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SUPPINI NOEMI

PhD THESIS

INTEGRATED PULMONARY FUNCTIONAL ASSESSMENT OF POST COVID19 PATIENTS

– A B S T R A C T –

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ABSTRACT

INTRODUCTION

In march of 2020, the World Health Organisation declared COVID-19 a global pandemic, marking a new era in global politics. Due to the possible clinical effects of this virus, including severe acute respiratory syndrome, high infection and fatality rates, many studies have been conducted. A lot of information was quickly acquired on the virus in 2020, including its transmission patterns and the efficacy of other therapies and procedures. After three years of the pandemic and over 700 million cases of SARS-CoV-2 infection, with a significant proportion of survivors, a new question arises: how and when should these patients be followed up?

A significant proportion of patients have had the resolution of the main illness, but have subsequently experienced an extended period of morbidity following the infection, marked by the persistence of symptoms for a duration of several months. One area of increased importance concerns the long-lasting lung damage caused by COVID-19.

Early SARS-CoV-2 variants were shown to be involved in the development lung fibrositic lesions and pulmonary hypertension. In this context the assessment of pulmonary function is crucial and it usually involves tests including spirometry, diffusion test, and lung volumes. Current clinical guidelines recommend pulmonary function testing for severe pneumonia patients after discharge.

The need to study this specific group of patients and their functional results led to the selection of this study theme, which focuses on integrated pulmonary functional assessment of post COVID-19 patients. The significance of forced oscillometry within this context should also be assessed. Thus, this study seeks to offer new insights on pulmonary function assessment in COVID-19 survivors. Implementing a variety of tests and analyzing imaging properties will improve evaluation and diagnosis.

The scientific objectives this doctoral research aims to address are firstly, to conduct a critical examination of data obtained from specialized literature on the post-covid condition, focusing specifically on sequelae on the respiratory system. Presentation of a comprehensive analysis of the clinical applications of oscillometry in the setting of respiratory disease among adult patients. Evaluation of the feasibility and efficacy of integrating spirometric measures, plethysmography, forced oscillometry, and CT scans for the assessment of lung function and composition after SARS-CoV-2 infection. Additionally, to explore potential correlations between these data. Determining whether forced oscillometry may improve the standard evaluation of lung function following infection by identifying subtler changes that may be overlooked when depending exclusively on spirometry and body

plethysmography. Evalution of the pulmonary function of individuals who have successfully recuperated from COVID-19, one year after their recovery. Additionally, to investigate any potential association between the severity of the first COVID-19 episode and subsequent changes in pulmonary function over time.

This thesis is composed of two sections: the general section and the specialized section. In the introductory section, a comprehensive overview was provided on the fundamental aspects of Covid-19, encompassing its etiopathogenesis, clinical presentations, diagnostic approaches, treatment modalities, and associated consequences. Particular attention was directed towards the long-term effects of Covid-19, with a specific focus on its pulmonary manifestations, and the methods employed in investigating this illness.

GENERAL PART
INTROSPECTION ON RECENT DATA FROM THE LITERATURE

The COVID-19 pandemic has monopolized the public agenda and paralyzed global trade, mobility, information, and culture. The global COVID-19 pandemic has motivated scientists and public health officials to quickly improve our understanding of this disease. This collaboration has led to new disease management, control methods and new strategies.

Based on a conservative estimation, the current global population of individuals enduring prolonged manifestations of COVID-19 is estimated to be no less than 65 million.

The phenomenon is distinguished by the presence of multiple complications, among these are cardiovascular, thrombotic, and cerebrovascular diseases. Furthermore, it is worth noting that type 2 diabetes, myalgic encephalomyelitis/chronic fatigue syndrome, and dysautonomia, including postural orthostatic tachycardia syndrome, are also frequently observed in individuals with Long COVID.

Respiratory manifestations represent a notable cluster of symptoms that have been identified after a comprehensive analysis of existing studies on the enduring consequences of COVID-19. The increasing prevalence of thromboembolic disease and fibrotic lung lesions in persons who have recovered from COVID-19 is being acknowledged. These aforementioned diseases possess the capacity to lead to the persistent symptom of breathlessness. Presently, there exists a dearth of considerable data pertaining to the increased prevalence of supplementary chronic respiratory conditions following acute COVID-19 infection.

