

Cancer Rehabilitation during the COVID-19 Pandemic: An Overview of Special Considerations

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Abstract

The global pandemic of coronavirus (COVID-19) is a major public health issue since identified in Wuhan, China in December 2019. It creates unique challenges from the perspective of cancer survivors, as they often require complex cancer treatments during the disease trajectory, disease surveillance, and rehabilitation. Given the vulnerability of this population, there is an urgent need to address the impact of such a pandemic on cancer rehabilitation. This article presents a narrative overview of the issues highlighted for rehabilitation services providing cancer care in this context, for risk mitigation, and for continued operation during this unprecedented public health crisis.

Keywords: Cancer rehabilitation, coronavirus, COVID-19

INTRODUCTION

In December 2019, the Coronavirus outbreak in China, termed “severe acute respiratory syndrome coronavirus 2” (SARS-CoV-2),^[1] was officially named by the WHO as “COVID-19.” Globally, this virus resulted in a pandemic with over 2 million people affected, and 165,153 deaths (as of April 20, 2020). Total worldwide cases are currently highest in the USA, Spain, and Italy, with Australia confirming 6542 cases for COVID-19, with 65 deaths so far. This pandemic has had a significant impact on global healthcare and economy. In the absence of a vaccine, no specific antiviral agent or other medications available, and experience from previous infections (such as the 2003 SARS-CoV, Middle East Respiratory Syndrome coronavirus, and 2009 H1N1 flu), has resulted in swift, effective implementation of public health measures in China, Singapore, South Korea, and Australia.^[2-5] These included strict border control, COVID-19 testing, contact-tracing, quarantine isolation, and “physical distancing” as part of a coordinated effort nationally and internationally to help contain the virus and its transmission. However, the challenge remains in keeping patients (and health-care staff) and the general population safe from the disease.

The mortality rates from COVID-19 are difficult to quantify, as they vary based on the characteristics of the affected

population, demographics, and available health-care resources. The mortality risk is higher in older age group and those with comorbidities: 11% for cardiovascular disease, 7% for diabetes, 6% each for chronic respiratory disease, hypertension, and for cancer.^[2] Cancer patients are a highly vulnerable group and more susceptible to sepsis compared with the general population. This may be due to the systemic immunosuppressive state caused by the cancer itself and therapy. Limited data is available on the incidence of COVID-19 in cancer patients compared with the general population.^[6]

Cancer patients with COVID-19 may present with similar clinical and imaging features as the general population, except they can demonstrate features of anemia and hypoproteinemia, contributing to increased immunosuppression from nutritional deficiency, and are more likely to progress rapidly to severe hypoxia.^[7] In a small nonrandomized retrospective study of COVID-19 affected cancer patients, lung cancer was

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reported as the most common cancer (25%), followed by esophageal (14.3%) and breast cancer (10.7%).^[7] Although the current evidence remains insufficient to explain a conclusive association between cancer and COVID-19, it has been suggested that cancer patients have a higher mortality risk when affected with COVID-19,^[2,7,8] and develop more severe forms of COVID-19 compared to noncancer populations.^[9] Patients with cancer also tend to have a higher risk of severe events (intensive care unit [ICU] admission, invasive ventilation, or death) compared with those without cancer (39% vs. 8%), and poorer clinical outcomes.^[9]

It is increasingly recognized that cancer survivors require rehabilitative interventions to deal with the acute and long-term consequences of cancer and cancer treatments.^[10] Cancer rehabilitation assists in addressing the physical and psychosocial needs of survivors using an interdisciplinary approach.^[10] Rehabilitative interventions identify and address impairments in cancer patients which are specific, individualized and tailored to the needs of the patient (and family); and to help prevent complications.^[11] Examples of common cancer impairments include: fatigue, pain, weakness, aerobic insufficiency (e.g. lung cancer), cognitive deficits due to encephalopathy (e.g. radiotherapy related, brain metastases), peripheral neuropathies (e.g. chemotherapy toxicities), pulmonary fibrosis (e.g. bleomycin use), and/or cardiomyopathy (e.g. doxorubin).^[11] The various rehabilitation interventions used to address cancer-related impairments aim to improve activity (e.g. related to mobility, function, cognition, mood) and increase participation in everyday activities. Cancer rehabilitation strategies factor in the progressive and sometimes rapid functional decline, toxic effects of cancer treatments, tumor recurrence, fatigue, medical fragility, and psychosocial issues of patients. Further, with often aligned goals between both cancer rehabilitation and palliative care (although distinct in approach), cancer rehabilitation also facilitates efforts in improving symptom burden, quality of life outcomes and discussions regarding goals of care and advance care planning among cancer patients.^[12,13]

