Pediatric cardiac surgery following severe acute respiratory syndrome coronavirus-2 infection: Early experience and lessons learnt

Supratim Sen¹, Vinay Joshi², Lopamudra Majhi³, Priya M. Pradhan¹, Sneha Jain¹, Vaibhav Dhabe³, Dipesh Trivedi⁴, Pradeep K. Kaushik⁴

¹Department of Pediatric Cardiology, NH SRCC Children's Hospital, Mumbai, Maharashtra, India, ²Department of Pediatric Intensive Care, NH SRCC Children's Hospital, Mumbai, Maharashtra, India, ³Department of Anesthesia, NH SRCC Children's Hospital, Mumbai, Maharashtra, India, ⁴Department of Pediatric Cardiac Surgery, NH SRCC Children's Hospital, Mumbai, Maharashtra, India

ABSTRACT

Background	:	We evaluated our early experience of cardiac procedures in children with congenital heart defects (CHD) after asymptomatic severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, to understand whether recent reverse transcription-polymerase chain reaction (RT-PCR) positivity had a negative impact on their postprocedural recovery and outcomes.
Materials and Methods	:	In this retrospective observational study, all patients with CHD who underwent cardiac surgery or transcatheter intervention at our institution between March 2020 and June 2021 who were detected to have asymptomatic SARS-CoV-2 infection on routine RT-PCR were included. Details of the cardiac procedure and postprocedural recovery were reviewed and compared with RT-PCR-negative patients who concurrently underwent similar cardiac surgeries or interventions at our center.
Results	:	Thirteen patients underwent cardiac surgery after recent SARS-CoV-2 positivity after a mean interval of 25.4 ± 12.9 days. One patient expired with multiorgan dysfunction and systemic inflammatory response with elevated D-dimer, serum Ferritin, C-reactive protein, and significant ground-glass opacities on chest radiograph. Another patient developed spontaneous thrombosis of the infrarenal abdominal aorta, bilateral iliac arteries, and bilateral femoral veins, requiring low-molecular weight heparin postoperatively. This patient's postoperative recovery was also prolonged due to lung changes delaying extubation. All other patients had uneventful postprocedural recovery with intensive care unit and hospital stays comparable to non-SARS-CoV-2-infected patients.
Conclusions	:	From our early experience, we can surmise that an interval of 2–3 weeks after asymptomatic SARS-CoV-2 infection is adequate to undertake elective or semi-elective pediatric cardiac surgeries. For patients requiring emergent cardiac surgery prior to this interval, there is potentially increased risk of inflammatory and/or thrombotic complications.
Keywords	:	COVID-19, multisystem inflammatory syndrome in children, pediatric cardiac surgery, severe acute respiratory syndrome coronavirus 2, surgical outcomes

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Address for correspondence: Dr. Supratim Sen, Department of Pediatric Cardiology, NH SRCC Children's Hospital, Mumbai, Maharashtra, India. E-mail: supratim80@gmail.com

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INTRODUCTION

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has had a major negative impact on the delivery of timely and optimum pediatric cardiac care in low- and middle-income countries.^[1-3] While public health resources, hospital and intensive care unit (ICU) beds were reallocated to the care of pediatric and adult patients with COVID-19 infection, resource-intensive specialties such as pediatric cardiology and cardiac surgery received less public funding.^[1] Furthermore, a generalized fear of potential increased exposure to COVID-19 in hospital environments led to parents and caregivers delaying elective and semi-elective cardiac procedures for their children with congenital heart defects (CHD).^[1,3]

As we adapted to the first wave of the pandemic in India and resumed pediatric cardiac surgery and interventions, our hospital protocols added routine SARS-CoV-2 reverse transcription-polymerase chain reaction (RT-PCR) testing of all patients admitted for a cardiac procedure. This led to incidental detection of asymptomatic SARS-CoV-2 infection in a few patients with CHD, who did not manifest any overt symptoms attributable to COVID-19. This study aims to analyze our evolving protocol and results for the management of these patients with CHD who underwent cardiac surgery after an initial positive RT-PCR result, to understand whether recent SARS-CoV-2 positivity had a negative impact on their postprocedural recovery and outcomes.

