Presentation and management of pneumomediastinum in patients with COVID-19 infection

Sulaiman Karim BS, Kenneth Nugent MD

ABSTRACT

Pneumomediastinum, characterized by the presence of air in the mediastinum, can be primary (spontaneous) or secondary. Although relatively rare and usually benign with an incidence of 1 in 7,000 to 12,000 hospital admissions, some cases can develop hemodynamic instability due to mechanical pressure, reducing venous return and may require emergency surgery. Prior to the COVID-19 pandemic, reports of tension pneumomediastinum were infrequent, and there was no consensus on the best surgical approach to manage this condition. This review considers the diverse presentations, underlying causes, and diagnostic and operative approaches in patients with COVID-19 infection and pneumomediastinum. A systematic search of databases, including PubMed and Scopus, was conducted. Articles were reviewed to identify the risk factors for pneumomediastinum, the hemodynamic consequences, and approaches to management in both COVID-19 and non-COVID-19 cases. In patients with COVID-19 infection, pneumomediastinum represents a risk factor for poor outcomes, especially in patients requiring mechanical ventilation. In patients with tension pneumomediastinum, surgical release of mediastinal air is essential and can use suprasternal incisions, lateral sternal incisions, or sternotomy, all with drains. These patients are also at increased risk for tension pneumothorax and may require surgical chest tubes.

Keywords: Pneumomediastinum, COVID-19, hemodynamics, surgical management, clinical challenges

INTRODUCTION

Pneumomediastinum (PM) is a rare condition characterized by the accumulation of air in the mediastinum. It is often benign and managed conservatively with oxygen therapy and monitoring. It can be divided into spontaneous or secondary causes, usually classified as traumatic or iatrogenic. In a few cases, mediastinal air can cause a tension pneumomediastinum (TPM), in which excessive mechanical pressure is exerted on major thoracic vessels, resulting in hemodynamic compromise. Immediate operative intervention is often necessary in TPM and can involve a range of surgical approaches from small parasternal incisions to full sternotomy.

The number of reports of PM has increased during the COVID-19 pandemic. The widespread use of high positive end-expiratory pressure ventilation in COVID-19 patients, coupled with the susceptibility of alveoli to barotrauma with this infection, has led to an increased incidence of PM cases. While the fundamental surgical approach for decompressing TPM remains the same in COVID-19 patients as in pre-pandemic patients, a consensus among critical care clinicians and surgeons has not yet emerged concerning the optimal surgical strategy for decompressing excessive mediastinal pressure, particularly in COVID-19 infections.
This uncertainty is compounded by the difficulty in stratifying the severity of pneumomediastinum, as direct measurements of intramediastinal pressures are technically difficult to establish categories of hemodynamic compromise. The combination of PM and COVID-19 poses unique clinical and technical challenges, and these cases require careful evaluation of surgical options. Addressing this knowledge gap is essential to improve patient care and establish evidence-based guidelines for the surgical management of PM in the context of COVID-19.

**Hemodynamic Considerations and Surgical Strategies for Pneumomediastinum in Non-COVID-19 Patients**

**Pneumomediastinum: Definition and Complications**

Pneumomediastinum, also termed mediastinal emphysema, is a rare, often benign condition in which air enters mediastinal fascial planes. This air often moves out of the mediastinum and causes subcutaneous emphysema, which prevents an increase in intramediastinal pressure. However, without the relief of pressure by air exiting out of this confined compartment, mediastinal air trapping can compress major thoracic vessels, compromise venous return, and lead to the serious complication of tension pneumomediastinum (TPM) with early signs manifesting as pulses paradoxus and electrical alternans. Although PM remains a relatively rare process with 0.001% to 0.01% of adult inpatients or 1 per 7,000 to 1 per 12,000 hospital admissions, some authors have suggested that PM is underreported due to underdiagnosis and because many patients do not seek medical assistance and attribute their symptoms to musculoskeletal pain.

**Diagnostic Evaluation**

In general, the diagnosis of PM starts with a standard chest x-ray. However, unless x-ray findings are unequivocal and clinical signs are not better explained by another diagnosis, computed tomography (CT) of the thorax is required for a definitive diagnosis. Studies have demonstrated that x-rays have limited sensitivity and detect approximately 30% of PM cases. Chest x-rays often miss small air amounts, a limitation that can be overcome using CT scans, which also help differentiate from pneumopericardium.

