

Management of cancer patients during COVID-19 pandemic at developing countries

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Abstract

Cancer patient care requires a multi-disciplinary approach and multiple medical and ethical considerations. Clinical care during a pandemic health crisis requires prioritising the use of resources for patients with a greater chance of survival, especially in developing countries. The coronavirus disease 2019 crisis has generated new challenges given that cancer patients are normally not prioritised for admission in critical care units. Nevertheless, the development of new cancer drugs and novel adjuvant/neoadjuvant protocols has dramatically improved the prognosis of cancer patients, resulting in a more complex decision-making when prioritising intensive care in pandemic times. In this context, it is essential to establish an effective and transparent communication between the oncology team, critical care, and emergency units to make the best decisions, considering the principles of justice and charity. Concurrently, cancer treatment protocols must be adapted to prioritise according to oncologic response and prognosis. Communication technologies are powerful tools to optimise cancer care during pandemics, and we must adapt quickly to this new scenario of clinical care and teaching. In this new challenging pandemic scenario, multi-disciplinary work and effective communication between clinics, technology, science, and ethics is the key to optimising clinical care of cancer patients.

Key words: Cancer; Oncology; Pandemic; COVID-19; SARS-CoV-2

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Core tip: Pandemics such as coronavirus disease 2019 (COVID-19) create new challenges in care of cancer patients, what makes necessary adapt the resources to be used, and consider the risk-benefit balance of cancer therapies. This review establishes a perspective on how COVID-19 pandemic affect cancer patients, and a proposal for managing these patients at developing countries.

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INTRODUCTION

In all of mankind history, humanity has experienced multiple health catastrophes caused by wars and famines. Pandemics have a special place in health catastrophes. The bloodiest were the bubonic plague during the 13th and 14th centuries and the Spanish flu during the 20th century. The coronavirus disease 2019 (COVID-19) pandemic has generated an unprecedented health crisis, challenging all health systems in every country of the world. This pandemic has led to large health expenditures, and the prioritisation of clinical care and resources for patients with the best prognosis. In this context, cancer patients may be displaced from priority of care^[1], making it necessary to create specific protocols for cancer patients. During the last ten years, there has been a revolution in cancer therapies. The development of immunotherapy, molecular targeted therapies, and new techniques of radiotherapy and surgery has led to an improvement in the survival and quality of life of these patients. The improvement in survival of cancer patients has led to more frequent medical complications, frequent admissions to critical care units, and sometimes transitory requirements of artificial life support, with good survival outcomes after critical care. For all these reasons, even in pandemics, it is necessary to consider cancer patients at the time of prioritising care during health crisis.

Historically, cancer has been associated with a poor vital prognosis and quality of life because of its related morbidity and high short-term mortality. In advanced or metastatic stages, cancer was treated with cytotoxic chemotherapy and resulted in low response rates and a large number of adverse events which could often be serious^[2]. In the last decade, the development of immunotherapy (with check point inhibitors) and molecular targeted therapies has generated a revolution in cancer management. The survival of cancer patients including those in metastatic stages has multiplied by several times^[3]. Molecular targeted therapies have been administered in multiple clinical settings *e.g.*, BRAF and MEK inhibitors have tripled survival in metastatic melanomas^[4]. In colorectal cancer, epidermal growth factor receptor (EGFR) inhibitor therapies have doubled overall survival of some patients^[5]. Vascular endothelial growth factor (VEGF) and VEGF-receptor inhibitors have improved survival in multiple types of cancer, such as colorectal, gastric, breast, ovarian, and endometrial cancer, among many others^[6]. The development of tyrosine kinase inhibitors has been applied in multiple types of tumours. The most successful cases have been its administration in renal cell cancer, hepatocellular carcinoma, refractory colorectal cancer, and kidney cancer, among many others^[7].

