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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Commentary

The effect of COVID-19 pandemic on daily oncology clinical practice

Recently, Boutros et al. (2020) have presented a critical review on the delay in the management of cancer patients during this coronavirus-2019 (COVID-19) era, its possible contributors and the impact on cancer patients' health. In this paper we discuss the effect of COVID-19 pandemic on the medical oncologists activity and on the life of our patients, with a focus on outpatient clinics. A proverb says that "every obstacle is in fact an opportunity": COVID-19 pandemic is certainly an obstacle, but it may force us to reconsider the real efficiency of many oncological activities by balancing the pro and contra, including in the contra also the risk of COVID-19 infection and of the severe complications it may cause. Many professional oncological associations issued directives suggesting to reconsider the real use of several oncological activities, so it may be worth considering some aspects of cancer keeping in mind that cancer is a complex disease which encompasses several entities associated with peculiar biology, clinical history and evolution, stage at presentation and prognosis.

First, we have to consider the real incidence of COVID-19 among cancer patients compared to the general population. Actually, published data are conflicting and not unique (Table 1). The fraction of cancer patients diagnosed with COVID-19 infection ranged from 2.2 % of Zhang L et al. (Zhang et al., 2020) to 30.9 % of Tian et al. (Tian et al., 2020), a pretty remarkable difference that probably originates from different inclusion criteria (to give an example in the Veneto Region with 4.879.133 residents cancer survivors represent around 6 % of the population while the new diagnoses affect only 0.6 % of the population); this percentage is remarkably similar to the reported incidence of a previous cancer diagnosis among residents in the Veneto region tested for COVID-19 (4,789/84,246, 5.7 %), with a slight increase among the SARS-CoV- 2-positive patients (723/9,275, 7.8 %) (Rugge et al., 2020). Males were prevalent in 5 out of 6 case series (Tian et al., 2020; Zhang et al., 2020; Kuderer et al., 2020; Lee et al., 2020; Dai et al., 2020; Yang et al., 2020) [2,3,5–8] (Table 1), median age ranges from 63 years (Yang et al., 2020) to 70 years (Lee et al., 2020). Table 1 reports also the clinical features of COVID-19 patients with cancer based on a literature review on published case studies updated to 31th December 2020, with the following key words: COVID-19, cancer. Second, we have to take into account the impact of the different types of anticancer treatments (immunotherapy, hormonal therapy, targeted therapy and radiotherapy) on the prognosis of COVID-19 infection. An extensive review on the interplay between the huge array of anti-cancer treatments at our disposal, cancer patient's age, comorbidity and outcome of Covid 19 infection have been made (Turnquist et al., 2020). Just to make a brief summary, some Authors investigated risk factors for COVID-19 severity and mortality in cancer patients who received an active treatment up to four weeks before getting infected by COVID-19 but could not find any predictive marker for increased mortality or COVID-19 severity (Lee et al., 2020; Yang et al., 2020). As expected the treatments more frequently administered 14–28 days before COVID-19 infection were chemotherapy alone (in 10.7 % (Zhang et al., 2020) to 17.0 % (Kuderer et al., 2020; Yang et al., 2020) of patients), followed by targeted therapy (in 3.8 % (Dai et al., 2020) to 8.0 % (Kuderer et al., 2020)), radiotherapy (in 1.0 % (Kuderer et al., 2020) to 12.4 % (Dai et al., 2020) and immunotherapy (in 2.0 % (Yang et al., 2020) to 5.7 % (Dai et al., 2020). The exception is the study by Tian et al. (2020), who described the combination of chemo and radiotherapy in 92.0 % of cases (213 patients). These data demonstrate that only a minority of the COVID-19 infected cancer patients were undergoing active cancer treatments within 14–28 days. Thus, since no predictive factors for COVID-19 infection incidence and severity have been identified among cancer patients under active treatment while the great majority of COVID-19 infected cancer patients were not in an active phase of the disease which are the factors, if any, making our patients more susceptible to the infection and to its sequelae. In facts, we are just starting to elucidate the mechanisms underlying the pathogenesis of COVID-19 infection whose severity seems to be characterized more by an exaggerated immune-inflammatory response to the virus, mediated by IL-6, rather than by a direct effect of the virus per se (Turnquist et al., 2020). A recent research has reported that severe cases of COVID-19 tend to have higher neutrophil to lymphocyte ratio (NLR) (Liu et al., 2020). Increasing NLR is a risk factor of mortality not only in infectious diseases but also in malignancy, acute coronary syndrome, intracerebral hemorrhage, polymyositis, and dermatomyostis (Liu et al., 2020). In most cases, chemotherapy leads to a reduction in neutrophils, which are important for the inflammatory response and thus might represent a mechanisms of defense against a severe form of COVID-infection in cancer patients on chemotherapy. On theoretical grounds, immunotherapy with immune-checkpoint blockers might simultaneous boost cytotoxic T lymphocyte (CTL) immune responses against virus-infected and neoplastic cells (Derosa et al., 2020). However, an association of checkpoint inhibitor–based immunotherapy with the aggravation of COVID-19, including increased hospitalization and severe respiratory conditions, was first reported in 31 patients (Robilotti et al., 2020). This negative prognostic link was independent of age, cancer type and other comorbid conditions or co-administered medications such as steroids (Robilotti et al., 2020).

