



Incidence and Clinical Features of Pneumomediastinum and Pneumothorax in COVID-19 Pneumonia

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Abstract

Background: Pneumothorax (PTX) and pneumomediastinum (PM), collectively termed here “air leak”, are now well described complications of severe COVID-19 pneumonia across several case series. The incidence is thought to be approximately 1% but is not definitively known.

Objectives: To report the incidence and describe the demographic features, risk factors and outcomes of patients with air leak as a complication of COVID-19.

Methods: A retrospective observational study on all adult patients with COVID-19 admitted to Watford General Hospital, West Hertfordshire NHS Trust between March 1st 2020 and Feb 28th 2021. Patients with air leak were identified after reviewing both chest radiographs (CXR) and axial imaging (CT Thorax) with confirmatory radiology reports inclusive of the terms PTX and/or PM.

Results: Air leak occurred with an incidence of 0.56%. Patients with air leak were younger and had evidence of more severe disease at presentation, including a higher median CRP and number of abnormal zones affected on chest radiograph. Asthma was a significant risk factor in the development of air leak (OR 13.4 [4.7-36.4]), both spontaneously and following positive pressure ventilation. CPAP and IMV were also associated with a greater than six fold increase in the risk of air leak (OR 6.4 [2.5-16.6] and 9.8 [3.7-27.8] respectively). PTX, with or without PM, in the context of COVID-19 pneumonia was almost universally fatal whereas those with alone PM had a lower risk of death.

Conclusion: Despite the global vaccination programme, patients continue to develop severe COVID-19 disease and may require respiratory support. This study demonstrates the importance of identifying that deterioration in such patients may be resultant from PTX or PM, particularly in asthmatics and those managed with positive pressure ventilation.

Keywords

pneumothorax, pneumomediastinum, COVID-19, air leak

Introduction

Pneumothorax and pneumomediastinum, collectively termed here “air leak”, are now well described complications of severe COVID-19 pneumonia across several case series.¹⁻⁶ The incidence of these complications is thought to be approximately 1%.⁴ In patients with air leak as a complication of COVID-19, mortality ranges from 33% to 66%.¹⁻⁶ This is higher than the overall reported mortality of COVID-19 patients (16.8% to 52.2%) admitted to hospital between March and May 2020.⁷

Both forms of air leak have been noted to occur in COVID-19 patients secondary to barotrauma associated with intubation, but also spontaneously in those with no pre-existing lung disease.⁴ Severe COVID-19 causes pathological changes consistent with acute respiratory distress syndrome (ARDS).⁸

Other forms of ARDS are associated with pneumothorax, as cystic and fibrotic changes in the lung parenchyma lead to alveolar tear, with injury to the visceral pleura resulting in air accumulation in the pleural space. In contrast, in

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pneumomediastinum it is thought that air from ruptured alveoli dissects along bronchovascular planes and into the mediastinum.⁹ Spontaneous and ventilation associated air leak have also previously been reported in ARDS caused by two other clinically significant coronaviruses- the closely genetically related SARS-CoV-1, aetiological agent of Severe Acute Respiratory Syndrome (SARS)¹⁰ and Middle Eastern Respiratory Virus, MERS-CoV^{10,11}

Herein we describe the demographic features, risk factors and outcomes of patients with air leak as a complication of COVID-19 in patients admitted to our institution with confirmed SARS-CoV-2 infection. This is the first study to report the true incidence of air leak as a complication of COVID-19, albeit in a single centre institution.

Study Design and Methods

Adult patients over 18 years with positive SARS-CoV-2 nucleic acid testing by real-time polymerase chain reaction (rRT-PCR) were retrospectively recruited at Watford General Hospital, West Hertfordshire NHS Trust between March 1st 2020 and Feb 28th 2021. A pre-specified study protocol including data collection methodology has been published elsewhere.¹²

Patients with air leak were identified after reviewing both chest radiographs (CXRs) and axial imaging (CT Thorax) by 2 respiratory physicians with confirmatory radiology reports inclusive of the terms pneumothorax and/or pneumomediastinum. Any scans performed for trauma or other likely secondary causes were excluded, for example, surgical or iatrogenic PTX and PM. We compared these cases to data from 993 randomly selected COVID-19 patients without air leak were drawn from the electronic records recruited as part of the PREDICT study.¹² For all patients with and without air leak we obtained demographic details, co-morbidities, laboratory investigations,

radiological imaging, clinical management including modes of ventilation, survival and outcome.

CXR scores were assigned according to number of zones (eg Upper, Middle, and Lower lung fields) demonstrating COVID-19 associated changes, and were scored according to the CARE chest radiography score¹³

Statistical Analysis

Statistical analysis was performed with Graphpad Prism statistics software (GraphPad, San Diego, USA). Categorical variables were assessed using Pearson's χ^2 tests. Initial exploratory analysis and statistical normality testing determined all continuously distributed variables of interest were non-normally distributed, therefore Mann-Whitney U-tests were used for analysis of continuous variables. P values <0.05 were considered statistically significant.

