2. Hemodynamics mathematical model of G. Poedinzev – O. Voronova

2.1 Hemodynamics equations of G. Poedinzev – O. Voronova

The blood circulatory system can be treated as optimal and effective hydraulic system that includes a pump (heart), and an elastic pipeline (vessels). Therefore, the knowledge of the cardio-vascular system functioning laws and the functioning regulation is hardly possible without taking into account the specific properties of the blood circulation hydrodynamics (i.e. hemodynamics).

According to classical hydrodynamics, there are two modes of liquid motion: laminar and turbulent. It is commonly supposed that, the blood flow in the whole vascular system is laminar, but at the aorta opening it is turbulent. This is written in all books dealing with blood circulation. Moreover, the Gagen-Poiseuille law can be applied to laminar flow of blood. The specific characteristic of this law is a parabolic distribution of speeds in the effective cross-section of vessel [28–30]. With the speed distribution like this, all the blood components are evenly distributed in the flow, and consequently, the average speed of their motion equals to the average speed of the flow as a whole.

However, in some papers we can find the data contradictory to affirmation of the in vivo sanguimotion in Gagen-Poiseuille mode. To begin with, Poiseuille himself has carried out investigations and admitted that the law is not applicative to the sanguimotion in vessels. This notwithstanding, the erroneous conception of the Poiseuille law of sanguimotion persists and was accepted as official. Let us mention briefly some contradictions that are most significant.

The analysis of the blood circulation in vessels proved that the blood circulation pattern has a specific regular three-dimension structure. It was found out that "when the concentration is normal or close to normal, the erythrocytes shall form inside the bloodstream the rouleaus arranged concentrically inside in orthogonal section" [31]. The search for the mechanism that structures the blood circulation (according to Poiseuille concept of sanguimotion in vessels) showed no prospects. For Poiseuille flow, the parabolic distribution of speeds and lack of lateral gradient of static pressure are characteristic. So, the hydrodynamic forces required for structurization of the moving blood, i. e. for the rouleaus formation, are not available.

Some of the experimental investigations of sanguimotion in vessels do not prove the concept of parabolic speed distribution and of blood flow uniform structure. In ascending aorta, the speed profile is flattened, while in descending aorta it assumes the M-shaped form [32].

Also it was experimentally proved that the dry blood (plazma) and erythrocytes linear motion speeds are not equal: the erythrocytes motion speed is higher than the speed of the plazma [33].

This specific velocity profile is not characteristic neither for Poiseuille flow nor for the turbulent motion.

To this must be added the following: Poiseuille blood flow concept is ajar with the principle of optimality that is the basic principle of the biological systems functioning by virtue of which all the processes that take place in the biology are characterized with the ultra-high efficiency [34]. Exactly the compliance with this principle can serve a key factor in the process of assessment of the theoretical models validity and adequacy, especially when we mean the organism systems functioning models.

Since the blood circulatory system is the optimum nature-made hydraulic system, the functioning of this system is characterized with the most high efficiency. So, one would expect that also the blood vessels show a very high hydraulic efficiency.

But, if the blood flow in the vessels would comply with Poiseuille law, the hydraulic efficiency would be hyperlow, i.e. the huge energy loss would be required to overcome the friction. Just for example, the hydraulic efficiency in the arterioles would be equal approximately to 3.1x10-6, it would not comply with the "principle of optimality" [35, 36].

The above-mentioned facts allow to come to conclusion: the sanguimotion in the blood vessels does not comply with the Poiseuille law, but it is effected in the mode that allows to essentially decrease the head pressure loss due to friction, and the flow structurization takes place. The classical hydrodynamics does not offer the solution to this matter.

The situation has changed fundamentally when the previously unknown "third" mode of fluid flow has been discovered. The third mode differs from the other two well-known modes (the laminar (Poiseuille) flow and the turbulent flow) and is distinguished by substantially lower loss in pressure head and by the particular undulant structure of stream. It was found out that exactly in this particular mode (not in Poiseuille mode), the blood flows in the blood vessels [35–37].