Literature findings indicated persistent decreases in lung function, as evaluated by pulmonary function testing, specifically in regards to diffusion capacity for carbon monoxide (DLco), throughout a period of up to two years subsequent to infection. The latest studies on SARS-CoV-2 have provided insights into the presence of pulmonary function abnormalities that manifest during the early stages of recuperation subsequent to COVID-19 infection.

The incorporation of easily accessible diagnostic technologies, such as spirometry, absolute lung volume measurement, and gas transfer assessment, has made a substantial impact on the improvement of clinical care and understanding of respiratory conditions. However, the determination of these characteristics requires significant patient participation and the ability to perform at maximum respiratory effort.

Oscillometry is a supplementary technique employed for evaluating the mechanical properties of the respiratory system, enhancing our understanding and management of pulmonary conditions. Impulse oscillometry has promise in the assessment of pulmonary sequelae in individuals who have recuperated from COVID-19, owing to its capacity to detect changes in the peripheral airways and its relatively safe nature within the context of the COVID-19 pandemic. The technique presents many benefits compared to conventional spirometry in terms of practicality, especially in specific populations such children, the elderly, and persons with restricted muscle capacity or cognitive impairments. Moreover, oscillometry has been shown to provide enhanced sensitivity in the detection of small airway illness and lung fibrosis. This approach is distinguished by its passive nature, since it necessitates minimal perceived exertion on the part of the individual undergoing the process. An additional advantage lies in the diminished generation of aerosols, rendering it appropriate for utilization amongst ongoing viral illnesses. Medical professionals have continually endeavored to find an alternative method for assessing lung function in difficult situations. The incorporation of oscillometry in conjunction with spirometry has the potential to yield supplementary advantages in the adult population.

SPECIAL PART

The research component of this thesis consists of three sections. Firstly, a comprehensive literature review is conducted to examine the role of oscillometry in the assessment of lung function. Secondly, the application of oscillometry in the assessment of lung function in post-COVID patients is explored. Lastly, the thesis investigates the assessment of lung function in post-COVID patients at two specific time points: 40 days after infection and one year after infection.

1. LUNG FUNCTION ASSESSMENT BY IMPULSE OSCILLOMETRY IN ADULTS

The forced oscillation technique (FOT) is commonly used in regular lung function testing to study respiratory mechanics, as it requires minimum patient involvement. The tidal breathing test provides information on the respiratory system's elastic properties and ventilation uniformity. The maneuver involves measuring respiratory tract flow-response

using external pressure signals, typically from a loudspeaker. The maneuver is based on the utilization of external pressure signals, often produced by a loudspeaker, in order to assess the flow-response of the respiratory tract. The investigation focuses on the examination of pressure and its corresponding flow, with particular attention given to the analysis of oscillatory mechanical parameters such as resistance and reactance.

Figure 10 illustrates the primary domains in which impulse oscillography is applied in diagnostic and/or therapeutic settings.

