International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2022): 7.942

COVID-19 Related "Pneumo" Complications: Regional Hospital Experience

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Abstract: ***Background: Coronavirus disease 2019 (COVID-19) presents from mild infection to severe pneumonia and "pneumo" complications such as pneumothorax (PNTX) and pneumomediastinum (PNM). The aim was to discuss the incidence, characteristics, and outcomes of PNTX/PNM in COVID-19 pneumonia. Methods: This was a prospective observational study. We enrolled adult patients with COVID-19 pneumonia treated at The COVID hospital, University Clinical Center of Vojvodina, Serbia from 1st September to 2nd December 2021. We collected data on demographic, clinical characteristics, and outcomes of patients with COVID-19 pneumonia and PNTX/PNM. Results: From total number (3117) of patients 44 (1.41%) had PNTX and/or PNM; mean age 63.7±14; dominantly males (n=29, 65.9%).4 (9%) patients had chronic pulmonary disease (one asthma, three chronic obstructive pulmonary disease of which one combined with bronchiectasis) and 15 (34.0%) were active or ex smokers. Clinical characteristics were that 31 (70.4%) had PNTX, 6 (13.6%) had PNM and 7 (15.9%) patients had combined PNTX and PNM. PNTX isolated or combined with PNM was right sided in 23 (52. %), left sided in 12 (27.2%) and bilateral in 3 (6.8%) patients. PNTX/PNM was associated with subcutaneous emphysema in 4 (9.0%) cases. Approximately two-thirds of patients were ventilated (n=1, 2.2% non-invasively and n=29, 65.9% invasively). The remaining patients were oxygen-supported only: 5 (11.3%) conventional oxygen support, 8 (18.1%) high-flow nasal cannula.35 (79.5%) out of the total 44 cases were deceased during hospitalization. Conclusions: Incidence of PNTX and/or PNM was relatively low, it was not associated with underlining pulmonary diseases or smoking, but with high in-hospital mortality.***

Keywords: COVID-19, pneumothorax, pneumomediastinum, mechanical ventilation

1. Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes coronavirus disease 2019 (COVID-19) which presents from self-limiting upper respiratory tract infection to acute respiratory distress syndrome (ARDS) and respiratory complications such as pneumomediastinum (PNM) and pneumothorax (PNTX) (1) . PNTX and PNM are defined as presence of free air in the pleural and mediastinal cavities (2) . Barotraumadueto noninvasive or invasive mechanical ventilation is one of the main causative mechanisms, even though it can also occur in patients without any respiratory support (3). COVID-19can cause emphysema-like changes which seem to be disease-specific and may explain the higher incidence of PNM and PNTXinCOVID-19compared to other pneumonias equal severity (4) . PNTX and PNM are important complications of COVID-19, and some studies indicate that they could be associated with worse prognosis including higher mortality and prolonged hospitalization (1, 3, 5, 6, 7, 8). The purpose of our work is to report the incidence, characteristics, and outcomes of PNTX/PNM in patients with COVID-19 pneumonia.

2. Methods

This was a prospective, single center observational study. We enrolled adult patients with COVID-19pneumonia, treated during the period from 1stSeptember 2021 to 2ndDecember 2021 at The COVID Hospital, University Clinical Center of Vojvodina, Petrovaradin, Serbia. We collected data on demographic, clinical characteristics, and outcomes of patients with COVID-19 pneumonia and PNTX/PNM.

