ENERGY OF BLOOD CIRCULATION IN PRIMARY REDUCTION OF MYOCARDIAL CONTRACTILITY

K. Mykhnevych

The aim: *to study the energy parameters of the circulatory system in heart failure in patients with acute coronary syndrome (ACS) against the background of coronary artery bypass grafting (CABG), depending on the degree of myocardial contractility decrease.*

Materials and methods. *In 48 patients with ACS in the perioperative period energy parameters of blood circulation have been determined: flow power (FP), oxygen reserve (OR) and circulatory reserve (CR). FP reflects the useful power of the myocardium, OR – the correspondence of oxygen absorption by tissues to their needs, CR is an integral energy parameter. Patients have been divided into 2 groups: group CF1 (n=18) – patients with an ejection fraction (EF) of less than 40 %, group CF2 (n=30) – patients with EF of at least 40 %. The same treatment has been performed in both groups.*

Results. *The initial energy parameters of circulation were significantly reduced, more so in the CF1 group. During treatment, FP, OR, and CR in the CF1 group increased more slowly than in the CF2 group, and remained significantly lower by the end of the study. The initial CR was highly correlated with the need for dobutamine, the duration of postoperative artificial blood circulation, and postoperative mechanical ventilation, so CR can also be used as a predictive criterion.*

Conclusions. *Determination of energy indicators of blood circulation allows you to fully assess the state of the circulatory system, predict the course of its insufficiency and monitor the effectiveness of its treatment. The severe decrease in myocardial contractility, accompanied by a decrease in the EF to 40 % or lower, slows down the recovery of energy parameters of circulation and requires the search for more effective methods of intensive therapy*

Keywords: *circulatory energy, heart failure, acute coronary syndrome, coronary artery bypass grafting*

1. Introduction

Unrelenting attention is rightly paid to the energy budget of the body, but in most of the works we have not been able to find a complete understanding of this issue. As a rule, the chemical (which is essentially electromagnetic) form of energy is studied. This component of energy exchange is well studied, but its connections with other forms of energy that take place in the body are, at best, veiled, and more often they are simply not considered. Meanwhile, the production of energy by the body already requires energy in itself: you need to get food (although today this is not a big problem in developed countries), and most importantly, you need to get oxygen, which is a kind of carrier of potential chemical energy, and then deliver it to the place use. It does not require new evidence that the process of oxygen transfer from the atmosphere to cells is energy dependent, and the circulatory system plays a key role in this process.

The human body consumes energy at a high rate even at rest – about 100 W [1, 2]. Regulation of energy consumption is extremely complex and includes numerous compensation mechanisms, which can hardly be fully taken into account in a particular patient. Even G. A. Ryabov in 1988 pointed out the need to take into account at least two indicators of the oxygen budget during hypoxia, and for different mechanisms of its development, pairs of indicators are different [3]. This situation is typical not only for living nature, but also for inanimate. An example is

the state of a gas in a vessel, the molecules of which move in different ways and unpredictably, but there are parameters that automatically take into account the behavior of all molecules – pressure and temperature. Thus, the uncertain characteristics of gas molecules (with a large number of them) can be estimated with complete certainty using integral indicators. In the microcosm, the situation is still not defined: even a single microparticle cannot be completely definitely characterized, which is expressed by the Heisenberg uncertainty principle, known today to any high school student. Biological objects also have uncertainty in many ways, in particular, in the sense that the same result of regulation of a particular function can be achieved with different combinations of the severity of different regulatory influences. This phenomenon was expressed in 1976 by Rushmer in the form of the principle of biological uncertainty [4].

Thus, the specific state of a particular function of the body, including the function of blood circulation, may be due to the implementation of an unpredictable combination of various adaptive mechanisms, and then the only universal method, which has long been used in the sciences of inanimate nature, remains to describe the state of the function – energy.

