

Perioperative COVID-19 in cardiac surgery: A toxic coexistence

Kalp cerrahisinde perioperatif COVID-19: Toksik birliktelik

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It has long been known that viral respiratory tract infections, particularly influenza, is associated with cardiovascular complications including acute myocardial infarction, heart failure, and myocarditis. As being another viral respiratory tract infection, it was not a surprise to realize that novel coronavirus 2019 disease (COVID-19) is also related to these complications, but it surpassed flu in that sense and associated with a great amount of cardiovascular complications such as myocardial injury, myocardial infarction, myocarditis, cardiac arrhythmias including sudden cardiac arrest, heart failure, cardiogenic shock, and thromboembolic events.

In a study including 53,913 patients with COVID-19, individuals who were infected with severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) had a 167% higher risk of developing a cerebral venous thrombosis within two weeks after infection than those who had influenza.^[1]

In another study, involving 153,760 COVID-19 cases and more than 10 million controls, individuals who had COVID-19 had a 52% increased risk of stroke, 63% increased risk of heart attack, and 72% increased risk of heart failure compared to controls after the first 30 days of infection, and the increased risks were evident irrespective of cardiovascular risk factors including age, sex, race, diabetes, hypertension, obesity, and hyperlipidemia; the risks and associated burdens were evident even among those who had mild COVID-19 and exhibited a gradual increase across the severity spectrum of COVID-19.^[2]

The main pathogenic mechanisms of those frequent cardiovascular complications of COVID-19 are widespread presence of SARS-CoV-2 receptor

angiotensin converting enzyme 2 (ACE-2) on the host cells including endothelial cells of the blood vessels and heart and cardiomyocytes, dysregulated immune response and inflammation, endothelial injury/infection, and dysregulation of renin-angiotensin-aldosterone system (RAAS).^[3]

Although cardiovascular surgical interventions (CVSI) performed with right indications are life-saving, a systemic inflammatory response with some adverse effects is induced in patients undergoing cardiac surgery with cardiopulmonary bypass (CPB) as a result of the combination of surgical trauma, activation of blood components in the extracorporeal circuit, ischemia/reperfusion injury, endotoxin release and activation of immune cells. This response frequently leads to transient immunosuppressive states including suppression of cellular immunity and T-cell dysfunction for several days.^[4,5]

It is evident that COVID-19 and CVSI may have some similar devastating effects on immune, inflammatory and coagulation systems and endothelium. As a result patients with perioperative COVID-19 may have poor clinical outcomes due to the additive or synergistic effects of COVID-19 and CVSI on these systems. Additionally, risk factors for severe COVID-19 and cardiovascular diseases requiring CVSI are also quite similar and include age, male sex, diabetes mellitus, obesity, atherosclerotic diseases, hypertension. Those shared risk factors may also contribute to the poor clinical outcomes of perioperative COVID-19 in patients undergoing cardiovascular surgery (CVS).

In this issue of the Turkish Journal of Thoracic and Cardiovascular Surgery, Aksu et al.^[6] and Venckus et al.^[7] reported consequences of having perioperative

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COVID-19 in patients undergoing CVSI. In both of the studies comparing patients without postoperative COVID-19 infection, patients who developed COVID-19 after CVSI had higher risks of longer hospitalization, re-sternotomy for bleeding, wound infection, pneumonia, and fatality.

In previous studies, it was shown that CVSI performed during or within eight weeks of the first date of confirmed SARS-CoV-2 infection was associated with an increased risk of developing postoperative complications, including postoperative pneumonia, respiratory failure, pulmonary emboly, and sepsis.^[8] Based on these findings, surgical societies recommend delaying elective major surgery such as CVSI for seven to eight weeks after a diagnosis of COVID-19 in unvaccinated patients.^[9] Similar to other viral illnesses, decisions about the timing of elective procedures should be based on comorbidities and residual symptoms of the patient, including exercise tolerance relative to baseline and type of procedure to be performed.

During the COVID-19 pandemic, despite widespread preoperative COVID-19 screening, there has been always a risk of COVID-19 in perioperative period among patients undergoing elective surgical procedures, particularly if the incidence of COVID-19 in the population remains high. In a multi-center, prospective study including nearly 100,000 patients who underwent elective surgery in the United States Veteran's Hospitals, complication rate for the patients who were infected with COVID-19 within 30 days after elective surgery was found to be 8.4, 3.0, and 2.6 times higher for pulmonary, major and any complications, respectively.^[10] The results of the studies among patients undergoing CVSI were also similar. In a multi-center, retrospective study including 104 patients having perioperative COVID-19 in Brazilian CVS centers, postoperative complications and mortality were significantly higher in the patients who had COVID-19 after CVS than patients who were infected before CVS.^[11] In another study from the United Kingdom, patients who caught COVID-19 postoperatively had a significantly higher rate of mortality compared to those with a preoperative diagnosis (37.1% vs. 0.0%, respectively).^[12] An Indian study also confirms those findings of increased mortality and morbidity among patients who were infected with COVID-19 postoperatively.^[13]

Although patients included in the Venckus et al.'s^[7] study were older and had more comorbidities than patients included in the Aksu et al.'s^[6] study, fatality rate was lower in the previous one, which was

7% (1/14) versus 36% (8/22) for the second. Fatality rate in patients who had COVID-19 after CVSI was also higher and quite similar with the Aksu et al.'s^[6] study in aforementioned studies.^[11-13] The lower mortality rate reported in the Venckus et al.'s^[7] study could be related to the usage of remdesivir in most of the patients probably early in the infection in that study. In a double-blind, prospective, randomized, placebo-controlled study, a three days course of remdesivir was shown to reduce the risk of death and hospitalization by 87% among patients with mild COVID-19 and who were at high risk for COVID-19 progression.^[14]

Some additional antivirals including nirmatrelvir/ritonavir and molnupiravir were also shown to reduce the risk of hospitalization or death due to COVID-19 and have already licensed to use in patients with mild-to-moderate COVID-19 who are at high risk of disease progression.^[15] All of the anti-viral treatments for COVID-19 should be initiated as soon as possible and within five to seven days of symptom onset. As patients having CVSI are always at high risk of COVID-19 progression due to their comorbidities and other risk factors, patients who developed perioperative COVID-19 should have either remdesivir, or nirmatrelvir/ritonavir, or molnupiravir as soon as possible.

Both of the Venckus et al.^[7] and Aksu et al.'s^[6] studies were conducted before widespread COVID-19 vaccinations and clearly highlight the importance of the prevention of COVID-19 among patients undergoing CVSI. As highly effective COVID-19 vaccines are available all over the world at the moment, completion of both primary and booster vaccinations of the patients scheduled for CVSI before the surgery is of utmost importance to prevent the deadly risk of getting perioperative COVID-19. Finally, nosocomial transmission of COVID-19 both between patients and from healthcare workers to the patients should be prevented with proper COVID-19 vaccinations of healthcare workers and isolation of infected patients and ensuring that infected healthcare workers stay at home.

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