Case Report

SARS-CoV-2 (COVID-19) PCR cycle threshold: can it help in the timing of urgent cardiac surgery?

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Summary
Background: The COVID-19 pandemic has resulted in a significant reduction in urgent cardiac surgery due to concerns about safety for both patients and care givers. The timing of safe cardiac surgery is yet to be clarified in the setting of COVID-19 diagnosis.

Methods: Due to the urgency of the cardiac conditions on presentation, we have operated on four patients who exhibited the spectrum of COVID-19 disease from asymptomatic to severe COVID-19 pneumonia. With the evolving knowledge about SARS-CoV-2 and its genetic determinants as well as the cycle threshold levels obtained from real-time reverse transcription polymerase chain reaction, we have attempted to develop a strategy to deal with these patients.

Results: All four patients underwent urgent cardiac surgery following a thorough evaluation and multidisciplinary team approach with guidance based on the virus cycle threshold values obtained by reverse transcription polymerase chain reaction.

Conclusion: We have shown that, with thorough preparations, consideration of the significance of the cycle threshold obtained on reverse transcription polymerase chain reaction and meticulous timing, COVID-19 diagnosed patients may undergo open heart surgery safely.

Keywords
cardiothoracic surgery, cardiovascular medicine, ischaemic heart disease, surgery

Introduction
The COVID-19 pandemic, caused by the SARS-CoV-2 virus, has had a negative impact on healthcare worldwide, with no guidelines for COVID-19 patients undergoing urgent cardiac surgery. Qatar has one of the highest incidences of SARS-CoV-2 positivity/million (extensive screening, Ministry of Public Health: moph.gov.qa), but one of the lowest death rates.

We report on four COVID-19 patients, who underwent urgent cardiac surgery with excellent outcomes. We utilised real-time reverse transcription polymerase chain reaction (rtRT-PCR) and the cycle threshold (C_T) of specific SARS-CoV-2 genes to help guide the timing of surgery.

Description
Molecular testing
rtRT-PCR for SARS-CoV-2 Virus: naso-/oropharyngeal swabs (Copan Diagnostics Inc, Italy) placed in Universal Transport Medium; aliquots extracted on the QIAsymphony platform (Qiagen, USA) and tested by rtRT-PCR with Thermo/Fisher TaqPath COVID-19 RT-PCR Kit (Thermo/Fisher, USA) for S, N and ORF1a&b genes, or onto Roche Cobas6800 using Cobas® SARS-CoV-2 Test (Roche, Switzerland) for ORF-1a/b and E-gene of SARS-CoV-2.

The C_T value is the PCR cycle number at which the fluorescence generated crosses a fluorescence signal threshold, and a detectable amount of target nucleic material has been generated during the PCR reaction. The lower the C_T value, the greater the amount of nucleic material present. At our institution, a C_T value below 33 for the E, N, ORF1a&b and S genes is diagnostic of COVID-19.

Anaesthesia in COVID-19 patients
(i) Full Personal Protective Equipment (PPE).
(ii) Patients covered with plastic tents.
(iii) Pre-induction oxygenation for 5 min using in-circuit High Efficiency Particulate Air (HEPA) filters.

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(iv) Rapid sequence induction technique: 1 min apnoea, video-laryngoscopic endotracheal intubation using a clamp applied after removing the stylet, cuff inflation and ventilator connection.

**Patient 1**

A 43-year-old man presented with chest pain, ST changes and an elevated troponin. Despite being asymptomatic, a COVID-19 rtRT-PCR test was positive (E 21, N 24, ORF1a&b 33). Coronary angiography (CAG) showed three vessel disease not amenable to angioplasty. Following a Multidisciplinary Team Discussion (Cardiologists, Cardiac Surgeons, Anaesthetists, Infectious Disease Specialists) and on-going symptoms, his coronary artery bypass grafting (CABG) was undertaken.

**Patient 2**

A 50-year-old man presented with chest pain, ST changes and an elevated troponin. A COVID-19 rtRT-PCR test was positive (E 33, N 38, ORF1a&b 31, S 35), although he was asymptomatic. CAG showed 90% left main stenosis and due to on-going symptoms proceeded to CABG.

