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Review article

Is cancer a prognostic factor for severe COVID-19, especially for breast cancer patients?

Le cancer est-il un facteur pronostique de la COVID-19 sévère, en particulier chez les patientes atteintes d'un cancer du sein ?

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ABSTRACT

The coronavirus disease 2019 (COVID-19) pandemic has caused a global upheaval in our health care system. Our hospital facilities have been subjected to a major influx of patients and the prevention of cross-contamination has been a key issue in the spread of the virus. New recommendations for good hygiene practice and new recommendations for disease management have emerged to limit the spread of the virus and reorganize the provision of care in key services. Many studies have attempted to identify factors that contribute to poor prognosis for COVID-19 infection. Among them, cancer patients, were considered more at risk of developing severe forms of COVID-19. In this article, we provide an overview of the current state of the pandemic as well as new recommendations for disease management that have emerged in oncology and radiation therapy in particular. In this article, we will try to provide some answers through a review of the literature to the question: is cancer a prognostic factor for severe COVID-19?

Mots clés :
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RÉSUMÉ

La pandémie de la *coronavirus disease* 2019 (COVID-19) est à l'origine d'un bouleversement mondial de notre système de santé. Nos structures hospitalières ont été soumises à une affluence majeure de patients et la prévention des contaminations croisées a constitué un enjeu déterminant dans la propagation du virus. Ainsi, de nouvelles recommandations de bonne pratique d'hygiène, ainsi que de nouvelles recommandations de prise en charge des pathologies, ont émergé afin de limiter la propagation du virus et réorganiser l'offre de soins dans les services déterminants. De nombreux travaux ont essayé de mettre en évidence des facteurs de pronostic défavorable de l'infection par le *severe acute respiratory syndrome coronavirus 2* (SARS-CoV-2). Parmi eux, les patients, atteints de cancer, ont été considérés comme plus à risque de voir se développer des formes sévères de la COVID-19. Dans cet article, nous dressons un état des lieux actuels de la pandémie, ainsi que des nouvelles recommandations de prise en charge ayant émergé en oncologie et, plus particulièrement, en radiothérapie. Nous essayerons d'apporter des éléments de réponse à travers une revue de la littérature à la question : le cancer constitue-t-il un facteur de risque de pronostic défavorable en cas d'infection par le SARS-CoV-2 ?

1. Introduction

The coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is responsible for a worldwide pandemic [1]. The first described case was

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in November 2019, in the city of Wuhan, China, and the infection then spread via the flow of people, especially tourists, around the world [2–4]. The World Health Organization (WHO) declared a state of public health emergency on 30 January 2020 [1]. About 200 countries have now been affected by this global health crisis.

SARS-CoV-2 is an RNA virus that mainly infects the airways [5]. It usually remains asymptomatic, but can cause fever (77.4–98.6%), cough (59.4–81.8%), asthenia (38.1–69.6%) and dyspnoea (3.2–55%) [6]. The mean age of hospitalized SARS-CoV-2-infected patients is 47 years, comprising 42% females and 58% males, and the mortality rate ranges between 1 and 3% depending on the country [7]. However, these data may be unreliable due to the disparity between countries in terms of the transparency of published data and the capacity of certain countries to implement optimal screening and management of COVID-19 patients [8,9]. The number of infected people also needs to be expressed in relation to the country's population. For example, in August 2020, in France, there have been 248,158 confirmed cases (0.37% of the population), while, in the United States, there have been 5,850,278 confirmed cases (1.8% of the population) [1].

2. Health care reorganization to limit the spread of COVID-19

This pandemic has prompted reorganization of the health system and the health care provided by health care facilities. New guidelines have emerged to limit the spread of the virus. Learned societies have also issued guidelines for hygiene and barrier measures (separate flows in health care facilities, use of masks and hand sanitizer, etc.), as well as new practices in each medical or surgical [10–17] specialty. New guidelines have also emerged for the chemotherapy management of cancer patients, with a preference for oral chemotherapy rather than intravenous chemotherapy, 3-week regimens rather than weekly regimens, home chemotherapy, and postponement of non-urgent care. Surgery for carcinomas in situ, was postponed for 3 to 6 months and surgery for some invasive cancers were also postponed for up to 6 weeks. Reorganization of radiotherapy has required larger use of shortened hypofractionated regimens as well as temporary suspension of time-consuming irradiation techniques (isocentric lateral decubitus, respiratory gating, etc.), and the use of dedicated machines for COVID-19 patients [18–22]. Health authorities have also encouraged outpatient care and teleconsultation [23]. Several institutions and societies have also published practice guidelines for the management of cancer patients by organ, especially for breast cancer [7,24–29]. De Azambuja et al., on behalf of the European Society for Medical Oncology (ESMO), proposed recommendations for the management of breast cancer patients according to three levels of priority: high priority, intermediate priority, low priority [29]. In the field of breast cancer radiotherapy, high-priority patients correspond to patients in whom treatment cannot be delayed. This group includes patients with factors of poor prognosis (less than 40 years, triple-negative, inflammatory cancer, etc.) or requiring urgent irradiation (spinal cord compression, bleeding, poorly controlled symptoms, etc.).