**Historical Perspectives and Terminology**

Recognition of this pathophysiological process was reported as early as 1827 by Laennec, who described “grating and bubbling” rales during respiration. Müller further expanded on the physical examination findings associated with PM in 1888 by describing subcutaneous emphysema as bubbling crepitations synchronous with the heartbeat. These early clinical descriptions were again described by Hamman in 1939 in a case series of postpartum patients, leading to the term “Hamman’s Crunch.” In 1944, Macklin and Macklin studied PM using animal models. They concluded that PM involved the following events: rupture of alveoli allows air to enter the lung interstitium and move toward the mediastinum along bronchovascular bundles, driven by a pressure gradient. This process is now referred to as the Macklin effect.

**Hemodynamics in Pneumomediastinum**

The Macklin effect associated with spontaneous pneumomediastinum (SPM) can develop as a result of the spread of any intrathoracic gas into the mediastinum; however, it is more frequently associated with rupture of alveoli located adjacent to bronchioles or pulmonary vessels by barotrauma. Spontaneous pneumomediastinum often develops as a consequence of a strong Valsalva maneuver, severe coughing, or vomiting in patients with parenchymal lung diseases, such as asthma, COPD and interstitial pneumonia, which predispose them to barotrauma. Secondary PM is usually associated with trauma or iatrogenic causes, such as surgery or positive pressure ventilation. In recent decades, the frequency of iatrogenic PM cases has increased due to the increased use of positive pressure ventilatory support.

The Macklin and Macklin study focused on describing the clinical features of mediastinal air trapping,
which included increased mediastinal pressure, decreased venous return, impaired cardiac function, and hypotension. However, their research did not report intrathoracic hemodynamics using central venous pressure (CVP) measurements, and they did not perform right heart catheterization, which was not available at that time.

There is an indirect mention of increased CVP in a study by Shennib and colleagues in which insertion of a central venous catheter demonstrated markedly elevated CVP in the setting of TPM secondary to barotrauma in a ventilated unresponsive status asthmaticus patient. In a case series, Dondelinger and colleagues reported four patients with elevated CVP in the setting of TPM. Their study findings were consistent with those of Macklin and Macklin, and they suggested that the limited availability of clear clinical and autopsy-based event sequences probably account for the limited number of reports in the literature.

Hemodynamics comparison with tension pneumothorax

The hemodynamic effects of complicated and uncomplicated PM have not been definitively investigated. However, there is detailed research on another condition involving air trapped in the thoracic cavity, i.e., tension pneumothorax (PTX).

Barton and colleagues did animal studies to determine whether cardiovascular collapse in PTX is caused by mechanical pressures or hypoxemia. Their results supported the hypothesis that significant cardiovascular collapse is primarily due to early hypoxia, contrary to the findings of the study by Macklin and Macklin. Barton et al. concluded that the significant decrease in cardiac output (CO) throughout the earlier stages of PTX is not associated with a reduction in mean arterial pressure. Instead, they found cardiovascular collapse is secondary to severe hypoxemia, with oxygen saturation dropping below 50%. To investigate this finding, Martin and colleagues created a tension pneumothorax with intrathoracic CO2 using a trocar in a swine model, thus allowing for better pressure titration. They recorded central hemodynamic changes, including CVP, wedge pressure, and cardiac output, linked to PTX. Their animal model replicated the classically described sequence in humans, specifically cardiovascular collapse secondary to mechanical pressures.

While PM is typically considered benign, its clinical importance significantly increases when associated with certain clinical situations such as mechanical ventilation, esophageal rupture, and severe trauma. The potential clinical significance and the absence of studies with controlled scientific data regarding the underlying physiology of PM indicate the need for more research to understand this syndrome.

