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Optimizing care for patients with interstitial lung disease during the COVID-19 pandemic

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The purpose of this commentary is to address common questions regarding the care of patients with fibrotic interstitial lung disease (ILD) during the COVID-19 pandemic. Our suggestions are based on limited available data and supplemented by current practices across Canadian ILD centres. This commentary summarizes the position statement on practical considerations for the diagnosis and treatment of fibrotic interstitial lung disease during the COVID-19 pandemic[1].

Diagnostic evaluation of patients with ILD

We suggest modifying the standard diagnostic evaluation to reduce in-person patient contact with the healthcare system in order to minimize the risk of SARS-CoV-2 transmission.

Rationale: The overall goal of modifications to the ILD diagnostic pathway is to reduce the risk of SARS-CoV-2 transmission, while minimizing delays in establishing an accurate diagnosis. This can be achieved by decreasing in-person contact (e.g., virtual clinic visits and multidisciplinary discussions), employing infection control policies during necessary visits, and limiting investigations to those that are required to direct management decisions. In some situations, accepting a lower diagnostic certainty for an ILD diagnosis may be justified,[2] which is particularly relevant if the differential diagnoses would be managed similarly. It may also be appropriate to temporarily observe stable patients without a clear diagnosis until community transmission of SARS-CoV-2 is low, at which time further evaluation can be pursued more safely. Patients may require reconsideration of a less confident working diagnosis after the pandemic.

Ancillary diagnostic procedures including bronchoscopy and surgical lung biopsy

Beyond usual risk-benefit considerations, additional risk factors associated with the transmission of SARS-CoV-2 and development of severe COVID-19 illness should be considered when contemplating aerosol generating medical procedures such as bronchoscopy and surgical lung biopsy.

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Rationale: The performance of bronchoscopy and surgical lung biopsy procedures during the COVID-19 pandemic pose risks to both patients and healthcare providers. Clinicians must consider the direct procedural risks to patients, as well as those of increased patient contact with the healthcare system. Although bronchoscopy is safe in many patients with ILD, it is an aerosol generating procedure and should be performed under airborne precautions with eye protection during the COVID-19 pandemic.[3] Patient factors associated with increased mortality following surgical lung biopsy in ILD (e.g., advanced age, comorbidities, need for supplemental oxygen) should be reviewed carefully prior to recommending a procedure,[4] particularly since these risk factors are similar to those for severe COVID-19 illness. Although data are limited, patients undergoing elective surgery during the incubation period of SARS-CoV-2 may have substantial perioperative morbidity and mortality.[5] Testing for SARS-CoV-2 in the 1-2 days prior to bronchoscopy or surgical lung biopsy is reasonable in adequately resourced areas, given the potential for asymptomatic patients to be infectious.[3] Elective bronchoscopy and surgical lung biopsy should be deferred in patients with SARS-CoV-2 infection.

Multidisciplinary discussion

We suggest conducting virtual multidisciplinary discussions (MDDs) using platforms that allow imaging and pathology to be shown in real-time.

Rationale: Virtual MDDs allow similar collaborative discussion between experts while respecting physical distancing recommendations. Various online meeting platforms provide the ability for participants to share radiology images and pathology slides in real-time with the entire group. Virtual meetings can increase attendance and access to MDD; however, it is critical to ensure that adequate privacy and security measures are in place to maintain patient confidentiality.

Immunomodulatory medications

(A) We suggest that immunomodulatory therapy should continue to be prescribed according to standard practice using the lowest effective dose.

(B) Temporary cessation of immunomodulatory therapy should be considered on a case-by-case basis in patients who have confirmed or suspected COVID-19.

Rationale: Immunomodulatory therapy is associated with increased risk of infection in patients with ILD.[6] However, there is an absence of robust data suggesting that these therapies are major risk factors for more severe disease in Severe Acute Respiratory Syndrome (SARS), Middle Eastern Respiratory Syndrom (MERS), or COVID-19. Evidence from previous human coronavirus infections has suggested that corticosteroid treatment may lead to increased viremia and delayed clearance of viral RNA from respiratory tract secretions.[7] Corticosteroids have also been associated with increased length of hospital stay in SARS and MERS;[7, 8] however, study design limitations prohibit definitive conclusions. Based on the totality of evidence, corticosteroids can be used with caution to treat steroid-responsive ILD in areas with a high prevalence of COVID-19 illness, but priority should be given to steroid-sparing therapies where possible.

