

## COVID-19 AND PULMONARY FIBROSIS: A LITERATURE REVIEW

---

***Antonio Lucas Gomes Fontenele***

University of Vassouras Medical Student  
(UV)

<http://lattes.cnpq.br/4258603490555000>

***Paulo Roberto Hernandez Júnior***

Medical Student at Vassouras University  
(UV) and Scientific Initiation Student  
at PIBIC - State University of Campinas  
(Unicamp)

<http://lattes.cnpq.br/7418862771895322>

***Patrick de Abreu Cunha Lopes***

Medical Student at the University of  
Vassouras (UV) and Scientific Initiation  
Student at PIBIC at the Foundation for  
Research Support of the State of Rio de  
Janeiro (FAPERJ)

<http://lattes.cnpq.br/9719714143799267>

***Juliana de Toledo Pierrri Ribeiro Sampaio***

Resident in Geriatrics at Hospital das  
Clínicas, Faculty of Medicine, University of  
São Paulo (HCFMUSP)

<http://lattes.cnpq.br/9403357997175959>

***Rossy Moreira Bastos Junior***

Doctoral Student at the Federal University of  
Rio de Janeiro (UFRJ)

<http://lattes.cnpq.br/0075913838823892>

***Paula Pitta de Resende Côrtes***

Professor of Medicine at the University of  
Vassouras (UV)

<http://lattes.cnpq.br/9207835681849532>

All content in this magazine is licensed under a Creative Commons Attribution License. Attribution-Non-Commercial-Non-Derivatives 4.0 International (CC BY-NC-ND 4.0).



**Abstract:** Pulmonary fibrosis as a possible consequence of a post-infectious condition caused by the SARS-CoV-2 virus in COVID-19 disease has been the subject of several studies. The analysis of imaging tests and their correlation suggestive of pulmonary fibrosis has been described in several of these studies. This article is a research with a qualitative approach and descriptive character through an integrative literature review. The databases used in this research were the Virtual Health Library (VHL), National Library of Medicine (PubMed) and Directory of Open Access Journals (DOAJ). The search for articles was performed using the descriptors: “Covid-19” and “Pulmonary Fibrosis”. Inclusion and exclusion criteria were: open access articles, clinical trial, journal article, articles published in Portuguese, Spanish, English, age group including elderly males over 45 years of age, clinical trials, randomized or non-randomized, articles originals, case-control studies, cohort studies and articles published in the period 2020 to 2021. The results of pulmonary findings in imaging exams are highly suggestive of pulmonary fibrosis, according to several researchers, however, there was still no final conclusion until the moment. There is a need, then, for more studies on the subject to prove it.

**Keywords:** Covid-19, Pulmonary Fibrosis.

## INTRODUCTION

The new SARS-CoV-2 coronavirus virus became known to cause numerous atypical respiratory disorders in the Hubei province of Wuhan, China, in December 2019. This virus has a genetic code made up of positive-sense, single-stranded RNA, surrounded by an extracellular membrane that contains a series of peak glycoproteins similar to a crown. This term “corona” translates, in Latin, into corona, relating its thorn coating that approached a structure in the shape of a crown, seen by

electron microscopy. Coronaviruses have caused disease in humans since the late 1960s. Seven strains of human coronaviruses have been identified, four of which stand out for their upper respiratory tract infection and mild symptoms. The other three stand out for causing serious diseases of the lower respiratory tract, such as: MERS-CoV (Middle East Respiratory Syndrome), SARS-CoV (Severe Acute Respiratory Syndrome) and SARS-CoV-2 (COVID-19) ( POLLARD, 2020).

Pulmonary fibrosis belongs to a group of chronic and fatal interstitial lung diseases that affect mainly elderly and middle-aged people. The most common histopathological features are fibrosis and changes in favor of honey in the subpleural and basement membranes, in addition to extracellular matrix (ECM) and collagen deposition around the fibrotic foci. Pulmonary fibrosis structurally modifies the lung with great damage that compromises pulmonary diffusion and ventilation, often with incompatibility for life. The most common type is idiopathic pulmonary fibrosis, whose average survival is only two to four years. Therefore, it is a serious disease that threatens human health. Diagnosis can be made through clinical history, high-resolution computed tomography (HRCT), clinical manifestations, bronchoscopy and lung biopsy, and pulmonary function tests (WU, 2020) (AESIF, 2021).