The third topic is the follow-up of cancer patients who are NED (not evidence of the disease). Looking at patients visited during the last month at our outpatient clinics we saw that almost 30 % were over-70 years old and we wonder whether it makes any sense to expose these persons to come to our clinics to bring normal blood exams, normal x-rays and normal ultrasounds. It also remains to be clearly defined the upper limit of patient's age to stop follow-up with its burden of medical examinations and radiological evaluations (annual mammography for women who underwent breast surgery, surveillance colonoscopy after

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colon cancer also considering the discomfort of procedure and preparation. No limit is actually set, but we would suggest that 75 years (similarly to what applies to standard screening) is a reasonable age (Freedman et al., 2021).

The fourth point to consider is cancer screening. Many associations (generally in total good faith) have launched alarming signals on the devastating consequences of reducing these procedures. Some authors have addressed the debate advising to reconsider cancer screening i.e for melanoma (Welch et al., 2021) and breast cancer (Lauby-Secretan et al., 2015). COVID-19 pandemic might stimulate more efficient ways of screening for cervical cancer, such as vaginal self-sampling (Feldman and Haas, 2020), a procedure being implemented in the Veneto Region.

This tragic pandemic might really stimulate a more effective use of health care resources and a kinder, less paternalistic approach to cancer patients that must involve them in a shared decision making regarding the use of chemotherapy, especially in subgroups for which this treatment can be of doubtful utility (eg. ER-positive breast cancer); a preference a the use of neoadjuvant hormonal treatment, instead of NACT where indicated (eg. ER-positive breast cancer (Spring et al., 2020), the indication of shorter adjuvant chemotherapies in colorectal cancer (eg. pT3pN1) (Grothey et al., 2018), the re-evaluation of survival benefit of adjuvant chemotherapy in some cancer subgroups (eg. stage II colon cancer and older patients with stage III colon cancer) (Glimelius and Osterman, 2020) and the re-evaluation of the usefulness of third or subsequent lines in advanced cancers (eg. colorectal, lung). We should also consider that receiving chemotherapy not only means coming to the hospital 1–4 times a month, it also implies going to a laboratory to have blood tests.

Finally we should take into account the need of specific anticancer treatments and what we can consider ancillary activities that are often necessary and important, like implanting a central venous access, undergoing minor surgery like closing a colostomy, or being admitted in hospital for febrile neutropenia.

Actually, what we can do is to maintain a high quality standard in oncological care (from diagnosis to follow-up, moving from active cancer treatments to palliative care) and possibly not to decrease the multidisciplinary cancer team meetings activities (eg. managed remotely), that could suggest a potential delay in patient management (Giuliani and Bonetti, 2020).

Disclosure

No founds were received to support this article.

Research involving human participants and/or animals

No human participants and/or animals were involved.

Informed consent

Not needed (no human participants were involved).

Declaration of Competing Interest

The authors report no declarations of interest.

Table 1
Clinical features of COVID-19 patients with cancer in published real world case studies.

Authors	Kind of study	N° of cancer patients/% towards overall COVID-19 patients	Median age (range)	Males/ Females (%)	Three most frequent type of cancer/%	Tumor stage/%	Type of oncological active treatments (%)	Mortality (%)
Zhang L et al [2]	retrospective	28/2.2	65 (56–70)	60.7/39.3	lung/25.0oesophagus/ 14.3 breast/10.7	I/III/III/ 64.3 IV/35.7	chemotherapy (10.7)[a] targeted therapy (7.1)[a] radiotherapy (3.6)[a] immunotherapy (3.6)[a]	28.6
Tian J et al [3]	retropective[b]	232/30.9	64 (58–69)	51.0/49.0	bladder/14.2 breast/13.4 colorectal/11.6	I/III/III/ 85.0 IV/15.0	chemotherapy or radiotherapy (92.0) targeted therapy or immunotherapy (14.0)	20.0
Yang K [4]	retrospective[b]	248/2.5	63 (56–70)	47.0/53.0	breast (20.0) colorectal (14.0) lung (12.0)	I/III/III/ 73.0 IV/27.0	chemotherapy (17.0)[c] targeted therapy (7.0)[c] radiotherapy (5.0)[c] immunotherapy (2.0)[c]	20.0
Kuderer NM et al [6]	retrospective[b]	928/NR[d]	66 (57–76)	50.0/49.0[e]	breast (21.0) prostate (16.0) gastrointestinal (12.0)	I/III/III/ 45.0[f] IV/43.0[f]	chemotherapy (17.0)[c] endocrine therapy (9.0)[c] targeted therapy (8.0)[c] immunotherapy (4.0)[c] radiotherapy (1.0)[c]	13.0
Lee LYW et al [5]	observational[b]	1044/NR	70 (60–77)	56.9/43.1	breast (13.7) Colorectal (11.9) prostate (10.9) lung (21.0)	NR	NR	35.2
Dai M et al [7]	retrospective[b]	105/19.6	64 (NR)	54.7/45.3	gastrointestinal (12.4) Breast (10.5)	NR	chemotherapy (16.2)[g] targeted therapy (3.8)[c] immunotherapy (5.7)[g] radiotherapy (12.4)[g]	NR

Legend: N°= number; COVID-19= coronavirus disease 2019.
[a] within 14 days of COVID-19 diagnosis; ARDS = acute respiratory distress syndrome; AMI = acute myocardial infarction.
[b] included any type of malignant solid tumors and haematological malignancy; NR = not reported.
[c] within 28 days of COVID-19 diagnosis.
[d] study on cancer patients affected by COVID-19.
[e] 1 % not specified.
[f] the remaining 12.0 % was missing.
[g] within 40 days of COVID-19 diagnosis.

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