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STUDY OF PULMONARY FUNCTION IN COVID 19 PATIENTS 3 MONTHS AFTER THE INFECTION IN A HOSPITAL SET-UP OF MANIPUR

Medical Science

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ABSTRACT

Objective:- Evaluation of pulmonary function impairment after COVID-19 in persistently symptomatic and asymptomatic patients of all disease severities and characterisation of risk factors **Methods:-** Patients with confirmed SARS-CoV-2 infection underwent prospective follow-up with pulmonary function testing 3 months after acute illness. Pulmonary function impairment (PFI) was defined as reduction below 80% predicted of TLC, FVC, or FEV1. Clinical data were analyzed to identify risk factors for impaired pulmonary function. **Results:-** 76 patients were included, hereof 35 outpatients with mild disease and 41 patients hospitalized due to COVID19. Sixteen patients had critical disease requiring mechanical ventilation, 25 patients had moderate–severe disease. After 3 months, 44 patients reported persisting respiratory symptoms. Significant PFI was prevalent in 40 patients (52.6%) occuring among all disease severities. The common causes for PFI were reduced TLC and FVC. The severity of PFI was signifcantly associated with mechanical ventilation that occurred in 1/5 of patients after mild disease course. **Conclusion:-** We characterized pulmonary function impairment in asymptomatic and persistently symptomatic patients of different severity groups of COVID-19 and identified further risk factors associated with persistently decreased pulmonary function.

KEYWORDS

Post-COVID, Pulmonary function impairment, COVID-19, SARS-CoV-2.

INTRODUCTION:-

The coronavirus disease 2019 (COVID-19) pandemic has put considerable strain on the health systems globally [1]. A signifcant percentage of patients develop COVID-19 pneumonia, which is the key determinant of prognosis in COVID-19 [2–4]. Risk factors for critical disease are mainly age, cardiovascular disease, diabetes and male sex [5].

Further pulmonary worsening is mediated by a cascade of hyperinfammatory responses, which is frequently observed after an initial period of symptom stability. COVID-19 pneumonia and the severe infammatory process are hypothesized to cause lasting parenchymal damage. Besides, patients with moderate to severe COVID-19 disease are more likely to develop multi-organ disease, e.g. myocardial injury, thromboembolic complications, liver failure, and pneumothorax [6–10]. Comparably, patients after Acute Respiratory Distress Syndrome (ARDS) suffer from long-term physical problems and lung function deterioration [6]. An unknown proportion of patients may develop subclinical COVID-19 pneumonia with a mild disease course without hospitalization. So far, few studies have analyzed. the impact of COVID-19 on lung function, and its long-term efects remain unclear. It is essential to identify risk factors for lasting pulmonary damage and define patients at risk who should receive specialized respiratory follow-up care after infection.

Here, we evaluate pulmonary function impairment after COVID-19 disease among all severity groups in persistently symptomatic and asymptomatic patients four months after infection. Furthermore, this study investigates predictors for lung function impairment according to disease severity in a highly diverse COVID-19 patient group.

METHODS-

Design and study population:-

This single-center cohort study included 76 patients with confirmed COVID-19 disease with acute illness during the first wave (June to December 2020). The Institutional Ethics Committee approved the study which was carried out in the Department of Physiology, Regional Institute Of Medical Sciences, Imphal in collaboration with the Department of Medicine.Up to December 2020, we prospectively included all adult patients (age>18 years) who presented to the Medicine outpatient department for follow-up 3 months after confirmed SARS-CoV-2 infection [positive RT-PCR test]. Hospitalized patients from the medicine ward were also sent to us after discharge. All patients provided written informed consent. Patients underwent a standardized interview to qualitatively evaluate COVID-19 related symptoms (yes or no) as previously described [11]. We diferentiated between any COVID-19-related symptoms (including dyspnea, cough, fatigue, or anosmia, yes or no) and specifc respiratory symptoms (dyspnea at rest or after exercise, cough, yes or no). Pulmonary Function Test was carried out by using computerised Medspiror (Helios).

Diagnosis of COVID 19:-

We diagnosed COVID-19 in patients with matching symptoms and documented positivity for SARS-CoV-2 RNA in a reverse transcriptase-polymerase chain reaction (RT-PCR) from nasopharyngeal swabs (NPS) as described previously [15].

Disease severity and comorbidity:-

Patients were divided into 3 groups (mild, moderate/severe, and critical severity) according to WHO criteria (https:// www.who. int/ publications/i/item/clinical-management-ofcovid-19). Moderate and severe disease courses were analysed as one group (moderate/severe). Symptomatic patients without hospitalization were classified as mild disease. Hospitalized patients with clinical signs of pneumonia without oxygen requirement were classifed as moderate disease and patients who needed low-flow oxygen supplementation via nasal cannula were classified as severe disease. Critically ill patients received non-invasive ventilation (NIV) or invasive mechanical ventilation.