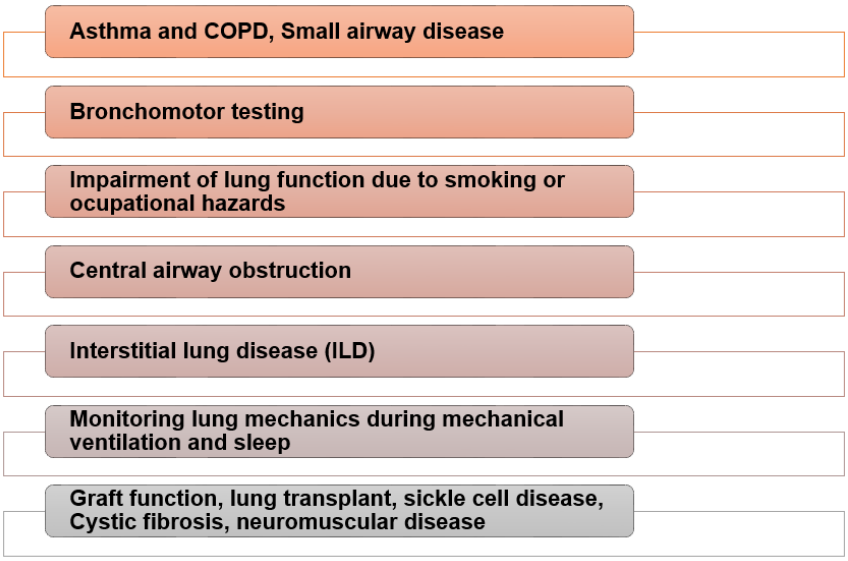

Figure 10. Clinical application areas of oscillometry

Oscillometry is used to assess bronchodilator response and it has been found to be more sensitive than spirometry for diagnosing and monitoring asthma in children. King et al. recommend defining a favorable response to bronchodilators (BD) as a 40% reduction in respiratory system resistance (Rrs5), a 50% increase in reactance (Xrs5), and an 80% decrease in area of reactance (AX).

Salbutamol-induced impedance changes in healthy and COPD patients were studied resulting that oscillometric parameters are sensitive to bronchodilation, especially in early stages of COPD. Moreover, the Forced Oscillation Technique can be as useful as spirometry in assessing COPD treatment efficacy. Many academic publications have examined the efficacy of long-acting beta agonists and corticosteroids in asthmatic airway responsiveness management.

In oscillometry studies, asthma is the most common pulmonary disease. Asthmatics' airway resistance, especially in smaller airways, increases during exacerbation. Typically, Rrs5 and Fres are elevated, while R20 is within the average range. Additionally, Xrs5 has a larger negative deviation. Between exacerbations, all parameters can be normal in young people. Oscillometry helps assess asthma management. Increases in Rrs5-Rrs20 and AX

may indicate poor disease control. In a comprehensive literature review, the relationship between small airway disease and asthma control was examenied. The authors found that oscillometry and other non-invasive approaches can diagnose small airway disease. They also claimed that diagnosing SAD may improve therapy. Oscillometry can also detect small airway disfunction before symptoms and spirometry changes. Implementing prompt therapy can prevent symptom onset. Oscillometry can also identify asthma medication response by evaluating reactance area changes. COPD patients showed a larger increase in Rrs5, leading in an elevation of the Rrs5-Rrs20 parameter.

Additionally, the severity of chronic obstructive pulmonary disease (COPD) as characterized by GOLD cryteria is strongly correlated with the amount of changes in Fres, Rrs5, Rrs20, Xrs5, and AX. Oscillometry is widely used to diagnose obstructive diseases, but its ability to detect disease development is limited, requiring further study.

In both obstructive and restrictive diseases, minor airway inflammation, changing elastic recoil pressure, and decreased lung volume can alter reactance and resistance. Both obstructive and restrictive lung illnesses have high Rrs5, Fres, AX, and a negative Xrs5. This may explain why oscillometry is better at diagnosing obstructive diseases.The only difference between both situations is Rrs20, which is normal for interstitial lung disease (ILD) but increases for obstructive diseases. It has been demonstrated that oscillometry can assess small airways disease in interstitial lung disease patients.

Additional diseases that were examined encompassed lung function impairment resulting from exposure to occupational hazards or smoking, central airways obstruction, cystic fibrosis, monitoring of lung mechanics during mechanical ventilation and sleep, neuromuscular diseases, lung transplant, and graft function.

Further research is necessary to examine quality control approaches for metrics that encompass a wide range of age groups and various pulmonary illnesses and clinical domains, such as critical care and population screening. The utilization of oscillometry in geriatric and pediatric healthcare facilities carries considerable importance in the identification and surveillance of illnesses, as well as in facilitating adjustments to therapeutic interventions. Additional inquiry is necessary within the domain of interstitial lung diseases, specifically pertaining to oscillometry, due to the urgent want for extensive scholarly exploration. The primary reason for considering the use of a radiation-free assessment technique in disease progression monitoring is the possible benefits it offers.

Regarding future directions, oscillometry exhibits promise as a diagnostic method with great sensitivity for the early identification of fibrosis, even before spirometric abnormalities become evident. Furthermore, given the advent of new fields of study, it is anticipated that the utilization of this methodology will continue to expand in academic research.

The potential for enhancing the acceptance and utility of oscillometry in everyday clinical practice lies in the development of more user-friendly and portable equipment, as well as the better understanding of interpreting oscillometry values.

