

COVID-19 and Cancer: Updating Epidemiological Issues

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Covid-19 e Câncer: Atualização de Aspectos Epidemiológicos

Covid-19 y Cáncer: Actualización de Aspectos Epidemiológicos

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Abstract

Introduction: The disease caused by the new coronavirus (COVID-19) is currently a global public health issue. Advanced age, male gender, history of tobacco addiction and presence of comorbidities, among them cancer, were reported in the literature as factors associated to the worse prognosis of the disease. **Objectives:** To review the literature about the new coronavirus infection in individuals with malignant neoplasms and to update the epidemiological aspects of the disease in oncologic patients. **Method:** Literature review on articles published in scientific journals that addressed the epidemiologic aspects of the infection by coronavirus in oncologic patients using the terms of the Medical Subject Headings (MeSH) and of the Health Sciences Descriptors (DeCs) in the MEDLINE/PubMed database. **Results:** Patients with cancer have worse clinical results when compared to the general population. **Conclusion:** Elderly oncologic patients with lung cancer or patients who have submitted to recent cancer surgery or chemotherapy when diagnosed with COVID-19 were more susceptible to the development of severe infection.

Key words: Neoplasms; SARS Virus; Coronavirus Infections; Epidemiology; Pandemics.

Resumo

Introdução: A doença causada pelo novo coronavírus (Covid-19) é atualmente um problema mundial de saúde pública. A idade avançada, sexo masculino, histórico de tabagismo e presença de comorbidades, entre as quais, o câncer, foram relatados na literatura como fatores associados ao pior prognóstico da doença. **Objetivos:** Revisar a literatura acerca da infecção pelo novo coronavírus em indivíduos portadores de neoplasias malignas e atualizar os aspectos epidemiológicos da doença em pacientes oncológicos. **Método:** Revisão de trabalhos publicados em periódicos científicos que abordavam os aspectos epidemiológicos da infecção por coronavírus em pacientes oncológicos por meio de termos do *Medical Subject Headings* (MeSH) e dos Descritores em Ciências da Saúde (DeCs) na base de dados MEDLINE/PubMed. **Resultados:** Pacientes com câncer apresentam piores resultados clínicos quando comparados à população geral. **Conclusão:** Pacientes oncológicos idosos, portadores de câncer de pulmão, ou que se submeteram à cirurgia oncológica ou à quimioterapia recentes ao diagnóstico de Covid-19 apresentaram maior suscetibilidade ao desenvolvimento da infecção grave.

Palavras-chave: Neoplasias; Vírus da SARS; Infecções por Coronavírus; Epidemiologia; Pandemias.

Resumen

Introducción: La enfermedad causada por coronavirus (Covid-19) es actualmente un problema de salud pública. Las personas con enfermedades crónicas como el cáncer, el sexo masculino, los antecedentes de tabaquismo y los ancianos tienen un mayor riesgo de adquirir formas graves, desarrollar complicaciones y morir por la enfermedad. **Objetivos:** Revisar la literatura sobre la infección con el nuevo coronavirus en individuos con neoplasias malignas y sintetizar los aspectos epidemiológicos de la enfermedad en pacientes con cáncer. **Método:** Revisión de la literatura como artículos publicados en revistas científicas utilizando los términos médicos (MeSH) y Descriptores en Ciencia de la Salud (DeCs) en la base de datos MEDLINE/PubMed. **Resultados:** Los pacientes con cáncer tienen peores resultados clínicos en comparación con la población general. **Conclusiones:** Pacientes oncológicos ancianos, portadores de cáncer de pulmón, o que se sometieron a cirugía de cáncer o a quimioterapia reciente al diagnóstico de Covid-19 fueron más susceptibles al desarrollo de infección severa.

Palabras clave: Neoplasias; Virus del SRAS; Infecciones por Coronavirus; Epidemiología; Pandemias.