Statistical analysis:-

Continuous variables were reported using mean with standard deviation (SD). We compared differences in means using unpaired t-test and ANOVA in the whole sample. When comparing repeated measurements of lung function testing, we used paired t test and Mann–Whitney test. Categorical variables were reported as absolute and relative frequencies and compared using $\chi 2$ test. In the univariate analysis we used Pearson correlation coeficient to test for association between variables. Statistical signifcance was considered at $p<0.05$. SPSS version 26 was used for statistical analysis. For descriptive purposes, pulmonary function impairment (PFI) was described as reduction in TLC,FVC or FEV1 to <80% of the predicted value.

RESULTS:-

Baseline characteristics- Up to December 2020, 76 patients were included. The mean age (±SD) was 49.6±17.4, and 43.3% of the patients were male. Thirty-five patients (46.1%) had mild disease treated as outpatients. In these mild patients, no imaging studies were performed during acute illness as patients were quarantined. 41 patients (53.9%) were hospitalized and had CT scan during acute illness. Hereof 25 patients (32.9%) had moderate/severe disease while 16 patients (21.1%) developed critical disease during hospitalization with the necessity for mechanical ventilation (Table 1). Patients with mild and moderate/severe disease were signifcantly younger than patients with critical disease with mean age (±SD) 44.3±14.6, 48.1±19.6 and 63.8±10.3 years, respectively). 10 patients (24%) who were scheduled for appointments were lost to follow-up (Fig. 1). The majority of patients (n=53, 69.7%) reported at least one persistent COVID-19 related symptom at presentation in our center four months after the initial diagnosis of COVID19. Persistent respiratory symptoms (dyspnea at rest, dyspnea after exercise, or cough) were documented in 43 (56.6%) patients. 21 patients (27.6%) reported

persistent fatigue, and 12 patients (15.8%) persistent anosmia (Table 2). One-third (24 patients) reported no residual symptoms at the follow-up presentation. According to patient interview, no patient had been diagnosed with interstitial lung disease previously.

Table 1 Baseline characteristics of the study population

Total Cohort n=76	Mild No hospitalization n=35	Moderate/Severe Hospitalisation No ventilation n=25	Critical pvalue Ventilation n=16
Age, mean ± SD 49.6±17	44.3±14.6	48.1±19.6	63.8±10.3 <0.001*
Male,n(%) 33(43.4)	13(37.1)	9(36)	12(70) 0.285
COPD(n%) 5(6.6%)	3(8.6%)	1(4%)	1(6.3%) 0.136
Hypertension 17(22.4%)	3(8.6%)	7(28%)	7(43.8%) 0.071
Obesity(n%) 8(13.6%)	1(2.9%)	3(12%)	5(31.3%) 0.045*
Diabetes mellitus 4(5.3%)	0(0%)	2(8%)	2(12.5%) 0.553
Coronary artery 5(7.6%) disease	1(2.9%)	2(8%)	2(12.5%) 0.462

Pulmonary Function testing at 3 months follow up:

TLC, FVC, and FEV1 were signifcantly decreased after critical disease course, while mean FEV1/FVC was normal in all disease severities (Table 2).

Table2:- Pulmonary function testing :-

	All patients Mild Disease	Moderate Disease	Severe p value Disease
Patients,n	n=76 n=35	n=25	n=16
TLC	5.8±1.5 6.1±1.3	5.9±1.6	5.1±1.7 0.11
TLC,% of predicted	96.3±19.1 99.8±11	101.8±21.4	77.5±11.4 <0.01*
FVC,L	3.7±1.1 4±1.1	3.7±.8	2.9±1.1 <0.01*
FVC,% of predicted	97.1±17.6 99.4±13	102.5±16	79.7±20 <0.01*
FEV1,L	3±0.9 3.3+_0.9	3.1±0.8	2.4±0.9 <0.01*
FEV1,% of predicted	97±18 97.1±14	104.3±16	84.1±23 <0.01*
FEV1/FVC	83.5±7.5 82.4±7	84.6±4.8	84.5±23 0.46

