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POSSIBILITIES OF PREDICTING THE OUTCOME OF THE COURSE OF ACUTE PURULENT-DESTRUCTIVE LUNG DISEASES IN PATIENTS WHO HAVE HAD SARS-COV-2

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Abstract: Since the discovery of COVID-19, purulent-destructive lung diseases have been increasingly described and diagnosed around the world in patients who have fallen ill with or have had covid pneumonia. Treatment of purulent diseases of the lungs and pleura invariably remains an urgent problem. This pathology, painful for the patient, time-consuming for the doctor and expensive for the medical institution, combines intoxication due to a purulent-destructive process and impaired respiratory function. The occurrence of infectious destruction of the lungs and pleura is facilitated by immunodeficiency and immunosuppression, which are characteristic of patients suffering from haematological diseases, increased tendency to thrombosis, diabetes mellitus, alcoholism, drug addiction, HIV infection, who have undergone extensive surgical interventions, organ and tissue transplantation. The peculiarity of the course of COVID lung infection is the consolidation of an inflammatory focus in the lungs, which can lead to the formation of abscesses and gangrene of the lungs, and sepsis, which is associated with high mortality in the long term after COVID disease. At the moment, the exact mechanism of development is not known, but it may be associated with diffuse alveolar damage, intraalveolar bleeding, stenosis or occlusion of alveolar arterioles, their thrombosis and, as a consequence of the above, necrosis of the cell parenchyma. Another factor in the occurrence of acute purulent-destructive lung diseases is pneumofibrosis, which is a frequent occurrence after covid pneumonia. A lung abscess is a necrotic lesion that forms a cavity filled with pus in the lung parenchyma with a characteristic level of fluid in the air on a chest X-ray. Most often, the cause of severe covid pneumonia is not only a virus but bacterial and fungal superinfection, including those associated with mechanical ventilation.

Key words: Acute purulent-destructive lung diseases, SARS-COV-2, prediction of disease outcome.

INTRODUCTION

Based on the results of clinical observations, most publications note that 2/3 of patients with SARS-CoV-2 developed acute respiratory distress syndrome at the dawn of the pandemic. These patients had an increased risk of developing ventilator-associated pneumonia [7, 12, 14, 17].

V. Beaucote et al. In their observations, we noted a characteristic trend in the development of purulent-destructive lung diseases in patients with SARS-CoV-2 who were under mechanical ventilation in the intensive care unit [8].

Indeed, pulmonary endotheliitis [11], which provokes the development of microthromboembolism of the peripheral parts of the lung tissue [10], has been widely reported among critical patients with COVID-19.

Wicky P.N. and co-authors [18] noted that it is in such patients, due to the insufficiency of the concentration of antibiotics in the lesion, that the risk of developing purulent-destructive diseases becomes very high.

RESEARCH ARTICLE

Libby L.S. and others argue that purulent-destructive lung diseases in severely ill patients with SARS-CoV-2 can also develop as a result of the addition of superinfection against the background of microthromboembolism of the pulmonary vessels and endophlebitis [9]. The prerequisites for the development of purulent-destructive lung diseases in such cases are also the development of a heart attack in areas of lung tissue [19].

Kalenchits T.I. et al. [1] described a case of polysegmental destructive viral-bacterial pneumonia complicated by acute lung abscess and pleural empyema in a 50-year-old patient who was being treated in a hospital for SARS-CoV-2. A month was diagnosed with an abscess in the lower lobe of the right lung, which subsequently spontaneously drained into the pleural cavity. The authors believe that one of the factors in the formation of a lung abscess in SARS-CoV-2 may be a violation of the blood coagulation system with the formation of microthrombi in small pulmonary vessels.

The frequency of registration of acute purulent-destructive lung diseases in patients with SARS-CoV-2 during the pandemic was ambiguous [2-6]. Thus, according to several hospitals in Europe, if during the first wave (from March to June 2020) the incidence of acute purulent-destructive lung diseases was noted in the range of 35-46%, then during the period of other waves (from August 2020 to April 2021) there was an increase in the number of patients with acute purulent-destructive lung diseases in the range of 52-65% [13, 16, 20].

Based on the above, we can state that any study regarding the features of the clinical, radiological and microbiological manifestations of purulent-destructive lung diseases in patients with SARS-CoV-2 deserves close attention.

