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## How to Treat Acute Purulent-Destructive Lung Diseases if they are Sequels to Covid-19? Problems and ways to solve them.

Sh.A. Bobokulova<sup>1</sup>, Sh.A. Khamdamov<sup>2</sup>, D.N. Korikhonov<sup>3</sup>,  
A.O. Okhunov<sup>4</sup>, K.Kh Boboev<sup>5</sup>, F.A. Abdurakhmanov<sup>6</sup>

### ABSTRACT

**Background.** The COVID-19 pandemic has shown how much coronavirus infection can be contagious. Even now, doctors are facing the consequences of this viral disease. A high lesion of the pulmonary system causes an increase in the proportion of consequences of respiratory disease. One of the difficult aspects in this direction is lung abscesses.

**Material.** An analysis of different approaches in the treatment of lung abscesses of patients who have had COVID-19 was carried out. All patients, depending on the severity of the course of purulent lung disease and treatment methods, were divided into 3 groups.

**Results.** The main positive therapeutic effect in the treatment of lung abscesses in patients who have had COVID-19 should be reduced to the impact of the effects of endothelitis. For this purpose, long-term intraarterial catheter therapy and local ultrasound cavitation of the lung destruction cavity were used. Significant positive results were obtained in all major groups where a differentiated treatment approach was applied.

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<sup>1</sup> Assistant, Department of General and Pediatric Surgery-1, Tashkent Medical Academy, Tashkent, Uzbekistan.  
E-mail: [shokhista.bobokulova@gmail.com](mailto:shokhista.bobokulova@gmail.com)

<sup>2</sup> Assistant, Department of General and Pediatric Surgery-1, Tashkent Medical Academy, Tashkent, Uzbekistan.  
E-mail: [doctorshoh1010@mail.ru](mailto:doctorshoh1010@mail.ru)

<sup>3</sup> Assistant, Department of General and Pediatric Surgery-1, Tashkent Medical Academy, Tashkent, Uzbekistan.  
E-mail: [dqorixonov@gmail.com](mailto:dqorixonov@gmail.com)

<sup>4</sup> Professor, DSc, PhD, MD, Head of the Department of General and Pediatric Surgery-1 of the Tashkent Medical Academy, member of the American (SIS) and European (S IS-E) Societies of Surgical Infection, Tashkent, Uzbekistan. E-mail: [general-surgery@mail.ru](mailto:general-surgery@mail.ru)

<sup>5</sup> Assistant, Department of General and Pediatric Surgery-1, Tashkent Medical Academy, Tashkent, Uzbekistan.  
E-mail: [qboboyev@bk.ru](mailto:qboboyev@bk.ru)

<sup>6</sup> Assistant, Department of General and Pediatric Surgery-1, Tashkent Medical Academy, Tashkent, Uzbekistan.  
E-mail: [sardorruss@mail.ru](mailto:sardorruss@mail.ru)

**Conclusion.** The use of the therapeutic and diagnostic algorithm developed by us leads to an improvement in the clinical, radiological and ultrasound picture of the disease, allows us to reduce the duration of inpatient treatment by 7 days, as well as improve clinical outcomes, including, to increase the proportion of patients with complete recovery by 23% and reduce the frequency of the transition of an abscess to a chronic form by half.

**Keywords:** acute lung abscesses, COVID-19, endothelialitis, long-term intraarterial catheter therapy, ultrasound cavitation

## INTRODUCTION

Secondary bacterial co-infections of the lungs, in patients with COVID-19, according to the literature, develop in approximately 7.2% of cases. At the same time, it is known that in influenza, bacterial co-infections appear in 65.1% of patients [17, 19]. This fact is very interesting since patients with severe COVID-19 have a number of negative factors associated with the immunosuppressive state of the body. These include factors such as the elderly age of the patient, the high incidence of concomitant diabetes mellitus, enhanced corticosteroid therapy, etc. [6, 32]. It is in such a contingent of patients that the accession of co-infection is accompanied by a severe course of COVID-19 or its fatal outcome [13].

