Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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COVID-19 and Cancer in Cuba

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ABSTRACT

The COVID-19 pandemic has called attention to the contribution of comorbidities, including cancer and brought additional challenges to previously existing programs for cancer treatment and control. The COVID-19 pandemic in Cuba was addressed through an integrated all-society action plan that to date has been largely successful with a low incidence of COVID-19 and mortality rates several-fold lower than worldwide averages. Despite downsizing many other health components all oncology services were maintained. Between March 11, when the first case was detected, until July 23, Cuba reported 2,449 cases of COVID-19 that included 28 (1.14%) with a diagnosis of cancer. Distribution among cancer diagnoses did not deviate from that expected according to cancer epidemiology in Cuba. However, although the probability of getting infected with the coronavirus for a cancer patient (0.012%), was not higher than that of the general population (0.020%), 9 of the 28 (32.1%) died, a lethality higher than that of COVID-19 patients without cancer (3.5%) a difference that is statistically significant ($P < .001$). We argue that going forward scientific research on the relationship of aging, inflammation and cancer, including identification of biomarkers and the development of novel therapeutic interventions, should become one of the priorities in the post-COVID agenda of both oncologists and infectious disease scientists.

The COVID-19 pandemic has had a dual impact on the treatment of cancer. First, the higher incidence of COVID lethality in older patients has called attention to the contribution of comorbidities, including cancer. Second, the demands the pandemic has placed on health systems have in turn brought additional challenges to previously existing programs for cancer treatment and control. Since the beginning of the pandemic, the attention of the worldwide scientific community to COVID-19 has produced more than 15,000 manuscripts. A multinational study that reported outcomes in more than 900 patients with a diagnosis of cancer and COVID-19 in Spain, Canada and the USA [1] found a lethality rate above 13% for patients diagnosed with COVID-19 who were concurrently suffering from cancer. The present communication summarizes how the Cuban Health System has addressed the challenge of the simultaneous occurrence of cancer and COVID-19 infection.

Cancer is the second cause of death in Cuba (25% of all deaths) and the leading cause of life-years lost. In 2015, Cuba reported 44,454 new cases of cancer, for a crude incidence rate of 425.6 cases per 100,000 inhabitants in males and 366.7 in females. The burden of cancer follows the demographics of an aging population where more than 60% of the island's inhabitants are more than 60 years old [2]. Since 1992, Cuba has had a National Cancer Program [3], led by the Ministry of Health, which coordinates all components of cancer control, including communication, the participation of individuals, prevention, early diagnosis and treatment. It also oversees resource management and research policy.

The COVID-19 pandemic in Cuba was addressed through an integrated all-society action plan, which was designed and implemented before the first cases appeared. The COVID-19 action plan was managed, on a daily basis, by the top authorities of the government and to date has been largely successful: the transmission of the disease has been controlled and the incidence of COVID-19 and the mortality rates have been kept at levels several-fold lower than worldwide averages. A description of the Cuban strategy and processes for COVID-19 has been recently published [4] available in supplementary material).

A component of the COVID-19 plan consisted of actions targeted to patients with cancer. Despite downsizing many other health

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programs in the epidemic phase, all oncology services were maintained, including oncological surgery, radiotherapy and chemotherapy [5]. Family physicians were requested to update the situation of cancer patients in their area, especially those under active treatment. Hospitalized cancer patients received COVID-19 tests if any respiratory symptoms appeared. Family visits to hospitalized patients were suspended. Inclusion on pivotal active clinical trials continued.

Between March 11, when the first case was detected, until July 23, Cuba reported 2,449 cases of COVID-19. Among them 28 (1.14%) had cancer as a comorbidity. Distribution among cancer diagnoses did not deviate from that expected according to cancer epidemiology in Cuba. Lung cancer was the most frequent cancer diagnosis, with six cases (21.4%), followed by head and neck cancer with four cases (14.3%), and breast cancer with three cases (10.7%). There were also cases two diagnoses each of esophageal, prostate, bladder and ovarian cancer, and one diagnosis of cervical, colon, pancreatic, and kidney cancer, and one case each of leukemia, lymphoma and multiple myeloma. As the epidemic in Cuba to date has been well contained, no statistically significant conclusion can be extracted from these descriptive data.

