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Pneumothorax in Non-ventilated Patients with COVID-19 Pneumonia: Management and Outcome of a Rare Entity

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ABSTRACT

Background: Rapid clinical deterioration of patients with COVID-19 pneumonia has three potential causes including: Disease progression, pulmonary embolism, and pneumothorax. Pneumothorax is a serious complication in patients with parenchymal lung disease, which may require rapid intervention.

Objective: This study aimed to review management and outcome of spontaneous pneumothorax in our hospitalized non-ventilated patients with COVID-19 pneumonia, and to evaluate the relation of pneumothorax with in-hospital outcome.

Patients and methods: This retrospective study included non-ventilated patients who had spontaneous pneumothorax associated with moderate or severe COVID-19 pneumonia. Pneumothorax was managed considering hemodynamics and size of pneumothorax. When indicated, tube thoracostomy was performed under strict protective measures.

Results: There were 12 cases of spontaneous pneumothorax out of 136 initially non-ventilated COVID-19 patients (8.82%), with median age of 62.5 years. The imaging features included unilateral pneumothorax (91.7%), bilateral pneumothorax (8.3%), subcutaneous emphysema (41.7%), tension pneumothorax (16.7%), pneumomediastinum (16.7%), and hydropneumothorax (8.3%). After median hospital stay of 13 days, the recovery rate was 41.7%, while death was reported in 58.3%. Treatment of pneumothorax was conservative in 58.3% and tube thoracostomy in 41.7% with median chest tube duration of 4 days. Pneumothorax resolved in all patients with no need for further surgical intervention. In comparison with survivors, died patients had higher frequency of severe pneumonia (P= 0.02) and higher ferritin levels (P= 0.04). Severe pneumonia at presentation and the need for invasive ventilation later on had significant impacts on survival after presentation of pneumothorax (P-values of Log Rank test = 0.011 and 0.027 respectively).

Conclusion: Pneumothorax is a rare but serious complication of COVID-19, which requires early diagnosis and treatment. Presentation with severe pneumonia and later on deterioration affected prognosis of initially non-ventilated COVID-19 patients with spontaneous pneumothorax.

Keywords: Coronavirus, COVID-19, Pneumothorax, Pneumomediastinum, Tube thoracostomy, Bullectomy.

INTRODUCTION

The respiratory infection caused by the novel coronavirus disease 2019 (COVID-19) has led to a global health problem since its first appearance in Wuhan, China at the end of December 2019, followed by widespread of the virus outside China and announcement of COVID-19 infection as a pandemic in March 2020. As of 26 December 2020, more than 80 million cases of COVID-19 infection have been reported worldwide including more than 1.75 million deaths [1, 2].

COVID-19 infection leads to viral pneumonia of varying degrees of severity, which may progress to severe lung damage, acute respiratory distress syndrome (ARDS), and death. Spontaneous pneumothorax is a rare complication of COVID-19 infection that has been reported in less than 1% of patients and may occur in the absence of mechanical ventilation [1, 2]. This study aimed to review our institutional experience with management and outcome of spontaneous pneumothorax in hospitalized non-ventilated COVID-19 patients, and to evaluate the relation of this rare entity with in-hospital outcome.

PATIENTS AND METHODS

Patients: This retrospective study included COVID-19 patients who developed spontaneous pneumothorax after their admission at our hospital, between June and September 2020.

Inclusion criteria: Peripheral oxygen saturation (SpO_2) < 93%, respiratory rate > 30 breath/minute, and imaging evidence of lung infiltrates. Patients with non-iatrogenic, non-traumatic pneumothorax (isolated or combined with pneumomediastinum) during their hospital stay for treatment of COVID-19 pneumonia.

Exclusion criteria: Patients not on mechanical ventilation before diagnosis of pneumothorax, but invasive ventilation could be indicated later on. Patients with traumatic, iatrogenic, or post-intubation pneumothorax and patients with isolated pneumomediastinum.

Protocol of hospital management: The diagnosis of COVID-19 was confirmed by RT-PCR test. Chest CT was performed for initial evaluation after admission and when it was indicated during hospitalization. Typical imaging findings of COVID-19 were peripheral ground-glass opacities and bilateral linear consolidation. In-hospital laboratory investigations included complete blood counts (leucocytes, lymphocytes, neutrophils, and platelets), blood biochemistry (liver function tests, renal functions tests, blood glucose, lactate dehydrogenase, and myocardial enzymes), coagulation profile (prothrombin time and

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D-dimer), inflammation biomarkers (C-reactive protein (CRP) and Ferritin), and blood gas analysis. The hospitalized patients had moderate or severe/critical illness. Patients with moderate severity of COVID-19 presented with fever and SpO_2 < 93%, while severe/critical disease was defined by fever with SpO_2 < 88%, and signs of acute respiratory distress syndrome (ARDS).