Any circulatory disturbance reduces the supply of oxygen to tissues, which is a stressful situation that activates the sympathoadrenal system (SAS), and this, in turn, leads to an increase in tissue energy requirements

against the background of the impossibility of adequately providing this growth [3]. One of the consequences of SAS activation is an increase in total peripheral resistance (TPR), bringing the volume of the receiving vessels into line with the reduced incoming blood volume. This requires an increased energy expenditure from the myocardium without increasing its efficiency (a phenomenon that has been known for a long time, but has not yet been explained) [5], and if the myocardium cannot provide sufficient energy for blood flow, circulatory failure will develop, namely, heart failure.

One of the reasons for the primary decrease in myocardial contractility is acute coronary syndrome (ACS), the only way to correct it in some patients is coronary artery bypass grafting (CABG) [6].

The aim of the study is to determine the energy characteristics of the circulatory system in heart failure in patients with ACS on the background of CABG, depending on the degree of myocardial contractility (MC) decrease.

2. Materials and methods

The state of circulatory function was studied in 48 patients with ACS who were admitted in the period from 2013 to 2017 for performing CABG at the State Institution Heart Institute of the Ministry of Health of Ukraine. To participate in the study, patients gave written informed consent. The study was conducted in accordance with the requirements of the Declaration of Helsinki on Human Rights (1964), the International Conference on the Harmonization of Good Clinical Practice (ICH GCP), the Council of Europe Convention for the Protection of Human Rights and Honor with regard to the Use of Biology and Medicine (Convention on Human Rights and Biomedicine) (ETS-164), including the additional protocol of the Convention on Biomedical Research of January 25, 2005 and the legislation of Ukraine (protocol No. 2 of June 10, 2020 of the meeting of the Commission on Ethics and Bioethics of Kharkiv National Medical University).

The examined patients were divided into 2 groups depending on the level of ejection fraction (EF) at admission. Group CF1 (cardiac failure) included 18 patients with EF less than 40 %, group CF2 – 30 patients with EF not less than 40 %. The principle of division into groups is associated with the prevailing clinical impression of a more severe course of ACS in patients with EF less than 40 %. The demographic and anthropometric characteristics of the examined patients are presented in Table 1.

The differences between the groups in the presented indicators concerned only age: patients with EF<40 % were significantly older.

Upon admission to the hospital, all patients underwent coronary angiography, after which they were transferred to the preoperative room, where, after induction into anesthesia (diprivan 1.5–2 mg/kg, fentanyl 1.5–3 µg/kg, arduan 0.08 mg/kg), they were intubated trachea and started mechanical ventilation (MV). In order to prevent fibrillation and achieve a coronary effect, β_1-adrenergic blocker Betalok (2–2.5 mg) was administered. After that, the patients were transferred to the operating room. Basis anesthesia – sevoflurane in a semi-closed circuit (1.5–5 vol %), gas flow 3.2–3.7 l/min, analgesia – fentanyl 3–5 µg/kg·hour. After a purse-string suture was applied to the aorta, heparin was injected at a dose of 300 U/kg and artificial circulation (AC) began. The gas flow into the lungs was 0.45–0.9 l/min under PEEP 4 mm H_2O, the sevoflurane evaporator was connected to the HLM gas line (1.5–2.5 vol %). At the end of the main stage of the operation, the AC was stopped, the patient was warmed up, after reaching a body temperature of 34–35 °C, electrical defibrillation with energy of 10 J was performed and infusion of dobutamine was started, the dose of which was controlled by pressure in the left atrium (target level 8–12 mm Hg). To normalize TPR, norepinephrine was used at a dose of 20–200 ng/kg·min, to provide a coronary effect – nitroglycerin at a dose of 2–4 µg/kg·min, to prevent fibrillation – Betaloc 3–7 mg bolus.

To determine the energy characteristics of blood circulation, we measured its mechanical parameters and parameters of the hemic oxygen transport link.

