



Coronary artery bypass grafting in active or recent COVID-19 infection: a systematic review

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Received: 30 August 2022 / Revised: 30 January 2023 / Accepted: 2 February 2023 / Published online: 9 March 2023
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Abstract

Introduction Even though there have been few studies on coronary artery bypass grafting (CABG), data on patients with coronavirus disease-2019 (COVID-19) infection show that cardiac surgery has poor outcomes in this subset. From the available studies in the literature, we conducted a systematic review with the aim of determining the outcome of COVID-19 patients who underwent CABG.

Methods Between December 2019 and October 2022, searches were conducted in PubMed, the Directory of Open Access Journals, and Google Scholar to find studies reporting results of COVID-19 patients undergoing CABG. We extracted data on the clinical profile and outcomes of the patients from the eligible studies. The quality of the studies was assessed using a standardised tool.

Results The total sample size across the 12 included studies was 99 patients who underwent CABG in active disease or within 30 days of COVID-19 infection. The median and interquartile range (IQR) for the length of time spent on a mechanical ventilator, stay in the intensive care unit (ICU), and the total hospital stay were 0.9 (0.47–2), 4.5 (2.5–8), and 12.5 (8.5–22.5) days respectively. Seventy-six patients developed postoperative complications, and there were eleven deaths.

Conclusion The findings of the present study indicate that mortality risk goes down when the time between COVID-19 diagnosis and surgery increases. When compared to data from other high-risk urgent or emergent CABG patients around the world who were not infected with COVID-19, patients who underwent CABG in the COVID-19 subgroup had similar postoperative outcomes.

Keywords Coronary artery bypass grafting · COVID-19 · Cardiac surgery · SARS-Cov-2 · Outcome

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Introduction

Within months of its onset, coronavirus disease-2019 (COVID-19), caused by a novel coronavirus — severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), shook the entire world and converted many healthcare facilities into dedicated COVID hospitals, with a major brunt on surgical facilities [1]. Cardiac surgery (CS) also suffered a major blow, and most of the centers stopped performing elective surgeries [2]. But gradually, it was realised that urgent or emergent cardiac conditions with no viable alternatives, like acute coronary syndrome (ACS), not amenable to percutaneous coronary intervention (PCI), need to be performed as waiting in these cases could have disastrous consequences [3]. Poor results are reported in the few data currently available for COVID-19-positive patients undergoing CS, with even less data on coronary artery bypass grafting (CABG) [4]. Hence, there is a reluctance of cardiac

surgeons to perform cardiac surgeries in such a cohort [5, 6]. We carried out this systematic review to determine the outcomes of COVID-19-positive cardiac surgical patients who underwent CABG within 30 days of COVID detection.

Material and methods

Search technique

The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines were adhered for this review [7]. We searched the articles in Pub Med, Directory of Open Access Journals (DOAJ), and Google Scholar using the following terms:

Cardiac surgery [OR] heart surgery [OR] open heart surgery [OR] cardiac surgical procedures [OR] coronary artery bypass grafting [OR] coronary artery surgery [OR] coronary artery bypass surgery [OR] coronary artery disease surgical treatment [OR] coronary artery revascularization [AND] Covid-19 [OR] SARS-Cov-2 (**severe acute respiratory syndrome coronavirus 2**) [OR] coronavirus [OR] Covid.

We looked for additional references in sub-references and similar articles. The search was performed for a period between December 2019 and October 2022.

Selection criteria

The following were the inclusion criteria for the studies included in this review:

- A. Participants with a confirmed preoperative diagnosis of COVID-19 who underwent CABG in the active disease or within 30 days after the diagnosis. If the preoperative pending report revealed that COVID-19 was present, patients subjected to CABG were also included.
- B. Studies in the English language.

Articles were excluded as follows: (i) suspected patients of COVID-19 with unknown or doubtful status undergoing surgery, (ii) patients with no preoperative testing for COVID-19, (iii) patients with negative preoperative or intraoperative COVID-19 report, (iv) CABG patients with their first SARS-Cov-2 infection detected in the postoperative period, (v) no clarity in the timing of surgery about COVID-19 diagnosis, (vi) patients operated after 30 days of COVID-19 diagnosis, (vii) patients with no data on the outcome of CABG.

Extraction of data

The following information was independently gathered by two authors from each included study: authors' names,

publication year, setting, kind of study, sample size, technique used for CABG, objectives, and outcomes. Disagreements were settled by dialogue or by the involvement of a third investigator. Zotero, the reference management software, was used for citation and management of included studies.