Several studies are being carried out, but still without conclusive results, regarding the proof of the capacity of SARS-CoV-2 to provoke massive inflammation, including a cytokine storm, a fibroblastic activation and increase of extracellular matrix components, extracellular matrix metalloproteinases (MMPs), in addition to tissue inhibitors of MMPs, which neutralize caused by inflammation, including proteases, in addition to other effector molecules (WIGÉN, 2020) (SHAH,

2021). There are still no solid conclusions about the existence of a relationship between Covid-19 and pulmonary fibrosis. Thus, this review aimed to analyze pulmonary fibrosis as a long-term side effect after post-Covid-19 conditions. Thus, evaluating the presence of pulmonary fibrosis caused by Covid-19 (LI; SHEN, 2021).

## **METHODOLOGY**

This is a bibliographical research with a qualitative approach and descriptive character through an integrative literature review. The databases used in this research were the Virtual Health Library (VHL), National Library of Medicine (PubMed) and Directory of Open Access Journals (DOAJ). The search for articles was performed using the descriptors: “Covid-19” and “Pulmonary Fibrosis” using, for this, the Boolean operator “and”. The descriptors used were mentioned only in the English language and can be found in the Health Sciences Descriptors (DeCs). This literature review was carried out through the following steps: establishing the theme; definition of eligibility parameters; definition of inclusion and exclusion criteria; verification of publications in databases; examination of the information found; analysis of the studies found and presentation of the results. Among the filters used in the research are the following: free access articles, clinical trial and journal article, in addition to articles published in Portuguese, Spanish, English and age group, including elderly males over 45 years of age. All clinical trials, randomized or non-randomized, original articles, case-control studies and cohort studies were also included. Inclusion and exclusion criteria were defined; articles published in the period 2020 to 2021 were used as inclusion criteria. The exclusion criteria defined are literature review articles, meta-analysis and abstracts. All articles that were in duplication when selected

by the inclusion criteria were excluded, they were excluded from this duplication. All other articles that were excluded were not in the context addressed, fleeing the objective of the theme about Covid-19 and Pulmonary Fibrosis.

## **RESULTS**

After the association of all descriptors in the search bases, 654 articles were found. We found 31 articles in the Virtual Health Library, 608 articles in the PubMed database and 15 articles in the DOAJ database. After applying the inclusion and exclusion criteria, seven articles from the VHL, 17 articles from the PubMed database and three articles from the DOAJ were selected. Of which, two articles were excluded for being duplicated between the PubMed and BVS platforms and one article was removed for being in duplication on the DOAJ and BVS platforms, totaling 25 articles for a complete analysis (ALARCÓN, 2021) (ZHAO, 2021).

The results of the studies were evaluated and selected and a comparative table was constructed, consisting of the number of individuals studied, year of publication, main pulmonary findings in laboratory and imaging tests, as shown in table 1 below (HU, 2020) (ZOU, 2021).

Of the 25 articles, all had some degree of fibrosis. The greater the severity of the disease caused by Covid-19, the greater the degree of fibrosis. The most common findings include: inflammatory infiltrate, hemorrhage, subpleural lines, consolidation, banding opacity, ground-glass opacity, and disseminated hyaline membrane. Less than 10% of cases presented with only pulmonary fibrosis. Between 80-90% of cases, pulmonary fibrosis was accompanied by other pulmonary findings (LI; SCHNEIDER, 2021) (ZHOU, 2020).

