









# Impacts of COVID-19 on cancer patients: a systematic review

## *Impactos da COVID-19 nos pacientes oncológicos: uma revisão sistemática*

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### ABSTRACT

**Introduction:** During the coronavirus pandemic, oncological patients, who are undergoing treatments in which the majority are immunosuppressant, have become a group very susceptible to severe forms of the infection. Therefore, as a form of protection, their going to hospital environments were restricted, delaying diagnosis and compromising the effectiveness of treatments. **Objectives:** This study aims to analyze the scientific about the production of the theme cancer and COVID-19 in order to contribute with informations on the subject. **Methods:** Systematic review of literature using the SciELO, LILACS and PubMed. The following keywords were used: “cancer” AND “COVID-19” according to the Medical Subject Headings (MeSH) and their translation to the Portuguese. Studies in English and Portuguese from inception were included. **Results:** 1,606 studies were screened and 9 were included in the systematic review after using the inclusion and exclusion criterias. Among the central themes addressed by the selected studies are the pandemic impacts in areas of monitoring oncological patients, such as: treatment, telemedicine, reduction of employees in the care of cancer patients, reduction of clinical trials, reduction of financial resources, and psychological support to that population. **Conclusion:** The pandemic directly affected the way of life of this group, which suffered from a reduction in medical care and the resources available to them. Therefore, there is a need to provide more specific care to these patients in such a delicate situation during the pandemic.

**Keywords:** Cancer; COVID-19; Health Impact Assessment.

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## RESUMO

**Introdução:** Com a pandemia de coronavírus os pacientes oncológicos, que estão em tratamentos, nos quais a maioria são imunossupressores, se tornaram um grupo muito suscetível a formas graves da infecção. Logo, como forma de proteção e prevenção, a realização de exames de rastreio no ambiente hospitalar foi restringida, atrasando diversos diagnósticos e comprometendo a eficácia de tratamentos.

**Objetivos:** Analisar a produção científica acerca do tema câncer e COVID-19, a fim de contribuir com informações sobre o assunto. **Métodos:** Revisão sistemática da literatura nas bases de dados SciELO, LILACS e PubMed. Os descritores utilizados foram “câncer” AND “COVID-19” de acordo com o *Medical Subject Headings* (MeSH) e seus equivalentes para a língua portuguesa, conforme os descritores de Ciências da Saúde (DeCS). Foram incluídos artigos originais em inglês e português, sem delimitação temporal. **Resultados:** Foram encontrados 1.606 artigos e, após utilizar os critérios de inclusão e exclusão, nove foram incluídos para análise na revisão. Dentre os temas centrais abordados pelos estudos selecionados estão o impacto da pandemia em algumas áreas de acompanhamento do paciente oncológico, como: tratamento, telemedicina, diminuição de funcionários no atendimento ao paciente com câncer, diminuição dos ensaios clínicos, redução dos recursos financeiros e apoio psicológico a essa população. **Conclusão:** A pandemia afetou diretamente o modo de vida desse grupo, que sofreu com uma redução no atendimento médico e nos recursos dispostos a eles. Portanto, nota-se a necessidade de prestar um cuidado mais específico a esses pacientes em situação tão delicada durante a pandemia.

**Palavras-chave:** Câncer; COVID-19; Avaliação do Impacto na Saúde.

## INTRODUCTION

Coronavirus disease 2019 (COVID-19), caused by an enveloped RNA beta-coronavirus named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), had its first cases described in December 2019 in Wuhan, China and quickly spread around the world, having been named by the World Health Organization (WHO) as a pandemic on March 11, 2020<sup>1</sup>. The severity of the disease ranges from asymptomatic disease to severe acute respiratory syndrome (SRAG) that requires an intensive care unit (ICU) for the support of patients<sup>2</sup>.

