Factors associated with deaths in hospitalized cancer patients and COVID-19 in an Amazon region: a cross-sectional study with data from epidemiological surveillance

Original Research Article

Abstract

Background: The COVID-19 pandemic has already affected Brazil dramatically, but the northern region of the country has suffered greater impacts due to regional vulnerability factors.

Objective: To describe the factors associated with deaths in hospitalized cancer patients and COVID-19 in the state of Pará, Brazil.

Method: Cross-sectional study with data from epidemiological surveillance of acute and severe respiratory syndromes of hospitalized cases notified from January 1, 2020, to December 31, 2020. Clinical and outcome variables, chi-square test, and Odds ratio were analyzed.

Results: 164 cases, lethality represented 94 (57.32%). The mean overall age was 63 years, of survivors was 60 years and of deaths was 66 years. Advanced age was associated with deaths (p-0.039). Male gender was associated with deaths (65.96% - p-0.006 - OR 2,438 - CI 1,291-4,604). Similarly, the signs and symptoms associated with death were dyspnea (80.85% - p- 0.028 - OR 2,203 - CI 1,080-4,491), respiratory distress (76.60% - p- 0.003 - OR 2,756 - CI 1,410-5,387), O2 saturation <95% represented almost four times to the chances of death (68.09% - p-<0.001 - OR 3,398 - CI 1,798-6,494). Comorbidities were not associated with deaths, however, Immunodeficiency/Immunodepression represented the most frequent in the cases (22.56%), followed by Chronic Cardiovascular Disease (21.95%) and Diabetes Mellitus (18.90%). ICU admission was associated with deaths with the highest odds ratio of the analysis almost five times (42.55% - p- <0.001 - OR 4,444 - CI 2,028-9,739).

Conclusion: In this study, we showed that the lethality was higher than in other studies of hospitalized cancer patients with COVID-19, as well as higher than the overall lethality of COVID-19 among hospitalized patients. The factors associated with deaths are similar to those in the literature, except that immunodeficiency is a specific condition in cancer patients and is associated with an unfavorable outcome.

Keywords: Oncology; Cancer; Neoplasm; Severe acute respiratory syndrome; COVID-19.

INTRODUCTION

The new coronavirus emerged in the province and Wuhan in China in December 2019, following an outbreak of pneumonia of unknown etiology associated with a fish market in the region. In January 2020 the causative infectious agent, SARS-CoV-2, was isolated and named for its similarity to SARS-CoV, a coronavirus that caused an epidemic of Severe Acute Respiratory Syndrome (SARS) in China in 2003, so the disease was named COVID-19, caused by the new coronavirus SARS-CoV-2 [1].

The similarity between the viruses also includes transmissibility, directly and by fomites, being a highly contagious disease, thus, it soon spread to neighboring countries, and on March 20, 2020, the World Health Organization (WHO) declared the outbreak by SARS-CoV-2 as a pandemic, thus the disease reached a global level, causing thousands of deaths, both in developed and developing countries and undeveloped countries [2].

The clinical features are presented in most cases on average (85%) mild and moderate cases, called Flu Syndrome (FS), with the presence of fever, cough, myalgia, chills, sore throat, loss of smell and taste. Severe cases, on average (15%), are associated with symptoms of GS and respiratory distress, dyspnea, oxygen saturation <95%, diarrhea, flapping of the wings of the nose, etc., and the severe cases are called SARS, which requires intensive care and is also associated with high mortality [3].

The literature cites that some risk factors are associated with the severity of COVID-19, for example, the elderly, obese, pregnant women, patients with chronic diseases, heart disease, diabetes, neurological diseases, cancer, immunosuppressed and immunosuppressed [4,5].