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INTRODUCTION

On December 2019 were identified the first cases of the coronavirus disease 2019 – COVID-19 caused by the presence of a novel coronavirus, the severe acute respiratory syndrome coronavirus 2 – Sars-CoV-2, whose origin was in Wuhan, Hubei, China¹. Advanced age, male gender, history of tobacco addiction and presence of comorbidities were reported in the literature among which, cancer, as factors associated to worse prognosis of the disease². The fast progression of the COVID-19 pandemic was declared by the World Health Organization (WHO) a Public Health Emergency of International Concern³. For being a disease with high potential of transmissibility through droplets from coughing, sneezing or talking, social distancing, quarantine and isolation were adopted in several countries, in addition to hygiene instructions and respiratory etiquette³⁻⁴.

The most frequent symptoms are fever (above 37.8°C), difficulty breathing and/or shortness of breath, headache, diarrhea, muscle pain, anosmia and ageusia. Although nearly 80% presenting asymptomatic infection³, either immunosuppressed, older adults or chronic diseases carriers, among them, cancer, are more susceptible to serious complications of the severe acute respiratory syndrome with evolution to multiple organs dysfunction syndrome, which includes respiratory and kidney failure⁵⁻⁸.

Among cancer patients, those with lung cancer, who underwent bone marrow transplantation or submitted to chemotherapy treatment had more risk of complications due to coronavirus infection^{5,9,10}. Therefore, the guiding question was: What is the epidemiological profile of the oncologic patients who developed Covid-19? The objective was to compile information of publications about Sars-CoV-2 infection in oncologic patients in order to warn and guide the assistance provided to relatives, caregivers and health professionals.

METHOD

To meet the proposed objectives, it was chosen the literature review. Articles published in scientific journals that addressed the epidemiological aspects of the coronavirus infection in oncologic patients were selected. The selection criteria were articles in English, Portuguese, Spanish and French available as full text published between December 1, 2019 and April 22, 2020 encountered in the databases MEDLINE/PubMed, utilizing the descriptors controlled of Medical Subject Headings (MeSH) and the Descriptors of Sciences of Health (DeCs) from the Boolean operator AND as well as its respective synonyms through the Boolean operator OR.

The search strategy elicited 198 publications by the combination of the terms Covid-19 and cancer ((Severe Acute Respiratory Syndrome Coronavirus 2[Supplementary Concept] OR COVID-19[Supplementary Concept] OR Severe Acute Respiratory Syndrome Coronavirus 2[tiab] OR Coronavirus Disease 2019[tiab] OR 2019 Novel Coronavirus[tiab] OR Wuhan Coronavirus[tiab] OR COVID-19[tiab] OR SARS-CoV-2[tiab] OR 2019-nCoV[tiab]) AND (Neoplasms[mh] OR Neoplas*[tiab] OR Cancer*[tiab] OR Tumor*[tiab] OR Tumour*[tiab] OR Carcinoma[mh] OR Carcinoma*[tiab] OR Malignan*[tiab] OR Medical Oncology[mh] OR Oncol*[tiab])) AND (English[lang] OR Portuguese[lang] OR Spanish[lang] OR French[lang]).

The exclusion criteria were those articles unrelated to the study object after reading the abstract and which did not address the target-population, oncologic patients. Grey literature was also searched including government reports, as well as other references were used to elaborate the introduction and discussion of results.

RESULTS

Titles and abstracts were evaluated by four reviewers in compliance with predefined exclusion and inclusion criteria to avoid biases of selection. The discordant cases (N=2) were decided by consensus, resulting in a final selection of 13 articles for full reading and elaboration of this study. The information gathered are presented in Table 1.

In its totality, the articles were published in 2020. In relation to the type of publication, 69.2% (N=9) were original articles, 15.4,0% (N=2) letter to the editor and 15.4% (N=2), editorials. Among the studies designs 30.7% (N=4) were cross-sectional, 23.1% (N=3) cohort studies, 23.1% (N=3) systematic reviews with meta-analysis, 15.4% (N=2) opinion of experts and 7.7% (N=1) case study, whose level of evidence 2a, 2b, 4 and 5 were identified in 23.1% (N=3), 30.7% (N=4), 7.7% (N=1) and 38.5% (N=5), respectively¹¹.