Immunotherapy has led to a historical revolution in cancer management. The development of check point inhibitors, such as programmed cell death protein 1 (PD-1), PD-1 ligand (PDL-1), and cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) inhibitors has improved the survival of patients with tumours with a high mutational burden^[8]. The first type of tumour where immunotherapy was successfully administered was melanoma, initially with CTLA-4 inhibitors and then with PD-1 inhibitors, significantly improving the survival of these patients^[9]. Currently, combination immunotherapy treatment has made dramatic progress in the long-term survival of these patients^[10]. Other tumours where these therapies have been successfully administered are non-small cell lung cancer, kidney cancer, and more recently, triple-negative metastatic breast cancer^[11], among many others. The

development of these therapies has generated a true revolution in the management of cancer patients. Even when patients have metastatic disease, these new therapies are capable of ostensibly improving the survival and quality of life^[12], while creating other challenges in cancer treatment that need to be solved, such as the management of long-term oncological complications and adverse reactions to these novel therapies.

Despite the fact that patients with metastatic cancer had an indication for being admitted into the intensive care units, it was not so because of their predicted poor prognosis^[13]. The development of new oncology therapies has improved survival in cancer patients, and therefore, increased the probability of developing medical complications requiring admission to the ICU, such as intestinal obstruction, infections, respiratory failure, acute kidney injury, among others, and complications associated with cancer treatment^[14]. It has been proven that patients with even advanced stage of cancer who have control over their disease through oncological treatment, *i.e.*, having stable disease or partial/complete response as well as acute medical morbidities have a similar prognosis as patients without cancer and admitted to the ICU^[15]. There have been multiple reports about the survival of cancer patients hospitalised in the ICU^[16-19]. The change in the prognosis of cancer patients and the improvement of their prognosis after critical care hospitalisation opens the challenging scenario of evaluating the risk-benefit balance of advanced life support and prioritisation of medical resources, especially in a complex scenario as a pandemic. In several countries, the COVID-19 crisis has forced physicians to choose patients to be admitted to ICUs. In this context, some cancer patients, even in the metastatic stage, should also be considered when prioritising critical care^[20].

CANCER PATIENTS IN PANDEMIC

During the last century, there have been major pandemics that have challenged health systems. The A(H1N1) pandemic, Severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) outbreaks previously revealed the challenges that health systems must face in the event of a large-scale pandemic, and this has now become more evident in the COVID-19 pandemic.

Historical aspects

A(H1N1): The A(H1N1) flu was declared on June 11, 2009 by the World Health Organization (WHO) as the first pandemic in the 21st century due to its rapid spread around the world^[21]. The first cases were reported in Mexico as atypical pneumonia in 2009^[22]. Subsequent reports showed a rapid trend towards saturation of critically ill units with patients with respiratory problems^[23-25]. During the pandemic, there was unprecedented coordination of the global medical and public health community to reduce the impact of a problem with potential lethality and morbidity^[23]. It is estimated that the mortality associated with the 2009 influenza pandemic during the first 5 years was 151700-575400 patients as a result of respiratory and cardiovascular deaths^[26], which would be far from the Spanish flu pandemic that is estimated to have caused a mortality of millions of people^[27,28].

Seasonal influenza has had an important impact in cancer patient mortality even before the pandemic. It has been described that they have a ten-times risk of death than the general population^[29]. There is a concern about the outcomes of cancer patients during the pandemic since cancer patients have a higher risk for influenza complications whether on chemotherapy or not such as parenchymal pulmonary compromise, bacterial infection, respiratory insufficiency, and sepsis^[30,31]. Cancer patients with the A(H1N1) flu have similar symptoms as the general population, but tend to have haematological abnormalities as anaemia, neutropenia or leukopenia^[32]. Different clinical series described that patients with solid or haematological tumours had a poor prognosis during the pandemic, such as increased hospitalization, bacterial infection, and death^[33-36]. In fact, it has been described that patients who received chemotherapy in the last month or had neutropenia on admission had fatal outcomes^[33,35]. Other risk factors for worse outcomes were a low albumin level and poor nutritional status^[34], which are very frequent in cancer patients. Another resulting problem from the pandemic was an interruption of chemotherapy^[37].