Quality and risk of bias assessment of included studies

Studies that were included were evaluated for quality and risk of bias by two independent reviewers. Discussion was used to settle disagreements between the reviewers at various stages of the review. The Joanna Briggs Institute (JBI) Critical Appraisal tools for case series, cohort study, and case reports, which are made up of 10, 11, and 8, yes/no/unclear or not applicable questions, respectively, were used to assess the standard of the included studies [8].

For a succinct assessment of the general quality of the included studies, these were categorised as follows: (1) low risk of bias (studies that met at least 75% of the standards for quality); (2) studies with a moderate risk of bias (compliant with 50 to 74% of the quality standards); (3) studies with a high risk of bias (those that only complied with less than 49% of the standards for quality) [9].

Data analysis

The demographics and clinical variables were reported using descriptive statistics. For continuous variables, we used median and interquartile range, and for dichotomous variables, we used frequencies and percentages. Two independent researchers evaluated the included studies' methodological quality and risk of bias using the JBI risk of bias checklist.

Results

Study selection and characteristics

A total of 5747 articles were discovered using the electronic search. After deleting duplicate records, 5319 articles were screened by the reviewers. Two reviewers separately reviewed the titles and abstracts of all the articles. After a thorough review of the titles and abstracts, 5147 articles were excluded. For the remaining 172 studies, full-text articles were retrieved and finally 160 studies were assessed for eligibility. After independent assessment, 148 articles were removed for a stated reason and 12 articles were included in the current review. The PRISMA flow diagram (Fig. 1) outlines the process of selecting studies and scrutinising publications.

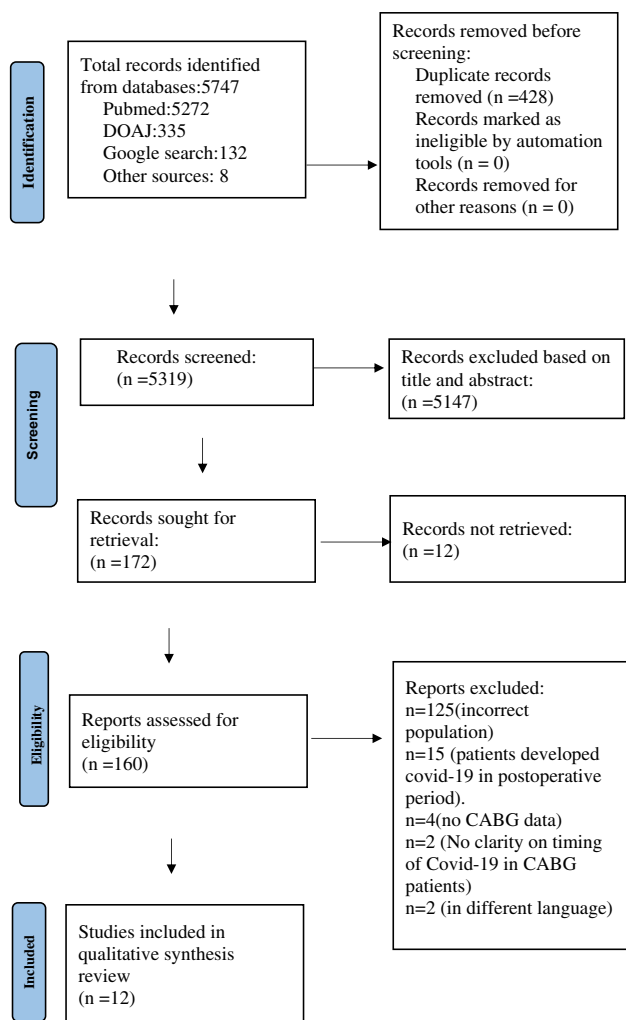


Fig. 1 PRISMA flow chart

Patient characteristics and outcomes

Ninety-nine COVID-19-positive patients underwent CABG in active disease or within 30 days of COVID-19 infection. Ninety-five (96%) patients were emergent or urgent procedures, and four (4%) were performed electively. Computed tomography (CT) of the chest was done preoperatively in 68 (78.2%) of the patients. Recent myocardial infarction (MI) (in the last 3 weeks) was reported in 6 (6%), ST elevation MI (STEMI) in 24 (24.2%), non-ST elevation MI (NSTEMI) in 18 (18.1%), and unstable angina (UA) in 55 (56%) patients. Coronary angiography (CAG) demonstrated critical left main (LM) or LM equivalent with triple-vessel disease (TVD) in 13 (14.3%), critical TVD in 18 (20%), double-vessel disease (DVD) in 5 (6%), and single-vessel disease (SVD) in 52 (57%) of patients.

