TEXTO & CONTEXTO ENFERMAGEM
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IMPACT OF COVID-19 IN PATIENTS WITH CANCER: A SCOPING REVIEW

Tâmara Taynah Medeiros da Silva[1]
Naryllenne Maciel de Araújo[2]
Sabrina Daiane Gurgel Sarmento[2]
Grayce Louyse Tinoco de Castro[1,3]
Daniele Vieira Dantas[2]
Rodrigo Assis Neves Dantas[2]

[1]Liga Norte Riograndense Contra o Câncer. Natal, Rio Grande do Norte, Brasil.
[2]Universidade Federal do Rio Grande do Norte, Programa de Pós-Graduação em Enfermagem. Natal, Rio Grande do Norte, Brasil.
[3]Serviço de Atendimento Móvel de Urgência. Natal, Rio Grande do Norte, Brasil.

ABSTRACT

Objective: to map the knowledge about SARS-CoV-2 infection in patients with cancer in terms of clinical manifestations, treatment, and prognosis.
Method: a scoping review based on the Joanna Briggs Institute theoretical framework, registered in the Open Science Framework (osf.io/64ems/). A search was carried out in nine databases and virtual libraries in June and July 2020.
Results: twenty-five articles were selected that answered the guiding question, demonstrating that the neoplasm most affected by the infection was the lung, and the main clinical manifestations were fever, cough, dyspnea, diarrhea, and fatigue. Regarding treatment, antivirals and antibiotics were the most mentioned. All articles cite the vulnerability of patients with cancer diagnosed with COVID-19, with a mortality rate of 21-30% in most articles and a prognosis for progression to severe forms of the disease. Still, most patients were cured, although in severe cases they worsened, compared to the general population.
Conclusion: this study demonstrated insecurity in disease treatment due to the variety of medications used and the uncertainty about whether to continue neoplastic treatment during this period.

DESCRIPTORS: Coronavirus infections. Pandemics. Oncology. Neoplasms. Signs and symptoms.

HOW CITED: Silva TTM, Araújo NM, Sarmento SDG, Castro GL, Dantas DV, Dantas RAN. Impact of COVID-19 in patients with cancer: a scoping review. Texto Contexto Enferm [Internet]. 2021 [cited YEAR MONTH DAY]; 30:e20200415. Available from: https://doi.org/10.1590/1980-265X-TCE-2020-0415

IMPACTO DA COVID-19 EM PACIENTES ONCOLÓGICOS: *SCOPING REVIEW*

RESUMO

Objetivo: mapear o conhecimento sobre a infecção pelo SARS-CoV-2 em pacientes oncológicos, em termos de manifestações clínicas, tratamento e prognóstico.
Método: revisão de escopo, com base no referencial teórico do *Joanna Briggs Institute,* registrada na *Open Science Framework (osf.io/64ems/)*. Realizou-se busca em nove bases de dados e bibliotecas virtuais, nos meses de junho e julho de 2020.
Resultados: selecionaram-se 25 estudos que respondiam à questão norteadora, demonstrando que a neoplasia mais acometida pela infecção foi a pulmonar, e as principais manifestações clínicas foram a febre, tosse, dispneia, diarreia e fadiga. No que fala sobre tratamento, os antivirais e antibióticos foram os mais mencionados. Todos os estudos citam a vulnerabilidade de pacientes oncológicos diagnosticados com COVID-19, com uma mortalidade de 21-30% na maioria dos estudos e um prognóstico de evolução para formas graves da doença. Ainda, a maioria dos pacientes evoluiu para a cura, embora nos casos graves a evolução tenha sido para o pior prognóstico, se comparado com a população em geral.
Conclusão: este estudo demonstrou a insegurança no tratamento da doença pela variedade de medicamentos utilizados e a incerteza em continuar ou não o tratamento neoplásico neste período.

DESCRITORES: Infecções por coronavírus. Pandemias. Oncologia. Neoplasias. Sinais e sintomas.

IMPACTO DEL COVID-19 EN PACIENTES COM CÁNCER: REVISIÓN DE ALCANCE

RESUMEN

Objetivo: mapear el conocimiento sobre la infección por SARS-CoV-2 en pacientes con cáncer, en términos de manifestaciones clínicas, tratamiento y pronóstico.
Método: revisión del alcance, basada en el marco teórico del Instituto Joanna Briggs, registrado en el Open Science Framework (osf.io/64ems/). Se realizó una búsqueda en nueve bases de datos y bibliotecas virtuales, en los meses de junio y julio de 2020.
Resultados: se seleccionaron 25 estudios que respondieron a la pregunta orientadora, demostrando que la neoplasia más afectada por la infección fue la pulmonar, y las principales manifestaciones clínicas fueron fiebre, tos, disnea, diarrea y fatiga. En cuanto al tratamiento, los antivirales y los antibióticos fueron los más mencionados. Todos los estudios citan la vulnerabilidad de los pacientes con cáncer diagnosticados con COVID-19, con una tasa de mortalidad del 21-30% en la mayoría de los estudios y un pronóstico de progresión a formas graves de la enfermedad. Aún así, la mayoría de los pacientes evolucionaron para curarse, aunque en los casos graves la evolución fue de peor pronóstico, en comparación con la población general.
Conclusión: este estudio demostró inseguridad en el tratamiento de la enfermedad debido a la variedad de medicamentos utilizados y la incertidumbre sobre si continuar el tratamiento neoplásico durante este período.

DESCRIPTORES: Infecciones por coronavirus. Pandemias. Oncología. Neoplasias. Signos y síntomas.

