Echocardiography and Lung Ultrasound in Long COVID and Post-COVID Syndrome A Review Document of the Austrian Society of Pneumology and the Austrian Society of Ultrasound in Medicine

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Abbreviations

2-ChV, apical two-chamber view; 4-ChV, apical four-chamber view; CT, computerized tomography; GLS, global longitudinal peak systolic strain; ICU, intensive care unit; LA, left atrium; LUS, lung ultrasound; LV, left ventricle; MCpEF, chronic myocarditis with preserved left ventricular ejection fraction; PLAX, parasternal long axis view; PSAX, parasternal short axis view; RV, right ventricule; RVF, right ventricular function

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Lung ultrasound has the potential to enable standardized follow-up without radiation exposure and with lower associated costs in comparison to CT scans. It is a valuable tool to follow up on patients after a COVID-19 infection and evaluate if there is pulmonary fibrosis developing. Echocardiography, including strain imaging, is a proven tool to assess various causes of dyspnea and adds valuable information in the context of long COVID care. Including two-dimensional (2D) strain imaging, a better comprehension of myocardial damage in post-COVID syndrome can be made. Especially 2D strain imaging (left and the right ventricular strain) can provide information about prognosis.

Key Words—COVID-19; lung ultrasound; echocardiography; rehabilitation

Introduction

The ongoing COVID-19 pandemic is a global crisis holding the world hostage and is continuing to present an immense burden on healthcare workers.¹ Millions of people have been infected, with numbers still rising, and variants of the virus are still being discovered. With widespread vaccination, this pandemic might come to an end.^{2,3} Nevertheless, follow-up after COVID-19 still presents some difficulties. Some patients still suffer from symptoms such as dyspnea after acute COVID-19. In this consensus document, the usefulness of lung ultrasound (LUS) in post-COVID-19 patients is underlined.

Furthermore, the combination of LUS and cardiac imaging, especially echocardiography with newer parameters, such as strain imaging, is discussed. One main aim was to illustrate how ultrasound can be easily implemented understandably. LUS can identify persistent reverberation artifacts after a COVID-19 infection, commonly known as B-lines.⁴ Echocardiography can show deterioration in

regional and global strain imaging.^{5,6} Informed consent of all published material was obtained.

Long COVID and post-COVID syndrome

There is yet a lack of data on the rehabilitation of COVID-19 patients after a critical or severe course of the disease. At the same time, there is concern about the difficulties that the tremendous need for rehabilitation after critical and severe COVID-19 disease presents.^{7,8} A recent study by Sonnweber et al. showed that post-COVID-19 patients suffered from persistent symptoms, such as dyspnea and impairment in lung function testing.⁵ This study indicated that follow-up care of patients after COVID-19 with persistent clinical symptoms should include serial echocardiographic scans, serial lung function testing, and imaging of the lung with computerized tomography (CT) scans.⁵

As the number of symptomatic patients after an acute COVID-19 infection increased, the terms "long COVID" (symptoms after 4 weeks of acute infection) and "post-COVID syndrome" (symptoms after 12 weeks of acute infection) were introduced and are now used to describe more than 100 different persistent symptoms after acute infection.⁹⁻¹¹ In a metaanalysis, Lopez-Leon et al identified symptoms significantly associated with long COVID, including fatigue (58%), headache (44%), and dyspnea (24%). Pulmonary fibrosis (5%), reduced pulmonary capacity (10%), palpitations (11%), increase in heart rate (11%), chest pain (16%), and myocarditis (1%) were also reported. A pathological chest CT was observed in imaging 35% of patients 60 to 100 days after initial presentation.⁹ Pathological chest radiographs were found in almost two-thirds of hospitalized but noncritical COVID-19 patients.¹² Even bronchoscopically verified organizing pneumonia following COVID-19 pneumonia was described.¹³ Regarding elevated laboratory parameters, NT-pro-BNP was elevated in 11% of diagnosed long COVID patients.9

