

COVID-19 in patients recovering from cardiac surgery: A surprising mild disease course

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Abstract

Background: We describe the baseline, operative, and postoperative features of a group of 18 patients who contracted the severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) infection in a rehabilitation facility after cardiac surgery, and present some potential explanations for the surprisingly benign course of the COVID-19 in this cohort.

Methods: All patients were operated on an urgent or emergency basis (acute aortic syndrome, 3; refractory heart failure, 12; and endocarditis, 3) during the first lockdown period of the COVID-19 pandemic. The mean age was 70 years, and 12 patients were male. After the diagnosis of COVID-19, patients were treated according to the most recent recommendations. Eleven asymptomatic patients were discharged home or to a COVID-19 hotel and underwent close monitoring. Patients with fever, dyspnea, or a significant rise of the polymerase chain reaction levels were hospitalized, three received antivirals, three azithromycine, and five hydroxychloroquine. Nasal swabs were repeated on a weekly basis, and all patients were quarantined until the collection of two consecutive negative samples.

Results: Diversely from other observations on perioperative COVID-19 reporting mortality rates of 30%–40%, the COVID-19 had a benign course in our cohort: only seven patients required hospitalization, and one required short intensive care unit admission. There were no deaths, and at the latest follow-up, all patients had been discharged home.

Comment: Our data show that the SARS-CoV2 infection after cardiac surgery may have a benign course. Further studies are needed to investigate the relationship between the timing of the infection, some potentially protective therapies (e.g., anticoagulants), and the course of the COVID-19.

KEYWORDS

COVID-19, postoperative care, postoperative infection

1 | BACKGROUND

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 23 and April 14, 2020, 19 patients were discharged from our unit to a rehabilitation clinic, where a hotbed of severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) infection was documented on April 17. After the outbreak, all patients underwent screening with real-time polymerase chain reaction (RT-PCR) on nasal swabs, and 18/19 patients were found positive. Diversely from other observations on perioperative COVID-19 reporting ubiquitous pulmonary complications and mortality rates of 30%–40%, the COVID-19 had a benign course in our cohort, with only one patient requiring admission in the intensive care unit (ICU) and 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.

2 | PATIENTS AND METHODS

A total of 18 patients who contracted the SARS-CoV2 infection in a rehabilitation clinic while recovering from cardiac surgery constitute the object of the present article. All patients had been operated on a nonelective basis during the first lockdown period of the COVID-19 pandemic. The RT-PCR on nasal swabs was performed before the admission for surgery and repeated before discharge: all these exams were negative, thus confirming that all patients became infected while in the rehabilitation clinic.

After the diagnosis, the patients were treated according to the most recent recommendations. Asymptomatic patients were discharged home or to a COVID-19 hotel and underwent close monitoring. Patients with fever, dyspnea, or a significant rise of the PCR levels were hospitalized and treated as needed.

RT-PCR on nasal swabs was repeated on a weekly basis, and all patients were quarantined until the collection of two consecutive negative samples.

Continuous variables are reported as mean \pm standard error. Categorical variables are expressed as percentages. The Internal Review Board approved this study. Oral informed consent was asked from all patients.

3 | RESULTS

The preoperative clinical features, the surgical details, and the postoperative outcome and complications are reported in Table 1. As can be easily appreciated, this was a group of critically ill, elderly patients with multiple severe comorbidities and high surgical risk scores. Twelve patients were male, and the mean age was 70 years. Only four patients who were all operated on an emergency basis for

TABLE 1 Patients characteristics

<i>Demographics and risk factors</i>	
Age (years)	70.1 \pm 11.9
Sex, M (N, %)	12 (63.1)
Hypertension (N, %)	11 (57.9)
Diabetes (N, %)	2 (11.1)
Smoking (N, %)	7 (36.8)
Obesity (N, %)	4 (21.1)
IV drug abuse (N, %)	2 (11.1)
COPD (N, %)	6 (31.6)
Renal failure (N, %)	3 (15.8)
CAD (N, %)	4 (21.1)
LVD (N, %)	4 (21.1)
Pulmonary hypertension	11 (57.9)
Preoperative inotropes/IABP	3 (15.8)
Other chronic condition	4 ^a (21.1)
<i>Surgical details</i>	
STS score	7.2 \pm 4.6
Emergency (N, %)	5 (26.3)
Redo	4 (21.1)
Complex combined procedures	12 (63.1)
Endocarditis (N, %)	2 (11.1)
Aortic dissection	2 (11.1)
Major complications	4 (21.1)
<i>COVID-19-related symptoms and course</i>	
Time to diagnosis	10.0 \pm 4.8
Asymptomatic	6 (31.6)
Fever	7 (36.8)
Cough	3 (15.8)
Sore throat	2 (11.1)
Dyspnea	1 (5.5)
GI symptoms	5 (26.3)
Major rise in PCR levels	5 (26.3)
Sent to a COVID-19 unit	7 (36.8)
Sent to a COVID-19 ICU	1 (5.5)
Warfarin/heparin at discharge	17 (94.4)

Abbreviations: COPD, chronic obstructive pulmonary disease; CAD, coronary artery disease; GI, gastro-intestinal; IABP, intra-aortic balloon pump; LVD, left ventricular dysfunction; M, male; PCR, polymerase chain reaction; STS, society of thoracic surgeons.