We suggest that clinicians use the lowest effective dose of immunomodulatory therapy in patients with ILD and recommend that initiation of immunomodulatory therapy be delayed in patients with newly confirmed or suspected COVID-19. Discontinuation of immunomodulatory therapy may be associated with accelerated lung function decline and increased mortality.[6] The

choice of whether to continue, decrease the dose, or temporarily cease previous immunomodulatory therapy in patients with ILD who develop COVID-19 illness is difficult and should be considered on a case-by-case basis.

Antifibrotic medications

We suggest that antifibrotic therapies should continue to be prescribed according to clinical practice guideline recommendations.

Rationale: There are no data to suggest that antifibrotic therapies are associated with increased risk of COVID-19 or more severe disease in those contracting the illness. It is also unknown if antifibrotics may attenuate COVID-19 infection or prevent post-infectious fibrotic lung disease, although ongoing studies will attempt to address these questions.[9] Given the absence of data, the decision to initiate or continue antifibrotic medication should follow standard clinical practice. Pulmonary function tests (PFTs) being performed solely to meet regional funding eligibility criteria without any other clinical indication should be considered non-urgent and should be postponed or waived during this time. This recommendation is supported by the sustained effects of antifibrotic medications beyond one year, in patients with severe ILD, and in patients with progression while on therapy,[10-12] suggesting the safety and likely efficacy of continued therapy in these situations.

Patient care after COVID-19 disease

We suggest that patients with persistent respiratory symptoms after COVID-19 illness be evaluated for the presence of post-COVID pulmonary fibrosis and/or exacerbation of pre-existing ILD, and that patients with confirmed post-COVID pulmonary fibrosis be assessed at a clinic that specializes in ILD.

The risks of morbidity and mortality associated with COVID-19 in patients with ILD are unknown. However, COVID-19 and IPF tend to affect older patients who have a smoking history, co-morbidities, and reduced pulmonary reserve,[13, 14] and the risk of having more severe infection is therefore likely increased for patients with ILD. Those patients with underlying ILD who survive COVID-19 may have substantially worsened respiratory symptoms, reduced lung function, and new or increased oxygen requirements. Referral to an ILD centre may facilitate initiation of therapies such as antifibrotic medications, pulmonary rehabilitation, oxygen, vaccinations, and access to multidisciplinary care, including palliative care when appropriate.

Some patients without prior lung disease develop imaging features of ILD following COVID-19 disease (e.g., ground glass and reticulation); however, there are no data on their long-term prognosis.[15] Data obtained from the SARS outbreak showed that 30-60% of survivors had lung fibrosis on chest imaging post-infection.[16] We therefore suggest evaluation for ILD with high resolution computed tomography of the chest and PFTs for patients who have persistent respiratory symptoms following recovery, with this assessment ideally performed in a standardized manner in order to support specific research questions on this topic.

Conducting ILD research

The decision to conduct clinical research should consider local and national policies, community prevalence of COVID-19, risk of study protocols to staff and patients, and patient preferences.

The risks associated with conducting ILD research during the COVID-19 pandemic depends largely on the study protocol and local community prevalence of infection. Consistent with recommendations for clinical care, study protocols should be modified to prioritize the safety of patients and research personnel, including allowance for virtual study visits and either delaying or cancelling non-urgent testing. Most clinical trial sponsors have suspended new patient enrollment for ongoing studies and postponed initiation of new clinical trials. In addition, many institutions have suspended non-COVID investigator-led research in an effort to shift resources to pandemic-related research questions and, in some cases, have re-deployed personnel to support frontline clinical work. As a result, studies are being delayed and investigators are attempting to maintain research programs despite financial strains. Solutions to these challenges have included the use of bridge funding or shifting focus to important COVID-related questions, such as risk factors for severe disease, outcomes of COVID-19 in those with ILD, and whether a subset of patients with COVID-19 will develop progressive fibrotic interstitial lung disease.

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