INTRODUCTION

At first, coronavirus was isolated in 1937, but only in 2002 did it become known as SARS-CoV, when it was responsible for causing severe acute respiratory syndromes (SARS).[1–4]

However, 18 years after the SARS-CoV epidemic, the first cases of COVID-19 (Coronavirus Disease 2019) were identified, caused by a new coronavirus, SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2), originated in Wuhan, Hubei, China.[1–4]

The cases spread rapidly across the world, initially on the Asian continent and then reaching other countries and continents. On January 26, 2020, the first case was registered in Brazil.[2,3] The global spread made the World Health Organization (WHO) declare the COVID-19 pandemic, configuring itself as a Public Health Emergency of International Concern.[5–7]

The most frequent symptoms are fever, headache, diarrhea, muscle pain, dry cough, anosmia, ageusia and, in more severe cases, dyspnea and/or respiratory distress, which can lead to death.[4] The worst prognosis of the disease is reported in the literature as associated with advanced age, male people, history of smoking and the presence of comorbidities, including cancer, thus being more susceptible to serious complications of COVID-19, with progression to multiple organ dysfunction syndrome.[3–4]

Knowing this, cancer organizations and authorities have made progress in developing guidelines and recommendations for cancer treatment in patients during the pandemic, since it is a group of diseases that increases its prevalence annually. Patients with cancer can often experience nausea, vomiting, diarrhea, constipation, fatigue, dyspnea, and pain, which makes the diagnosis of COVID-19 difficult, since several patients with cancer have these symptoms due to complications due to antineoplastic treatment or due to particular conditions of the neoplasm itself.[7–9]

A study conducted this year makes it clear that the outbreak of COVID-19 requires immediate action in cancer practice. These patients have a high risk of mortality (28.6% versus 5.3% of the general population) and are more susceptible to serious events of infection by the virus, probably due to immunosuppression by treatment and by the neoplasm itself.[8–9]

Even with these data, since COVID-19 is a newly discovered pathology, there is still little literature that addresses individuals with cancer infected by SARS-CoV-2 with regard to signs and symptoms, the treatment chosen and how is the prognosis after infection. Thus, the study is justified because it is essential to obtain scientific knowledge that can be applied in practice as a way of preparing health professionals to deal with COVID-19 in patients with cancer in a safer and more comprehensive way.

Just as we emphasize the importance for public health, considering the pandemic character and the magnitude of the issue worldwide, this study may have significant importance in the foundation for developing effective guidelines and protocols for COVID-19 treatment.

The impact can be defined as a decisive influence in some event; therefore, although the pandemic has rapid consequences for the entire world population, it is noticeable that some groups with pre-existing fragile conditions are more vulnerable to the repercussions promoted by the COVID-19 pandemic.

In this sense, the present study aims to map the knowledge about SARS-CoV-2 infection in patients with cancer, in terms of clinical manifestations, treatment and prognosis.

METHOD

This is a scoping review about the impact of COVID-19 on patients with cancer. The study was based on the Joanna Briggs Institute (JBI) theoretical framework.[10] It was registered in the Open Science Framework (OSF) (osf.io/64ems/) and adopted the recommendation of the protocol established by the PRISMA Extension for Scoping Review (PRISMA-ScR)[11] for writing and review. OSF is an online tool that promotes workflows for researchers, promoting improvements in the practices of reproducibility, transparency and management of research data.

To formulate the research question, PCC strategy was used, which represents Population, Concept, and Context. Thus, P (Population) - patients with cancer diagnosed with COVID-19; C (Concept) - clinical characteristics, treatment and prognosis; C (Context) - pandemic. In this regard, the following guiding question was raised: what are the characteristics of SARS-CoV-2 infection in patients with cancer, in terms of clinical manifestations, treatment and prognosis?

To identify scoping reviews with a similar objective to this study, a search was conducted in the JBI Clinical Online Network of Evidence for Care and Therapeutics (COnNECT +), Database of Abstracts of Reviews of Effects (DARE), The Cochrane Library and International Prospective Register of Ongoing Systematic Reviews (PROSPERO). The results pointed to the absence of scoping reviews on the theme.

For the collection of publications for this study, firstly, publications were identified in the data sources; subsequently, a reverse search was carried out, in which publications were found in the references of the publications collected in the first and second phases, and which had not been previously collected.

The following descriptors indexed to MESH were used for search: “Coronavirus”, “Coronavirus Infections”, “Signs and symptoms”, “Drug Therapy”, “Therapeutics”, “Prognosis” and “Medical Oncology”, as well as the keywords “Oncological patients” and “COVID-19”, in addition to using the Boolean operators “AND” and “OR”, as shown in Chart 1.

Chart 1 – Descriptors and keywords used for search. Natal, RN, Brazil, 2020.

PCC	MESH/DeCS		Keywords
Population	Medical Oncology/*Oncologia*	**OR**	Oncological patients
	AND		
Concept	Signs and symptoms/*Sinais e Sintomas* **OR** Therapeutics/*Terapêutica* **OR** Prognosis/*Prognóstico*		
	AND		
Context	Coronavirus/*Coronavírus* **OR** Pandemics/*Pandemias*	**OR**	COVID-19

From the access to the Journal Portal of the Coordination for the Improvement of Higher Education Personnel (CAPES - *Coordenação de Aperfeiçoamento de Pessoal de Nível Superior*) and the Virtual Health Library, nine data sources were used: 1. Web of Science, 2. Latin American & Caribbean Literature in Health Sciences (LILACS), 3. Scopus, 4. Medical Literature Analysis and Retrieval System Online (MEDLINE), 5. Cumulative Index to Nursing and Allied Health Literature (CINAHL), 6. ScienceDirect, 7. Scientific Electronic Library Online (SciELO), 8. Cochrane Library, 9. Wiley Online Library, 10. Catalog of Theses and Dissertations (CAPES - *Catálogo de Teses e Dissertações*) and 11. Google Scholar, considering the importance of finding all the available articles related to the subject.