The fatality of co-infection cases in patients with COVID-19 is due to the development of necrotizing pneumonia. Necrotizing pneumonia is mainly described in the setting of community pneumonia as a rare and severe complication [18, 38]. The disease proceeds with the formation of many lung abscesses, which are better known to clinicians than the above forms of lung damage [9,18].

The problem of treating acute lung abscesses in patients who have had COVID-19 is one of the most complex and relevant in thoracic surgery due to its relatively high frequency and unsatisfactory outcomes [3,4,16]. The number of patients in the world suffering from them tends to increase reaching 4-5 or more cases per 100 thousand inhabitants per year. The overall mortality rate for acute abscesses in patients who have had COVID-19 is 4.4%, and for gangrenous abscesses, it reaches 15.2% [7, 14].

Such a high specific percentage of negative outcomes of treatment of patients is due to the development of a specific pathological process against the background of COVID-19 - endothelialitis. It is its development and the presence of co-infection that is considered the main pathomorphological substrate of the development of purulent-destructive lung diseases [20-27].

The basis for the treatment of purulent destruction of the lungs is intensive complex conservative therapy. However, impaired blood rheology, blockade of micro-circulation in the affected lung, due to the presence of the consequences of endothelialitis and the associated low concentration of antibiotics in the lesion, as well as the development of endotoxemia and immunological disorders in patients, cause insufficient effectiveness of conservative treatment. This, in turn, leads to the progression of the purulent-destructive process with the development of life-threatening complications or the formation of a chronic abscess, which are indications for highly traumatic surgical interventions.

At the same time, the priority direction of surgeons is organ-sparing methods of treatment, the purpose of which is to preserve the organ as a morphological structure, as well as its functional properties. To date, many endobronchial and transthoracic methods have been developed for the timely and effective emptying of the pulmonary abscess. The first, for example, include long-term transbronchial catheterization or endoscopic drainage of the abscess cavity. And to the second category - flow-washing drainage. But they do not affect the pathomorphological basis of lung abscesses in patients who have had COVID-19.

The Department of General and Pediatric Surgery of the Tashkent Medical Academy is actively developing organ-preserving technologies in the field of thoracic surgery, and the main goal of this work was to improve the results of treatment of acute lung abscesses in patients who have had COVID-19, through the use of long-term intra-arterial catheter therapy and combined intracorporeal ultrasound cavitation of the abscess cavity in the complex of therapeutic measures.

## MATERIAL AND METHODS OF RESEARCH

Under our supervision from 2020 to 2022, 103 patients with acute lung abscess who had a history of COVID-19 were in the department of

purulent surgery of the multidisciplinary clinic of the Tashkent Medical Academy.

95.2% of the patients were male and 4.8% were female. The age of patients ranged from 38 to 72 years. Acute purulent lung abscess was detected in 87 (84.5%) patients, acute gangrenous abscesses were observed in 16 (15.5%) patients.

Often, destruction of the lungs occurred against the background of chronic obstructive pulmonary disease with diffuse pneumosclerosis and emphysema of the lungs - in 28 (27.2%) cases. The most common complication - pyopneumothorax was observed in 10 (9.7%) patients. There were 2 (1.9%) cases of other complications (contralateral pneumonia, pleural empyema, formation of a bronchopleural fistula, hemoptysis, and acute pulmonary heart failure).

The majority (n = 78; 75.7%) of patients had a moderate severity of the disease, and 25 (24.3%) had - moderate degree.

Depending on the methods of treatment used, all patients were divided into 3 clinical groups comparable in clinical and radiological data - a comparison group (n = 35), in which standard treatment was used and 2 main ones in the treatment of which long-term intraarterial catheter therapy and ultrasound cavitation of the abscess cavity were additionally used.

