Cardiovascular Care of the Oncology Patient During COVID-19

KUMS-2021
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Introduction

• Cardiovascular complications of COVID-19 were recognized early in the pandemic and include myocardial injury that can be due to acute coronary syndrome; myocarditis; disseminated intravascular coagulation or cytokine storm; cardia arrhythmias, including malignant arrhythmias; arterial and venous thromboembolism; heart failure; and cardiogenic shock.

• Recent data also demonstrate subclinical myocardial dysfunction early post recovery from the infection.
Introduction

- Patients with cancer have reduced physiologic reserve from underlying disease and, in many cases, prior cardio-toxic exposure, resulting in a higher risk for cardiovascular complications. The prevalence of cancer cases in COVID-19–infected patients was 4.5%.
Introduction

• The risk of being in the intensive care unit was threefold higher for patients with cardiac or cerebrovascular disease and twofold higher for patients with hypertension.

• Although patients with no comorbidities had a case-fatality rate of 1.4%, rates were much higher for those with hypertension, CVD, or cancer, with case-fatality rates of 8.4%, 13.2%, and 7.6%.
It is reasonable to obtain baseline LVEF assessment in those considered to be at high risk for CTRCD, with repeat LVEF assessment during therapy if indicated for cardiac-related symptoms.
Screening and Monitoring of Cardiac Function

- Patient specific risk factors that are considered high risk are older age (>60 years), 2 or more traditional cardiovascular risk factors (smoking, hypertension, diabetes, hyperlipidemia, obesity), prior cardiotoxic cancer therapy or mediastinal irradiation, and compromised cardiac function (LVEF<55%, more than moderate valvular heart disease, or CAD).
The Cancer Patient With Suspected or Confirmed COVID-19 Infection

• Before cancer treatment, the decision and timing of when to start should be based on the likelihood that urgent therapy will be disease modifying.

• The need to mitigate exposure risk to healthcare workers and other cancer patients must be considered.
The Cancer Patient With Suspected or Confirmed COVID-19 Infection

• Although there is an underlying proinflammatory state in patients with cancer or CVD.

• Modern cancer therapies can exhibit complex immunological effects by not only directly targeting malignant cells with “on-target” effects but also depleting circulating or tumor-infiltrating immunosuppressive cell populations resulting in immunomodulation via “off-target” effects.
The Cancer Patient With Suspected or Confirmed COVID-19 Infection

• The interplay of inflammation, cancer, and CVD is complex.
• In COVID-19 patients with acute myocardial injury, a subset of patients demonstrates hyper inflammation consistent with cytokine storm.
• Active treatment with cardiotoxic agents should be avoided if possible until resolution of COVID-19 infection in cancer patients.
The Cancer Patient With Suspected or Confirmed COVID-19 Infection

• Though *biomarker elevation* denotes an increased risk in cardio-oncology patients receiving cardio-toxic chemotherapy, their elevation in COVID-19–infected patients may not imply a similarly elevated oncologic-specific risk, but may be related to the infection instead.
The Cancer Patient With Suspected or Confirmed COVID-19 Infection

- COVID-19 infection may, as do other severe viral infections, increase the risk of plaque rupture and the occurrence of acute coronary syndrome.

- COVID-19 itself can manifest with clinical features of myocarditis.
The Cancer Patient With Suspected or Confirmed COVID-19 Infection

- Post recovery from active COVID-19 infection, cancer patients with either overt or subclinical myocardial injury should undergo repeat cardiac imaging before their next treatment cycle.
The Cancer Patient With Suspected or Confirmed COVID-19 Infection

• It is reasonable to image recovered cancer patients with risk factors for cardiotoxicity (hypertension, diabetes, CAD).

• Cardiac biomarkers can be considered and compared with those that may have been drawn during the course of the COVID-19 infection.
Angiotensin Converting Enzyme Inhibitors or Angiotensin Receptor Blockers

• The causative pathogen in COVID-19, the Severe acute respiratory syndrome coronavirus-2 virus, binds to the spike protein of angiotensin converting enzyme 2, a membrane-bound immunopeptidase highly expressed in lung and heart tissue, facilitating viral entry into the respiratory epithelium.
Angiotensin Converting Enzyme Inhibitors or Angiotensin Receptor Blockers

• Because angiotensin converting enzyme 2 levels may be elevated in patients on ACEi and ARBs and a higher risk of adverse complications has been noted in patients with preexisting CVD, there was initial controversy surrounding continued ACEi and ARB use in COVID-19 infections.
Angiotensin Converting Enzyme Inhibitors or Angiotensin Receptor Blockers

- Society guidelines recommend *against* withdrawal of these therapies due to the risk of hypertension and resulting kidney injury that may result.