In the context of the COVID-19 pandemic, medical and rehabilitative interventions must be weighed against the risk for inadvertent COVID-19 exposure or the potential for increased vulnerability as a result of oncological treatment. The evidence for critical issues concerning treatment principles for COVID-19 affected cancer patients is as yet unclear. This is because of limited studies (small sample sizes, heterogeneity in clinical presentation and cancer population, and disease trajectory). Additional challenges exist in terms of preparedness plans including the re-prioritization of hospital regimes for patients with cancer, service delivery, safety and equipment, workforce planning, and business continuity plans, in line with evolving updates in guidelines, policies, and recommendations.^[14]

This article outlines the challenges faced by cancer patients in the context of the COVID-19 pandemic. It also provides

a rehabilitation perspective on the contingency measures undertaken in response to hospital-wide and national developments to help mitigate risk, facilitate continue operation and optimize service delivery during this global health crisis.

ACUTE AND REHABILITATION CARE CHALLENGES

From an organizational perspective, acute cancer services are considered critical services in a tertiary hospital, and its operations are expected to continue even in the context of a pandemic. The risk of death and morbidity from COVID-19 needs to be weighed against the magnitude of benefit of intended cancer treatments.^[15] Acute care challenges need to be recognized in the treatment of cancer patients in the context of COVID-19.

Clinically, COVID-19 disease is frequently associated with fever (90%), cough (68%), fatigue (38%), sputum production (34%), and/or shortness of breath (19%).^[16] Factors such as other infectious agents, chemoradiotherapy side effects or cancer progression may mimic symptoms of COVID-19 (e.g. flu-like symptoms and/or low-grade fever). Clinical presentations, for example, sore throat due to radiation-induced mucositis (e.g. post head and neck radiotherapy), respiratory symptoms of varying severity (e.g. lung cancer), fever (e.g. acute leukemia), or cough (e.g. mediastinal lymphoma) can complicate diagnostic work-up and likely result in missed or delayed diagnosis of COVID-19.^[17,18] COVID-19 is associated with a high inflammatory burden, greater propensity for vascular inflammation, pneumonitis, myocarditis, and cardiac arrhythmias; these share features of and/or exacerbate chemoradiotherapy effects.^[19,20]

The COVID-19 pandemic has resulted in the cancellation of most elective surgeries and limited surgical cases to emergencies and some cancer resections. As oncology treatments tend to be time sensitive, there can be adverse outcomes due to the cancellation of elective surgery, although data regarding the impact of delayed surgery in the longer term are still unclear.^[21] On the other hand, quarantine requirements and cessation of surgical activity may help reduce the need for blood products. Currently, blood product shortages present an issue in most COVID-19 affected countries due to transport restrictions, fear of virus transmission and blood donors having self-isolation requirements.^[17]

Interruption of chemotherapy treatment protocols (due to medication shortages, resource limitation, reduced hospital-isolation beds and reduction in immunosuppressive treatment) may negatively affect prognosis, particularly in active disease treatment in those with favorable or intermediate risk of disease. For instance, delayed adjuvant chemotherapy for colorectal cancer and breast cancer are associated with inferior survival rates.^[22,23] Radiotherapy, as the mainstay of treatment of many cancers, with a course taking up to several weeks, has its own unique challenges. The reduced availability

of radiation oncology workforce due to cautionary isolation or redeployment to other settings results in delayed radiotherapy treatment regimes. Patients who require isolation would have difficulty accessing a dedicated linear accelerator and CT simulation room due to their high costs. There is also the risk of cross-infection if staff are working at multiple hospitals (i.e. satellite centers and clinics), leading to reduced workforce capability. Radiotherapy is also critical for the treatment of oncological emergencies such as spinal cord compression, tumor bleeding, malignant airway obstruction, or for the management of palliative symptoms. Delayed radiotherapy can contribute to reduced cancer control of up to 14% with each week of delay in treatment.^[24]