We divided the mechanical indicators into kinetic ones, describing the movement of blood through the vessels without considering the reasons for the movement (end diastolic and systolic volumes – EDV and ESV, stroke volume – SV, heart rate – HR, cardiac output – CO) and dynamic, describing the causes of blood movement (systemic perfusion pressure – SPP, equal to the difference between effective arterial and central venous pressure – APe and CVP, and TPR).

Of the hemodynamic parameters, EDV and ESV were directly measured by the echocardiographic method (apparatus "Aplio XG SSA-770A", "Toshiba", Japan), as well as HR, AP and CVP. Based on the measured values, SPP, CO, TPR and energy values were calculated.

Hemic indicators were calculated on the basis of a modified by us generally accepted method for determining the oxygen content in blood according to the formula [1]:

$$C_{O_2}[mol/ml] = K_H[mol/g] \cdot C_{Hb}[g/ml] \cdot S_{O_2} + K_B^2[mol/ml \cdot b] \cdot (1 - C_{Ht}) \cdot p_{O_2}[b], \quad (1)$$

Table 1

Distribution of patients with primary heart failure by groups

Group	Age, years M±σ	Body weight, kg, M±σ	Height, cm, M±σ	BSA, m², M±σ	BMI, kg/m², M±σ	Men n (%, p±m)	Women n (%, p±m)
CF1 (n=18)	60.4±5.1	87.3±9.9	174.8±8.9	2.13±0.15	28.5±3.6	11 (61.1±11.5)	7 (38.9±11.5)
CF2 (n=30)	56.8±4.3	88.7±8.2	177.0±7.4	2.16±0.11	28.5±3.6	21 (70.0±10.8)	9 (30.0±10.8)

where $K_H = 5.98 \cdot 10^5$ mol/g – Hüfner's constant reflecting the mass of oxygen bound by 1 gram of hemoglobin; C_{Hb} – hemoglobin concentration, g/ml; S_{O_2} – proportion of oxygenated haemoglobin; $K_B = 1.04 \cdot 10^{11}$ mol/ml·b – Bunsen constant, which reflects the mass of dissolved oxygen per unit volume of plasma at a unit partial pressure of oxygen in it (b = dyn/cm²); p_{O_2} – partial pressure of oxygen in plasma.

Oxygen transport, consumption and extraction ratio (OER) was calculated using conventional methods.

On the basis of the above-described indicators, the energy parameters of blood circulation were calculated: blood flow power (BFP), oxygen reserve (OR) and circulatory reserve (CR). BFP was calculated based on the laws of hydrodynamics as the product of SPP and CO. The OR indicator was used as an indicator of the adequacy of oxygen consumption by tissues to their needs and was calculated as one third of the quotient from the division of the arteriovenous difference in the oxygen content (mol/L) and the concentration of lactate (L) in the blood (mol/L), that is, OR is a dimensionless value:

$$OR = \frac{1}{3} \frac{C_{(a-v)o_2}}{L}. \qquad (2)$$

The calculation of OR is based on the fact that aerobic oxidation of 1 mole of glucose requires 6 moles of oxygen, and during anaerobic oxidation, 2 moles of lactate are formed from 1 mole of glucose, that is, 1 mole of lactate corresponds to non-oxidation of 0.5 mole of glucose, or the non-use of 3 moles of oxygen [7].

For an integral assessment of the energy of blood circulation, we introduced the CR indicator, which is equal to the product of BFP and OR. Its decrease corresponds to circulatory failure of any genesis, while its increase corresponds to adequate provision of increased tissue energy requirements.

All measured and calculated parameters, with the exception of those not subject to normalization (SPP, C_{O_2}, OR), were normalized to body surface area to obtain the corresponding indices: stroke (SI), cardiac (CI), specific peripheral vascular resistance (SPVR), index BFP (BFPI) and index CR (CRI).

Blood circulation indicators were recorded at the following stages:
1) before the operation;
2) exit from perfusion;
3) transfer to the intensive care unit (ICU);
4) transfer from ICU.