Fluid in the interstitium of the lung and the partial filling of alveolar spaces create vertical artifacts arising from a smooth pleural line with a bilateral symmetric distribution. Such lines are called B-lines.¹⁴ In the differential diagnosis of B-lines, echocardiography and scans of the inferior vena cava can be used to verify a cardiogenic cause of pulmonary edema.¹⁴

LUS can be of considerable value for predicting the clinical course and outcome in patients with COVID-19.¹⁵ Typical findings in patients with COVID-19 pneumonia are bilateral areas of fragmentation of the pleural line with reverberation artifacts.¹⁶ In a 2020 publication of the world federation of ultrasound in medicine and biology, a differentiation of reverberation artifacts depending on the origin was proposed.¹⁴ Artifacts that arise from a smooth pleural line and denote pulmonary edema should be called "B-lines." In contrast, artifacts arising from a fragmented pleural line are described as "comet tails."¹⁴ To avoid confusion and as reverberation artifacts in COVID-19 are called B-lines, B-lines will stay as the nomenclature in this publication with the note that comet tails are a more detailed term to differentiate reverberation artifacts.^{14,17–20} Reverberation artifacts in the case of sub-pleural consolidations and a reduction or absence of pleural sliding can be seen, as well.²¹ Reverberation artifacts arising from a fragmented pleural line indicate diffuse alveolar damage, diffuse parenchymatous lung diseases, and inflammatory diseases such as COVID-19.^{14,16}

Consolidations can be visualized using ultrasound. Hypoechoic areas with small hyperechoic (bronchograms) or hypoechoic (fluid bronchograms) structures within them, as well as a "tissue-like appearance" or hepatization of the lungs, are described as consolidations in lung ultrasound.^{22–24}

Pleural effusions in post-COVID-19 patients indicate a bacterial superinfection (small and localized effusions) or other differential diagnoses, such as left heart failure leading to elevated filling pressures, right heart failure, and loss of protein in kidney failure, or liver disease.^{16,25}

Lung Ultrasound for COVID-19 Pneumonia

Artifacts in LUS are created by air and, in the case of reverberation artifacts, by air and fluid mismatch.¹⁴

12-Zone LUS Scanning Protocol for Long COVID

Follow-up examinations, such as those in a rehabilitative setting, for COVID-19 patients should be consistent

with previous scans, and scanning must be performed thoroughly to identify changes in the LUS in detail. Patients with persistent symptoms, such as dyspnea, should be imaged.⁵ A reduction in B-line artifacts, a reduction in the size of consolidations, and a reduction or disappearance of pleural effusions in the case of complications (bacterial pneumonia, right and left heart failure) can be seen in LUS and should be documented.²⁶ Chest radiographs are an alternative and cheap diagnostic tool for bacterial or viral pneumonia in general and the follow-up of COVID-19.^{27,28} Chest radiographs are widely available but have a lower sensitivity in detecting COVID-19 pneumonia compared to LUS.²⁸

Overall, no international consensus exists on which transducer should be used for COVID-19 in which exact situation. The usage of a convex transducer with a low frequency or a linear transducer for better evaluation of the pleural line is recommended.^{19,20,29,30} In the author's opinion, in order to detect optimally and follow up on ultrasound artifacts associated with COVID-19 pneumonia, a specific lung preset with a low mechanical index, singlefocal point modality, and without harmonic imaging or other cosmetic filters should be chosen.¹⁷ The focal zone should be placed at the area of the pleural line.

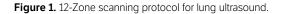
In the literature, several protocols are described, and no standardized international consensus has yet been achieved.^{17,20,29,30} The authors' agreement regarding feasibility is a 12-zone scanning protocol described in the literature.^{20,29} Starting with zone one in a longitudinal view, followed by a transverse view, a scan of all intercostal spaces should be performed in a supine patient. Posterior zones should always be included in follow-up examinations and performed in an upright position. A linear transducer with a specific preset should be used whenever possible. Depth settings should be adapted to patient size but ought to be in the range of 4 to 8 cm. In cases of larger, persistent pleural effusions or obese patients, a convex transducer should be selected.³⁰ The depth setting should be adapted to patients' sizes and will be in the range of 8 to 15 cm for optimal detection below fatty tissue. A 12-zone scanning protocol with pathologies as seen in critically ill, severely ill, and post-COVID-19 patients is presented in figures one and two (Figures 1 and 2). 31