A potent strategy to avoid infections in the years following the pandemic was periodic immunization of these high-risk patients^[38,39], which was effective in preventing nosocomial outbreaks^[40]. There are lessons following the 2009 influenza pandemic that need to be taken into consideration for cancer patients for next pandemic: It necessary a rapid response and massive diversification of scientific

information in crisis preparation, with the final objectives to ameliorate cancer poor outcomes due to immunosuppression status and lack of access to anti-cancer treatments during time is ongoing the pandemic.

SARS and MERS: SARS and MERS are two major coronavirus outbreaks in the last 20 years prior to the COVID-19 pandemic. The first report of SARS was in the Guangdong province of China in November 2002, and it spread later to Vietnam, Canada, and Hong Kong^[41]. The first reports of MERS was in Saudi Arabia in 2012, and it became an endemic zoonosis in the Middle East^[42]. Both diseases quickly caught the attention of the public health community due to their high mortality rates, and nosocomial transmission to health care workers and patients^[42-44]. They have a similar clinical presentation ranging from no symptoms to pneumonia, and in more severe cases, respiratory failure^[45]. Although both require a large amount of resources in the ICU, there are differences in the severity of both pathologies. It is estimated that 20%-30% of the patients with SARS and 50%-89% of patients with MERS will require ICU hospitalization^[43,45-47]. According to WHO, the MERS case fatality rate was 34% and for SARS 10%^[48,49].

It has been described that the presence of comorbidities, such as cancer increases the risk of poor outcomes in SARS patients^[43], but there exist only few patients with cancer affected by SARS. In the case of MERS, a meta-analysis found that immunosuppressed patients and patients with the human immunodeficiency virus (HIV) have poor clinical outcomes^[50]. In a retrospective analysis, cancer patients showed an 80% admission rate to the ICU and 84% mortality rates. Mortality rates could reach 100% in advanced solid tumours and haematologic neoplasms, but in this study only hospitalised patients were included and the sample size was small (19 patients)^[51]. Despite the high mortality rates of these diseases, it was possible to control their worldwide spread given the rapid action of the authorities to track and isolate contacts^[52]. We theorise that patients with a high risk due to immunosuppression, such as cancer probably do not show worse outcomes due to a low number of cases despite a high severity of both infections. This prevented the discussion of prioritisation of critical care resources for patients with malignancies which is a relevant issue in the times of another coronavirus crisis by SARS coronavirus 2 (SARS-CoV-2).

SARS-CoV-2 pandemic

In December 2019 in Wuhan, Hubei Province, China, rare cases of unknown pneumonia were reported to the local authorities that were related to the seafood and wet animal wholesale market^[53]. Subsequently, epidemiological and molecular data described a novel coronavirus and its genetic material was rapidly identified and described as similar to that detected in bats^[54]. This new virus was renamed recently to SARS-CoV-2 by the International Committee on Taxonomy of Viruses^[55], it was found to be related with SARS (79% similarity) and MERS (50% similarity)^[56,57]. The virus spread rapidly round the world and was declared a new pandemic by WHO on 11 March 2020^[58]. The clinical syndrome associated with SARS-CoV-2 infection was globally denominated COVID-19 (coronavirus disease). The high mortality rates are of public health concern. The estimated global mortality rate is 4.7%, and varies in different countries, *e.g.*, it is as low as 0.7% in Germany and as high as 10.8% in Italy^[59]. Another important preoccupation is the high use of critical care resources in COVID-19 patients. In a Chinese series, 5% to 32% of hospitalised patients required ICU^[60,61] and in an Italian series, 9% of the patients in ICU had a positive test^[62]. The problem of the lack of resources to treat critically ill patients became more obvious when nearly twenty million confirmed COVID-19 cases are registered by WHO (as at August 2020)^[63]. The discussion about the rationalization of critical resources for the care of patients with COVID-19 or other critical diseases during pandemics is a fact^[64-66], and that is undoubtedly affecting to cancer patients.