An important feature of the perioperative period in the examined category of patients was a significant decrease in the oxygen capacity of the blood by stage 2, due to the need for hemodilution to provide AC.

In a preliminary study, the values of energy parameters of blood circulation were determined in 30 healthy volunteers [8], with which the results obtained in patients were then compared.

The significance of the differences between the indicators was assessed using the Student's test; the differences were considered significant if the p value was less than 0.05. Correlation dependences were assessed by calculating the Pearson correlation coefficient.

3. Research results

Naturally, the initial kinetic parameters of patients in the CF1 group were lower than in patients in the CF2 group (Fig. 1), but in both groups they were lower than the reference values. All baseline differences were significant and were caused by different MC.
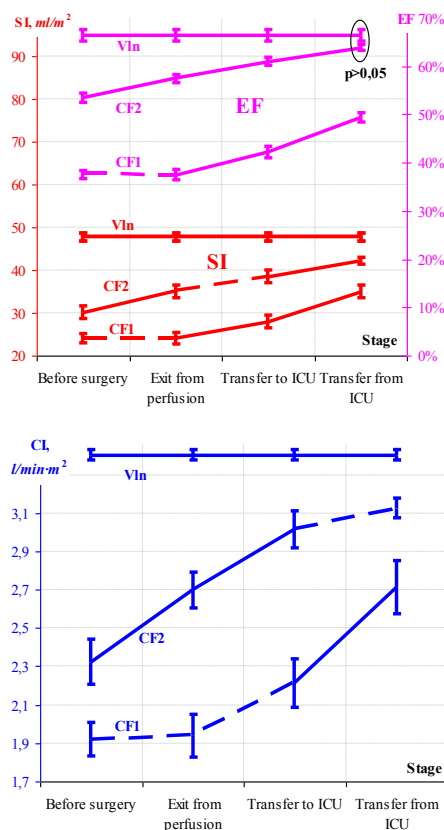

Fig. 1. Kinetic parameters of blood circulation depending on MC (hereinafter M±m); Vln – a group of healthy volunteers

The response to the decrease in CI was an increase in vascular tone due to the activation of SAS in response to hypoxic stress, which was manifested in an increase in SPVR (Fig. 2). This imposed increased energy requirements on the myocardium to maintain CI, which requires an increase in SPP. The myocardium of patients of the CF1 group could not fulfil this requirement, as a result of which the SPP was reduced. In patients of the CF2 group, the myocardium possessed greater energy reserves, but they were only enough to prevent a fall in SPP, as a result of which the CI in these patients was also reduced, although to a significantly lesser extent.

The complex of therapeutic measures (CABG and perioperative intensive therapy) increased the energy reserves of the myocardium and improved the state of microcirculation, as a result of which the SPVR decreased and the energy reserves of the myocardium made it possible to increase the CI even without a significant increase in the SPP. However, with an initially lower MC, treatment outcomes were worse: CI increased to a lesser extent, and SPVR also

decreased to a lesser extent; only SPP and only in the CF2 group did not differ from the level of healthy volunteers.
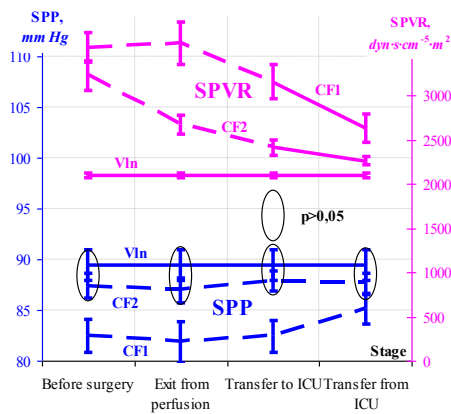

