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ORIGINAL RESEARCH

**13. Vagus Nerve Neuropathy in SARS-CoV-2 Infection: An
Ultrasound Study**

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Serbia

https://www.youtube.com/watch?v=hJicJ1w8oM&list=P_LhqNq3xJClbafO0Y5bvBcgMmXpgzJxd44&index=5&t=7183s

Background: The vagus nerve regulates systemic inflammation through the inflammatory reflex arc. Afferent fibers detect cytokines and relay signals to the brainstem, which activates parasympathetic pathways to suppress inflammation via acetylcholine release in the spleen. Disruption of this “brake system” can lead to cytokine storm, a driver of severe COVID-19. Beyond COVID-19, vagal dysfunction is also implicated in atherosclerosis, asthma, diabetes, Crohn’s disease, ulcerative colitis, and autoimmune thyroiditis.

Aim: To determine whether vagus nerve neuropathy can be detected in SARS-CoV-2-infected patients using ultrasound, and to assess its contribution to COVID-19 pathophysiology and related inflammatory conditions.

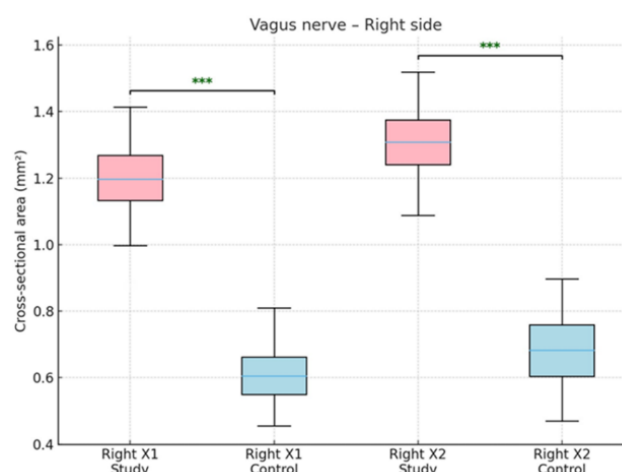
Methods: A prospective study was conducted between October 2021 and April 2022, including 68 patients (mean age 53.1 ± 14.3 years) with PCR-confirmed Delta variant infection and 50 healthy controls (mean age 22.7 ± 2.4 years). Exclusion criteria for controls included chronic illness or medication affecting autonomic function. Ultrasound was performed with a 10–18 MHz linear probe, with patients supine or in lateral decubitus position. The vagus nerve was examined bilaterally at two levels: X1 (carotid bifurcation) and X2 (cricoid cartilage). Cross-sectional area (CSA) was traced just outside the hyperechoic rim. Each measurement was repeated by two independent operators. Data were analyzed using Mann–Whitney U tests (IBM SPSS v26).

Results: On the left side, X1 values did not differ, while X2 showed a borderline increase in the COVID group ($p=0.05$). On the right side, both X1 and X2 were nearly doubled in COVID-19 patients compared to controls ($p<0.001$). Median CSA values were consistently higher in patients (Left X1: 0.77 vs 0.70 mm²; Left X2: 0.87 vs 0.70 mm²; Right X1: 1.20 vs 0.60 mm²; Right X2: 1.30 vs 0.70 mm²). Importantly, this enlargement was observed despite the older age of the patient group, where smaller nerve dimensions would normally be expected. This contrast reinforces the likelihood of pathological involvement rather than age-related variation.

Conclusion: Ultrasound revealed enlargement of the vagus nerve in COVID-19 patients, most prominently on the right side. Although

ultrasound cannot fully distinguish edema from structural neuropathy, the consistent enlargement justifies use of the term neuropathy in a broad sense. These findings support the hypothesis that vagus nerve dysfunction contributes to cytokine storm and severe outcomes in SARS-CoV-2 infection. Moreover, ultrasound emerges as a simple, bedside, non-invasive tool to study cranial nerves in vivo. Given the role of the inflammatory reflex in many chronic diseases, these results may extend beyond COVID-19, offering opportunities for diagnostics, monitoring, and therapeutic interventions targeting vagal pathways.

Figure 1. Box Plot: Comparison of Right Vagus Nerve Cross-sectional Area (Study vs. Control).



Legend: Box plots of vagus nerve cross-sectional area (CSA, mm²) at two levels (X1 – carotid bifurcation, X2 – cricoid cartilage) on the right side in COVID-19 patients and healthy controls. * $p < 0.001$; n.s. = not significant (Mann–Whitney U test).

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