- Moreover, the results of 2 meta-analyses, 31 observational studies, and interim results from at least 1 randomized controlled trial indicate that ACE inhibitors and ARBs are *not associated* with either the incidence or severity of COVID-19 infection.
Angiotensin Converting Enzyme Inhibitors or Angiotensin Receptor Blockers

• Although there is a signal toward improved outcomes among patients with COVID-19 who continue these medications, the risk-vs benefit decision of newly initiating these therapies in the context of COVID-19 is an area of active study.

• Although not stipulated, such guidelines should also apply to angiotensin receptor-neprilysin inhibitors or other medications containing ACE inhibitors or ARBs.
Angiotensin Converting Enzyme Inhibitors or Angiotensin Receptor Blockers

• Beta blockers can be considered as first line for cardioprotective therapy in patients treated with cardiotoxic therapy and/or with CTRCD.

• In individuals with chemotherapy-induced LV dysfunction already prescribed ACE inhibitors or ARBs, these medications may contribute to positive ventricular remodeling and should be continued in the setting of COVID-19 infection.
Anticoagulants

• Based on multiple reports, elevated clotting factors such as D-dimer, PT, and fibrinogen have been associated with worsened septic coagulopathy and outcomes in COVID-19–infected patients.

• Among cancer patients with COVID-19, 1 study found that 39% have an elevated D-dimer.
Anticoagulants

• The International Society of Thrombosis and Haemostasis has put forth guidelines recommending the use of low-molecular-weight heparin (LMWH) for thromboprophylaxis in all hospitalized patients (including those non critically ill) with COVID-19 in the absence of contraindications (ie, active bleeding or platelet count <25 109/L).
Anticoagulants

• Individuals with a sepsis-induced coagulopathy score 4 or greater or a D-dimer value greater than six-fold the upper limit of normal had a lower in-hospital mortality with LMWH prophylaxis.

• Additionally, LMWH has been shown to have anti-inflammatory properties that may be useful adjunctively in treating COVID infection.
Anticoagulants

• Continuation of anticoagulation post hospitalization can be considered in some patients considered at low risk for bleeding and at high risk for VTE, although it is not routinely recommended in all patients upon discharge.

• As with all anticoagulants in cancer patients, the benefits of treatment must be weighed against the risk of hemorrhage on an individual basis and warrant further study.
QT Interval Prolongation From COVID-19 or Cancer-Related Treatments

- Treatment of COVID-19 (eg, chloroquine, hydroxychloroquine, lopinavir, ritonavir, and azithromycin) have been implicated in corrected QT (QTc) prolongation and sudden cardiac death; caution is advised in starting these medications, and drug–drug interactions should be evaluated.
QT Interval Prolongation From COVID-19 or Cancer-Related Treatments

• Cardio-oncology patients may be receiving QT-prolonging cancer therapy (eg, arsenic) or medications (eg, antifungals and antiemetics) at baseline and therefore may be more susceptible to electrolyte disturbances that can cause further QTc prolongation.

• To reduce the risk of torsade de pointes, QT-prolonging COVID-19 medications should not be initiated in patients with a baseline QTc of 500 milliseconds or longer or with known congenital long-QT syndrome.
Exosomes contribution in COVID-19 patients’ treatment

• MSCs exert an immunomodulation effect due to the secretion of endogenous factors, such as vascular endothelial growth factor (VEGF), insulin growth factor (IGF), and nerve growth factor (NGF), transforming growth factor (TGF)-β and growth differentiation factor (GDF)-11.
Exosomes contribution in COVID-19 patients’ treatment
Home Message

- **Collaboration** between the oncology and cardiology communities will continue to be of utmost importance in taking care of cardio-oncology patients, now even more than ever, during this COVID-19 pandemic.

- The **cardio-oncology community** will carry these skills into the future and continue to build on this experience to even further strengthen the care of patients in this growing field.
Thank you