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MATHEMATICAL MODEL FOR THE INVESTIGATION OF HYPOXIC STATES IN THE HEART MUSCLE AT VIRAL DAMAGE

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The main complications of organism damaged by SARS-CoV-2 virus are various cardiovascular system lesions. As a result, the secondary tissue hypoxia is developed and it is relevant to search the means for hypoxic state alleviation. Mathematical modeling of this process, followed by the imitation of hypoxic states development, and subsequent correction of hypoxia at this model may be one of the directions for investigations.

Aim. The purpose of this study was to construct mathematical models of functional respiratory and blood circulatory systems to simulate the partial occlusion of blood vessels during viral infection lesions and pharmacological correction of resulting hypoxic state.

Methods. Methods of mathematical modeling and dynamic programming were used. Transport and mass exchange of respiratory gases in organism, partial occlusion of blood vessels and influence of antihypoxant were described by the systems of ordinary nonlinear differential equations.

Results. Mathematical model of functional respiratory system was developed to simulate pharmacological correction of hypoxic states caused by the complications in courses of viral infection lesions. The model was based on the theory of functional systems by P. K. Anokhin and the assumption about the main function of respiratory system. The interactions and interrelations of individual functional systems in organism were assumed. Constituent parts of our model were the models of transport and mass exchange of respiratory gases in organism, self-organization of respiratory and blood circulatory systems, partial occlusion of blood vessels and the transport of pharmacological substance.

Conclusions. The series of computational experiments for averaged person organism demonstrated the possibility of tissue hypoxia compensation using pharmacological substance with vasodilating effect, and in the case of individual data array, it may be useful for the development of strategy and tactics for individual patient medical treatment.

Key words: functional respiratory system; transport and mass exchange of respiratory gases; hypoxic state; partial occlusion of blood vessels.

Review of some publications with cardiovascular complications of COVID-19 and necessity of mathematical modeling use. The series of cases of strange pneumonia were registered in China on December 2019. New strain of coronavirus SARS-CoV-2, which was the causative agent of acute respiratory disease — coronavirus disease 2019 (COVID-19) have been identified in course of the subsequent studies. The epidemic turned into pandemic during brief period of time. Currently, there are quite a lot of publications with the attempts to trace and systematize current information about coronavirus

infection SARS-CoV-2 since the beginning of the epidemic. Out of the domestic authors, we should like to mention the review of S. V. Komisarenko [1] first of all; it includes up-to-date data on etiology, epidemiology, pathogenesis, clinical manifestations, and principles of diagnosis and treatment of new type of coronavirus infection, including the ideas about COVID-19 influence on cardiovascular system.

The reports about various cardiovascular complications of COVID-19 appeared in scientific literature quite quickly [2, 3]. Some types of cardiovascular system damages have been described already in literature [4]: acute myocardial damage, heart rhythm disturbances, myocarditis, the onset and/or aggravation of heart failure, pulmonary embolism [5–8]. High mortality rates: 10.5% among the patients with cardiovascular diseases (CVD), and 6.0% — with arterial hypertension [6, 7] were registered among the patients with COVID-19 and concomitant cardiovascular diseases in the studied reviews. In general, the potential mechanisms of SARS-CoV-2 influences on cardiovascular system were summarized according to [2–8], and demonstrated on Fig. 1.

The mechanisms causing the damage of cardiovascular system under the influence of SARS-CoV-2 have not been fully established. But in [9] the factor of the patients' age was mentioned as the first one in the list, as well as aggravation of the courses of many chronic diseases (including cardiovascular diseases) with SARS-CoV-2 background.

Since the information on the mechanisms of COVID-19 action was limited still, the analysis of the data from previous studies about the outbreaks of viral pneumonia and acute respiratory syndrome in the Middle East, as well as seasonal influenza, will help to understand better the mechanisms of coronavirus action on cardiovascular system, as it was emphasized in [10]. Understanding of SARS-CoV-2 cardiovascular effects is seen as quite important for the development of ways to provide timely comprehensive medical care during such lesions. Coronavirus influence on humans, and potential mechanisms of this infection effects on cardiovascular system based on the analysis of the large number of publications and clinical studies were described in [10] (Fig. 1).