The target of arterial O_2 level ($SatO_2$) was 93–96%. Patients with moderate severity of COVID-19 had symptomatic treatment and oxygen therapy through nasal cannula or face mask. Patients with severe disease were admitted to intensive care unit and received oxygen therapy through nasal cannula or face mask, or received non-invasive O_2 therapy using CPAP. Patients with ARDS had mechanical ventilation with high positive end-expiratory pressure (PEEP).

Medical treatment of our patients with COVID-19 included chloroquine for 5–20 days, antibiotic prophylaxis with Azithromycin, Meropenim or Imipenim, and third-generation Cephalosporins, and anticoagulation therapy particularly in patients with high D-dimer. Steroids were given for patients with severe or critical illness for 7-10 days. At our institution, the proposed plan for management of spontaneous pneumothorax in non-ventilated patients with COVID-19 pneumonia was on the based-on guideline recommendations by the British Thoracic Society considering the hemodynamic status and the size of pneumothorax on imaging studies (Figure 1).

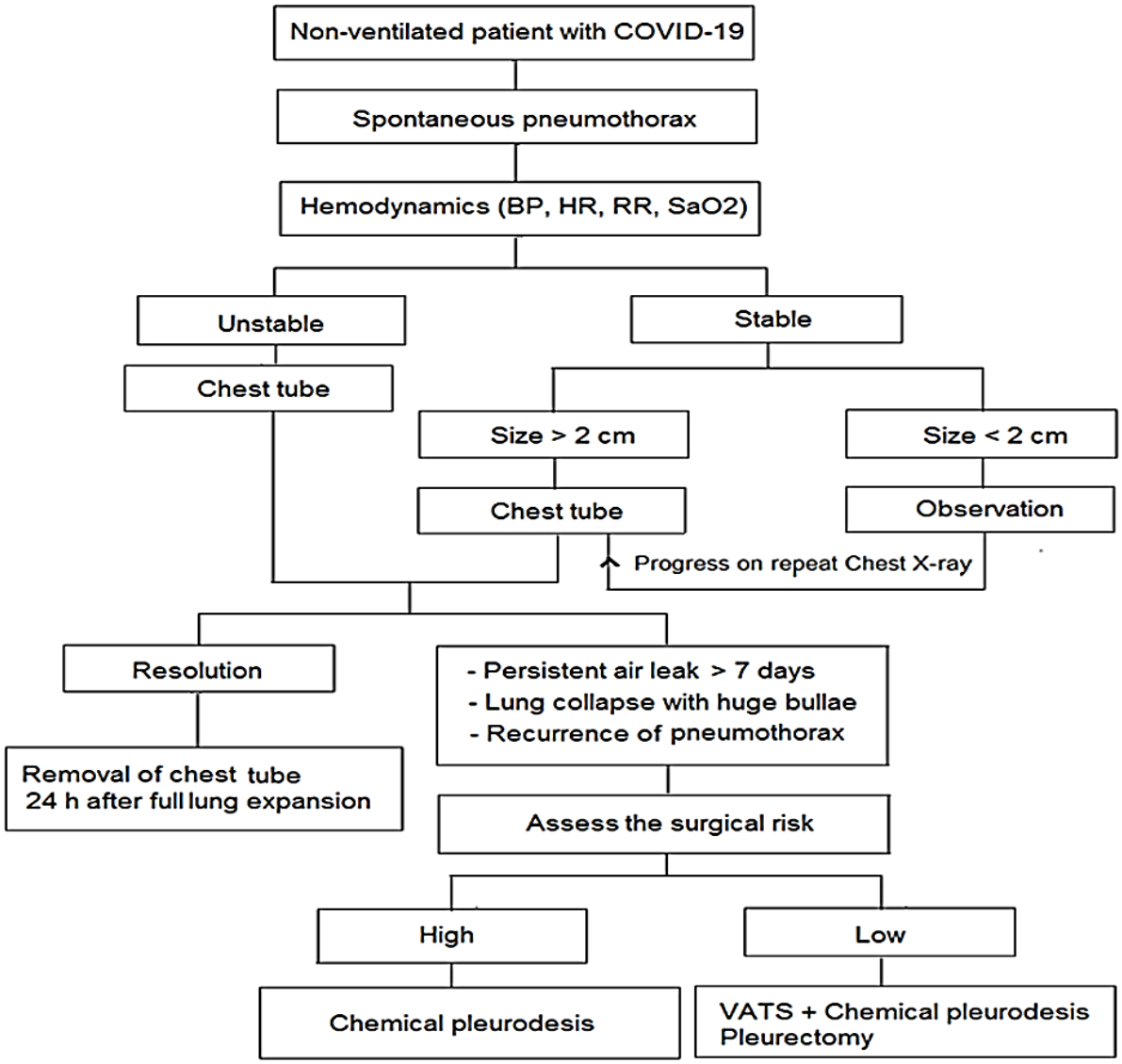

Figure (1): Algorithm for surgical management of spontaneous pneumothorax in non-ventilated patients with COVID-19 pneumonia.