Clinical experience has shown that early recognition of infected individuals is crucial. Since disease severity is highly correlated with its prognosis, the essential strategies to improve outcomes remain early detection of high-risk patients and early intervention guided by intensivists. As there are still no effective treatments for COVID-19, mortality reduction is achieved by early and strong intervention to prevent contamination and progression, especially in groups with greater vulnerability, notably elderly patients, those with cardiovascular disease and patients with cancer<sup>3</sup>.

Current epidemiological data show that patients with active cancer or in remission are frequently affected and have a worse evolution when infected with COVID-19<sup>4</sup>. The incidence and mortality are higher in these patients due to systemic immunosuppression, which can be attributed to both antineoplastic treatments (chemotherapy and tumor resection surgeries) as well as the tumor malignancy itself<sup>5</sup>.

In addition to this greater chance of evolution to severe forms, with a faster rate of deterioration and death<sup>6</sup>, cancer patients had to adapt to new treatment routines, with a reduction in outpatient care to reduce the flow of patients in cancer treatment units as a way to reduce the circulation of the virus in this population, in addition to living with the suspension and/or postponement of surgeries and exams (essential for the diagnosis and staging of the disease).

Thus, due to the various losses and challenges faced by cancer patients at this time, this systematic review of the literature aimed to analyze the scientific production on the topic of cancer and COVID-19 in order to contribute with information on the subject.

## METHODS

This review article was prepared according to the items in the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) list<sup>7</sup>. For the literature survey, the PICO approach was used, in which the acronym represents patient (cancer patient undergoing treatment), intervention (coronavirus pandemic), comparison (period before the pandemic), outcome (success and adherence to therapy). A search was carried out in July 2020 in the LILACS (Latin American and Caribbean Literature in Health Sciences), SciELO (Scientific Electronic Library Online) and PubMed databases. The descriptors used were “cancer” and “COVID-19”, according to the Health Sciences Descriptors (DeCS), and their equivalents in English were used, according to the Medical Subject Headings (MeSH). To connect such descriptors, the Boolean operator “AND” was used.

This systematic review included original articles, without time frame, published in English or Portuguese and that responded to the pre-established PICO. Books, book chapters, editorials, experimental reports, studies with a specific type of cancer, correspondence, letters to the editor, comments, opinion articles and guidelines were excluded, as they did not go through a rigorous process of peer review, as occurs in scientific articles.

The selection of studies was made by 5 authors independently and blindly, which met the inclusion and exclusion criteria. Possible differences were resolved by consensus. To analyze the chosen articles, a table was created with the year and place of publication, authors, study design and its main theme (Table 1).

## RESULTS

Initially, 1,606 articles were found in the databases, after eliminating duplicate studies and adapting to the pre-established PICO, 1,451 articles were excluded. Among the 155 evaluated in full text, only 9 met all eligibility criteria and were included in this review (Figure 1).

Among the selected articles, there were five<sup>8-12</sup> systematic literature reviews, two<sup>13,14</sup> epidemiological studies, one<sup>15</sup> prospective cohort, and one<sup>16</sup> retrospective cohort. Data from selected articles are described in Table 1.

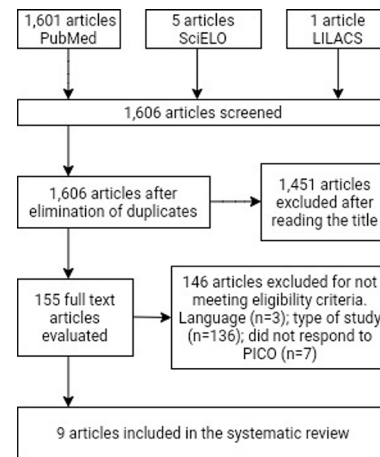


Figure 1. Flowchart of literature review and article selection.

Table 1. General information about the articles included in the study.