AUTHOR - YEAR - NUMBER - LUNG FINDINGS - AGE
Aesif S., et al10 2020 3 frosted glass opacities, solid. and fibrosis. 46-57
Alarcon J., et al11 2021 15 consolidation, fibrosis 43-88
Ball L., et al12 2021 10 frosted glass and fibrosis 60-77
Roquetallade., et al13 2021 287 inflammation and fibrosis 54-71
Ducloyer M., et al14 2020 1 fibrosis, consolidation 75
Fang Y., et al15 2020 12 consolidation, fibrosis 35-74
Francone M., et al16 2020 130 inf. Inflammatory, fibrosis 27-90
Froidure A., et al17 2021 134 subpleural lines, Banding opacity and fibrosis 53-68
Hu Z., et al18 2020 102 suppleural lines, fibrosis 70-95
Li X., et al19 2021 462 inf. Inflammatory, fibrosis 35-65
Lia Y., et al20 2021 300 hemorrhage, fibrosis, ground glass 40-65
Merdiji H., et al21 2021 22 fibrosis 63-74
Peng D., et al22 2021 113 frosted glass opacities, fibrosis 20-75
Picchi G., et al23 2020 2 consolidation and fibrosis 63-88
Radermecker C., et al24 2020 4 inflammation, hemorrhage and fibrosis 51-73
Schuliang Z., et al32 2020 195 consolidation, fibrosis 56-76
Shang Y., et al25 2020 307 frosted glass, fibrosis 33-55
Shi P., et al26 2020 134 34-58
Uememura Y., et al27 2021 60 subpleural lines, fibrosis 62-80
Wu J., et al28 2020 27 subpleural lines, fibrosis 38-79
Wu M., et al29 2020 9 m. disseminated hyaline, inf. inflammatory and fibrosis. 51-86
Xue M., et al31 2021 289 consolidation, fibrosis 41-69
Yang J., et al30 2021 85 subpleural lines, fibrosis 29-51
Zou N., et al33 2021 284 inf. Inflammatory, fibrosis 48-56

Table 1 - Characterization of articles according to year of publication, number of individuals studied and main pulmonary findings in laboratory and imaging tests.

## DISCUSSION

Several mechanisms have been suggested in the genesis of pulmonary fibrosis in patients with COVID-19, some suspect the ability of the SARS-CoV-2 virus to interact with the Angiotensin-2 Converting Enzyme (ACE-2), present in large quantities in the lung, and which is increased in individuals infected with SARS-CoV-2 (FANG, 2020) (UMEMURA, 2021). ACE-2 would, therefore, function as a receptor for the virus. Physiologically, ACE-2 promotes the conversion of Angiotensin-1 into Angiotensin-2. Angiotensin-2, in turn, participates in the process of pulmonary remodeling and fibrosis, promoting the expression of transforming growth factor-beta-1, a pro-fibrotic cytokine that converts fibroblasts into myofibroblasts, depositing collagen in lung tissue (YIM, 2021) (SHANG, 2020) (WU, 2020).

Several studies on Covid-19 analyzed patients who showed radiographic changes consistent with pulmonary fibrosis, in addition to characteristic findings in histopathology (ROQUETAILLADE, 2021). Some authors classify pulmonary fibrosis resulting from post-covid-19 infection, based on radiological criteria, based on extensive and persistent fibrotic changes, such as parenchyma bands, irregular interfaces, reticular opacities and traction bronchiectasis with or without honeycombing (FRANCONE, 2020). Other studies show, through computed tomography, immediate extensive pulmonary fibrosis. In 131 lung samples from individuals with covid-19, three histological patterns of lung injury were identified and often found overlapping: epithelial, vascular, and fibrotic. In an autopsy study, it was concluded that the pattern of fibrosis was seen more commonly and typically showed fibrosis of the alveolar duct or diffuse thickening of the alveolar walls (AMBARDAR, 2021) (MERDJI, 2021).

Other studies also suggest that chest computed tomography findings, such as bronchovascular bundle distortion, fibrotic bands, architectural distortion, and interlobular septal thickening, are suggestive of pulmonary fibrosis caused by Covid-19 (ALI, 2021).