There are several clinical characteristics that are related to mortality in COVID-19 patients, including old age and the presence of chronic conditions, such as cardiovascular disease, diabetes, chronic respiratory disease, hypertension, and cancer^[67,68]. An estimated prevalence of cancer in a cohort of COVID-19 cases was 2% in a pooled meta-analysis^[69]. It has also been suggested that the incidence of COVID-19 in cancer patients could be greater than in the general population^[70]. Indeed, there is a concern about an immunosuppression status in patients with cancer and outcomes in COVID-19, which may increase due to treatments, such as chemotherapy and radiotherapy^[70]. In addition, there is no clarity about the optimal treatment for patients diagnosed with cancer requiring treatments such as surgery, chemotherapy, and radiotherapy which have been cancelled or rescheduled during this ongoing pandemic^[71]. Clinical symptoms of COVID-19 in cancer patients are similar as that of

the general population. These symptoms are fever, dry cough, fatigue, and dyspnoea, although anaemia and hypoproteinaemia are more frequent in cancer patients^[72]. Reports in Chinese patients have described that cancer patients have a 3.5 times higher risk for the need of ICU beds, mechanical ventilation, or death, compared to patients without cancer^[73,74]. Moreover, patients who have started chemotherapy or undergone surgery have more severe events (ICU, mechanical ventilation, or death)^[74]. Similarly, Zhang *et al*^[72] (2020) described that cancer patients who received oncologic therapies (chemotherapy, targeted therapy, radiotherapy, or immunotherapy) in the last 14 days developed more frequent severe adverse events. This series reported a 28.6% mortality rate in 28 cancer patients. Likewise, Dai *et al*^[75] observed a high mortality rate with the need of ICU and mechanical ventilation in 126 cancer patients compared to a matched sample of COVID-19 patients without cancer. In addition, Yang *et al*^[76] also reported a 20% mortality rate and in its cohorts is described that receiving chemotherapy 4 wk before symptoms onset and male sex are risk factors for fatal outcomes. A Major cohort from Cancer Consortium (CCC19) database include 928 patients with COVID-19, reporting 13% death rate. Also, in this cohort older age, male sex, former smoking, two or more comorbidities, ECOG > 2 and active cancer status are described as risk factors for 30-d mortality. However, contrarily to other cohorts is not observed a worse prognostic with recent anti-cancer treatments^[77]. A special preoccupation has emerged in patients with thoracic malignancies and SARS-CoV-2 infection, an international collaboration The Thoracic Cancers International COVID-19 Collaboration (TERAVOLT) registry has recollected data in these patients showing higher mortality rate (33%). Risk factors for worse outcomes are similar to previous studies, such as more than 65 years old, current or former status, receiving chemotherapy alone and the presence of comorbidities in a univariate analysis, but in a multivariate analysis only smoking status was associated with mortality. Interestingly, admission to ICU was lower than other series, authors suggest a difficulty in ICU admission in the context of a lack of material and human resources^[78].

Recently, a report published by the Gustave Roussy Institute in 137 patients reported that the Eastern Cooperative Oncology Group (ECOG) performance status, cancer type, and prior cancer therapy can predict the risk of clinical worsening or death in cancer patients with COVID-19. The majority of cancer patients had active/metastatic disease (59%), and the remaining (41%) were in remission or had localised disease. The investigators reported that ECOG performance status > 1 (hazard ratio, HR 4.6), patients with hematologic malignancies (HR 2.7), and patients who received chemotherapy for their disease within the past 3 months had a higher risk for poor clinical outcome. Although prior chemotherapy correlated with a greater chance of clinical deterioration, treatment with immunotherapy or targeted agents in the past 3 mo did not^[79]. **Table 1** shows a summary of up-to-date retrospective published studies in cancer patients infected with SARS-CoV-2.