Chart 2 addresses the search syntax used in data sources that were used for search. It is worth mentioning that, in the second phase, search was carried out on Google Scholar.

Chart 2 – Search syntax in data sources. Natal, RN, Brazil, 2020.

Data source	Syntax adopted
Web of Science	TS: (Medical Oncology OR Oncological patients) AND TS: (Signs and symptoms OR Therapeutics OR Prognosis) AND TS: (Coronavirus OR COVID-19 OR Pandemics)
LILACS*	Medical Oncology [Words] OR Oncological patients [Words] AND Signs and symptoms [Words] OR Therapeutics [Words] OR Prognosis [Words] AND Coronavirus [Words] OR COVID-19 [Words] or Pandemics [Words]
Scopus†	(TITLE-ABS-KEY (Medical Oncology OR Oncological patients) AND TITLE-ABS-KEY (Signs and symptoms OR Therapeutics OR Prognosis)) AND (TITLE-ABS-KEY (Coronavirus OR COVID-19 OR Pandemics))
MEDLINE‡	(“Medical Oncology” [All Fields] OR “Oncological patients” [All Fields]) AND (“Signs and symptoms” [All Fields] OR “Therapeutics” [All Fields] OR “Prognosis” [All Fields]) AND (“Coronavirus” [All Fields] OR “COVID-19” [All Fields] OR “Pandemics” [All Fields])
CINAHL§	(Medical Oncology OR Oncological patients) AND (Signs and symptoms OR Therapeutics OR Prognosis) AND (Coronavirus OR COVID-19 OR Pandemics)
Science Direct	(SU (Medical Oncology OR Oncological patients)) AND (SU (Signs and symptoms OR Therapeutics OR Prognosis)) AND (SU (Coronavirus OR COVID-19 OR Pandemics))
SciELO‖	(*”Medical Oncology” OR “Oncological patients”) AND (“Signs and symptoms” OR “Therapeutics” OR “Prognosis”) AND (“Coronavirus” OR “COVID-19” OR “Pandemics”)
Cochrane Library	(Medical Oncology OR (Oncological patients)) AND (Signs and symptoms OR (Therapeutics OR (Prognosis)) AND (Coronavirus OR (COVID-19) OR (Pandemics))
Wiley¶	(“Medical Oncology” OR “Oncological patients”) AND (“Signs and symptoms” OR “Therapeutics” OR “Prognosis”) AND (“Coronavirus” OR “COVID-19” OR “Pandemics”)
Catalog of Theses and Dissertations (CAPES)	(“Medical Oncology” OR “Oncological patients”) AND (“Signs and symptoms” OR “Therapeutics” OR “Prognosis”) AND (“Coronavirus” OR “COVID-19” OR “Pandemics”)
Google Scholar	(“Medical Oncology” OR “Oncological patients”) AND (“Signs and symptoms” OR “Therapeutics” OR “Prognosis”) AND (“Coronavirus” OR “COVID-19” OR “Pandemics”)

Note: *LILACS: Latin American & Caribbean Literature on Health Sciences; †Scopus: Elsevier’s SCOPUS; ‡MEDLINE: Medical Literature Analysis and Retrieval System Online; §CINAHL: Cumulative Index of Nursing and Allied Health; ‖SciELO: Scientific Electronic Library Online; ¶Wiley: Wiley Online Library.

To guide and organize the data collection, a search protocol was created containing the study theme, the research question, the objective, the data sources, the intersections, the inclusion and exclusion criteria. Articles available in the data sources used that addressed the theme, accessible in full and produced in the last ten years, in English, Portuguese or Spanish were included. Opinion articles, letters to the editor and editorials were excluded.

The ClinicalKey platform was used to select articles that did not have free access through CAPES or the Virtual Health Library (VHL). The platform, developed by Elsevier is considered a virtual medical library, with approximately 25 articles inserted per second, and allows free access to books, journals, and guidelines.

Article screening was carried out by two researchers, independently, after reading titles and abstracts, and, under any incongruity during the selection process of the articles, a third researcher was consulted.

It should be noted that, after selecting the articles, the data extraction aimed to include relevant data to obtain the results expected by the scoping review. For this, study data were collected using a structured form with data source, study title, country, language, author and year of publication, level of evidence and degree of recommendation, main results, methodology, type of approach, population and sample, signs and symptoms, associated comorbidities, therapy and mortality rate.

Regarding the classification of articles according to level of evidence and degree of recommendation, the guidelines established by the Oxford Center for Evidence-based Medicine were followed,[12] which recommend that the lower the number, the greater the level of evidence of the study. Still, the degree of recommendation “A” is considered the one with the highest recommendation and “D”, the one with the lowest.

Subsequently, the data extracted from the included articles were organized and presented in chart formatting, aiming at a clear conformation and that the information can be related to the objectives and issues addressed in this study.

RESULTS

The initial data survey obtained 3,192,372 papers (513,887 on Web of Science; 65 on LILACS; 468 on Scopus;59,369 on MEDLINE;959,100 on CINAHL;1,619,060 on Science Direct; 20 on SciElO; two on Cochrane; 297 on Wiley; four on Theses and Dissertations platform;40,100 on Google Scholar). After applying the filter for publications in the last ten years,1,665,551 were analyzed from reading titles and abstracts.