3. Results

During above mentioned period 3117 patients were treated due to COVID-19 pneumonia. From total number of patients44 (1.4%) had PNTX and/or PNM. Mean age of enrolled patients with PNTX and/or PNM was 64±14 years. The majority of patients were males (n=29, 66%). There was 15 (34%) active or ex smokers. Vaccinated patients were 6 (14%). Only 4 (9%) had underlying chronic pulmonary disease (one asthma, three chronic obstructive pulmonary disease of which one combined with bronchiectasis). CTPA and/or CT of thorax was performed in 14 cases. Mean CT severity index of pneumonia was 18. Clinical characteristics were that 31 (71%) patients had PNTX, 6 (14%) patients had PNM and 7 (16%) patients had combined PNTX and PNM. PNTX isolated or combined with PNM was on the right side in 23 (53 %) patients, on the left side in 12 (27 %) patients and bilateral in 3 (7%) patients. PNTX/PNM was associated with subcutaneous emphysema in 4 (9%) cases. Majority of PNTX patients (n=32) required treatment with a chest drainage. As shown inTable1, in patients with PNTX/PNM, approximately more than two-thirds of patients were ventilated (n=1, 2% non-invasively and n=29, 66% invasively), while the remaining patients were on oxygen-supported only: 5 (11%) with conventional oxygen support and 8 (18%) with high-flow nasal cannulas and one patient did not require oxygen therapy. From 44 PNTX and/or PNM patients 35 (80%) were deceased during hospitalization.

4. Discussion

The significance of PNTX and PNM in COVID-19, initially limited to several case reports/series, has been increasingly described and analyzed in multiple observational studies (1). PNTX and PNM are potentially fatal complication in patients with COVID-19 ARDS specially in those requiring mechanical ventilation. Among our study group incidence of PNTX and/or PNM was 1.41 %, dominantly PNTX and

around sixteen percent combined. PNTX/PNM was associated with subcutaneous emphysema in 9 % of patients. According to the one of the largest systematic reviews, the incidence of PNTX is low at 0.3 % among the nine studies but increases up to 12.8-23.8 % in critically ill COVID-19 patients requiring invasive mechanical ventilation (1). Bonato et al. (5) reported 41.5 % of combined PNTX and PNM, 33.5 % only PNTX and 24.5 % PNM alone. According to three observational studies, less than 20% of hospitalized COVID-19 patients developed PNM concurrently with PNTX (1). Lemmers et al. (10) reported pneumomediastinum/subcutaneous emphysema in 13.6% patients with SARS-CoV-ARDS. Among our study group 9 % patients had underlying chronic pulmonary disease. In systematic review most COVID-19 patients diagnosed with PNTX did not have pre-existing lung diseases, with a reported frequency of lessthan 30% (1). The structural changes in lungs caused by COVID-19 and lung damage associated with mechanical ventilation may be responsible for PNM in these patients. A recent study by Lemmers et al. (10) have shown that there is significant increase in PNM/subcutaneous emphysema in COVID-19 ARDS (14%) patients compared tonon-COVID-19 ARDS (2%) despite the use of low tidal volume and low airway plateau pressure as a lung protective ventilator strategies in COVID-19 patients. Thus, if barotrauma is eliminated, the underlying lung pathology due to infection should be considered as cause for development of PNM. COVID ARDS is associated with increased risk of pulmonary vascular thrombosis, and subsequent necrosis and damage to alveolar membrane that can contribute to barotrauma (7). In our study one third of patients were active or ex-smokers which is consistent with four observational studies which revealed that less than 34% of COVID-19 patients diagnosed with pneumothoraces were smokers (1) . Most of the patients in these four studies presenting with PNTX/PNM were non-smokers and did not present previous respiratory comorbidities, indicating that smoking history or prior pulmonary status do not appear to influence PNTX/PNM pathogenesis (5) . On contrary data from the ISARIC4C study of 131 679 patients admitted with COVID-19 that reveal an overall incidence of pneumothorax of 0.97%. Male sex, smoking, chronic pulmonary disease (which includes COPD, interstitial lung disease and sarcoidosis, but not and asthma) and invasive ventilation were associated with increased risk of pneumothorax. Pneumothorax is associated with increased mortality in COVID-19 (3).

Half of our patients had right sided PNTX. Infour observational studies describing the locality of PNTX, COVID-19-related PNTX was commonly unilateral and predominantly right-sided in 57% of cases (1) .