Author/year	Country/Continent	Study design	Theme
Gosain et al., 2020 <sup>8</sup>	United States	Literature review	Discusses the challenges of treating cancer patients infected with COVID-19 and proposes approaches to manage this vulnerable population during the pandemic.
Raymond et al., 2020 <sup>9</sup>	Asia and Europe	Literature review	Impact of the COVID-19 outbreak on cancer-related diagnosis, treatment and research, in addition to the impact on the global economy.
Cancarevic et al., 2020 <sup>10</sup>	United States	Literature review	Analyzes the impact of COVID-19 infection in patients with malignant comorbidities.
Denys et al., 2020 <sup>11</sup>	France	Literature review	Discusses the changes and necessary solutions in the organization, safety and management of interventional oncology patients in the context of the COVID-19 pandemic.
Tsamakis et al., 2020 <sup>12</sup>	Greece	Literature review	Discusses the challenges faced by cancer patients and new strategies to treat and care for cancer patients in the pandemic.
Zuliani et al., 2020 <sup>13</sup>	Italy	Epidemiological study	Impact on oncological treatment in a period of 2020 compared to the same period of 2019, observation of both the perception of risks and the acceptance of protective measures by patients and measurement of the COVID-19 infection rate in health professionals.
Ning et al., 2020 <sup>14</sup>	United States	Prospective cohort	Monitoring of cancer patients using RT-PCR tests. Assessment of delay in treatment and clinical results, in addition to employee exposure.
Lou et al., 2020 <sup>15</sup>	United States	Cross-sectional epidemiological study	Research that evaluated the impacts of the COVID-19 pandemic in patients with metastatic and non-metastatic cancer undergoing active treatment or not.
Turaga e Girotra, 2020 <sup>16</sup>	United States	Retrospective cohort	Assesses the impact of postponing elective cancer surgery due to the COVID-19 pandemic on survival and cancer progression in patients.

## DISCUSSION

### TREATMENT

The treatment of cancer patients is very complex and variable, it depends on factors such as the type and stage of the tumor, location, the patient's general health status and possible side effects. Some possible approaches are radiotherapy, chemotherapy, bone marrow transplantation, surgery, among others. However, with the COVID-19 pandemic, such treatments, which mostly require the patient to go to the hospital, were compromised.

The studies analyzed in the review by Gosain et al. (2020)<sup>8</sup> pointed to the practice of reducing chemotherapy sessions as a form of prevention against the new virus. Furthermore, in an attempt to reduce patient visits to hospitals, potentially contaminated sites, there was a shift from parenteral medication to oral medication, when possible. This change in the route of application allowed these people to use a drive-thru system to pick up the medication periodically and thus reduce their exposure to the disease. In addition, it is mentioned that patients with more stable cancer had the onset of chemotherapy postponed, since people who were diagnosed with COVID-19 and had received such medication up to 14 days before infection, had a greater chance of developing severe forms of the disease, when compared to cancer patients who were not on therapy (HR=4,079; 95%CI: 1,086-15,322;  $p=0.037$ )<sup>8</sup>.

Another treatment that has been postponed in this group is bone marrow transplantation<sup>8</sup>. According to Gosain et al. (2020)<sup>8</sup>, this procedure involves the use of immunosuppressive medications, which considerably increases the risk of nosocomial infection, hence the practice of delaying the transplant while the patient is asymptomatic, has been adopted in the analyzed health systems.

Surgery in cancer patients was also identified as a treatment that could be delayed due to the new scenario<sup>8,9,11,16</sup>. The possibility that, during the postoperative period, the patient may need an ICU bed, at a time when these are lacking, is one of the main factors for most of the studies analyzed to bring it as a frequent practice among health services. Furthermore, the delay of up to 60 days in surgical intervention in women with breast cancer did not impact the final outcome of the disease<sup>8</sup>. Turanga and Girotra et al. (2020)<sup>16</sup> on the other hand, found that for 48% cancer types the safe period for postponing surgery would be a maximum of four weeks, whereas for cancers treated with neoadjuvant therapy, this period was increased to eight weeks.