This approach provided the new opportunities for the investigating the functions and regulation principles of blood circulatory system when it is considered an optimal biological transportation system.

The hemodynamic processes in the blood circulatory system have been investigated using the crucially new scientific basis, i.e. based on the third mode of sanguimotion in vessels. Following is the brief description of the theoretical basis and of the work fulfilled.

The initial theoretical and experimental investigations in the Hydrodynamics were undertaken in the 60-th years of the 20-th century by G. M. Poedinzev (1929 ÷ 2006). They resulted in development of the new theory of "third" mode of the fluid flow. In the end of 70th, O. K. Voronova joined the work. More than twenty years, the creative working team of this book co-authors have been working at further theoretical treatment and practical implementation of this concept.

The mathematical process aimed at derivation of the real liquid motion equation started with the verification of the prerequisites that made the basis for the Navier-Stokes equation (classical equation of viscous fluid motion). All the prerequisites and assumptions have been checked for consistency, self-sufficiency and independence. For this purpose, they have been represented as the set of axioms. The set has been analyzed and as a result it was proved that two axioms were irrelevant.

The first axiom contains the statement of the liquid incompressibility.

In incompressible media, the sound speed is taken to be equal to infinity. It follows that the relative shift of individual particles is not feasible in this media because the agitation in one spot immediately is translated to all other particles of the media. It means that this hypothetical media will possess the properties inherent to a perfectly rigid body but not to fluid. Thus, the notion "incompressible" is in contrast to notion "fluid". In actual practice, the fluid compressibility is rather low. This property could be ignored in calculations, but it should not be neglected in the motion modeling process. Otherwise, we lose one parameter of prime importance, namely the sonic velocity in liquid media, that actually is of the final value.

The second axiom establishes the linear dependence of tangent stress vs shearing rate.

This prerequisite implies that the tangent stress in liquid is proportional to shear velocity (Newton's law of friction), and in this context, it is rather a theorem than an axiom by virtue of the fact that the fluid motion is predetermined not only by the action of external forces but also by the action of the internal friction mechanism. It means that as a matter of fact the friction law is the law of the fluid motion that shall be worked out through modeling. Accordingly, when we derive the real liquid motion equation, the law of friction belongs to theorem category and, pursuant to the axiomatic method, it can't be included into set of axioms.

Elimination of the contradictions and restrictions (that are at root of Navier-Stokes equation derivation method allowed to revise the set of axioms and to derive the real liquid motion equations. They differ from Navier-Stokes equations, and their solutions were obtained only through the analytical approach.

The further investigations proved the applicability of the newly developed mathematical model for describing the principles and regularities of the real liquid motion. The model was used for description of the laminar (Poiseuille) and turbulent flow modes, as well as for description of the period from the instant of the fluid motion onset in the pipe to the instant of the unsteady flow transformation to stationary motion. This stage of investigation appeared to be exceptionally interesting.

It was found out that the actual internal friction mechanism is much more complicated than one represented by the Newton linear friction law. It appeared that the friction occurring in the flowing liquid is of nonstationary wave nature.

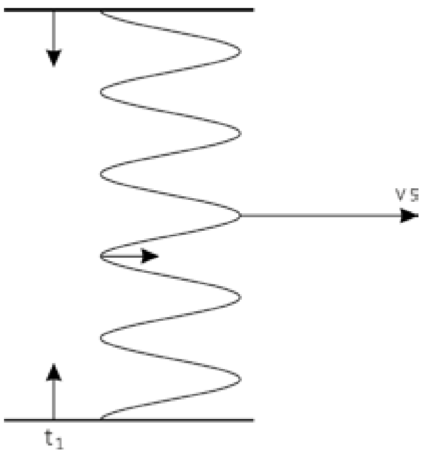

Fig. 1 Formation of the running friction waves at the onset of fluid motion in tube

For example: in tube at the instant of the fluid flow onset (while fluid is in quiescent state), in the superfine boundary layer nearest to the tube inside surface, the concentric friction waves packet is originated and immediately (like connection bellows) is spread into the depth of the flow. At that, the edge wave is not detached from the inside surface of the tube, while the frontal wave spreads about and runs at sound velocity to the tube axis, it is shown schematically in Fig.1.

