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Small airway function after Covid-19 infection

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Background: Lingering respiratory symptoms is common after covid-19. The pathophysiology behind this is unclear, with spirometry often being normal. We hypothesised that impairment in the small airways can be an explanation.

Aim: To investigate if the function of the small airways is impaired after covid-19.

Methods: 58 (36 females) post covid-19 subjects aged 21-65 years performed spirometry, DLCO, nitrogen (N2) multiple breath washout (MBW) and impulse oscillometry (IOS). Seven out of 58 were hospitalized in the acute phase. Median (IQR) days between infection and participation was 216 (172; 549). Lung function were reported in z-score related to GLI reference equations for spirometry and DLCO, while two healthy cohorts (n=400 and n=158) provided local reference values for N2 MBW and IOS, respectively. Limits of normality were defined as ±1.96 z-score.

Results: Small airway dysfunction was present in 20/58 assessed lung clearance index, in 18/58 assessed by Sacin and in 10/58 assessed by Scond., while 31/58 had abnormality in at least one of these N2 MBW derived indices. IOS identified increased resistance in small airways in 5/58 and increased reactance (“stiffness”) in small airways in 10/58. Spirometry was abnormal in 2/58 and another two subjects had abnormal DLCO.

Only Sacin differed significantly between subjects with respiratory symptoms (n=26) and those without (n=32), median (IQR) z-score, 1.66 (0.28; 3.36) versus 0.50 (-0.45; 1.74), p=0.014. Abnormal Sacin was demonstrated in 11/26, and 16/26 demonstrated abnormality in at least one N2 MBW outcome. However, 10/26 with respiratory symptoms had all lung function outcomes within the normal range.

Conclusion: Small airway dysfunction was common in this sample of post covid-19 subjects, despite spirometry and DLCO being normal. Ventilation heterogeneity at the entrance to the acinar airways (Sacin) may partly explain the experience of dyspnea in these subjects, but other reasons beyond reduced lung function may also contribute to lingering respiratory symptoms.