Radiotherapy, in turn, was a treatment reported as more difficult to be interrupted, since it requires daily sessions and without such periodicity, the treatment would be lost<sup>8</sup>. For Gosain et al. (2020)<sup>8</sup> it is necessary to consider the risk *versus* the benefit of maintaining radiotherapy, since patients at more advanced stages of cancer may die after discontinuing the medication. Therefore, for patients undergoing palliative treatment or those for which a break in therapy would not cause extensive damage, it is necessary to consider it. Another point raised is the greater susceptibility to severe forms of coronavirus disease in patients undergoing radiotherapy during the infection, so this increased risk factor should also be considered by the medical team when deciding on maintenance or interruption of treatment<sup>14</sup>.

### TELEMEDICINE

Telemedicine is defined as the use of information and communication technologies in health, making the provision of services related to health care viable. According to Tsamakidis et al. (2020)<sup>12</sup>, it is increasingly being used by oncologists and patients with largely positive experiences for both groups. In this context, this process needs to be accelerated, increasing the accessibility and quality of interaction and data collected.

Before the pandemic, some oncology services were already evaluating the use of telemedicine, mainly with patients in remote or needy areas and for case discussion meetings involving different specialists. With the COVID-19 pandemic, there was an increase in the interest and use of telemedicine by the medical community, in an attempt to stop the spread of the virus through less exposure of patients and medical staff in some health care situations<sup>12</sup>. In this context, on March 19, the Federal Council of Medicine issued a declaration authorizing the practice of telemedicine during the COVID-19 pandemic, in order to continue to provide assistance and monitoring of oncological services. Therefore, physicians can remotely guide and refer patients, monitor and inspect health and disease parameters, and exchange information and opinions among other physicians, as a form of diagnostic assistance<sup>17</sup>.

In addition, a resource similar to telemedicine, which is the implementation of the telephone, mainly for presence screening, was considered accepted by patients and there was almost no interference in the delivery of cancer care<sup>13</sup>. In addition, psychologists and psychiatrists can also use telemedicine to provide psychological support to patients, which can decrease non-essential hospital visits or admissions<sup>12</sup>. Thus, the rapid need to implement virtual care during the COVID-19 pandemic will require further research to help improve the understanding of the effectiveness of e-Health in cancer patients.

### REDUCTION OF EMPLOYEES IN THE CARE OF PATIENTS WITH CANCER

In addition to infection-related outcomes, continued use of rapid diagnoses and aggressive control measures can help mitigate the adverse effects of treatment delays and workforce incapacitation. In a study by Ning et al. (2020)<sup>14</sup>, the use of dual PPE (personal protective equipment) policies decreased viral transmission among high-risk patients and minimized the impact on the workforce, providing additional protection to employees and changing exposures to the low-risk category. Moreover, there was a drop in the post-exposure extended quarantines, and the number of quarantined employees decreased by six times.

Furthermore, according to Zuliani et al. (2020)<sup>13</sup>, the timely and careful adoption of organizational and protective measures, coordinated efforts of all figures involved in modern cancer treatment (physicians, psychologists, nurses, assistants, and support staff) and effective communication strategies to frankly share the risks and necessary sacrifices with patients/caregivers can lead to effective protection of health professionals and cancer patients.



### REDUCTION OF CLINICAL TRIALS

Clinical trials are an extremely important part of advancing medicine and introducing new therapies, and ensuring the safety of participants is critical in any setting. In the midst of the current crisis, the Food Drug and Administration (FDA) has issued guidelines for institutions to protect study participants while administering the product under investigation with an altered monitoring approach<sup>18</sup>.

Clinical trial activities during COVID-19 are being adapted to the changing setting. According to Gosain et al. (2020)<sup>8</sup>, non-therapeutic interventional tests that require the collection of samples in person were suspended until the request to “stay at home” is withdrawn, with specific studies on the current virus being prioritized. This scenario may generate, in the near future, a deficit in the advancement of oncotherapy.