Patients of all groups received complex treatment that included 1) ensuring timely comprehensive and adequate drainage and sanitation of purulent cavities in the lungs and tracheobronchial tree, 2) exposure to pathogenic microbial fluoride foci of destruction and inflammation, 3) correction of homeostasis disorders.

Patients of the second group (n=32), along with standard treatment, underwent long-term intraarterial catheter therapy. The main indication for the appointment of this type of therapy was the low effectiveness of the complex conservative treatment of acute lung abscesses with adequate drainage of the pulmonary abscess.

Patients of the third group (n=36). along with standard treatment, long-term intra-arterial catheter therapy was carried out in combination with ultrasound cavitation of the cavity of a drained lung abscess. An indication for the additional appointment of intracavitary ultrasonic cavitation was the low efficiency of transthoracic sanitation of purulent cavities.

All patients were examined according to a single scheme including physical, general clinical, instrumental, biochemical and microbiological research methods.

Clinical indicators included the duration of bronchopulmonary symptoms and general symptoms of intoxication, the total time of the patient's stay in the hospital, the number of minimally invasive interventions and operations, clinical and morphological outcomes of diseases, complications and mortality.

## RESULTS

In the process of treatment, positive changes in the morphological composition of the blood were noted, which were more significant in the "white" blood. The content of leukocytes decreases by 9.5%. The number of eosinophils increased in all groups, but reliable changes were noted only in the third group - by 82.0% (from  $1.22 \pm 0.22$  to  $2.22 \pm 0.25\%$ ;  $p < 0.05$ ).

Neutrophilia also stopped most reliably in all groups decreased the content of stab forms - by 38.0% ( $p < 0.01$ ) in the comparison group, and by 57.7% ( $p < 0.001$ ) and 59.3% ( $p < 0.001$ ) in the second and third groups, respectively. The number of segmented neutrophils decreased less pronounced and unreliable. A decrease in the shift of the leukocyte formula to the left indicated subsidence of inflammatory phenomena.

The number of lymphocytes significantly increased in the second group of patients by 49.2% ( $p < 0.005$ ), and in the third group of patients by 53.0% ( $p < 0.001$ ). The content of monocytes significantly increased by 25.9% ( $p < 0.05$ ) in the third group.

A decrease in the relative content of neutrophils and an increase in lymphocytes, monocytes and eosinophils in peripheral blood led to a decrease in the leukocyte index of intoxication by 45.5% (from  $2.23 \pm 0.35$  to  $1.21 \pm 0.16$  conventional units;  $p < 0.01$ ) in the third group of patients by 42.2% (from  $2.23 \pm 0.35$  to  $1.29 \pm 0.20$  conventional units;  $p < 0.05$ ) in the second group. In the comparison group, the leukocyte index of intoxication will inaccurately decrease by 27.4%.

In the study of biochemical parameters, we identified dysproteinemia in the form of a decrease in the albumin fraction to 49.2% of the total serum protein content. In the process of treatment, there was an inaccurate growth of the total protein in all groups. More pronouncedly, its qualitative composition of albumin content significantly increased by 23.2% (from  $35.08 \pm 1.68$  to  $43.21 \pm 1.18$  g/l;  $r < 0.0011$ ; and 20.7% (from  $35.08 \pm 1.68$  to  $42.3 \pm 1.07$  g/l;  $p < 0.001$ ) in the second and third groups, respectively. In the comparison group, this indicator increased inaccurately by 11.3%.

A significant decrease in the content of aminotransferases and urea in the blood serum was revealed. Alanine aminotransferase - by 59.6% ( $p < 0.001$ ), aspartate aminotransferase - by 51.4% ( $p < 0.05$ ), urea by 30.8% ( $p < 0.05$ ). There was a downward trend in bilirubin and creatinine in all groups, but more pronounced in the second and third. All this indicates an improvement in the function of the liver and kidneys and the normalization of metabolic processes in the body.

The content of fibrinogen in the blood significantly decreased by 19.5% (from  $7.737 \pm 0.229$  to  $6.231 \pm 0.258$  g/l;  $r < 0.001$ ), which also indicates a decrease in the severity of inflammatory phenomena.

