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COVID-19 Patients With Previous Coronary Artery By-Pass Graft Have a Higher Mortality Risk

Subjects with previous coronary bypass graft (CABG) have per se a higher mortality rate in both the short- and long-term period compared with the general population.[1] Over the latest months, several analyses have demonstrated that cardiovascular (CV) comorbidities are common in patients with COVID-19 infection, increasing their morbidity and mortality risk.[2,3] However, data regarding the prevalence and prognostic impact of previous CABG in patients with SARS-CoV-2 infections are still scant. Therefore, aim of the present manuscript is to perform a systematic review and meta-analysis to evaluate the prevalence and mortality risk associated with a history of CABG in COVID-19 patients.

The study was performed in accordance with the Preferred Report Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines.[4] For this purpose, PubMed-MEDLINE and Scopus databases were systematically searched for articles, published in English language, from inception through August 1, 2021, using the following Medical Subject Heading (MESH) terms: "COVID-19" AND "Non-survivors" OR "CABG." Inclusion criteria were: (1) studies enrolling subjects with a confirmed diagnosis of COVID-19, (2) stratifying the population as survivors and nonsurvivors, and (3) providing data on the presence of previous CABG. Conversely, case reports, review articles, editorials/letters, and case series with less than 10 participants, randomized controlled trials and studies including duplicate populations, if any, excluded. References from the included studies were screened to potentially identify other investigations meeting the inclusion criteria. Ethical approval and informed consent were not required as the study did not directly enroll human subjects. The quality of the included studies was graded using the Newcastle-Ottawa quality assessment scale (NOS).[5] The cumulative prevalence of previous CABG, defined as the ratio between patients with previous CABG (n) and the number of patients enrolled in each study (N), were pooled using a random effects model and presented with the corresponding 95% confidence interval (CI). Similarly, mortality risk data were pooled using the Mantel-Haenszel random effects models with odds ratio (OR) as the effect measure with 95% CI. Heterogeneity among studies was assessed using Higgins and Thomson I^2 statistic where I^2 values correspond to the following levels of heterogeneity: low (<25%), moderate (25% to 75%) and high (>75%). The presence of potential publication bias was verified by visual inspection of the funnel plot. Due to the low number of the included studies (<10), small-study bias was not examined as our analysis was underpowered to detect such bias. A predefined sensitivity analysis (leave-one-out analysis) was performed removing 1 study at the time, to evaluate the stability of our results regarding the mortality risk. To further appraise the impact of potential baseline confounders, a meta-regression analysis using age, gender, arterial hypertension (HT) and diabetes (DM) as moderator variables was performed. All meta-analyses were conducted using Comprehensive Meta-Analysis software, version 3 (Biostat, USA).

Initial search resulted in 712 articles. After removing duplicates (n = 215) and applying our inclusion criteria only 4 studies,[5–9] enrolling 3,070 patients (mean age 67.9 years old, 2,036 males) were included in the analysis. The general characteristics of patients enrolled are showed in Table 1. The mortality rate was 21.6% (n = 664). Previous CABG was presents in 3.1% (95% CI 1.7% to 5.5%, I2: 80.7%) of COVID-19 patients (Figure 1). On pooled analysis, patients with previous CABG showed a significant higher mortality risk in the short-term period (OR: 2.78, 95% CI 1.54 to 5.040, p = 0.001, I^2 = 24.6%; Figure 1). Visual inspection of the relative funnel plot did not reveal significant evidence of publication bias. Sensitivity analysis yielded consistent results. Meta-regression showed a direct correlation with gender (male vs female, Coeff. 0.331, p = 0.04), but no effect when considering age (p = 0.51), HT (p = 0.55), and DM (p = 0.56) as moderating variables.

The results of present analysis showed that previous CABG is present in about 3% of COVID-19 patients. Despite its relative low prevalence, this cardiac condition significantly increases the short-term mortality risk. Our findings confirm

Table 1
General characteristics of the population enrolled

Author years [IQR]	Number of pts, N	Males	Mean age,	Nonsurvivors	HT	DM	Previous CABG	NOS
Cereda et al[6]	1683	1131 (67.2%)	67 ± 14	370 (29%)	910 (55%)	319 (19.3%)	51 (4.3%)	8
Giannini et al[7]	1093	742 (68.3%)	68 [58-76]	211 (19.3%)	590 (54.8%)	178 (16.5%)	15 (2.3%)	8
Silverio et al[8]	226	141 (62.4%)	68.9 ± 13.9	68 (30%)	138 (61.1%)	64 (28.3%)	13 (5.8%)	8
Aladağ et al[9]	68	22 (44%)	68 [55-75]	15 (22%)	36 (72%)	24 (48%)	3 (6%)	8

Pts = patients; HT = arterial Hypertension; DM = diabetes mellitus; CABG = coronary artery by-pass graft; NOS = Newcastle-Ottawa quality assessment scale; IQR = interquartile range.