MATERIALS AND METHODS

This is a retrospective observational cohort study. The hospital ethics committee approved this study and individual patient consent was waived. Patients who underwent cardiac surgery between March 2020 and June 2021, and whose routine preprocedural RT-PCR was initially positive for SARS-CoV-2, were included. Patients with symptoms of COVID-19 such as high-grade fever, cough, or recent worsening of breathlessness and those patients whose close contacts were SARS-CoV-2 RT-PCR positive but who themselves were RT-PCR negative, were excluded from the study. Patients who underwent cardiac procedures more than 60 days after an initial positive RT-PCR report were also excluded as we did not expect previous SARS-CoV-2 exposure to influence outcomes after an interval of 8–9 weeks.

Our hospital's protocol for preprocedural COVID-19 testing is outlined in Figure 1. For patients who initially tested positive for SARS-CoV-2 in whom emergency cardiac surgery was not clinically indicated, the RT-PCR testing was repeated after a minimum home or institutional quarantine of 2 weeks, as mandated by government guidelines.



Figure 1: Institutional preprocedural testing protocol for COVID-19 in cardiac patients

The details including patient's age, weight, diagnosis, and intervention were obtained from hospital records. The interval between the initial SARS-CoV-2 RT-PCR report and the cardiac procedure was recorded, and details of postprocedural recovery including days of ICU stay and hospital stay were noted.

To evaluate whether recent SARS-CoV-2 infection impacted postprocedural recovery and outcomes, we compared the postprocedural recovery and outcome data of the study patients with RT-PCR-negative patients with similar cardiac defects who concurrently underwent similar cardiac surgeries at our center during the study.

Statistics

For this descriptive analysis, the data were summarized using means with standard deviation for normally distributed data. Categorical variables were expressed as numbers and percentages. Due to the small numbers, further statistical analysis was not done.

RESULTS

In the study period, a total of 13 children were detected to be SARS-CoV-2 RT-PCR positive on routine preprocedural screening and fulfilled inclusion criteria. These patients did not have symptoms attributable to COVID-19, such as high-grade fever, cough, or recent worsening of breathlessness. Any baseline tachypnea or desaturation was ascribed to their congenital heart disease.

Patient characteristics, procedural details, and outcomes are summarized in Table 1. All patients were confirmed to be SARS-CoV-2 RT-PCR negative on repeat testing prior to their cardiac surgery. The mean (\pm standard deviation) interval between the first positive SARS-CoV-2 RT-PCR test and the procedure was 25.4 \pm 12.9 days.

Table 2 summarizes the comparison of postoperative ICU and hospital stay in these patients who were previously SARS-CoV-2 RT-PCR positive with a cohort of

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Patient	Age (months)	Weight (kg)	Diagnosis	Surgery done	Interval between COVID positivity and surgery (days)	CPB (min)	XC (min)	ICU stay (days)	Hospital stay (days)	CRP (mg/L)	Outcome
1	31	9.7	DORV VSD PS	ICR, PA plasty, RV-PA conduit	19	161	117	6	14	3	Good
2	9	5.9	DORV VSD PS	IVTR+TAP	42	294	211	18	26	11	Expired
3	16	8.8	VSD	VSD closure + RVOT Resection	18	48	33	3	7	7	Good
4	7	4.6	VSD, ASD, LPA Sling	VSD+ASD closure, LPA reimplantation	18	147	45	2	7	35	Good
5	10	3.7	VSD	VSD closure	15	52	31	2	8		Good
6	12	4.6	VSD	VSD closure	35	61	37	2	7		Good
7	0.27	3.2	TGA	ASO	8	115	78	12	21		Thrombotic complications. Good outcome
8	7	5.6	TGA VSD	ASO, VSD closure	30	145	118	4	7	14	Good
9	3	3.8	TGA VSD	ASO VSD closure	18	133	97	5	8		Good
10	7	5.5	Congenital MS, VSD, PDA	VSD closure, supramitral membrane excision, PDA ligation	55	86	57	3	12	222	Culture positive sepsis requiring IV antibiotics. Good outcome
11	12	6.8	Tricuspid Atresia 1B	BD Glenn, atrial septectomy	23	30	19	1	13		Good
12	9	3.4	Supracardiac TAPVC	TAPVC repair	30	49	31	3	11		Good
13	132	18.1	Secundum ASD	ASD closure	18	32	13	2	6		Good

DORV: Double outlet right ventricle, VSD: Ventricular septal defect, PS: Pulmonary stenosis, ASD: Atrial septal defect, LPA: Left pulmonary artery, TGA: Transposition of great arteries, MS: Mitral stenosis, TAPVC: Total anomalous pulmonary venous connection, ICR: Intracardiac repair, IVTR: Intraventricular tunnel repair, TAP: Transannular patch, RVOT: Right ventricular outflow tract, ASO: Arterial switch operation, CPB: Cardiopulmonary bypass time, XC: Cross clamp time, CRP: C-reactive protein, ICU: Intensive care unit, IV: Intravenous, PDA: Patent ductus arteriosus, BD Glenn: Bidirectional Glenn

RT-PCR-negative patients who underwent similar cardiac procedures during the study at our center.