After reading all titles and abstracts, 119 articles were selected, of which 25 were excluded by duplicity. In this way, 94 proceeded to read the full text. Of the 94 articles read in full, 69 were excluded for not responding to the objectives of the study, and 25 articles were included for this review, as shown in Figure 1. All articles were published in 2020, with ten articles conducted in China, four in the USA, four in Spain, three in Italy, one in the UK, one in Japan, one in France and one in France and one in Italy, the United Kingdom and Spain. Moreover, 18 articles had evidence level 2B and seven articles obtained evidence level 3A, and the 25 articles with recommendation grade B, as shown in Chart 3.

Chart 4 exposes the synthesis of data extracted from the 25 records selected for this review, according to type of cancer, associated comorbidities, clinical manifestations and mortality rate of COVID-19 in patients with cancer. The second column refers to articles addressing the theme referring to the first column, which are identified using Chart 3 ID. Also, in the third column, we have how many articles (number and percentage) cited the topic addressed.

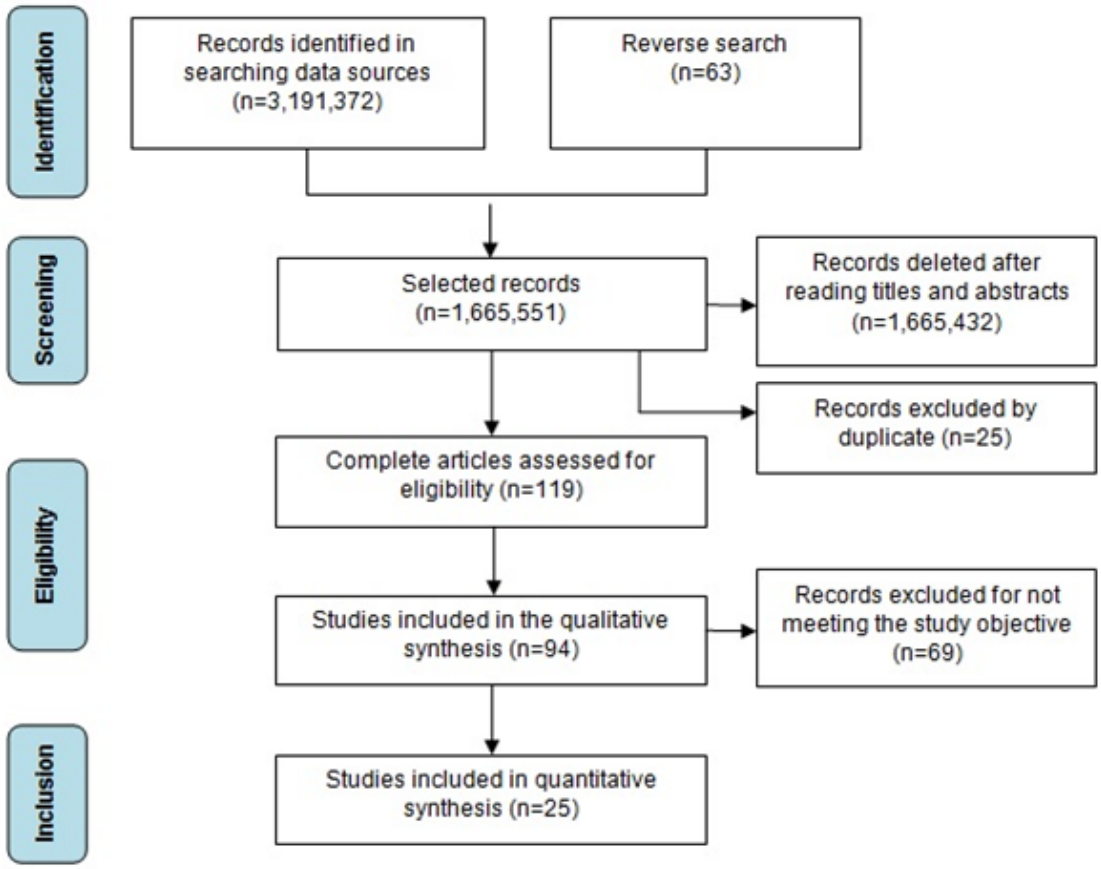

Figure 1 – Flow diagram according to PRISMA-ScR guidelines (adapted). Natal, RN, Brazil, 2020.

Chart 3 – Characterization of publications according to title, year of publication, country of origin, data source, level of evidence and degree of recommendation of articles included in the scoping review. Natal, RN, Brazil, 2020. (n = 25)

ID	Title	Country Year	Data source	Study sample	Level of evidence/ Degree of recommendation
A1	High mortality rate in patients with cancer with symptoms of COVID-19 with or without detectable SARS-COV-2 on RT-PCR[13]	France 2020	Web of Science	302	Cohort study 2B/B
A2	Patients with Cancer Appear More Vulnerable to SARS-CoV-2: A Multicenter Study during the COVID-19 Outbreak[14]	China 2020	Web of Science	105	Cohort study 2B/B
A3	COVID-19 in patients with thoracic malignancies (TERAVOLT): first results of an international, registry-based, cohort study[15]	Italy 2020	Web of Science	200	Cohort study 2B/B
A4	COVID-19 mortality in patients with cancer on chemotherapy or other anticancer treatments: a prospective cohort study[16]	United Kingdom 2020	Web of Science	800	Cohort study 2B/B

Chart 3 – Cont.