The protective measures during tube thoracostomy at our institution included: (1) Performing the procedure in an airborne infection isolation room, (2) Wearing personal protective equipment, (3) Preparing the chest tube drainage system before starting the procedure, (4) Providing all requirements of the procedure within the room, and assigning a person outside the room to provide any additional requirements, (5) Reducing the number of staff in the room, (6) a 14-28 Fr chest tube is securely connected to the drainage system before its insertion, (7) Reducing aerosol dissemination by adding anti-viral filter to the output vent of the bottle or connecting the tube drainage system to wall suction, (8) Performing the procedure under complete aseptic condition, (9) Making small skin incision and applying wet gauze to control gush of air after opening of the pleura, (10) Tightening the skin closure around the chest tube, and (11) Reduction of tube handling after its placement.

Data collection: The data of interest were collected from the medical records of the patients including: i) Demographic characteristics; ii) COVID-19 related data including initial symptoms and signs, prior health status and comorbidities, initial imaging features, average of laboratory results during hospitalization, ICU and hospital length of stay, methods of treatment, complications, and outcome (death or recovery); and iii) Pneumothorax-related data including specific imaging features and methods of treatment.

Ethical approval: This study has been approved by Minia Faculty of Medicine's Ethics Committee. Following receipt of all information, signed consent was provided by each participant. The study adhered to the Helsinki Declaration throughout its execution.

Statistical analysis

All data were tabulated using Microsoft Excel spreadsheets. The statistical analysis was performed using IBM SPSS statistical software version 20.0 and R version 4.0.3. Quantitative data were expressed as median and interquartile range (IQR), while qualitative data were expressed as number and percent. Due to small sample size of the studied condition, Fisher's exact test was used to compare qualitative data and Exact Mann-Whitney rank-sum test was used to compare quantitative data. Kaplan–Meier survival curves were used to evaluate survival data. Log Rank (Mantel-Cox) test was used to examine equality of survival distributions for selected risk factors. P-values ≤ 0.05 were considered significant.

RESULTS

Out of 136 patients with confirmed diagnosis of COVID-19 pneumonia who were admitted at our institution, 12 patients (8.82%) had spontaneous pneumothorax (not induced by mechanical ventilation, medical procedures, or trauma) during their hospitalization. Our series included 7 male and 5 female patients with median age of 62.5 years (range: 40-75 years). Demographics, symptoms, comorbidities, diagnostic imaging features, laboratory results, treatment, and complications of COVID-19 pneumonia in the studied patients are presented in table (1). The median duration of COVID-19 symptoms before admission was 6 days (range: 2- 10 days). After median ICU stay of 8.5 days (range: 3-18 days) and median total hospital stay of 13 days (range: 5-21 days), 5 patients (41.7%) showed recovery and were discharged home while 7 patients (58.3%) died. The causes of death were respiratory failure (25%), multiorgan failure (16.7%), renal failure (8.3%), and septic shock (8.3%).

Table (1): Demographics, symptoms, comorbidities, diagnostic imaging features, laboratory results, treatment, and complications of COVID-19 pneumonia in 12 non-ventilated patients with COVID-19-related pneumothorax (PTX)

Characteristics	**COVID-19 with PTX (n=12)**
Age (years)	62.5 (40-75)
Age (≥70 years)	2 (16.7%)
Gender, male	7 (58.3%)
Smoking (current or ex-smoker)	6 (50%)
COPD	5 (41.7%)
Comorbidities:	
Hypertension	5 (41.7%)
Diabetes mellitus	4 (33.3%)
Renal failure	2 (16.7%)
Heart disease	1 (8.3%)
Duration of symptoms before admission	6 (2-10)
Initial symptoms of COVID-19:	
Fever	12 (100%)
Cough	12 (100%)
Dyspnea	10 (83.3%)
Fatigue	8 (66.7%)
Headache	7 (58.3%)
Diarrhea	2 (16.7%)
Vomiting	1 (8.3%)
Initial imaging features of COVID-19:	
Bilateral ground glass opacities	12 (100%)
Bilateral consolidations	10 (83.3%)
Crazy paving	9 (75%)
Severity of COVID-19:	
Moderate	
Severe	5 (41.7%)
Laboratory results:	
Leucocytes ($\times 10^9$/L)	12.30 (8.30-20)
Neutrophils ($\times 10^9$/L)	10.17 (5.78-18)
Lymphocytes ($\times 10^9$/L)	1.41 (0.50-2.68)