We had one early postoperative mortality and 12 patients recovered with good early outcomes. The child who expired (patient 2) underwent intraventricular tunnel repair with transannular patch for double outlet right ventricle, ventricular septal defect (VSD) with pulmonary stenosis. He was operated 42 days after an initial positive SARS-CoV-2 RT-PCR but was RT-PCR negative on repeat testing prior to surgery. He required a second bypass-run and prolonged cardiopulmonary bypass (CPB) and cross-clamp times to address residual lesions detected on the epicardial echocardiogram. Postoperatively, he had normal biventricular function and no residual cardiac defects and was extubated on the 7th postoperative day (POD). On POD 10, he developed fever with worsening respiratory distress requiring reintubation and had persistent hypoxia and hypercarbia on arterial blood gas with diffuse ground-glass opacities in both lungs on chest radiograph. Acute phase reactants were elevated: D-dimer was 1804 ng/ml, serum Ferritin 772 ng/ml, and C-reactive protein (CRP) 11 mg/L. Repeat SARS-CoV-2 RT-PCR and blood cultures at this stage were negative. Antibiotics and inotropes were escalated but the patient had a progressive deterioration to multi-organ dysfunction (MODS) and refractory shock. The child succumbed 18 days' postsurgery.

line insertion, a peripheral Doppler ultrasound study was done and confirmed spontaneous thrombosis of the infrarenal abdominal aorta extending to bilateral iliac arteries as well as partial thrombosis in both (right > left) femoral veins. No previous arterial puncture or umbilical arterial line insertion had been done or attempted prior to the detection of spontaneous thrombosis. There was adequate collateral flow distal to the thrombi, and perfusion was mildly decreased but acceptable. D-dimer was elevated (2682 ng/ml) immediately postsurgery. This patient did require prolonged ventilation, which was attributed to lung changes on chest radiograph as cardiac findings were normal on echocardiogram. Although the ICU and hospital stay were prolonged, the child had a good outcome. Low-molecular weight heparin was initiated for the thrombosis and continued for 6 months postoperatively, prior to transitioning to oral aspirin. Subsequent thrombophilia workup for this baby was done 3 months' postoperatively and revealed a heterozygous methylenetetrahydrofolate reductase (MHTFR) mutation without elevated homocysteine levels. There were no further complications detected on mid-term follow-up of 12 months.

One patient (patient 7) with d-TGA was SARS-CoV-2

RT-PCR positive at birth. He had significant desaturation despite a balloon atrial septostomy and hence was taken

up for arterial switch operation on day 8 of life. Repeat

RT-PCR immediately prior to surgery was negative. In view

of feeble femoral pulses detected during perioperative

Table 2: Comparison of intensive care unit stay and hospital stay in previously severe acute respiratory
syndrome-coronavirus-2 positive cases and coronavirus disease-2019 negative controls

	Grou	p 1-VSD closure	
	Previous SARS-CoV-2	No previous COVID-19 (n=4)	Inference
	infection (<i>n</i> =2)		
Mean ICU stay (days)	2±0	2.3±1.5	No negative impact of RT-PCR
Mean hospital stay (days)	7.5±0.7	6.0±1.2	positivity on postoperative recovery,
Mean CPB (min)	57±6.4	47.8±15.6	with similar CPB and cross-clamp
Mean XC (min)	34±4.2	31.0±10.4	times
	Group 2-TOF/V	SD, PS intracardiac repair	
	Previous SARS-CoV-2	No previous COVID-19 (n=4)	Inference
	infection (<i>n</i> =2)		
Mean ICU stay (days)	12±8.5	3.25±0.5	Outcomes not comparable as
Mean hospital stay (days)	20±8.5	7.75±2.2	CPB and cross-clamp times in the
Mean CPB (min)	227.5±94.0	68.5±17.4	SARS-CoV-2 group are longer and
Mean XC (min)	164±66.4	47.5±17.3	can affect the postoperative recovery
	Group 3-Art	terial switch operation	
	Previous SARS-CoV-2	No previous COVID-19 (n=4)	Inference
	infection (<i>n</i> =1)		
Mean ICU stay (days)	12	8.5±0.7	With comparable CPB and
Mean hospital stay (days)	21	13±1.4	cross-clamp times, the ICU stay and
Mean CPB (min)	115	107.5±9.1	hospital stay were longer in the patient
Mean XC (min)	78	79±9.9	with previous COVID-19 infection
	Group 4-Arterial s	witch operation+VSD closure	
	Previous SARS-CoV-2	No previous COVID-19 (n=4)	Inference
	infection (<i>n</i> =2)		
Mean ICU stay (days)	4.5±0.7	8±2.2	No negative impact of RT-PCR
Mean hospital stay (days)	7.5±0.7	11.2±1.7	positivity on postoperative recovery,
Mean CPB (min)	139±18.5	124.5±24.1	with similar CPB and cross-clamp
Mean XC (min)	107.5±14.8	94.75±22.0	times