ID	Title	Country Year	Data source	Study sample	Level of evidence/ Degree of recommendation
A5	Case Fatality Rate of Patients with cancer with COVID-19 in a New York Hospital System[17]	USA* 2020	Web of Science	218	Cohort study 2B/B
A6	Clinical characteristics and risk factors associated with COVID-19 disease severity in patients with cancer in Wuhan, China: a multicentre, retrospective, cohort study[18]	China 2020	Web of Science	232	Cohort study 2B/B
A7	Clinical characteristics, outcomes, and risk factors for mortality in patients with cancer and COVID-19 in Hubei, China: a multicentre, retrospective, cohort study[19]	China 2020	Web of Science	205	Cohort study 2B/B
A8	SARS-CoV-2 infection in patients with cancer undergoing active treatment: analysis of clinical features and predictive factors for severe respiratory failure and death[20]	Spain 2020	Web of Science	63	Cohort study 2B/B
A9	Clinical characteristics of COVID-19-infected patients with cancer: a retrospective case study in three hospitals within Wuhan, China [21]	China 2020	Web of Science	28	Cohort study 2B/B
A10	COVID-19 in persons with haematological cancers[22]	China 2020	MEDLINE†	13	Cohort study 2B/B
A11	*Mortalidad por covid-19 en pacientes con cáncer en un hospital de Madrid durante las primeras 3 semanas de epidemic* [23]	Spain 2020	Science Direct	15	Retrospective 3A/B
A12	Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study[24]	USA* 2020	Science Direct	928	Cohort study 2B/B
A13	COVID-19 in patients with lung cancer[25]	USA* 2020	Science Direct	102	Retrospective 3A/B
A14	Determinants of COVID-19 disease severity in patients with cancer[26]	USA* 2020	Science Direct	423	Cohort study 2B/B
A15	Covid-19 and lung cancer: A greater fatality rate [27]	Spain 2020	Science Direct	17	Cohort study 2B/B
A16	Outcomes of Novel Coronavirus Disease 2019 (COVID-19) Infection in 107 Patients with Cancer from Wuhan, China[28]	China 2020	Wiley Online Library	107	Retrospective 3A/B

Chart 3 – Cont.

ID	Title	Country Year	Data source	Study sample	Level of evidence/ Degree of recommendation
A17	Clinical characteristics and outcomes of patients with cancer with COVID-19[29]	China 2020	Wiley Online Library	52	Retrospective 3A/B
A18	Characteristics and outcome of SARS-CoV-2 infection in patients with cancer[30]	China 2020	Google Chrome Scholar	141	Cohort study 2B/B
A19	Infection rate and clinical management of patients with cancer during the COVID-19 pandemic: experience from a tertiary care hospital in northern Italy[31]	Italy 2020	Google Chrome Scholar	81	Retrospective 3A/B
A20	Characteristics and outcomes of coronavirus disease 2019 (COVID-19) patients with cancer: A single-center retrospective observational study in Tokyo, Japan[32]	Japan 2020	Google Chrome Scholar	32	Cohort study 2B/B
A21	Presenting Features and Early Mortality from SARS-CoV-2 Infection in Patients with cancer during the Initial Stage of the COVID-19 Pandemic in EuropA3[3]	Italy Spain 2020	Google Chrome Scholar	204	Cohort study 2B/B
A22	Covid-19 transmission, outcome and associated risk factors in patients with cancer at the first month of the pandemic in a Spanish hospital in Madrid[34]	Spain 2020	Google Chrome Scholar	45	Cohort study 2B/B
A23	Coronavirus disease-2019 in patients with cancer. A report of the first 25 patients with cancer in a western country (Italy)[35]	Italy 2020	Google Chrome Scholar	25	Cohort study 2B/B
A24	Systematic investigations of COVID-19 in 283 patients with cancer[36]	China 2020	Google Chrome Scholar	283	Retrospective 3A/B
A25	A Multicenter Study of Coronavirus Disease 2019 Outcomes of Patients with cancer in Wuhan, China[37]	China 2020	Google Chrome Scholar	67	Retrospective 3A/B

Note: *USA: United States of America; †MEDLINE: Medical Literature Analysis and Retrieval System Online.

Chart 4 – Characterization of publications according to type of cancer, comorbidities, clinical manifestations and mortality rate of COVID-19 in patients with cancer from the articles included in the scoping review. Natal, RN, Brazil, 2020.