DISCUSSION:-

Here we report comprehensive pulmonary function evaluation of COVID-19 patients 3 months after acute illness in a broad cohort of patients ranging from mild to critical disease course including patients with persisting symptoms as well as patients who were asymptomatic at the time-point of follow--up. We found impaired pulmonary function in more than half of the patients. Recent studies reported reduced TLC, and FVC one to six months after COVID-19 disease in selected patients; however, so far, most studies focused on hospitalized cohorts[21,22]. Contrary to these studies, we included 46% (n = 35) patients who had a mild disease course without hospitalization and also 33% (n = 25) who reported no persistent COVID-19-related symptoms. Even though patients with critical disease had more severe PFI at mean, we also found PFI defined as values < 80% predicted in a proportion of patients who had mild and moderate/severe COVID-19. Reduced lung capacities after COVID-19 may indicate interstitial lung damage. Interstitial lung disease after COVID-19 disease is an important clinical manifestation in the convalescent phase. Recent studies report up to 62% of pulmonary interstitial fibrosis-like changes two months after critical disease courses[18]. Similar to ARDS, long-term mechanical ventilation likely plays an important role in the development of interstitial fibrosis. As preexisting COPD was rare, this suggests non-critical COVID-19 pneumonia as likely cause in most patients. Long-term follow-up has not been established yet. It is unclear whether impaired difusion capacity will improve and which risk factors for persistence over more extended time courses exist. Early identifcation of restrictive disease and identifcation of risk factors might be essential for early treatment interventions. TLC and FVC are less frequently impaired and thus secondary markers for identifying patients at risk. If progressive fibrosing interstitial lung disease after COVID-19 is confirmed by further diagnostic assessment, antiifbrotic agents, e.g. Nintedanib might be a treatment option that needs to be studied in RCTs. To elucidate risk factors for pulmonary function impairment, we integrated clinical data during acute illness. As mentioned above, the most substantial risk factor for impaired TLC, FVC, and FEV1 was mechanical ventilation, in line with findings from other recent cohorts [16,17]. Contrary to other studies, we have also included patients with mild disease course and patients who did not report symptoms at follow-up and thus analyzed the infuence of disease severity and persistent symptoms on PFI. This approach revealed that PFI might also be present after mild COVID-19, and such patients should also be included in future studies. However, it should be noted that this was not a population-based study. At the time of presentation in our aftercare unit 23 patients (65.7%) had persistent symptoms, whereas 12 patients (34.3%) negated persistent COVID-19 related symptoms. Asymptomatic patients (n=12) were referred or presented themselves due to intrinsic or scientific interest after announcing the post-COVID-19 aftercare offer after the first COVID-19 wave. Nevertheless, we assume that negative effects on lung function are less frequent in patients who do not present in an aftercare unit after mild disease courses. Potential selection bias might be present in the mild disease course group. Thus, the frequencies of symptomatic versus asymptomatic follow-up patients are not representative for an overall post-COVID-population. Additionally, analyses are limited due to moderate sample size, and symptoms were analyzed only qualitatively. As PFT values before the disease were not available for the majority of the patients, mild preexisting abnormalities cannot be excluded. According to our data and recent publications, we recommend pulmonary aftercare to patients after severe and critical COVID-19 disease courses [11]. In sum, we describe that PFI may be present in symptomatic and asymptomatic post-COVID-19 patients but is most frequent in those who had severe acute illness.

REFERENCES:-

1. Li Q, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N Engl J Med. 2020;382:1199–207.
2. Chen N, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020; 395: 507–13.
3. Huang C, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395:497–506.
4. Wang D, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA. 2020;323:1061–9.
5. Jakob CEM, et al. First results of the "Lean European Open Survey on SARS-CoV-2-Infected Patients (LEOSS)." Infection. 2021;49:63–73.
6. Needham DM, et al. Improving long-term outcomes after discharge from intensive care unit: report from a stakeholders' conference. Crit Care Med. 2012;40:502–9.
7. Bieber S, et al. Left and right ventricular dysfunction in patients with COVID-19-associated myocardial injury. Infection. 2021;49:491–500.
8. Spiro JE, et al. Secondary tension pneumothorax in a COVID-19 pneumonia patient: a case report. Infection. 2020;48:941–4.
9. Weber S, et al. Severe liver failure during SARS-CoV-2 infection. Gut. 2020;69:1365–7. 10. Tan BK, et al. Arterial and venous thromboembolism in COVID.
10. Tan BK, et al. Arterial and venous thromboembolism in COVID19: a study-level meta-analysis. Thorax. 2021. https://doi.org/10. 1136/thoraxjnl-2020-215383.
11. Huang C, et al. 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study. Lancet. 2021;397:220–32.
12. Quanjer PH, et al. Lung volumes and forced ventilatory flows. Report Working Party Standardization of Lung Function Tests, European Community for Steel and Coal. Official Statement of the European Respiratory Society. Eur Respir J. 1993;6:5–40.
13. Quanjer PH, et al. Multi-ethnic reference values for spirometry for the 3–95-yr age range: the global lung function 2012 equations. Eur Respir J. 2012;40:1324–43.
14. Huang Y, et al. Impact of coronavirus disease 2019 on pulmonary function in early convalescence phase. Respir Res. 2020;21:163
15. Munker D, et al. Dynamics of SARS-CoV-2 shedding in the respiratory depends on the severity of disease in COVID-19 patients. Eur Respir J. 2021. https://doi.org/10. 1183/13993003. 02724-2020.
16. Huang Y, et al. Impact of coronavirus disease 2019 on pulmonary function in early convalescence phase. Respir Res. 2020;21:163.
17. You J, et al. Anormal pulmonary function and residual CT abnormalities in rehabilitating COVID-19 patients after discharge. J Infect. 2020;81:e150–2.
18. Zou H, Li SQ. Pulmonary fbrosis in critically ill patients with novel coronavirus pneumonia during the convalescent stage and a proposal for early intervention. Acta Pharmacol Sin. 2020. https:// doi.org/10.1038/s41401-020-00566-4.