**Patient 3**

A 47-year-old man presented with chest pain, ECG changes and an elevated troponin. The initial COVID-19 rtRT-PCR test was indeterminate. CAG showed significant complex three vessel disease. Repeat COVID-19 rtRT-PCR was positive (E 33, ORF1a&b 31). Due to on-going symptoms, he proceeded to CABG. Patients 1 to 3 all had surgery within one week of a positive result and made uneventful recoveries and were transferred to COVID-19 facilities.

**Patient 4**

A 37-year-old man (with known Marfan’s Syndrome) presented with cough/breathlessness from a COVID-19 quarantine facility, having arrived from a high incidence COVID-19 country where he had undergone elective thoracoabdominal aortic aneurysm (8 cm) repair. Before discharge, he underwent a computerised tomogram (CT) showing a new innominate artery dissection with the ascending aorta poorly visualised. He was tachypnoeic and hypoxic. He denied chest pain.

Our CT scan (Figure 1) showed a Stanford Type A aortic dissection, with typical COVID-19 pneumonic changes. Echocardiogram showed an ejection fraction of 25% with moderate aortic regurgitation. The patient’s rtRT-PCR was negative, but his wife tested positive. He was managed conservatively although he came close to intubation. He was treated with Azithromycin and Hydroxychloroquine as this was the recommended treatment at that time.

We felt there was chronicity to the dissection (no pain and previous institutions CT scan), and with his radiologically diagnosed COVID-19 pneumonia, we treated him conservatively initially. Pulmonary CT (Figure 2) 14 days later showed resolution of the pneumonia and he underwent root replacement for his Type A dissection. He made an uneventful recovery and subsequently had positive serology (BioMedomics COVID-19 IgM-IgG Rapid Test, Morrisville, NC, USA).

All Intensive Care Staff wore full PPE (no short-ages) with routine post-operative cardiac surgery care given in a designated COVID-19 Isolation Room in a partitioned intensive care unit. No staff involved developed COVID-19 infection, and family were excluded from visiting.

**Comment**

The COVID-19 pandemic has overwhelmed healthcare systems with no specific COVID-19 treatment...
available it is important to utilise available evidence when managing patients. The diagnostic effectiveness of rtRT-PCR\(^3,4\) for COVID-19, as well as the C\(_T\) value means that guidelines for the timing of surgery are evolving.\(^5,6\) We have employed rtRT-PCR for the SARS-CoV-2 E, N, ORF1a&b and S genes, with a C\(_T\) value of 33 used as a cut-off for positivity. If the C\(_T\) value (at least two genes) is greater or equal to 33, then COVID-19 is deemed negative, whereas a C\(_T\) value less than 33 is considered positive for COVID-19. The relationship between the viral load and C\(_T\) as determined by rtRT-PCR has been well characterised for SARS-CoV-2 virus and other pathogens.\(^5,6\)

There is no published guidance for cardiac surgeons so we have relied on the C\(_T\) value to determine the timing of urgent surgery, when it is not possible to delay. Patient 1 had a low C\(_T\) value, (significant viral load); Patient 2 (C\(_T\) indeterminant) and Patient 3 (C\(_T\) 31); all had excellent post-operative outcomes. Patient 4 presented with severe COVID-19 pneumonia (Figure 1). Pulmonary CT is well established as the standard for the diagnosis of COVID-19 disease\(^7\) with high sensitivity. All patients were given a higher than normal risk on consenting, but their underlying cardiac conditions were felt to be more of a risk. Where possible, we delayed surgery until the C\(_T\) value was higher (low viral load), or the chest CT had improved (Figure 2). The Korean Centre for Disease Control published data on patients discharged following two weeks of quarantine and high C\(_T\) values and subsequently showing had low infectivity.\(^8\)

In this short report, we aim to show the possible importance of the rtRT-PCR C\(_T\) value and its relevance to COVID-19 disease in the setting of cardiac surgery. Also, we have shown that COVID-19 diagnosed patients may undergo cardiac surgery, safely.

**Declarations**

**Competing Interests:** None declared.

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**Guarantor:** A Alkhulaifi.

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