

Relatively High Heart-Rate Variability Predicts Greater Survival Chances in Patients with Covid-19

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Abstract : Background: The worldwide pandemic of severe acute respiratory syndrome coronavirus 2 (SARS-COV2), which began in 2019, also known as Covid-19, has infected over 136 million people and tragically took the lives of over 2.9 million people worldwide. Many of the complications and deaths are predicted by the inflammatory “cytokine storm.” One way to progress in the prevention of death is by finding a predictive and protective factor that inhibits inflammation, on the one hand, and which also increases anti-viral immunity on the other hand. The vagal nerve does precisely both actions. This study examined whether vagal nerve activity, indexed by heart-rate variability (HRV), predicts survival in patients with Covid-19. Method: We performed a pseudo-prospective study, where we retroactively obtained ECGs of 271 Covid-19 patients arriving at a large regional hospital in The Netherlands. HRV was indexed by the standard deviation of the intervals between normal heartbeats (SDNN). We examined patients’ survival at 3 weeks and took into account multiple confounders and known prognostic factors (e.g., age, heart disease, diabetes, hypertension). Results: Patients’ mean age was 68 (range: 25-95) and nearly 22% of the patients had died by 3 weeks. Their mean SDNN (17.47msec) was far below the norm (50msec). Importantly, relatively higher HRV significantly predicted a higher chance of survival, after statistically controlling for patients’ age, cardiac diseases, hypertension and diabetes (relative risk, H.R, and 95% confidence interval (95%CI): H.R = 0.49, 95%CI: 0.26 - 0.95, $p < 0.05$). However, since HRV declines rapidly with age and since age is a profound predictor in Covid-19, we split the sample by median age (40). Subsequently, we found that higher HRV significantly predicted greater survival in patients older than 70 (H.R = 0.35, 95%CI: 0.16 - 0.78, $p = 0.01$), but HRV did not predict survival in patients below age 70 years (H.R = 1.11, 95%CI: 0.37 - 3.28, $p > 0.05$). Conclusions: To the best of our knowledge, this is the first study showing that higher vagal nerve activity, as indexed by HRV, is an independent predictor of higher chances for survival in Covid-19. The results are in line with the protective role of the vagal nerve in diseases and extend this to a severe infectious illness. Studies should replicate these findings and then test in controlled trials whether activating the vagus nerve may prevent mortality in Covid-19.

Keywords : Covid-19, heart-rate Variability, prognosis, survival, vagal nerve

Conference Title : ICBM 2021 : International Conference on Behavioral Medicine

Conference Location : Bangkok, Thailand

Conference Dates : December 16-17, 2021