Characteristics	COVID-19 with PTX (n=12)
Platelets count ($\times 10^9$/L)	114 (65-314)
C-reactive protein (mg/L)	96 (12-196)
Ferritin (µg/L)	879.50 (33-2400)
D dimer (mg/L)	2.30 (0.20-4)
Lactate dehydrogenase (U/L)	765 (288-1600)
Arterial blood gases:	
pH	7.39 (7-7.83)
P_aO_2 (mmHg)	47.50 (40-74)
P_aCO_2 (mmHg)	32 (20-52)
HCO^- (mEq/L)	20.50 (16-28)
Treatment of COVID-19:	
Chloroquine	12 (100%)
Azithromycin	12 (100%)
Meropenim	9 (75%)
Imipenim	1 (8.3%)
Cephalosporins	2 (16.7%)
Non-respiratory complications of COVID-19:	
Acute renal failure	2 (16.7%)
Hepatic injury	1 (8.3%)
Uncontrolled diabetes mellitus	3 (25%)
Hospital durations:	
ICU stay (days)	8.50 (3-18)
Hospital stay (days)	13 (5-21)
Outcome of COVID-19:	
Death	7 (58.3%)
Recovery	5 (41.7%)
Causes of death:	
Respiratory failure	3 (25%)
Multiorgan failure	2 (16.7%)
Renal failure	1 (8.3%)
Septic shock	1 (8.3%)

Median and IQR: Non-parametric test. Data were expressed as number (percent) or median (IQR).

Diagnostic features and treatment of pneumothorax in 12 non-ventilated patients with COVID-19 pneumonia are presented in table (2) and figure (2). The median time interval from admission to presentation of spontaneous pneumothorax was 5 days (range: 1-12 days). The imaging features were unilateral pneumothorax in 11 patients (91.7%), bilateral pneumothorax in one patient (8.3%), subcutaneous emphysema in 5 patients (41.7%), tension pneumothorax in 2 patients (16.7%), concomitant pneumomediastinum in 2 patients (16.7%), and hydropneumothorax in one patient (8.3%). Our patient with bilateral pneumothorax had a history of COPD, and manifested concomitant subcutaneous emphysema, pneumomediastinum, and lung bullae. This female patient showed resolution of pneumothorax after insertion of chest tubes, but she died due to multiorgan failure. Both patients of tension pneumothorax were male patients who had unilateral tension pneumothorax, and one of them had a history of COPD. Tension pneumothorax resolved in both patients using chest tube, but one patient died due to multiorgan failure. Two female patients (16.7%) had additional pneumomediastinum; one of them had COPD and bilateral pneumothorax. The treatment of pneumothorax was conservative in one patient and chest tube in the other patient. Both patients expired due to septic shock in one patient and multiorgan failure in the other patient. Treatment of pneumothorax was conservative in the most of cases (58.3%). Chest tube placement was required in 5 patients (41.7%) with median duration of 4 days (range: 2-7 days). Pneumothorax resolved in all of patients with no need for further surgical intervention (Bullectomy and pleurodesis). Nine patients (75%) required nasal cannula or non-invasive ventilation for oxygen therapy while three patients (25%) required mechanical ventilation.

Table (2): Diagnostic features and treatment of pneumothorax in 12 non-ventilated patients with COVID-19 pneumonia

Characteristics	COVID-19 with PTX (n=12)
Time interval from admission (days)	5 (1-12)
Imaging extent of pneumothorax:	
Unilateral (Right)	8 (66.7%)
Unilateral (Left)	3 (25%)
Bilateral pneumothorax	1 (8.3%)
Tension pneumothorax	2 (16.7%)
Pneumomediastinum	2 (16.7%)
Sucutaneous emphysema	5 (41.7%)
Hydropneumothorax	1 (8.3%)
Treatment:	
Conservative	7 (58.3%)
Chest tube insertion	5 (41.7%)
Duration of chest tube (days)	4 (2-7)
Oxygen therapy:	
Nasal cannula or non-invasive ventilation	9 (75%)
Intubation and mechanical ventilation	3 (25%)

Data were expressed as number (percent) or median (IQR)