In conclusion, oscillometry is a suitable method for individuals of many age groups, including youngsters and the elderly, as it does not require active patient cooperation due to its reliance on tidal breathing. Furthermore, it demonstrates itself as a feasible option for persons who are incapable of undergoing spirometry. The application of oscillometry holds significance in the surveillance of temporal fluctuations in chronic illnesses and the assessment of broncho-motor reactions in airway function. There is a noticeable increase in worldwide attention towards impulse oscillometry, as it is being increasingly applied in the fields of physiology and other clinical illnesses

2. POST-INFECTION OSCILLOMETRY AND PULMONARY METRICS IN SARS-COV-2 PATIENTS

The SARS-CoV-2 virus has resulted in notable effects on pulmonary function during the COVID-19 pandemic.

Data from this section of the thesis were published this year in an article entitled " Post-Infection Oscillometry and Pulmonary Metrics in SARS-CoV-2 Patients: A 40-Day Follow-Up Study". This is the first article about the use of forced oscillometry, as a tool for evaluating lung function in in post-covid patients Romania.

Therefore, the main aim of this study was to comprehensively evaluate the pulmonary function and structure in individuals who have recently acquired acute SARS-CoV-2 infection, specifically at the 40-day milestone subsequent to the initial infection.

The rationale for choosing this particular time period was predicated on its relevance in recording the early phases of recuperation and the potential consequences linked to the illness. By centering the analysis on this specific timeframe, it facilitates an exploration of immediate physiological responses without delving into the complexities associated with enduring post-infective syndromes, such as the condition commonly referred to as protracted COVID.

The primary objectives of this study were to evaluate the feasibility and efficacy of integrating spirometric parameters, plethysmography, forced oscillometry, and CT scans for the assessment of lung function and composition in individuals who have contracted SARS-CoV-2. Additionally, the study aimed to explore potential correlations between these parameters. Furthermore, the aim of this study was to determine whether forced oscillometry may improve the standard evaluation of lung function following infection by identifying more

subtle changes that may be overlooked when depending exclusively on spirometry and body plethysmography.

This study was conducted at the Pneumology Clinic of the Victor Babeș Hospital of Pneumophtisiology and Infectious Disease Timisoara, between 2021 and 2022. 66 patients, diagnosed with SARS-CoV-2 infection who agreed to participate in this study and were able to perform spirometry,body-pletismography and oscillometry were enrolled.

The design of this study is observational and allowed the analysis of patient data obtained during their periodical investigations.

The severity of SARS-CoV-2 infection was assessed according to World Health Organization (WHO) guidelines and the period of testing postinfection was recorded. Demographic data collected included personal numeric code (unique identifying number), age, sex, height, weight, and location of residence (either urban or rural). We took into consideration comorbidities and smoking status of the participants. Lung function was evaluated through multiple modalities. Spirometry was employed to measure Forced Vital Capacity (FVC), Forced Expiratory Volume in one second (FEV1), and Forced Expiratory Flow at 25–75% (FEF25–75). Plethysmography tests were utilized to determine Total Lung Capacity (TLC), Residual Volume (RV), Specific Airway Resistance (sRAW), Airway Resistance (RAW), Airway Conductance (GAW), and the ratio and percentage of Residual Volume to Total Lung Capacity (RV/TLC and RV/TLC%). Several oscillometry parameters were collected, including Resonant Frequency (RF), Resistance at 4 Hz (R4), 6 Hz (R6), and 20 Hz (R20), and Reactance at 4 Hz (X4) and 6 Hz (X6). These tests were carried out using the Cosmed Quark PFT equipment, respecting the ATS/ERS quidelines. Additionally, computerized tomography (CT) scans were carried out to assess lung composition and pathology, using specific software. These analyses allowed for the determination of total lung capacity as well as the capacity of the right and left lungs separately. The scans helped identify the presence and volume of emphysema, normal lung tissue, ground-glass opacities, crazy-paving patterns, and lung consolidations. CT scans also facilitated the visualization and recording of calcifications and blood vessels.