A subgroup of patients, after three months of SARS-CoV-2 infection, had abnormalities on computed tomography, which included ground-glass opacity and subpleural bands (PICCHI, 2020). Six months after infection, the ground-glass pattern resolved, but there was persistence or development of changes suggestive of pulmonary fibrosis, such as reticulation with or without a distortion of the lung parenchyma (YANG, 2021). Another, more recent analysis with 118 infected patients diagnosed with moderate or severe pneumonia by SARS-CoV-2, adopting a stricter definition of fibrotic changes, found fibrotic-like changes in 72% of cases (SOLOMON, 2021) (BALL, 2021).

In a case study of two patients, findings suggestive of pulmonary fibrosis were also found after three weeks of symptoms in mild, moderate and severe disease (SHI, 2020). Changes suggestive of pulmonary fibrosis were: irregular areas of subpleural and perilobular consolidation, ground-glass pattern with fibrotic changes, interstitial thickening, traction bronchiectasis and subpleural bands (PENG, 2021). In another case study with three patients, two had post-covid-19 pulmonary fibrosis. Findings suggestive of pulmonary fibrosis were as follows: subpleural bands, residual ground-glass opacity, and fibrotic changes. According to this study, pulmonary fibrosis associated with pneumonia caused by COVID-19 has a spectrum that can range from fibrosis associated with organizing pneumonia to severe acute injury, progressing to generalized fibrotic change in the lung (RAI, 2021) (DUCLOYER, 2020).

## CONCLUSION

Post-Covid-19 pulmonary fibrosis appears to be a pulmonary complication present in most cases of SARS-CoV-2 infection and may persist for a long period of time. It can therefore be deduced from all imaging findings that pulmonary fibrosis may indeed be present and that it is a very common pulmonary complication in Covid-19 cases and therefore attention must be paid and further studies in order to better understand it and avoid, as much as possible, its consequences in individuals infected with Sars Cov-2. In addition to the need to prove the association of COVID-19 and pulmonary fibrosis.

## REFERENCES

- Aesif, S. W., Bribriescio, A. C., Yadav, R., Nugent, S. L., Zubkus, D., Tan, C. D., Mehta, A. C., & Mukhopadhyay, S. (2021). Pulmonary Pathology of COVID-19 following 8 Weeks to 4 Months of Severe Disease: A Report of Three Cases, including One with Bilateral Lung Transplantation. *American Journal of Clinical Pathology*, 155(4), 506–514. <https://doi.org/10.1093/ajcp/aqaa264>
- Alarcón-Rodríguez, J., Fernández-Velilla, M., Ureña-Vacas, A., Martín-Pinacho, J. J., Rigual-Bobillo, J. A., Jaureguizar-Oriol, A., & Gorospe-Sarasúa, L. (2021). Radiological management and follow-up of post-COVID-19 patients PALABRAS CLAVE COVID-19; Seguimiento radiológico; Secuelas; Radiografía de tórax. *In Radiología* (Vol. 63). [www.elsevier.es/rx](http://www.elsevier.es/rx)
- Ali, Rasha Mostafa Mohamed, e Mai Bahgat Ibrahim Ghonimy. “Post-COVID-19 pneumonia lung fibrosis: a worrisome sequel in surviving patients”. *Egyptian Journal of Radiology and Nuclear Medicine*, vol. 52, no 1, abril de 2021, p. 101. **BioMed Central**, <https://doi.org/10.1186/s43055-021-00484-3>.
- Ambardar, Shiva Rattan, et al. “Post-COVID-19 Pulmonary Fibrosis: Novel Sequelae of the Current Pandemic”. *Journal of Clinical Medicine*, vol. 10, no 11, junho de 2021, p. 2452. PubMed Central, <https://doi.org/10.3390/jcm10112452>.
- Ball, L., Barisione, E., Mastracci, L., Campora, M., Costa, D., Robba, C., Battaglini, D., Micali, M., Costantino, F., Cittadini, G., Patroniti, N., Pelosi, P., Fiocca, R., & Grillo, F. (2021). Extension of collagen deposition in covid-19 post mortem lung samples and computed tomography analysis findings. *International Journal of Molecular Sciences*, 22(14). <https://doi.org/10.3390/ijms22147498>
- Ducloyer, M., Gaborit, B., Toquet, C., Castain, L., Bal, A., Arrigoni, P. P., Lecomte, R., Clement, R., & Sagan, C. (2020). Complete post-mortem data in a fatal case of COVID-19: clinical, radiological and pathological correlations. *International Journal of Legal Medicine*, 134(6), 2209–2214. <https://doi.org/10.1007/s00414-020-02390-1>
- Fang, Y., Zhou, J., Ding, X., Ling, G., & Yu, S. (2020). Pulmonary fibrosis in critical ill patients recovered from COVID-19 pneumonia: Preliminary experience. *American Journal of Emergency Medicine*, 38(10), 2134–2138. <https://doi.org/10.1016/j.ajem.2020.05.120>
- Francone, M., Iafrate, F., Masci, G. M., Coco, S., Cilia, F., Manganaro, L., Panebianco, V., Andreoli, C., Colaiacomo, M. C., Zingaropoli, M. A., Ciardi, M. R., Mastroianni, C. M., Pugliese, F., Alessandri, F., Turriziani, O., Ricci, P., & Catalano, C. (2020). Chest CT score in COVID-19 patients: correlation with disease severity and short-term prognosis. *European Radiology*, 30(12), 6808–6817. <https://doi.org/10.1007/s00330-020-07033-y>