As soon as the tube axis is reached, the wave disappears (its radius gets equal to zero). But the other next wave comes up to the axis and disappears as well. And so on and so forth. The steady-state (laminar) flow condition (defined by Gagen-Poiseuille) is settled when all the waves of the wave-packet (with the exception of the minor parietal area) disappear after they have reached the tube. Exactly to this current the Newton law of friction can be applied. Objectively, the process of the unsteady flow reshaping to a steady-state flow takes just fraction of a second. This process is shown in Fig. 2.

So, when the liquid motion is set up in the tube, the fluctuating wavelike velocity profile exists within a very short time, and in addition to that, the peak-to-valley pattern of the static

pressure is observed in conformity with the Bernoulli law. If the suspended particles appear in the flow of this kind, then the lateral static pressure gradients shall push them out into the layers where the pressure is the lowest. According to Bernoulli law, those are the layers where the motion speed is the highest. That is, the formation of the moving liquid stream occurs.

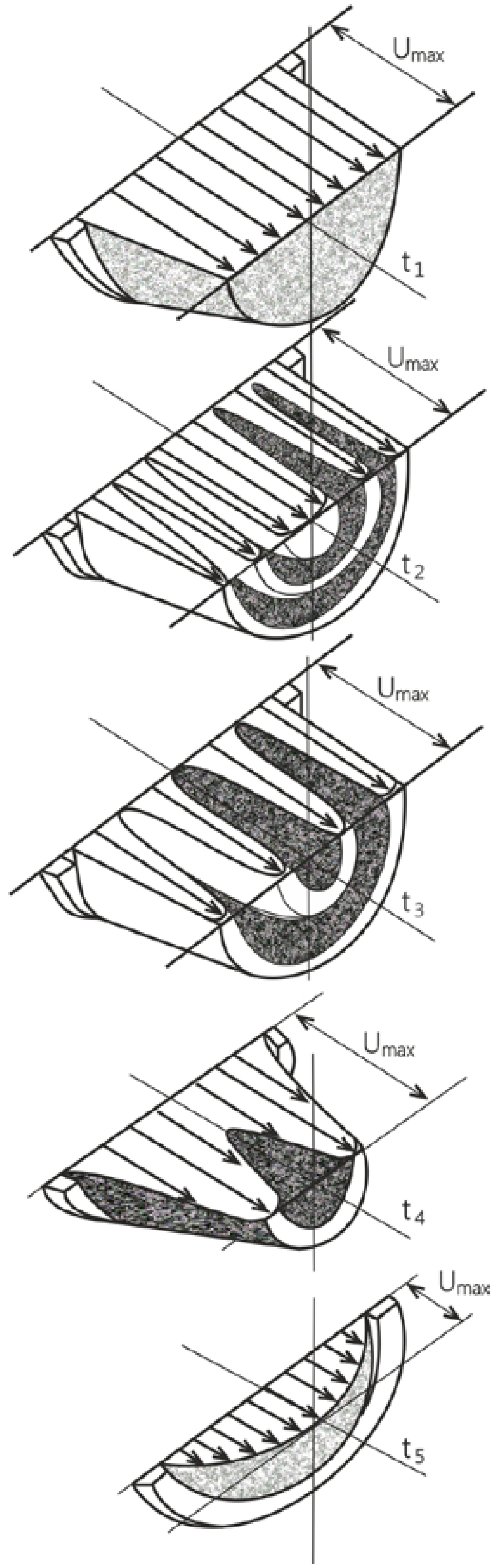

Fig. 2. Liquid flow velocity profiles for the same flow section of the pipe at different acceleration time ($t1<t2<t3<t4<t5$), where t5 is the time within which the nonstationary motion of the liquid transfers to stationary motion

