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ORIGINAL ARTICLE

# Quality of Life Assessment of Patients Infected With COVID-19 and Prior Coronary Artery Bypass Graft Surgery in Brazil: Four Years Follow-up

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## Abstract

**Background:** The COVID-19 pandemic has been a worldwide challenge. In patients with coronary artery disease (CAD), previously submitted to coronary artery bypass graft surgery (CABG), such impact should be analyzed.

**Objectives:** Evaluate the impact on quality of life of COVID-19 infection in patients with prior CABG.

**Methods:** Patients undergoing isolated CABG between July 2016 and July 2017 were enrolled. This is an observational, cross-sectional, prospective study. Patients were divided into two groups: Group (COVID-19) and Group (No-COVID), for analysis of variables. The World Health Organization's (WHO) definitions of confirmed cases were used to define the diagnosis of COVID-19 infection. Quality of life was assessed using the Quality of Life in Cardiovascular Surgery (QLCS) questionnaire, applied 30 days, 6 months, 1 year, and 4 years after surgery. The primary endpoint was improvement in quality of life at 4 years after CABG. The local ethics committee approved the study. Continuous variables were described by their means and standard deviations (SD). Categorical variables were described using absolute or relative frequencies. The items that make up the quality of life questionnaire were added together to calculate the score. A linear mixed model was used to assess the effect of time on the score. The significance level adopted was 5%. The analyses were carried out using R software, version 4.2.1.

**Results:** The total sample consisted of 434 patients who underwent isolated CABG; the mean age was 63 years, with a prevalence of males (71%). Among the patients followed up at the 4-year follow-up (115), 60 (52%) were positive according to the WHO's definitions. After multiple comparisons, there was a statistical difference in quality of life in all periods (P<0.001). Between patients with and without COVID-19, a statistical difference was observed at 1 and 4 years (p = 0.0039).

**Conclusion:** Patients who underwent CABG and had a history of COVID-19 infection experienced worsening quality of life within 4 years. There was no difference between groups regarding new acute myocardial infarction (AMI), stroke, or hospitalization.

**Keywords:** Quality of Life; Myocardial Revascularization; COVID-19.

## Introduction

The respiratory failure syndrome caused by SARS-CoV-2 began in the city of Wuhan, China, in December 2019 and was officially declared a pandemic by the World Health Organization (WHO) on March 11, 2020.[1] It has similarities with viruses such as SARS-CoV and MERS-CoV, responsible for previous pandemics, but with specific characteristics demonstrated over the years of the pandemic.[2,3]

The viral structure is composed of a single-stranded RNA molecule with positive polarity, surrounded by a lipid bilayer where the S protein, membrane (M), and envelope (E) are anchored, responsible for the infection and cellular multiplication of the virus. The main clinical manifestations

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**Central Illustration: Quality of Life Assessment of Patients Infected With COVID-19 and Prior Coronary Artery Bypass Graft Surgery in Brazil: Four Years Follow-up**

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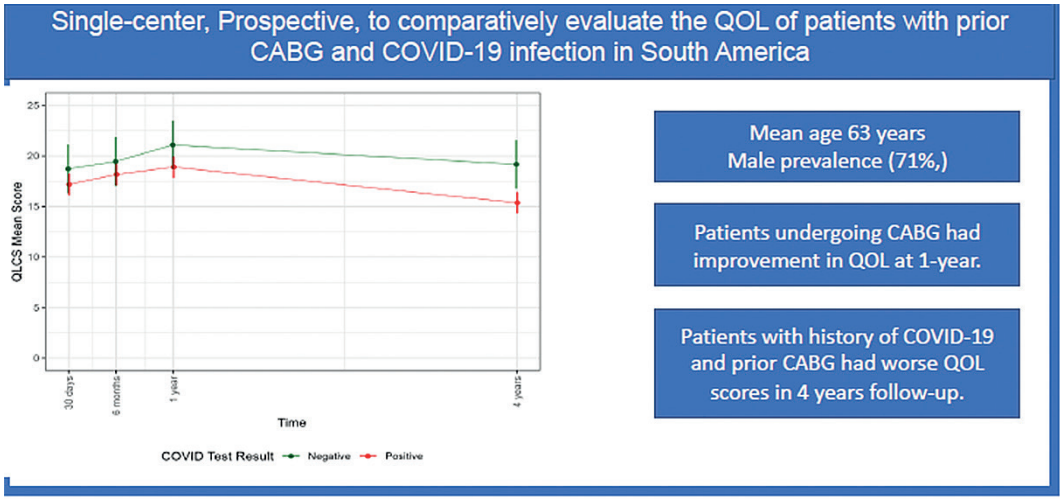