In the context of neoplasms, they are a set of pathologies that start from the differentiation and loss of cell function, thus the affected tissue or organ loses its function and the cells multiply disorderly, if the malignant cells migrate to other organs can multiply systemically and cause metastasis from the organ primarily affected. Early diagnosis is fundamental for the best prognosis and is confirmed by biopsy of the

affected tissue. The treatment is based on some approaches such as radiotherapy, chemotherapy, and surgery, which can be performed in association or individually. Chemotherapy and radiotherapy cause immunosuppression, which makes the cancer patient vulnerable to secondary and opportunistic infections, thus becoming a group of patients at risk for the development of infections that can be serious [6,7].

According to the National Cancer Institute (INCA), in 2020 in Brazil the prevalence in men was of Prostate (65,840-29.2%), Colon and Rectum (20,540-9.1%), Trachea, Bronchus and Lung (17,760-7.9%), Stomach (13,360-5.9%) Oral Cavity (11. 200-5.0%) Esophagus (8,690-3.9%) Bladder (7,590-3.4%), Larynx (6,470-2.9%), Leukemias (5,920-2.6%), Central Nervous System (5,870-2.6%), totaling in men, except non-melanoma skin (225,980) cases in 2020, including melanoma reaches (309,750). In women, Breast (66,280-29.7%), Colon and Rectum (20,470-9.2%), Cervix (16,710-7.5%), Trachea, Bronchus and Lung (12,440-5.6%), Thyroid Gland (11,950-5.4%), Stomach (7,870-3.5%), Ovary (6,650-3.0%), Body of the Uterus (6. 540-2.9%), Non-Hodgkin Lymphoma (5,450-2.4%) Central Nervous System (5,230-2.3%), totaling, except non-melanoma skin (223,110) cases in 2020, including melanomas reaches (316,280). thus the neoplasms in 2020 reached more than 600,000 cases in Brazil [8]. Thus, the high prevalence is associated with the greatest impacts of COVID-19 on cancer patients.

One survey cited that the pandemic by COVID-19 affected the treatment of cancer patients, impacting on mortality, as well as the specific characteristics of COVID-19 in these patients [9].

Given this problem, this study aims to describe the factors associated with deaths in hospitalized cancer patients and COVID-19 in the state of Pará, from an analysis of severe SARS cases reported to the Brazilian Ministry of Health (MS), since Brazil's Amazon region has distinct characteristics from other regions, and that these results can subsidize the best management and direct public policies to reduce mortality by COVID-19 in cancer patients in this region of the Brazilian Amazon.

METHOD

This is a cross-sectional epidemiological study, analytical, quantitative, secondary-based, from data provided by the OpenDataSUS platform (https://opendatasus.saude.gov.br/) of the Brazilian Ministry of Health, which

corresponds to the surveillance database of Severe Acute Respiratory Syndromes (SARS), which is performed by the platform of the Information System for Epidemiological Surveillance of Influenza (SIVEP-GRIPE). The study period was from March 1, 2020, to December 31, 2020, including all the notifications of this time frame. (https://sivepgripe.saude.gov.br/sivepgripe/login.html?1).

The database was made available from the OpenDataSUS platform in Excel 2019 format on March 31, 2021, with the last update on March 24, 2021. The SIVEP-GRIPE notification form is composed of 80 variables, on sociodemographic and clinical-epidemiological data [10]. The variables extracted according to the form were: gender (item 8), age (item 10), signs and symptoms (item 35), has risk factors/comorbidities (item 36), admission to intensive care unit (item 47), ventilation (item 44), closure criteria (item 60), final classification: 5-SARS by COVID-19 (item 72) and evolution: 2- death (item 74). The case definition for notification is: hospitalized individual with fever, even if referred, accompanied by cough or sore throat and presenting dyspnea or O2 saturation < 95% or respiratory distress or that evolved to death by SARS regardless of hospitalization.

Inclusion criteria were notifications from residents of Pará with final classification confirmed for COVID-19 and evolution completed, with the variable other comorbidity completed (cancer or neoplasms). Blank notifications were excluded.