Direct damaging effect of SARS-CoV-2 on cardiomyocytes was proved in [11]. In addition, the severe courses of COVID-19 (pneumonia, ARDS — acute respiratory distress syndrome) were accompanied by significant disorders in gases exchange, which caused hypoxemia. Oxygen delivery to tissues decreased during hypoxemia. Thus, the energy supply of

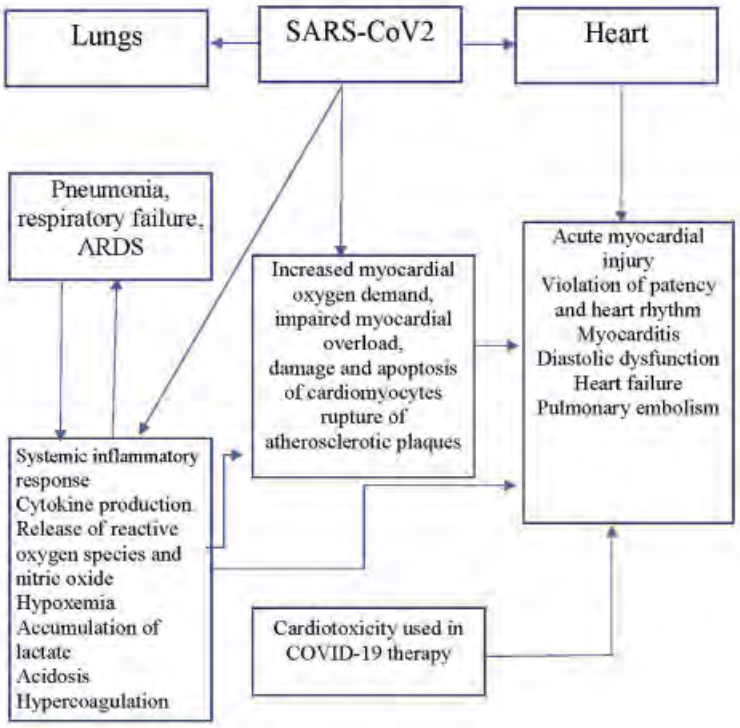

Fig. 1. **Potential mechanisms of SARS-CoV-2 effects on cardiovascular system [2–8]**

cellular metabolism decreased and anaerobic fermentation increased causing intracellular acidosis and reactive oxygen species release, which, consequently, destroyed phospholipid layer of cell membranes with the damage and apoptosis of cardiomyocytes [4].

Lactate accumulation and hypoxia caused by respiratory failure leaded to the formation of diastolic dysfunction, insufficient myocardial perfusion, accompanied by hypercoagulation, which can cause the development of acute myocardial infarction [12].

In general, the scheme of cardiovascular system involvement into described phenomena basing on [5, 9, 12–20] was represented on Fig. 2 [10].

Coronavirus infection influence on cardiovascular system was described in [21], in order to clear up and develop the algorithm for correct medical care provision for the people with cardiovascular diseases. This study was based on already known data on epidemiological characteristics of SARS and MERS [6, 7, 22–24], and studies of cardiovascular system damages in cases of pre-existing diseases and studied viral pathology.

The potential impact of COVID-19 on cardiovascular system was observed in [25]. The statistics of complications during COVID-19 from [19, 26, 27] were suggested; in particular, it was noted that in study with 75 patients hospitalized with COVID-19, the acute myocardial infarction caused 2 of 5 deaths. Also, an analysis of [22, 23, 28–30] had demonstrated the presence of large percentage of cardiovascular pathologies in patients with COVID-19; but these patients had not such pathologies before. It was concluded that until specific medical preparations against SARS-CoV-2 become available, the treatment of COVID-19 will be limited mainly by supportive therapy and treatment of complications [25].

An analysis of literature sources from Pub Med database was carried out in [31] using the keywords COVID-19 and SARS-CoV-2. The aim of the work was to collect and systematize contemporary information accumulated recently on pathophysiological mechanisms of SARS-CoV-2 effects on cardiovascular system, and the main acute cardiovascular complications of COVID-19. The sources [7, 29, 30, 32–57] with the description of pathophysiological mechanisms of the influence of SARS-CoV-2 on cardiovascular system were analyzed in [31]. The author concluded that in many cases SARS-CoV-2 caused various cardiovascular complications through the acute inflammatory damage of myocytes, provoking ventricular dysfunction, coagulopathy. Hypoxemia lead to insufficient