Regarding the statistical analysis, continuous data were shown as means with SD, whereas categorical data are frequencies and percentages. Group differences were analyzed using Student's t-test or ANOVA for continuous data, and Mann-Whitney U-test or Kruskal-Wallis test for non-parametric data. When anticipated cell counts were below five, categorical data differences were assessed using the X_2 or Fisher's exact test. A cox regression model was used to analyze COVID-19 severity prognostic variables based on lung data. All statistical analyses were conducted using SPSS v.26 (IBM Corporation, Armonk, NY, USA).

Spirometric findings demonstrated a decline in forced vital capacity and forced expiratory flow between 25% and 75% of forced vital capacity as the severity of COVID-19 increased. In particular, it was observed that patients with severe forms demonstrated a statistically significant reduction in forced vital capacity (86.8 ± 25.5), in comparison to patients with mild forms (106.0±18.9, p=0.017). The FEF25–75 demonstrated a comparable pattern, wherein individuals with severe forms had an average value of 77.7 ±6.0 , while those with mild forms had an average value of 82.9 ± 5.6 (p = 0.017). These findings suggest a trend toward restrictive disfunction and possibly small airway disease.

Regarding body-pletismography, in relation to the severity of the disease, the data suggests a deteriorating pattern in Total Lung Capacity as indicated by the body-plethysmography parameters. Patients with mild forms of acute COVID-19 exhibited a mean total lung capacity value of 119.1 ± 29.0. In contrast, patients with moderate and severe forms of COVID-19 demonstrated lower TLC values of 109.4 ± 40.6 and 100.8 ± 44.6, respectively. The statistical analysis revealed that the observed differences in total lung capacity among the different severity groups did not reach statistical significance (p-value = 0.297). This suggests that TLC was comparable across all categories. The Residual Volume demonstrated a decreasing pattern as the severity rose, however, this disparity did not yield statistical significance (p = 0.465).

In addition, in oscillometric measurements it was observed that the resonant frequency showed an increase with the severity of the condition. Specifically, the group with severe forms demonstrated a statistically significant higher resonant frequency(17.4 ± 4.4) compared to the group with moderate forms ((15.6 ± 2.9; p = 0.042). In the instance of Resistance at 4 Hz, there was a notable reduction observed when comparing the moderate group (4.6 ± 2.1) to the severe group (3.5 ± 1.1). The results indicate that there was a notable difference in reactance at 4 Hz among the three groups. The mild group exhibited an average of -2.2 ± 1.4, the moderate group had a mean of -1.8 ± 1.1, and the severe group showed a mean of -2.8 ± 1.4, with a statistically significant difference between the moderate and severe groups. These oscillometry parameter changes are compatible with both restrictive and peripheral airway obstructive modifications.

Upon further examination of the existing literature regarding post-infection oscillometry and pulmonary metrics in individuals affected by SARS-CoV-2, a number of studies indicate the possibility of oscillometry serving as a more discerning indicator of lung function impairment in comparison to conventional spirometry. In recent research it was found that oscillometry can be clinically valuable in detecting persisting lung function problems among patients with mild to moderate COVID-19 disease, even when their spirometric values appear normal

The CT scans revealed a correlation between disease severity and an increase specially in ground-glass opacities.

When assessing the correlation between the CT findings and other methodologies, it was observed that spirometry, body plethysmography, and oscillometry exhibited similar levels of accuracy in detecting ventilatory dysfunction and post-COVID-19 fibro-reticular modifications.

The results of the multiple regression analysis indicated a significant relationship between COVID-19 severity and three variables: Reactance at 4 Hz, Forced Expiratory Flow 25–75%, and Resonant Frequency. The study found that for every unit increase in these parameters, there was an estimated increase in the probability of the occurrence by a factor of 3.16, 2.09, and 1.90, respectively. In contrast, it was shown that the resistance at a frequency of 4 Hz and airway resistance exhibited a notable reduction in the occurrence of hazards, thereby underscoring their potential as protective factors.