### DECREASE IN FINANCIAL RESOURCES

As a consequence of the COVID-19 outbreak, most countries decided to adopt aggressive prevention measures that are currently heavily impacting the global economy. Both unfavorable economic factors and a high unemployment rate contribute to the increase in cancer cases in a society. World Bank and World Health Organization (WHO) data generated by more than 2 billion people from 1990 to 2010 showed that rising unemployment was significantly associated with an increase in mortality from cancer and all specific cancers<sup>19</sup>.

According to Raymond et al. (2020)<sup>9</sup>, an increase in the mortality rate among cancer patients is expected as a direct consequence of COVID-19 infection and a remote residual effect of the outbreak on the global economy. It is expected that high-performance health systems will be sufficiently resilient to the consequences of the COVID-19 epidemic and may be better able to neutralize the remote impact on cancer mortality.

### PSYCHOLOGICAL SUPPORT FOR PATIENTS WITH CANCER

According to Lou et al. (2020)<sup>15</sup>, rates of generalized anxiety and depression were high among people undergoing active treatment and patients who were not currently in therapy. In addition, most respondents reported that they considered COVID-19 to be a moderate or very serious threat and patients with a history of previously treated cancer or those undergoing active cancer treatment were more likely to report practicing complete social distancing. In this sense, given this current pandemic scenario, psychological support is even more important, being considered an integral tool for cancer treatment. One of the studies reports the importance of social contacts for cancer patients, as they are more likely to develop psychiatric illnesses including anxiety and depression<sup>10</sup>. However, the need for measures of distancing and social isolation caused by the COVID-19 pandemic made this population more vulnerable to these psychological pathologies.

In this sense, the partnership between the patient and the physician is essential at this time. Furthermore, according to Tsamakis et al. (2020)<sup>12</sup>, psychological interventions through additional virtual care tools, such as phone and

video calls, are needed to ensure the quality of life of these patients and support them. It is also worth emphasizing the need for proper multidisciplinary care to help patients and their families/caregivers to obtain information and adequate support to overcome doubts, fears, uncertainties regarding changes, signs and symptoms of the treatment and of the disease<sup>10</sup>.

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### CONCLUSION

The COVID-19 pandemic generated impacts in several areas, directly affecting the population's way of life. The cancer community is highlighted, which was affected by the postponement of treatment such as surgery, radiotherapy, chemotherapy, and bone marrow transplantation, in addition to the reduction in outpatient visits due to the need for a lower flow of people in cancer treatment centers. In addition, this group suffered from the redirection of financial resources to health issues involving the COVID-19 pandemic, which directly impacted cancer-related studies. Also, social isolation brought the aggravation of psychological disorders in cancer patients.

Given all that has been exposed, it is possible to have a general idea of the current panorama of cancer in this COVID-19 scenario and to analyze the advances and challenges that still exist in the management of this disease. Thus, there is a need to provide care to patients suffering from cancer, especially in the midst of this pandemic, as they are immunocompromised and vulnerable to serious results of a SARS-CoV-2 infection, due to the underlying malignancy and various anti-cancer treatments.

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### AUTHOR'S CONTRIBUTION

We describe contributions to the papers using the taxonomy (CRediT) provide above: Conceptualization, Investigation, Methodology, Visualization & Writing - review & editing: Author Amanda Carvalho Girardi Teixeira; Author Arthur Castro de Sá; Author Diogo Augusto Martins Silva; Author Isabelle Lina de Laia Almeida; Author Jaqueline Ferraz Rego; Author João Domingos Barreto Saraiva Barros; Author Marília Rodrigues Moreira; Author Stefan Vilges de Oliveira. Project administration, Supervision & Writing - original draft: Author Amanda Carvalho Girardi Teixeira; Author Arthur Castro de Sá; Author Diogo Augusto Martins Silva; Author Isabelle Lina de Laia Almeida; Author Jaqueline Ferraz Rego; Author João Domingos Barreto Saraiva Barros; Author Marília Rodrigues Moreira; Author Stefan Vilges de Oliveira. Validation & Software: Author Marília Rodrigues Moreira. Resources & Funding acquisition: Not applicable. Data curation & Formal Analysis: Author Marília Rodrigues Moreira.

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