METHODS

Information on the comprehensive examination and treatment of 128 patients with acute purulent-destructive lung diseases who have had SARS-CoV-2 is analysed.

The patients were treated and examined in the purulent surgery department of the multidisciplinary clinic of the Tashkent Medical Academy. The period of study and collection of clinical material began in the second quarter of 2020 and ended in December 2022 (XI quarters). At the same time, for the period from April to August 2020, the clinic also functioned as a specialised covid centre, with the involvement of specialists in all areas by quarantine requirements.

Taking into account the different flow of patients depending on the pandemic situation for SARS-CoV-2, all patients were divided into two groups.

The first group of patients (control) consisted of 65 (50.8%) patients with acute purulent-destructive lung diseases who had undergone SARS-CoV-2 and underwent traditional methods of treatment from April to December 2020. The second group of patients (the main one) consisted of 63 (49.2%) patients with acute purulent-destructive lung diseases who had had SARS-CoV-2, who underwent improved methods of diagnosis and treatment of these diseases, approved and recommended for practical use by the Ministry of Health of the Republic of Uzbekistan.

All patients were subdivided according to clinical and nosological forms of acute purulent-destructive lung diseases. Most of the patients were represented by acute purulent abscess (32.8%) and abscessed pneumonia (31.3%). To a lesser extent, there were patients with acute gangrenous lung abscesses (25.8%) and lung gangrene

RESEARCH ARTICLE

(10.2%). At the same time, in the control group of patients, cases with abscessed pneumonia prevailed (32.3%), while in the study group – with acute purulent abscess (38.1%). There were two times more patients with lung gangrene in the control group than in the main group, which was associated with the peak of the SARS-CoV-2 pandemic. Bilateral lung lesions were noted in 35.9% of cases, unilateral – in 64.1% in a ratio of 0.56 units. Moreover, in the control group of patients, bilateral lesions were 5.2% higher than in the main group.

The distribution of patients by sex and age is confirmed by the well-known trends characteristic of purulent lung diseases: men aged 31 to 60 years (81.3%), among whom manual workers prevail (69.2%) employed in industry and agriculture. Intellectual workers accounted for 24.5%, students and pensioners 6.3%.

The overwhelming majority of patients (77.3%) smoked, more than half abused alcohol, and did not comply with household and hygienic standards.

Most of the patients were transferred to us directly from a specialised clinic after the exclusion of infectious pathology (subgroup I – 51.6%). However, along with this, there was a cohort of patients who were admitted to the clinic from various therapeutic hospitals, where, as a rule, they underwent purely conservative therapy (subgroup II of patients – 48.4%). At the same time, patients of subgroup I prevailed in the control group (56.9%), and patients of subgroup II (54.0%) prevailed in the study group.

The state of the endothelial system in the lungs was studied by the indicators of the molecules of vascular intercellular adhesion-1 (ng/ml) and endothelin-1 (f/μmol/l) in samples of mixed venous and arterial blood using the enzyme-linked immunosorbent analyser AT 858 (PRC).

Von Willebrand factor (IU/dL) was determined in mixed venous and arterial blood samples using an automatic closed-type analyser HumacLOT DUO (Germany) using a reagent kit from Human (Germany).

The activity of inducible NO synthase (mmol/l/h) and the content of peroxynitrite (mmol/l) in venous and arterial blood samples was determined by the Griss method modified by A.P. Solodko et al. (e.g.). [45]. The concentration of the indicators was calculated according to the equation of the calibration graph, taking into account the dilution during deproteinisation. The optical density was measured on an SF-46 spectrophotometer at a wavelength of 520 nm.

The study of the physical and biochemical parameters of the fluid of bronchoalveolar swabs provided for the determination of its surface-active properties on modified Wilhelm-Langmuir balances. Phosphatidylcholine and lysophosphatidylcholine were extracted and studied by thin-layer chromatography on silica gel glass plates.

One of the main methods of analysis and interpretation of the results obtained was the determination of the correlation relationship between the indicators. At the same time, all the criteria for the significance of the correlation in our studies assumed the Gaussian distribution of quantitative features. In this regard, the correlation relationship was established by the graphic representation of the measurement results on the plane, where the values of the studied features (correlation plane).