Conservative management of spontaneous pneumomediastinum in non-COVID-19 patients

The diagnostic and therapeutic guidelines for benign SPM remain uncertain in the literature. Supportive treatment is the primary approach for hemodynamically stable patients with PM with minimal symptoms, and this includes analgesia, oxygen therapy, and antitussives. As with pneumothorax, supplemental oxygen therapy speeds up the spontaneous resolution of PM by increasing the gradient for nitrogen washout from the mediastinal tissue into the blood. Most patients will be safe for eventual discharge with outpatient follow-up care. However, a small minority of patients, depending on the underlying cause, may require further diagnostic evaluation and, in some cases, surgical management in the rare instance of developing TPM.

Surgical management of spontaneous pneumomediastinum in non-COVID-19 patients

The first reported successful surgical approach to PM was recorded by Tietgal when he performed a mediastinotomy in 1911. Operative management is recommended for patients with a deteriorating hemodynamic status or patients presenting with significant subcutaneous emphysema. Since then,
the therapeutic approach has focused on alleviating compromised venous return with less invasive measures, including minor suprasternal or supraclavicular incisions.3,18,20

Surgical intervention for SPM is infrequently required, and there is limited information in the medical literature. Gunluoglu and colleagues reported a series of 23 patients who developed SPM, and three required subcutaneous air drainage to evacuate extensive subcutaneous emphysema.26 Their surgical approach involved an incision at the supra-ternal notch or the pectoral area. Another case series reported by Mondello and colleagues included 18 patients who developed SPM between 1998 and 2005, and ten required drainage of subcutaneous air, but the exact technique was not described in detail.27 In this series, the recovery of two patients was complicated by PTX, which required chest tube decompression. Perna and colleagues followed 47 patients who presented with SPM between 2000 and 2008.28 A single case evolved to TPM with PTX, which was decompressed with right-sided thoracotomy; the patient was discharged on postoperative day 3.

While surgical interventions for SPM remain underreported in the literature, insights can be obtained by examining surgical techniques used to treat TPM secondary to traumatic or iatrogenic causes. Dondelinger and colleagues describe their “limited mediastinostomy” approach as another method of treating TPM, in which an incision is created above or below the sternum, below the clavicle, or lateral to the sternum.20 Subsequently, blunt dissection into the retrosternal space or placement of a chest tube into the mediastinum is performed. Dondelinger and colleagues also described percutaneous CT-guided insertion of mediastinal drainage catheters, and insertion of a large-bore chest tube through the subxiphoid space was described by Moore and colleagues.20,29 Cases involving mediastinal shift and tracheal compression have required thoracotomy, and emergency situations have required emergency cervical mediastinotomy.23,28,30 If these methods do not successfully alleviate TPM, sternotomy may be necessary.3,20

As the surgical approaches for managing complicated PM continue to evolve, future studies should assess the techniques used, outcomes, and complications.

**ETIOLOGY AND SURGICAL MANAGEMENT PNEUMOMEDIASTINUM IN PATIENTS WITH COVID-19**

**SPONTANEOUS PNEUMOMEDIASTINUM IN COVID-19 PATIENTS**

The suspected etiology of spontaneous pneumomediastinum (SPM) in COVID-19 patients probably has a mechanism similar to that found in acute respiratory distress syndrome (ARDS). This idea is supported by prior research during the SARS-CoV-1 pandemic, when it was found that damage to the lung tissue and surrounding interstitial space makes the alveoli more prone to rupture, leading to subsequent air dissection along the peribronchovascular sheath, a phenomenon explained by the Macklin effect.15,31,32 The incidence of PM in COVID-19 patients is higher (1:5498) than in the general population (1:7000 to 1:12000).33–35

Several case reports recommend managing spontaneous PM using conservative approaches, in the absence of hemodynamic compromise and in the context of COVID-19 infection.34,36,37 Nonetheless, in the context of COVID-19, the risks associated with SPM are considerably higher than in patients without this infection. A case series by Chowdhary and colleagues, which included 22 reports and 35 cases of SPM in COVID-19 positive patients, concluded that an SPM diagnosis may correlate with a severe illness trajectory and increased mortality rates.38 Therefore, the occurrence of SPM necessitates increased clinical caution.