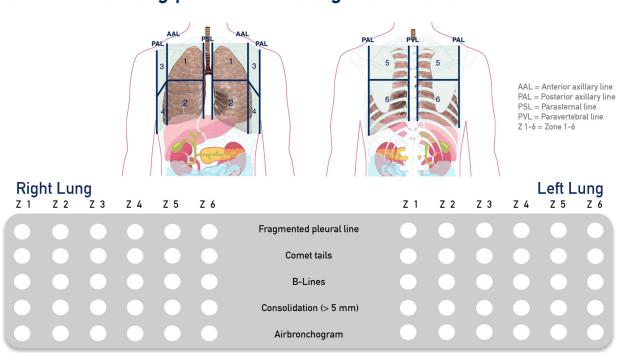
Findings are comparable with CT-Imaging (Video S1—LUS and CT imaging, from the ICU to the rehabilitation-left: after acute infection with a ground-glass pattern, consolidation and pleural effusion/corresponding ultrasound image of zone one, hemithorax, right lateral; right: CT and corresponding lung ultrasound four months later).²⁰ It has to be noted that ultrasound evaluation of the phrenic nerve and the diaphragm may be an additional tool in LUS to diagnose unilateral or bilateral paralysis of the diaphragm. The longitudinal assessment of respiratory patterns in patients with lung disease can be monitored, and in a standardized setting, monitoring is possible.³²

Comprehensive Echocardiography in Long COVID

In follow-up during rehabilitation after COVID-19 with cardiac involvement, a comprehensive TTE exam should be performed only if a clinical benefit is expected.^{33,34} In a post-COVID-19 setting, patients often present with symptoms of potential cardiac involvement such as palpitations and chest pain.³⁵ In a UK cohort, it was displayed that after a COVID-19 infection, the risk for death and readmission to the hospital is increased compared to matched controls.³⁶ In a median follow-up of 140 days of 47780 individuals, 29.4% were readmitted to the hospital, and 12.3% died after discharge after an acute COVID-19 infection. The risk for major adverse cardiovascular events was approximately threefold higher than in the matched cohort.³⁶ Cases of myocarditis were even reported in asymptomatic or mild COVID-19 diseases.³⁷

Echocardiography is the key investigation tool for assessing cardiac function and provides information on cardiac chamber size, wall thickness, regional wall motion abnormalities, pericardial effusion, valvular pathology, stiffness of the LV, and pulmonary hypertension.³⁸ After assessing the clinical status, the electrocardiogram, blood tests (NT-proBNP), echocardiography, and lung ultrasound can diagnose and classify patients with heart failure.³⁸ Furthermore, in patients with suspected cardiomyopathy, echocardiography is the first-line diagnostic tool recommended by the European Society of echocardiography.³⁸





12-zone scanning protocol for Lung Ultrasound

Designated lung preset :

For deep structures or in obese patients (primarly zone 4-6) → convex transducer (alternatevly phased array transducer) For superficial structures (primarily zone 1-3) → linear transducder. Possible for superficial structures in Zone 4-6 as well. For consolidations → use appropriate depth

• Altersberger et al. 2022

In the author's opinion, patients after COVID-19 who suffered from cardiac injury, myocarditis, acute coronary syndromes, pericarditis, stress-induced cardiomyopathy, worsening cardiovascular disease, persistent dyspnea with the clinical suspicion of cardiomyopathy, and thoracic pain should be evaluated with echocardiography concordant to the indications for echocardiography in existing guidelines.^{38–42}

A comprehensive TTE protocol, as recommended by the American Society of Echocardiography and the European Society of Echocardiography, with applying routine measurements.^{38,43,44}