The data obtained during the study were subjected to statistical processing on a Pentium-IV personal computer using the Microsoft Office Excel-2016 software package, including the use of built-in statistical processing functions and BioStat

RESEARCH ARTICLE

for Windows (version 2007). The methods of variational parametric and nonparametric statistics were used with the calculation of the arithmetic mean of the studied indicator (M), standard deviation (σ), standard error of the mean (m), relative values (frequency, %), the statistical significance of the measurements obtained when comparing the mean quantitative values were determined by the parametric Student's test (t) with the calculation of the probability of error (p) when checking the normality of the distribution (by the kurtosis criterion) and the equality of general variances (F is the Fisher test).

The confidence level $p < 0.05$ was taken as a statistically significant changes. The results of the research were expressed in units of the International System of Units.

RESULTS AND DISCUSSION

To assess the significance of the studied parameters of changes in the endothelial system among patients with acute purulent-destructive lung diseases after SARS-COV-2, we carried out a correlation analysis of the relationship between the dynamics of changes in venous-arterial difference indicators and the level of these products in mixed venous and arterial blood samples. It should be noted that the first analysis was based on the standard division of patients into three subgroups.

The correlation between the dynamics of venous-arterial difference and the dynamics of changes in the content of the studied metabolites in mixed venous blood in patients of the control group was ambiguous. Among patients of subgroup I, the maximum direct correlation was registered about phospholipase-A2, von Willebrand factor and peroxynitrite. Lysophosphatidylcholine, inducible nitric oxide synthase and intercellular adhesion factor were distinguished by a slight decrease in significance. The dynamics of

changes in the content of such indicators as phosphatidylcholine and endothelin-1 in the ICS had an inverse correlation concerning the venous-arterial difference.

Among the patients of subgroup II, a decrease in the level of correlation dependence of venous-arterial difference on the dynamics of the studied parameters in mixed venous blood was generally noted. Phosphatidylcholine, lysophosphatidylcholine, and phospholipase-A2 decreased slightly (by $r = -0.125$, $r = 0.083$, and $r = 0.031$, respectively). All these parameters belonged to the category of those responsible for the production of lung surfactant, and their changes in patients of subgroup I did not have a significant value. However, the indicators characterising endothelial dysfunction in the lungs in patients of subgroup II underwent great changes. The correlation parameters decreased significantly, namely the intercellular adhesion factor by 8.9 times, nitric oxide synthase by 4.3 times, von Willebrand factor by 3.9 times, peroxynitrite by 3.0 times, and endothelin-1 by 2.4 times.

In patients of subgroup III, the decrease in correlation concerning the data of lysophosphatidylcholine and phospholipase-A2 of patients of subgroup I was 7.9 ($p < 0.05$) and 4.3 ($p < 0.05$) times, respectively. For all other parameters, the correlation dependence acquired the opposite value. At the same time, the maximum values of the inverse correlation were about the intercellular adhesion factor and endothelin-1.

Regarding the changes in the correlation dependence of the content of the studied markers in the arterial blood sample and the venous-arterial difference, a mirror contrast between the I and III subgroups of patients can be noted. At the same time, the data of patients of subgroup II acquire an

RESEARCH ARTICLE

intermediate value in the general cloud of the dispersion value of the data, being mainly within the values of patients of subgroup I.

Thus, the change in the values of the correlation between the studied markers showed that the course of acute purulent-destructive lung disease in patients who have had SARS-COV-2 has a natural relationship with the outcome of treatment. Changes in the venous-arterial difference in the studied parameters in patients with a relatively mild course of the pathological process have more reliable values, which indicates the normal functional ability of the lungs to correct the products of the endothelial system before they enter the universal arterial environment. At the same time, among patients with unsatisfactory treatment outcomes, the functional capacity of the endothelial system of the lungs undergoes pronounced insufficiency, which, in our opinion, was already associated with the initial damage to the endothelial system of the lungs in the process of SARS-COV-2. On the other hand, pronounced disorders in the endothelial system of the lungs during SARS-COV-2 lead to a disruption of the compensatory capabilities of the non-respiratory function of the lungs, in this case, known as insufficiency of its barrier-filtration function [15]. At the same time, as our studies have shown, these changes are closely interrelated and have a pattern in the form of the development of endothelial dysfunction of a compensatory and decompensatory nature. Such a conditional division was because, at the compensatory level, the surfactant system of the lungs was not disturbed, and the endothelial dysfunction was local, capable of making appropriate corrections in the arterial system. At the same time, in patients with a decompensated level of damage, all of the above functional abilities are completely impaired. It is this division of the nature of

the identified disorders, in our opinion, that will allow for a randomised approach in the choice of treatment tactics for patients with acute purulent-destructive lung diseases after SARS-COV-2.