Type of cancer	ID of articles	N (%)
Lung	A1[13], A2[14], A3[15], A4[16], A5[17], A7[19], A8[20], A9[21], A11[23], A12[24], A13[25], A14[26], A15[27], A16[28], A17[29], A18[30], A19[31], A20[32], A21[33], A22[34], A23[35], A24[36], A25[37]	23 (92)
Hematologic	A1[13], A2[14], A4[16], A5[17], A7[19], A10[22], A11[23], A12[24], A14[26], A18[30], A20[32], A21[33], A23[35], A24[36]	14 (56)
Breast	A2[14], A4[16], A5[17], A7[19], A8[20], A9[21], A12[24], A14[26], A17[29], A18[30], A19[31], A21[33], A22[34], A24[36]	14 (56)
Gastrointestinal	A2[14], A4[16], A7[19], A8[20], A12[24], A16[28], A17[29], A18[30], A20[32], A21[33], A23[34], A24[36]	12 (48)
Colorectal	A5[17], A7[19], A8[20], A11[23], A14[26], A17[29], A19[31], A20[32], A22[34], A24[36]	10 (40)
Genitourinary	A4[16], A5[17], A11[23], A16[28], A17[29], A18[30], A21[33], A23[35]	8 (32)
Head and neck	A5[17], A7[19], A8[20], A9[21], A16[28], A17[29], A18[30], A21[33]	8 (32)
Prostate	A8[20], A9[21] A11[23], A12[24], A14[26], A17[29], A20[32], A22[34]	8 (32)
Thyroid	A2[14], A7[19], A24[36]	3 (12)
Comorbidities		
SH*	A1[13], A2[14], A3[15], A4[16], A5[17], A6[18], A7[19], A8[20], A9[21], A10[22], A11[23], A13[25], A14[26], A15[27], A16[28], A17[29], A18[30], A19[31], A20[32], A21[33], A22[34], A23[35], A243[6], A25[37]	24 (96)
DM†	A1[13], A2[14], A3[15], A4[16], A5[17], A6[18], A7[19], A8[20], A9[21], A11[23], A13[25], A14[26], A15[27], A16[28], A17[29], A18[30], A19[31], A20[32], A21[33], A22[34], A23[35], A243[6], A25[37]	23 (92)
COPD‡	A1[13], A3[15], A4[16], A5[17], A6[18], A7[19], A8[20], A9[21], A11[23], A13[25], A14[26], A15[27], A16[28], A17[29], A18[30], A20[32], A21[33], A22[34], A23[35], A243[6]	20 (80)
Heart disease	A2[14], A3[15], A4[16], A6[18], A7[19], A8[20], A13[25], A14[26], A16[28], A17[29], A18[30], A20[32], A22[34], A243[6], A25[37]	15 (60)
CKD§	A2[14], A31[5], A5[17], A6[18], A7[19], A8[20], A11[23], A14[26], A15[27], A17[29], A19[31], A21[33], A22[34], A243[6]	14 (56)
Smoking	A1[13], A2[14], A3[15], A6[18], A18[30], A19[31], A21[33], A23[35]	8 (32)
Obesity	A11[23], A12[24], A13[25], A15[27], A19[31]	5 (20)
Clinical manifestations		
Fever	A1[13], A2[14], A3[15], A4[16], A6[18], A7[19], A8[20], A9[21], A10[22], A11[23], A12[24], A13[25], A14[26], A15[27], A16[28], A17[29], A18[30], A19[31], A21[33], A22[34], A23[35], A24[36], A25[37]	23 (92)
Cough	A1[13], A2[14], A3[15], A4[16], A6[18], A8[20], A9[21], A10[22], A11[23], A12[24], A13[25], A14[26], A15[27], A16[28], A17[29], A18[30], A21[33], A22[34], A23[35], A24[36], A25[37]	21 (84)

Chart 4 – Cont.

Type of cancer	ID of articles	N (%)
Dyspnea	A1[13], A3[15], A4[16] A6[18], A7[19], A8[20], A9[21], A10[22], A11[23], A12[24], A13[25], A14[26], A15[27], A16[28], A18[30], A21[33], A22[34], A24[36], A25[37]	19 (76)
Diarrhea	A1[13], A3[15], A4[16] A6[18], A7[19], A8[20], A10[22], A11[23], A13[25], A14[26], A15[27], A16[28], A17[29], A18[30], A21[33], A22[34], A25[37]	17 (68)
Fatigue	A2[14], A3[15], A7[19], A8[20], A9[21], A12[24], A16[28], A17[29], A21[33], A24[36], A25[37]	11 (44)
Myalgia	A2[14], A3[15], A10[22], A11[23], A15[27], A16[28], A17[29], A21[33], A22[34], A25[37]	10 (40)
Nausea and vomiting	A2[14], A4[16], A6[18], A7[19], A13[25], A21[33], A25[37]	7 (28)
Headache	A2[14], A3[15], A6[18], A10[22], A17[29], A18[30], A21[33]	7 (28)
Anosmia and ageusia	A1[13], A3[15], A4[16], A18[30], A21[33]	5 (20)
Treatment		
Antivirals	A2[14], A6[18], A7[19], A8[20], A9[21], A10[22], A11[23], A15[27], A16[28], A17[29], A18[30], A21[33], A22[34], A23[35], A24[36], A25[37]	16 (64)
Antibiotics	A2[14], A6[18], A7[19], A8[20], A9[21], A10[22], A11[23], A12[24], A15[27], A16[28], A17[29], A18[30], A21[33], A22[34], A24[36]	15 (60)
IMV ||	A3[15], A5[17], A6[16], A7[18], A9[21], A10[22], A12[24], A13[25], A14[26], A16[28], A21[33], A24[36], A25[37]	13 (52)
Oxygen therapy	A2[14], A4[16], A6[18], A7[19], A9[21], A10[22], A13[25], A14[26], A17[29], A21[33], A23[35], A25[37]	12 (48)
Non-Invasive	A2[14], A3[15], A7[19], A9[21], A10[22], A17[29], A18[30], A21[33], A22[34], A25[37]	10 (40)
Glucocorticoids	A8[20], A11[23], A12[24], A13[25], A15[27], A16[28], A21[33], A22[34], A23[35]	9 (36)
Chloroquines	A6[18], A7[19], A16[28], A17[29], A25[37]	5 (20)
Mortality rate		
Between 11 - 20 %	A2[14], A7[19], A12[24], A14[26], A18[30], A25[37]	6 (24)
Between 21- 30 %	A1[13], A4[16], A5[17], A6[18], A9[21], A13[25], A17[29], A19[31], A21[33]	9 (36)
Between 31 - 40%	A3[15], A20[32], A24[36]	3 (12)
Between 41% - 50%	A11[23], A22[34]	2 (8)
Higher than 50%	A10[22], A15[27]	2 (8)

Note: *SH: Systemic Hypertension; † DM: Diabetes Mellitus; ‡ COPD: Chronic Obstructive Pulmonary Disease; §CKD: Chronic Kidney Disease; ||IMV: Invasive Mechanical Ventilation.

