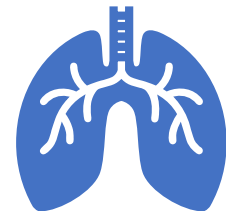


# Pulmonary Function Testing and COVID-19- Long Term Implications

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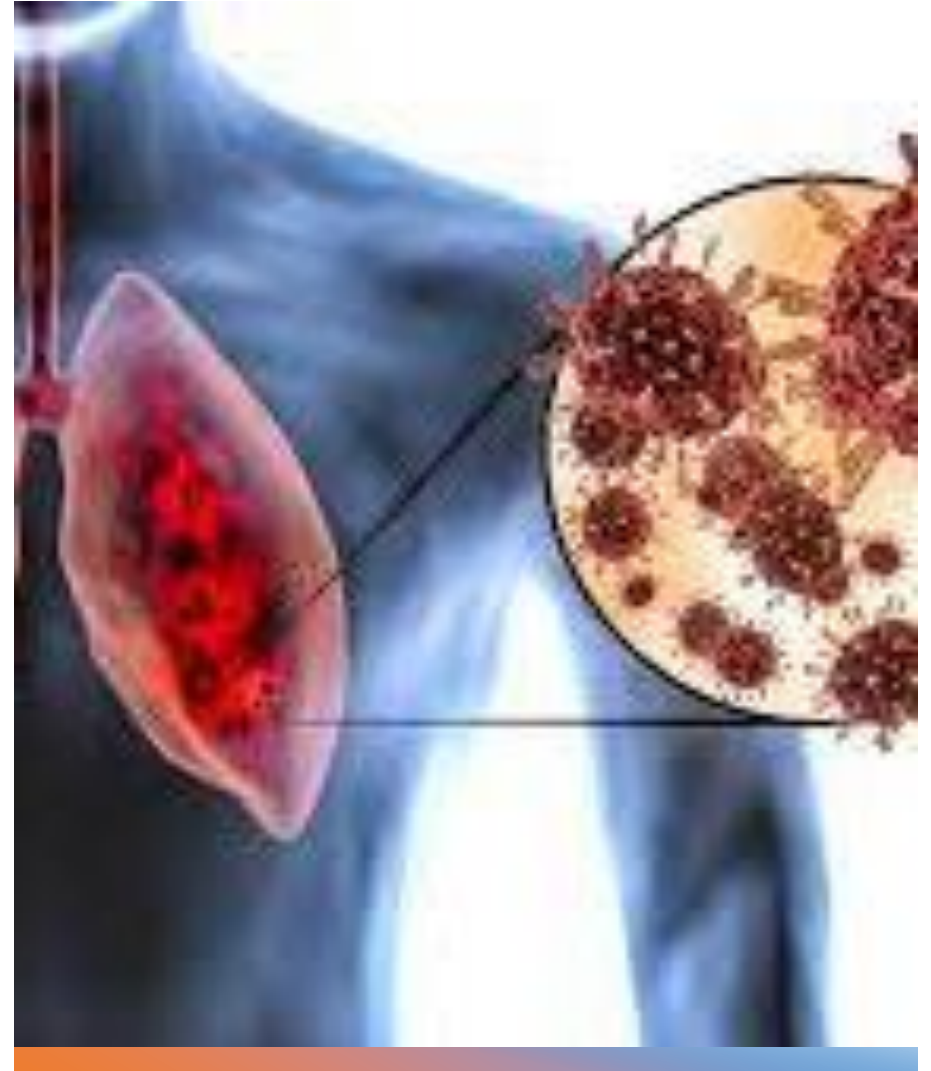
# Objectives

- Background of COVID-19
- Pulmonary function testing
- DLCO
- Ramifications of Post COVID PFT's
- Long term consequences of COVID-19
- Long term improvement of PFT's



# Background

- The COVID-19 pandemic created significant problems regarding the morbidity and mortality of patients and represents a global challenge to healthcare systems
- Patients who recovered from COVID-19 may have potential long term pulmonary impairment in lung function
- Common findings include dyspnea, fatigue, exercise fatigue
- Pulmonary function testing has proven to be quite beneficial the management of these patients