The data were organized in an Excel 2019 spreadsheet, and the analysis was performed by the Statistical Package for the Social Sciences (SPSS) 20.0 statistical program. A table was made with the number of cases per municipality of residence. The analysis was performed using the absolute (Fa) and relative (Fr) frequency distributions of the study variables. To measure the association between the outcome variables (dependent) and the predictors (independent) the Chi-square test or Fisher's exact test was used when unable to use the former. Odds Ratio (OR) was performed on the variables significant in the chi-square. To verify the age difference between survivors and deceased, the Shapiro Wilk normality test was applied to verify which test to use. The Shapiro Wilk test was significant 0.035 and thus the sample does not have normality, and we used the Mann-Whitney test to verify the difference between the groups. The alpha level of significance was equal to or less than <0.05.

The data of this study were publicly available, not containing personal data of patients such as name, address, and telephone contact, thus presenting no risk to the

research participants, besides being exempt from ethical opinion. This study is conducted by Law No. 12.527 of 18/11/2011 (Access to Information Law) [11].

RESULTS

The study totaled until the study period 164 cases of COVID-19 hospitalized in oncology patients according to the information in the notification and investigation form of SIVEP-GRIPE. Of these 164, the lethality represented 94 (57.32%), on the closure criteria, most were laboratory 149 (90.90%) (Table 1).

The average age of the survivors was 63, of the survivors 60, and the deceased 66. The average age for deaths is higher.

Table 1 - Closure criteria for hospitalized cases of COVID-19 in oncology patients, Pará, Brazil, 2022.

Closing criteria	**N**	**%**
Laboratory	149	90,9
Clinical-epidemiological	9	6,4
Clinical	5	3,0
Clinical-imaging	1	0,6
Total	164	100,0

Source: OpenDataSUS. SIVEP-GRIPE.

In table 2 we observe the cases per municipality of residence, Belém represented 51 (31.10%), followed by Santarém 25 (15.20%) and Marabá 12 (7.30%), Ananindeua 8 (4.90%) and Parauapebas 6 (3.70%). The others were equal to or less than 3 cases for each municipality.

Table 2 - Number of cases of COVID-19 in oncology inpatients by the municipality of residence, Pará, Brazil, 2022.

Cases per municipality	**N**	**%**
Belém	51	31,1
Santarém	25	15,2
Marabá	12	7,3
Ananindeua	8	4,9

Parauapebas	6	3,7
Itaituba	3	1,8
Marapanim	3	1,8
Paragominas	3	1,8
Tucuruí	3	1,8
Abaetetuba	2	1,2
Altamira	2	1,2
Canaã dos carajás	2	1,2
Juruti	2	1,2
Marituba	2	1,2
Mocajuba	2	1,2
Oeiras do para	2	1,2
Portel	2	1,2
Rurópolis	2	1,2
Salinópolis	2	1,2
Água azul do Norte	1	0,6
Alenquer	1	0,6
Anapu	1	0,6
Aurora do para	1	0,6
Baião	1	0,6
Braganca	1	0,6
Brasil novo	1	0,6
Breves	1	0,6
Bujaru	1	0,6
Cametá	1	0,6
Capanema	1	0,6
Castanhal	1	0,6
Curionópolis	1	0,6
Curuá	1	0,6
Dom Eliseu	1	0,6
Ipixuna do para	1	0,6
Jacundá	1	0,6
Mae do rio	1	0,6
Moju	1	0,6
Monte alegre	1	0,6
Ourilândia do Norte	1	0,6
Pacajá	1	0,6
Primavera	1	0,6
Santa Isabel do Pará	1	0,6
Santo Antônio do Tauá	1	0,6
São domingos do Araguaia	1	0,6
São Geraldo do Araguaia	1	0,6
São Miguel do Guamá	1	0,6
Tucumã	1	0,6
Uruará	1	0,6
Total	164	100,0

Source: OpenDataSUS. SIVEP-GRIPE.