In most literary sources, acute purulent-destructive lung diseases are designated as lung abscesses. However, unfortunately, in clinical practice, it is often necessary to use a term that is not quite correct, such as "multiple lung abscesses". We focus on this fact since it is known that an abscess is a limited purulent-inflammatory process, that is, an abscess with a pyogenic capsule. At the same time, clinical and radiological comparisons indicate that in limited acute purulent-destructive diseases of the lungs, the purulent process prevails, while in widespread - necrotic. Therefore, when determining the type of acute purulent-destructive lung disease, it is necessary to focus on the morphological substrate of changes in the lung parenchyma.

Based on the multivariate correlation analysis of the state of the endothelial system of the lungs and the clinical and radiological results of the studies, we have developed criteria for determining the activity of the course of the purulent-destructive process in the lungs in patients who have had SARS-COV-2. From the studied indicators of the activity of the purulent-destructive process and endothelial dysfunction in the lungs, we selected 12 signs that were the most informative, equivalent, and correlated with the prevalence and nature of the process. Of these, two are clinical, 2 are X-ray, and 8 are laboratory.

Statistical analysis of the information array made it possible to determine the most characteristic indicators, which formed the basis for the construction of linear integral data characterising the degree of endothelial lung dysfunction in patients

RESEARCH ARTICLE

with acute purulent-destructive diseases after SARS-COV-2.

When building models of the severity and outcome of diseases using the least squares method, the model parameters were subject to a condition of their effectiveness not lower than the level of $p < 0.05$ according to the t-test. Based on the graphical construction of clinical and laboratory data and the identification of their correlation, we have developed a method for assessing endothelial lung dysfunction in acute purulent-destructive diseases after SARS-COV-2.

When building a prediction rule using the least squares method, the values of the weights were determined from the original data sample, and they were the best in the class of linear functions. This made it possible to more objectively take into account the contribution of each laboratory sign to the prognosis of the further course of the pathological process.

The variation of numerical arithmetic values in the dynamics of the development of endothelial lung dysfunction had a graphic form of compaction within the phases (compensated and decompensated) of the development of this pathological process identified by us. The selected optimal model for determining the degree of endothelial lung dysfunction facilitated the assessment of the functional ability of the barrier-filtration function of the lungs in their acute purulent-destructive diseases in patients who have had SARS-COV-2.

Comparison of the results of our studies with clinical data allows us to consider the detected changes sufficiently specific and justified to be used as tests in the diagnosis and prediction of the course of acute purulent-destructive lung diseases in patients who have had SARS-COV-2.

By the intensity of manifestation, each sign was evaluated according to integrated, formatted research data combined into a digital program describing the degree of endothelial dysfunction in acute purulent-destructive lung diseases in patients who have had SARS-COV-2.

Laboratory criteria were based on information on the endothelial and surfactant-forming systems. Laboratory criteria were compiled based on the amount (up to 100 ml, up to 300 ml and more than 300 ml) and the nature (mucous, purulent, putrid) of the sputum secreted. Radiographic features included the determination of the extent of lung tissue lesions (within a segment of the lobe of the lung, within the lobe of the lung, and more than one lobe of the lung). Pleural complications were graded according to the nature of the substrate of the inflammatory process (exudate or pus).

The numerical value reflected the severity of the disease and the extent of lung tissue damage in the form of compensatory and decompensatory manifestations of disorders.

As mentioned above, the correlation analysis of the dependence of the indicators of endothelial dysfunction of the lungs in their acute purulent-destructive diseases in patients who have had SARS-COV-2 made it possible to establish that normal synthesis of surfactant by the lungs is possible only if the level of disorders is at a compensated value.