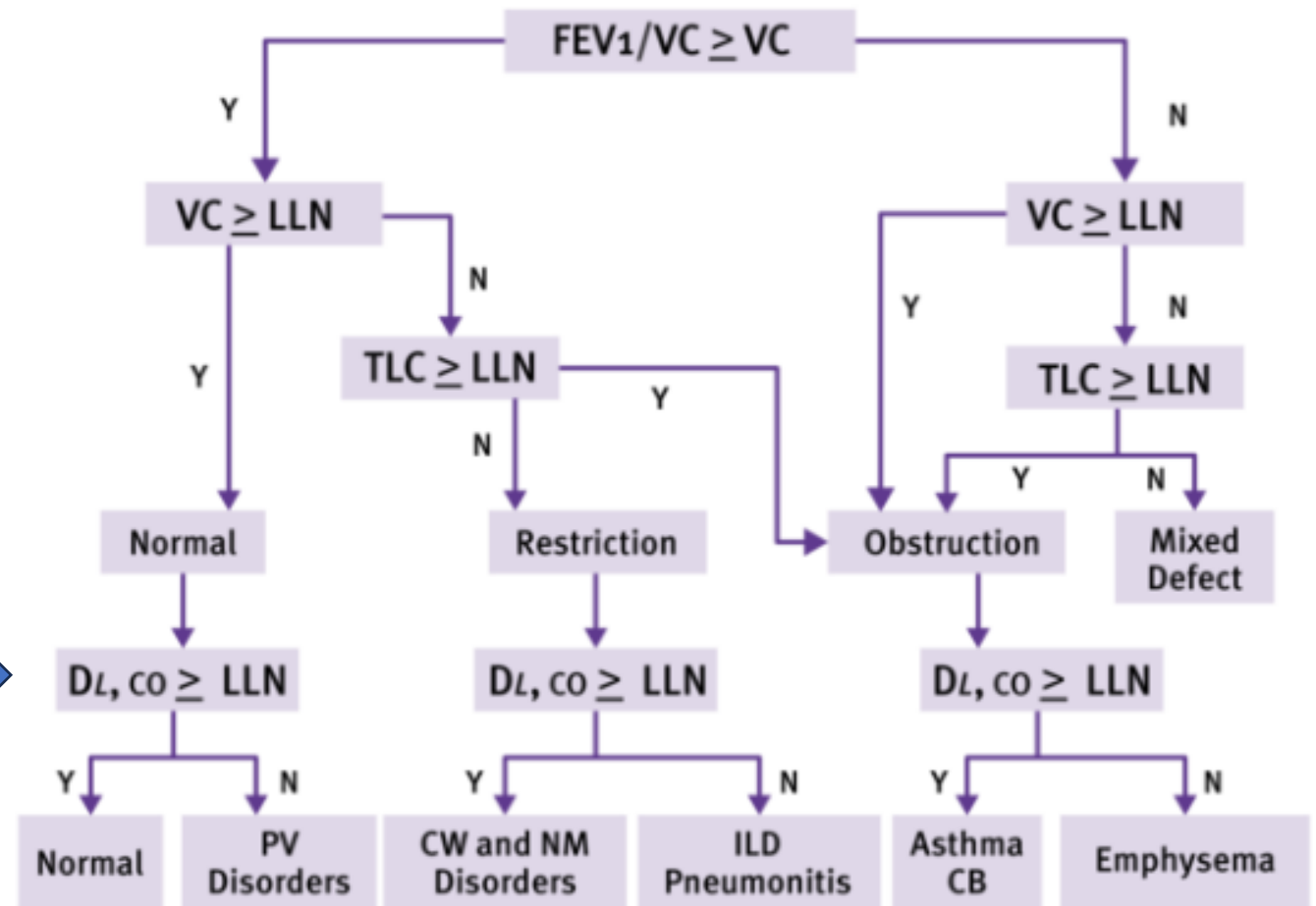


# What is DLCO?

- Lung Diffusion Testing (DLCO)
- It is a pulmonary function test that determines how oxygen diffuses from the lungs into the blood When we take a breath
- It is done in the pulmonary function laboratory
- Small amounts of carbon monoxide are inhaled with a breath hold of 10 seconds and then you exhale
- The amount of gas carbon monoxide with a known value when you inhale is then measured after you exhaled, and it is determined how much CO is absorbed
- Normal DLCO: Between 75% and 140% of the predicted value
- Mildly reduced DLCO: 60% to 75% or the lower limit of normal (LLN) predicted value
- Severely reduced DLCO: Less than 40% of the predicted value

# DLCO

- DLCO is a measurement that helps to determine the lung's ability to transfer gas from inspired air through the bloodstream.
- It measures the uptake of carbon monoxide (CO) after holding breath for 10 seconds