About the characteristics of the cases, we observed that advanced age is associated with deaths (Mann-Whitney p- 0.039), as well as male gender (65.96% - p- 0.006 - OR 2.438 - CI 1.291-4.604) with twice as many chances of death according to the odds ratio in the bivariate analysis. Similarly on signs and symptoms, dyspnea (80.85% - p- 0.028 - OR 2,203 - CI 1,080-4,491) with two times more chances of death, followed by respiratory distress with almost three times more chances of death by Odds ratio (76.60% - p- 0.003 - OR 2. 756 - CI 1,410-5,387), O2 saturation <95% represented almost four times to the chances of death (68.09% - p-<0.001 - OR 3,398 - CI 1,798-6,494). Comorbidities were not associated with deaths, however, Immunodeficiency/Immunodepression represented the most frequent in the cases (22.56%), followed by Chronic Cardiovascular Disease (21.95%) and Diabetes Mellitus (18.90%). ICU admission was associated with deaths with the highest odds ratio of the analysis almost five times (42.55% - p- <0.001 - OR 4,444 - CI 2,028-9,739).

Table 3 - Clinical, epidemiological, and outcome characteristics of hospitalized oncology cases of COVID-19, Pará, Brazil, 2022.

Characteristics	Total (164)	%	Survivor (70)	%	Death (94%)	%	p-value	OR	CI	
Age										
Median	65,00		73,61		89,12		0,039**			
Sex							0,006	2.438	1.291	4.604
Male	93	56.71	31	44.29	62	65.96				
Female	71	43.29	39	55.71	32	34.04				
Signs and Symptoms										
Fever	108	65.85	51	72.86	57	60.64	0,103			
Cough	108	65.85	47	67.14	61	64.89	0,764			
Sore throat	32	19.51	18	25.71	14	14.89	0,084			
Dyspnea	122	74.39	46	65.71	76	80.85	0,028	2.203	1.080	4.491
Respiratory distress	110	67.07	38	54.29	72	76.60	0,003	2.756	1.410	5.387
O2 saturation <95%	91	55.49	27	38.57	64	68.09	<0,001	3.398	1.798	6.494
Diarrhea	19	11.59	7	10.00	12	12.77	0,584			
Vomit	18	10.98	7	10.00	11	11.70	0,730			
Another symptom	45	27.44	23	32.86	22	23.40	0,180			
Comorbidities										
Chronic cardiovascular disease	36	21.95	18	25.71	18	19.15	0,315			
Chronic hematological disease	1	0.61	1	1.43	0	0.00	0,427*			
Chronic liver disease	2	1.22	1	1.43	1	1.06	0,673*			
Asthma	4	2.44	0	0.00	4	4.26	0,137*			
Diabetes Mellitus	31	18.90	15	21.43	16	17.02	0,476			
Immunodeficiency/Immunodepression	37	22.56	13	18.57	24	25.53	0,292			
Chronic kidney disease	5	3.05	2	2.86	3	3.19	0,637*			

Obesity	1	0.61	0	0.00	1	1.06	0,573*			
Hospitalized in ICU	50	30.49	10	14.29	40	42.55	<0,001	4.444	2.028	9.739

Source: OpenDataSUS. SIVEP-GRIPE. *Fisher's exact test, **Mann-Whitney. OR Odds Ratio, CI Confidence Interval.

DISCUSSION

This study analyzed the cases of COVID-19 hospitalized oncologists in the state of Pará, and we identified a high lethality of (57.32%), because the lethality in hospitalized oncologists for COVID-19 generally reaches a lower rate, for example in the studies of Duarte et al[12] which analyzed those hospitalized in Brazil at the beginning of the pandemic, which still only included health professionals. However, another study performed another analysis of those hospitalized for COVID-19 in the state of Pará in the first year of the pandemic and showed a lethality rate of (42.47%)[13]. Thus, the lethality in cancer patients is higher than in those hospitalized for COVID-19 overall.

A study of 218 patients hospitalized for COVID-19 diagnosed with cancer in New York showed a lethality rate of (28%) lower than the rate in our study. [14].