Although there is limited information about outcomes in cancer patients, previous reports suggest a complex scenario. In this line, guidelines and protocols are needed that can decrease the risks in cancer management in these pandemic times.

Cancer therapies during the pandemic

The current COVID-19 pandemic challenges oncologists to profoundly organise oncological care to reduce hospital visits and admissions, and therapy-induced immune-related complications without compromising cancer outcomes. The following section presents relevant information and publications regarding the management of cancer with different oncological therapies in the context of the COVID-19 pandemic, and in **Table 2**, we present a scheme for prioritisation of cancer therapies during pandemic.

Curative therapies: Curative therapies in cancer patients include surgery, adjuvant, and neoadjuvant protocols. Surgery has a pivotal role in the management of cancer, as a diagnostic, curative, and palliative tool. Surgeries are procedures with risks surgical complications, and non-surgical-associated complications (pneumonia, deep venous thromboembolism, respiratory insufficiency, and others), ICU admission, and death. Not all surgeries have the same risk. Breast cancer-related surgeries are associated with a 1.7% risk of readmission^[80], the readmission risk 2 weeks after a radical gastrectomy for gastric cancer was 3%^[81], 12% in lung cancer surgery^[82] and 20% after an oesophagectomy^[83]. Oncology surgeries require a huge amount of material, infrastructure, and human resources in a setting where there is a lack of materials^[1] or they are redistributed for COVID-19-related care. In this global pandemic wherein all cancer patients do not have a similar prognosis or prioritisation for surgery, many centres and professionals are redirected to triage patients. Many of the proposed

Table 1 Retrospective reports about cancer patients with severe acute respiratory syndrome coronavirus 2 infection

Ref.	n ¹	Mean age	Outcomes	Results
Liang <i>et al</i> ^[74] , 2020	18	63	Severe clinical events (ICU admission and mechanical ventilation or death)	Severe clinical events: 39% (7/18 patients) <i>vs</i> 8% (126/1572 patients without cancer) ($P = 0.0003$)
Zhang <i>et al</i> ^[72] , 2020	28	65	Severe clinical events (ICU admission, life-threatening complications or death)	Severe clinical events: 53.6% (15/28 patients). Death rate: 28.6% (8/28 patients)
Dai <i>et al</i> ^[75] , 2020	105	64	Death rate, ICU admission and severe or critical symptom	Death rate: 11.4% (OR 2.34, $P = 0.03$); ICU admission: 19.0% (OR 2.84, $P < 0.01$); Severe or critical symptom: 34.3% (OR 2.79, $P < 0.01$)
Barlesi <i>et al</i> ^[79] , 2020 ²	137	61	ICU admission or death	ICU admission: 11.0% (15/137 patients); Death rate: 14.6% (20/137patients)
Yang <i>et al</i> ^[76] , 2020	205	63	ICU admission or death	ICU admission: 15.0% (30/205 patients); Death rate: 20.0% (40/205 patients)
Kuderer <i>et al</i> ^[77] , 2020	928	66	ICU admission, mechanical ventilation or death	ICU admission: 14.2% (132/928 patients); Mechanical ventilation: 12.5% (116/928 patients); Death rate: 13.0% (121/928patients)
Garassino <i>et al</i> ^[78] , 2020 ³	200	68	ICU admission, mechanical ventilation in hospitalised patient and death in all patients	ICU admission: 8.8% (13/147 patients); Mechanical ventilation: 6.1% (9/147 patients); Death rate: 33.0% (66/200 patients)

¹Patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) confirmed and cancer.

²Results reported at congress, some patient are not discharged at the time of calculate finals outcomes.

³Results from a cohort with thoracic malignancies and SARS-CoV-2 confirmed infection. ICU: Intensive care unit.

triages are based on experience or expert consensus.

