An ABC approach to cardiothoracic complications and sequelae of COVID-19: a tertiary centre experience

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ABSTRACT

The Coronavirus disease 2019 (COVID-19) pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has caused unprecedented challenges to healthcare professionals (HCPs) worldwide. HCPs faced an unknown disease causing many complications, including now well-established acute respiratory distress syndrome (ARDS) and pulmonary artery thromboembolic disease, and some not so well known, for instance, tracheobronchomalacia, tracheal tear or dehiscence, granulation tissue formation and pulmonary hypertension. Many of these complications require highly specialist care warranting early recognition of complications and involvement of appropriately trained professionals. Here, we review the complications and sequelae encountered at our tertiary care centre with follow-up data and potential management strategies using the A (Airway), B (Breathing), C (Circulation) approach. This will not only familiarise HCPs with the different complications of COVID-19, but also arm them with a systematic approach to these complications.

KEYWORDS: large airway injury, pulmonary fibrosis, pulmonary hypertension, pulmonary thromboembolic disease, sildenafil

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Introduction

Since its origin in 2019 from Wuhan, China, Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has resulted in 767 million cases and 6.95 million deaths worldwide.[1] Acute respiratory distress syndrome (ARDS) resulting from diffuse alveolar damage is the most common and most well-recognised cause of hospitalisation, need for ventilatory support and death.[2] There is also a higher incidence of pulmonary embolism (PE) and *in situ* thrombosis leading to ventilation–perfusion (VQ) mismatch and respiratory failure associated with this condition.[3]

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To assist with appropriate diagnosis and management of this unfamiliar disease, at the beginning of the pandemic, an acute respiratory disease support team was set up in our tertiary care centre in South London to deal with patients critically unwell with COVID-19. All surviving patients were followed up in an ARDS follow up clinic at 3 months after discharge with 2D echocardiography, computed tomography pulmonary angiogram (CTPA) and 6-min walk test (6MWT) as minimum follow-up investigations. The team comprised a professor of cardiothoracic medicine, a consultant cardiothoracic intensivist, a registrar in respiratory medicine, a pulmonary hypertension (PH) specialist nurse and an experienced cardiothoracic medical secretary. The work of this team has already been published.[4–8] Here, we summarise our single-centre experience of cardiorespiratory complications of COVID-19 in a systematic way using a practical and easy-to-remember A (Airway), B (Breathing), C (Circulation) approach.

The ABC approach

A: Airway (Table 1)

Central airway malacia is a well-known late complication of invasive mechanical ventilation and attributed to inflammation, infection and barotrauma.[9] COVID-19 is associated with significant large airway inflammation, which can lead to structural distortion of the airway.[10] This can cause distal lobar collapse leading to difficulty in mechanical ventilation or failed weaning attempts from ventilatory support. Bronchoscopy will offer diagnosis and endobronchial stenting can be indicated in proximal (tracheal and/or main bronchial) disease to help recruit the distal airways to mitigate these effects.[4]

Large and upper airway mucosal oedema not only occurs because of the direct inflammatory effects of SARS-CoV-2 virus, but is also associated with duration of intubation.[10,11] Examples include subglottic, glottic and supraglottic oedema. In the case of a tracheostomised patient, large airway inflammation, including granulation tissue, might occur the tracheostomy tube and can be easily missed if flexible bronchoscopy via tracheostomy tube alone is performed.[4] If this is suspected, bronchoscopy (via vocal cords or tracheal stoma) or nasendoscopy to examine the epiglottis, glottis, vocal cords and proximal trachea is required.

Granulation tissue can develop at the site of tracheostomy and can lead to serious airway obstruction and haemorrhage, both of which can be immediately life-threatening.[4] Airway obstruction resulting from granulation tissue can present with difficult ventilation, difficulty weaning from ventilatory support, copious

Table 1. Airway-related complications of COVID-19 encountered by the acute respiratory disease support team

Pathology	Main learning to consider
Tracheobronchomalacia	Role of stenting
Glottitis	Large airway inflammation can be above tracheostomy site
Granulation tissue formation	Granulation tissue formation can be above tracheostomy site; laser therapy is useful
Tracheal tear and dehiscence	Cover with endotracheal tube/ temporary stenting/role of BioGlue
Tracheal diverticulum	Surveillance
Covid swab retention	Unconventional approach might be needed in difficult cases

COVID-19 = Coronavirus disease 2019.

secretions or a weak voice. This must be identified and considered before decannulation.[12] Endobronchial laser therapy can be used to clear granulation tissue and/or to secure haemostasis.