When studying the microbial flora in 70 results of cultures of secreted sputum, as well as the contents of drained pulmonary abscesses, 76 strains of microorganisms were isolated. In sputum, streptococcus (28.6%), staphylococcus (25.6%) and conditionally pathogenic enterobacteria (28.6%) prevailed. Less common were *Pseudomonas aeruginosa* and Gram-negative bacilli - 8.6% each. In the contents of lung abscesses, along with the above bacteria, a noticeable place in the microbial spectrum was occupied by *Escherichia coli* and proteus - 9.8% each; the proportion of gram-positive rods and enterococci was 7.3% each.

Microbial associations of 2-3 and even 4 microbes were observed in 70.5% of cases. In associations, staphylococcus was most often found in combination with gram-negative bacteria - Intestinal and *Pseudomonas aeruginosa*. In 21 (35%) crops, there was no growth of bacteria, which, in the presence of a clear purulent-inflammatory process, indicates the presence of anaerobic flora. After treatment, the number of cultures without bacterial growth in the third group of patients increased to 23 (71.9%,  $p < 0.05$ ) in sputum and to 16 (75.2%,  $p < 0.05$ ) - in the contents of abscess cavities. At the same time, in the comparison group, it was 55% ( $p > 0.05$ ) and 52% ( $p > 0.05$ ), respectively. It should be noted that in cases with negative results of cultures in the third group of patients in 3 cases, clinical signs of the presence of anaerobic flora persisted. Thus, indeed, complete sanitation was achieved in 61.1% of cases, and in the comparison group - only in 27%.

The most sensitive to local ultrasonic cavitation were Gram-positive microorganisms. And pathogens such as *Pseudomonas aeruginosa*, Proteus, enterobacteria and fungi were more resistant.

It should be noted that patients of the second and third groups were not administered antibiotics in the ab-

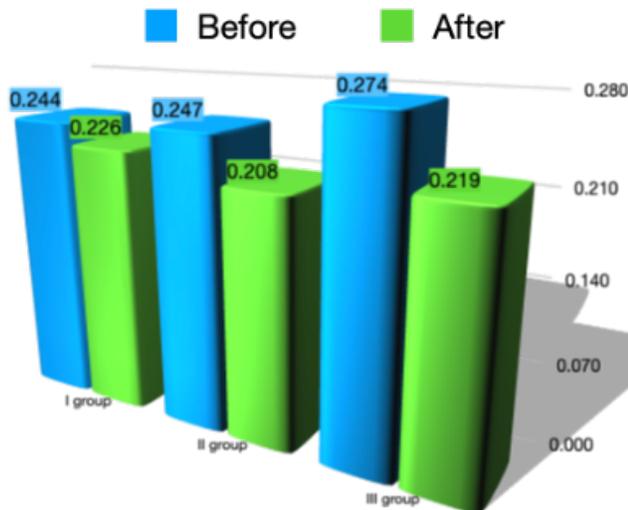
cess cavity. The bactericidal effect was probably due to both the direct effect of ultrasound on microorganisms and the improvement of microcirculation in the zone of perifocal infiltration and the rheological properties of the blood, which in turn leads to easier penetration of antibiotics from the blood into the focus of destruction.

When analyzing the data of clinical and instrumental studies against the background of the treatment, positive dynamics were revealed in all groups, but it was especially pronounced in the third group of patients, where combined long-term intraarterial catheter therapy and ultrasound cavitation of the abscess cavity were used. Already after two or three days of such treatment, there was an improvement in the general condition of patients, the normalization of hemodynamic parameters, and a decrease in the general symptoms of intoxication. Fever and tachycardia, which are objective criteria for the purulent-inflammatory process and intoxication of the body, were stopped 7-8 days earlier in the group using long-term intra-arterial catheter therapy and 9-10 - when combined with ultrasound cavitation of the abscess cavity. The excretion of purulent sputum in the second group of patients stopped a day earlier than in the group with traditional treatment, mucopurulent for three days. In the third group of patients, a more pronounced positive dynamics was observed - these manifestations were stopped 2 days earlier than in the second group of patients. Thus, the combined use of long-term intraarterial catheter therapy and local ultrasound cavitation of the destruction cavity makes the positive change in the clinical picture more prominent than isolated catheter therapy.