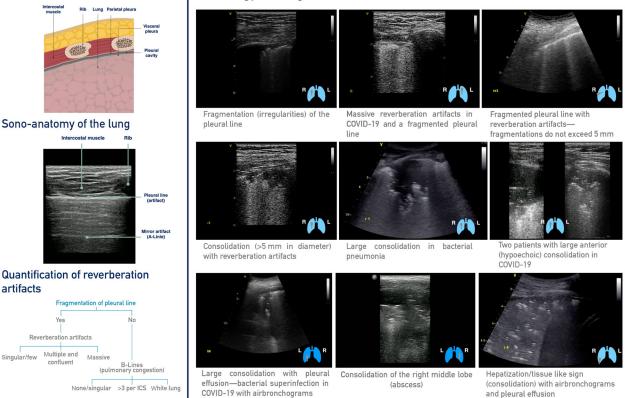
As there are no specific recommendations for post-COVID syndrome patients, a diagnostic workup as provided by the European Society of Echocardiography and the American Society of Echocardiography might be appropriate to apply.^{38,43,44}

A comprehensive exam starts with a parasternal long-axis view (PLAX), applying color Doppler and measuring the left ventricular enddiastolic diameter, the thickness of the interventricular septum, and the posterior wall.⁴⁴ In a parasternal short axis view (PSAX), the aortic valve should be visualized at the basis of the heart. The basal segments of the left ventricle (LV) and the opening of the mitral valve is the second view in a PSAX achieved by tilting the transducer. The mid- and apical segments can be visualized with further tilting. In a PSAX, radial left ventricular function can be visually assessed.⁴³

There is a special focus on regional wall motion abnormalities in the apical views. The apical fourchamber view (4-ChV), the apical two-chamber-view (2-ChV), and the apical long-axis view have to be Figure 2. LUS pathologies seen in critical, severely ill, and post COVID-19 scans with a suggestion to quantify reverberation artifacts.

Anatomy of the lung





visualized.⁴³ Diastolic dysfunction should be assessed according to current guidelines.⁴⁵

A specific focus in post-COVID-19 patients should be on the right heart as it can be involved in case of complications such as pulmonary embolism and may also provide prognostic information.^{41,46,47} An assessment of right ventricular function (RVF) and size should be performed. Additionally, systolic pulmonary artery pressure should be estimated by measuring the peak velocity of the tricuspid regurgitation signal.⁴⁸ Moreover, the pulmonary acceleration time and the size of the pulmonic trunk can be assessed.^{43,44,48} To complete the evaluation of the right ventricle (RV) and longitudinal RVF, the strain of the free RV wall in a focused view on the RV should be performed^{43,44} (Video S2: RV strain in a focused apical 4-ChV of the RV).

Schneider et al. reported that a ratio of pulmonary trunk diameter to ascending aorta diameter >1 provides additional information on pulmonary hypertension and should be taken into account in the context of routine assessment of pulmonary hypertension in echocardiography.⁴⁹

Subcostal views, such as the subcostal 4-ChV, are essential for detecting pericardial effusions.⁵⁰ Additionally, the inferior vena cava should be scanned to estimate right atrial pressure.⁴⁴

In echocardiography protocols in follow-up settings after COVID-19, strain imaging should be included. Changes in regional and global longitudinal systolic strain (GLS) should be reported^{6,43} (Video S3: Strain imaging in post-COVID-19 patients with reduction in basal regional strain).

As there is evidence that diastolic function after an acute inflammation with COVID-19 is impaired, the routine evaluation should also include diastolic parameters.^{33,34,43,45} In recent literature, left atrial (LA) strain is used to determine filling pressures; it

• Altersberger et al. 2022

might give valuable information in the future, but, as of now, LA strain did not show to correlate with prognosis in acute COVID-19 disease.^{46,51} Dilatation of the LA is an important marker of prognosis of patients with prior cardiovascular diseases.^{52–54}

In our experience, a thorough evaluation of all heart chambers is necessary to detect potential cardiac complications, such as myocarditis, pericarditis, and acute coronary syndromes, which occur in acute and long COVID patients, and to identify the actual underlying cause of dyspnea^{35–37} (Video S4: Strain imaging in a post-COVID-19 patient after an acute coronary syndrome with a reduction in GLS and regional basal and mid-segmental strain).