For hematopoietic stem-cell transplants, both donor and recipients must be healthy for the procedure to be feasible and successful. Ongoing immunosuppression, mucositis, malnutrition and/or graft-versus-host disease may increase the risk of complications in those with COVID-19. Delays in the identification of compatible donors, travel/transport restrictions and delayed transplant procedure due to the pandemic may result in disease recurrence, with a reduced survival outcome.^[25]

Given these challenges, critical measures in acute cancer care services are aimed at protecting patients and staff, with implementation of treatment modification strategies and infection precaution measures to minimize risk. Clinicians need to evaluate individual patient risk of COVID-19 based on risk factors for severe manifestation of respiratory viruses in cancer patients. Early recognition and treatment of other possible differential diagnoses remain vital, especially in severely neutropenic patients. In suspected or confirmed COVID-19 cases, recommendations include delaying the start of treatment or stopping ongoing treatment temporarily until the patient is no longer infectious, if possible. These cases should be ideally discussed with infectious disease teams and/or other relevant specialty teams to weigh specific risk and benefits to continuing or stopping treatment, in order to avoid compromising oncological outcomes. Some chemotherapy drugs that are delivered as infusions conventionally can be changed to oral administrations or administered in prolonged intervals based on the patient's condition.^[15] Those requiring blood transfusion may be impacted from reduced supply during the pandemic and encouraged to refer to their health service guidelines and capacity. Alternative options such as iron, Vitamin B12, or erythropoietin transfusion may be considered and/or transfusion to those at highest risk of bleeding. Post hematopoietic transplant care should be guided by clinical principles and monitored in the period of highest risk prior to immune recovery. Physicians should be aware of drug interactions with targeted therapies and those used to treat COVID-19 infections/complications such as antibiotics, antiviral drugs, and other QTc prolongation agents.^[17]

Radiotherapy treatment should be delayed in those considered low-risk patients, given the limited oncological impact. For

those who have already started radiotherapy (and at risk if treatment was postponed or ceased), these treatments should continue. The focus should be on reducing elective new cases starting radiotherapy and consideration of alternative options. There is evidence to support hypo-fractionation of radiotherapy to reduce treatment time.^[26,27] Consensus recommendations for radiotherapy options exist for management of cancers of: the breast, central nervous system, lung, prostate, leukemia, and palliative metastases.^[28-33] Some centers have radiation oncologists remotely providing treatment to contour treatment target volume and organ affected.

Although there is evidence for cancer rehabilitation along the cancer care continuum,^[34,35] the evidence for cancer rehabilitation in this COVID-19 pandemic is still limited. Nevertheless, rehabilitative interventions remain critical in COVID-19 survivors. Following ICU and/or acute hospital stay, COVID-19 survivors may suffer from multiple short-and longer-term complications. Some of those with prolonged stay in ICU develop acute respiratory distress syndrome and complications, such as intubation, reduced lung function, copious secretions, or ineffective cough. These complications can be compounded by a patient's history of comorbidities (e.g. chronic obstructive airways disease, neuromuscular disease, and cystic fibrosis), or other factors such as radiotherapy side effects or drug toxicities. Although the disease presentation of COVID-19 involves pneumonitis rather than exudative consolidation, copious secretions require physical interventions.^[36] In these severe cases, the management includes postural drainage, prone positioning to optimize oxygenation, and airway clearance techniques (breathing exercises, mechanical insufflation-exsufflation, percussion, vibration therapy, and cough maneuvers).^[37]