We have studied the dynamics of the disease severity index against the background of the application of the therapeutic and diagnostic algorithm developed by us in a comparative aspect with traditional treatment. In the main third group, before treatment, the moderate severity of the disease with a disease severity index of 0.15 to 0.25 conventional units was in 24 patients (66.7%), and 12 (33.3%) - of moderate degree with a disease severity index from 0.275 to 0.5 conventional units. After treatment using combined long-term intraarterial catheter therapy and ultrasound cavitation of the abscess cavity, the picture changed - 5 (13.9%) patients already had a mild degree of severity of the disease with a disease severity index of 0.075 to 0.125 conventional units, 23 (63.9%) - moderate with a disease severity index of 0.15 to 0.25 conventional units, and 8 (22.2%) - moderate

with a disease severity index of 0.275 to 0.4 conventional units.

The dynamics of the average values of the disease severity index is presented on figure-1. Significant changes were observed in the third group of patients, where the severity index of the disease decreased by 20.1% ( $p < 0.05$ ). In the remaining groups, the decrease in the severity index of the disease was unreliable.



**Figure 1. Dynamics of changes in the severity index of the disease in patients with acute lung abscesses after suffering COVID-19**

The observed changes, both individual clinical signs and the integral indicator of the severity index of the disease, characterize combined therapy as an effective additional method of treating purulent-destructive lung diseases. It allows to achieve the speedy relief of clinical manifestations of such a severe pathology as an acute lung abscess in patients who have had COVID-19.

In addition to improving laboratory and clinical parameters, positive clinical, radiological and ultrasound dynamics were observed in the area of lung damage and around it. Echocopy, performed on the 10-12th day from the start of treatment, recorded positive changes in patients of the third group in the form of a decrease in the size of the cavities by more than half, as well as the thickness of the abscess wall and the perifocal infiltration zone. Similar changes were identified during fluorographic examination. In the comparison group, the rate of reduction in the size of the cavity and perifocal infiltration zone was significantly slowed (similar changes after 3 weeks or more).

The proportion of patients with complete recovery in the second group of patients increased significantly - 84.4% ( $p < 0.05$ ), as well as in general in 79.4% ( $p < 0.05$ ) of patients of the main groups (second and third groups). In 11 (16.2%) patients, clinical recovery occurred, and in another 3 (4.4%) patients there was a transition to the chronic form of the abscess. In the comparison group, these rates were worse - 18 (52.0%), 12 (33.0%) and 5 (15%), respectively. No deaths were observed in any of the groups. The duration of inpatient treatment was significantly reduced by 7 days ( $r < 0.01$ ) in the second group and by 5.4 days ( $r < 0.05$ ) in the third group of patients. The best outcomes of treatment of acute lung abscesses in the second group are associated with the fact that in the third group the contingent of patients was somewhat heavier.

All surgical interventions are divided by volume into "small" (punctures and drainage of pulmonary and pleural abscesses) and "large" (lobectomy and lung resection with pleuroectomy). The bulk (85.7%) were operations performed before the use of long-term intraarterial catheter therapy and ultrasound cavitation of the lung destruction cavity, and only 14.3% - after.

In most cases (91.1%) it was possible to limit themselves to minimally invasive interventions. Basically (50.0%) transthoracic microdrainage of abscess cavities was performed. In the presence of a blocked abscess or in the presence of a large size, transthoracic external drainage with a tube with a wide lumen (17.9%) was performed. In the case of an abscess breakthrough with the development of pyopneumothorax, the pleural cavity was drained (23.2%).