DISCUSSION

In this scoping review, the impact of COVID-19 on patients with cancer was exposed through the thematic approach in the scientific articles selected from the researched data sources.

In relation to the country where the study was carried out, China hosted the largest number of publications (40%), since the country was the birthplace of the pandemic. There is still a close relationship with the year of publication, with the first case discovered in late 2019 in the same country. The new disease caused an increase in the number of researches due to the potential for spread and severity caused by COVID-19.[14]

Moreover, of the 25 articles included in this review, none had been developed in Brazil. This is justified by the study's own limitation, since the data collection for this investigation took place in the months of June and July 2020. In other words, although the first case in Brazil took place in January, only in March did the greatest actions investigations and control of COVID-19 were initiated, influencing the production of scientific knowledge, added to the time required for data collection, analysis and publication. In spite of this, we have evidenced that fundamental initiatives are carried out on the development of articulated strategies to encourage and offer the necessary support so that all countries can develop research on the theme due to the situation of global calamity and the increasing mortality rate.[13,37]

When related to type of cancer, lung and hematologic cancer are seen as predictors for viral infection. The installed lung disease already promotes impairment of functionality and increased resistance, predisposing to anoxia and rapid evolution of COVID-19. Lung patients with cancer, in general, have other comorbidities (such as COPD or SH) and are mostly smokers. These diseases are risk factors for severe presentations by coronavirus, which, together with lung cancer itself, can limit the lung condition of patients, and a coronavirus pneumonia can bring serious risks to life.[33–34,37]

In hematological involvement, patients experience a decrease in cells responsible for fighting infection, being aggravated by viral infection.[37] Furthermore, using corticosteroids by patients with hematological diseases is common, but also in infectious diseases; however, research has shown that corticosteroids in COVID-19 treatment can cause immunosuppression, which may have a significant impact on the clinical outcome.[35,37]

The Brazilian Guideline for Diagnosis and Treatment of COVID-19 defined that the risk factors for clinical complications are age equal to or above 65 years old, presence of comorbidities (SH, DM, pre-existing lung diseases, cardiovascular diseases, immunosuppression and cancer) and use of corticosteroid therapy and immunosuppressants. Thus, among the analyzed records, the comorbidities most frequently identified were SH and DM. National and international studies[38-39] support this finding, demonstrating that comorbidities such as hypertension and diabetes are related to more severe versions of the disease, increasing the risks related to clinical complications, and making these patients more susceptible to death associated with the infection by COVID-19.

Therefore, it is necessary to understand that oncological individuals are already considered a risk group. This risk is exacerbated by the underlying comorbidities, making them more susceptible to the development of COVID-19 in its most severe form, as they already compromise the functions of their organism, requiring early detection and effective prevention and treatment measures.[23,29]

Considering the clinical manifestations, 92% of the studies included in the research pointed out fever as the main symptom presented in patients, characterizing the inflammation caused by the disease. This was a complicating symptom for the diagnosis of COVID-19, since many patients with cancer have fever after treatment or even due to neoplastic complications.[22,23,29] As a result, especially in patients with lung cancer, epidemiological data and clinical history correlated with laboratory and

imaging tests should be applied in cases of symptoms, making it possible to properly and carefully identify COVID-19 in neoplastic patients.[40]

Regarding COVID-19 treatment, we highlight that all studies included in this research address using prescription drugs in the context of COVID-19 diagnoses, not being medicines previously used for other disorders or comorbidities. Antivirals are the most widely used drugs, however, with percentages ranging from 7-100%[29,30], explained by the availability of studies so far, since research needs time to be developed according to protocols and safely. Thus, we reinforce that scientific evidence needs to be developed regarding the use of these drugs, in order to better understand the efficacy and safety of antivirals in patients with cancer. However, evidence has shown that early treatment with antivirals can reduce the incidence of severe and critical cases.[40–42]

However, caution and direct observation of these patients are necessary, as there are reports of the development of gastrointestinal symptoms, such as abdominal pain and diarrhea, due to viral infections directly in the intestinal mucosa or the use of antiviral drugs, which can cause bacterial translocation and severe secondary infections. Thus, the importance of adequate monitoring of drug therapy used in these patients is reinforced, as well as the correct use of modulators of the intestinal microbiota and adequate nutritional support.[40–42]

Treatment with antibiotic therapy demonstrates elevated uses in patients with cancer diagnosed with COVID-19, ranging from 70-100%.[20–22] However, manuals clarify that antibiotics are not recommended as a means of preventing bacterial infections in patients with mild or moderate degrees of the disease, and their use in critically ill patients, especially those on IMV, is indicated, but should also be carefully assessed according to clinical conditions of each individual, being recommended in severe acute respiratory syndromes or when the thoracic image presents deterioration and/or pulmonary impairment.[22,23]

In a study carried out in Spain[34], in patients with cancer diagnosed with COVID-19, with a sample of 45 patients, the mortality rate was 42%, worth noting that, in this study, all patients used hydroxychloroquine. Thus, we show that the use of chloroquine and hydroxychloroquine for patients undergoing treatment for COVID-19 is still under analysis, and there is no consensus between researchers and health professionals, since most studies are in vitro and clinical studies have small samples, methodological limitations or are still under development. Therefore, although some initial studies suggest beneficial effects with the use of these medications, there is still insufficient data to state that they should be used routinely.[22–23,40–42]