In the short-term, those from acute care may be transferred to rehabilitation wards to lessen the impact on acute care demands or other settings (e.g. home with post-acute care services, supported accommodation). Higher severity cases may require inpatient rehabilitation whereas rehabilitation at home models could manage lower-acuity patients with COVID-19.^[38] In assessing COVID-19 survivors for rehabilitation, clinicians need to consider clinical assessment, cardiorespiratory status, and impairment-driven evaluation including physical and functional deficits. Complications relevant to rehabilitation include: physical deficits (loss of muscle mass, ataxia, plantar flexion contractures, critical illness myopathy/neuropathy) and/or peripheral/central nervous system issues (headache, dizziness, hypogeusia, hyposmia, neuralgia, altered conscious state, stroke, epilepsy, and posterior reversible encephalopathy syndromes).^[39,40] Fatigue is a prevalent symptom in an estimated 40% of patients, along with mental health issues such as depression, anxiety, and hallucinations.^[41,42] The management of these impairments is crucial, with early delivery of care including interventions such as: joint range of movement exercises, mobilization, strength and cardiorespiratory conditioning, balance exercises, functional task retraining, fatigue management strategies, adaptive equipment, cognitive

rehabilitation, and psychosocial strategies, to help patients return to a safe environment and reintegrate into society.

REHABILITATION CONTINGENCY MEASURES

There are limitations that need to be considered from an infectious-risk perspective in the delivery of rehabilitation. The potential organizational and operational challenges in providing rehabilitation for COVID-19 patients has been previously outlined.^[38] Ongoing infectious risk (despite clinical recovery in the affected cases) is still uncertain.^[43] All immediate focus is on global efforts to collaborate and mitigate the risk of virus transmission, lessen the impact of reduced workforce and ensure business continuity plans as patients transition from hospital to home. These risk reduction measures should be reviewed regularly and follow evolving institutional, local, state-wide and national policies and recommendations. Some of the rehabilitation contingency measures undertaken in response to hospital-wide and national developments are highlighted below and summarized in Table 1.

Acute care/inpatient rehabilitation

First, for efficient management a COVID-19 affected cancer survivor, rehabilitation physicians (and/or allied health or nursing) should be included in acute cancer care teams to maintain coordination and care continuity. The rehabilitation team should assess patient history for tumor details (type/stage/presence of metastatic disease), details of treatment (e.g. surgery, chemotherapy, radiotherapy and/or complications), review pathology and imaging, as well as evaluate performance status, through telehealth where possible. Face-to-face sessions should be avoided, where possible. An evidence-based approach from a rehabilitation perspective will support the cancer management plan, consider the patient's level of risk, prognosis, and goals of care. The integration of rehabilitation teams can help explore alternative models of care delivery to reduce demand on hospital capacity, including rehabilitation at home services, postacute care or other community providers.

The rehabilitation interdisciplinary leadership team can coordinate, manage and execute existing hospital care in line with policies and procedures during the outbreak. This team should have clear communication channels with acute cancer teams (oncology, hematology, etc..) for contingency plans to reduce the risk of sepsis based on individual patient status. This team should coordinate patient screening prior to transfer to inpatient rehabilitation units, infection control requirements, staff re-configured into enclosed wards (assign clinical and work areas into different protection zones), staff education and training, roster workflows and modifications, management of personal protective equipment (PPE), emphasizing physical distancing, hand hygiene, appropriate exercise prescriptions/equipment use, medical waste disposal, and emergency responses.

Prior to cancer patients being transferred to inpatient rehabilitation, screening protocols should be implemented

as per organizational guidelines. These include temperature checks, blood tests, nucleic acid tests and negative swabs, with infection control precautions/plan in place as required. Symptoms that are potentially associated with COVID-19 (such as fever or cough) should be routinely monitored. If a patient exhibits fever or suspected COVID-19 on the rehabilitation ward, staff must arrange the patient into the COVID-19 screening tool, work up and clinical workflow pathways as per local hospital and government guideline; and perform PPE/isolation precautions while the patient is tested and awaiting swab results. Those who deteriorate will require full PPE precautions and escalation for further management.