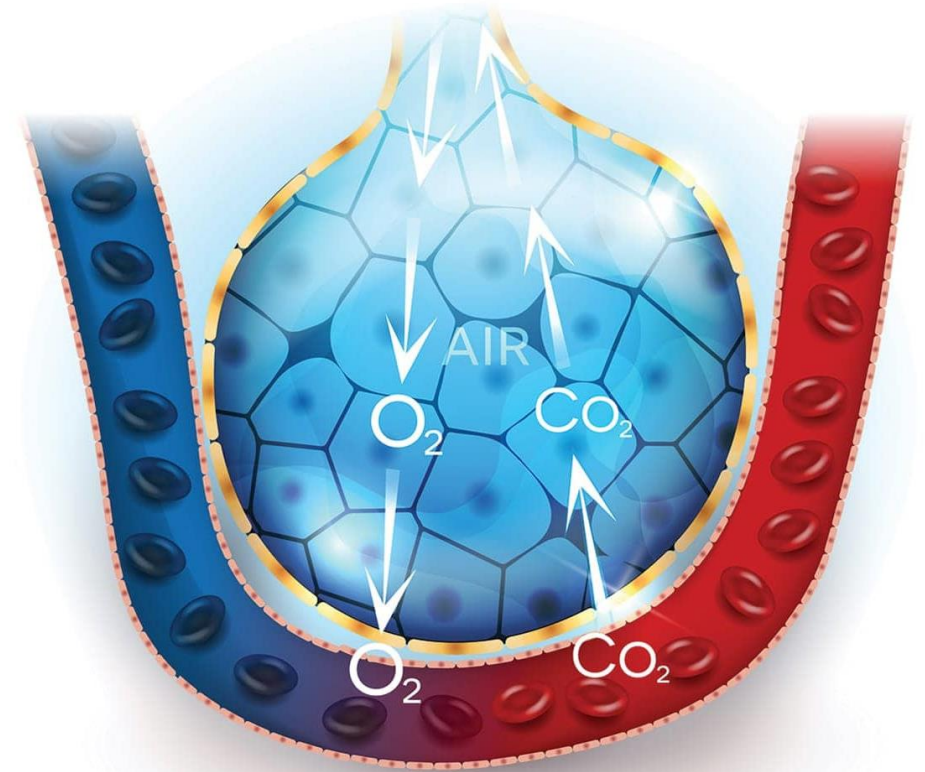
ATS ERS Interpretation Decision Tree

# Impact of COVID-19 on Pulmonary Function

- Around 120 million people worldwide have been affected by the SARS-CoV-2 virus
- Pulmonary function data remains scarce due to the temporary closure of pulmonary function laboratories during the early phases of the pandemic
- One of the first studies describing pulmonary function tests with COVID-19 patients was published in 2020 by Mo et al.



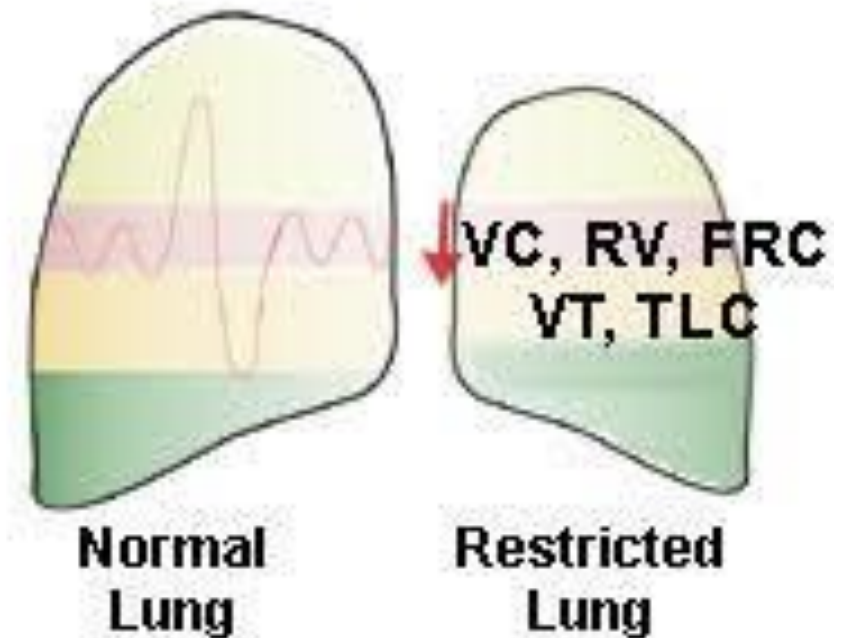
- Mo X, Jian W, Su Z, Chen M, Peng H, Peng P et al.: Abnormal pulmonary function in COVID-19 patients at time of hospital discharge. Eur Respir J 2020, 55
- Study:
  - 110 patients
  - 49Y/O =/- 14
  - 50% women
  - Previously healthy individuals
    - mild (n = 24)
    - moderate (n = 67)
    - severe disease (n = 19)
    - three patients had pre-existing lung disease
- Findings:
  - In discharged survivors with COVID-19, impairment of diffusion capacity is the most common abnormality of lung function, followed by restrictive ventilatory defects such as reduction in total lung capacity and residual volumes
  - Typical PFT defect that might be expected in an individual with an interstitial-based process





