Early View

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Cardiopulmonary Exercise Test might be Helpful For Insight Interpretation of Impaired Pulmonary Function on Recovered COVID-19 Patients

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Cardiopulmonary Exercise Test might be Helpful For Insight Interpretation of Impaired Pulmonary Function on Recovered COVID-19 Patients

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To the Editor,

We are grateful to have the opportunity for an in-depth discussion with Dr Nusair et al[1]and Dr Chapman et al[2] who we sincerely appreciate their insightful comments on our study about the impaired pulmonary function in COVID-19 patients[3,4], which helps to interpret the parameters of abnormal lung diffusion capacity more accurate.

According to the algorithm pointed out by Dr. Chapman[2], the mean VA for total, mild, pneumonia, severe pneumonia patients with COVID-19 in our study were 84.9%, 85.3%, 86.4%, 78.5%, respectively[3]. Recently, another retrospective study by Frija-Masson[5] showed more than half of patients with COVID-19 pneumonia presented abnormal lung function 30 days after symptom onset. Similarly, a rough value VA for total, none/mild, moderate, severe patients with COVID-19 were 85.1%, 87.9%, 80.2%, 78.9%, respectively. If we plotted these data into the curve of DLCO/DLCO$_{TLC}$ and KCO/KCO$_{TLC}$ plotted against volume loss VA/VA$_{TLC}$ presented by J. Michael et al[6], we can see a greater impairment in DLCO and a normal but not increased KCO especially in severe cases, which isn't in parallel with the expected result if a reduction in VA is the sole factor that results in lung diffusion abnormality. Both studies supported the view that loss of alveolar units is not sufficient to cause the observed impairment in DLCO.

DLCO depends on both VA and the KCO. The same DLCO may occur with various combinations of KCO and VA, each suggesting different pathologies. Currently, limited data on pathology showed the diffuse alveolar damage (DAD) was the predominant lung pathology, with various levels of progression and severity and residual interstitial abnormalities[7]. Additionally, pulmonary microangiopathy, fibrin clotting within small capillaries around alveoli, small vessel thrombosis and thickening of alveolar capillaries were also found in different post-mortem studies[8,9]. From this perspective, it suggested that not only reduced VA, but also residual interstitial abnormalities, pulmonary vascular abnormalities contributed to the abnormal diffuse function in patients with COVID-19. We agree with Dr. Chapman's point that "Use of more specific measures of the alveolar-capillary membrane, such as combined DLCO and DLNO measurements or advanced imaging techniques, are likely required to determine whether interstitial abnormalities or pulmonary vascular abnormalities contribute to reduced DLCO". Moreover, a combination of dynamic chest CT scans help to assess the status of patients with COVID-19 having abnormal lung function.

In the clinical practice, part of rehabilitated patients with COVID-19 presented various level of exertional dyspnea. Besides the impairment of static pulmonary function tests (PFT), a decreasing capability of oxygen uptake or utilize should be noted. Therefore, we performed the dynamic functional evaluation through cardiopulmonary exercise test (CPET) in 10 rehabilitated patients with COVID-19 (i.e. 3 moderate cases, 2 severe cases, 5 critical ill cases) 1-month post-discharge in our center between January to March 2020.

Our result showed the spirometry was within the normal range in all cases and abnormal DLCO (<80% pred) was only found in 3 cases. However, noteworthy, all cases had reduction of the peak oxygen uptake (PeakVO2) and seven cases displayed decreasing oxygen pulse of predicted (VO2/HR%pred). On the contrary, 8 cases displayed normal ventilatory equivalents for carbon dioxide at anaerobic threshold (VE/VCO2@AT). This indicated pulmonary dysfunction and gas transfer inefficiency was not the sole reason for exercise limitation of patients with COVID-19, extrapulmonary factors especially the cardiac dysfunction after long-term bed rest during hospitalization should be concerned.

Up to date, no data regarding the CPET on patients with COVID-19 was reported. Previous study on SARS by Ong et al [10] showed despite half of the recovered patients with SARS had pulmonary function defects, the impairment was mild in majority of cases. Many patients had decreased exercise capacity that cannot be accounted for impairment of pulmonary function, which was consistent with our preliminary results. Thus, it is necessary to further evaluate the impairment of exercise endurance in patients with COVID-19.

References

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Table1：Clinical Characteristics, PFTs and CPET at 1-month post-discharge follow-up

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9	Case 10	Mean± SD
Illness severity	moderate	moderate	moderate	severe	severe	critical	critical	critical	critical	critical	
Gender	Male	Female	Female	Male	female	Male	Male	Male	Male	Male	NA
Age	50	25	56	26	83	65	58	41	50	53	50.7±17.3
BMI	19.83	20.43	20.63	26.58	23.13	21.63	23.42	28.18	25.43	24.27	23.4±2.8
PFTs											
FEV1 %pred	111	98	106	102	138	115	99	87	92	93	104.1±14.7
FVC %pred	107	93	111	106	138	106	90	87	85	95	101.8±15.7
FEV1/FVC	85.5	92.6	80.6	81.3	79.1	85	87.7	83.8	87.3	78.8	84.2±4.4
FEF25%-75% %pred	101	111	75	87	90	109	127	81	116	69	96.6±19.1
DLCO %pred	86	93	88	95	61	85	69	80	78	84	81.9±10.5
KCO %pred	74	103	92	89	70	90	81	88	86	84	85.7±9.3
CPET											
PeakVO2 %pred	73	76	74	61	77	66	44	73	58	60	66.2±10.5
VO2@AT %pred	55.9	53.5	/	37.8	/	52.2	43.5	50	42.8	44.7	47.6±6.3
Breath reserve	66.6	65.3	65.5	46.9	70.9	66.4	58.3	65.3	53.9	59.9	61.9±7.2
VO2/HR %pred	74	94	107	64	106	65	54	76	66	74	78±18.3
VE/VCO2 @AT	25.4	26.5	/	27.7	/	30.4	34.6	28.7	31.3	32.1	29.6±3.1

Abbreviation: PFTs: pulmonary function tests; FEV1%pred: forced expiratory volume in one second of predicted; FVC%pred: forced vital capacity of predicted; FEF25%-75%%pred: mean forced expiratory flow between 25% and 75% of predicted; DLCO%pred: carbon monoxide diffusion capacity of predicted; KCO%pred: carbon monoxide transfer coefficient of predicted; CPET: cardiopulmonary exercise test; PeakVO2 %pred: peak oxygen uptake of predicted; VO2@AT%pred: oxygen uptake at anaerobic threshold of predicted; VO2/HR%pred: Oxygen pulse of predicted; VE/VCO2@AT: Ventilatory equivalents for carbon dioxide at anaerobic threshold.