

## COVID-19 and the autonomic nervous system

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**Background:** COVID-19 infection has been shown to have an adverse impact on the cardiovascular system. Cardiac injury, as indicated by elevated cardiac troponin and NT-proBNP levels have been confirmed in COVID-19 cases. There is still ambivalent data on the effect of left ventricular function. Cases of left ventricular impairment, persistent hypotension, acute myopericarditis, myocarditis, arrhythmia and heart failure have been reported in the short term, but there is a significant lacuna when it comes to medium and long-term follow-up of subjects previously infected with COVID-19.

**Purpose:** To assess any residual myocardial and autonomic injury in subjects previously infected with COVID-19 at a median follow-up of 5 months.

**Methods:** A case-control study was performed. Cases were randomly selected subjects who were previously diagnosed with COVID-19 infection following nasopharyngeal swabbing. Controls were subjects who had not been found to be infected with COVID-19 following swabbing and were negative for COVID-19 IgG antibodies. All participants were submitted a standardised questionnaire regarding past medical history. Blood investigations were taken including NT-proBNP and troponin I levels. In addition, all participants underwent 24-hour ambulatory blood pressure monitoring (ABPM) and 24-hour ECG monitoring. The latter was used to assess both for underlying arrhythmias as well as heart rate variability (HRV), a measure of autonomic regulation of the heart. All data was analysed using SPSS version 23.0.

**Results:** The study comprised 259 subjects, whereby cases included 174 participants while 75 subjects were age- and gender-matched controls. The study cohort was relatively young with a mean age of  $46.1 \pm 13.8$  years. The median follow-up was of approximately 5 months (median 173.5 days, IQR 129–193.25 days). There was no statistically significant difference between cases and controls with regards cardiovascular risk factors and underlying medical conditions. Likewise, there was no difference in blood investigations, including troponin I and NT-proBNP levels at 5-months follow-up. No difference was noted between the two groups in both awake and asleep blood pressure (BP) readings, as well as dipping BP status. No significant arrhythmias were noted in both groups on 24-hour ECG monitoring. However, when assessing for heart rate variability, it was shown that subjects who had been previously infected with COVID-19 exhibited lower root-mean square differences of successive R-R intervals (RMSSD),  $p=0.028$ . This indicates poor vagus nerve-mediated autonomic control of the heart.

**Conclusion:** Subjects previously infected with COVID-19 exhibited lower HRV as exhibited by low RMSSD as compared to controls. Reduced HRV is a known biomarker for mortality and sudden death in cardiac disease. The possible long-term implications of reduced HRV in subjects previously infected with COVID-19 merits further investigation.