However, some preliminary hints can be discerned, and these provide insights for future research. The first is that the probability of getting infected with the coronavirus for a cancer patient (0.012%), as calculated according to our best estimates of cancer prevalence, is not higher than that of the general population (0.020%). It could be even slightly lower, which might be expected given the heightened isolation and protection of cancer patients. However, the second observation, one that concerns lethality is less encouraging. Of the 28 patients with a diagnosis of COVID-19 who had a concurrent cancer diagnosis, nine (32.1%) died, a lethality higher than that of COVID-19 patients without cancer (3.5%). This difference in lethality is statistically significant ($P< .001$). Furthermore, it does not appear this effect of cancer on COVID-19 lethality can be explained by age. In the subgroup above 60 years of age, lethality was 13.5% for patients not having cancer (including those with other comorbidities), but 41.2% for COVID-19 patients older than 60 years having a concurrent cancer diagnosis. Cognizant that the small numbers of patients requires us to be careful with regards to any generalizations, our data suggest that a diagnosis of cancer does not lead to a higher probability of getting infected with coronavirus, but does introduce a higher probability of severe evolution and death if infected. The small size of the sample does not allow us to make any adjustments by type of treatment.

Our experience provides some insight that might be considered going forward. The incidence of cancer will continue to increase driven by the aging of the population. Moreover, for a variety of cancer diagnoses, the disease is becoming a more chronic illness, that while not amenable to cure, can often be controlled for several years [6]. Aging, cancer progression and most cancer treatments are associated with systemic inflammation, including an increase in the concentration of several pro-inflammatory cytokines, with infiltration of lymphoid and myeloid cells, whose complex interplay is not yet well understood. Moreover, if zoonotic virus epidemics continue to emerge, driven by increasing population, urbanization and environmental damage, it can be expected that systemic hyper-inflammation will become common in severely ill patients.

Several biotechnology drugs initially developed by Cuban biotechnology industries for cancer indications could be repurposed for the management of COVID-19 or similar infections, a possibility that underscores the fundamental science connections among aging, cancer and inflammation. Three such therapeutics – (i) Biomodulina-T, thymic peptides developed for treatment of immunosenescence [7] and the potentiation of cancer vaccines, (ii) Heberferon, a combination of interferons alpha and gamma developed for cancer [8], and (iii) itolizumab, an anti-CD6 monoclonal antibody, initially developed for lymphoproliferative disorders and autoimmune diseases [9] – were all tested in different phases of the evolution of COVID-19 with encouraging results. We would thus argue that scientific research on the relationship among aging, inflammation and cancer, including identification of biomarkers and the development of novel therapeutic interventions, should become one of the priorities in the post-COVID agenda of both oncologists and infectious disease scientists.

Conflicts of interest

Authors do not have any commercial or financial conflict of interest.

References

[1] Kuderer Nicole M, Choueiri Toni K, Shah Dimpy P, et al. Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study. Lancet 2020;28. May https://doi.org/10.1016/S0140-6736(20)31187-9.
[2] MINSAP. Dirección Nacional de Registros Médicos y Estadística de Salud. Anuario Estadístico de Salud 2019. La Habana: MINSAP; http://files.sld.cu/dne/files/2020/05/Anuario-Electrónico-Inglés-2019-ed-2020.pdf.
[3] Lage A, Romero T. Back and forth between cancer treatment and cancer control programs: insights from the Cuban experience. Semin Oncol 2018;45:12–17.
[4] Díaz-Canel Bermúdez M, Núñez Jover J. Gestión gubernamental y ciencia cubana en el enfrentamiento a la COVID-19. Anales de la Academia de Ciencias de Cuba 2020;10(2):e881.
[5] Actions adopted in Cuba for cáncer patients during the COVID-19 epidemics.: http://instituciones.sld.cu/sicc/2020/07/23/medidas-adoptada...etapa-de-covid19/.
[6] Lage A, Crombet T. Control of Advanced Cancer: The road to chronicity. Int J Environ Res Public Health 2011;8:683–97. doi:10.3390/ijerph8030683.
[7] Saavedra D, et al. Biomodulina T partially restores immunosenescent CD4 and CD8 T cell compartments in the elderly. Exp Gerontol 2019;124:110633. doi:10.1016/j.exger.2019.110633.
[8] Bello-Rivero I, et al. HeberFERON, a new formulation of IFNs with improved pharmacodynamics: perspective for cancer treatment. Semin Oncol 2018;45:27–33.
[9] Hernandez P. Therapeutic targeting of CD6 in autoimmune diseases: a review of Cuban Clinical Studies with the antibodies IOR-T1 and Itolizumab. Curr Drug Targ 2016;17:666–77.