Out of the cohort's total of 99 patients, 4 operations were required due to the failure or complications of percutaneous interventions (PCI), of which 2 were urgent and

2 were elective. Eighty-six (87%) patients performed on-pump CABG and the rest, 13 (13%), as off-pump surgery (OPCABG). The saphenous veins (SV) and the left internal mammary artery (LIMA) were the most frequently used grafting conduits. Eleven (11.1%) patients died. One died because of acute respiratory distress syndrome (ARDS), one due to refractory cardiogenic shock, one from severe encephalopathy, six due to heart failure, one due to septic shock, and the last patient due to stroke. Two patients developed COVID pneumonia in the postoperative period. There was excessive bleeding in 2 patients; one was managed medically and the other via hemostatic re-exploration. Two patients required renal replacement therapy, and eight patients developed renal failure. Eleven patients developed stroke, 26 patients developed pleural effusion (PE), and 19 patients developed atrial fibrillation (AF).

Six patients (6.5%) had a length of mechanical ventilation (LOV) greater than 48 h, and 85 (93%) patients had a hospital stay (LOS) of more than 7 days.

Five (5%) patients were operated upon within 1 day of diagnosis, 79 (80%) within 2–14 days, and 15 (15%) within 15–30 days of the disease. Table 1 summarises the major characteristics of the patients that were included in the review.

The mortality rate of patients operated on for intraoperative active disease was 20%, and 50% had a LOV greater than 48 h (Table 2).

When reported, the median and interquartile range for the length of time spent on a mechanical ventilator, stay in the intensive care unit (ICU), and total hospital stay were 0.9 (0.47–2), 4.5 (2.5–8), and 12.5 (8.5–22.5) days, respectively. The median hospital stay for patients operated on within 1 day of COVID-19 was 22 days.

Risk of bias

The quality assessment of the included studies is shown in Table 3. The mean of the two reviewers' scores was calculated and the risk of bias was determined as per pre-defined criteria. The JBI checklist with reviewer's scores is available as supplementary material "(Online resource 1)." There is no significant bias risk in any of the studies. Nine studies [10, 12, 13, 15, 17–21] fell into the low-risk bias group.

Discussion

This systematic review attempted to analyze the available information to inform surgeons about the consequences of CABG in the COVID-19 subset of patients. The key findings generated are discussed below.

Table 1 Patient characteristics

Study Country Year Type	Included patients (n)	MI (n)	CAG (n)	Timing of COVID-19 diagnosis and surgery (n)	Length of ventila- tion > 48 h (n)	Length of hospital stay > 7 days (n)	Postoperative complica- tion (n)	Death (n)
Yandrapalli USA 2020 Case report [10]	1	NSTEMI (1)	TVD (1)	2–14 days (1)	0	0	Pleural effusion (1)	0
Shoman Qatar 2020 Case series [11]	3	ACS (3)	-	2–14 days (1)	0	-	None	0
Romiti Italy 2021 Case report [12]	1	NSTEMI (1)	DVD (1)	1 day (1)	0	1	None	0
Omar Qatar 2021 Case report [13]	3	STEMI (2) NSTEMI (1)	LM+TVD (2) TVD (1)	2–14 days (3)	0	3	None	0
Farsky Brazil 2021 Case series [14]	8	NSTEMI (3) UA (5)	-	15–30 days (5) 1 day (3)	4	7	Stroke (1) AF (1) Pneumonia (1) Renal replacement therapy (2)	2
Montandru France 2021 Case report [15]	1	NSTEMI (1)	TVD (1)	15–30 days (1)	0	1	None	0
Parra Colombia 2021 Case report [16]	1	STEMI (1)	LM+LAD (1)	1 day (1)	-	-	None	0
Salah Egypt 2021 Case series [17]	3	UA (3)	LM+TVD (3)	2–14 days (3)	1	3	Re-exploration (1)	0

Table 1 (continued)