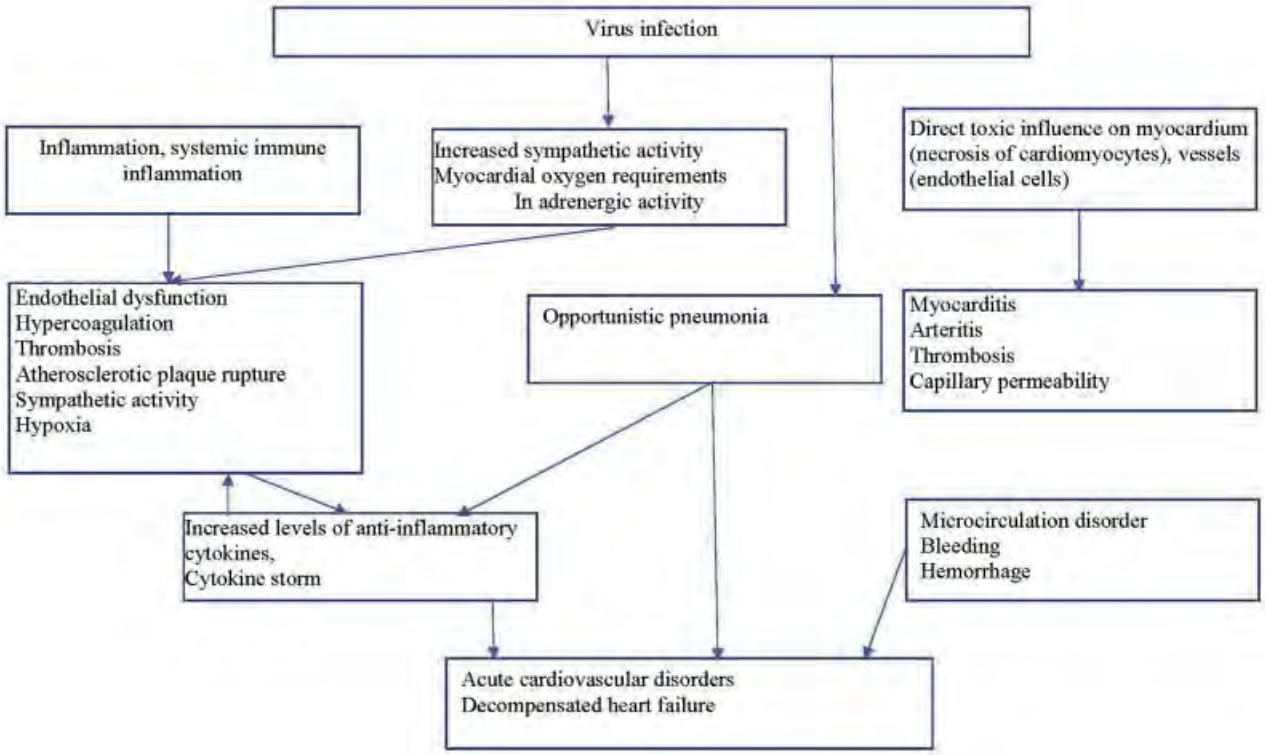

Fig. 2. **Influence of coronavirus infection (COVID -19) on cardiovascular system [10]**

oxygen supply to the myocardium [53], with the decrease of cardiac output and circulating blood volume; the sympathetic nervous system was activated to maintain circulatory homeostasis and perfusion of vitally important organs; all this leaded to even greater imbalance between the oxygen demand of the heart and oxygen delivery, as a result of which the heart muscle was damaged [54]. Other systemic factors lead to myocardial damage were acid-base imbalance, respiratory and metabolic acidosis, and electrolyte imbalance [55].

The publications from Pub Med, Google Scholar E-library databases for 2020 devoted to SARS-CoV-2 influences on cardiovascular system were analyzed in [58]. According to some authors [6, 7, 19, 30, 59–72], the spreading of concomitant cardiovascular diseases in patients with identified COVID-19 and the mechanisms of COVID-19 influence on cardiovascular system were analyzed [7, 30, 64, 73–75].

Summarizing the above, one has to note that all this evidenced not only about the need of symptomatic treatment, which was quite obvious, but also that it was desirable to have at least some ideas or approaches of possibility of patient's state alleviation. Therefore, for such cases it seems appropriate to apply mathematical modeling, which allows simulating such disturbances in organism. So, the aim of this work was the development of mathematical model of partial vascular occlusion and simulation of antihypoxant influence.

Mathematical model. The mathematical model of controlled part of respiratory system [76–78] was represented by the system of ordinary differential equations, which described the dynamics of oxygen tension at all stages of its path in the organism; and in brief form it was [79–80]:

$$\frac{dp_iO_2}{d\tau} = \phi(p_iO_2, p_iCO_2, \eta_i, \dot{V}, Q, Q_{t_i}, G_{t_i}O_2, q_{t_i}O_2), \quad (1)$$

$$\frac{dp_iCO_2}{d\tau} = \psi(p_iO_2, p_iCO_2, \eta_i, \dot{V}, Q, Q_{t_i}, G_{t_i}CO_2, q_{t_i}CO_2), \quad (2)$$

where the functions φ and ψ were described in details in [76–78]; V – ventilation; η — degree of hemoglobin saturation with oxygen; Q — volumetric rate of systemic and Q_{t_i} — local blood flows; $q_{t_i}O_2$ — rate of oxygen consumption by the i-th tissue reservoir; $q_{t_i}O_2$— rate of carbon dioxide release in i-th tissue reservoir.

The flow rates $G_{t_i}O_2$ of oxygen from the blood to the tissue and carbon dioxide from the tissue to the blood were determined by the ratio

$$G_{t_i} = D_{t_i}S_{t_i}(p_{ct_i} - p_{t_i}), \quad (3)$$

where D_{t_i} are coefficients of gases permeability through the air-blood barrier, S_{t_i} is the surface area of gas exchange.