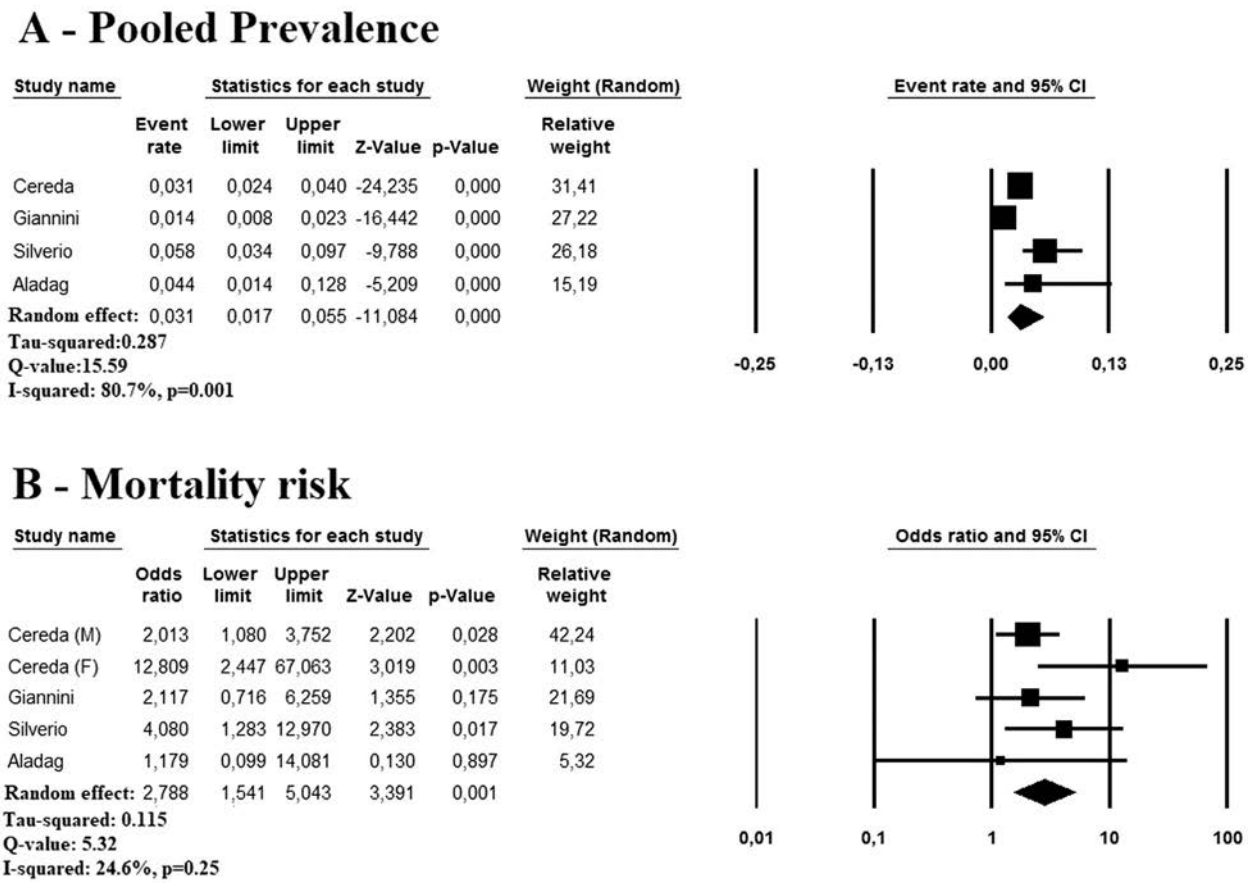

Figure 1. (A) Forest plot investigating the prevalence of previous coronary artery by-pass graft among COVID-19 patients; (B)Forest plot evaluating the mortality risk due to previous coronary artery by-pass graft in COVID-19 patients using a random-effect model.