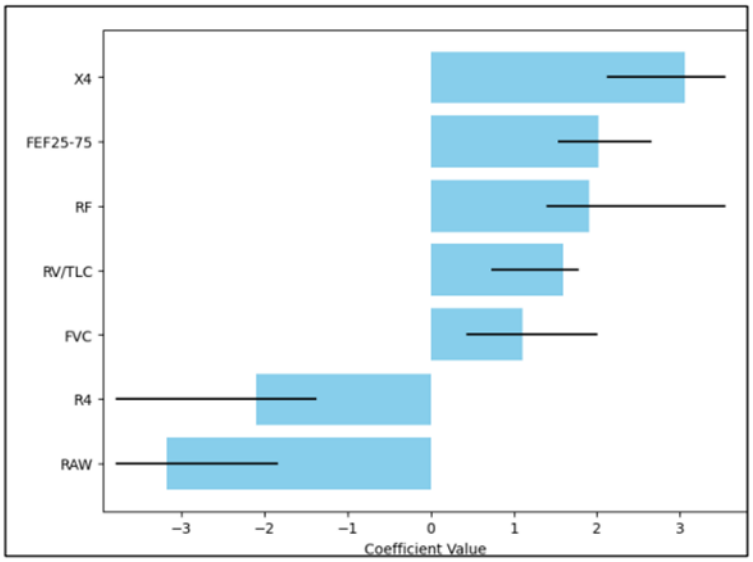

Figure 14. Multivariate regression

The utilization of non-invasive and readily available approaches presents an opportunity to gain useful insights into the respiratory well-being of individuals in the process of recuperating from SARSCoV-2 infection. These techniques serve as viable alternatives to the use of CT scans for regular assessments. Additional research is necessary to enhance the integration of these approaches and examine their long-term association with clinical results.

In brief, this study undertook a comprehensive evaluation of respiratory function and morphology in patients who were diagnosed with acute SARS-CoV-2 infection, with particular emphasis on the 40-day duration subsequent to infection.

The study's findings revealed significant reductions in Forced Vital Capacity and Forced Expiratory Flow 25-75% with increasing illness severity. The data reveals a downward trajectory in overall lung capacity, while the absence of statistical significance prevents making conclusive assertions.

The oscillometry tests demonstrated a significant increase in Resonant Frequency and a reduction in negative reactance (X4) in cases of severe COVID-19 forms. The results derived from computed CT demonstrated a higher prevalence of ground-glass opacities among patients with severe COVID-19 forms.

The findings derived from the regression analysis revealed statistically significant correlations between the variables X4, FEF25–75, and Fres. Nevertheless, the results of this research provide a significant contribution to the understanding of pulmonary function following SARS-CoV-2 infection and give vital insights for further investigation and therapeutic approaches.

3. LONGITUDINAL ANALYSIS OF PULMONARY FUNCTION IMPAIRMENT ONE YEAR POST-COVID-19

The need for bigger cohort studies is underscored by the variety shown in the available data, in order to gain a more comprehensive understanding of the characteristics and outcomes of COVID-19.

Hence, the objective of this investigation was to assess the pulmonary function among a group of individuals who have survived COVID-19, one year following their recovery, and examine the potential correlation between the severity of the acute COVID-19 episode and pre-existing lung conditions. Data from this section of the thesis were published this year in an article entitled “Longitudinal Analysis of Pulmonary Function Impairment One Year Post-COVID-19: A Single-Center Study”. This is the first article evaluating lung function in post-covid patients Romania, over one year.

The study was conducted at the Pneumology Clinic of the Victor Babeș Hospital of Pneumophtisiology and Infectious Disease Timisoara, between 2021 and 2022. This single-center observational study aims to longitudinally evaluate pulmonary function in 140 COVID-19 survivors one year after recovery, assessing associations with disease severity and pre-existing lung conditions. Participants aged 18 and older, with confirmed SARS-CoV-2 infection, were evaluated using spirometry and Diffusion Capacity of Lungs for Carbon Monoxide (DLCO) tests. Pulmonary function parameters like Forced Expiratory Volume at 1 s (FEV1), Forced Vital Capacity (FVC), and Total Lung Capacity (TLC) were measured. Participants were stratified by age, gender, body mass index, smoking status, and lung damage severity via computed tomography (CT).

In order to aid clinical interpretation, the obtained PFT data underwent normalization to population averages and it is presented as percentages of predicted values. For normally distributed continuous data, the mean and standard deviation (SD) were reported.