Summing up the results of the study, we can state that the combined long-term intraarterial catheter therapy and ultrasound cavitation of the abscess cavity has anti-inflammatory, detoxification, protein-correcting effects.

## DISCUSSION

Even though COVID-19 is a respiratory virus, studies have shown that this viral infection can involve many other organs in the body. Cardiovascular involvement, heart failure, kidney failure, liver damage, shock, and multiple organ failure are other manifestations of COVID-19. [40] Studies have even shown neurological complications of COVID-19. [8] Coronavirus can cause some hematological complications, such as lymphocytopenia, thrombocytopenia, coagulopathy. [37]

A lung abscess is usually the formation of a cavity as a result of necrosis of the lung tissue. [11] Bacterial infection and aspiration can lead to the formation of an abscess. [10] Lung tissue diseases cause primary abscesses. [15] On the other hand, secondary abscesses are usually caused by other diseases, such as pulmonary thromboembolism or the spread of extrapulmonary abscesses to the lungs. [39]

To the best of our knowledge, none of the previous studies have reported a lung abscess as a complication of COVID-19 infection [2,5,12]. It is important to monitor patients after discharge for such complications, especially if patients have symptoms. [1,14,21,22]

Long-term intra-arterial catheter therapy has the property of unblocking areas of the microvasculature and potentiating the capabilities of anti-inflammatory and detoxification drugs. The combined use of methods of long-term intraarterial catheter therapy and ultrasound cavitation of the lung abscess cavity not only synergize with each other, but also enhance the process of exposure to endothelitis and its consequences. The combination of general and local targeted effects in the treatment of lung abscesses in patients who have had COVID-19 contribute to the acceleration of the timing of the purulent cavity and the relief of the local inflammatory process, which allows to reduce the duration of conservative treatment, as well as improve the outcomes of the disease.

## CONCLUSION

**D**elayed intracavitary ultrasound cavitation complements the method of long-term intraarterial catheter therapy, helping to accelerate the timing of sanitation of the purulent cavity and stop the local inflammatory process. This method is easy to use, and is also well tolerated by patients. It meets the modern principles of treatment of acute purulent-destructive lung diseases, as it has a complex effect on the etiology and on the main links in the pathogenesis of acute lung abscesses in patients who have had COVID-19. The use of the therapeutic and diagnostic algorithm developed by us leads to an improvement in the clinical, radiological and ultrasound picture of the disease, allows us to reduce the duration of inpatient treatment by 7 days and also improve clinical outcomes, including, to increase the proportion of patients with complete recovery by 23% and reduce the frequency of the transition of an abscess to a chronic form by half.

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**Conflict of Interest** – The authors state that they have no conflict of interest.

**Ethical Statement** - to publish these results we obtain the Ethics Committee of the Tashkent Medical Academy. All patients were informed about the research process. All of them signed the relevant letter of consent.

**Data Availability Statement** - Data supporting the results of this study are available at the request of the respective author. The data is not publicly available because it contains information that could compromise the privacy of study participants.

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**O'TKIR YIRINGLI-DESTRUKTIV O'PKA KASALLIKLARINI QANDAY DAVOLASH MUMKIN, AGAR ULAR COVID-19-NING KETMA-KETLIGI BO'LSA? MUAMMOLAR VA ULARNI HAL QILISH USULLARI.**

Bobokulova Sh.A., Xamdamov Sh.A., Korikhonov D.N., Oxunov A.O., Boboev K.Kh., Abduraxmanov F.M.

**Toshkent tibbiyot akademiyasi**

**ABSTRAKT**

**Dolzarbli.** COVID-19 pandemiyasi koronavirus infeksiyasi qancha yuqumli bo'lishi mumkinligini ko'rsatdi. Hozir ham shifokorlar ushbu virusli kasallikning oqibatlarini bilan yuzlashmoqda. O'pka tizimining yuqori lezyonlari nafas yo'llari kasalliklari oqibatlarining ortishiga olib keladi. Bu yo'nalishdagi qiyin jihatlardan biri o'pka xo'ppozlaridir.