the results of several recent investigations which demonstrated that the clinical outcomes in patients with SARS-CoV-2 infection are closely related to the burden of associated comorbidities. Understanding the risk factors associated with a poor outcome in these patients remains critical to promptly identify vulnerable populations, especially patients with pre-existing CV diseases, who would require prioritization in treatment and prevention and close monitoring if infected. This aspect must be carefully considered especially among older patients with previous CABG, as demonstrated by our meta-regression, which partially explain the low heterogeneity observed. However, also the design of the single studies reviewed, due to the participants' inclusion criteria, design and inherited biases may have contributed to the heterogeneity observed. Further larger clinical studies are needed to confirm our preliminary results, also analyzing the number of by-pass and the vessels involved.

Disclosures

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Meta-Analysis of Percutaneous Coronary Intervention of Chronic Total Occlusions

Chronic total coronary occlusions (CTO) represent a revascularization challenge and have a reported prevalence of 30%.[1] CTO is associated with worse early and late outcomes; nevertheless, its optimal treatment strategy remains unknown. The majority of CTO patients are medically treated by titrating antianginal therapy and modifying the coexisting cardiovascular risk factors, with only 10% of patients undergoing attempted percutaneous coronary intervention (PCI).[2] Recent studies examined the clinical utility of CTO-PCI[3–5]; however, data regarding the impact of PCI revascularization on short- and mid-term outcomes remain scarce.

The primary endpoint was all-cause mortality. Secondary endpoints included cardiac death, myocardial infarction (defined as a CK-MB level >3 times the upper limit of lab normal value with or without new pathologic Q wave), and target vessel revascularization (defined as revascularization at the target vessel (inclusive of the target lesion) after the completion of the index procedure with PCI or coronary artery bypass grafting (CABG). All outcomes were tested at 1 and 4 years after the index procedure. Pooled relative risk (RR) and their corresponding 95% confidence intervals (CI) were calculated using the random-effects model.

A total of 6 RCTs including 1,890 patients (1014 patients who underwent PCI + OMT vs 876 patients who had OMT only) were included. The median follow-up period was 12 months (range 4 to 48 months). The mean age was 63 ± 9.8 years, 83.4% males, 28% had diabetes, 39% were smokers, 62% had hypertension, and 51% had hypercholesterolemia. The baseline ejection fraction was 53 ± 13. Half of the lesions were in the right coronary artery with an average SYNTAX score of 21.4 ± 10.1, and the average Japanese-CTO Registry score was 2.0 ± 1.4.

All-cause mortality and cardiac mortality were comparable between CTO-PCI and OMT groups at 1-year (RR: 1.70; 95% CI: 0.50 to 5.80; p = 0.40; and RR: 1.77; 95% CI: 0.19 to 16.06; p = 0.61) and at 4-year follow-up (RR: 1.14; 95% CI: 0.38 to 3.40; p = 0.81; and RR: 2.05; 95% CI: 0.8 to 5.28; p = 0.14). Moreover, MI risk was comparable between the two groups at 1 and 4-year follow up (RR: 1.01; 95% CI: 0.43 to 2.36; p = 0.98) and (RR: 1.46; 95% CI: 0.75 to 2.87; p = 0.27) respectively. However, PCI group was associated with lower risk of TLR at 1-year follow-up (RR: 0.28; 95% CI: 0.17 to 0.49; p <0.001) but not at 4-year (RR: 0.55; 95% CI: 0.28 to1.09; p = 0.09). (Figures 1 and 2)

Our study demonstrated that PCI revascularization for CTO patients did not lower the risk of all-cause mortality at 1 and 4 years compared with OMT alone. Furthermore, the two groups had a similar risk of cardiac mortality and MI; however, the PCI group had fewer TLR at 1-year follow-up.

Several observational studies investigated the clinical effectiveness of PCI revascularization among patients with CTO and have reported a lower risk of Major Adverse Cardiac Events (MACE) with CTO-PCI strategy.[6,7] however, the methodological limitations of such studies preclude any firm conclusion from being drawn from such analyses. Furthermore, a recently published single-center clinical study showed a lower 10-year rate of cardiac death in the CTO-PCI group mainly