- Froidure, A., Mahsouli, A., Liistro, G., de Greef, J., Belkhir, L., Gérard, L., Bertrand, A., Koenig, S., Pothén, L., Yildiz, H., Mwenge, B., Aboubakar, F., Gohy, S., Pilette, C., Reychler, G., Coche, E., Yombi, J. C., & Ghaye, B. (2021). Integrative respiratory follow-up of severe COVID-19 reveals common functional and lung imaging sequelae. **Respiratory Medicine**, 181. <https://doi.org/10.1016/j.rmed.2021.106383>
- Hu, Z. J., Xu, J., Yin, J. M., Li, L., Hou, W., Zhang, L. L., Zhou, Z., Yu, Y. Z., Li, H. J., Feng, Y. M., & Jin, R. H. (2020). Lower Circulating Interferon-Gamma Is a Risk Factor for Lung Fibrosis in COVID-19 Patients. **Frontiers in Immunology**, 11. <https://doi.org/10.3389/fimmu.2020.585647>
- Li, X., Shen, C., Wang, L., Majumder, S., Zhang, D., Deen, M. J., Li, Y., Qing, L., Zhang, Y., Chen, C., Zou, R., Lan, J., Huang, L., Peng, C., Zeng, L., Liang, Y., Cao, M., Yang, Y., Yang, M., ... Liu, Y. (2021). Pulmonary fibrosis and its related factors in discharged patients with new coronavirus pneumonia: a cohort study. **Respiratory Research**, 22(1). <https://doi.org/10.1186/s12931-021-01798-6>
- Li, Y., Schneider, A. M., Mehta, A., Sade-Feldman, M., Kays, K. R., Gentili, M., Charland, N. C., Gonye, A. L. K., Gushterova, I., Khanna, H. K., LaSalle, T. J., Lavin-Parsons, K. M., Lilley, B. M., Lodenstein, C. L., Manakongtreecheep, K., Margolin, J. D., McKaig, B. N., Parry, B. A., Rojas-Lopez, M., ... Li, J. Z. (2021). SARS-CoV-2 viremia is associated with distinct proteomic pathways and predicts COVID-19 outcomes. **Journal of Clinical Investigation**, 131(13). <https://doi.org/10.1172/JCI148635>
- Merdji, H., Mayeur, S., Schenck, M., Oulehri, W., Clere-Jehl, R., Cunat, S., Herbrecht, J. E., Janssen-Langenstein, R., Nicolae, A., Helms, J., Meziani, F., & Chenard, M. P. (2021). Histopathological features in fatal COVID-19 acute respiratory distress syndrome. **Medicina Intensiva**, 45(5), 261–270. <https://doi.org/10.1016/j.medin.2021.02.007>
- Peng, D. H., Luo, Y., Huang, L. J., Liao, F. L., Liu, Y. Y., Tang, P., Hu, H. N., & Chen, W. (2021). Correlation of Krebs von den Lungen-6 and fibronectin with pulmonary fibrosis in coronavirus disease 2019. **Clinica Chimica Acta**, 517, 48–53. <https://doi.org/10.1016/j.cca.2021.02.012>
- Picchi, G., Mari, A., Ricciardi, A., Carucci, A. C., Sinatti, G., Cosimini, B., di Norcia, M., Iapadre, N., Balsano, C., & Grimaldi, A. (2020). Three cases of covid-19 pneumonia in female patients in Italy who had pulmonary fibrosis on follow-up lung computed tomography imaging. **American Journal of Case Reports**, 21, 1–11. <https://doi.org/10.12659/AJCR.926921>