Patients with a prolonged course of COVID-19 disease may be facing symptoms such as dyspnea, fatigue, and palpitations. Pathological changes can be found in pulmonary function test, lung imaging, and echocardiography.^{9,13,55–57} Significant pathological residuals of clinical, functional, and morphological changes are often found in post-COVID-19 patients. Sonnweber et al. conclude that follow-up care should be considered in patients with persistent symptoms, including serial measures of pulmonary function test-ing, echocardiography, and CT-imaging.⁵

In the case of pulmonary imaging, we recommend a 12-zone scanning protocol in LUS to visualize residual changes such as reverberation artifacts and the reduction thereof over time.²⁰ LUS can be a lowcost, easy-to-use, widely available, and radiationsparing alternative to serial chest radiographs or CT scans for tracking clinical improvement. CT scans are costly and should be reserved for unclear cases.^{20,30} Chest radiographs have lower sensitivity than LUS but are widely available, cheap, and standardized.^{27,28,30} LUS might serve as an early tool for detecting long-term complications such as pulmonary fibrosis.^{18,58} If pleural effusions are present in post-COVID-19 patients, differential diagnoses such as left and right heart failure, kidney disease, or liver disease will have to be considered.²⁰

To detect cardiac complications and possible residual findings in strain imaging, comprehensive transthoracic echocardiography, including strain imaging, should be considered for implementation during rehabilitation after COVID-19 disease. In the authors' opinion, for patients with clinical findings which are suggestive of cardiomyopathy or elevated cardiac markers such as NT-proBNP, a comprehensive TTE should be performed as the risk of cardiac complications after COVID-19 is increased compared to controls.^{5,6,36,38,43} In particular, in myocarditis or myocardial injury cases, echocardiography, including strain imaging, should be applied.^{6,46,47,59} Given that myocarditis is a cause of sudden cardiac death, cardiac MRI should be considered the gold standard. Still, optimal resource management should be taken into consideration, and echocardiography might serve as the first screening tool.⁶⁰ However, the combination of imaging modalities has an even higher accuracy than cardiac MRI or speckle tracking echocardiography alone for detecting the entity of chronic myocarditis with preserved left ventricular ejection fraction (MCpEF).⁵⁵

A GLS of -13.8 in critically ill COVID-19 patients was defined as a predictor of mortality.⁶¹ A reduction in GLS can be seen when the EF is still normal and can be considered an early marker of myocardial damage.⁶¹

RV strain is a marker of poor prognosis (values >-23%) in critical COVID-19 and is considered to be a potential marker for long-term prognosis in follow-up in long COVID patients.⁴⁷

In the case of the post-COVID syndrome, there are yet no international recommendations for performing echocardiography. In a large UK cohort with a median follow-up of 140 days, cardiac complications were described as occurring substantially higher than in a cohort that never had COVID-19.³⁶ Sequels of COVID-19 described in a meta-analysis in a median time to assessment of 41 days included a reduction in ejection fraction in 23 of 811 participants.³⁵ Overall, the included studies did show an increased risk of cardiovascular sequels after acute COVID-19 disease with a higher rate of heart failure, myocarditis, pericarditis, myocardial infarction, and arrhythmias.³⁵

Conclusion

The usage of ultrasound should be encouraged not only in the context of this pandemic but also in future challenges.²⁹ Advanced techniques, such as 2D strain imaging of the cardiac chambers, can identify subclinical myocardial damage and are mentioned more and more in current guidelines. Still, there is a lack of data on the outcome for COVID-19 patients. Lung ultrasound and echocardiography hold great potential in the aftermath of COVID-19 disease. Still, more literature is needed in the context of the post-COVID syndrome to evaluate which patient population profits the most from standardized ultrasound exams.

Conflict of Interest

All authors have read the manuscript and approved its submission. The authors declare that there is no conflict of interest.

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