- Frija-Masson J, Debray M-P, Gilbert M, Lescure F-X, Travert F, Borie R et al.: Functional characteristics of patients with SARS-CoV-2 pneumonia at 30 days post-infection. Eur Respir J 2020, 56
- Study:
  - 45 patients
  - 54 Y/O +/- 8
  - 44% women
  - Previously healthy individuals
    - mild (n = 12)
    - moderate (n = 17)
    - severe disease (n = 16)
    - three patients had pre-existing lung disease
- Findings:
  - In this cohort of patients, 81% had abnormal PFTs with the majority displaying a reduced TLC and reduced DLCO
  - Extensive injury to alveolar epithelial cells and endothelial cells
  - Chronic vascular and alveolar remodeling leading to lung fibrosis

## Restrictive Lung Disorders



# Take Home Points on Post COVID PFT's

- COVID was first described in November 2019 and therefore there are not many studies on pulmonary function testing because of closure of labs
- Observational studies have demonstrated that approximately 42% of patients demonstrated PFT impairment
- Approximately 27% of them show their restrictive pattern on spirometry and 11% showed reduced total lung capacity via body plethysmography
- Approximately 31% showed a reduction in DLCO



# Studies evaluating pulmonary function following SARS-CoV-2 infection ( $n = 30+$ participants)

Author (Date; Country)	Title	Methodology	Measurements	Main findings
Mo et al. (April 2020; China) [15*]	Abnormal pulmonary function in COVID-19 patients at time of hospital discharge	Prospective observational study measuring pulmonary function at discharge across the severity spectrum ( $n = 110$ )	Spirometry, diffusing capacity, static lung volumes	Spirometry was normal, reduced lung volume was more frequent in those with severe disease (47% having a TLC lower than 80% predicted). Reduced DLco was the most common pulmonary function finding (47% of all patients) and was increasingly more common in more severe symptoms (84% in severe disease)
Liu Kai et al. (April 2020; China) [16**]	Respiratory rehabilitation in elderly patients with COVID-19: A randomised controlled study	RCT with six weeks of pulmonary rehabilitation compared with controls ( $n = 72$ )	Spirometry, diffusing capacity, 6MWT, CT, SF-36	DLco was reduced in both groups before intervention. Pulmonary rehabilitation led to an improvement in DLco, spirometry and 6MWT compared to controls
Lv et al. (April 2020; China) [34]	Pulmonary function of patients with 2019 novel coronavirus induced pneumonia: A Retrospective Cohort Study	Retrospective analysis of pulmonary function data measured 14 days after discharge ( $n = 137$ )	Spirometry	Patients with severe disease had lower FVC and FEV <sub>1</sub> with preserved FEV <sub>1</sub> /FVC ratio suggesting a restrictive pattern
Daher et al. (October 2020; Germany) [12]	Follow up of patients with severe coronavirus disease 2019 (COVID-19): Pulmonary and extrapulmonary disease sequelae	Prospective observational study following patients with severe COVID-19 disease ( $n = 33$ )	Spirometry, diffusing capacity, body plethysmography, 6MWT, TTE, ABG, SGRQ	At follow-up, spirometry and static lung volumes were normal. Median DLco was 65% predicted (IQR 53-73). 45% of patients were below the LLN for 6MWT distance and 45%



# Some good news study by Fortini, Alberto et al.2022

- Study

One-year evolution of DLCO changes and respiratory symptoms in patients with post COVID-19 respiratory syndrome

- Purpose

During a follow-up program of patients admitted for COVID-19 at our non-ICU Unit, we found that 37% of them had decreased diffusing lung capacity for carbon monoxide (DLCO) 3–6 months after discharge. This prospective observational study aimed to evaluate the evolution of changes in DLCO and respiratory symptoms at the 1-year follow-up visit.

- Conclusion

These results suggest that DLCO and respiratory symptoms tend to normalize or improve 1 year after hospitalization for COVID-19 in most patients. However, there is also a non-negligible number of patients (about one-third) in whom respiratory changes persist and will need prolonged follow-up.



