Risk factors of pneumothorax and pneumomediastinum in COVID-19: a matched case-control study

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Background

- During the novel coronavirus disease-2019 pandemic, a considerable number of pneumothorax (PNX)/pneumomediastinum (PNM) associated with COVID-19 have been reported, and the incidence is higher in critically ill patients.
- Despite using a protective ventilation strategy, PNX/PNM still occurs in patients on invasive mechanical ventilation (IMV).

Objectives

- This matched case-control study aims to identify the risk factors and clinical characteristics of PNX/PNM in COVID-19.

Methods

- This retrospective study enrolled adult patients with COVID-19, admitted to a critical care unit from March 1, 2020, to January 31, 2022. COVID-19 patients with PNX/PNM were compared, in a 1 to 2 ratio, to COVID-19 patients without PNX/PNM, matched for age, gender, and worst National Institute of Allergy and Infectious Diseases ordinal scale.
- Conditional logistic regression analysis was performed to assess the risk factors for PNX/PNM in COVID-19.

Results

Table 1. Clinical characteristics and outcomes of the study population

	PNX/PNM (n=24)	Control group (n=48)	*P* Value
Age, y	65.4 ± 10.9	65.4 ± 10.9	.994
Sex, male	21 (87.5)	42 (87.5)	>.99
BMI, kg/m^2	22.8 ± 3.2	24.7 ± 4.2	.048
NIAID - Ordinal scale			>.99
5	2 (8.3)	4 (8.3)	
6	4 (16.7)	8 (16.7)	
7	8 (33.3)	16 (33.3)	
8	10 (41.7)	20 (41.7)	
Hypertension	15 (62.5)	27 (56.2)	.800
Diabetes mellitus	8 (33.3)	20 (41.7)	.669
COPD	1 (4.2)	2 (4.2)	>.99
Asthma	4 (16.7)	1 (2.1)	.039
Interstitial lung disease	0	1 (2.1)	>.99
Chronic kidney disease	1 (4.2)	6 (12.5)	.412
Charlson comorbidity index	3.0 (2.0-4.0)	3.0 (2.0-5.0)	.976
Smoking			.542
Current	0 (0.0)	2 (4.2)	
Previous	8 (33.3)	13 (27.1)	
Never	16 (66.7)	33 (68.8)	
COVID-19 treatment			
Steroid	22 (91.7)	48 (100.0)	.128
High-dose steroid (higher than dexamethasone 6mg)	16 (66.7)	36 (75.0)	.323
Remdesivir	20 (83.3)	44 (91.7)	.300
2nd immunomodulatory agents			.562
Baricitinib	1 (4.2)	2 (4.2)	
Tocillizumab	12 (50.0)	26 (54.2)	
SOFA score	6.5 (2.0-8.0)	5.0 (2.0-8.0)	.990
PaO_2/FiO_2 ratio	156.3 (140.9-179.4)	141.7 (110.0-196.4)	.674
In-hospital mortality	10 (41.7)	20 (41.7)	>.99
Length of stay, d	33.0 (17.5-63.0)	20.5 (13.0-31.0)	.061

PNX/PNM = pneumothorax/pneumomediastinum; BMI = Body mass index; NIAID = National Institute of Allergy and Infectious Diseases; SOFA = Sequential Organ Failure Assessment

Table 2. Clinical characteristics and outcomes of the patients with IMV

	PNX/PNM (n=18)	Control group (n=36)	*P* Value
Age, y	66.6 ± 11.1	66.6 ± 11.0	.993
Sex, male	15 (83.3)	30 (83.3)	>.99
Prone position during treatment	12 (66.7)	14 (38.9)	.102
Neuro-muscular blocker	11 (61.1)	17 (47.2)	.500
Ventilator associated pneumonia	12 (66.7)	15 (41.7)	.149
COVID-19 treatment			
Steroid	17 (94.4)	36 (100.0)	.721
High-dose steroid (higher than dexamethasone 6mg)	14 (77.8)	31 (86.1)	.339
Remdesivir	16 (88.9)	33 (91.7)	.344
2nd immunomodulatory agents			.472
Baricitinib	0	1 (2.8)	
Tocillizumab	10 (55.6)	21 (58.3)	
From Symptom onset to intubation date, d	13.0 (9.0-18.0)	9.5 (4.0-13.5)	.032
Ventilator mode			.668
APV-CMV	2 (11.1)	4 (11.1)	
Pressure-controlled	10 (55.6)	24 (66.7)	
Volume-controlled	6 (33.3)	8 (22.2)	
Tidal volume, mL	416.0 (345.0-467.0)	430.5 (401.5-459.0)	.627
TV/Ideal body weight, mL/kg	6.8 (5.3-7.3)	6.7 (6.1-7.4)	.472
PEEP, cmH_2O	9.7 ± 3.3	10.6 ± 2.7	.294
Peak pressure, cmH_2O	33.9 ± 7.5	31.6 ± 6.0	.224
PaO_2/FiO_2 ratio	161.4 (141.8-197.0)	118.9 (94.2-191.1)	.191
Arterial blood gas analysis			
pH	7.4 (7.3-7.4)	7.4 (7.3-7.4)	.790
$PaCO_2$	39.0 (35.8-53.3)	41.7 (36.9-54.1)	.607
In-hospital mortality	10 (55.6)	20 (55.6)	>.99
Weaning from mechanical ventilation	5 (27.8)	14 (38.9)	.614
Ventilator days, d	30.0 (15.0-74.0)	17.5 (10.5-30.0)	.083
Length of stay, d	37.5 (22.0-74.0)	23.5 (18.0-31.5)	.052

IMV = Invasive mechanical ventilation; APV-CMV = Adaptive Pressure Ventilation - Controlled Mechanical Ventilation; TV = Tidal volume; PEEP = Positive end-expiratory pressure

Table 3. Risk factors analysis for PNX/PNM in COVID-19

	Univariate analysis			Multivariable analysis		
	OR	95% CI	*P* Value	OR	95% CI	*P* Value
BMI	0.85	0.72-0.996	.044	0.87	0.74-1.02	.086
Asthma	8.000	0.89-71.58	.063	6.01	0.65-55.86	.115

PNX/PNM = pneumothorax/pneumomediastinum; OR = Odds ratio; CI = Confidence interval; BMI = Body mass index

Major Findings

- 427 patients with COVID-19 were admitted during the period, and 24 patients were diagnosed with PNX/PNM.
- Body mass index (BMI) was significantly lower in the case group (22.8 kg/m2 and 24.7 kg/m2; P = .048).
- BMI was statistically significant risk factor for PNX/PNM in univariate conditional logistic regression analysis (odds ratio (OR), 0.85; confidence interval (CI), 0.72–0.996; P = .044).
- For patients on IMV support, univariate conditional logistic regression analysis showed the statistical significance of the duration from symptom onset to intubation (OR, 1.14; CI, 1.006–1.293; P = .041).

Limitation

- The number of case patients was small since the data were collected from a single institution.
- In particular, the lack of clear risk factors with statistical significance in the multivariable analysis could be attributed to the relatively small sample size of our study.

Conclusions

- In this case-control study, using a control group matched for age, sex, and disease severity, low BMI showed a tendency to be associated with PNX/PNM due to COVID-19, and delayed application of invasive mechanical ventilation was found to be a contributive factor for this complication.