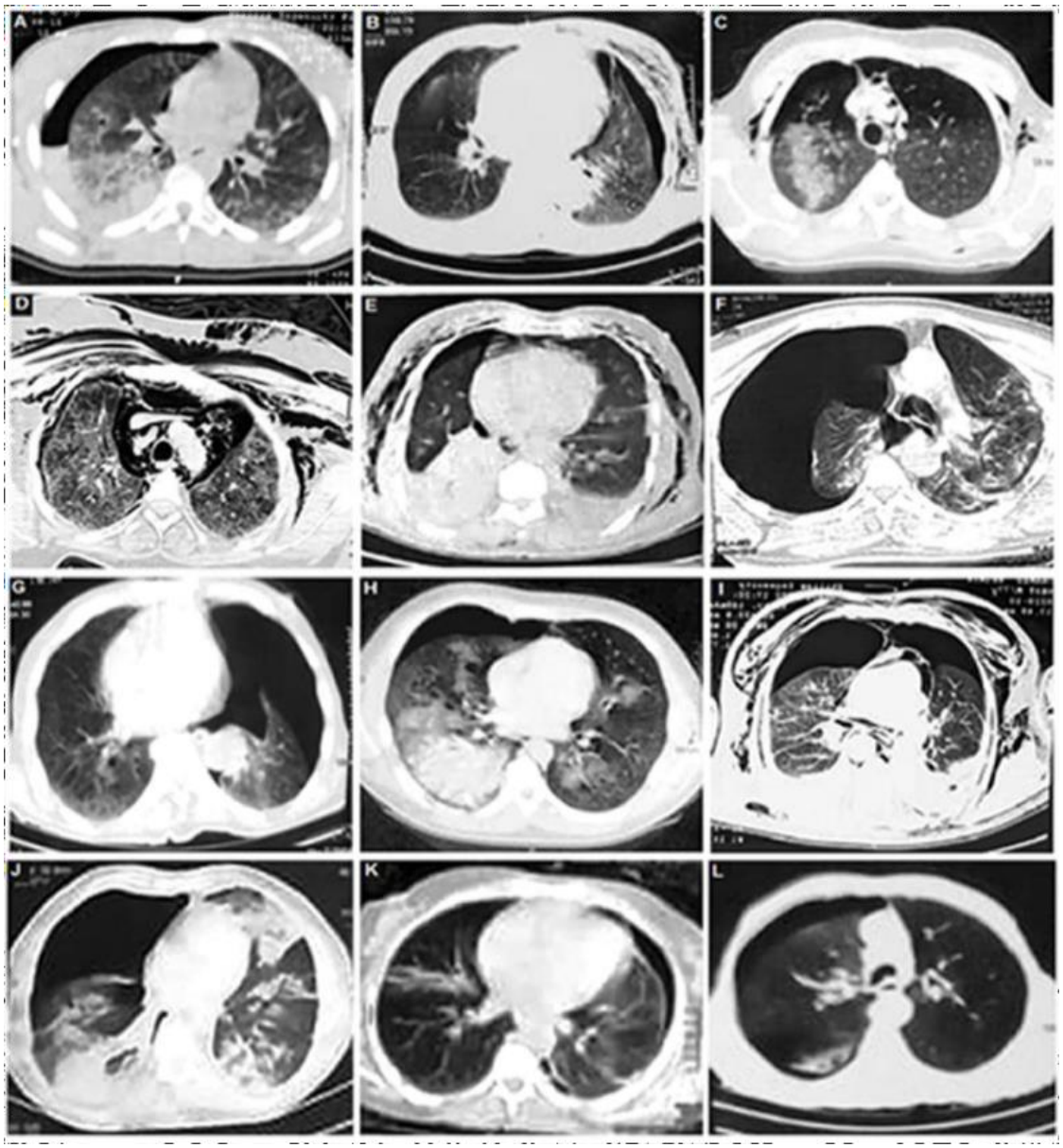

Figure (2): Images of chest computed tomography of 12 non-ventilated patients with COVID-19 related pneumothorax. (A) Hydropneumothorax, (B, C, E, G, H, K & L) isolated pneumothorax, (D & I) pneumothorax with pneumomediastinum and (F & J) tension pneumothorax.

Comparing clinical and diagnostic features of COVID-19 between survivor and died patients with COVID-19 related pneumothorax (Table 3) revealed non-significant differences except for significantly higher frequency of severe pneumonia (P= 0.028) and higher ferritin levels in died patients (P= 0.04). Kaplan–Meier survival curves of 12 non-ventilated patients with COVID-19 related pneumothorax during their hospital stay after diagnosis of pneumothorax are presented in figure (3). In all patients, the median survival time after diagnosis of pneumothorax was 16 days (95% Confidence Interval: 4.84-27.15). Comparison of the survival distributions for different levels of selected risk factors showed P-values of 0.31 for history of COPD, 0.027 for moderate versus severe pneumonia at admission, and 0.011 for invasive versus non-invasive oxygen therapy, which reflects a significant impact of severe pneumonia at presentation and the need for invasive ventilation on survival time after diagnosis of pneumothorax.

Table (3): Clinical and diagnostic features of COVID-19 in survivor and died patients with COVID-19 related pneumothorax