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*CABG: coronary artery bypass graft surgery; QOL: Quality of Life*

are cough, fever, dyspnea, and loss of taste and smell, observed in different populations worldwide. In this context, the impact of the COVID-19 pandemic on patients with cardiovascular disease has been significant, despite many of these individuals having multiple comorbidities.[4,5]

This fact was reinforced when the first cases of COVID-19 infection were described in the literature, where the most severe cases with comorbidities such as coronary artery disease (CAD), systemic arterial hypertension (SAH), and diabetes mellitus (DM) were associated with worse clinical outcomes, such as the need for intensive care unit (ICU) admission and mortality.[6]

This study aimed to assess the impact of COVID-19 infection on quality of life in patients with prior coronary artery bypass graft surgery (CABG).

## Materials and Methods

### Ethical Statement

The study was approved by the local Research Ethics Committee and all the patients included signed an informed consent form.

### Study Design

This is an observational, cross-sectional, and prospective study. It initially included 434 patients who underwent CABG without other associated procedures between July 2016 and July 2017. They were followed up at 30 days, 6 months, 1 year, and 4 years to assess quality of life using the Quality of Life in Cardiovascular Surgery (QLCS) questionnaire (Appendix 1).

To analyze the variables, the patients were divided into two groups: Group (COVID-19) and Group (No COVID-19). The WHO definitions of confirmed cases were used to diagnose COVID-19 infection.

### Outcomes Definitions

We included patients over the age of 18 who had undergone CABG using cardiopulmonary bypass alone. Patients with inadequate characterization of COVID-19 infection and those who could not be contacted for follow-up were excluded. The primary outcome was considered to be improved quality of life at 4 years after CABG. Secondary outcomes included all-cause mortality, new myocardial infarction or stroke, hospitalization for treatment of COVID-19 infection, and the need for orotracheal intubation in the treatment of COVID-19 infection.

Quality of life was assessed using the QLCS questionnaire (Appendix 1), validated by Bond et al.[7,8] For internal validation of the questionnaire, the authors identified a Cronbach's alpha of 0.74. This questionnaire was thus validated for the Brazilian population of

patients undergoing CABG, the subgroup analyzed in this study.

## Statistical analysis

According to the normality of the data, continuous variables were described by their means and standard deviations (SD) or medians and interquartile ranges. Categorical variables were described using absolute or relative frequencies. Normality was assessed using the Shapiro-Wilk test.

The items in the symptoms questionnaire were compared and distributed using the generalized mixed model of the binomial (logistic) family. Multiple comparisons were conducted to assess differences among various time points. The distribution of the items comprising the quality of life questionnaire was compared using the mixed model for ordinal data. Multiple comparisons were also employed to assess differences among various time points.

The items comprising the quality of life questionnaire were aggregated to calculate the score. A linear mixed model was used to assess the impact of time on the score. Estimated means were illustrated graphically over time, accompanied by their respective 95% confidence intervals. The effects were reported as differences in estimated means between time points, accompanied by their respective 95% confidence intervals and P values.

Analyses were also conducted, considering patients with a COVID test, to assess the impact of test results on quality of life scores at 4 years. A linear mixed model was used for this purposed, and the effects, alongside their confidence intervals and P values, were reported.

The significance level adopted was 5%. The analyses were conducted using R software, version 4.2.1.

## Results

A total of 434 patients undergoing isolated CABG were included, with a mean age of 63 years and male prevalence of 71%. The main comorbidities identified were hypertension (85%), dyslipidemia (61%), DM (53%), and prior acute myocardial infarction (AMI) (53%). Out of the initial cohort, 115 completed the 4-year follow-up, during which they were contacted by telephone to complete the quality of life questionnaire. Among these, 60 patients were confirmed to have COVID-19 based on WHO criteria. The demographic characteristics are shown in Table 1.