The most frequent scenario was China (N=9; 69.2%), having been identified other countries such as, India (N=1; 7.7%), Iran (N=1; 7.7%), United States (N=1; 7.7%) and Brazil (N=1; 7.7%).

Regarding the severity of COVID-19 disease, severer cases were observed in oncologic patients. This evaluation was realized and presented in articles 1, 3, 7, 11 and 12 listed in Table 1.

DISCUSSION

Of the publications selected, five revealed more prevalence of individuals with cancer in confirmed

Table 1. Description of the publications selected according to author, type of cancer, title, scenario, design and study population and measures of effect

| N° | Author/year | Title | Type of publication | Study scenario, design and population | Level of evidence ^a | Type of cancer | Measures of effect |
|----|----------------------|--|----------------------|--|--------------------------------|---|---|
| 1 | Liang et al., 2020 | <i>Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China</i> | Article | China, multicenter retrospective cohort study, N = 1,590 | 2b | Any malignant neoplasm | Intensive care: P = 39% (N = 18) of the patients with cancer versus 8% (N = 1,572) of the patients with cancer (p = 0.0003) |
| 2 | Xia et al., 2020 | <i>Risk of COVID-19 for patients with cancer</i> | Letter to the editor | China, cross-sectional, N = 1,590 | 5 | Any malignant neoplasm | - |
| 3 | Yu et al., 2020 | <i>SARS-CoV-2 transmission in patients with cancer at a tertiary care hospital in Wuhan, China</i> | Article | China, cross-sectional, N = 1,524 | 2b | Any malignant neoplasm | Rate of infection by coronavirus in oncologic patients: 0.79% (CI95% 0.3%-1.2%) |
| 4 | Shankar et al., 2020 | <i>Cancer care delivery challenges amidst coronavirus disease - 19 (COVID-19) outbreak: specific precautions for cancer patients and cancer care providers to prevent spread</i> | Editorial | India, experts opinion. | 5 | Any malignant neoplasm | - |
| 5 | Guan et al., 2020 | <i>Comorbidity and its impact on 1590 patients with covid-19 in China: a nationwide analysis</i> | Article | China, multicenter, retrospective case study, N = 1,524 | 4 | Any malignant neoplasm | HR = 1.79 (CI95% 1.16-2.77) |
| 6 | Zhang et al., 2020 | <i>Clinical characteristics of COVID-19-infected cancer patients: a retrospective case study in three hospitals within Wuhan, China</i> | Article | China, multicenter, cohort retrospective study, N = 28 | 2b | Lung, esophagus, breast, larynx, liver, prostate, cervix, colon, rectum, nasopharynx, endometrium, ovary and testicle | Most frequent types of cancer: lung (25.0%), esophagus (14.3%) and breast (10.7%). Antitumor therapy until 14 days prior to COVID-19 infection: 21.4% |
| 7 | Shi et al., 2020 | <i>Host susceptibility to severe COVID-19 and establishment of a host risk score: findings of 487 cases outside Wuhan</i> | Article | China, retrospective cohort study, N = 487 | 2b | Any malignant neoplasm | Severe cases of COVID-19: P = 4.1% oncologic patients versus 0.7% patients without comorbidities (p = 0.025) |
| 8 | Emami et al., 2020 | <i>Prevalence of underlying diseases in hospitalized patients with covid-19: a systematic review and meta-analysis</i> | Article | Iran, systematic review and meta-analysis, N = 76,993 | 2a | Any malignant neoplasm | P = 0.92 (CI95% 0.56-1.34) |
| 9 | Wang et al., 2020 | <i>Does comorbidity increase the risk of patients with COVID-19: evidence from meta-analysis</i> | Article | China, systematic review and meta-analysis, N = 1,558 | 2a | Any malignant neoplasm | OR = 2.29 (CI95%: 1.00-5.23, p = 0.627) |