Characteristics	**Survivors (n=5)**	**Died (n=7)**
Age (years)	62 (45-65)	65 (40-75)
Age (≥70 years)	0	2 (28.6%)
Gender, male	3 (60%)	4 (57.1%)
Smoking	3 (60%)	3 (42.9%)
COPD	2 (40%)	3 (42.9%)
Comorbidities:		
Hypertension	2 (40%)	3 (42.9%)
Diabetes mellitus	2 (40%)	2 (28.6%)
Renal failure	0	2 (28.6%)
Duration of symptoms (days)	7 (6-9)	6.5 (5-10)
Initial symptoms of COVID-19:		
Fever	5 (100%)	7 (100%)
Cough	5 (100%)	7 (100%)
Dyspnea	4 (80%)	6 (85.7%)
Fatigue	3 (60%)	5 (71.4%)
Headache	1 (20%)	6 (85.7%)
Diarrhea	1 (20%)	1 (14.3%)
Vomiting	0 (0%)	1 (14.3%)
Initial imaging features of COVID-19:		
Bilateral ground glass opacities	5 (100%)	7 (100%)
Bilateral consolidations	4 (80%)	7 (100%)
Crazy paving	4 (80%)	5 (71.4%)
Severity of COVID-19:		
Moderate	5 (100%)	2 (28.6%)
Severe	0 (0%)	5 (71.4%) *
Laboratory results:		
Leucocytes ($\times 10^9$/L)	11.6 (8.4-13.4)	16.4(8.3-20)
Neutrophils ($\times 10^9$/L)	8.12 (5.88-10.56)	14.76(5.78-18)
Lymphocytes ($\times 10^9$/L)	2.1(1.08-2.68)	1.19 (0.5-2.22)
Platelets count ($\times 10^9$/L)	113 (70-314)	115 (65-196)
C-reactive protein (mg/L)	96 (12-96)	98 (24-196)
Ferritin (µg/L)	600 (46-870)	1500 (33-2400) *
D dimer (mg/L)	0.95 (0.5-3.4)	2.5 (0.2-4)
Lactate dehydrogenase (U/L)	600 (488-1532)	960 (288-1600)
Arterial blood gases:		
pH	7.39 (7-7.47)	7.4 (7.32-7.83)
P_aO_2 (mmHg)	55 (45-68)	45 (40-74)
P_aCO_2 (mmHg)	32 (30-52)	32 (20-50)
HCO^- (mEq/L)	20 (18-28)	21 (16-26)

Median and IQR: Non-parametric test. Data are expresed as number (percent) or median (IQR).
*Significant p-value on comparison to survivors