In addition to the demographic analysis, the patients' quality of life was assessed using the QLCS questionnaire, comprising 5 questions: 1) How is the patient's performance in daily activities/work/school?; 2) How is the patient's health after surgery?; 3) How is the patient's physical capacity after surgery?; 4) From an emotional standpoint, how is the patient feeling?; 5) In their relationship with family members, how is the patient feeling? The questionnaire has a maximum score of 25 points and has been validated in previous studies for the analyzing patients undergoing CABG.

A statistical difference was observed between 1 and 4 years for all components of the QLCS questionnaire. Additionally, the comparison of scores over the follow-up period, accompanied by their respective 95% CI and P values, is presented in Table 2, showing a statistically significant difference across all periods.

**Table 1 – Baseline characteristics.**

| Variables | N = 434 |
|---|---|
| Age, mean (SD) | 63 (9) |
| Gender, n/N(%) | |
| Male | 309/434 (71%) |
| Height, mean (SD) | 165 (9) |
| Weight, mean (SD) | 77 (15) |
| BMI, mean (SD) | 28.0 (4.4) |
| SAH, n/N(%) | 371/434 (85%) |
| Dyslipidemia, n/N(%) | 265/434 (61%) |
| Chronic obstructive pulmonary disease, n/N(%) | 16/434 (3.7%) |
| Peripheral arterial disease, n/N(%) | 22/434 (5.1%) |
| Chronic kidney disease, n/N(%) | 45/434 (10%) |
| DM, n/N(%) | 232/434 (53%) |
| Stroke, n/N(%) | 22/434 (5.1%) |
| Acute myocardial infarction, n/N(%) | 228/434 (53%) |
| Arrhythmia, n/N(%) | 11/434 (2.5%) |
| Smoker, n/N(%) | 241/434 (56%) |
| COVID test results, n/N(%) | |
| COVID-19 Positive | 60/115 (52%) |

*SAH: systemic arterial hypertension; DM: diabetes mellitus; SD: standard deviations; BMI: body mass index.*

Afterward, we specifically assessed patients diagnosed with COVID-19 during follow-up, according to the WHO definition of confirmed cases. Out of 115 patients, 60 were confirmed cases. The boxplot graphs below (Figure 1) depict the distribution of the quality of life scores in each group, showing that the median score among COVID-19-positive patients is lower compared to those without a history of infection. It is important to note that in the first year of follow-up, therefore a period predating the COVID-19 pandemic, the scores exhibited similar patterns.

In addition, we compared the quality of life scores between the follow-up periods for these groups. Multiple comparisons analysis revealed a difference only between 1 and 4 years (p = 0.0039), as indicated by their respective 95% CI and p values (Table 3).

There was no difference between the groups of patients with and without a history of COVID-19 infection during follow-up with regard to the study's secondary outcomes, including the need for ICU or ward admission, orotracheal intubation, new AMI, stroke, or thromboembolic event.

**Table 2 – Comparisons between scores over time.**

| Comparison | Difference | Confidence Interval 95% | | P Value |
|---|---|---|---|---|
| | | Inf | Sup | |
| 30 days - 6 months | -1.12 | -1.52 | -0.73 | <0.001 |
| 30 days - 1 year | -1.83 | -2.22 | -1.43 | <0.001 |
| 30 days - 4 years | 1.32 | 0.71 | 1.92 | <0.001 |
| 6 months - 1 year | -0.70 | -1.10 | -0.30 | 0.0005 |
| 6 months - 4 years | 2.44 | 1.84 | 3.05 | <0.001 |
| 1 year - 4 years | 3.14 | 2.54 | 3.75 | <0.001 |