In result, the cohort consisted of mostly males (58.6%), with a mean age of 53.8 years and body mass index of 24.9 kg/m2. Post-COVID fibro-reticular modifications were seen in 22.7%, 27.3%, and 51.9% of mild, moderate, and severe disease patients, respectively. This association between disease severity and the development of fibro-reticular changes post-recovery was found to be statistically significant ($p=0.003$), indicating a strong correlation.

Regarding pulmonary function testing at 40 days post viral clearance it was found that the Forced Vital Capacity (FVC) exhibited notable variations among the groups ($p<0.001$). The mean values declined progressively from 97.8±9.6 in the mild group to 89.9±15.0 in the moderate group, and further to 84.9±17.7 in the severe group. These findings indicate that there is an association between illness severity and a decrease in FVC. Despite observing a drop in the Forced Expiratory Volume in 1 second (FEV1) as the severity of the condition increased, it is important to note that this decrease did not reach statistical significance ($p=0.074$). In a similar vein, it was seen that the Forced Expiratory Flow 25%-75% and the Diffusing Capacity of the Lungs for Carbon Monoxide (DLCO) exhibited a tendency towards decreased values as the severity of the disease increased. However, it is important to note that these alterations did not reach statistical significance, with p-values of 0.059 and 0.052, respectively. It is worth noting that there was an observed increase in the ratio of forced expiratory volume in one second (FEV1) to forced vital capacity (FVC) as the severity of the disease rose ($p=0.033$). This finding suggests that there may be a somewhat greater preservation of FEV1 compared to the loss in FVC. The study findings revealed notable decreases in Total Lung Capacity (TLC) and Residual Volume (RV) as disease severity increased ($p=0.023$ and $p=0.003$, respectively). These results suggest that individuals with severe COVID-19 may experience enduring reductions in these specific measures of lung function, consistent with a growing tendency to restriction.

A one-year follow-up indicated a non-significant change in FVC, FEV1, FEV1/FVC ratio, FEF25-75, and RV compared with the 40-day measurement, but it revealed significant improvements in DLCO and TLC ($p = 0.010$). There were significant mean increases in FVC, FEV1, DLCO, TLC, and RV across all disease severities over one year.

Imptovements were most pronounced in the patients with a history of severe COVID-19, who had a better recovery over one year, compared with the mild and moderate COVID-19 patients whose lung function almost normalized. One year after the SARSCoV- 2 infection, we observed a significant association between disease severity and post-COVID

fibrotic changes. Though some lung function parameters remained stable over the year, significant improvements were noted in DLCO and TLC.

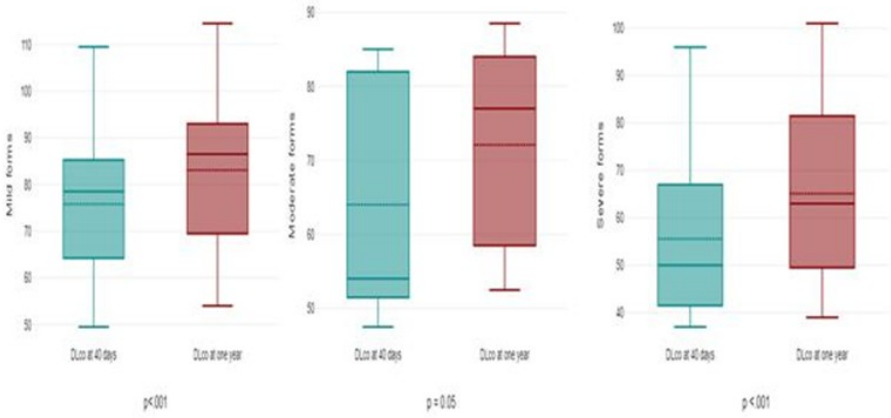

Figure 17. Evolution of DLCO in one year after acute COVID-19 disease by disease severity