Some recommendations have proposed using a general criteria for all types of surgeries, depending on the risk itself, like that proposed by the American College of Surgeons who recommend that high-acuity surgeries in healthy patients should not be postponed unlike intermediate-acuity surgeries in healthy patients and those with a low risk for cancer in whom surgeries could be postponed or they could consider an ambulatory surgery centre^[84]. Moreover, another strategy is considering the stage, previous treatment, and specific tumour site in the choice of the more appropriate treatment for the patients, as is recommended by the Society of Surgical Oncology^[85]. Furthermore, it has also been proposed that the tumour type, natural progression, and short-term aggressiveness should be considered in making the most appropriate decision^[86-90]. The decision to schedule or delay surgery in some centres has been made through the decision of experts (surgeons, oncologists, pathologists, and radiologists) through a video conference triage where cases are discussed considering the patient preference, urgency, local logistic conditions, and other non-surgery treatment options^[89-91].

Adjuvant and neoadjuvant protocols with chemotherapy and/or radiotherapy have a major role in the treatment of many cancers in different stages. Both treatments have adverse effects that can lead to immunosuppression associated with infections^[92]; these should be considered because cancer patients have a higher mortality associated with viral pneumonia due to respiratory viruses, such as parainfluenza or other non-COVID-19 coronaviruses^[93]. Additionally, delaying some therapies with a curative intent may lead to adverse outcomes in cancer patients. A decrease in overall survival has been reported among patients with locally advanced breast cancer who had a delayed adjuvant or neoadjuvant chemotherapy^[94-96]. In stage II-III colon cancer, delaying adjuvant chemotherapy was also found to have a worse overall survival^[97,98]. Similarly, delayed radiotherapy also has deleterious effects. A study showed that delayed radiotherapy initiation has been associated with a higher local recurrence rate in head and neck cancers and breast cancer^[99].

Therefore, it is necessary to compare the potential benefits and risks of delays in therapy initiation to which the patients are exposed during the current pandemic at the time of planning the administration of therapies. The European Society for Medical Oncology (ESMO)^[100] has proposed a 3-tier classification for prioritisation of treatment during the COVID-19 pandemic. The high-priority group comprises patients with vital commitment or who could gain a significant improvement in mortality or quality of life with treatment. The medium-priority group are non-critical patients, but a delay in starting their therapy beyond 6 wk could have consequences. Finally, the low-priority group could be treated after the pandemic since the benefit of treatment is marginal.

Table 2 Proposal for an approach to cancer therapies that should be prioritized in the event of a pandemic

Priority	Clinical scenario	Examples
High	Tumors with high early mortality associated and high response rate to treatment	Advanced germ cell tumors, lymphomas or acute leukemias
	Definitive curative cancer treatments	CRT for head and neck, cervical or anal cancers
Intermediate	Neoadjuvant or adjuvant therapies with high survival benefit	Perioperative ChT for gastric cancer and neoadjuvant CRT for localized rectal cancer. Adjuvant ChT for stage III or high risk stage II colorectal cancer, or stage III melanoma. ChT and RT for high risk breast cancer
	Neoadjuvant or adjuvant indications with modest survival benefit	Neoadjuvant ChT for muscle invasive bladder cancer. Adjuvant ChT for NSCLC, gallbladder and pancreatic cancer or gynecologic malignancies
	Palliative indications with high survival benefit	Immunotherapy for melanoma, NSCLC (with PDL1 > 50%) or high risk kidney cancer. Systemic ChT for metastatic breast or colorectal cancer. Molecular targeted therapy for NSCLC with driver mutation. TKI for GIST or low risk kidney cancer, and ADT and abiraterone or docetaxel for castrate-sensitive prostate cancer
Low	Palliative indications with modest survival benefit	Palliative chemotherapy for upper gastrointestinal cancers. Chemotherapy for gallbladder or pancreatic cancer, SCLC or bladder cancer
	Palliative indications without benefits in terms of overall survival	Second and third line palliative ChT for many solid tumors, as regorafenib for colorectal cancer or ramucirumab and paclitaxel for gastric cancer

CRT: Chemoradiotherapy; ChT: Chemotherapy; NSCLC: Non small cell lung cancer; RT: Radiotherapy; SCLC: Small cell lung cancer; TKI: Tyrosin kinase inhibitors; ADT: Androgen deprivation therapy; PDL1: Programmed death-ligand 1; GIST: Gastrointestinal stromal tumors.

