ORIGINAL ARTICLE

Oncology practice during COVID-19 pandemic: a fast response is the best response

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SUMMARY

The first confirmed case of coronavirus disease 2019 (COVID-19) in Brasil was reported on February 25th, 2020, and by April 3rd, 8076 were confirmed in the country. As COVID-19 disease incidence escalates in Brasil, management of cancer patients requires immediate action and oncology clinics are urged to establish a contingency plan. We have installed a COVID-19 Management Committee to elaborate and implement best practices to assist cancer outpatients as well as to provide a safe environment for clinical staff and other employees at the outpatient clinics. The challenges of cancer treatment in the midst of COVID-19 global pandemic highlight the importance of a rapid response by institutions, where organizational structure, strategic planning, agility in guidelines implementation and alternative ways to protect and support clinical staff, employees and patients may be the key to mitigate pandemic effects.

KEYWORDS: *COVID-19. Coronavirus. Medical oncology. Public Health. Pandemics*

INTRODUCTION:

The Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is rapidly spreading all over the world, affecting 180 countries and threatening the health of all mankind, leading the World Health Organization (WHO) to classify Coronavirus Disease (COVID-19) as a pandemic on March 12th, /2020 and its risk as *very high* at global level[1].

By April 3rd, 1.039.166 cases were confirmed worldwide, among which 55.092 patients (5,3%) died. Updated statistics for Brasil have shown 8076

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confirmed cases and 329 (4%) COVID-19 associated deaths[2]. Nonetheless, as testing for SARS-CoV-2 is restricted to severe cases and health professionals, these numbers are likely to be underestimated[3].

Clinical experience in other countries has shown that early recognition of infected individuals is crucial. Since the severity of disease is highly related to its prognosis, the essential strategies to improve outcomes remain the early detection of high-risk patients and early intervention guided by intensivists. As there has been no effective antiviral treatments for COVID-19, reduced mortality is achieved by early and strong intervention to prevent contamination and disease progression[4-6].

Management of cancer patients during COVID-19 disease outbreak requires immediate action and oncology clinics are urged to establish a contingency plan, as mortality among these at risk individuals reaches 28,6%[7], contrasting to 5,3% in the general population[2]. The immunosuppressive state caused by either anticancer treatments and/or surgery renders cancer patients more susceptible to infections. A recent study has shown that these patients have a statistically significant higher risk of developing severe events associated to SARS-CoV-2 infection, with a hazard ratio of 3.56[8]. This study enrolled a small number of patients, but nonetheless, it reflects the general position undertaken by most hospitals and clinics around the world, where adjuvant chemotherapy or elective surgery for less aggressive cancers is being postponed and personal protection should be reinforced for patients with cancer or cancer survivors. Intensive surveillance or treatment should be considered for those cancer patients with active disease who are infected with SARS-CoV-2 virus, as mortality can be as high as 28% among these individuals. As COVID-19 disease incidence escalates in Brasil, it poses a challenge to medical practice and presses for a crisis management plan. AMO is a network of outpatient clinics currently operational in 6 cities in 2 states. In 2019, our 247 physicians assisted 41.429 patients on a total of 97.110 medical visits and 3917 patients underwent 33.524 chemotherapy sessions. As the largest oncology group in the Bahia state, we undertook the task to install a COVID-19 Management Committee to elaborate and implement best practices to assist cancer outpatients as well as to provide a safe environment for clinical staff and other employees at the outpatient clinics.

COVID-19 MANAGEMENT COMMITTEE INSTALMENT AND INITIAL CONTINGENCY PLAN

WHO declared COVID-19 outbreak as a Public Health Emergency of International Concern on January 30th, raising general awareness on timing and pattern of virus spreading from China to other countries. The first positive case in Latin America was registered on February 25th in São Paulo[9], Brasil. Thus, the Committee was installed on March 11th and the 1st version of the contingency plan was elaborated in this meeting and implemented on March 12th, the very same day that COVID-19 was declared as pandemic by WHO. The timeline of subsequent resolutions and actions of the Committee are detailed in Figure 1.