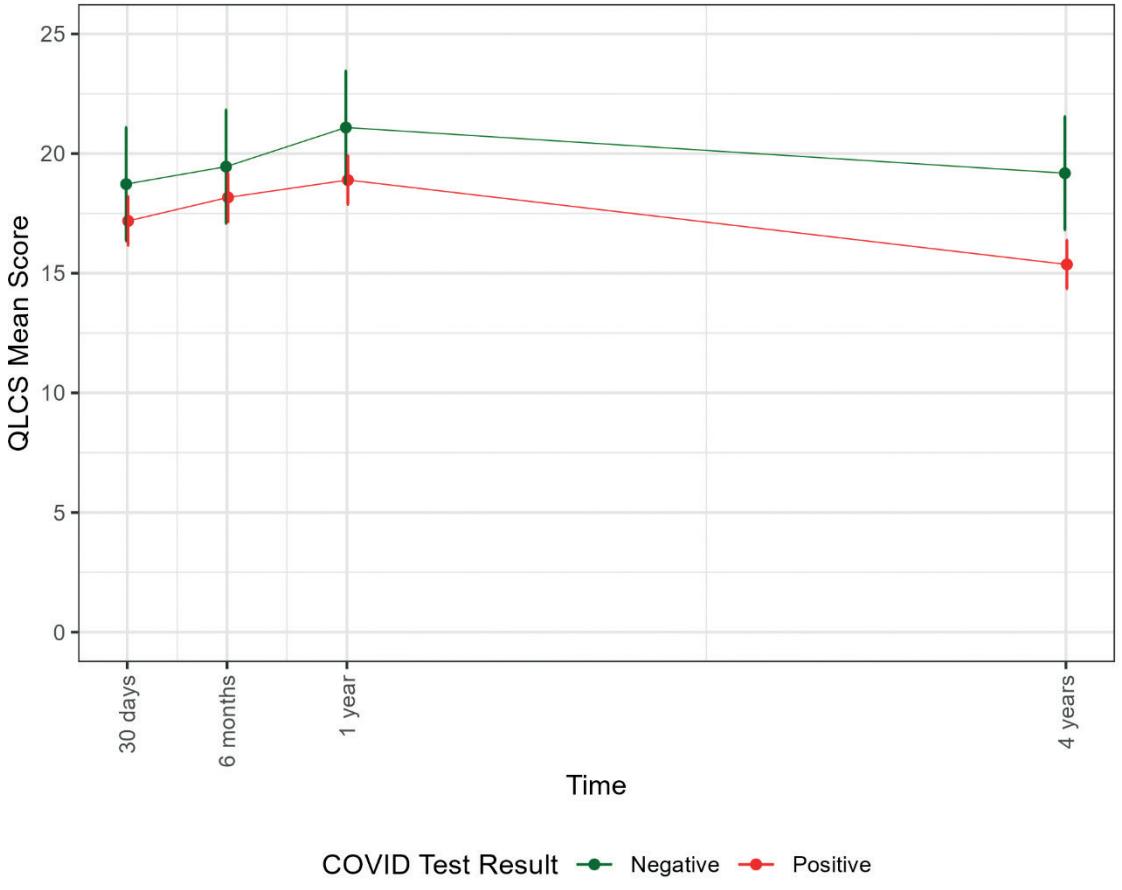


**Figure 1 – Average QLCS scores estimated over time according to WHO definitions for confirmed COVID-19 cases at 4 years follow-up..**
*QLCS: Quality of Life in Cardiovascular Surgery.*

**Table 3 – Comparisons between groups at each time point.**

| Comparison | Time | Estimate | CI 95% | | P Value |
|---|---|---|---|---|---|
| | | | Inf | Sup | |
| Negative COVID - Positive COVID | 30 days | 1.54 | -1.03 | 4.12 | 0.2390 |
| Negative COVID - Positive COVID | 6 months | 1.29 | -1.29 | 3.86 | 0.3257 |
| Negative COVID - Positive COVID | 1 year | 2.19 | -0.38 | 4.77 | 0.0946 |
| Negative COVID - Positive COVID | 4 years | 3.82 | 1.24 | 6.39 | 0.0039 |

## Discussion

This study reveals that patients with a history of COVID-19 infection experienced worse quality of life scores. The context of the COVID-19 pandemic has impacted several cardiovascular surgery centers worldwide, showcasing a broad spectrum of patient symptoms, discussion on therapies, the emergence of SARS-CoV-2 variants, and the historical progression of vaccines.[1,3,9]

Understanding the mechanisms of viral infection has been fundamental to understanding the impact of COVID-19 on patients with cardiovascular disease. Chung et al.[10] demonstrated in a review the significance of the angiotensin-converting enzyme 2 (ACE2), which is present in cells of the respiratory system, kidneys, heart, and blood vessels. ACE2 serves as a substrate for binding the SARS-CoV-2 virus via its surface proteins, and subsequently viral replication, enabling the infection of other cells. The organic response to infection relies on the action of the immune system (both innate and adaptive), which, in association with the "cytokine storm," contributes to cell damage and the disease severity, particularly among patients with cardiovascular disease.[10,11]

Thakker et al.,[12] in a systematic review of patients diagnosed with acute coronary syndrome both with and without COVID-19, observed higher mortality rates in the former group. This outcome can be attributed to several factors, including pre-existing comorbidities such as SAH, DM, and dyslipidemia, as well as diagnostic delays. Many of these factors were present in the patients included in this study, given the various changes in healthcare amid the pandemic.