A retrospective analysis of the degree of endothelial dysfunction in patients with acute purulent-destructive lung diseases after SARS-COV-2 showed that out of 65 patients in the control group, all cases were found to be impaired to some extent of functional insufficiency of the endothelial system of the lungs. In 49.2% of cases (32 patients), compensated endothelial

RESEARCH ARTICLE

dysfunction was diagnosed, and in 50.8% of cases (33 patients) – decompensated endothelial dysfunction.

Exactly half of the patients with compensated endothelial dysfunction were patients with abscessed pneumonia. In 46.9% of cases, these were patients with acute purulent lung abscess and one patient (3.1%) with acute gangrenous abscess.

Patients with decompensated endothelial lung dysfunction were represented by all nosological forms of acute purulent-destructive lung diseases. In 48.5% of cases, they were represented by patients with acute gangrenous lung abscesses, and in 27.3% of cases by patients with lung gangrene. Patients with abscessed pneumonia (15.2%) and acute purulent abscess were the fewest patients.

In the course of treatment, the dynamics of endothelial dysfunction among the patients of the control group change. In 13 (20%) patients, no endothelial lung dysfunction was detected as a result of treatment. Compensated endothelial dysfunction was noted among 25 patients with acute purulent-destructive lung diseases. Among them, the main proportion were patients with abscessed pneumonia (48.0%) and patients with acute purulent abscess (40.0%). There were only three patients with gangrenous abscesses (12.0%).

The number of patients with decompensated endothelial dysfunction was reduced by only 7.0%. Most of them were represented by acute gangrenous lung abscess (48.1%) and lung gangrene (33.3%). In 18.5% of cases, decompensated endothelial lung dysfunction was found among patients with abscessed pneumonia (11.1%) and acute purulent lung abscess (7.4%).

Thus, already at the first stage of randomisation of patients by nosological

forms of manifestation of acute purulent-destructive lung diseases, confirmation was obtained of the reliable significance of the method developed by us for assessing the patient's condition. Of course, it should be noted that in this analysis, the information on the dynamics was not complete since in patients of the control group with a lethal outcome, it was not possible to assess the final result on the same days of the study. To assess the sensitivity and specificity of the diagnostic method developed for us, we carried out a comparative assessment of these criteria with traditional laboratory and clinical methods of assessment (Marchuk index). As a basis for the comparative nature, we took the final results of the treatment of patients in the control group.

The sensitivity of the Marchuk clinical index in patients with acute purulent-destructive lung diseases after SARS-COV-2 on the day of admission to the clinic was 98.3%, while the sensitivity of the Marchuk laboratory index was 1.4% higher. In comparison with this, the index of endothelial dysfunction in this contingent of patients was also very high (92.4%), but it was inferior to the clinical indicator by 5.9% and to the laboratory indicator by 7.3%.

Retrospective analysis of the results of the treatment showed that the importance of the clinical and laboratory signs of Marchuk, as well as the original method developed by us, is decreasing. However, in all subsequent cases, the level of the original methodology remained higher than traditional methods of assessment. For example, if the prognostic mortality rate according to the Marchuk clinical index was only 10.3%, then according to the Marchuk laboratory index, it was 15.3%. At the same time, the original method exceeded the reliability of traditional methods by 4.7 and 3.2 times.

RESEARCH ARTICLE

A comparative assessment of the specificity of the studied methods revealed the maximum complete value for the Marchuk clinical index and 8% less than the laboratory index. The specificity of the original method was 98.4%.

For other criteria, the decrease in the specificity of diagnostic values was ambiguous. A progressive decrease was noted in the Marchuk laboratory index with a minimum value for mortality (10.2%). The specificity of the original method of diagnostic criteria in patients with complete recovery was 88.3%, with clinical recovery – at 79.8% and chronicity – at 56.3%. In terms of indicators among patients with fatal outcomes, this figure was 45.8%.

CONCLUSION

A comparative analysis of the effectiveness of traditional and original methods for assessing the diagnostic criteria for the course and prognosis of acute purulent-destructive lung diseases in patients who have had SARS-COV-2 showed the high sensitivity and specificity of the proposed technique, which is based on the assessment of the degree of endothelial dysfunction in the lungs.

Conflict of Interest – None

Ethical aspect – the article is reviewed, and the information presented has a cited reference to primary sources.

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RESEARCH ARTICLE

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