The COVID-19 Management Committee is composed by staff from the AMO Clinic, as follows: Medical Director (Hematologist), Medical Manager (Pulmonologist), Director of Assistance and Reception, Director of Pharmacy and Logistics, Quality and Safety Manager, two Risk Management and Ambulatory Health Care Infection Prevention and Control Service (SCIA) Nurses, Nursing Coordinator and Coordinator of Communication and Marketing and an *ad hoc* Infectologist. The Committee meetings are held daily or on-demand and any modifications in the protocol to manage suspected and/or confirmed cases of COVID-19 are communicated to staff immediately. Updated literature was used as source of information/best practice (see References) and all protocols are adjusted according to data updates.

The Initial Contingency Plan, implemented on March 12th, had as main objective to instruct employees on how to identify suspected cases of COVID-19 among patients and employees, to instruct patients, family members, clinical staff and employees about prevention and adequate hygienic/decontamination procedures of themselves as well as working areas, and how to proceed upon occurrence of unexpected events. The plan defined the roles of those professionals involved in its execution, as well as the communication procedures (both internal and external) to ensure access to information, guaranteeing the continuation of the activities developed by employees, prioritizing safety and adequate care for patients, avoiding financial losses and customer dissatisfaction. Also, a triage procedure was adopted and performed by the call center using a scripted approach. Follow up appointment of patients

reporting suspected COVID-19 symptoms where postponed and for those symptomatic patients scheduled to undergo infusion treatment, the assistant physician was contacted and upon decision to maintain the infusion, patients would be listed at the reception hall as required to wear a mask at all times while at the clinic. Infusion treatment would only proceed if after clinical examination the suspicion of COVID-19 was discarded or rejected/dismissed. Objectives and topics covered in the contingency plan were modified according to subsequent deliberations of the Committee and grouped into recommendations for oncology practice (elaborated and validated in collaboration with clinical oncologists staff) , monitoring and managing of outpatient/clinical research patients, clinical staff /employees safety and well-being, telemedicine implementation and observational data collection of COVID-19 pandemic consequences upon clinical outcome of cancer patients.

RECOMMENDATIONS FOR THE MANAGEMENT OF ONCOLOGY PRACTICE DURING THE COVID-19 PANDEMIC

The COVID-19 pandemic has imposed a scenario of resource contingency and reassessment of the benefit of exposing patients to treatments that will increase the risk of severe complications. In order to facilitate decision-making and patient management, the COVID-19 Management Committee postulated the following general recommendations for oncology practice[6,8,10-12]:

1. Provide guidance about the importance of vaccination against influenza (strain 2020) except when acute fever is detected. In order to avoid agglomerations, patients are suggested to undergo vaccination in a drive-thru vaccination facility, by scheduled appointment or to undertake it at home, depending on availability.