Fig. 2. Dynamic indicators of blood circulation depending on MC

Circulatory patterns associated with MC influenced energy performance (Fig. 3). The useful power that the myocardium was able to deliver to the bloodstream (BFPI) was reduced in both groups of patients. Operation and intensive therapy in the CF2 group, already after the cessation of cardiopulmonary bypass, made it possible to significantly increase this indicator, whereas in the CF1 group it significantly increased only at the end of the study, but remained significantly lower than in the CF2 group. At the same time, in the CF1 group, only 33.3 ± 11.1 % of patients had BFPI achieved the reference values, and in the CF2 group – in 93.3 ± 4.6 %.
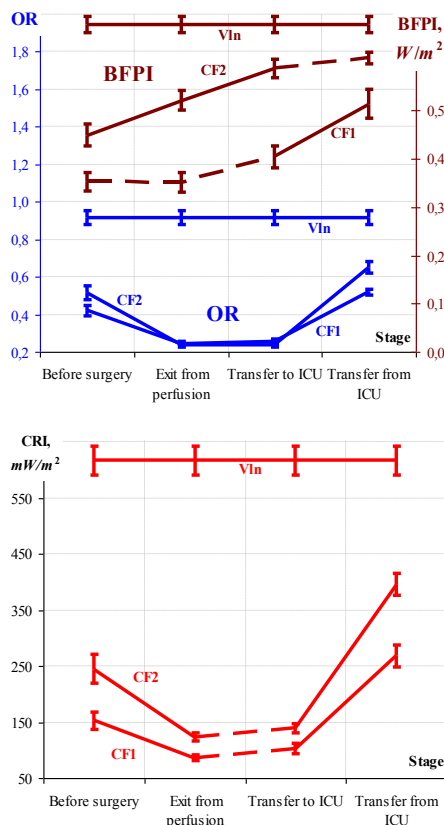

Fig. 3. Energy indicators of blood circulation depending on MC

OR and CRI reflected the dynamics of all the studied parameters of blood circulation, changes in which were sometimes uncertain and multidirectional. With a more pronounced decrease in MC, they were significantly lower than with a less pronounced one. At critical moments of the operation, they were minimal; at the end of the study, they became much higher than at the beginning. In the CF1 group, CRI reached the level of volunteers in 22.2 ± 9.8 % of patients, in the CF2 group – in 63.3 ± 8.8 %. Thus, CRI allows predicting the course of the perioperative period and evaluating the effectiveness of treatment in patients with ACS. The lower this indicator, the slower adequate blood circulation is restored.

CRI also correlated with such clinical characteristics as the need for inotropic support with dobutamine, the duration of postoperative AC and AV. The correlation coefficient of baseline CRI in the CF1 group with the dobutamine dose was $r=-0.87\pm0.06$; $p=0.02$, with the duration of postoperative AC – $r=-0.81\pm0.08$; $p<0.03$, with the duration of postoperative AV – $r=-0.90\pm0.04$; $p=0.01$. In the CF2 group, these indicators were lower (respectively, $r=-0.72\pm0.09$; $p=0.04$, $r=-0.64\pm0.11$; $p==0.049$ and $r=-0.71\pm0.09$; $p=0.04$), which can be regarded as a lower compensation intensity.

4. Discussion of research results

Despite the fact that the kinetics and dynamics of blood flow has been studied for a long time and successfully, the study of the energetics of blood circulation in the presented form has not been carried out before, although attempts of this kind have been made [5, 9]. As a result of the analysis of these attempts, it was revealed that they do not meet the strict requirements of physical science and lead to many inaccuracies, which we tried to neutralize [7, 10].

Currently, the fact that a decrease in MC leads to a decrease in such a kinetic indicator as CI and such a dynamic indicator as SPP does not require additional evidence, which is caused by a compensatory increase in the dynamic indicator of TPR against the background of reduced myocardial ability to overcome it [5]. Our research has shown that such changes are accompanied by a drop in the energy indicators of blood circulation, first of all, the power of blood flow. As a result, as a response to circulatory hypoxia, a stress reaction develops in the form of an increase in vascular tone, which makes increased demands on the myocardium, the adequate implementation of which is impossible due to a decrease in MC [5]. Lack of oxygen supply to tissues is reflected in a significant decrease in OR and integral energy index – CR. The degree of decrease in these indicators corresponds to the clinical manifestations of the course of the disease and the severity of the decrease in MC, determined by EF.