Emergency responses are attended by the CODE Blue/Medical Emergency Team (MET) call response teams. This scenario will vary based on hospital setting, location, protocols, and staff capacity. To conserve PPE, the policies instituted limit the number of health-care professionals required to come into direct contact with patients with suspected or confirmed COVID-19. Two doctors, usually one as the most senior and 1 nurse attend the emergency situation. The nurse-in-charge coordinates provision of PPE for staff and emergency response. Staff should be familiar with escalation and clinical review criteria. Full PPE is required for any patient deterioration requiring a MET response or cardiopulmonary resuscitation required given the high risk of aerosol transmission. Aerosol generating procedures such as bag-valve-mask ventilation, noninvasive ventilation, high flow oxygen requirements, intubation, airway suctioning, bronchoscopy, and other procedures require appropriate PPE and negative pressure isolation single rooms.^[36]

Further risk mitigation procedures include: staff temperature screening entering the hospital from ports of entry, including rehabilitation units, and to avoid work if they develop symptoms of COVID-19. Staff must be trained in standardized PPE training (masks, protective eyewear, gowns, and gloves), hand hygiene and equipped with COVID-19 diagnosis and management, including disinfection policies and procedures. Staff may also be faced with additional tasks, given hospital-wide consequences with staff shortages and patient overload. There will be a need for adaptations on the departmental workflows. All planned staff leave should be avoided or postponed as appropriate, in anticipation of potential staff shortages and ancillary workload.

With zoning of areas, rehabilitation units can be re-configured into COVID-19 and non-COVID-19 zones of varying contamination/protection levels based on risk exposure, staff occupancy, and ventilation condition. We propose "clean," "semi-contaminated," and "contaminated zones." Deployment of staff to COVID-19 and non-COVID-19 zones should be planned, and staff judged at high risk (i.e. those who are pregnant, have significant chronic respiratory illness, immunosuppressed, older, e.g. >70 years of age, immune deficiencies) should not enter the isolation zone. Minimizing movement across contaminated and noncontaminated areas is crucial.

Table 1: Recommendations for rehabilitation contingency measures in response to the COVID-19 pandemic (in the context of cancer rehabilitation service delivery)

Setting	Contingency measures
Acute care	Integration of rehabilitation team within acute cancer care service and COVID-19 response team Identify/address common and relevant COVID-19/cancer-related impairments, prevent complications Stringent patient risk assessment prior to transfer to inpatient rehabilitation/ambulatory care settings Explore alternative models of care (e.g., rehabilitation at home, postacute care services)
Rehabilitation - Inpatient	Address relevant COVID-19 and cancer-related impairments, prevent complications, optimize function, establish goal setting, support community reintegration from subacute hospital settings Establish goals of care, advance care planning discussion Symptom monitoring and temperature screening of patients/staff/visitors prior to entering rehabilitation unit Infrastructure (e.g., ward reconfiguration - COVID-19 zones, reallocation of office spaces) Hygiene measures for patients/staff (e.g., hand hygiene, cough/sneezing etiquette) Stringent safety and cleaning procedures (e.g., equipment allocation/decontamination, environmental decontamination) Staff allocation and workflow roster management Therapy modification strategies (e.g., bedside therapy) Establish telehealth platforms to communicate with patients, interdisciplinary teams, acute care specialty teams, and primary care providers Education/training/planning - physical distancing, self-isolation, hygiene measures, PPE, emergency responses, and escalation procedures Physical distancing (e.g., limit - staff in enclosed areas, staff entering patient rooms, visitor numbers, community day leaves, group training sessions) Support for psychological well-being of patients/staff
Rehabilitation - Ambulatory care	Address long-term cancer survivorship issues, optimize function and support reintegration into community activities of daily living, family roles, employment Encourage advance care planning and improve quality of life outcomes Ensure awareness of cancer patients regarding COVID-19 symptoms requiring medical care, hygiene measures, physical distancing, lifestyle risk reduction strategies, psychosocial support Symptom monitoring and temperature screening (where possible) for staff/patients (outpatient clinics, home therapy visits, e.g., rehabilitation at home, postacute care services) Staff education - physical distancing, self-isolation, hygiene measures, PPE, emergency responses and escalation procedures Stringent safety and cleaning procedures (e.g., equipment, environment) Staff allocation and workflow roster management Establish telehealth services (outpatient clinics, community therapy services, interdisciplinary meetings, liaison with acute/primary care providers)