In case of partial occlusion of the artery, which is divided into arterial vessels of right and left sides, the equations of mathematical models of mass transfer and mass exchange of respiratory gases in the blood of tissue capillaries were presented in [78, 81]:

$$\frac{dp_{ct_i}O_2}{d\tau} = \frac{1}{V_{ct_i}(\alpha_1 + \gamma \cdot Hb\frac{\partial \eta_{ct_i}}{\partial p_{ct_i}O_2})}(\alpha_1 Q_{t_i}(p_aO_2 - p_{ct_i}O_2) +$$
$$+ \gamma \cdot Hb \cdot Q_{t_i}(\eta_a - \eta_{ct_i}) - G_{t_i}O_2), \quad (4)$$

$$\frac{dp_{t_i}O_2}{d\tau} = \frac{1}{V_{t_i}(\alpha_1 + \gamma_{Mb} \cdot Mb\frac{\partial \eta_{t_i}}{\partial p_{t_i}O_2})}(G_{t_i}O_2 - q_{t_i}O_2), \quad (5)$$

Description of changes in oxygen tensions in heart tissues in the model of respiratory gas transport in organism, in case of partial artery occlusion have the form [78, 81]:

$$\frac{dp_{ct_k}O_2}{d\tau} = \frac{1}{(V_{ct_k} - \int_{\tau_0}^{T}(Q_{t_k} - \tilde{Q}_{t_k})d\tau \cdot (\alpha + \gamma \cdot Hb\frac{\partial \eta_{ct_k}}{\partial p_{ct_k}O_2})} \times$$
$$\times(\alpha_1 \cdot \tilde{Q}_{t_k} \cdot p_{t_k}O_2 + \gamma \cdot Hb \cdot \tilde{Q}_{t_k} \cdot \eta_{ct_k} -$$
$$-G_{t_k}O_2 - \alpha_1 \cdot Q_{t_k} \cdot p_{ct_k}O_2 + \gamma_{Hb} \cdot Hb \cdot Q_{t_k} \cdot \eta_{ct_k}), \quad (6)$$

$$\frac{dp_{t_k}O_2}{d\tau} = \frac{1}{V_{t_k}(\alpha_1 + \gamma_{Mb} \cdot Mb_k\frac{\partial \eta_{t_k}}{\partial p_{t_k}O_2})}(G_{t_k}O_2 - q_{t_k}O_2), \quad (7)$$

where the index $k = r, l$ corresponded to the left or right side of the heart; α_1, α_2 — solubility of gases in blood plasma; Hb, BH — the concentration of hemoglobin and buffer bases in the blood; γ, γ_{BH} — Hüfner constants; V_v — the volume of venous fluid; z_j — the degree of blood saturation with oxygen or carbon dioxide; Q_{t_k} — volumetric rate of coronary blood flow determined by the model of functional respiratory system (FRS); Q_{t_k} its actual rate in case of pathological changes in the heart. It is clear that $\tilde{Q}_{t_k} < Q_{t_k}$, i. e. the

actual blood flow rate with partial vascular permeability is lower than for the organism of healthy person.

If we assume that coronary vessels of the left and right parts of the heart are not damaged, then, with partial occlusion of the artery, the oxygen stress gradients in absolute value will be greater than corresponding gradients in case of vessel damage and, depending on occlusion degree, hypoxia in the heart muscle will be less pronounced.

If the vessels of the left or right side of the heart were damaged, then hypoxia occurred, being caused by partial occlusion of one part of the heart muscle, in the other, the volumetric blood flow rate would be greater than necessary. This would lead to the increase in oxygen tension in this part, i.e. an asymmetry in oxygen tensions distribution in the heart muscle appeared. When the degree of damage of arterial vessels that supply the blood to left and right sides of the heart was different, hypoxia was developed in the tissues of both parts of the heart, which was caused by different degrees of vascular occlusion, and then the distribution of oxygen tension will also be asymmetric.

Using this model, it was possible to analyze the situations when complete occlusion of the capillary bed occurred in elementary part of the heart muscle. In the initial period, there will be a sharp depletion of oxygen reserves from the blood, a mismatch in its supply with the needs of the tissues that surround the capillary, then the oxygen tension in this tissue area will become critical and this part will not be able to take part in the pumping function of the heart. Thus, in case of coronary vessels damage, the distribution of oxygen in the heart muscle depends on the degree of capillary bed damage and its localization.

In order to alleviate the hypoxic state, a number of medical substance are used for today; and for the optimization of the choice of medical substance, we proposed to use mathematical models that will simulate the effect of this substance, on organism of individual person.