Spontaneous tracheal tears can arise as a result of the inflammatory effects of the disease on airway mucosa and changes in intrathoracic pressure because of prolonged coughing, and should be suspected in cases of unexplained surgical emphysema or spontaneous pneumomediastinum.[5] They can also occur secondary to endotracheal (ET) intubation, particularly if a bougie is deployed and especially when the tracheal intubation is carried out in an emergency. Therapeutic strategies can include a conservative approach; covering the tear with an ET tube; temporary stenting with a covered stent; or the use of BioGlue. A multidisciplinary team discussion is suggested to determine therapeutic strategy because mechanical ventilation can complicate matters further. Acute tracheal tear appears to be associated with a poor prognosis because all three of our patients with tracheal tears succumbed to multiorgan failure.[5]

Tracheal diverticulum is a rare entity that has been described in patients with COVID-19. Herniation resulting from chronic cough, tracheostomy-related injury, obstructive airway disease and tracheobronchomalacia are implicated risk factors.[13] Most of these diverticulae are asymptomatic and are managed conservatively. Rarely, they can cause recurrent tracheobronchial infection, which might necessitate surgical intervention.[14]

Some patients have had viral swabs deployed through tracheostomy tube, leading to swab fracture and retention in large airways. This requires rigid/fibreoptic bronchoscopic retrieval either via the vocal cord approach or, if indicated, through tracheal stoma.[6,15] Education of staff involved in COVID testing is essential to avoid taking COVID swabs via a tracheostomy tube.

Out of 44 consecutive patients seen between April and June 2020 by the acute respiratory disease support team, five (11%) patients had the above-mentioned large airway pathologies.[4] Based on our experience, we recommend that large airway pathology should be considered in patients requiring prolonged mechanical ventilatory support, difficulty in weaning from ventilatory support, unexplained air-leak, surgical emphysema and pneumomediastinum.

Table 2. Breathing-related complications of COVID-19 encountered by the acute respiratory disease support team

Pathology	Main learning to consider
ARDS	Mortality benefit with dexamethasone and IL6 inhibitors
Evolving lung fibrosis	Methylprednisolone therapy
	No recurrent respiratory tract infection

ARDS = acute respiratory distress syndrome; COVID-19 = Coronavirus disease 2019 IL6 = Interleukin 6.

B: Breathing (Table 2)

Acute hypoxemic respiratory failure (AHRF) secondary to ARDS is the most common organ dysfunction seen in patients hospitalised with COVID-19. This accounts for 90% of COVID-19 related mortality seen in the intensive care setting.[2] The Recovery trial established a role for dexamethasone and Interleukin 6 inhibitors in the management of SARS-CoV-19.[16,17] However, to date, there is no clear role for steroid therapy in the management of post-COVID interstitial lung disease (PC-ILD).

In our cohort of 44 consecutive patients, 10 (23%) patients with immunologically driven severe ARDS and CT features of evolving lung fibrosis (extensive ground glass changes, peripheral airspace dilatation and traction bronchiectasis) were pulsed with methylprednisolone based on its similarity to connective tissue disease-related interstitial lung disease (CTD-ILD), which is characterised by non-specific interstitial pneumonia overlapping with organising pneumonia (OP/NSIP overlap).[18] Three-month follow-up CT imaging of the thorax showed significant improvement from admission CT scans in most patients. However, long-term sequelae of ARDS were unsurprisingly present in most of the follow-up imaging. Parenchymal bands and pulmonary fibrosis were the most common of these radiological abnormalities.[7]

On lung function tests, reduction in the diffusing capacity of the lung for carbon monoxide (DLCO) was the most frequent finding. This was worse in patients with established fibrosis. A similar trend was seen in 6MWD, which was reduced overall in the whole group, but was much worse in patients with established fibrosis.[7]

Most importantly, none of these patients developed infection or sepsis secondary to steroid usage.[8]

PC-ILD is prevalent in 10% of hospitalised patients at 12 months post COVID-19 infection. Multiple pathogenic mechanisms have been implicated, including direct tissue damage resulting from the inflammatory nature of the illness, ARDS, ventilator induced lung injury (VILI) and autoimmunity with the generation of, as of yet, unidentifiable autoantibodies.[19] PC-ILD is an exciting area of research to assess a potential role for immunomodulation.