Adoption of these recommendations has been translated to different types and stages of cancer, such as prioritisation of radiotherapy treatment in head and neck cancer^[101] and lung cancer^[102] in this current pandemic by the American Society of Radiation Oncology (ASTRO) and the European Society for Radiotherapy and Oncology (ESTRO). In pandemics, strategies such as triage are necessary. In the categorisation process, multiple factors, such as the type of tumour, stage, comorbidities, short-term progression, local material resources, and alternatives to surgery must be considered and discussed in order to allocate a beneficial treatment to oncology patients.

Non-curative treatments: Non-curative treatments with systemic chemotherapy have a main role in advanced cancer stages and a great impact in the overall survival and quality of life of patients. In recent decades, important advances have taken place in some disseminated diseases with systemic therapies or target therapies for palliative treatment, such as molecular targeted therapy in the presence of some mutations in non-small cell lung cancer^[103], or EGFR and VEGF inhibitors in colorectal cancer^[104]. These systemic treatments with high response rates could be prioritised in some cases of optimal clinical conditions with close clinical follow-up and a careful and transparent risk-benefit analysis with the patient and family. In another group of patients with poor ECOG performance statuses or advanced malignancies with systemic therapies of low effectiveness and high risk of complications, the initiation of

systemic therapy should be evaluated case-by-case. In case of oncologic emergencies, such as spinal compression, hypercalcaemia, severe anaemia, hip fracture, and others according to the ESMO guidelines, these problems represent high priority and require urgent interventions^[100].

Immunotherapy is a common treatment in different malignancies, such as melanoma, non-small cell lung cancer, kidney cancer, triple negative metastatic breast cancer, among many others. A concern with the use of immune checkpoint inhibitors in the COVID-19 era is pneumonitis reported in 2% of patients within 2.5 (0.5-11.5) months of therapy onset^[105], with nonspecific symptoms similar to those of COVID-19 infection^[106]. It has been theorised that a synergic lung injury with COVID-19 and immune checkpoint inhibitor pneumonitis occurs, although there is not enough information to affirm this hypothesis^[107]. Moreover, immunotherapy-related serious infection rate is low. In a series of melanoma and anti-CTLA-4, its incidence is only 7.3%^[108]. However, a recent report in a small sample of patients with COVID-19 on immunotherapy (6 patients) suggested that patients tend to have a high mortality. ESMO^[100] recommends a double dosing of anti-PD-1 drugs with a double interval for reducing visit exposition in patients with lung cancer and melanoma.

CONCLUSION

The COVID-19 pandemic has created an unprecedented change in the lives of people worldwide, especially in patients with chronic diseases. Cancer patients are an especially vulnerable population, because cancer has been associated with high mortality, and its treatment is associated with multiple and frequent adverse events. In parallel, COVID-19 has led to a high occupancy rate of ICUs, and patients with metastatic cancer are not a priority at the time of admission to these units. However, new cancer therapies have led to a radical change as cancer patients have a longer survival, treatments are better tolerated, and patients have better outcomes after hospitalisation in the ICU. This situation has led to the need for the establishment of specific care protocols for cancer patients in these current times.