Our study showed that advanced age was associated with deaths. A study of 37 hospitalized patients with COVID-19 and cancer did not associate advanced age with severe cases of the disease, one hypothesis is the limitation in the small sample [15]. Another study of 1,590 patients found that among cancer patients, advanced age was the only risk factor for serious events (OR 1,43, IC 95% 0,97–2,12; p=0,072) [16].

Regarding the signs and symptoms, we identified that dyspnea, respiratory distress, and altered O2 saturation were associated with deaths, similar to other studies of patients hospitalized in general for COVID-19[17,18]. As well as in another study specifically of oncology patients with COVID-19[19].

A survey of 423 cancer patients and COVID-19, showed that fever (78%) and cough (82%) were the most common clinical features, while shortness of breath (44%) and diarrhea (26%) were less common but not. 168 (40%) of 423 patients were hospitalized and 87 (20%) developed severe respiratory illness, including 47 (11%) who required high-flow oxygen and 40 (9%) who required mechanical ventilation. The

illness in seven pediatric cases was mild and uncomplicated. The overall lethality rate was 12% (51 of 423). The case fatality for hospital and ICU admission was 24% (41 of 168) and 35% (17 of 48), respectively. [20].

The same New York study cited above identified increased mortality significantly associated with older age, multiple comorbidities, need for ICU support, and elevated levels of D-dimer, lactate dehydrogenase, and lactate on multivariate analysis [14]. Similar to our results regarding ICU admission for risk of death. Another study also associated the risk of death in ICU in those hospitalized for COVID-19 in general [21].

Immunodeficiency/immunodepression was significant in occurrence in our study, representing the most common comorbidity. According to Al-quteimat and amer[22], the immunosuppressed state of some cancer patients (whether caused by the disease itself or by treatment) increases the risk of infection compared to the general population. Immunosuppression can also expose cancer patients to severe complications from an infection, which can result in delayed treatment and unnecessary hospitalizations that can negatively affect the prognosis of the disease.

A meta-analysis of 15 studies with 3,019 patients, of whom 1,628 were men; 41.0% were from the United Kingdom and Europe, followed by the United States and Canada (35.7%) and Asia (China, 23.3%). The overall lethality rate for COVID-19 patients with cancer measured 22.4% (95% confidence interval [CI] = 17.3% to 28.0%). Univariate analysis revealed age (OR = 3.57, 95% CI = 1.80 to 7.06), male gender (OR = 2.10, 95% CI = 1.07 to 4.13), and comorbidity (OR = 2.00, 95% CI = 1.04 to 3.85) were associated with increased risk of serious events (defined as individuals admitted to the intensive care unit or requiring invasive ventilation or death). In multivariate analysis, only age greater than 65 years (OR = 3.16, 95% CI = 1.45 to 6.88) and being male (OR = 2.29, 95% CI = 1.07 to 4.87) were associated with increased risk of serious events. In this analysis, the authors concluded that COVID-19 patients with cancer have a higher lethality rate compared to COVID-19 patients without cancer. Age and sex appear to be risk factors associated with a worse prognosis [23]. However, the lethality of our study was still higher, but we emphasize that we only analyzed hospitalized patients, while the meta-analysis did not specify whether it included only hospitalized patients.

Cancer patients have an increased risk of serious infections, with a 3.5-fold increase in the risk of needing mechanical ventilation or ICU admission or dying

compared to patients without cancer. The increased susceptibility of cancer patients to serious complications from COVID-19 may be attributed to the immunosuppressive state caused by the malignancy and anticancer treatments, such as chemotherapy or surgery. Patients who received chemotherapy or underwent surgery in the 30 days before presenting with COVID-19 were at higher risk of serious events than patients who were not treated with chemotherapy or surgery. It was also found that a history of cancer conferred the highest risk of serious complications and was correlated with worse COVID-19 results. Notably, patients with lung cancer did not have a higher likelihood of serious complications compared to patients with other types of cancer [16].