Results

A total of 3377 COVID PCR positive patients were admitted to West Hertfordshire hospital between 1st March 2020 and 28th February 2021. A total of 19 patients with air leak were identified. The overall incidence of air leak as a complication of COVID-19, in our institution, was 0.56%. Of the 19 patients with air leak, 3/19 (15.7%) patients had PTX only, 11/19 (57.8%) had PM, 5/19 (26.3%) patients had both complications of PTX and PM simultaneously.

Table 1 shows the baseline characteristics of the patients with air leak compared to a group of 993 SARS CoV 2 patients without air leak. Patients with air leak were significantly younger (median age 63 years [IQR 48-65] compared to 74 years [IQR 59-85] than those without air leak ($p=0.0002$). There was no significant difference in gender between the groups. Patients with air leak had evidence of increased disease severity at admission including a significantly higher median CRP (125 [IQR 85-167] compared to 65 [IQR 26-126] as well as more zones affected on CXR (4 vs. 2 in those without air leak)

Patients with air leak were significantly more likely to have an underlying diagnosis of asthma (31.5%) compared to those who did not (3.3%) ($P<0.001$). Asthma was associated with an odds ratio of 13.4 [4.7-36.4] for air leak in COVID-19 infection. 2 patients with asthma had spontaneous pneumothorax or pneumomediastinum. The remaining 4 patients had received ventilatory support prior to the development of these complications.

Air leak in COVID-19 was associated a number of adverse outcomes. Firstly, there was an increased risk of admission to intensive care; 16/19 (84.2%) of patients were admitted versus 15.8% of patients without air leak. Air leak was also associated with a greater length of stay (LOS) of 15 days versus 7 days. Air leak was associated with a higher overall mortality 52.6% compared to 35.3% but this was not statistically significantly different.

Table 1. Demographic and Clinical Characteristics of COVID-19 Patients with and Without air Leak.

	Air leak (N= 19)	No air leak (N= 1029)	P- Values
Median Age (years) [IQR]	63 [48-65]	74 [59-85]	0.0002
Male sex	11 (57.8%)	570 (55.3%)	>0.9999
Respiratory co- morbidities			
COPD	0 (0%)	64 (6.2%)	0.6239
Asthma	6 (31.5%)	49 (4.7%)	0.0003
Median CRP ng/ml	125 [85-167]	70 [31-127]	0.008
Median abnormal CXR zones (at presentation) [IQR]	4 [3-5]	2 [1-4]	0.0008
Mode of ventilation			
CPAP	7 (36.8%)	93 (9.0%)	0.0008
IMV	5 (26.3%)	34 (3.3%)	0.0006
ICU admission			
All (Spontaneous)	16 (84.2%) 6/7 (85.7%)	163 (15.8%)	0.0006
Mortality	52.6%	35.3%	0.147
Median LOS (days) [IQR]	15 [8-36]	7 [3-13]	<0.0001

Air leak occurred both spontaneously and following initiation of non-invasive and invasive ventilation. 36.8% (7/19) of air leaks were spontaneous, 36.8% (7/19) occurred following continuous positive airways pressure (CPAP) ventilation and 26.3% (5/19) occurred post invasive mechanical ventilation (IMV). The average interval from CPAP initiation to air leak was 6.6 days and post initiation of IMV was 5 days.

CPAP and IMV were associated with an increased risk of air leak with an odds ratio (OR) 6.4 [2.5–16.6] and 9.8 [3.7–27.8] respectively. The mode by which air leak occurred as a complication of COVID-19 did not appear to result in significantly different mortality rates as 4/7 (57.1%) of patients with spontaneous air leak died versus 3/7 (42.8%) with CPAP associated air leak and 3/5 (60%) with IMV associated air leak.

Of 8 patients with PTX, either alone or in conjunction with PM, all were managed with intercostal drain insertion. In most of these cases (6/8) the pneumothorax resolved following intercostal drain insertion. Of those with PM alone, most were managed conservatively. Intervention was performed in one patient with pneumomediastinum. The patient was deteriorating with haemodynamic instability and increasing oxygen requirements. While PM is normally managed conservatively, there is no guidance on the management of severe PM in COVID-19, except an isolated case report where mediastinal drains were inserted for tension PM.¹⁴ Our patient did not have a tension PM but in view of the clinical deterioration and extent of PM, a mediastinal drain was inserted via an incision below the xiphoid process. This patient survived and was discharged from the hospital following a length of stay of 54 days. It is unclear if the mediastinal drain was necessary for survival in this case.

