juliana Bogoya, Angela Barrero, Gilberto de Lima Lopes Jr.

Collection and/or assembly of data: Aylen Vanessa Ospina, Ricardo Bruges, William Mantilla, Iván Triana, Pedro Ramos, Sandra Aruachan, Alicia Quiroga, Isabel Munevar, Juan Ortiz, Néstor Llinás, Paola Pinilla, Henry Vargas, Henry Idrobo, Andrea Russi, Ray Manneh, Giovanna Rivas, Héctor González, Daniel Santa, Jesús Insuasty, Laura Bernal, Jorge Otero, Carlos Vargas, Javier Pacheco, Carmen Alcalá, Paola Jiménez, Milton Lombana, Fernando Contreras, Javier Segovia, Luis Pino, José Lobatón, Manuel González, Javier Cuello, Juliana Bogoya, Angela Barrero, Gilberto de Lima Lopes Jr.

Data analysis and interpretation: Aylen Vanessa Ospina, Ricardo Bruges, William Mantilla, Iván Triana, Pedro Ramos, Sandra Aruachan, Alicia Quiroga, Isabel Munevar, Juan Ortiz, Néstor Llinás, Paola Pinilla, Henry Vargas, Henry Idrobo, Andrea Russi, Ray Manneh, Giovanna Rivas, Héctor González, Daniel Santa, Jesús Insuasty, Laura Bernal, Jorge Otero, Carlos Vargas, Javier Pacheco, Carmen Alcalá, Paola Jiménez, Milton Lombana, Fernando Contreras, Javier Segovia, Luis Pino, José Lobatón, Manuel González, Javier Cuello, Juliana Bogoya, Angela Barrero, Gilberto de Lima Lopes Jr.

Manuscript writing: Aylen Vanessa Ospina, Ricardo Bruges, William Mantilla, Iván Triana, Pedro Ramos, Sandra Aruachan, Alicia Quiroga, Isabel Munevar, Juan Ortiz, Néstor Llinás, Paola Pinilla, Henry Vargas, Henry Idrobo, Andrea Russi, Ray Manneh, Giovanna Rivas, Héctor González, Daniel Santa, Jesús Insuasty, Laura Bernal, Jorge Otero, Carlos Vargas, Javier Pacheco, Carmen Alcalá, Paola Jiménez, Milton Lombana, Fernando Contreras, Javier Segovia, Luis Pino, José Lobatón, Manuel González, Javier Cuello, Juliana Bogoya, Angela Barrero, Gilberto de Lima Lopes Jr.

Final approval of manuscript: Aylen Vanessa Ospina, Ricardo Bruges, William Mantilla, Iván Triana, Pedro Ramos, Sandra Aruachan, Alicia Quiroga, Isabel Munevar, Juan Ortiz, Néstor Llinás, Paola Pinilla, Henry Vargas, Henry Idrobo, Andrea Russi, Ray Manneh, Giovanna Rivas, Héctor González, Daniel Santa, Jesús Insuasty, Laura Bernal, Jorge Otero, Carlos Vargas, Javier Pacheco, Carmen Alcalá, Paola Jiménez, Milton Lombana, Fernando Contreras, Javier Segovia, Luis Pino, José Lobatón, Manuel González, Javier Cuello, Juliana Bogoya, Angela Barrero, Gilberto de Lima Lopes Jr.

Disclosures

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