In a cohort of non-ventilated COVID-19 patients who developed SPM, there is limited documentation on the surgical management of cases that progress to hemodynamic compromise (TPM). A previous study from 2004 focused on non-ventilated SARS-CoV-1 patients and described institutional experiences with five cases of SPM that required surgical intervention.31 Subsequent research in the context of COVID-19 reported similar institutional experiences, detailing
two cases of non-ventilated patients with SPM who required surgical management due to hemodynamic compromise. Lin and colleagues reported a case series that included a rare instance of TPM in a patient who was readmitted seven days after being taken off mechanical ventilation. Notably, the patient did not require supplemental oxygen at the time of discharge, and while the condition was not entirely spontaneous, its presentation was notably delayed. The paucity of comprehensive reports on the surgical management of SPM in non-ventilated COVID-19 patients, particularly those progressing to hemodynamic compromise, indicates a significant gap in the current medical literature that warrants more investigation.

Secondary pneumomediastinum in COVID-19 patients

Mechanical ventilation is more likely to cause barotrauma in individuals with underlying lung disease, especially in patients with ARDS, SARS, or COVID-19 infection. Some debate exists on the exact cause of increased susceptibility from mechanical ventilation; however, the consensus is that SARS and COVID-19 cause severe diffuse damage to the alveoli. This damage can lead to alveolar rupture and the subsequent development of PM. Urigo and colleagues cite Gralinski and Baric, who hypothesize this is due to the breakdown of membrane integrity caused by infection of both type I and II pneumocytes.

Hospitalized COVID-19 patients may receive intensive respiratory support, including high positive end-expiratory pressure ventilation. Due to a pronounced vulnerability to barotrauma, PM occurs fairly often in COVID-19 patients undergoing mechanical ventilation, with documented occurrences reaching up to 15% in randomized controlled trials. A more recent study by Bellentti and colleagues found that nearly 25% of their mechanically ventilated patients developed PTX or PM. In another study of mechanically ventilated patients, COVID-19 ARDS patients had a higher incidence of pneumomediastinum (13.6%) than non-COVID-19 ARDS patients (1.9%). Consequently, mechanical ventilation-induced pneumomediastinum occurs frequently in COVID-19 patients and has a higher morbidity and mortality risk compared to SPM.

Management

Compared to non-COVID-19 patients, surgical management is not entirely different. To the best of our knowledge, only one case series features a PM case unrelated to mechanical ventilation in which mediastinal emphysema improved with chest tube decompression. In this case, Brito and colleagues concluded that progressive PM, TPM, or PTX can be managed by the insertion of a chest tube connected with continuous suction.

There is limited literature describing the surgical approaches for managing SPM in the context of COVID-19. Nonetheless, prior reports on surgical approaches for progressive PM in non-COVID patients provide an outline for surgical approaches for managing progressive secondary PM. Thuan and colleagues outline three broadly used approaches. The first method to surgically decompress the mediastinum creates an incision in the suprasternal notch followed by blunt dissection. Thuan and colleagues made two attempts using this approach in a single report; unfortunately, both patients died, prompting these clinicians to consider alternative methods. The second approach described includes a modified Chamberlain procedure in which a left parasternal anterior mediastotomy is performed; one case reports this approach at bedside in the ICU with improvement in hemodynamic status. The third surgical approach described involves mediastinal drainage via suprasternal and subxiphoid incisions. Seven cases were managed with this approach, and the hemodynamic status improved in all seven patients. Additional methods use bilateral pleural or intercostal drains and sub-clavicular incisions to evacuate air-trapping. Nevertheless, using these methods continues to be discussed among various authors.

Clinical studies

Two case series have provided important information about the management of pneumomediastinum in the context of COVID-19 infection. These series effectively highlight the increased occurrence of pneumomediastinum in ventilated patients, as discussed
by Wali et al., and in non-ventilated patients, as discussed by Chowdhary et al.\textsuperscript{38,50}