When considering the global impact of the COVID-19 pandemic, its effects on the treatment of patients with cardiovascular disease become evident. In England, the number of CABGs decreased by 64%, while in the USA, according to STS data, there was a 52.6% reduction in the volume of heart surgeries. Additionally, in Canada, patients referred for CABG experienced higher mortality rates during the pandemic, with COVID-19 infection identified as a predictor of mortality in several studies.[13-16]

In Brazil, Khalil et al.[17] conducted and analysis involving 281,760 CABGs carried out between January 2008 and December 2020, revealing a reduction of around 25% in surgical volume in 2020. This reduction was accompanied by an increase in mortality rates in certain regions of the country, such as the southeast and center-west. Mejia et al.,[18] in an analysis of 650 patients, reported a 62% reduction in CABG volume, highlighting a devastating impact on surgical outcomes in Brazil. The authors noted a higher mortality among the subgroup of patients with COVID-19, as well as an increased incidence of associated complications. In the multivariate analysis, COVID-19 and postoperative pneumonia were identified as markers of post-CABG mortality.

Secondary outcomes such as ICU admission, acute myocardial infarction, and thromboembolic events did not differ statistically in this study. This outcome may be attributed to national public policies observed during follow-up, including a notable prevalence of vaccinated patients, with 100% of the sample having received at least one to two vaccine doses.

The reduction in surgical volume, associated with higher mortality and post-operative complications, directly impacts patients' quality of life. Algahtani et al.,[19] in an analysis of 754 patients, used the WHOQOL-BREF questionnaire to demonstrate that patients with chronic conditions such as hypertension, diabetes, and cardiovascular disease reported worse quality of life scores, findings consistent with those of this study. Al Dhaheri et al.[20] investigated the mental health

implications for patients during the COVID-19 pandemic, emphasizing on the role of family support.

The impact on the quality of life of patients undergoing CABG is notorious; in our study, for instance, quality of life remained stable during the first year of follow-up in a pre-pandemic context.[21,22] Bond et al.[7,8] demonstrated the improvement in patients' quality of life scores at the 1-year follow-up using the QLCS score. However, the COVID-19 pandemic has brought major challenges in the management of CAD patients undergoing CABG, whose long-term implications are yet to be fully understood.

Huang et al.[23] observed persistent symptoms such as fatigue, anxiety, and depression six months after hospital discharge among patients who had been admitted to an ICU. These findings are supported by other studies, where quality of life, measured by other tools such as the SF-36 score, was reduced in patients with COVID-19.[24,25]

Patients with CAD undergoing CABG present multiple comorbidities. Quality of life serves as an important metric for assessing the therapeutic impact of surgery, with different questionnaires currently validated. Discussions concerning socioeconomic factors, public policies, and rehabilitation programs are pertinent in the ongoing treatment of patients dealing with COVID-19 sequelae.[26-28]

Furthermore, it is important to note that this study reflects real-life conditions. For reasons inherent to the COVID-19 pandemic experienced in Latin America, such as appointment cancellations and the inability to conduct necessary postoperative tests, follow-up data for all the initially enrolled patients could not be collected, impacting the final 4-year sample. This was a significant limiting factor in this analysis.

## Conclusion

In this study, it was observed that patients with prior CABG and a history of COVID-19 infection experienced worse quality of life scores at the 4-year follow-up. However, there was no statistical difference in acute myocardial infarction, stroke, or thromboembolic events between the groups with and without COVID-19. To the best of the authors' knowledge, this is the first study in the literature to assess the impact of COVID-19 infection on the quality of life of patients with prior CABG using the QLCS questionnaire.

## Author Contributions

Conception and design of the research, statistical analysis, obtaining financing and writing of the manuscript: Maia AS, Santos MA; acquisition of data and snalysis and interpretation of the data: Maia AS, Maia M, Maia ALS, Santos MA; critical revision of the manuscript for intellectual content: Maia AS.

### Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

### Sources of Funding

There were no external funding sources for this study.

### Study Association

This article is part of the thesis of master submitted by Adnaldo da Silva Maia, from USP.

### Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of the Dante Pazzanese under the protocol number 47467040.0.000.1462. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

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