- Pollard, C. A., Morran, M. P., & Nestor-Kalinowski, A. L. (2020). MINI-REVIEW The COVID-19 pandemic: a global health crisis. **Physiol Genomics**, 52, 549–557. <https://doi.org/10.1152/physiolgenomics.00089.2020.-The>
- Rai, Deependra K.1.; Kumar, Subhash2; Sahay, Nishant3 Post-COVID-19 pulmonary fibrosis, **Journal of Family Medicine and Primary Care**: May 2021 - Volume 10 - Issue 5 - p 2028-2031doi:10.4103/jfmpc.jfmpc\_2126\_20
- Roquetaillade, C., Bredin, S., Lascarrou, J. B., Soumagne, T., Cojocar, M., Chousterman, B. G., Leclerc, M., Gouhier, A., Piton, G., Pène, F., Stoclin, A., & Llitjos, J. F. (2021). Timing and causes of death in severe COVID-19 patients. **Critical Care**, 25(1). <https://doi.org/10.1186/s13054-021-03639-w>
- Shah, A. S., Wong, A. W., Hague, C. J., Murphy, D. T., Johnston, J. C., Ryerson, C. J., & Carlsten, C. (2021). A prospective study of 12-week respiratory outcomes in COVID-19-related hospitalisations. In *Thorax* (Vol. 76, Issue 4, pp. 402–404). **BMJ Publishing Group**. <https://doi.org/10.1136/thoraxjnl-2020-216308>
- Shang, Y., Xu, C., Jiang, F., Huang, R., Li, Y., Zhou, Y., Xu, F., & Dai, H. (2020). Clinical characteristics and changes of chest CT features in 307 patients with common COVID-19 pneumonia infected SARS-CoV-2: A multicenter study in Jiangsu, China. **International Journal of Infectious Diseases**, 96, 157–162. <https://doi.org/10.1016/j.ijid.2020.05.006>
- Shi, P., Ren, G., Yang, J., Li, Z., Deng, S., Li, M., Wang, S., Xu, X., Chen, F., Li, Y., Li, C., Yang, X., Xie, Z., Wu, Z., & Chen, M. (2020). Clinical characteristics of imported and second-generation coronavirus disease 2019 (COVID-19) cases in Shaanxi outside Wuhan, China: A multicentre retrospective study. **Epidemiology and Infection**. <https://doi.org/10.1017/S0950268820002332>
- Solomon, Joshua J., et al. “CT of Post-Acute Lung Complications of COVID-19”. **Radiology**, vol. 301, no 2, novembro de 2021, p. E383–95. [pubs.rsna.org](https://pubs.rsna.org) (Atypon), <https://doi.org/10.1148/radiol.2021211396>.
- Umemura, Y., Mitsuyama, Y., Minami, K., Nishida, T., Watanabe, A., Okada, N., Yamakawa, K., Nochioka, K., & Fujimi, S. (2021). Efficacy and safety of nintedanib for pulmonary fibrosis in severe pneumonia induced by COVID-19: An interventional study. **International Journal of Infectious Diseases**, 108, 454–460. <https://doi.org/10.1016/j.ijid.2021.05.055>