Other common complications seen in severe COVID-19 infection, such as superadded bacterial or fungal infection and pneumothoraces, should also be considered in the event of an unexplained clinical deterioration. In patients with severe COVID-19 infection requiring intensive care unit (ICU) admission, there is a 10% risk of developing pneumothorax with statistically significant prolongation of mechanical ventilation and length of hospital stay associated with it.[20]

Table 3. Circulation-related complications of COVID-19 encountered by the acute respiratory disease support team

Pathology	Main learning to consider
Right ventricular dysfunction and pulmonary hypertension	Successful use of sildenafil to improve pulmonary haemodynamics Normalised in 90% patients at 3 months; Sildenafil subsequently discontinued
Pulmonary thromboembolic disease	*In situ* thrombosis: resolved at 3 months Pulmonary emboli: risk of CTEPH; VQ scan can be useful
Atrial fibrillation	Digoxin used as preferred drug for rate control because of risk of bronchospasm and ILD associated with beta-blockers and amiodarone, respectively

COVID-19 = Coronavirus disease 2019; CTEPH = chronic thromboembolic pulmonary hypertension; ILD = interstitial lung disease; VQ scan = ventilation–perfusion scan.

C: Circulation (Table 3)

COVID-19 is a primary respiratory infection with effect on pulmonary haemodynamics. Approximately 15% of patients with SARS-CoV-19 infection develop PH.[21] This is believed to reflect multifactorial pathophysiology, including the sequelae of venous thromboembolism (Group 4: PH associated with chronic pulmonary artery occlusion), ILD and hypoxia (Group 3: PH associated with lung diseases and/or hypoxia), myocarditis and other cardiac pathologies, such as myocardial infarction (Group 2: PH associated with left heart disease) and endothelial injury (Group 1: pulmonary arterial hypertension).[21,22] In our cohort, 84% patients (37/44) had echocardiographic evidence of PH with right ventricular dysfunction (RVD) and/or raised estimated pulmonary artery systolic pressure (PASP).[8]

Based on the experience in managing chronic thromboembolic PH (CTEPH) and PH in non-COVID-19 cases, sildenafil was used as pulmonary vasodilator therapy (PVT) in carefully selected patients.[23] Use of nebulised nitric oxide and prostacyclin was limited because of their availability, complexity of administration and concerns of contamination of ambient air. However, sildenafil had wide availability, was easy to administer via the oral route or through nasogastric tube and had good patient tolerance. Sildenafil can also be administered intravenously if the enteral route is not possible. These were important factors to consider in the midst of the pandemic with low nurse to patient ratios, stretched resources and HCP working outside their area of practice. On follow-up echocardiography, significant improvement was documented in all the right ventricular parameters. None of our patients experienced any side effects of sildenafil and it was stopped in 90% of the patients at 3 months follow-up.[8]

There is a 16.5% incidence of PE in all patients hospitalised with COVID-19 and this is associated with worse clinical outcomes.[3,24] A distinct phenotype with peripheral distribution of clot burden is seen suggestive of *in situ* thrombosis and has been attributed to local and systemic inflammation.[3,25] In our ITU cohort, PE or peripheral *in situ* thrombosis was seen in 52% (23/44) of patients. Of these, 35% (8/23) patients had proximal clot and 65% (15/23) patients had peripheral pulmonary arterial thrombosis. Seven out of the eight patients with proximal clot required thrombolytic therapy. All the patients received appropriate full-dose anticoagulation.[8]

Thrombolysis and aggressive treatment of PE do not necessarily reduce the risk of development of CTEPH, which has an incidence of ~3%.[26] Guidelines recommend CT pulmonary angiography (CTPA) and ventilation perfusion scintigraphy (VQ scan) to rule out chronic thromboembolic disease.[23] VQ scan is thought to be more sensitive for distal disease; an important consideration in patients with COVID-19-related distal *in situ* thrombosis.