2. Maintain adjuvant chemotherapy with curative intent for those patients who are already in treatment.

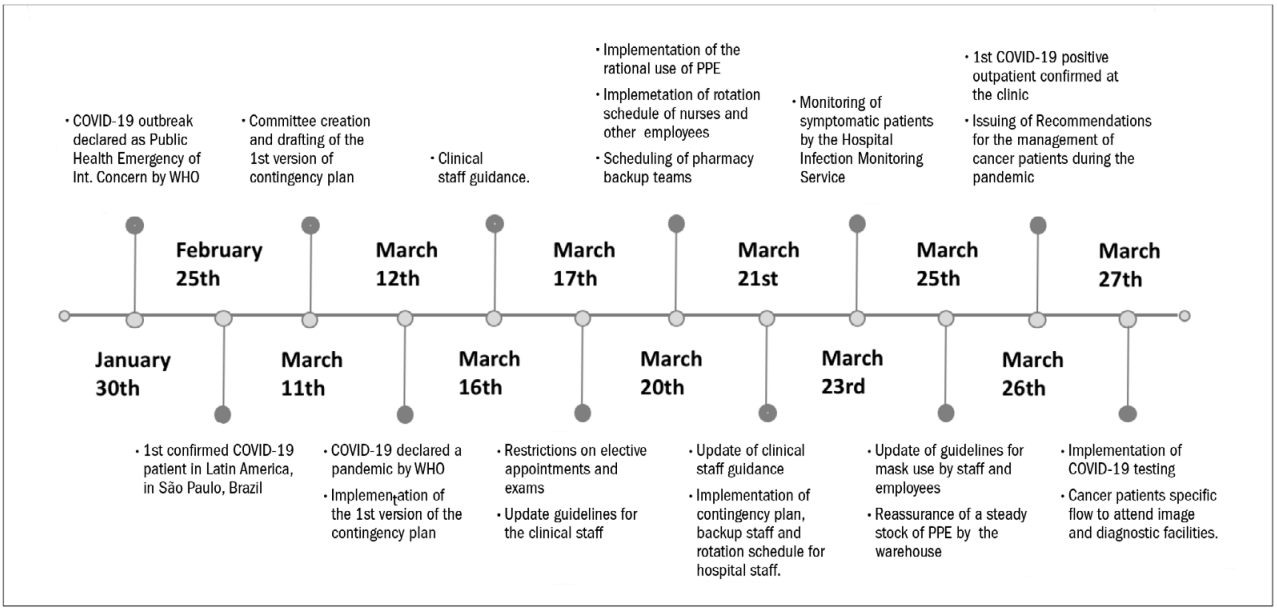
3. Consider reducing adjuvant duration for those who have already started treatment, when the benefit is not impaired (e.g. patients with low risk stage III colon cancer, early ovarian or breast cancer)

4. In non-indolent tumors, with indication for curative surgical treatment, prioritize surgery. If the situation evolves to a shortage of hospital beds, consider neoadjuvant therapy in tumors where literature evidence supports equivalence to adjuvant therapy (e.g. stage II-IIIA non-small cell lung cancer, T2N0M0 gastric cancer, EC I-III breast cancer).

5. Do not delay or postpone chemotherapy in high-risk tumors with a clear indication of adjuvancy. As far as possible, choose the least toxic and /or oral schemes when equivalents in terms of clinical benefit.

6. Consider not performing adjuvant chemotherapy in situations where a small benefit is expected (e.g.

FIGURE 1. TIMELINE OF EVENTS LEADING TO THE CREATION OF THE COVID-19 MANAGEMENT COMMITTEE AND ITS SUBSEQUENTE ACTIONS. WHO: WORLD HEALTH ORGANIZATION; COVID-19: CORONAVIRUS DISEASE 2019; PPE: PERSONAL PROTECTION EQUIPMENT.



stage Ib lung cancer, stage II colon cancer) or in those tumors where a non-immunosuppressive treatment is an option (e.g. ER-positive early-stage breast cancer).

7. Consider the use of prophylactic G-CSF in protocols with a higher risk of neutropenia and allow more permissive use in cases of previously verified neutropenia.

8. For patients with metastatic disease undergoing chemotherapy:

- Do not interrupt treatment in symptomatic patients with active disease or in those at high risk of progression

- Consider interrupting maintenance therapy if the disease shows improved remission. Share the decision with the patient, weighing risks of progression and/or infections.

- Switch intravenous medications to oral medications when possible (e.g. 5-FU, vinorelbine, anticoagulants).

9. Radiotherapy should be maintained to:

- Treatment with curative intent of fast-growing tumors.

- Treatment of oncological emergencies. Ex: spinal cord compression, bleeding, etc.

- When radiotherapy, combined or not with chemotherapy, is the standard of treatment (e.g. anal, cervix, esophagus and head and neck tumors.

- In those patients who have already started treatment.

Note: Whenever possible, give preference to hypofractionation schemes (shorter duration).

10. Consider delaying radiation therapy for indolent tumors

11. Postpone supportive medications or reconcile with chemotherapy days (e.g. denosumab and zoledronic acid, except in cases of hypercalcemia)

12.Patients on cancer follow-up, without active treatment and asymptomatic may have their appointments postponed.

MANAGING AND MONITORING OUTPATIENTS

Our outpatient clinic assists the population of a large urban area, and concerns for exposing patients to COVID-19 grew as SARS-CoV-2 spread in the country. Outpatients are allowed in with only one companion, which are advised to join the appointment only when patients are underage or non-self-sufficient.