The equations for the changes in tensions of oxygen and pharmacological substance in the blood of arterial flows were as follows [78, 82]:

$$\frac{dp_aO_2}{d\tau} = \frac{1}{V_a(\alpha_1+\gamma\cdot Hb\frac{\partial\eta_a}{\partial p_aO_2})}[\alpha_1(Q-Q_{sh})p_{Lc}O_2 + \\ +\gamma\cdot Hb\cdot(Q-Q_{sh})(\eta_{Lc}-\eta_a)+ \\ +\alpha_1 Q_{sh}p_{\bar{v}}O_2]+\frac{1}{V_a(\alpha_1+\gamma\cdot Hb\frac{\partial\eta_a}{\partial p_aO_2})}+ \\ +[\gamma\cdot BH\cdot Q_{sh}\eta_{\bar{v}}-\alpha_1 Qp_aO_2-\gamma\cdot BH\cdot q\eta_a], \quad (8)$$

$$\frac{dc_{f_a}}{d\tau} = \frac{1}{V_a}((Q-Q_{sh})c_{f_{lc}}+Q_{sh}c_{f_{\bar{v}}}-Qc_{f_a}. \quad (9)$$

It should be taken into account that the levels of gases tensions and substance concentrations is formed as a result of instant mixing of flows coming from the blood of pulmonary capillaries and the blood mixed with gases and substance.

Arterial blood vessels are branched into microcirculatory networks of organs and tissues. The classical mathematical model of mass transfer and mass exchange of respiratory gases presented above, describes the dynamics of respiratory gases tensions in m tissue reservoirs, among which, as a rule, tissues of the brain, kidneys, liver, gastrointestinal tract, cardiac and skeletal muscles, bone and adipose tissues are distinguished.

Equations (6) and (7), which described the changes in respiratory gases tensions in the blood washing the tissue and in tissue fluid of the reservoir, were supplemented by following equations for the concentrations of pharmacological substance for the blood of tissue capillaries:

$$\frac{dc_{f_{ct_i}}}{d\tau} = \frac{1}{V_{ct_i}}(Q_{t_i}(c_{f_a}-c_{f_{ct_i}})-G_{f_{t_i}}), \quad (10)$$

and for tissue fluid we supplemented the equations (6)–(7) with the expression

$$\frac{dc_{f_{t_i}}}{d\tau} = \frac{G_{f_{t_i}}}{V_{t_i}}, \quad (11)$$

where

$$G_{f_{t_i}} = D_{f_{t_i}}S_{t_i}(c_{f_{ct_i}}-c_{f_{t_i}}). \quad (12)$$

During the development of mathematical model of transport and mass exchange of respiratory gases and pharmacological substance, it was assumed that the substance

did not participated in metabolic processes directly, but it was regulatory factor for hypoxia stabilizing and compensation.

Let's suppose that pharmacological substance *f* belongs to pharmacological group that promotes vasodilation of capillary walls. Its effect on smooth muscles leads to more free penetration of oxygen and carbon dioxide through the barriers separating blood and tissue fluid and, at the same time, to the decrease of the rate of oxygen utilization by smooth muscles of capillaries.

Therefore, the amount of gas flow through the membrane between blood and tissue fluid can be expressed by the ratio:

$$G_{j_{t_i}} = K(c_{f_{t_i}}) \cdot D_{j_{t_i}} \cdot S_{t_i}(p_{j_{ct_i}} - j_{t_i}), \qquad (13)$$

where $K(c_{f_{t_i}})$ — functional enhancer of diffusion process of respiratory gases into the tissue reservoir. According to [82], some experimental studies permit to suggest that $1 \le K(c_{f_{t_i}}) \le 2$ for most pharmacological substance of this type.

In the venous bed the blood from the organs and tissues was mixed and transported to the lungs for oxygenation. Therefore, the equations for oxygen transport in mixed venous blood

$$\frac{dp_{\bar{v}}O_2}{d\tau} = \frac{1}{V_{\bar{v}}(\alpha_1 + \gamma \cdot Hb \frac{\partial \eta_{\bar{v}}}{\partial p_{\bar{v}}O_2})} \times$$

$$\times[\alpha_1(\sum_{t_i} Q_{t_i} \cdot p_{ct}O_2 - Q \cdot p_{\bar{v}}O_2) -$$

$$-\gamma \cdot Hb \cdot Q \cdot \eta_{\bar{v}}], \qquad (14)$$

have to be supplemented by the equation for concentration of pharmacological substance:

$$\frac{dc_{f_v}}{d\tau} = \frac{1}{V_{\bar{v}}}(\sum_{t_i} Q_{t_i} c_{f_{t_i}} + c_{f_a} Q_{f_{t_i}} - Qc_{f_v}). \qquad (15)$$

Differential equations and algebraic relations (1–15) describe fully the transport and mass exchange of respiratory gases and pharmacological substance in selected structure of respiratory system of respiratory cycle. The described mathematical model makes it possible to predict oxygen, carbon dioxide and nitrogen regimes of organism under the disturbing influences in forms of inhalation, oral, intramuscular and intravenous administration of pharmacological preparation.