to be continued

Table 1. continuation

| N° | Author/year | Title | Type of publication | Study scenario, design and population | Level of evidencea | Type of cancer | Measures of effect |
|----|---|---|----------------------|---|--------------------|---|--|
| 10 | Desai et al., 2020 | <i>COVID-19 and cancer: lessons from a pooled meta-analysis</i> | Article | USA, systematic review and meta-analysis, N=3,661 | 2a | Any malignant neoplasm | P=2.0% (CI95% 2.0%-3.0%) |
| 11 | Ma et al., 2020 | <i>Clinical characteristics and prognosis in cancer patients with COVID-19: a single center's retrospective study</i> | Letter to the editor | China, cross-sectional, N=1,380 | 5 | Colorectal, lung, breast, gynecological and other neoplasms | P=54.1% Covid-19 severe patients with cancer. Comorbidities associated to adverse events P=40% |
| 12 | <i>Novel Coronavirus Pneumonia Emergency Response Epidemiology Team, 2020</i> | <i>The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China</i> | Article | China, cross sectional, N=72,314 | 5 | Any malignant neoplasm | Rate of fatality in oncologic patients 5.6% versus 0.9% patients without comorbidities |
| 13 | Thuler e Melo, 2020 | Sars-CoV-2/Covid-19 em pacientes com câncer | Editorial | Brazil, experts opinion | 5 | Any malignant neoplasm | - |

Caption: ^aBased in the adaptation of the levels of evidence in Szklo, 2015.

COVID-19 cases compared to general population (1.0% versus 0.29%)⁵. Yu et al.¹² referred twofold higher odds of infection susceptibility by patients with cancer (OR=2.31; CI95% 1.89-3.02). Shankar et al.² suggest that the magnitude of the risk of infection by COVID-19 is twofold higher for individuals with malignant neoplasms in comparison with the general population. The Desai et al.¹³ meta-analysis, also referred prevalence twofold higher in patients with cancer infected by COVID-19 (P=2.0%; CI95% 2.0%-3.0%). In a review, Thuler e Melo¹⁴ suggest that the individuals with cancer have higher risk for the development of the disease by COVID-19 comparing with the general population. On the other hand, the findings of the meta-analysis conducted by Wang et al.¹⁵ do not corroborate the correlation between individuals with neoplasms and the evolution to severe clinical status of COVID-19 when compared with all the patients included in the study (OR=2.29; CI95% 1.00-5.23) even if borderline.

Oncologic patients, especially those in treatment, are more susceptible to infection, considering that some therapeutic modalities compromise its immune system¹⁶⁻¹⁷, being corroborated by four publications encountered in this review. Liang et al.⁵ observed that 25% of 16 individuals with cancer have been submitted to the treatment in less than one month from the infection by COVID-19 and in 75% of 18 patients, it was performed primary resection of the tumor in the month prior to infection. It was observed by Zhang et al.¹⁸ that 35.7% of the oncologic patients (N=10) presented clinical staging IV of the tumor and 21.4% (N=6) have

undergone anti-tumor therapy in until 14 days preceding the diagnosis of COVID-19. In addition, an increased risk of developing the most severe infection was observed in this study in patients undergoing antitumor therapy (HR=4.079; CI95% 1.086-15.322, p=0.037). Of the 12 oncologic patients infected by Sars-CoV-2 (N=1,254) observed in the study realized by Yu et al.¹², 41.7% (N=5) were in treatment (immune therapy, chemotherapy or radiotherapy). Ma et al.¹⁹ identified that 35.0% cancer carriers with moderate or severe coronavirus infection have submitted to anti-tumor therapy within one month before COVID-19 diagnosis.

Liang et al.⁵ indicated that 39.0% of the patients with cancer (N=18) needed intensive care compared with 8% (N=124) of the 1,572 patients (p=0.0003). In the study conducted by Shi et al.²⁰, of the 487 cases of COVID-19, 49 (10.1%) evolved to severe symptoms, in which 4.1% had neoplasms in comparison with 438 (89.9%) who presented moderate symptoms in which 0.7% were oncologic patients (p=0.025). For Ma et al.¹⁹, the proportion of severe COVID-19 cases or critically ill was 54.1% in cancer patients, a percentage higher than that found in the study conducted by Wang et al.²¹ with 138 COVID-19, in which 26.1% (N=36) were patients in severe conditions. The coronavirus lethality rate in patients with any neoplasm was 5.6% in a study conducted by the Chinese epidemiological group, Novel Coronavirus Pneumonia Emergency Response Epidemiology Team²². The study carried out by Yu et al.¹² found no increased risk of severe COVID-19 infections in oncologic patients.