ICU stay and hospital stay in days (mean±SD). VSD: Ventricular septal defect, TOF: Tetralogy of fallot, PS: Pulmonary stenosis, CPB: Cardiopulmonary bypass time in min (mean±SD), XC: Cross clamp time in minutes (mean±SD), ICU: Intensive care unit, SARS-CoV-2: Severe acute respiratory syndrome coronavirus-2, SD: Standard deviation, RT-PCR: Reverse transcription-polymerase chain reaction, COVID-19

DISCUSSION

The COVID-19 pandemic has adversely impacted pediatric cardiac services internationally, and this trend has been reported in India too.^[1,3] A recent multicenter retrospective observational study from 24 pediatric cardiac centers across India conducted by the Pediatric Cardiac Society of India analyzed hospital data from April to August 2020 and compared this to corresponding months in 2019.^[3] The authors reported a 74.5% reduction in outpatient visits, 66.8% reduction in hospitalizations, 73.0% decrease in cardiac surgeries, and 74.3% decrease in catheterization procedures in April-August 2020 compared to the preceding year.[3] The overall in-hospital mortality was higher in 2020 (8.1%) as compared to 2019 (4.8%), with a higher postoperative mortality (9.1% vs. 4.3%). The authors observed that a greater proportion of complex surgeries, neonatal surgeries, emergency surgeries, and operating on patients with an active or recent COVID-19 infection were likely reasons for the higher postoperative mortality during the first wave of the pandemic.^[3]

Patients with CHD are thought to be at potentially higher risk of developing severe COVID-19,^[4-6] especially

in those patients with uncorrected CHD, cyanotic CHD with saturation <85%, infants, and patients with pulmonary hypertension.[5-7] SARS-CoV-2 infection is known to cause cardiac injury indirectly with the immune-inflammatory response and cytokine storm, and directly by invasion of cardiomyocytes.^[4] Cardiac involvement with ventricular dysfunction is also seen in 30%-40% of patients with multisystem inflammatory syndrome in children (MIS-C).^[8,9] Haji Esmaeil Memar et al. reported a series of nine patients with CHD who developed COVID-19.^[10] There were two deaths in this series, in a 14-year-old patient with aortic stenosis and a 10-month-old infant with hypoplastic left heart syndrome, respectively. Patients with a wide spectrum of CHD including total anomalous pulmonary venous connection (TAPVC), truncus arteriosus, pulmonary atresia-intact ventricular septum, Tetralogy of Fallot (TOF), patent ductus arteriosus, and VSD recovered from their primary COVID-19 infection in this cohort, although surgical correction was reported in only two.^[10] Simpson and colleagues reported their multicenter experience with COVID-19 infection in seven children with preexisting cardiac conditions including atrioventricular canal defect, anomalous left coronary artery from the pulmonary artery, dilated cardiomyopathy, hypertrophic cardiomyopathy and status-postheart transplant.[11] This series comprised five infants and three patients with atrioventricular canal defect and trisomy 21. Worsening heart failure and arrhythmias were the common presentations. The authors reported 1 early death, 1 late death, and 5 (71%) ICU admissions including 2 prolonged ICU stays of over 30 days. In a recent multicenter retrospective observational study from India, Sachdeva et al. reported data of COVID-19 infection in children with heart disease and grown-ups with CHD (GUCH).^[7] The cohort included 94 patients with COVID-19 infection seen at the 13 participating pediatric cardiac centers, comprising 10 neonates (10.6%), 37 infants (39.4%), 36 children aged 1-18 years (38.3%), and 11 GUCH patients (11.7%) (aged 18-62 years). The median age was 13 months (range 3 days-62 years). One-third (n = 31, 33%) of the patients had acyanotic CHD, and 41.5% (n = 39) were cyanotic. Eighteen of these patients (19.1%) had undergone a previous cardiac surgery or intervention. Only 30 patients (31.9%) were symptomatic for COVID-19 at the time of testing, and the rest (64 patients) had incidental SARS-CoV-2 detected as part of preprocedural screening. Hospitalization following a positive COVID test was required in 51.1% of the patients (n = 48) and the rest were managed at home. Three patients had thrombotic complications including a left ventricular thrombus in a patient with dilated cardiomyopathy, prosthetic mitral valve thrombosis in a child with rheumatic heart disease, and ischemic stroke in an infant following the closure of VSD. Of the 13 patients requiring intubation and ventilation at admission, nine died. There were 13 total deaths in this series (case fatality rate: 13.8%), including 3 among 19 patients operated for heart disease during the index hospitalization.^[7] During the index hospitalization, three patients required emergency interventions, two required emergency surgery and the rest underwent cardiac surgery 10-28 days after recovery from COVID-19 infection. The authors highlighted the high case fatality rate observed in this cohort amongst predominantly young unoperated children with serious CHD and COVID-19 infection.^[7] Admittedly, one of our greatest concerns during the pandemic has been SARS-CoV-2 exposure and infection of our unoperated and operated patients with CHD. In our study cohort, although we had 10 infants and seven patients with cyanotic CHD (both risk factors for COVID-19 complications), fortunately, no patient deteriorated or manifested signs of COVID-19 prior to their procedures despite being RT-PCR positive.