7/8 patients with PTX died. 8/11 patients with PM survived. PM appeared to be associated with a better outcome than PTX. (Table 2). In order to ascertain if PTX itself was associated with increased mortality or whether it was simply a marker of parenchymal damage, we compared mortality in age and sex matched controls with similar disease severity based on number of abnormal CXR zones. We found the mortality in 18 matched controls without PTX to be 38.8% (7/18) versus 87.5% (7/8) in those with PTX.

Discussion

Pneumothorax and Pneumomediastinum are severe complications of COVID-19 pneumonia. In this retrospective observational analysis, we find that air leak occurred with an

incidence of 0.56% that remained consistent across both waves of the UK COVID-19 pandemic. CPAP and IMV were associated with a greater than six fold increase in the risk of air leak.

Air leak was associated with several adverse outcomes including longer LOS and admission to ICU. PTX, with or without PM, in the context of COVID-19 pneumonia was almost universally fatal whereas those with alone PM had a lower risk of death. Pneumothoraces were managed with the insertion of intercostal drains while pneumomediastinum was managed mainly conservatively.

Asthma is a recognised underlying risk factor for pneumothorax, as pleural blebs are prone to rupture with increased pleural pressure secondary to bronchospasm and hyperinflation. In this study asthma was associated with a greater risk of air leak, with an OR 13.4, even greater than the risk from barotrauma. This could be due to a combination of increased pleural pressure in asthma worsened by COVID-19 infection, as well as the increased risk of requiring positive pressure ventilation. Clinicians should be aware of the increased risk of air leak in asthmatic patients and be vigilant for PM/PTX in these patients if they deteriorate. Further studies are required to interrogate the relationship between COVID-19, asthma and risk of air leak with its associated adverse outcomes, in order to optimise the management of these patients.

No other studies have specifically investigated the incidence of pneumomediastinum and pneumothorax in COVID-19, but one large retrospective multicentre case series based in the UK estimated an incidence of approximately 1%,³ which is consistent with our own observations. A study investigating PTX alone in COVID-19 also found the incidence to be 0.56%.¹⁵ The overall mortality of 52% from air leak, in our centre, is in line with some studies,^{16,17} but higher than reported in others.³ The mortality difference in our patients with and without air leak is not statistically significant. However, the trend toward increased mortality from air leak, and specifically pneumothorax, may reflect the underlying disease severity of COVID-19 infection^{16,17} or may be due to the PTX itself. It may also be due to the specific mode of ventilation and airway pressures employed in our intensive care setting and the use of higher CPAP positive end expiratory pressures (PEEP) in the early days of the pandemic, or the way in which pneumothoraces were managed with intercostal drain insertion rather than observation. Limited literature exists in the management of pneumothorax in ARDS¹⁸ or COVID-19 pneumonia¹⁹ and further guidance on this would be helpful.

Our study had several limitations. First, the small number of patients with pneumothorax and pneumomediastinum was dependent on the incident caseload during the first and second waves of the COVID-19 pandemic in a single centre institution. This makes the analysis less generalisable. Second, the radiographic data were not analysed in detail. Third, this is a retrospective study in which we did not interrogate the relationship between the onset of COVID-19 symptoms and occurrence of air leak, nor the ventilation parameters in real time. Different ventilation strategies have

Table 2. Management of patients with COVID-19 associated pneumothorax and pneumomediastinum.

		PTX	PTX/PM	PM
Management	Drainage	2	4	1
	Conservative	1	1	10
Mortality		3/3 (100%)	4/5 (80%)	3/11 (27%)

PTX = pneumothorax, PM = pneumomediastinum.

been employed in COVID-19 given the multiple mechanisms of lung injury and the different presentations of the disease, therefore conventional forms of ventilation will not always be the most appropriate.²⁰ A larger study investigating whether ultra-protective ventilation strategies might be employed to prevent and/or manage barotrauma related air leak would be valuable.²¹ Finally, the COVID-19 pandemic appears to have changed significantly over time in terms of available therapy and outcomes. It is possible that our results, including the severity of lung disease and mortality, cannot be extrapolated to future critically ill COVID-19 infected patients.

To our knowledge, this is the first study to date to specifically look at the incidence of PTX and PM in COVID-19 pneumonia, which we find to be 0.56%. This study further adds to the literature by highlighting the risk of asthma (as well as the known risk of barotrauma) in patients with COVID-19 pneumonia in causing air leak, which is associated with adverse outcomes particularly when PTX is present. As the global pandemic continues, studies are urgently required to understand the optimal ventilation strategies to prevent air leak in COVID-19, and its management if pneumothorax or pneumomediastinum do occur.

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Declaration of Conflicting Interests

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Ethical Approval


Not applicable, because this article does not contain any studies with human or animal subjects.

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