In our model it was assumed that intravenous influence of antihypoxant was the most effective. In this case, the dynamics of substance *f* in mixed venous blood was:

$$\alpha_f V_v \frac{dc_{f_v}}{d\tau} = \sum_{t_i} \alpha_f Q_{t_i} c_{f_{t_i}} + d_f Q_{f_{t_i}} - \alpha_f Q c_{f_v}, \qquad (16)$$

where ($c_{f_{t_i}}$ — concentration of pharmacological substance in the blood of tissue capillaries of the region; t_i, ($c_{f_{t_i}}$ –concentration of substance in tissue fluid of the region t_i.

It is assumed that the removal of antihypoxant *f* from the organism is carried out through the kidneys, and the change in substance *f* concentration in the renal tissue is determined by the equation:

$$\alpha_{f_i} V_{t_i} \frac{dc_{f_{t_i}}}{d\tau} = G_{f_{i_i}} - \alpha_{t_i} Q_f c_{t_i}, \qquad (17)$$

where Q_f is the filtration rate of the liquid. It was assumed that the volumetric filtration rate was 0.035 mg/s.

Pharmacological correction of tissue hypoxia in case of vascular patency lesions. Results of numerical experiment. Series of experiments was carried out on mathematical model of hypoxic states pharmacological correction. The scheme of software package was shown on Fig. 3.

The results of computer analysis of the effect of antihypoxant influence on the organism of averaged person have been demonstrated below. Injected dose was 10 mg, preparation administration was done by pulsed intramuscular injection. The used substance had the ability to dilate blood vessels. The data on organism functional state with basal metabolism and during hypoxia caused by diseases of cardiovascular system were demonstrated in Table 2 [78].

The dynamics of partial pressures and tensions of respiratory gases in the organism after the imitation of antihypoxant injection were presented in Table 2.

The data given in Table 2 indicated that through 20 hours after the injection of pharmacological substance a new round of tissue hypoxia development had started. Oxygen tensions in tissues began to fall, and carbon dioxide tensions began to increase. Let's note that current concentration of the preparation in arterial blood reached the norm, equal to half of the average concentration of the substance earlier — through 18.5 hours after the injection.

Table 1. **Indicators of partial pressures and tensions of respiratory gases in healthy organism and with vascular occlusion**

Functional state		Tensions of respiratory gases in parts of the structure of respiratory system in mmHg									
		alveoli	arteria	brain	heart	liver	kidney	skelet. muscles	skin	other tissues	veins
Healthy organism	O_2 CO_2	125 38.5	95.2 41.5	38.1 46.54	27.7 48.73	42.4 45.6	66.7 48.6	31.8 54.1	37.0 51.8	37.0 51.3	39.9 51.02
CAD patient	O_2 CO_2	128 37.1	95.6 41.9	35.8 47.6	24.6 48.8	40.0 47.3	51.1 49.2	25.3 55.3	35.7 53.1	36.7 53.1	37.8 52.0

Note. CAD — coronary artery disease, CAD patient — patient with CAD.

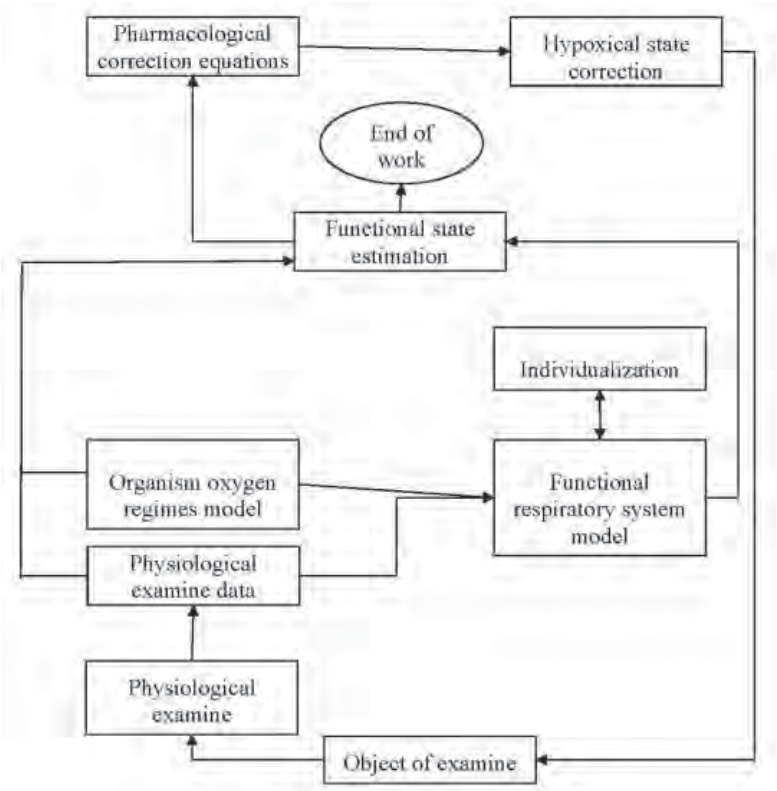

Fig. 3. **Scheme of the work of software package for simulation of pharmacological correction of hypoxic state at vascular occlusion**