^aThree patients had severe orthopedic conditions and major functional limitations. One patient had lymphoma. One patient had hepatitis C virus-related liver disease.

critical, high-risk conditions (two for aortic dissection and two for bacterial endocarditis) were younger than 70.

The indications to urgent/emergency surgery were as follows: aortic dissection/pathology of the ascending aorta (three), refractory congestive heart failure for aortic (four) mitral (three), or multiple (three) valve disease, combined valvular and ischemic heart disease (two), acute endocarditis (two), and syncope in hypertrophic obstructive cardiomyopathy (one). During the early postoperative course, seven patients had atrial fibrillation and two patients required re-exploration for bleeding. Two patients had a transient increase of the creatinine

levels, three needed inotropic support, and three required prolonged ventilatory assistance. One patient developed a complete heart block and underwent pacemaker implantation.

The median interval between the operation and the discharge to the rehabilitation clinic was 8 days (range: 5–31), being significantly prolonged in three patients who experienced major postoperative complications. Eighteen patients were on oral anticoagulants at discharge, and all received prophylactic subcutaneous low-molecular-weight heparin. The indications to anticoagulation were the presence of a prosthesis/prosthetic ring (16) and/or postoperative atrial fibrillation (7). Before discharge, all patients underwent screening with real-time PCR on nasal swabs to exclude a subclinical SARS-CoV2 infection. All these exams were negative.

Patients were referred to the rehabilitation clinic, where some cases of COVID-19 were documented; thus, all patients underwent further nasal swabs for SARS-CoV2. After a median period of 9 days in the rehabilitation clinic (range: 4–24), 18/19 patients presented a SARS-CoV2-positive nasal swab. Surprisingly, the SARS-CoV2 infection had a benign course in this cohort: six patients were completely asymptomatic, and most of the remaining had only mild symptoms. Only seven patients had fever ($>38^{\circ}\text{C}$ in six), and a significant rise in the C reactive protein levels was recorded in only five of them. A single patient complained of dyspnea. Seven patients were hospitalized. Three patients received antivirals (ruxolitinib or darunavir/cobicistat), three azithromycin and five received empirical therapy with hydroxy-chloroquine. Only one patient needed admission in the COVID-19 ICU for dyspnea and mild hypoxemia, which was treated by continuous positive airway pressure. The remaining 11 asymptomatic or mildly symptomatic patients were discharged home or to a COVID-19 hotel (Table 1). At the latest follow-up (October 31), all patients had been discharged home. The last nasal swab was negative in all patients.

4 | COMMENT

The SARS-CoV2 infection can be pauci-symptomatic, causing a flu-like disease. In some patients, however, it causes severe interstitial pneumonia and acute respiratory distress syndrome (ARDS), which is frequently associated with thrombotic microangiopathies.^{1,2} 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 the 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, chronic obstructive pulmonary disease, 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 study group reported on the 30-day mortality and pulmonary complications in 1128 patients with perioperative SARS-CoV2 infection. Pulmonary complications were frequent and associated with 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 et al.⁴ reported similar results: all their patients had pulmonary complications, the postoperative hospital stay was prolonged, and the mortality was 44.4%. Considering all these data, the benign course of the COVID-19 in our patients might appear paradoxical.

5 | 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 is 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. 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 exposed 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 ± 4.8 days, while the 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.

6 | LIMITATIONS

This is a single institution, observational study on a small group of patients undergoing urgent/emergency cardiac surgery during the initial phases of the COVID-19 pandemic, when the Italian National

Health System had to face a tremendous crisis, characterized by high levels of uncertainty, by a tremendous scarcity of resources, and by the lack of solid guidelines. As a consequence, many decisions were based on empirical observations, and the therapeutic protocols were repeatedly reviewed and changed. However, we believe that our study group offers a very interesting staccato on the COVID-19 pandemic: the patients in this series shared several features of interest (anticoagulant therapy, recent open-heart surgery), and came in contact with the SARS-CoV2 infection during a well-defined, limited time frame. This gave us a unique opportunity to follow the course of the infection from the very beginning till the complete recovery in a homogeneous group of high-risk patients.

7 | CONCLUSION

Our data suggest 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 could support 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.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

Study design, data collection, analysis and interpretation, manuscript preparation: Alfredo Giuseppe Cerillo. Study design and supervision, critical revision, and approval of the article: Niccolò Marchionni. Data collection and approval of the article: Beatrice Bacchi. Study design and supervision, critical revision, and approval of the article: Pierluigi Stefano.

DATA AVAILABILITY STATEMENT

Data available upon request.

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