Study Country Year Type	Included patients (n)	MI (n)	CAG (n)	Timing of COVID-19 diagnosis and surgery (n)	Length of ventila- tion > 48 h (n)	Length of hospital stay > 7 days (n)	Postoperative complica- tion (n)	Death (n)
Keskin Turkey 2021 Case series [18]	4	STEMI (4)	SVD (4)	2–14 days (4)	-	-	Pneumonia (1)	1
Hussain London 2020 Case report [19]	1	STEMI (1)	TVVD (1)	2–14 days (1)	-	1	None	0
Ayati Iran 2022 Retrospective cohort study [20]	62	STEMI (16) NSTEMI (11) UA (35)	TVVD (10) DVD (4) SVD (48)	2–14 days (62)	0	62	Stroke (8) AF (16) Pleural effusion (25) Pericardial effusion (5) Renal failure (8)	7
Bhattacharya India 2022 Case series [21]	11	Recent MI (6) UA (11)	LM+TVVD (2) LM+DVD (1) LM equivalent+TVVD (3) TVVD (5)	2–14 days (2) 15–30 days (9)	1	7	Stroke (1) AF (1)	1

Abbreviations: MI myocardial infarction, STEMI ST elevation myocardial infarction, NSTEMI non-ST elevation myocardial infarction, UA unstable angina, CAG coronary angiography, LM left main disease, TVVD triple-vessel disease, DVD double-vessel disease, ACS acute coronary syndrome, SVD single-vessel disease, AF atrial fibrillation, LAD left anterior descending artery

Duration of mechanical ventilation and hospital stay

Overall, 6.5% of patients required mechanical ventilation for more than 48 h, which is consistent with global studies on COVID-negative high-risk profile patients undergoing urgent or emergency CABG, ranging from 2.9 to 13.8% [22, 23]. However, when CABG was performed within 1 day of COVID diagnosis, 50% of patients had LOV > 48 h. The mean duration of hospital stay in COVID-negative patients ranged from 9.2 days in urgent CABG to 14.2 days in emergent CABG, with 39% and 83% of patients having a duration of stay greater than 7 days [24]. Similarly, in the study by Malmberg et al. [25], the median duration of hospital stay varied between 12 and 13 days in NSTEMI and STEMI patients undergoing CABG. The median total hospital stay of 12.5 days found in this study is at par with the above studies, but the patients operated on within 1 day of COVID had a higher stay. Thus, COVID-19 contributes to prolonged mechanical ventilation and prolonged hospital stays in high-risk patients operated on within 1 day of the disease’s diagnosis, but has no effect in a similar subset operated on within 30 days of the disease. All the data depicted above is of patients undergoing emergent or urgent CABG, because only 4% of patients underwent elective CABG [18], which did not mention the duration of mechanical ventilation or hospital stay.

Postoperative complications

The frequency of postoperative problems: pneumonia (2%), re-exploration (1%), ARDS (1%), renal dysfunction (10%), stroke (10%), PE (26%), pericardial effusion (5%), and AF (19%) matches that reported for high-risk emergency CABG in COVID-negative patients [26, 27]. The incidence of pneumonia in the intraoperative active disease subset was 20%, which is nearly the same as the global figure of 23.9% in high-risk patients [26]. The incidence of re-exploration [17] is quite low (1% in this study), in contrast to the marked increase observed by Chiariello et al. [28]. This may be due to the small sample size. Stroke was seen in 10% of the patients in this review and was the cause of mortality in one patient [21]. The risk of stroke in CABG ranges from 0.0 to 5.2% [29], which may be further aggravated by COVID-19-induced cerebral thrombosis as a plausible mechanism [30]. One patient in the case series of Farsky et al. [14] died due to severe encephalopathy. The researchers found that the patient’s brain magnetic resonance imaging (MRI) results matched those of COVID-19. AF is the most common atrial arrhythmia after CABG, with an incidence of 15–45% [31]. The low incidence observed in this study (19%) may be due to the small sample size. COVID-19 has been linked to a greater risk of developing AF due to myocardial inflammation [32]. Except for stroke, the frequency of postoperative complications is therefore the same as in other high-risk CABG patients.