Wigén, J., Löfdahl, A., Bjermer, L., Elowsson-Rendin, L., & Westergren-Thorsson, G. (2020). Converging pathways in pulmonary fibrosis and Covid-19 - The fibrotic link to disease severity: Common molecular pathways in Covid-19 and pulmonary fibrosis. **In Respiratory Medicine: X** (Vol. 2). W.B. Saunders Ltd. <https://doi.org/10.1016/j.yrmex.2020.100023>

Wu, J., Zhou, X., Tan, Y., Wang, L., Li, T., Li, Z., Gao, T., Fan, J., Guo, B., Li, W., Hao, J., Wang, X., & Hu, B. (2020). Phase 1 trial for treatment of COVID-19 patients with pulmonary fibrosis using hESC-IMRCs. **In Cell Proliferation** (Vol. 53, Issue 12). Blackwell Publishing Ltd. <https://doi.org/10.1111/cpr.12944>

Wu, M., Chen, Y., Xia, H., Wang, C., Yee Tan, C., Cai, X., Liu, Y., Ji, F., Xiong, P., Liu, R., Guan, Y., Duan, Y., Kuang, D., Xu, S., Cai, H., Xia, Q., Yang, D., Wang, M.-W., Chiu, I. M., ... Kasper, D. L. (n.d.). Transcriptional and proteomic insights into the host response in fatal COVID-19 cases. <https://doi.org/10.1073/pnas.2018030117/-/DCSupplemental>

Wu, Q., Zhang, K. J., Jiang, S. M., Fu, L., Shi, Y., Tan, R. bin, Cui, J., & Zhou, Y. (2020). P53: A key protein that regulates pulmonary fibrosis. **In Oxidative Medicine and Cellular Longevity** (Vol. 2020). Hindawi Limited. <https://doi.org/10.1155/2020/6635794>

Yang, J., Chen, C., Chen, W., Huang, L., Fu, Z., Ye, K., Lv, L., Nong, Z., Zhou, X., Lu, W., & Zhong, M. (2021). Proteomics and metabonomics analyses of Covid-19 complications in patients with pulmonary fibrosis. **Scientific Reports**, 11(1). <https://doi.org/10.1038/s41598-021-94256-8>

Yim, Joowon, et al. "COVID-19 and Pulmonary Fibrosis: Therapeutics in Clinical Trials, Repurposing, and Potential Development". *Archives of Pharmacal Research*, vol. 44, no 5, maio de 2021, p. 499–513. **Springer Link**, <https://doi.org/10.1007/s12272-021-01331-9>.

Zhao, L., Wang, X., Xiong, Y., Fan, Y., Zhou, Y., & Zhu, W. (2021). Correlation of autopsy pathological findings and imaging features from 9 fatal cases of COVID-19 pneumonia. **Medicine**, 100(12), e25232. <https://doi.org/10.1097/MD.00000000000025232>

Zhou, S., Yang, Y., Zhang, X., Li, Z., Liu, X., Hu, C., Chen, C., Wang, D., & Peng, Z. (2020). Clinical Course of 195 Critically Ill COVID-19 Patients: A Retrospective Multicenter Study. **Shock** (Augusta, Ga.), 54(5), 644–651. <https://doi.org/10.1097/SHK.0000000000001629>

Zou, J. N., Sun, L., Wang, B. R., Zou, Y., Xu, S., Ding, Y. J., Shen, L. J., Huang, W. C., Jiang, X. J., & Chen, S. M. (2021). The characteristics and evolution of pulmonary fibrosis in COVID-19 patients as assessed by AI-assisted chest HRCT. **PLoS ONE**, 16(3 March). <https://doi.org/10.1371/journal.pone.0248957>