Sildenafil was used in 21 (91%) patients with thromboembolic disease and echocardiographic evidence of PH. All surviving patients demonstrated improvement in measured parameters on follow-up echocardiography.[8] This is suggestive of a beneficial effect of PVT in this cohort, but warrants more studies to evaluate it further.

Two of our patients developed atrial fibrillation. In these patients, after consultation with our cardiac electrophysiologist colleagues, digoxin was used as the drug of choice for rate control. Beta-blockers were avoided because of a potential side effect of bronchospasm in the context of already-diseased small airways with COVID-19 pneumonitis. In addition, amiodarone was not favoured because of the associated risk of ILD, independent of the risk of lung fibrosis due to COVID-19-associated ARDS.

Several cardiac complications of COVID-19 have been described in the medical literature.[27–29] However, some patients might have coexisting cardiac conditions, which might be exacerbated by the consequences of COVID-19 infection. Heart failure is the most common complication reported, with an incidence of 23% in hospitalised patients.[27] The aetiology of heart failure in severe COVID-19 infection is not fully understood. Hypoxia, volume overload, direct effect of SARS-CoV-2 on the myocardium, changes in pulmonary vascular resistance and unmasking of already existing subclinical heart failure in the setting of acute illness are hypothesised as possible aetiologies. There is an association between severe COVID-19 disease and acute coronary syndrome (ACS), with 8% of patients presenting with ACS at the outset.[28] Up to 40% of these patients lack an identifiable coronary lesion on angiography, indicating acute thrombosis or coronary vasospasm as potential causes.[28] Myocardial injury as defined by the increase in cardiac biomarkers is an independent marker of poor prognosis and is associated with increased mortality within the setting of severe COVID-19 infection. It is encountered in as many as 27.8% of patients hospitalised with SARS-CoV-2 infection.[29] Factors contributing to this increase in cardiac biomarkers include ACS, heart failure, arrythmias, RVD in setting of pulmonary thromboembolic disease and myocarditis, among others. Myocarditis is a rare cause of myocardial injury and has a reported incidence of 0.01% in patients hospitalised with SARS-CoV-2 infection.[30] Definitive diagnosis of myocarditis can be made by endomyocardial biopsy demonstrating lymphocytic infiltration of the myocardium, although this is not usually performed. An increase in cardiac biomarkers together with appearances on transthoracic echocardiogram and cardiac magnetic resonance (CMR) imaging in the right clinical context are usually sufficient for diagnostic purposes.

Conclusion

In this review, we have summarised different complications and sequelae of COVID-19 infection that we have encountered in our patients at a tertiary care hospital in an easy-to-remember ABC approach. We hope that this will reinforce the importance of a holistic approach in assessing the cardiorespiratory system in patients with severe COVID-19 infection. We believe that the complexity of these issues is best served by a multidisciplinary approach with early involvement of appropriate expertise. This is more likely to best optimise the care of these complex patients. We believe that early diagnosis and management of these conditions (which can be coexistent) will lead to better outcomes. Finally, it is important to remember that other common and unrelated pathologies, such as cancer, acute coronary syndrome, heart failure, obstructive airway disease and bacterial pneumonia, must be considered in the differential diagnosis. ■

Summary

What is known?
COVID-19 is an inflammatory condition with many potential complications and sequelae.

What is the question?
Is there a systematic methodology to approach these complications and sequelae of COVID-19?

What was found?
We propose an 'ABC approach' as a methodology that takes the clinician through the complications and sequelae of COVID-19 in a systematic way.
We also summarise our experience for the reader in this article. Main learning points for each complication are summarised in Tables 1–3 in the main text.

What is the implication for practice now?
We hope that this will reinforce the importance of a holistic approach in assessing the cardiorespiratory system in patients with severe COVID-19 infection. ABC assessment in a deteriorating patient is already well known to clinicians. This is expected to help with early recognition of the cardiorespiratory complications of COVID-19 and hopefully improve patient outcomes.

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