PPE: Personal protective equipment

Given that COVID-19 is easily spread in limited spaces, delivery of rehabilitation interventions presents a challenge. Patients with general rehabilitation issues (e.g. stroke, orthopedic, etc.), without suspected COVID-19 (and no contact precautions) should receive routine rehabilitation. In confirmed or suspected cases, including those requiring contact precautions for other reasons (e.g. influenza), staff should don appropriate PPE and limit clinicians entering the room and clinical examination, with review of the medical record and discussions ideally performed outside of room. Careful observation and therapy modification to bedside therapy in isolation will decrease spread (even if results are negative). The identification of equipment which increases risk of cross-infection is important (e.g. respiratory equipment, tilt-tables, gait aids, rehabilitation equipment, and storage), with strict allocation of equipment and decontamination procedures followed in-between patient use. Departmental cleaning is critical to avoid infectious spread through high touch areas such as toilets, lifts, doctors' and nurses' tables, or patient changing rooms.

To emphasize physical distancing, measures implemented include strict "single to no visitor" policy, limiting community day leave and avoidance of group training sessions. Interdisciplinary team meetings should utilize teleconferencing. The staff should keep interpersonal spacing (1.5 m or more) in open and closed spaces. Staff who can perform duties (e.g. research coordinators and administrative staff) from home should be encouraged. Based on the patient volume and complexity, minimum levels of staffing to maintain safe treatments should be implemented. At an organizational level, healthcare professionals should participate in telemedicine for good communication from senior administration to clinical teams and patients (and caregivers) for shared decision-making.^[44] This involves electronic messaging systems, E-mails or videoconferencing to minimize face-to-face and group meetings.

Ambulatory care rehabilitation

Rehabilitation contingency measures in ambulatory care settings remain mostly similar to risk mitigation principles used in acute hospital settings. Along with addressing longer

term cancer survivorship issues and ongoing COVID-19 related impairments, clinicians should also encourage patients/families (and/or carers) to be aware of COVID-19 symptoms or complications that would require medical attention and educate patients regarding self-isolation, hygiene, physical distancing and lifestyle risk reduction measures, as well as provide psychosocial support mechanisms.

Telemedicine has previously been found to be successful in assisting cancer patients in the community, including symptom management, survivorship care and chronic disease management follow up.^[18] Outpatient clinic appointments and therapy services are converted to telehealth and electronic platforms, where possible. Communication with interdisciplinary team colleagues and liaison with acute or primary care providers can also be performed through telehealth services. Patients who need to attend the rehabilitation center should receive a notification screening phone call, prior to their appointment. Given community restrictions in many countries, participation in regular rehabilitation group outpatient programs (e.g. pulmonary/cancer rehabilitation) among COVID-19 survivors is almost nonexistent, and limited in-home physiotherapy or occupational therapy. There is currently limited evidence regarding rehabilitative interventions including exercise programs in the community for COVID-19 survivors and cancer patients.

Finally, with prolonged hospitalization and COVID-19 complications, there is an increased risk of anxiety, depression, and posttraumatic stress disorder in COVID-19 affected patients which need appropriate evaluation and treatment.^[42] In addition, the issue of staff anxiety due to workload, personal safety, and concern for family member health should be recognized and appropriate support during and beyond this pandemic provided. This includes employee assistance programs, facilitated debriefing sessions and counseling, peer support, or care from primary care providers.

CONCLUSION

Given the evolving nature of this pandemic, business continuity plans are critical to prevent disruption of services. These measures require frequent review as new information about the virus comes available and guidelines from governmental health organizations and local institutions are updated. This article summarizes challenges in the delivery of cancer rehabilitation services, preparedness plans, based on clinical consensus, using evidence to date. This will change given the epidemiological curve, capacity of the health systems and resource limitations.

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Conflicts of interest

There are no conflicts of interest.

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