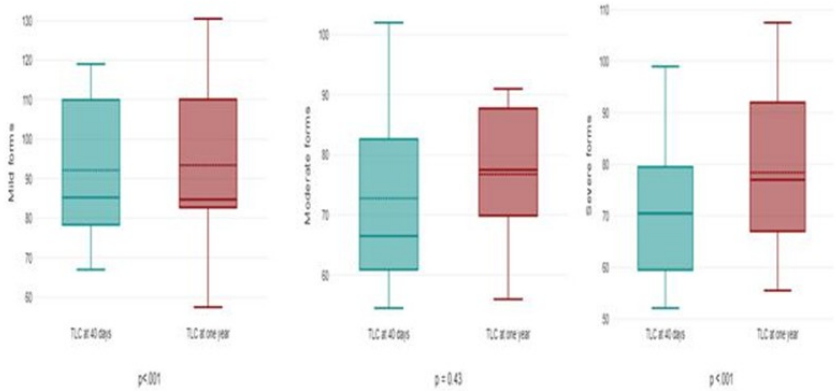

Figure 18. Evolution of TLC in one year after acute COVID-19 disease by disease severity

In conclusion, results suggest significant improvements in many lung function indices, particularly in patients who had severe indications of COVID-19, when evaluating pulmonary function impairment one year post-infection.

Despite the absence of substantial alterations in forced vital capacity and forced expiratory volume in one second over the duration of the year, a discernible decline was noted, particularly among patients with severe cases. Concurrently, a significant increase in the FEV1/FVC ratio was seen in severe cases, suggesting a comparatively conserved FEV1 in relation to the decline in FVC. This implies that the initial illness severity upon infection has an impact on the subsequent recovery of lung function. Despite the absence of statistical significance, the observation of post-COVID fibrotic lesions was evident in individuals with varying degrees of disease severity, suggesting the possibility of long-lasting

changes in lung structure after infection. Notably, there were detected statistically significant increases in the diffusing capacity of the lungs for carbon monoxide and total lung capacity over a period of one year.

The results of this study indicate a significant degree of resilience and adaptation in pulmonary function. Moreover, it underscores the significance of continuous monitoring and medical care for the respiratory health of those impacted by COVID-19, particularly those experiencing severe manifestations. Furthermore, it provides insight into the complex and enduring effects of COVID-19 on pulmonary function, hence underscoring the need for further longitudinal research to get a thorough comprehension of the long-term ramifications of COVID-19.

PERSONAL CONTRIBUTION

The scientific research objectives have been achieved, as the assessment of the feasibility and efficacy of spirometric measurements, plethysmography, forced oscillometry, and CT scans in evaluating lung function and composition after SARS-CoV-2 infection has been accomplished.

Regarding the individual contributions, they were executed in a progressive manner, delineated as follows:

This thesis begins with an extensive examination of the consequences of COVID-19, with a special emphasis on its influence on the respiratory system. It aims to examine various approaches for measuring and assessing these effects.

The current study conducted a comprehensive investigation of the therapeutic effectiveness of oscillometry in the setting of respiratory illness among adult adults. Furthermore, a comprehensive investigation was undertaken to ascertain prospective implementations of this methodology in individuals recovering from the COVID-19 pandemic. I have formulated and elaborated upon an innovative methodology for integrating oscillometry into the extensive array of pulmonary function assessments for persons in the process of recuperating from COVID-19. I have conducted an investigation on the potential feasibility and efficacy of utilizing spirometric measures, plethysmography, forced oscillometry, and CT scans as diagnostic modalities for assessing pulmonary function and composition subsequent to SARS-CoV-2 infection. Moreover, a comprehensive analysis has been undertaken to explore potential corelations between the aforementioned data, revealing noteworthy connections between the severity of COVID-19 infection and functional impairment. Additionally, I have identified associations between spirometric attributes, particularly FEF25-75 (a valuable marker for small airway disease), and oscillometric parameters.

I have performed an evaluation of pulmonary function in individuals who have achieved full recovery from COVID-19, examining the differences in lung function between one year after recovery and 40 days following the acute phase of the illness. The findings of this assessment demonstrate noteworthy improvements in pulmonary function, particularly in the parameters of DLco, TLC, and RV. This study underscores the significance of continuous monitoring and medical care for the respiratory health of those impacted by COVID-19, particularly those experiencing severe manifestations. Moreover, this study provides insight into the complex and enduring effects of COVID-19 on pulmonary function, hence underscoring the need for further longitudinal research to get a thorough knowledge of the long-term implications of COVID-19.

The aforementioned findings provide a significant addition to the understanding of pulmonary function following SARS-CoV-2 infection and give vital insights for further research and treatment approaches.