COVID-19 may potentially increase the morbidity and mortality of cardiac procedures, especially surgery on CPB. The activation of immunological and inflammatory cascades and a potential for systemic inflammatory response syndrome (SIRS) is a known phenomenon following cardiac surgeries on CPB.[5,12,13] COVID-19 can itself cause inflammation and an exaggerated immune response, which may progress to acute respiratory distress syndrome, SIRS, and MODS.^[12] As we know from our experience with MIS-C,^[8,9] the inflammatory sequelae of COVID-19 can persist and recur even weeks after recovery from the primary infection. Since the onset of the COVID-19 pandemic, hospital protocols incorporated routine SARS-CoV-2 RT-PCR testing of all patients for cardiac procedures to detect asymptomatic infection and minimize risks of cross-infection to others. This has led to incidental RT-PCR positivity in asymptomatic patients, which is a new dilemma we face as clinicians. Even in these patients with recent asymptomatic infection who have subsequently recovered with negative repeat RT-PCR, there is a theoretical risk of exaggerated inflammatory response postcardiac surgery, especially for surgeries on CPB. Such inflammatory response and progression to MODS were seen in one of our patients (patient 2). Although the postoperative complications may have been secondary to low cardiac output state following long CPB and cross-clamp times or sepsis, the patient had an initial recovery allowing weaning of inotropes and extubation by the 7th POD. From the 10th POD, the patient progressively deteriorated with a generalized multisystem inflammatory response, MODS, and elevated acute phase reactants, prompting us to treat this as MIS-C.

The data regarding CHD surgery and the associated risks of perioperative COVID-19 are scarce.^[7,14] To the best of our knowledge, there are no studies which have analyzed the safe interval between asymptomatic SARS-CoV-2 infection and elective or semi-elective invasive pediatric cardiac procedures. A recent international, multicenter, prospective cohort study by Nepogodiev et al. from the COVIDSurg collaborative and the GlobalSurg collaborative analyzed surgical patients who underwent elective or emergency surgery in October 2020 with preoperative SARS-CoV-2 infection and compared them with those without previous SARS-CoV-2 infection.[15] The patient ages in this study ranged from 0 to >80 years, and a total of 140,231 patients were included across 1674 hospitals in 116 countries, of whom 3127 (2.2%) patients had a preoperative SARS-CoV-2 diagnosis. In those patients with preoperative SARS-CoV-2 diagnosis, mortality was increased in patients having surgery within 0-2 weeks, 3-4 weeks, and 5-6 weeks of the diagnosis (odds ratio [95% confidence interval (CI)] 4.1 [3.3-4.8], 3.9 [2.6-5.1], and 3.6 [2.0-5.2], respectively). Overall, patients operated within 6 weeks of SARS-CoV-2 diagnosis were at an increased risk of 30-day postoperative mortality and 30-day postoperative pulmonary complications. Surgery performed ≥7 weeks after SARS-CoV-2 diagnosis was associated with a similar mortality risk to baseline (odds ratio [95%CI] 1.5 [0.9-2.1]). The authors concluded that if possible, surgery should be delayed for at least 7 weeks following SARS-CoV-2 infection, with a caveat that patients with ongoing symptoms \geq 7 weeks from diagnosis may benefit from further delay.^[15]