The Call Center contacts each patient the day before its appointment and through a scripted questionnaire, accesses if patients display respiratory symptoms and are suspected of COVID-19 infection, as well as screens for non-urgent follow up appointments that are rescheduled within 15 days (see Telemedicine Service Implementation) (Figure 2).

Asymptomatic outpatients whose appointment should not be rescheduled proceed through regular patient flow but within longer intermission between appointments and assigned to specific seats in the waiting room (2 meters apart from each other). Suspected COVID-19 infected patients (here forward referred to as "Symptomatic") outpatients on follow-up are rescheduled, but suspicion of COVID-19 infection is reported to SCIA and subsequently monitored (see Cancer Patients Monitoring during COVID-19 Pandemic). Initially, Front Desk received a daily report of the patients required to wear masks upon arrival at the clinic (all symptomatic patients), however, following a recent recommendation of the Ministry of Health, all patients are required to wear it now (compliance ensued as soon as clinic warehouse reassured adequate mask supply).

Patients undergoing infusion treatments are classified as asymptomatic or symptomatic – the former will follow the regular pre-infusion workup and treatment plan. The latter will undergo clinical triage and its management will be determined by prescribing Physician or Physician on Duty, either cleared to proceed treatment or put on hold and requested to be tested for COVID-19. Either way, SCIA is notified and patient monitoring proceeds (see Cancer Patients Monitoring during COVID-19 Pandemic).

Accrual of patients for clinical trials and monitoring visits of ongoing protocols were brought to a halt, while on protocol patients were scheduled for visits/procedures in off-peak hours. Clinical trials staff was divided on shifts, drug and/or sample kits delivery by sponsors was all concentrated in one day of the week and when feasible, already providing a 4-months supply.

Access to COVID-19 testing is guaranteed through a commercial agreement between the Clinic and a private laboratory to assure adequate sample collection and analysis. Furthermore, a specific protocol was adopted for patients required to perform imaging and/or other tests in our diagnostic facility located in another facility, where a specific flow dictates access at exclusive schedules, at large and patient density-controlled waiting rooms and private parking.

