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Editorial article

Coronavirus infection in cancer patients, last update[☆]

Infección por coronavirus en pacientes oncológicos, evidencias a fecha de hoy

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The coronavirus pandemic is redefining routine clinical practice in most medical specialties. Within this need to adapt to the health crisis, two fundamental aspects stand out. On the one hand, the novelty of the change. Medical care in the West has not faced such a health emergency in our times. On the other hand, the speed at which change is occurring. In barely two months we have had to adapt to a constant, daily change in different ways: volume of infected patients, knowledge, and clinical management, etc.

We have to temporarily contextualize the evolution of the pandemic in order to understand and face where we are and where we are going. The first article of scientific relevance regarding the coronavirus was an Original published in the *New England Journal of Medicine* the 28th of February.¹ Furthermore, in the first week of March Spain had only several hundred infected patients and few patients admitted to intensive care units (ICU).² Since then, we have experienced two months of health revolution, with a disproportionate number of infected patients, dead patients, collapsed hospitals, etc. The adaptation and response to the health and humanitarian crisis by Spanish health personnel has been commendable.

If we look at many of the protocols for the diagnosis and treatment of patients with suspected or confirmed coronavirus infection, we observe that most cancer patients are classified as risk patients. It is not usually specified if this risk is of infection, mortality, or both. The question arises as to whether it is real that the cancer history behaves as a risk factor with respect to this new infection, or whether the cancer population is a health population that is usually classified as being at high risk for all pathological processes in general. In the following paper we propose to reflect and investigate what evidence exists to establish such a status and whether or not it is correct.

We must be aware that many of the clinical strategies on which we have based the fight against coronavirus have been empirical, have not yet been studied or published, or come from studies with a low level of evidence. This is mainly the result of the speed at which the pandemic has developed, with many studies still to come.

We have therefore moved, in the two long months since the pandemic arrived in Spain, in a diagnostic-therapeutic management that sought and longed for protocols and facts, but which for the moment has often had to be approached as a syndrome, as symptoms, as pathophysiology. Strategies used in other clinical scenarios perceived as similar to this one have been extrapolated to this new disease. On many occasions we have been skilful in the chosen path, however, on other occasions, we have been surprised day by day with the complex behaviour of a disease whose natural history is being written. Internal medicine specialists, intensive care specialists and emergency doctors are the paradigm of the medical specialist who best responds to clinical situations of this morphology. They are capable of taking leadership in the management of healthcare teams based on their broad spectrum of knowledge and their versatility of action, especially useful in the novelty and constant change that we are experiencing.

In relation to the data we have on the behaviour of the coronavirus pandemic in cancer patients, there are many studies that are being carried out and few already published. However, we already have four retrospective studies that begin to explore the effect of the pandemic on this health population.^{3–7} There are many biases when extrapolating the results of these studies to our population, mainly ethnic (Chinese and American studies) and temporal (retrospective studies and patients admitted in the months of January, February, and March). The summary of the data of these studies also adds the usual bias of the comparison between studies with a non-homogeneous structure, objective, and population, making a cautious interpretation of the results essential. However, a correct and careful analysis of the data already published is of great value in order to guide the clinical and management measures that we are currently adopting and will continue to adopt over the coming months.

The analysis of current knowledge begins with a constructive criticism regarding the definition of the cancer patient. In these four studies analysed and in most of the literature referring to these patients as a specific and homogeneous population, what it means to be a cancer patient is usually not clearly defined. It is not the same to have suffered a solid tumour at some point in life, to have suffered it in the last five years, to be in active treatment, etc. Any clinical-epidemiological study that analyses cancer patients should start from the definition and clear inclusion and exclusion criteria of belonging to this group. Otherwise, we know that it may be a het-

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erogeneous population from which extrapolating some evidence is difficult.

We observe that the percentage of cancer patients admitted with coronavirus infection compared to the total number of patients admitted for this reason is small, between 1%–6% of the total. It is a figure of important value and significance, perhaps the most important that we can extrapolate from these studies. It is a small proportion, which refutes the inclusion of these patients in the risk group for coronavirus, at least as far as the need for hospitalization is concerned. The debate, discussion, and research on why this patient population has this low rate of hospitalization due to coronavirus infection is open. It could be that they are actually suffering fewer infections due to a stricter and earlier social lockdown compared to the general population. It could be that they are seeking less medical help and therefore there are less admissions. It could be that the immunosuppression inherent to cancer and secondary to most of its therapies behaves as a protective factor.