# Why is DLCO Reduced in Post COVID Patients?

- Evidence has supported that a deficit in DLCO is the primary pulmonary function defect and is relative to severity of the disease
- Typically, patients with COVID have ground glass opacities with their X-rays.
- Local dysregulations involving endothelial and epithelial injury can be seen with these patients as well as with various degrees of thromboembolism and endothelial dysfunction
- Also, abnormalities and cardiopulmonary circulatory physiology
- This could be the root cause of DLCO abnormalities



# Why does COVID19 lead to restrictive lung disorders?

- Decreased TLC with a preserved FEV1/FVC ratio (greater than 70%) is an indicator of restrictive lung disease found in post COVID19 patients.
- DLCO measurement will be decreased on patients with intrinsic pulmonary restriction caused by inflammation of the pulmonary parenchyma with deposition of collagen in the interstitium
- Ultimately leads to pulmonary fibrosis with restrictive disorder



# Long term consequences of COVID-19

- COVID-19 is relatively new as is being first described in November 2019
- Most prospective multicenter observational data demonstrated pulmonary function impairment
- Interstitial lung disease is a known long-term pulmonary sequelae of ARDS and reported in over 60% of severe acute COVID-19 ARDS survivors
- Pulmonary rehab may be beneficial to the select group of patients who are severely impacted
- More research needs to be done



# Findings of Post COVID19 Infection

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- Pulmonary function testing is very important for patients with post COVID infection
- The most common defect in PFT encountered following COVID19 infection is contained within the interstitial compartment rather than the airways so its not a obstructive disorder
- Radiographic findings of a disease in most cases causes a diffuse airspace/interstitial-based process
- This inflammatory process leads to impacted gas exchange we have the DLCO is markedly reduced
- Little impairment of the respiratory system seems to be related to muscle deconditioning
- Recovery normally takes place within the year to an almost normal function
- Long term consequences of post COVID infection will manifest itself in time





# Summary

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- Early findings from patients who had a severe post COVID-19 infection shows an impaired diffusing capacity and a restrictive pattern associated with interstitial changes
- This manifest itself in long term dyspnea complaints from patients
- In some cases, patients have developed pulmonary fibrosis which may benefit from an antifibrotic therapy, but new research is now be conducted
- Most cases resolve overtime but there are outliers who may benefit from long term pulmonary rehab



# References

- Fortini A, Rosso A, Cecchini P, Torrigiani A, Lo Forte A, Carrai P, Alessi C, Fabbrizzi F, Lovicu E, Sbaragli S, Faraone A. One-year evolution of DLCO changes and respiratory symptoms in patients with post COVID-19 respiratory syndrome. *Infection*. 2022 Apr;50(2):513-517. doi: 10.1007/s15010-022-01755-5. Epub 2022 Jan 21. PMID: 35061232; PMCID: PMC8777423.
- Frija-Masson J, Debray M-P, Gilbert M, Lescure F-X, Travert F, Borie R et al.: Functional characteristics of patients with SARS-CoV-2 pneumonia at 30 days post-infection. *Eur Respir J* 2020, 56
- Lissan S, Tesar T, Tisonova J, Lissanova M. Pharmacological approaches to pulmonary fibrosis following COVID-19. *Front Pharmacol*. 2023 Jun 15;14:1143158. doi: 10.3389/fphar.2023.1143158. PMID: 37397477; PMCID: PMC10308083.
- Mo X, Jian W, Su Z, Chen M, Peng H, Peng P et al.: Abnormal pulmonary function in COVID-19 patients at time of hospital discharge. *Eur Respir J* 2020, 55 Available from: <http://erj.ersjournals.com/lookup/doi/10.1183/13993003.01217-2020>
- Thomas, M., Price, O. J., & Hull, J. H. (2021). Pulmonary function and COVID-19. *Current opinion in physiology*, 21, 29-35.
- Wichman D, Sperhake JP, Lütgehetmann M, Steurer S, Edler C, Heinemann A, et al. Autopsy findings and venous thromboembolism in patients with COVID-19: a prospective cohort study. *Ann Intern Med*. 2020;173(4):268–77.
- Whiteson JH. Pulmonary Sequelae of Coronavirus Disease 2019. *Phys Med Rehabil Clin N Am*. 2023 Aug;34(3):573–584. doi: 10.1016/j.pmr.2023.04.005. Epub 2023 Apr 12. PMID: 37419533; PMCID: PMC10090325.