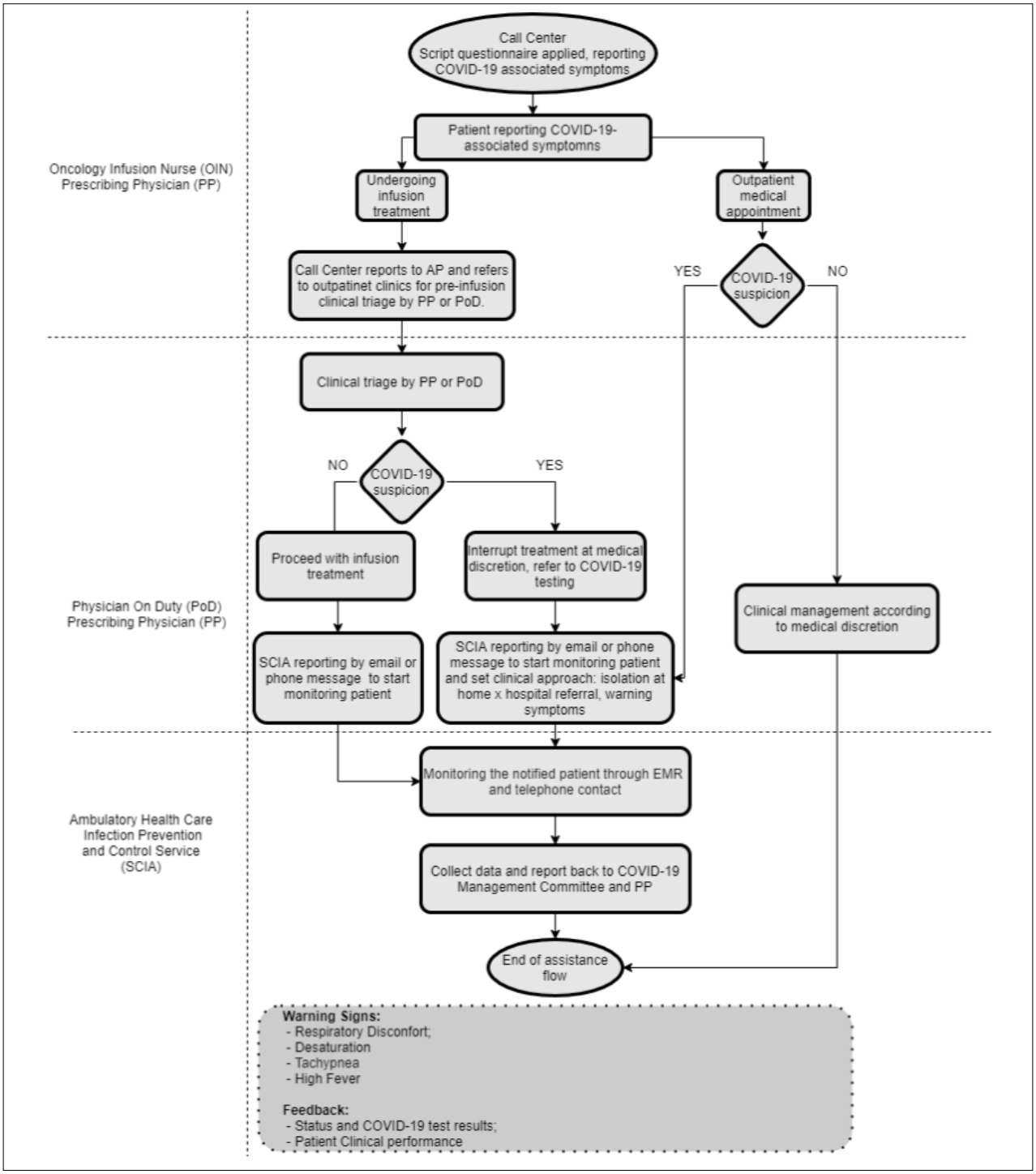


FIGURE 2. FLOWCHART FOR MANAGING AND MONITORING OUTPATIENTS. PP: PRESCRIBING PHYSICIAN; POD: PHYSICIAN ON DUTY; SCIA: AMBULATORY HEALTH CARE INFECTION PREVENTION AND CONTROL SERVICE, EMR: ELETRONIC MEDICAL RECORD.

EMPLOYEE AND LEADERSHIP SAFETY AND WELL-BEING

Psychological and physical well-being of clinical staff and employees is crucial to avoid the anticipated burnout imprinted by COVID-19 Pandemic and, therefore, clinics should abide by guidelines of best practice to ensure a safe work environment. We have provided training on prevention, personal protection and decontamination of working areas to all clinical staff and employees. Staff who are immunocompromised, have significant comorbidities, > than 60yo or are at any high-risk category were withdrawn from clinical practice.

As the number of outpatient appointments were

reduced, we have temporarily closed one of our Clinics branches and redesign the schedule of shifts, reducing working hours. Clinical staff was either assigned to practice at the outpatient clinics or at the hospital, reducing risks of cross-contamination. Hospital attending staff is considered to be at higher exposure to SARS-CoV-2 infection and, therefore, were scheduled to one week working/one week off shifts.

Staff shortage is expected due to several anticipated limitations, such as school closings and the need to quarantine staff on short notice, thus Human Resources reached out to our database to create a backup labor pool and started the hiring process of a temporary taskforce for subsequent training.

Personal Protection Equipment (disposable mask, gloves and gown) was provided at first for all staff in contact/attending symptomatic patients, later on the use of masks became mandatory to all staff and patients once the clinic warehouse reassured a steady supply of PPE. Recently, the Brazilian Ministry of Health recommended mask use for all health care providers, and because we took an early action upon it, we will be likely to fully comply with this recommendation in the near future.

Clinicians that also undertake administrative duties were advised to do it remotely, laptops were provided for those who needed it, and any other professional gatherings, such as scientific meetings and educational sessions were either canceled or postponed from March 12th on, and all weekly tumor boards are being held online.

