

# The role of surfactant system dysfunction in the formation of dyspnea in patients with COVID-19-associated pneumonia

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**Conflict of interest:** none

**OBJECTIVE.** To determine the contribution of surfactant system dysfunction (by level surfactant protein A (SP-A) of serum) to the formation of dyspnea in the subacute post-COVID (coronavirus disease) period in patients with COVID-19-associated pneumonia.

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## ОРИГІНАЛЬНЕ ДОСЛІДЖЕННЯ

**MATERIALS AND METHODS.** We screened 102 patients with dyspnea who had COVID-19-associated pneumonia in April – November 2021. The study was conducted in the subacute period of COVID-19 on day 47 (38; 62) after the first symptoms of coronavirus infectious. We excluded 25 patients whose dyspnea was associated with bronchial obstructive syndrome, signs of heart failure or anemia, and formed the main group of 77 patients with dyspnea due to lung parenchyma damage: mean age – 56 (49; 65) years, men – 37 (48.1 %), women – 40 (51.9 %). The control group consisted of 15 practically healthy individuals: mean age – 51 (45; 60) years, men – 6 (40.0 %), women – 9 (60.0 %). The main group was divided into three subgroups depending on the severity of COVID-19 in the acute period: subgroup 1 – 26 patients with dyspnea (mean age – 57 (53; 64) years; men – 12 (46.2 %), women – 14 (53.8 %)) who had a moderate course of the acute period of the disease; subgroup 2 – 36 patients (mean age – 55 (49; 61) years, men – 18 (50.0 %), women – 18 (50.0 %)) who had a severe course of the acute period of COVID-19; subgroup 3 – 15 patients (mean age – 55 (52; 63) years, men – 7 (46.7 %), women – 8 (53.3 %)) who had a critical course of the acute period of COVID-19. The examination of patients had consist general clinical methods, determination of level SpO<sub>2</sub>, assessment of dyspnea severity by the modified Borg scale, the 6-minute walk test (6MWD), and measurement levels SP-A of serum.

**RESULTS AND DISCUSSION.** Patients of subgroups 3 of COVID-19 in the subacute period had quite severe dyspnea both before 6MWD (4 (3; 6) points on the Borg scale) and after it (7 (5; 9) points on the Borg scale), whereas patients of subgroups 1 and 2 had less severe dyspnea both before 6MWD (1 (0.5; 2) and 2 (1; 4) points, respectively) and after it (2 (1; 3) and 5 (4; 7) points, respectively). The level of SP-A in the subacute period was significantly higher in patients of subgroups 2 and 3 compared to patients of subgroup 1 (73.8 (59.0; 87.2), 88.1 (51.1; 100.8) ng/ml and 46.6 (21.1; 77.1) ng/ml, respectively) ( $p < 0.05$ ). There was no significant difference between patients in subgroup 1 and the control group (46.6 (21.1; 77.1) vs 29.6 (14.0; 53.1) ng/ml) ( $p > 0.05$ ). Analysis of the area under the ROC curve between patients in subgroup 1 and subgroups 2 and 3 showed a high diagnostic ability of the test: AUC 0.866 (95 % confidence interval 0.766-0.935;  $p < 0.0001$ ) with an optimal cut-off point of 59 ng/ml (sensitivity – 78.4 %, specificity – 95.5 %). At a serum SP-A level  $> 59$  ng/ml, the risk of lung surfactant system dysfunction in severe or critical patients in the subacute period of the disease increases 6-fold (odds ratio 6.1; 95 % confidence interval 2.2-17.3;  $p = 0.0006$ ).

**CONCLUSIONS.** The severity of dyspnea in the subacute period of COVID-19 due to lung parenchymal damage depends on the severity of the acute course of the disease. Elevated SP-A levels ( $> 59$  ng/ml) in the subacute period of COVID-19 are observed in patients with severe or critical acute disease and reflect the presence of signs of long-term surfactant system dysfunction.

**KEY WORDS:** coronavirus disease, COVID-19, COVID-19-association pneumonia, dyspnea, post-COVID-19 period, surfactant protein A.