Wali and colleagues report a cohort of five patients with severe secondary PM after intubation referred to their tertiary thoracic surgery department in a 7-day period in April 2020.\textsuperscript{50} The results reported by Wali and colleagues agree with the consensus that mechanically intubated COVID-19 patients are at greater risk for barotrauma-induced PM. The authors describe the tracheobronchial injury in the setting of “aggressive” ventilation measures and larger-bore endotracheal tubes. Nonetheless, the study does not discuss the etiology beyond this. The authors attribute repositioning maneuvers as one possible contributing factor to tracheobronchial injury leading to PM. Risk factors were not directly measured in this cohort, but comorbid conditions included hypothyroidism, smoking, insulin-dependent diabetes, and asthma. The Carlson comorbidity score ranged from 0 to 2. Beyond this, risk factors were not discussed. Surgical management in this cohort ranged from conservative measures (n = 1) to bilateral intrapleural and subcutaneous drains (n = 2). They report a mortality rate of 40% and recommend that future research investigate the effectiveness of subxiphoid and suprasternal incisions. Outcomes were not discussed in detail; the two patients with bilateral intrapleural chest drains with bilateral subcutaneous drains (n = 2) survived, and two patients without subcutaneous drains died. The supportive treatment patient survived, but overall severity was rated relatively moderate. This study reports that the development of PM is an adverse prognostic marker, and the authors advocate using bilateral chest and subcutaneous drains to manage severe PM.

Chowdhary and colleagues reviewed 22 reports from the medical literature, which included 35 patients with COVID-19-associated spontaneous pneumomediastinum in March 2021.\textsuperscript{38} Their case series findings were consistent with the three cases they reported from their institution. The reported etiology was also consistent with previous studies, and they attributed SPM to the well-described Macklin effect. Their cohort included 35 patients (28 males, mean age 55.6 ± 16.7 years). Of the included patients in this cohort, 57.1% (n = 18) had chronic disease, 25.7% (n = 9) were previously healthy, and 17.1% (n = 6) did have chronic disease recorded in their report. Risk factors beyond this were not reported. While this paper did not directly discuss operative management for SPM, they used decompressive chest tubes for concomitant PTX. Their cohort of three patients was managed with supportive treatment. The mortality rate in their case series was 28.6% (n = 10 out of 35), comparable to the 33.3% (n = 1 out of 3) rate observed in their institutional cases. The authors agree with the consensus that the presence of SPM may indicate a poor prognostic marker in COVID-19 patients. In this context, the authors urge more studies to investigate the disease severity and poor outcomes associated with SPM.

Both studies agree that the development of PM or SPM represents as an unfavorable prognostic indicator in patients infected with COVID-19. They also agree on this disease’s general etiology and underlying risk factors. Nonetheless, neither study provides a comprehensive set of risk factors for adverse outcomes other than the use of mechanical ventilation in one study. Chowdhary and colleagues provide limited details on operative management for patients who develop SPM. Future research should focus on evaluating the efficacy of different surgical methods and identifying the underlying risk factors for SPM development.

**Conclusions**

The studies considered in this review have reported that pneumomediastinum can occur in patients with COVID-19 infection prior to the use of any positive pressure ventilation. COVID-19 infection is a risk factor for the development of pneumomediastinum during mechanical ventilation with positive pressures. The accumulation of air in the mediastinum can cause a significant hemodynamic compromise with a reduction in blood return to the right heart, decreasing cardiac output and blood pressure. This results in an emergency situation in which the mediastinal air must be vented out of the mediastinum, usually using a surgical procedure. Several surgical approaches are used in this situation; in general, most approaches require inserting a drainage tube into the
mediastinum. Patients who also have a pneumothorax should have surgical chest tubes placed.

The medical information available on COVID-19 patients with pneumomediastinum is limited. Important considerations include the simultaneous presence of a pneumothorax and the accumulation of air in other locations, such as subcutaneous tissue, the pericardium, and the abdomen. Patient stratification by severity is difficult due to lack of direct measure of mediastinal pressure. Patient stratification might be based on central venous pressure, blood pressure, oxygen requirements, and PEEP levels, but these methods might confuse cause with effect. Patients with pneumomediastinum and severe hemodynamic compromise or extremely abnormal gas exchange likely have persistent pneumomediastinum and potentially benefit from more definitive surgical procedures to evacuate mediastinal air. Finally, COVID-19 patients with spontaneous pneumomediastinum need to be characterized and compared with COVID-19 patients who develop pneumomediastinum during mechanical ventilation support.

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**From:** Department of Internal Medicine, Texas Tech University Health Sciences Center, Lubbock, Texas

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