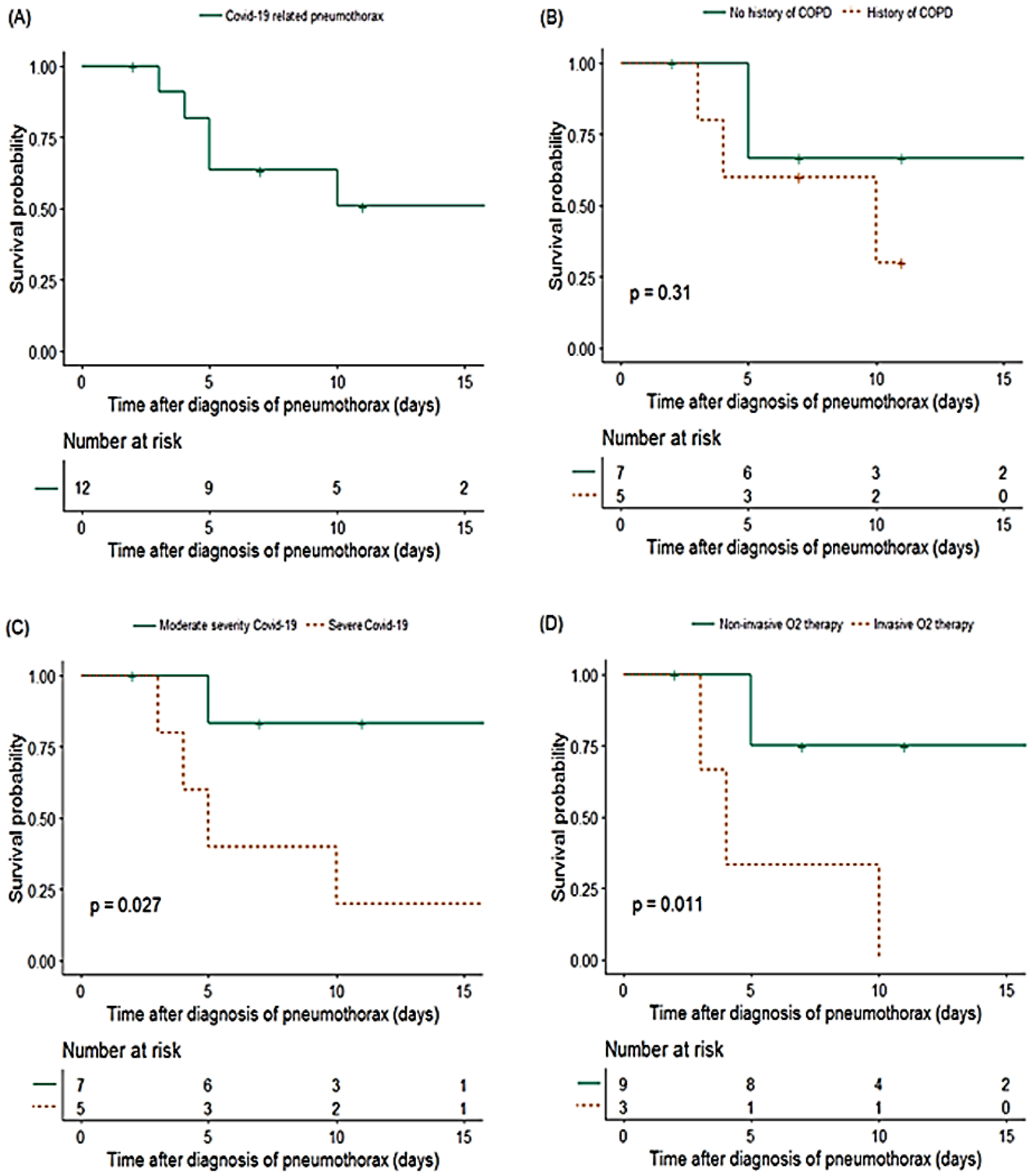

Figure (3): Kaplan–Meier survival curves of 12 non-ventilated patients with COVID-19 related pneumothorax during their hospital stay after diagnosis of pneumothorax. A) All patients, B) History of COPD, C) Severity of COVID-19 pneumonia at admission, D) Need for invasive versus non-invasive O_2 therapy.

DISCUSSION

Rapid clinical deterioration of patients with COVID-19 pneumonia has three potential causes including: Disease progression, pulmonary embolism, and pneumothorax [3]. Pneumothorax is a serious complication in patients with parenchymal lung disease, which may require rapid intervention. Ventilated patients have a risk to develop pneumothorax, however pneumothorax associated with lung damage in non-ventilated patients can occur to a lesser extent. Till December 2020, there were 36 published articles [1, 3] reporting 75 cases of pneumothorax in non-ventilated COVID-19 patients. It seems that these cases are not extremely rare, but there may be a lack of interest in its evaluation and presentation. In the absence of mechanical ventilation, the supposed mechanisms are related mainly to: Increased intra-alveolar pressure with cough or other respiratory efforts followed by rupture of the peripheral cystic lesions [1], inflammation-induced parenchymal injury and necrosis [4] and extensive tissue damage with bullae formation [5].

Only two large studies have been published in literature. **Zantah *et al.*** [2] reported spontaneous pneumothorax in six out of 902 patients (0.66%) with confirmed diagnosis of COVID-19 pneumonia. **Martinelli *et al.*** [4] reported the largest multi-center case series of COVID-19 related pneumothorax from sixteen UK hospitals that included 23 non-ventilated patients and 38 invasively ventilated patients.

In our series, the incidence of spontaneous pneumothorax was 8.82%, which reflects the highest reported incidence yet. The imaging strategy for CT chest on admission and daily chest X-ray might help our early and proper detection of patients with such complication. However, this incidence should be carefully interpreted as all of our hospitalized patients had only moderate to severe COVID- 19 pneumonia with a policy of home isolation for patients with mild illness. Most of our cases had unilateral pneumothorax (8 patients, 91.7%). Bilateral pneumothorax was reported only in one patient (8.3%). Handful cases of bilateral pneumothorax have been reported in literature. Our case of bilateral pneumothorax had COPD, lung bullae, and pneumomediastinum. This patient died due to severity of COVID-19 despite resolution of pneumothorax. Similarly, the reported cases in literature had resolved pneumothorax after emergent placement of chest tubes without a negative impact on patients' outcome [6-8]. **Ahluwalia *et al.*** [6] **and Alhakeem *et al.*** [20] reported bilateral pneumothorax with no predisposing risk factors which could be explained by cystic changes induced by COVID-19. **Ahluwalia *et al.*** [6] reported additional pneumomediastinum and pneumopericardium with excessive cough as an inciting factor for pneumothorax.

We reported two patients (16.7%) of COVID-19 and tension pneumothorax who were emergently and successfully treated by chest tubes, but one of them died due to multiorgan failure associated with severe pneumonia. Fighting two powerful enemies may result in quick losses when compared to fighting only one of them. Thus early detection and management of tension pneumothorax is essential to reduce mortality in patients with COVID-19. In literature, there is an important recommendation for thorough history-taking and clinical evaluation of COVID-19 patients with worsening of respiratory status [9-11]. **Flower *et al.*** [9] avoided blind initiation of CPAP in patients with COVID-19 and $SpO_2 < 94\%$ before exclusion of tension pneumothorax. **Khurram *et al.*** [10] emphasized the importance of considering additional pathologies such as acute pulmonary embolism and tension pneumothorax in patients with COVID-19. **Yasukawa *et al.*** [11] highlighted the role of follow-up chest imaging in evaluation of bulla formation and cystic changes with COVID-19 pneumonia, which may explain the occurrence of spontaneous tension pneumothorax.