Curigliano[24] draws attention and highlights that two recent articles in the Lancet and Lancet Oncology report that cancer patients with acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection have higher mortality rates. Common independent factors associated with increased risk of death were older age, smoking history, number of comorbidities, more advanced performance status, and active cancer.

As a limitation of the study, we highlight the risk of data bias because we analyzed a retrospective epidemiological surveillance database. However, the surveillance of SARS in Brazil is performed since 2009 because of the Influenza pandemic, thus the investigation form is well prepared and it is already routine in hospitals to fill it out and follow the flow of surveillance, such as sample collection for molecular investigation and closure of the case in the system. The form is filled in after the case is defined by the patient's primary care team, and during the outcome, the form continues to be filled in until the case is closed. The fact of not having the variable cancer comorbidity increases the risk of bias because the screening was performed by the variable other comorbidity and we filtered the neoplasms that were filled in manually by health professionals.

CONCLUSION

In this study, we show that the lethality was higher than other studies of hospitalized cancer patients with COVID-19, as well as higher than the overall lethality of COVID-19 among hospitalized patients. The clinical features associated with a death such as dyspnea, respiratory distress, and change in oxygen saturation were similar to

the other studies. As for the outcomes such as ICU admission and immunodeficiency associated with death that we identified, ICU admission is similar in patients without cancer, however, immunodeficiency is a factor specifically in cancer patients that influences the severity and death of those hospitalized by COVID-19 with cancer in this study, being similar to the literature.

REFERENCES

[1] Lima LNGC, De Sousa MS, Lima KVB. As descobertas genômicas do SARS-CoV-2 e suas implicações na pandemia de COVID-19. J Heal Biol Sci 2020;8:1. https://doi.org/10.12662/2317-3076jhbs.v8i1.3232.p1-9.2020.

[2] Velavan TP, Meyer CG. The COVID-19 epidemic. Trop Med Int Heal 2020;25:278–80. https://doi.org/10.1111/tmi.13383.

[3] Cespedes M da S, Souza JCRP de. Sars-CoV-2: A clinical update - II. Rev Assoc Med Bras 2020;66:547–57. https://doi.org/10.1590/1806-9282.66.4.547.

[4] Tian W, Jiang W, Yao J, Nicholson CJ, Li RH, Sigurslid HH, et al. Predictors of mortality in hospitalized COVID-19 patients: A systematic review and meta-analysis. J Med Virol 2020;92:1875–83. https://doi.org/10.1002/jmv.26050.

[5] Bello-Chavolla OY, Bahena-López JP, Antonio-Villa NE, Vargas-Vázquez A, González-Díaz A, Márquez-Salinas A, et al. Predicting Mortality Due to SARS-CoV-2: A Mechanistic Score Relating Obesity and Diabetes to COVID-19 Outcomes in Mexico. J Clin Endocrinol Metab 2020;105. https://doi.org/10.1210/clinem/dgaa346.

[6] Brasil M da S. ABC do Câncer Abordagens Básicas para o Controle do Câncer. 2nd ed. Rio de Janeiro: Instituto Nacional do Câncer; 2011.

[7] Abbas Z, Rehman S. An Overview of Cancer Treatment Modalities. Neoplasm, InTech; 2018. https://doi.org/10.5772/intechopen.76558.

[8] INCA IN do C. Estatísticas de câncer | INCA - Instituto Nacional de Câncer. Ministério Da Saúde 2020. https://www.inca.gov.br/numeros-de-cancer (accessed March 30, 2021).

[9] Moujaess E, Kourie HR, Ghosn M. Cancer patients and research during COVID-19 pandemic: A systematic review of current evidence. Crit Rev Oncol Hematol 2020;150:102972. https://doi.org/10.1016/j.critrevonc.2020.102972.

[10] Brasil M da S. Ficha de notificação SIVEP-GRIPE. OpenDataSUS 2020:1–2. https://opendatasus.saude.gov.br/dataset/ae90fa8f-3e94-467e-a33f-94adbb66edf8/resource/54a46c6d-e0b5-40b7-8b74-85450d22ace3/download/ficha-srag-final-27.07.2020_final.pdf (accessed August 27, 2021).