In framework of our mathematical model we would like to emphasize that the results of computer analysis relate to the effect of pharmacological substance with only the characteristic we picked up for this model — the ability to dilate blood vessels, increasing the ability of respiratory gases to penetrate tissue reservoirs. As a rule, pharmacological substance s consist of several biologically active compounds. We hope that inclusion into pharmacological substance of substances that increase the oxygen capacity of the blood, in particular, increase the hemoglobin content in the blood, and will contribute to greater effectiveness of the substance for hypoxia compensation. However, the stimulation of erythropoiesis can contribute to an increase in hematocrit, higher density of red blood cells in circulating blood, and this can cause vascular thrombosis.

And in this case, for individual choice of the substance, the method of its influence and dosage, it is possible to use the algorithmic and software supply for mathematical model of respiratory gases transport in the organism in modification [79].

The iterative procedure for applying of proposed software package in this case will be as follows:

1. An instrumental examination of the patient is carried out. We get the data about

Table 2. **Indices of partial pressures and tensions of respiratory gases after antihypoxant injection**

Time after injection		Tensions of respiratory gases in parts of the structure of respiratory system in mmHg after the substance administration									
		alveoli	arte-ria	brain	heart	liver	kidney	skelet. muscles	skin	other tissues	veins
1 h	O_2 CO_2	125.6 36.2	95.0 41.2	36.5 47.3	25.1 47.8	40.8 46.9	52.0 48.7	26.5 54.8	35.8 52.8	36.5 53.0	38.0 52.3
5 h	O_2 CO_2	125.58 36.8	95.2 41.8	36.7 47.2	25.8 47.6	41.3 47.1	55.6 48.8	28.1 54.6	36.1 52.4	36.6 52.4	38.2 53.0
10 h	O_2 CO_2	125.2 37.3	95.1 41.3	37.1 46.4	25.9 47.95	41.6 45.7	60.1 48.6	29.6 54.2	36.3 51.9	36.6 51.9	38.5 51.0
15 h	O_2 CO_2	125.0 38.0	95.3 41.0	37.3 46.1	26.0 47.5	41.4 44.2	58.0 48.0	29.3 54.3	36.3 52.0	36.3 52.0	38.3 51.1
20 h	O_2 CO_2	125.1 37.8	95.2 40.9	37.1 46.8	25.6 48.1	40.65 46.2	56.3 48.2	28.75 54.5	36.0 52.2	36.1 52.2	37.9 53.0

lungs ventilation, composition of alveolar and exhaled air, frequency of respiration, blood pressure, frequency of heart construction, hemoglobin, blood acidity, and etc., which are the initial data for the model of organism oxygen regimes [78, 83, 84]

2. Basing on the data of instrumental examination, we calculate such indicators as minute volume of the respiration, minute volume of the blood, rate of oxygen consumption by the organism, the economy, intensity and efficiency of oxygen regimes of the organism, the data characterizing the hypoxic state.

3. The data of instrumental examination and the part of the data obtained in calculation of organism oxygen regimes were used as input ones for the operation of respiratory gas transport model described above. Thus, in such a way, the individualization of the model was carried out.

4. On individualized model we simulated the state of the rest of individual person. We obtained the values of the tensions of oxygen and carbon dioxide in the tissues of individual organs, which allow us to estimate the degree of tissue hypoxia.

5. Further we simulated the injection of pharmacological substance. Obtained data were analyzed and, thus, the optimal options for the use of specific preparation were selected.

We would like to note in addition that on Fig. 3 the immune response model was not subdivided separately, as it was done in [80]. This is due to the fact that we deal with already disturbed respiratory and blood circulatory systems and this is taken into account in given initial data. It was also inappropriate, from the point of view of the authors, to give any physiological interpretation of the data obtained in numerical experiment. It is clear that for the test task they can be erroneous. It is important that with the help of developed complex of information support, with the array of individual initial data, it is possible to simulate various doses of pharmacological substance and, thus, to objectify and optimize this process.

