

Long COVID syndrome: a case-control study

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Funding Acknowledgement: Type of funding sources: None.

Background: Cardiovascular complications are rapidly emerging as a major threat in COVID-19 infection. Nonetheless, the mechanisms underlying the disproportionate effect of SARS-CoV-2 infection on patients with cardiovascular comorbidities remain incompletely understood.

Purpose: To assess whether COVID-19 infection has an adverse clinical outcome at medium-term follow-up.

Methods: A case-control study was performed. Cases were subjects who were diagnosed with COVID-19 infection following nasopharyngeal swabbing. Controls were age- and gender-matched subjects who were not found to be infected with COVID-19 following swabbing and were negative on testing for COVID-19 IgG antibodies. All participants were submitted a standardised questionnaire regarding past medical history. Baseline blood investigations were taken including N-terminal pro-B-type natriuretic peptide (NT-proBNP) and troponin levels. High-sensitivity C-reactive protein (hsCRP) was taken as marker of inflammation and von Willebrand factor (vWF) was taken as marker of endothelial dysfunction.

Results: 270 subjects were recruited, comprising 174 cases and 96 controls. Of the latter, 21 were found to be COVID-19 IgG positive and were excluded from the analysis. Hence, the study cohort comprised 174 cases and 75 controls. The mean age of the participants was 46.1±13.8 years. The median follow-up was of 173.5 days (IQR 129–193.25 days). There was no statistically significant difference in the baseline demographics be-

tween cases and controls with regards age, gender as well as cardiovascular risk factors and underlying medical conditions. Regarding symptomatology at follow-up, there was a statistically significant difference between the groups in deterioration in general condition ($p < 0.001$), shortness of breath (SOB) ($p = 0.008$), fatigue ($p = 0.044$), arthralgia ($p < 0.001$), abnormal taste ($p < 0.001$) and anosmia ($p < 0.001$), all being more frequent in subjects with prior COVID-19 infection. At follow-up, the blood investigations showed that only hsCRP was statistically significantly higher in the cases as compared to the controls ($p = 0.03$, Figure 1). Correlation analysis consequently revealed a negative correlation in both troponin ($p = 0.013$, $r = -0.19$) and vWF levels ($p = 0.026$, $r = -0.169$) with time. Finally, the association between the cases experiencing dyspnoea and the blood investigations at follow-up was assessed. Multivariate analysis revealed that COVID-19 positive cases experiencing dyspnoea have significantly higher white cell count (WCC) (OR 1.22, 95% CI 1.02–1.46, $p = 0.029$) and troponin levels (OR 1.15, 95% CI 1.02–1.29, $p = 0.015$) and lower haemoglobin levels at follow-up (OR 0.66, 95% CI 0.5–0.86, $p < 0.002$), Figure 2.

Conclusion: Patients previously infected with COVID-19 have persistent symptomatology at medium-term follow-up. The role of troponin, together with markers of inflammation and endothelial dysfunction at long-term follow-up merit further investigation.