[11] Brasil M da J. LEI Nº 12.527, DE 18 DE NOVEMBRO DE 2011. Diário Of Da União - DOU 2011. http://www.planalto.gov.br/ccivil_03/_ato2011-2014/2011/lei/l12527.htm (accessed July 25, 2020).

[12] Duarte MMS, Haslett MIC, Freitas LJA de, Gomes NTN, Silva DCC da, Percio J, et al. Descrição dos casos hospitalizados pela COVID-19 em profissionais de saúde nas primeiras nove semanas da pandemia, Brasil, 2020. Epidemiol e Serviços Saúde 2020;29:e2020277. https://doi.org/10.1590/S1679-49742020000500011.

[13] Sardinha DM. CARACTERÍSTICAS EPIDEMIOLÓGICAS E DISTRIBUIÇÃO ESPACIAL DA SÍNDROME RESPIRATÓRIA AGUDA GRAVE POR COVID-19 NO ESTADO DO PARÁ NO PRIMEIRO ANO DA PANDEMIA. Instituto Evandro Chagas, 2021.

[14] Mehta V, Goel S, Kabarriti R, Cole D, Goldfinger M, Acuna-Villaorduna A, et al. Case Fatality Rate of Cancer Patients with COVID-19 in a New York Hospital System. Cancer Discov 2020;10:935–41. https://doi.org/10.1158/2159-8290.CD-20-0516.

[15] Ma J, Yin J, Qian Y, Wu Y. Clinical characteristics and prognosis in cancer patients with COVID-19: A single center's retrospective study. J Infect 2020;81:318–56. https://doi.org/10.1016/j.jinf.2020.04.006.

[16] Liang W, Guan W, Chen R, Wang W, Li J, Xu K, et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. Lancet Oncol 2020;21:335–7. https://doi.org/10.1016/S1470-2045(20)30096-6.

[17] Abu-Raya B. Predictors of Refractory Coronavirus Disease (COVID-19) Pneumonia. Clin Infect Dis 2020;71:895–6. https://doi.org/10.1093/cid/ciaa409.

[18] Yadaw AS, Li Y-C, Bose S, Iyengar R, Bunyavanich S, Pandey G. Clinical predictors of COVID-19 mortality. MedRxiv Prepr Serv Heal Sci 2020. https://doi.org/10.1101/2020.05.19.20103036.

[19] Yang F, Shi S, Zhu J, Shi J, Dai K, Chen X. Clinical characteristics and outcomes of cancer patients with COVID-19. J Med Virol 2020;92:2067–73. https://doi.org/10.1002/JMV.25972.

[20] Robilotti E V., Babady NE, Mead PA, Rolling T, Perez-Johnston R, Bernardes M, et al. Determinants of Severity in Cancer Patients with COVID-19 Illness. Nat Med 2020;26:1218. https://doi.org/10.1038/S41591-020-0979-0.

[21] Jain V, Yuan J-M. Predictive symptoms and comorbidities for severe COVID-19 and intensive care unit admission: a systematic review and meta-analysis. Int J Public Health 2020;65:533–46. https://doi.org/10.1007/s00038-020-01390-7.

[22] Al-Quteimat OM, Amer AM. The Impact of the COVID-19 Pandemic on Cancer Patients. Am J Clin Oncol 2020. https://doi.org/10.1097/COC.0000000000000712.

[23] Zhang H, Han H, He T, Labbe KE, Hernandez A V., Chen H, et al. Clinical Characteristics and Outcomes of COVID-19–Infected Cancer Patients: A Systematic Review and Meta-Analysis. JNCI J Natl Cancer Inst 2021;113:371–80. https://doi.org/10.1093/JNCI/DJAA168.

[24] Curigliano G. Cancer Patients and Risk of Mortality for COVID-19. Cancer Cell 2020;38:161–3. https://doi.org/10.1016/J.CCELL.2020.07.006.

366

367