First, it is imperative to define which cancer treatments should be prioritised in pandemic times. The NCCN^[109] and ESMO^[100] guidelines propose treatment prioritisation in tumours with high early mortality and high response rate to chemotherapy or radiotherapy, such as haematologic malignancies and advanced testicular cancer. In these cases, the early start of cancer therapy can be curative; therefore, these therapies should not be delayed. Intermediate priority cases are neoadjuvant and adjuvant treatments with a high response rate, such as perioperative chemotherapy for gastric cancer, adjuvant treatment for stage III or high-risk stage II colon cancer, or high-risk breast cancer, among others. Systemic therapies in advanced diseases [*e.g.*, immunotherapy for melanoma and high risk kidney cancer, and target therapy in non-small cell lung cancer with driver mutation (EGFR, ALK or ROS1 mutation)] with high response rates are also at this priority level. The initiation of these therapies should be planned by evaluating the risk-benefit balance. It is important to consider the start time especially in adjuvant treatments, which should not be longer than 6-8 wk after surgery. Lastly, we have cancer therapies with low priority of initiation during this pandemic. These therapies have a low response rate and high associated toxicity, such as chemotherapy for upper gastrointestinal malignancies (gastric, gallbladder, or pancreas), metastatic bladder cancer, small cell lung cancer, triple negative breast cancer, among many others. The initiation of second or third-line cancer therapies after progression to a first line of cancer therapy can also be considered at this priority level (*i.e.*, regorafenib for colorectal cancer, ramucirumab and paclitaxel for gastric cancer, among others), and the risk-benefit balance of its initiation during the pandemic should be carefully evaluated. Table 2 shows a summary of the proposed prioritisation of oncological therapies during the pandemic. It is important to clarify that this proposed approach is transitory while we are in the period of greatest contagiousness. This scheme can help to optimise health resources and minimise the mobility of cancer patients to prevent possible infections.

In patients who are on cancer therapies during the pandemic, it is important to minimise their visits to hospitals through the use of telemedicine technologies, which has had very good results^[110], especially in terms of quality of life and patient satisfaction^[111]. Patients can send the results of their blood tests and computed tomography by email or message, and the medical evaluation is done by streaming, thus minimising the mobility of patients to the hospital. In addition, telemedicine can be used for communication, counselling, and disease monitoring^[112] especially for low-

priority symptoms (nausea, constipation, leg swelling, among others). In this context, the role of navigating oncology nurses is key^[113], because this process requires complex coordination between the medical team, laboratory team, radiology team, and administrative staff.

Finally, it is important to define which cancer patients affected with COVID-19 could be prioritised in case of a need for ICU admission. This very complex scenario is very likely to occur in countries where intensive care beds are scarce, especially in developing countries. This theme was recently addressed by the American Society of Clinical Oncology (ASCO)^[114]. First, it is imperative to maximise positive outcomes in patients hospitalised in ICU, and to choose patients with a higher probability of having better outcomes. Clinicians have a duty of care (principle of charity) and to optimise resources (principle of justice). For this reason, multi-disciplinary evaluation of the oncology team is critical to establish and communicate the prognosis of cancer patients to the ICU and emergency physicians with transparency and consistency. To establish the prognosis of a cancer patient with COVID-19, the oncology team has to consider the previous ECOG performance status, type and stage of cancer (localised or advanced), type and goal of cancer therapy (adjuvant, neoadjuvant, or palliative) and the line of cancer treatment (first, second, or third-line). In this process, communication and teamwork are key to achieving the best decision. In case of complex clinical scenarios, it is imperative to request the opinion of palliative care and medical ethics teams early.

Care of the health team is a very important issue. In our centre, we divide the medical staff into two teams to be able to maintain the continuity of cancer patient care in case of disability of a member by infection or a high-risk SARS-CoV-2 contact. In addition, we carry out clinical and oncology committee meetings through remote videoconferences with optimal results. With regards to oncology residents' training, teachings have been adapted to be carried out remotely and with limited clinical practices to optimise the availability of personal protection elements in accordance with the ESMO and NCCN recommendations for this pandemic^[100,109].

In summary, it is essential that oncology teams adapt to these new times of great challenges. Medical teams must adapt cancer treatment protocols and prioritise them according to patient response and prognosis. In cancer patients infected with SARS-CoV-2, it is essential that an effective and transparent communication is built between the oncology and critical care team to make the best decisions regarding the complex care of these patients. Optimising clinical care using technology and telemedicine have become powerful tools in facing this pandemic, and we must adapt quickly to this new reality of medical care.

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