The majority of cancer patients admitted for coronavirus infection were men, between 55%–60%, with a mean age in the seventh decade of life. The most common tumour in hospitalized patients is lung cancer, followed by other highly prevalent tumours such as colon cancer, breast cancer and prostate cancer.

The number of infections classified as hospital-acquired, which represent almost a third of the patients admitted, is important. Patients with hospital-acquired infection rather than community-acquired were categorized as those who had contact with the hospital in the previous weeks, either in the form of hospitalization or by visiting outpatient clinics or day hospitals.

The presence of comorbidities in these patients appeared in approximately 40%, with cardiovascular risk factors being the most common. Cancer patients with severe infection generally have more comorbidity than non-severe patients. The symptomatology has been the usual one observed in the general population with coronavirus infection, highlighting dyspnoea as the main symptom that defines seriously ill patients. The median number of days from the onset of symptoms to hospital admission was six.

The usual laboratory abnormalities can be extrapolated to those observed in the rest of the infected population. However, two important observations stand out. On the one hand, cancer patients have more anaemia and hypoproteinaemia, common laboratory abnormalities in this population. On the other hand, a more serious relationship is found in those patients who show a higher elevation of the enzyme lactate dehydrogenase (LDH) and interleukin-6 (IL-6). These abnormalities are also common and a severity prognostic factor in the non-cancer population.

With regard to the radiological findings, the Chinese population studies show that a large number of patients admitted to the hospital have had a thoracic tomography (CT) scan on admission. Almost all of the cancer patients had radiological abnormalities compatible with viral infection, with more bilateral than unilateral involvement. The debate about this diagnostic approach to hospital admission in China has been important. Given the high sensitivity for the diagnosis of chest CT, and taking into account the situation in China in the first months of the pandemic, it seems logical to have used it together with the microbiological tests that rapidly developed at the beginning of the pandemic.^{1,8}

Regarding the severity of the infection in cancer patients, it is observed that around 20% of the patients required admission to the ICU. The most common complication was respiratory distress, which appears in approximately 30% of patients. Other complications are not commonly observed. Approximately 30% of cancer patients admitted for coronavirus died during admission, after a median of 16 days of admission. Risk factors for the development of serious events include having received anti-tumour treatment the two weeks prior to admission and showing pulmonary consolidations on CT scan on admission.

Whether anti-tumour treatment confers a greater risk of serious infection is under debate. Some studies suggest that cancer patients in active treatment have a higher incidence of serious events than those not in active treatment. Serious event is usually defined in most studies as admission to the ICU, need for mechanical ventilation or death. However, other studies do not show such differences, and the occurrence of serious events in patients with and without active treatment is equivalent. It should be taken into account that those patients under active treatment are in contact with the hospital environment most of the time, and this activity does seem to be clearly related to a higher risk of infection and admission.

Another interesting analysis is the comparison between the cancer and non-cancer populations. In most studies, there are differences in the incidence of serious events in cancer patients compared to non-cancer patients. The low percentage of the population of cancer patients must be taken into account in most studies, limiting the interpretation that can be made of these data. In addition, age stratification is particularly relevant. The risk of intubation, for example, is higher overall in the cancer population than in the general population, but, when stratified by age, is only increased in the 66–80 age group. On the other hand, as far as mortality is concerned, it is not increased overall in cancer patients, but, after adjusting for age, it is increased in the cancer population under 50 years of age. These data must be interpreted with caution. The hypothesis arises that cancer patients may have a lower pulmonary inflammatory response due to the immunosuppression inherent to cancer and its treatments. However, in younger patients, with a low overall mortality rate, the inherent frailty of the cancer patient predisposes them to a higher rate of complications and mortality.

Structuring and adapting routine care in oncology outpatient clinics and day hospitals will be an essential task in the coming months and will have to be justified and guided by the data we are gathering.^{9–13}

We hope that the global pandemic is close to reaching its peak in incidence and severity, and that in a short time the clinical and social situation of all countries will return to normal.

We hope that clinical and therapeutic studies of coronavirus infection will soon emerge, to shed light on the health crisis we are experiencing.

We will soon return to social and health normality.

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