TELEMEDICINE SERVICE IMPLEMENTATION

To ensure continuity of oncology assistance to our patients, our clinic has put forward Telemedicine Practice as a follow up option. On March 19th, the Federal Council of Medicine issued a statement[13] authorizing Telemedicine Practice during COVID-19 pandemic, based on following terms:

-Teleguidance: medical professionals can remotely carry out guidance and referral of patients in isolation

-Telemonitoring: performed under medical supervision, for remote monitoring or enforcement of health and/or disease parameters.

-Teleinterconsulting: exclusively for the exchange of information and opinions among doctors, for diagnostic or therapeutic assistance.

From April 6nd, the Call Center Triage will offer telemedicine-based assistance to eligible patients upon remote informed consent signature. The Telemedicine Assistance can be contracted as out of pocket or reimbursed from health care providers, as authorized by the National Health Agency (ANS)[14] on March 30th.

CANCER PATIENTS MONITORING DURING COVID-19 PANDEMIC

All symptomatic patients (confirmed or not) undergoing infusion therapy during the COVID-19 pandemics are going to be closely monitored by the Ambulatory Health Care Infection Prevention and Control Service. Clinical data of these patients will be collected for assistance purposes and after COVID-19 pandemic resolution, data will be released as a scientific report, accounting for the impact of infection and/or mandatory changes in oncology practice during the pandemic.

CLOSING REMARKS

COVID-19 pandemic called for a fast response from Oncology Care Professionals to provide proper prevention, guidance and appropriate identification and treatment of critical cases, including decisions on whether to postpone or interrupt treatment. The effects of these compulsory modifications in cancer patient management and their clinical outcomes are yet to be known. Nonetheless, promotion of prevention, monitoring and early intervention are key to avoid or lessen the effects of COVID-19 pandemic upon this very high-risk group. Our oncology outpatient clinic (AMO Clinic, Bahia) staff responded very early to the warning of an upcoming epidemic, so when COVID-19 pandemic was announced by WHO, all the strategy and structure to face the challenge of providing cancer care on such conditions was already in place. We expect that the fast implementation of an early contingency plan and all the subsequent and continuous recommendations elaborated by our COVID-19 Management Committee will contribute to lessen the pandemic burden brought upon patients and staff/employees, as well as avoid infection, clinical complications and preventable deaths associated to SARS-CoV-2.

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Authors Contribution

CS: Data analysis and interpretation, drafting the article, critical revision of the article, final approval of the version. TL: Conception or design of the work, data analysis and interpretation, critical revision of the article, final approval of the version. APGAVN: Data analysis and interpretation, final approval of the version to be published. BVF; APLF; CDA; ABA; LOH; SSND Data collection, final approval of the version. PN: Data collection, data analysis and interpretation, critical revision of the article, final approval of the version. AC: AKC Data collection, critical revision of the article, final approval of the version. AP: Conception or design of the work, data analysis and interpretation, critical revision of the article, Final approval of the version.

RESUMO

O primeiro caso confirmado de Doença Associada ao Coronavírus 2019 (COVID-19) no Brasil foi confirmado em 25 de fevereiro de 2020 e em 3 de abril já haviam 8076 casos confirmados no país. A medida que a incidência de COVID-19 aumenta no Brasil, o tratamento de pacientes com câncer exige ação imediata e as clínicas oncológicas são instadas a estabelecer um plano de contingência. Instalamos um Comitê de Manejo de COVID-19 para elaborar e implementar as melhores práticas para ajudar pacientes ambulatoriais com câncer, bem como proporcionar um ambiente seguro para a equipe clínica e outros funcionários das clínicas ambulatoriais. Os desafios do tratamento do câncer em meio à pandemia global do COVID-19 destacam a importância de uma resposta rápida das instituições, onde a estrutura organizacional, o planejamento estratégico, a agilidade na implementação de diretrizes e formas alternativas de proteger e apoiar a equipe clínica, funcionários e pacientes podem ser a chave para mitigar os efeitos da pandemia.

PALAVRAS-CHAVE: *COVID-19. Coronavirus. Oncologia. Saúde Pública. Pandemias*

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