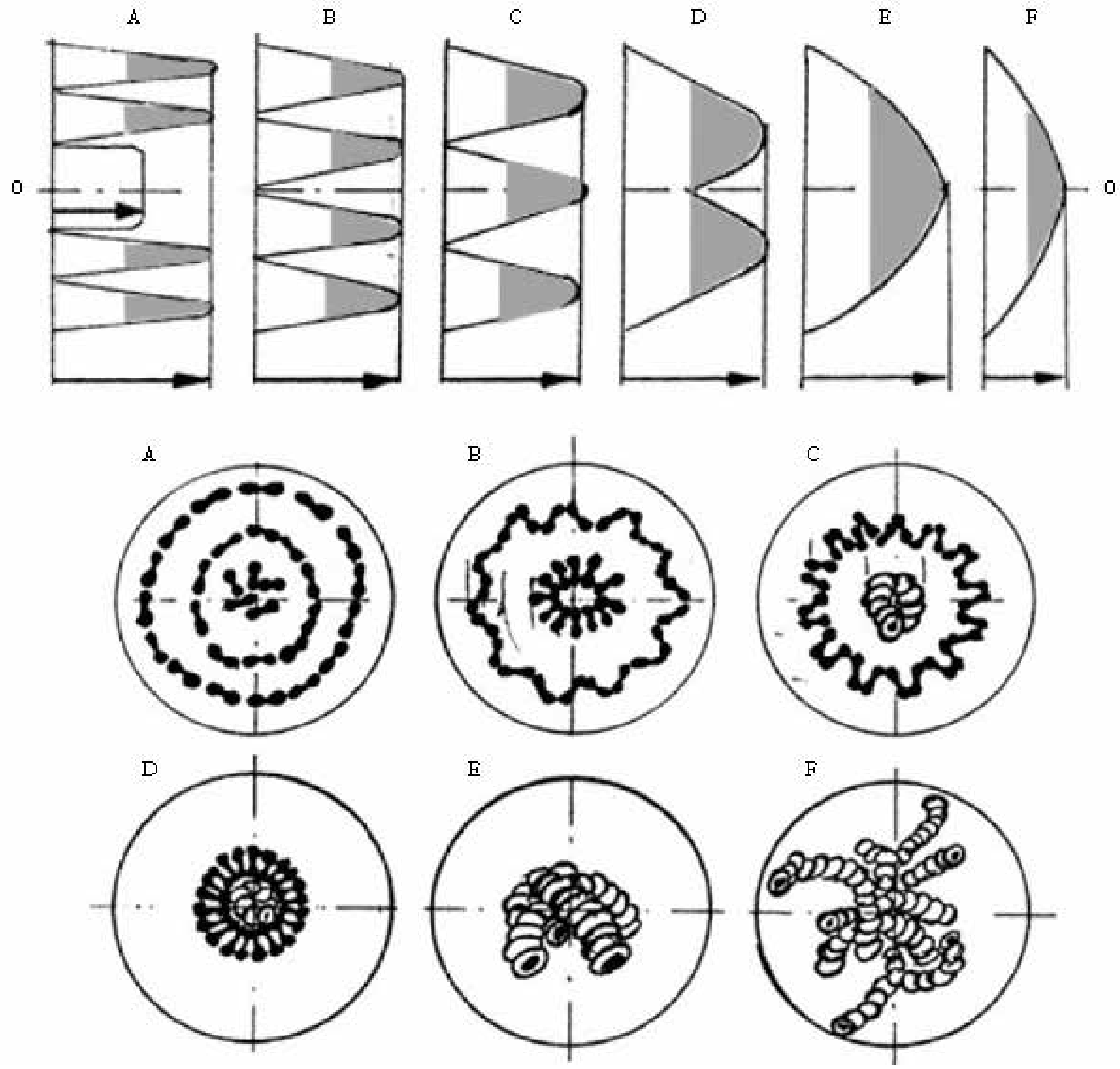

Fig. 3. Formation of two-phase fluid flow structure in tube at the moment of transition from quiescent state to motion (according to G. M. Poedinzev and O. K. Voronova)

There is one more unique feature: during this period, the head loss due to friction during the liquid motion is incomparably smaller then in the steady–state laminar flow.