Risk stratification guidelines for CHD were published in 2020 to triage cardiac procedures to minimize unnecessary exposure of patients with CHD to SARS-CoV-2.^[12,16] As a tertiary referral cardiac center, we too followed this stratification system for a few months during the first pandemic wave in India, but then realized the limitations of indefinitely delaying semi-elective cardiac procedures as the pandemic continued. While cases such as VSD closure and TOF repair may safely be deferred for a few weeks, prolonged delays can lead to worsening congestive cardiac failure, recurrent pneumonias, failure to thrive, progression of pulmonary hypertension, and multiple cyanotic spells depending on the type of CHD. Other critical CHD such as transposition of great arteries with intact ventricular septum and obstructed TAPVC need emergency cardiac surgeries even if found to be SARS-CoV-2 RT-PCR positive. Hence, the 6-7 weeks' interval generally recommended for elective and semi-elective surgeries after asymptomatic SARS-CoV-2 is often not clinically attainable in many children presenting with symptoms secondary to CHD. Our mean interval between SARS-CoV-2 positivity and cardiac surgery was 25.4 ± 12.9 days. In most of our patients treated after an interval of 2 weeks, we observed similar postoperative ICU and hospital stays when compared to the RT-PCR negative patients treated in the same time period. The only patient operated within an interval of <2 weeks after the RT-PCR positivity was patient 7 who underwent arterial switch operation, and this baby had elevated D-dimer levels and spontaneous thrombosis. This baby was found to have a heterozygous MHTFR mutation on subsequent thrombophilia work-up, which by itself is not known to predispose to thrombosis.^[17] In a recent multicenter retrospective study, Whitworth et al. analyzed the incidence of thrombosis in children with COVID-19, asymptomatic SARS-CoV-2, and MIS-C.^[18] Among a total of 853 admissions in 814 patients (426 COVID-19, 138 MIS-C, and 289 asymptomatic SARS-CoV-2), 20 patients had thrombotic events. Patients with MIS-C had the highest incidence of thrombotic events (6.5%, 9/138) compared to COVID-19 (2.1%, 9/426) or asymptomatic SARS-CoV-2 (0.7%, 2/289). The authors observed that D-dimer >5 times upper limit of normal was significantly associated with thrombotic events in their study and that asymptomatic SARS-CoV-2 infection may not significantly increase the risk of thrombosis.^[18] Sachdeva et al. and colleagues also reported thrombotic complications in three patients (3/94; 3%) in their cohort.^[7] In our patient cohort, while we did not routinely test for D-Dimer or ferritin levels on all our study patients, the levels were elevated in the two patients where we faced complications (thrombosis and death, respectively).

This study has limitations due to its retrospective observational design, and since D-dimer, serum ferritin, and CRP were not done routinely in all patients to quantify subclinical inflammation, either preoperatively or postoperatively. Moreover, the effect of CPB itself on D-dimer and serum ferritin in normal postoperative cardiac patients is not well defined, and it is difficult to unequivocally differentiate inflammatory effects of CPB from those of SARS-CoV-2. Biomarkers help in stratifying disease severity and prognosis in COVID-19^[19] and perhaps even in asymptomatic SARS-CoV-2 infection, preoperative inflammatory biomarkers may have a role in detecting subclinical inflammation and predicting the postoperative course. Further prospective studies are required to evaluate this.

CONCLUSIONS

In our experience, an interval of 2 to 3 weeks between asymptomatic SARS-CoV-2 detection and the cardiac surgery was sufficient. For patients requiring emergent cardiac procedures prior to this interval, the clinician should anticipate a potentially increased risk of COVID-19 related inflammatory and/or thrombotic complications.

Disclosures

The authors state that they had full control of the design of the study, methods used, outcome parameters, analysis of data, and production of the written report.

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Conflicts of interest

There are no conflicts of interest.

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