Table 2 Patient traits and outcomes as per timing of surgery in relation to COVID

S. no	Number of patients (n)	MI (n)	Length of ventilation > 48 h (n)	Length of hospital stay > 7 days (n)	Postoperative complication (n)	Death n (%)	Postoperative complication (%)
Timing of COVID-19 to CABG within 1 day							
A	5	STEMI (1) NSTEMI (3) UA (1)	n (2) NR-1	n (3) NR-1	Pneumonia (1) Renal replacement therapy (2) None (1)	1 (20)	60
Timing of COVID-19 to CABG within 2–14 days							
B	79	STEMI (23) NSTEMI (13) UA (40)	n (2) NR-2	n (70) NR-2	Re-exploration (1) Pneumonia (1) ARDS (1) Pleural effusion (26) Renal failure (8) Stroke (9) AF (16) Pericardial effusion (5) None (3)	9 (11.4)	84.8
Timing of COVID-19 to CABG within 15–30 days							
C	15	NSTEMI (2) UA (13)	n (2)	n (12)	Stroke (2) AF (3) None (10)	1 (6.7)	33.3

Abbreviations: CABG coronary artery bypass grafting, STEMI ST elevation myocardial infarction, NSTEMI non-ST elevation myocardial infarction, UA unstable angina, NR not reported, ARDS acute respiratory distress syndrome, AF atrial fibrillation

Table 3 Mean Joanna Briggs Institute (JBI) Critical Appraisal tool results and risk of bias of included studies

Study	Shoman, et al	Farsky, et al	Salah, et al	Keskin, et al	Omar, et al	Yandrapalli, et al	Montandrau, et al	Parra, et al	Romiti, et al	Hussain, et al	Ayati, et al	Bhat-tacharya, et al
Mean score	5	7	8.5	8	7.5	8	7.5	4	7.5	7	9	9
Risk of bias (%)	Moderate (50)	Moderate (70)	Low (85)	Low (80)	Low (93)	Low (100)	Low (93)	Moderate (50)	Low (93)	Low (87)	Low (82)	Low (90)

Mortality

There were 11 (11.1%) deaths in the study. One died because of ARDS [18], another due to refractory cardiogenic shock [14], one from severe encephalopathy [14], six due to heart failure [20], one due to septic shock [20], and one due to stroke [21]. This is consistent with international data on mortality (8.7–12.2%) in high-risk COVID-negative patients who received urgent/emergent CABG [25, 26]. One in five patients who underwent surgery within a day of developing COVID illness died from cardiogenic shock [14], resulting in a mortality rate of 20% in this subset. Hence, COVID-19 causes substantial mortality among high-risk CABG patients who are exposed to the intraoperative active disease, but has little to no effect on other patients.

There are currently no comprehensive studies on CABG in COVID-positive patients, but our findings show that those who underwent the procedure had comparable outcomes to other high-risk COVID-negative patients who underwent emergent or urgent CABG as per global studies. However, patients operated on during the intraoperative active phase have a greater duration of mechanical ventilation, length of hospital stay, and mortality. Additional observational studies on COVID-19 and CS, with a focus on disease timing and the effect of vaccination, are required to support decision-making.

Limitations

The studies included in the review were lacking in multiple data points. Because most of the studies were retrospective case studies with small sample sizes or case reports, statistical analysis was not possible, and the results obtained cannot be extrapolated to the population. The sample of patients operated on within 1 day of diagnosis was very small to make firm inferences. Given the continually shifting COVID-19 spectrum and the availability of disease vaccination, the findings of our study might change in the future. Despite this, the information gathered from all these articles can prove to be useful, especially considering the novelty of the disease and the absence of literature.

Conclusion

The findings of the present study indicate that mortality risk goes down when the time between COVID-19 diagnosis and surgery increases. Except for stroke, the risk of major post-operative complications in the COVID-19 subset is similar to other high-risk patients. The impact of vaccination and the recent COVID-19 mutants on the results of our study requires further investigation.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s12055-023-01495-7>.

Author contribution 1. Dr Rajat Agarwal: substantial contributions to the conception of the work, and the acquisition and analysis of data for the work, drafting the work, final approval of the version to be published.

2. Dr Shiv Mudgal: substantial contributions to the conception of the work, and the acquisition and analysis of data for the work, drafting the work, final approval of the version to be published.

3. Dr Amiy Arnav: substantial contributions to the conception of the work, and the acquisition and analysis of data for the work, drafting the work, final approval of the version to be published.

4. Dr Nishit Ranjan: substantial contributions to the conception of the work, and the acquisition and analysis of data for the work, drafting the work, final approval of the version to be published.

The author and co-authors contributed significantly to final revisions of the manuscript and agree to be accountable for all aspects of the work in ensuring that issues related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Funding None.

Data availability Not applicable.

Code availability Not applicable.

Declarations

Ethics committee approval Not applicable.

Human and animal rights statement Not applicable.

Informed consent Not applicable.

Consent for publication Not applicable.

Conflict of interest The authors declare that they have no conflict of interest.

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