# COVID-19 IN PATIENTS RECOVERING FROM CARDIAC SURGERY: A SURPRISING MILD DISEASE COURSE

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### Abstract

Cardiac surgical patients are often discharged to a rehabilitation facility to complete the convalescence in a protected setting. This care pathway is usually reserved for elderly and fragile patients, with severe and invalidating comorbid conditions. Between March and April 2020, nineteen patients were discharged from our unit to a rehabilitation clinic where a hotbed of SARS-CoV-2 infection was documented on April 17. After the outbreak, all patients underwent screening with real-time PCR on nasal swabs, and 18/19 patients were found positive. Diversely from other observations on perioperative COVID-19 reporting mortality rates of 30-40%, the COVID-19 had a benign course in our cohort: six patients were completely asymptomatic, and only seven patients required hospitalization (no deaths). We describe the baseline, operative and postoperative features of these patients, and present some potential explanations for the surprisingly benign course of the COVID-19 in this cohort.

## COVID-19 IN PATIENTS RECOVERING FROM CARDIAC SURGERY: A SURPRISING MILD DIS-EASE COURSE

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#### Abstract

Cardiac surgical patients are often discharged to a rehabilitation facility to complete the convalescence in a protected setting. This care pathway is usually reserved for elderly and fragile patients, with severe and invalidating comorbid conditions. Between March and April 2020, nineteen patients were discharged from our unit to a rehabilitation clinic where a hotbed of SARS-CoV-2 infection was documented on April 17. After the outbreak, all patients underwent screening with real-time PCR on nasal swabs, and 18/19 patients were found positive. Diversely from other observations on perioperative COVID-19 reporting mortality rates of 30-40%, the COVID-19 had a benign course in our cohort: six patients were completely asymptomatic, and only seven patients required hospitalization (no deaths). We describe the baseline, operative and postoperative features of these patients, and present some potential explanations for the surprisingly benign course of the COVID-19 in this cohort.

Cardiac surgical patients are often discharged to a rehabilitation facility, to complete the convalescence in a protected setting. This care pathway is usually reserved for elderly and fragile patients, or for those with severe comorbid conditions. Between March 23 and April 14, nineteen patients were discharged from our unit to a rehabilitation clinic where a hotbed of SARS-CoV-2 infection was documented on April 17<sup>th</sup>. After the outbreak all patients underwent screening, and 18 were found positive. Here we describe this patient population. The Internal Review Board approved this study. Oral informed consent was asked to all patients.

## A mild COVID-19 in a high-risk population

The patients' data are reported in Table 1. This was a group of critically ill patients with severe comorbidities and high risk scores. The indications to surgery were: aortic dissection (3), congestive heart failure (13) and endocarditis (2). Five patients had complications (low output syndrome 3, bleeding 2, renal failure 2, prolonged ventilation 3).

The median interval between the operation and the discharge was 8 days (range 5 - 31). Before discharge, all patients underwent screening to exclude a subclinical SARS-CoV2 infection: all these exams were negative.

After a median period of 9 days in the rehabilitation clinic (range: 4-24), 18/19 patients presented a SARS-COV2 positive swab. Surprisingly, the infection had a benign course in this cohort: six patients were completely asymptomatic, and the remaining had only mild symptoms. Only six patients had fever and one complained of dyspnea. Seven patients were hospitalized, and only one needed a short admission in the COVID-19 ICU for dyspnea and mild hypoxemia, that was treated by CPAP. The remaining eleven patients were discharged home, or to a COVID-19 hotel. At the latest follow-up (October 31<sup>st</sup>), all patients had been discharged home.

#### Comment

The SARS-COV2 infection can be pauci-symptomatic, causing a flu-like disease. In some patients, however, it causes severe interstitial pneumonia and ARDS (1). In a meta-analysis of 34 studies, totaling 6263 patients, the incidence of severe disease and ICU admission ranged between 9.6% and 56.3% (2). Recently, there has been a consistent effort to identify the risk factors and the mechanisms leading to the development of severe disease, and there is evidence that comorbid chronic diseases and acute organ injury might predispose to the development of ARDS. Older age, obesity, arterial hypertension, COPD and cardiovascular diseases have been repeatedly indicated as major risk factors for the development of severe symptoms and death: all these conditions were highly prevalent in our cohort.