**Material.** COVID-19 bilan kasallangan bemorlarning o'pka xo'ppozlarini davolashda turli xil yondashuvlarni tahlil qilish amalga oshirildi. Barcha bemorlar, yiringli o'pka kasalligi va davolash usullarining og'irligiga qarab, 3 guruhga bo'lindi.

**Natijalar.** COVID-19 bilan kasallangan bemorlarda o'pka xo'ppozlarini davolashda asosiy ijobiy terapevtik ta'sir endotelit ta'siriga tushishi kerak. Shu maqsadda uzoq muddatli intraarterial kateter terapiyasi va o'pka destruktiv bo'shlig'ining mahalliy ultratovush kavitatsiyasi qo'llanildi. Differentsiatsiyalangan davolash usuli qo'llanilgan barcha asosiy guruhlarda sezilarli ijobiy natijalarga erishildi.

**Xulosa.** Biz tomonidan ishlab chiqilgan diagnostika va davolash algoritmidan foydalanish kasallikning klinik, radiologik va ultratovushli tasvirini yaxshilashga olib keladi, bu bizga statsionar davolanish muddatini 7 kunga qisqartirishga, shuningdek, klinik natijalarni yaxshilashga imkon beradi, shu jumladan, to'liq tiklanish bilan og'rigan bemorlarning ulushini 23% ga oshirish va xo'ppozning surunkali shaklga o'tish chastotasini yarmiga kamaytirish imkonini beradi.

**Kalit so'zlar:** o'tkir o'pka xo'ppozlari, COVID-19, endotelit, uzoq muddatli intraarterial kateter terapiyasi, ultratovush kavitatsiyasi

**КАК НУЖНО ЛЕЧИТЬ ОСТРЫЕ ГНОЙНО-ДЕСТРУКТИВНЫЕ ЗАБОЛЕВАНИЯ ЛЕГКИХ, ЕСЛИ ОНИ СИКВЕЛЫ КОВИД-19? ПРОБЛЕМЫ И ПУТИ ИХ РЕШЕНИЯ.**

Бобокулова Ш.А., Хамдамов Ш.А., Корихонов Д.Н., Охунув А.О., Бобоев К.Х., Абдурахманов Ф.М.

**Ташкентская Медицинская Академия**

**АБСТРАКТ**

**Актуальность.** Пандемия КОВИД-19 показала на сколько коронавирусная инфекция может быть контагиозной. Даже в настоящее время врачи сталкиваются с последствиями этой вирусной болезни. Высокое поражение легочной системы обуславливает и увеличения удельного веса последствий заболевания органов дыхания. Одним из сложных аспектами в этом направлении являются абсцессы легких.

**Материал.** При провели анализ разных подходов в лечении абсцессов легких больных, перенесших КОВИД-19. Все больные в зависимости от тяжести течения гнойного заболевания легких и методов лечения были разделены нами на 3 группы.

**Результаты.** Основной положительный терапевтический эффект при лечении абсцессов легких у больных перенесших КОВИД-19 должен сводиться к воздействию последствий эндотелиита. Для этого были применены длительная внутриаартериальная катетерная терапия и локальная ультразвуковая кавитация полости деструкции легких. Значительные положительные результаты получены во всех основных группах, где применялся дифференцированных подход лечения.

**Заключение.** Применение разработанного нами лечебно-диагностического алгоритма приводит к улучшению клинко-рентгенологической и ультразвуковой картины заболевания, позволяет сократить сроки стационарного лечения на 7 суток, а также улучшить клинические исходы в том числе, увеличить долю больных с полным выздоровлением на 23% и снизить частоту перехода абсцесса в хроническую форму вдвое.

**Ключевые слова:** острые абсцессы легких, КОВИД-19, эндотелиит, длительная внутриаартериальная катетерная терапия, ультразвуковая кавитация