More than two-thirds of our patients were invasively ventilated. PNTX is a common complication of invasive mechanical ventilation in critically ill patients, with reported incidence up to 15%. Generally, critically ill patients with PNTX experienced a 2-fold increase in the risk of ICU and hospital mortality than those without PNTX. Among those who develop pneumothoraces, the mortality and recovery rate are poor in the setting of invasive mechanical ventilation, septic shock, and the evidence of tension physiology compared to those with procedure-related PNTX (1) . Belletti et al. (9) found that almost one of four patients with COVID-19 ARDS requiring mechanical ventilation develops PNTX/PNM, which was associated with increased risk of mortality. They also identified time from symptom onset to intubation and total bilirubin as the only independent predictors of PNTX/PNM development, and mechanical ventilation parameters did not differ between patients with and without PNTX/PNM. Almost all of the patients who developed PNX/PNM had the Macklin effect on baseline chest CT. Wang et al. reported the overall incidence of pneumothorax 2%, 10% in patients with ARDS, 24% in patients receiving mechanical ventilation, and 56% in patients requiring invasive mechanical ventilation. Four of five patients died during hospitalization, with a 80% high mortality, and the remaining one patient had prolonged hospitalization. Bonato et al. (5) showed that patients with PNM/PNTX had higher in-hospital mortality, increased length of hospitalization and higher mortality rate at follow-up.

Based on our findings and literature review we can conclude that clinicians caring for patients with COVID-19 ARDS should be aware of the high risk of developing PNX/PMD despite protective mechanical ventilation strategies, especially if the Macklin effect is identified on chest CT scan or present chronic pulmonary disease. Therefore, a high index of suspicion always should be present when dealing with unclear respiratory or hemodynamic deterioration in patients. The incidence of PNTX/PNM and subcutaneous emphysema observed during the COVID-19crisis is worrying and deserves a careful assessment. Even though the mortality rate is high in this group of patients, future studies should also focus on the follow-up of surviving patients who developed PNTX, PNM and subcutaneous emphysema. This is essential in determining its effect on long-term outcomes, such as on lung function or on the development of lung diseases like chronic obstructive pulmonary disease or pulmonary fibrosis.

5. Conclusion

Despite the small sample size and observational character of study we can conclude that presence of PNTX and/or PNM in COVID-19 patients is important. It can influence on mortality specially in mechanically ventilated patient combined with underlining pulmonary diseases or smoking history.

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Table 1: Demographics, clinical characteristics, and outcome of COVID-19 patients with PNTX/PNM

Male, n (%)	29 (65.9)
Age (y) ± SD	63, 7±14
Active or ex-smokers, n (%)	15 (34)
Underlining chronic pulmonary disease, n (%) • asthma, • chronic obstructive pulmonary disease, • chronic obstructive pulmonary disease combined with bronchiectasis	4 (9) 1 (2.2) 2 (4.5) 1 (2.2)
CT and/or CTPA, n (%) CT severity index of pneumonia Pulmonary thromboembolism	14 (31.8) 18 3 (6.8)
PNTX, n (%)	31 (70.4)
PNM, n (%)	6 (13.6)
PNTX and PNM, n (%)	7 (15.9)
Side of PNTX Left, n (%) Right, n (%) Bilateral, n (%)	 12 (52.7) 23 (27.2) 3 (6.8)
Prevalence of subcutaneous emphysema, n (%)	4 (9)
Chest drainage, n (%)	32 (72.7)
Respiratory support, n (%) Conventional oxygen therapy High flow nasal cannula Invasive mechanical ventilation Non-invasive mechanical ventilation	 5 (11.3) 8 (18.1) 29 (65.9) 1 (2.2)
Patient outcome, n (%) Discharge home Deceased Transferred to another hospital	 1 (2.2) 35 (79.5) 8 (18.1)