The COVIDSurg Collaborative reported 30-day mortality and pulmonary complications in 1128 patients with perioperative SARS-CoV-2 infection. Pulmonary complications were frequent, and associated with an increased mortality. In the subgroup of 51 cardiac surgical patients, the incidence of pulmonary complications was as high as 94.1%, and the mortality was 34% (3). Yates and coworkers reported similar results: all their patients had pulmonary complications, the postoperative hospital stay was prolonged, and the mortality was 44.4% (4). Considering all these data, the benign course of the COVID-19 in our patients might appear paradoxical.

#### Chance or causality?

A first, possible explanation of this paradox is stochastic: given that the true prevalence and mortality rate of the SARS-COV2 infection are not known, it is possible that the low rate of symptoms and complications was simply due to chance. Indeed, all patients - not only those with a clinical suspect of COVID-19 - were tested in the rehabilitation clinic, and this could have maximized the sensitivity of the screening program.

However, the prevalence of severe comorbid chronic diseases and risk factors was extremely high in our cohort, increasing the theoretic risk of a severe covid-19. In fact, data from other series of perioperative COVID-19 in cardiac surgery showed ubiquitous pulmonary complications and very high mortality rates (3, 4).

An attractive hypothesis is that our patients were somehow "protected" from the COVID-19. All our patients received low molecular weight heparin during the perioperative period, and all except one were discharged on oral anticoagulants. An altered hemostasis plays a major role in the development of severe COVID-19, and anticoagulants might have exerted a protective effect (5).

Severe COVID-19 is characterized by the development of ARDS, which eventually leads to ICU admission and death (6). A maladaptive immune response, involving activation of the innate immunity has been indicated as the pathogenetic mechanism of ARDS. Cardiac surgery promotes a strong systemic inflammatory response (7). It is possible that the recent activation of the innate immunity related to the surgical stress caused a secondary immunodeficiency in our patients, resulting in a blunted immune response to the SARS-COV2 infection.

While the potential protective role of a blunted immune response and/or of the anticoagulant therapy may only be speculated, our population offers an interesting view on a delicate aspect of the COVID-19 pandemic, that is the occurrence of a cluster of infections in a group of high-risk hospitalized patients. Eighteen out of 19 patients were infected, highlighting the contagiousness of the disease. The timing of the infection is also of interest. All our patients came in contact with the SARS-CoV2 postoperatively, after  $10.0\pm4.8$  days, while previous series included cases of preoperative infection and/or early postoperative infection: this could explain the severity of the perioperative COVID-19 observed by others.

Our data show that the SARS-CoV2 infection after cardiac surgery may have a benign course. We believe the favorable outcome observed in our patients along with the negative experiences previously reported highlight the importance of an aggressive screening to rule out a preoperative infection (and to postpone the operation in positive patients whenever possible), and suggest that anticoagulation could help to prevent the development of severe COVID-19 in these patients. Further studies are needed to investigate the relationship between the surgery-induced inflammatory response, anticoagulation and severity of COVID-19.

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### Table 1. patients characteristics

Demographics and risk factors Age (y) Sex, M Hypertension Diabetes Smoking Obesity drug abuse COPD Renal failure CAD lvd Pulmonary hypertension Preoperative inotropes/IABP other chronic condition Surgical details sts score Emergency REDO complex combined procedures endocarditis Aortic dissection Major complications covid-19 related syptoms and course time to diagnosis asymptomatic fever cough sore throat dyspnoea gi symptoms Major rise in PCR levels sent to a covid 19 unit sent to a covid 19 icu warfarin/heparin at discharge COPD: chronic obstructive pulmonary disease, cad: coronary artery disease, lvd: left ventricular dysfunction, iabp: intra-ac