Lung cancer has been mentioned in four publications as one of the types of cancer possibly most susceptible COVID-19 infection. When compared to the 18 patients with cancer (N=1,590), 28% (N=5) had lung cancer, according to Liang et al.⁵. However, a greater probability of developing severe infection was not encountered in patients with lung cancer when compared to other neoplasms – one (20%) of five patients with lung cancer *versus* eight (62%) of 13 patients with other types of cancer (p=0.294)⁵. In the study conducted by Zhang et al.¹⁸, among the 1,276 patients infected, 28 (2.2%) had malignant neoplasms, the most frequent was lung cancer (in 25% of the cases), followed by esophagus (N=4; 14.3%) and breast (N=3; 10.7%). Yu et al.¹² identified in its study population 58.3% of patients with lung cancer (N=12). For Ma et al.¹⁹, of the 37 individuals with cancer and COVID-19, 20 evolved to severe forms of the disease. Of these, 35.0% (N=7) had colorectal cancer and 20.0% (N=4) were patients with lung cancer (N=8). Other types of cancer were also investigated, but the differences encountered were not statistically significant. Emami et al.¹⁶, in a study of systematic review and meta-analysis (N=3,403), suggest that cancer is among the most prevalent diseases (0.92% CI95% 0.56-1.34).

The analysis of cancer patients with other comorbidities was carried out in five publications. In the study by Guan et al.²³, a composite measure was used to assess the need of intensive care (ICU and mechanic ventilation) and death as a measure of risk of severity of COVID-19 infection and a 79.0% higher risk was identified in individuals with any comorbidity, including cancer, diabetes, hypertension, cardiovascular and cerebrovascular diseases compared to individuals without comorbidities (HR=1.79; CI95% 1.16-2.77). For patients with two or more associated comorbidities, the risk was 2.5-fold higher (HR=2.59; CI95% 1.61-4.17). The adjusted analysis per age and tobacco smoking showed a 3.5-fold increase in risk (HR=3.5; CI95% 1.60-7.64). And in Zhang et al.¹⁸, 39.2% (N=11) presented other comorbidities associated to cancer. Ma et al.¹⁹ observed that, among the individuals with malignant neoplasms and COVID-19 with moderate or severe complications, 40% (N=8) of the severe cases (N=20), presented more than one comorbidity and evolved to severe forms of infection by coronavirus.

Two publications pointed out that the evidence of cancer as a risk factor for development of COVID-19 was based in small samples, considered a limitation of the findings^{23,24}.

It is worth mentioning the lack of familiarity with the effects of coronavirus in oncologic patients, in terms of survival or mortality due to discontinuation or delay of treatment caused by the saturation of the health services.

Despite there is not yet scientific evidence to change the therapeutic protocol during the pandemic^{2,17}. Mourey et al.²⁵ emphasized the need to limit hospitalizations and the application of prior restrictive measures before the beginning or discontinuation of the oncologic treatment due to accumulated risk of advanced age and cancer diagnosis.

Since advanced age and the presence of comorbidities are common in oncologic patients¹⁴, care strategies must consider the susceptibility to the development of the most severe form of infection, including measures for prevention, early detection, cure and recovery from infection for cancer care planning^{16,26,27}.

CONCLUSION

The analysis of the epidemiological profile of the oncologic patients infected by COVID-19 was summarized in this study. Since advanced age and comorbidities have been indicated as risk factors and cancer can be considered an age-related disease, oncologic patients are actually more vulnerable to develop COVID-19 in its most severe form.

CONTRIBUTIONS

All the authors contributed equally in the conception, analysis and interpretation of the study, wording and critical review with intellectual contribution and in the approval of the final version for review.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

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