We reported two cases (16.7%) of concomitant pneumomediastinum who died due to deterioration of COVID-19 pneumonia. Isolated or combined pneumothorax and pneumomediastinum are serious complications of COVID-19 that led to sudden decompensation and poor prognosis [12]. Inflamed pulmonary alveolar epithelium or repeated cough and straining in patients with COVID-19 may result in alveolar rupture followed by air escape from the ruptured alveoli to the mediastinum through perivascular and peribronchial fascia (The Macklin effect) with sudden onset of pneumothorax and pneumomediastinum. To improve outcome in such patients, **Brogna *et al.*** [13] highlighted the need for early imaging studies to obtain more details and initiate proper treatment. **Wang *et al.*** [14] administered steroids, which remains controversial as they suspected a cytokine storm.

In our series, five patients (41.7%) had a history of COPD and three of them (60%) died due to severe COVID-19. However, COPD did not reduce the survival time after diagnosis of spontaneous pneumothorax (Log-rank P-value = 0.31). Thus, the severity of COVID-19 rather than the presence of pneumothorax could explain the death of infected COPD patients. Generally, patients with COPD are at a high risk for infection with respiratory viruses. The most common pathogens are influenza virus in patients with acute exacerbations and human coronaviruses in patients with concomitant pneumonia [15]. The rate of COPD in patients with COVID-19 seems lower than other comorbidities such as hypertension, cardiovascular disease and diabetes [16]. COPD is known risk factor for spontaneous pneumothorax, particularly in patients with emphysematous subtype. Infection with COVID-19 has been reported to increase the risk for pneumothorax in patients with COPD and pulmonary emphysema [17]. These findings indicate the need for early diagnosis and treatment of spontaneous pneumothorax in patients with COVID-19 concomitant with COPD.

To date, the data regarding survival of patients with COVID-19 related pneumothorax are sparse. In our series, seven patients (58.33%) died. This rate lies within the reported range in literature by the largest reports. **Martinelli *et al.*** [4] reported death in 5 out of 23 patients (21.7%), while **Zantah *et al.*** [2] reported higher rate in 4 out of 6 patients (66.7%). These rates should be considered cautiously till reporting of more studies. Died patients in our series had higher levels of D-dimer and ferritin with lower counts of lymphocytes, which reflect the severity of COVID-19 with subsequent hyperinflammation and thrombosis. The causes of death were related to the deterioration of COVID-19 pneumonia not the extent of pneumothorax. Moreover, our analysis determined that presentation with severe COVID-19 pneumonia and the need for mechanical ventilation for oxygen therapy in severe cases associated with reduced survival time after diagnosis of spontaneous pneumothorax (Log- rank P-values <0.05). Still more studies are needed to evaluate prognosis in these patients.

Tube thoracostomy was indicated in 41.7% of our non-ventilated patients. Strict precautions were followed during the procedure, including connection of the chest tube to the drainage system before its insertion to prevent air leakage into the room. Also, closed drainage was created or an anti-viral filter was attached to the drainage system to minimize dissemination of the aerosol particles. These considerations were consistent with the recommendations of British Thoracic Society [18] and American Association for the Surgery of Trauma [19]. Additionally, there is experimental evidence that adding an anti-viral filter to the drainage system reduces aerosol emission from the bottle, and hence reduces in-hospital spread of COVID-19 [20, 21].

The surgical intervention in the form of bullectomy or pleurodesis was not required for any of our patients but it was reported by other authors. **Ahluwalia *et al.*** [6] performed chemical pleurodesis in a patient with recurrent bilateral pneumothoraxes. **Martinelli *et al.*** [4] performed right upper lobe bullectomy and pleurodesis for persistent air leak, which facilitated home discharge. **Janssen *et al.*** [5] reported bullectomy and talc age through video-assisted thoracic surgery (VATS) in a patient with multiple new bullae on CT after insertion of chest tube. Moreover, **Aiolfi *et al.*** [22] described two patients with iatrogenic persistent pneumothorax related to mechanical ventilation that successfully treated with VATS, bleb resection, and pleurectomy. Therefore, based on the currently available reports, we think that surgical treatment for lung bullae can increase the positive outcomes in patients with COVID-19 and persistent pneumothorax considering the guideline recommendations and the surgical fitness of the patient.

Limitations: Retrospective nature, single center experience, small sample size, and inclusion of non-ventilated patients with moderate to severe illness. However, these limitations could not reduce the importance of this analysis considering the rarity of the studied condition and the urgent need to assess all clinical aspects in emerging serious disease.

CONCLUSION

Pneumothorax and pneumomediastinum should be excluded in non-ventilated patients with COVID-19 pneumonia who had sudden clinical deterioration and worsening dyspnea, or decompensation. Pneumothorax often resolved after conservative treatment or tube thoracostomy, but bullectomy and pleurodesis may be considered in some cases. Outcome of patients with COVID-19 related pneumothorax is affected by the severity of viral pneumonia and the need for invasive ventilation. Large multicenter studies are recommended.

Conflict of interest: None.
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