Conclusions

Thus, a complex mathematical model for simulating of cardiovascular system damage and correction of the resulting hypoxic state was suggested in present article. Our united model consists on the models of transport and mass exchange of respiratory gases, self-organization of respiratory and blood circulatory systems, partial vascular occlusion and pharmacological correction. On the developed software package, a series of computational experiments was carried out for the organism of averaged person, the imitation of antihypoxant injection — pharmacological influence with only characteristic — the ability to expand blood vessels, increasing the ability of respiratory gases to penetrate into tissue reservoirs. Naturally, since the test task was examined, it could be concluded that this approach could be used to alleviate the complicated course of the disease. For more specific conclusions the arrays with patient's individual data have to be used.

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МАТЕМАТИЧНА МОДЕЛЬ ДЛЯ ДОСЛІДЖЕННЯ ГІПОКСИЧНИХ СТАНІВ СЕРЦЕВОГО М'ЯЗА ЗА ВІРУСНОГО УРАЖЕННЯ

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У зв'язку з тим, що одним з основних ускладнень за вірусного ураження SARS-CoV-2 є різні патології серцево-судинної системи і, як наслідок, вторинна тканинна гіпоксія, актуальним є пошук засобів для полегшення гіпоксичного стану. Одним із напрямів може бути математичне моделювання цього процесу з наступною імітацією розвитку гіпоксичного стану і подальшої корекції гіпоксії.

Мета. Побудувати математичну модель функціональної системи дихання і кровообігу для імітації часткової оклюзії судин за ураження вірусною інфекцією і фармакологічної корекції спричиненого гіпоксичного стану.

Методи. Застосовували методи математичного моделювання та динамічного програмування. Транспортування та масообмін респіраторних газів в організмі, часткову оклюзію судин і введення антигіпоксантів записували системою звичайних нелінійних диференціальних рівнянь.

МАТЕМАТИЧЕСКАЯ МОДЕЛЬ ДЛЯ ИССЛЕДОВАНИЯ ГИПОКСИЧЕСКИХ СОСТОЯНИЙ В СЕРДЕЧНОЙ МЫШЦЕ ПРИ ВИРУСНОМ ПОРАЖЕНИИ

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В связи с тем, что одним из основных осложнений при поражении организма вирусом SARS-CoV- 2 являются различные патологии сердечно-сосудистой системы и, как следствие, вторичная тканевая гипоксия, актуальным является поиск средств для облегчения гипоксического состояния. Одним из направлений может быть математическое моделирование этого процесса с последующей имитацией развития гипоксического состояния и последующей коррекции гипоксии.

Цель. Построить математическую модель функциональной системы дыхания и кровообращения для имитации частичной окклюзии сосудов при поражении вирусной инфекцией и фармакологической коррекции возникшего гипоксического состояния.

Методы. Применялись методы математического моделирования и динамического программирования. Транспортировка и массообмен респираторных газов в организме, частичная окклюзия сосудов и введение антигипоксанта записывали системой обыкновенных нелинейных дифференциальных уравнений.

Результати. Розроблено математичну модель функціональної системи дихання для імітації фармакологічної корекції гіпоксичного стану, спричиненого ускладненим перебігом вірусної інфекції. Модель ґрунтується на теорії функціональних систем П. К. Анохіна і припущенні щодо основної функції системи дихання Передбачається взаємовплив і взаємозв'язок окремих функціональних систем організму. Складовими частинами комплексної моделі є моделі транспортування і масообміну респіраторних газів в організмі, самоорганізації системи дихання і кровообігу, часткової оклюзії судин і транспортування фармакологічного препарату.

Висновки. Проведено серію обчислювальних експериментів для організму середньостатистичної людини, яка показала можливості компенсації тканинної гіпоксії за допомогою фармакологічного препарату із судинорозширювальною дією. Запропонована модель, у разі наявності масиву індивідуальних даних, може бути корисною для вироблення стратегії і тактики лікування конкретного хворого.

Ключові слова: функціональна система дихання; транспортування та масообмін дихальних газів; гіпоксичний стан; часткове закупорювання судин.

Результаты. Разработана математическая модель функциональной системы дыхания для имитации фармакологической коррекции гипоксического состояния, вызванного осложненным течением вирусной инфекции. Модель базируется на теории функциональных систем П. К. Анохина и предположении об основной функции системы дыхания. Предполагается взаимовлияние и взаимосвязь отдельных функциональных систем организма. Составными частями являются модели транспортировки и массообмена респираторных газов в организме, самоорганизации системы дыхания и кровообращения, частичной окклюзии сосудов и транспортировки фармакологического препарата.

Выводы. Проведенная серия вычислительных экспериментов для организма среднестатистического человека показала возможности компенсации тканевой гипоксии с помощью фармакологического препарата с сосудорасширяющим действием и, при наличии массива индивидуальных данных, модель может оказаться полезной для выработки стратегии и тактики лечения конкретного больного.

Ключевые слова: функциональная дыхательная система; транспортировка и массообмен дыхательных газов; гипоксическое состояние; частичная окклюзия кровеносных сосудов.