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Research Letter

Impact of Bacillus Calmette-Guérin (BCG) vaccination on postoperative mortality in patients with perioperative SARS-CoV-2 infection

COVIDSurg Collaborative

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Members of the COVIDSurg Collaborative are co-authors of this study and are listed under the heading Collaborators. For details of role see *Appendix S1*.

Dear Editor

During the COVID-19 pandemic, multiple theories were proposed based on the observation that countries with an ongoing national Bacillus Calmette-Guérin (BCG) immunization programme had lower SARS-CoV-2 case rates and COVID-19 mortality than countries that had stopped BCG vaccine administration. There was, however, no evidence supporting or disputing this theory[1,2]. Owing to the uncertainty on the role of BCG vaccine on the outcomes of patients with perioperative SARS-CoV-2 infection, this international study aimed to determine whether previous BCG vaccination was associated with reduced postoperative pulmonary complications (PPC) and 30-day mortality in patients undergoing surgery who developed SARS-CoV-2 infection.

This COVIDSurg study[3–5] was an international prospective cohort study that included patients who had surgery between 1 February and 31 July 2020 and were diagnosed with SARS-CoV-2 within 7 days before or 30 days after surgery. The primary outcome was the rate of 30-day PPC and the secondary outcome was 30-day postoperative mortality rate. These were compared in patients with and without BCG vaccination. A logistic regression model was used to find the odds of association. The full methodology is available in the *Appendix S2*.

This study included 2391 patients from 428 hospitals across 64 countries from February 2020 to July 2020. Overall, 1165 (48.9 per cent) patients were male and 524 (21.9 per cent) were aged 70 years or older (*Table S1*). The BCG vaccine had been administered to 1649 (69.0 per cent) patients, of whom 1518 (63.5 per cent) had received it at least 15 years before surgery. Patients who had received a BCG vaccination were younger than patients who had not been vaccinated (70 years of age or older: 16 *versus* 35 per cent ($P < 0.001$)), had lower ASA (grades III–V: 30 *versus* 51 per cent ($P < 0.001$)), and were more likely to have surgery for benign conditions (71 *versus* 60 per cent; $P < 0.001$). There were no significant differences in the rates of emergency surgery, major surgery, or timing of SARS-CoV-2 infection between the groups. Of the 2391 patients, 759 (31.7 per cent) developed PPC. The 30-day mortality was 11.1 per cent ($n = 265$). Although rates of PPC were significantly lower in patients who had previously been vaccinated against BCG than those who did not (29 *versus* 38 per cent; $P < 0.001$) (*Table 1*), this did not persist on adjusted analysis (odds ratio (OR) 0.98, 95 per cent c.i. 0.79–1.22; $P = 0.3$) (*Table 1*). There were no significant differences in 30-day mortality rates in previously BCG-vaccinated patients *versus* unvaccinated patients (10 *versus* 13 per cent; $P = 0.062$), which remained on adjusted analysis (OR 1.25, 95 per cent c.i. 0.92–1.69; $P = 0.156$) (*Table 1*). Full models are presented in *Tables S2* and *S3*.

Stratified analysis performed by timing of vaccination demonstrated that patients who were vaccinated 15 years previously or longer were less likely than patients vaccinated less than 15 years

Table 1 Impact of BCG vaccination on postoperative pulmonary complications and 30-day mortality in patients with SARS-CoV-2 infection undergoing surgery

	No. of patients (%)	Unadjusted OR (95% c.i.)	P	Adjusted OR (95% c.i.)	P
Pulmonary complications					
No BCG	278 (37.5)	REF		REF	
BCG	481 (29.2)	0.69 (0.57–0.83)	0.001	0.98 (0.79–1.22)	0.878
30-day mortality					
No BCG	96 (12.9)	REF		REF	
BCG	169 (10.2)	0.77 (0.59–1.01)	0.053	1.25 (0.92–1.69)	0.156

OR, odds ratio; BCG, Bacillus Calmette-Guérin; REF, referent.

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ago to be ASA grades III–V (30 *versus* 41 per cent; $P = 0.033$) and were more likely to have surgery for benign disease (72 *versus* 57 per cent; $P < 0.001$) (*Table S4*). There were no significant differences in rates of postoperative pulmonary complications (29 *versus* 34 per cent; $P = 0.208$) or 30-day mortality (10 *versus* 14 per cent; $P = 0.221$), on adjusted analysis (*Tables S5* and *S6*).

There were important limitations to the present study. There was a broad inclusion of patients from low-, middle-, and high-income countries with varying pre- and postoperative procedures and availability of resources such as a well-equipped ICU for the management of the patient. Mortality and morbidity could have been greatly impacted by this difference. Some countries had a much higher prevalence and severity of disease, which could have also influenced outcomes.

According to these findings, prior BCG vaccination does not appear to protect SARS-CoV-2-infected patients against PPCs and 30-day mortality.

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Supplementary material

Supplementary material is available at *BJS Open* online.

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