Intermediate priority patients are patients for whom management can be delayed by up to 6 weeks without affecting the patient's prognosis (less than 65 years, Scarff Bloom and Richardson score [SBR] of 2–3, expression of hormone receptors [HR+]).

Low priority patients correspond to patients for whom management can be delayed until the end of the pandemic (older than 70 years, SBR 1, HR+, without expression of the Human epidermal growth factor receptor [HER2–]).

These new modalities of patients' treatment help to limit spread of the virus by reducing patient flows in radiotherapy departments, allowing decreased patient/patient and physician/patient contact, while observing barrier measures and separate patient flows.

3. Does cancer constitute a factor of poor prognosis in COVID-19 patients?

Many authors have addressed the issue of whether cancer constitutes a risk factor for severe forms of COVID-19 [30–35]. Based on the discordant data on this subject, due to underrepresentation of cancer patients in COVID-19 case series, cancer cannot be considered to be independent risk factor of poor prognosis. However, the literature tends to suggest a non-significant association between cancer and more severe forms of COVID-19 [34,35].

A retrospective study by Dai et al. based on 641 patients, including 105 cancer patients, primarily designed to study the association between cancer and the risk of COVID-19-related complications, found a statistically significant association between the mortality rate of COVID-19 patients and cancer (odds ratio [OR]: 2.34; 95% confidence interval [95% CI]: 1.15–4.77; $P = 0.03$) [32]. This study also found a higher rate of admission in intensive care unit (ICU) (OR: 2.84; 95% CI: 1.59–5.08; $P < 0.01$) and more severe symptoms (OR: 2.79; 95% CI: 1.74–4.41; $P < 0.01$). In subgroup analyses, patients with lung cancer or haematological malignancies and patients receiving immunotherapy, chemotherapy or undergoing surgery presented an excess risk of severe forms of COVID-19. However, no statistically significant relationship with severe forms of COVID-19 was observed in patients treated by radiotherapy.

Other studies did not find any evidence in favour of a higher rate of severe forms of COVID-19 directly related to cancer, but suggested that the comorbidities presented by cancer patients would account for the more severe forms of COVID-19 observed in this population [34,35]. For example, Basse et al. conducted a prospective study of 141 patients, in which the primary objective was to assess the characteristics and risk factors of cancer patients with COVID-19 [35]. Contrary to mostly Chinese retrospective studies [30–33], multivariate analysis of this prospective study did not find any statistically significant increase in severe forms of COVID-19 according to the type or stage of cancer.

However, in line with the results of the main retrospective studies, this study did not show any excess risk of severe forms of COVID-19 in patients with a history of radiotherapy or with radiation-induced sequelae. Like most prospective studies, this study did not find any significant association between cancer and severe forms of COVID-19, but identified an association between comorbidities in cancer patients, especially age, hypertension, WHO performance status, male gender, and obesity and severe forms of COVID-19 [34,35].

At the present time, the literature therefore tends to suggest that the susceptibility of cancer patients to severe forms of COVID-19 is related more to deterioration of the general state of health and comorbidities than to the cancer *per se* or its treatments, especially radiotherapy.

4. Discussion

The COVID-19 pandemic is currently receding in Europe and Asia, but is continuing to progress in the United States and South America. Development of a vaccine constitutes a major health, economic and political challenge. However, the risk of a new wave of the pandemic could overwhelm the capacities of our health system, hence the need to identify prognostic factors for people at risk of severe forms of COVID-19 in order to adapt our management and prevention measures [4–6]. Many retrospective studies have tried to identify risk factors for severe forms of COVID-19. In these studies, cancer appeared to be a factor of poor prognosis.

However, due to underrepresentation of cancer patients in these series, cancer cannot be considered to be an independent prognostic risk factor. Recent prospective studies have shown that severe forms of COVID-19 are not directly associated with cancer and cancer treatments, but can be attributed to the many comorbidities and poor general status of this patient population [14]. As no drug has yet been formally demonstrated to be effective in the treatment of COVID-19, some authors have studied the possibility of using the anti-inflammatory and immunosuppressive effects of low-dose lung irradiation to treat or limit the development of severe forms of COVID-19. If successful, this treatment modality would constitute a real revolution in the management of COVID-19 patients [20].

The next step will be to evaluate the outcome of irradiated COVID-19 positive breast cancer patients treated during the pandemic period; our single centre study is currently running.

5. Conclusion

International collaboration is needed to evaluate the impact of COVID-19 in the population of breast cancer patients and adapt and optimize the protocols of treatment to their comorbidities.

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Disclosure of interest

The authors declare that they have no competing interest.

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