Surgical treatment and intensive therapy aimed at increasing MC had a positive effect on the energy of blood circulation, which was restored the faster, the less pronounced the initial decrease in MC was.

The study of energy indicators of blood circulation, thus, makes a more complete description of the state of hemodynamics and allows predicting the course of the early postoperative period, as well as monitoring intensive therapy.

Study limitations. The small number of examined patients does not allow to extend the obtained data to the entire population of patients, which requires further research.

Prospects for further research. The study of the energy of blood circulation is necessary for circulatory disorders of various origins, in particular – with vascular insufficiency and with hypovolemia associated or not associated with blood loss. This will clarify the pathogenesis of circulatory failure and the prognostic value of energy indicators.

5. Conclusions

1. A pronounced drop in myocardial contractility against the background of acute coronary syndrome, ac-companied by a decrease in the ejection fraction to 40 % and below, leads to a violation of the energy balance of tissues, which is expressed in a decrease in their oxygen reserve below 0.6 and circulatory reserve below 300 mW/m^2, which below the level of reference values by about 1.5–2 times.

2. The more pronounced the initial disturbances in myocardial contractility in acute coronary syndrome, the slower the recovery of the energy parameters of blood circulation after coronary artery bypass grafting, which requires the search for more effective methods of intensive therapy.

Conflict of interest

The authors declare that they have no conflicts of interest.

References

1. Ivanov, K. P. (2016). Novye biologicheskie problemy v energetike zhivykh sistem. Uspekhi sovremennoi biologii, 136 (6), 586–592.

2. Ivanov, K. P. (2008). Energiia i zhizn. Uspekhi sovremennoi biologii, 128 (6), 606–619.

3. Riabov, G. A. (1988). Gipoksiia kriticheskikh sostoianii. Moscow: Meditsina, 288.

4. Rashmer, R. F.; Kositskii, G. I. (1981). Dinamika serdechno-sosudistoi sistemy. Moscow: Meditsina, 600.

5. Folkov, B., Nil, E. (1976). Krovoobraschenie. Moscow: Meditsina, 463.

6. Eagle, K. A., Guyton, R. A., Davidoff, R., Edwards, F. H., Ewy, G. A., Gardner, T. J. et. al. (2004). ACC/AHA 2004 Guideline Update for Coronary Artery Bypass Graft Surgery: Summary Article. Journal of the American College of Cardiology, 44 (5), 1146–1154. doi: http://doi.org/10.1016/j.jacc.2004.07.021

7. Mykhnevych, K. H., Volkova, Yu. V., Khartanovych, M. V., Lyzohub, M. V. (2020). Enerhetychni aspekty krovoobihu. Kharkiv: TOV «Planeta-Prynt», 165.

8. Mykhnevych, K. G., Volkova, Y. V., Baranova, N. V., Boiko, O. V. (2020). Determination of reference values of energy parameters of circulation. Ukraïns′kij Žurnal Medicini, Bìologìï Ta Sportu, 5 (4 (26)), 182–188. doi: http://doi.org/10.26693/jmbs05.04.182

9. Usenko, L. V., Shifrin, G. A. (2007). Intensivnaia terapiia pri krovopotere. Dnepropetrovsk: Novaia ideologiia, 290.

10. Mikhnevich, K. G. (2018). Some questions of hydrodynamics and energetics of circulatory and hemic links of the oxygen transport system (part 3). Emergency medicine, 6 (93), 28–34. doi: http://doi.org/10.22141/2224-0586.6.93.2018.147639

Mykhnevych Kostiantyn, PhD, Associate Professor, Department of Emergency, Anesthesiology and Intensive Care, Kharkiv National Medical University, Nauky ave., 4, Kharkiv, Ukraine, 61022
E-mail: kmikhnevich@yahoo.com