Regarding treatment with oxygen therapy, we observed that patients who do not have a current history of cancer use therapy in approximately 42% of cases, as explained in a recent meta-analysis[19]. Meanwhile, studies with patients with cancer reported an oxygen use rate above the incidence for patients without cancer, 73%19,29, 76%22, 78%.[21] We must highlight that factors can influence the high rates of need for oxygen therapy, since cancer is predominantly a disease of elderly people, and cancer is not an isolated influence in these data.[19]

Furthermore, in a cohort study carried out in China[9], involving 1,590 individuals diagnosed with COVID-19, of which 18 had neoplasia, it was observed that these patients showed a higher risk of developing serious adverse events, such as the need for invasive mechanical ventilation, in comparison with cancer-free patients: 39% versus 8%, respectively. Scientific evidence indicates that the average number of non-patients with cancer submitted to IMV is approximately 2.5%, while studies with patients with cancer report using IMV with percentages up to 15 times higher: 18%[36], 20%[15] and 35%.[21]

Concerning mortality rate, when comparing the group of patients without cancer, the average time from the onset of symptoms to death was 21 days, while in patients with cancer, this average

varied between 4 and 12 days. We understand that this is due to a sum of conditions, such as advanced age, the various side effects resulting from treatment, associated comorbidities, the performance and status of patients with cancer, and the existing immunosuppression itself, which makes it difficult to identify the signs and symptoms infection, considering the deficient immune response in these patients.[16,20] Moreover, studies confirm that the mortality rate of these patients ranged from 28%.[21]

There is a variation in studies on the mortality rate of this population from 18% to 61%.[22,30] Metastatic neoplasms proportionally increase this statistic. Studies still cite that there is a difficulty in isolating the factor that leads to the prognosis of patients with cancer with COVID-19, since many have advanced neoplasms, not only being SAR-CoV-2 infection a factor for a poor prognosis, but an additional factor to the neoplasia accompanied.

Furthermore, the fact that antitumor treatment is ongoing may increase the likelihood of developing serious events, as shown by studies in which treatment with myelosuppressive chemotherapy increases the risk of reaching the severe form of COVID-19.[32,43]

Reflections are being developed in the current scenario of the pandemic caused by Covid-19, as health centers have directed all their efforts to fight the pandemic, causing a sharp drop in cancer diagnoses; however, there is no reason to believe that the actual incidence of cancer has fallen. In many hospitals, elective surgery to remove a newly detected tumor is being postponed, and in other cases, some patients are receiving less intense chemotherapy and/or radiation. Undiagnosed cancers will still surface eventually, but at a more advanced stage and with worse prognosis.[28,32,35]

In addition to clinical care, the COVID-19 pandemic caused an unprecedented disruption, across the scientific community, to cancer research, closing many laboratories and slowing down carrying out clinical trials related to cancer. The scientific community must ensure that this interval is only momentary, as testing is the most effective way to make progress in developing new cancer therapies.[28–30]

However, we realize that studies available in literature do not yet provide detailed information on the proper management of patients with cancer diagnosed with COVID-19. Other limitations were the lack of studies that discussed the type of diagnostic approach for COVID-19, as well as the findings in laboratory and imaging tests in patients with suspected or diagnosed COVID-19.

In short, the results of this scoping review have enabled, worldwide, to map the current studies on the subject, providing professionals in the field with an initial understanding of the influence of COVID-19 in patients with cancer. It is believed that research such as these can assist and support the development of well-structured protocols that guide professionals in the diagnosis, treatment and prevention of the disease in this public, in addition to other research in the field.

CONCLUSION

In view of analysis of all articles included in this research, it is evident that the characteristics presented by SARS-CoV-2 infection in patients with cancer are mostly patients with lung, followed by hematology, and breast cancer. They had SH and DM as their main comorbidities, and their most common clinical manifestations in the articles were fever, cough and dyspnea, characterizing an inflammatory disease of the respiratory tract.

There are still divergences in literature on the treatment used, as it is a new disease and patients with cancer are already weakened by neoplastic treatment. Thus, the most used were still antivirals and antibiotics, with more use of IMV intervention, compared to the general population. It has led to a poor prognosis, as patients with cancer are more likely to develop the severe form of COVID-19 disease, with a mortality rate between 21-30% in most articles.

Thus, it is in common agreement in international literature that patients with cancer need direct and emerging interventions in the case of confirmation of SARS-CoV-2 infection, and that treatment should be discussed according to its benefits and harms in light of scientific evidence. Therefore, this study brings the need for protocols and more research on oncology, in order to support the teams' approach and interventions towards patients.

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NOTES

CONTRIBUTION OF AUTHORITY

Study design: Silva TTM, Araújo NM, Sarmento SDG, Castro GL, Dantas DV, Dantas RAN.
Coleta de dados: Silva TTM, Araújo NM, Sarmento SDG, Castro GL, Dantas DV, Dantas RAN.
Data analysis and interpretation: Silva TTM, Araújo NM, Sarmento SDG, Castro GL, Dantas DV, Dantas RAN.
Discussion of results: Silva TTM, Araújo NM, Sarmento SDG, Castro GL, Dantas DV, Dantas RAN.
Critical writing and/or content review: Silva TTM, Araújo NM, Sarmento SDG, Castro GL, Dantas DV, Dantas RAN.
Review and approval of the final version: Silva TTM, Araújo NM, Sarmento SDG, Castro GL, Dantas DV, Dantas RAN.

CONFLICTS OF INTEREST

There is no conflict of interest.

EDITORS

HISTORICAL

Received: August 17, 2020.
Approved: October 26, 2020.

CORRESPONDING AUTHOR

Rodrigo Assis Neves Dantas
rodrigoenf@yahoo.com.br