At first, it was calculated and then proved by experiment.

As a matter of fact, the mathematical model of internal friction wave mechanism was developed. The model represents the set of equations that describe the motion of the real fluid. The model analysis proved that the friction mechanism can be controlled by changing the fluid motion speed by a definite law. The existence of then unknown fluid motion mode was predicted. This mode differs form the two already known ones: laminar (Gagen-Poiseuille) mode and turbulent mode. The losses of pressure required to overcome the friction are substantially lower and it has a particular flow pattern. The flow pattern is formed by the steady undulations of velocity and static pressure profiles with high transverse gradients of these parameters. Initially this mode was referred to as "initial stage of acceleration current", later on as "elevated fluidity mode", then as "the third mode of fluid flow" (in contrast to the laminar (Poiseuille) and turbulent modes).

As noted above, the "third" mode is characterized with high gradients of lateral speed and, consequently, of static pressure. If the fluid contains suspended particles that are similar to blood cells, then as the above-mentioned wave process is in progress, the particles will concentrate in the waves maximums, while the pure fluid will concentrate in the wave minimum. As a consequence of this process, the flow structure will become similar to the layer cake. When this structure is moving along the center line of the pipe, the speed of concentric layers with particles shall be twice as higher than the speed of the layers without particles. The speed vectors shall be parallel to the axes of current. And this is just the elevated fluidity condition associated with low friction that exists between the layers and the tube walls. Fig. 3 shows the erythrocytes arrangement in the stream of blood in every instant of time in the described process.

While in the initial stage of the accelerating current (third mode) the alternate ring-shaped layers of the blood and plasma are observed, in the laminar flow conditions (ref. Fig. 3, E and F) all elements are concentrated in the flow center. At that, they are very close to each other, just producing a solid mass. This process can result in red blood cell aggregation and haemolysis. To avoid these pathological after-effects, it is necessary to control the flow structure so that the quantity of the ring-shaped layers does not decrease in course of time and remains constant.

Discovered was the method of maintaining in tube for unlimited time the fluid motion mode with the stationary axial-symmetric profile of flow velocity and static pressure [35, 36].

This is feasible only in pulsed mode. The fluid motion in pulsed mode inside a springy tube is the most efficient, at that the fluid flow speed and the tube radius shall change in each impulse by well-defined law, namely:

- instantaneous speed of fluid flow motion in elastic tube changes within an impulse according the law:

$$U_t = U_0\left(\frac{t_0}{t}\right)^{0,4} \tag{1}$$

instantaneous radius of elastic tube lumen at the instant of tube expansion varies according the law:

$$r_{+t} = r_0\left(\frac{t}{t_0}\right)^{0,2} \quad \text{при } t_0 \le t \le t_1 \tag{2}$$

- instantaneous radius of elastic tube lumen at the instant of tube contraction varies according the law:

$$r_{-t} = r_0\left\{\varepsilon + \frac{\beta}{2}\left[\varepsilon - \left(\frac{t}{t_0}\right)^{0,2}\right]\right\} \quad \text{при } t_1 \le t \le t_2 \tag{3}$$

- maximum fluid flow speed in elastic tube within the impulse equals:

$$U_0 = 37{,}5\, g t_0 \frac{(5\varepsilon - 2)^3 - 27}{(5\varepsilon - 2)^5 - 243} \tag{4}$$

where:

$$\varepsilon = \left(\frac{t_1}{t_0}\right)^{0,2} = \left(1 + \frac{\Delta t_1}{t_0}\right)^{0,2} \tag{5}$$

$$\alpha = \left(\frac{t_2}{t_0}\right)^{0,2} = \left(1 + \frac{\Delta t_1 + \Delta t_2}{t_0}\right)^{0,2} \tag{6}$$

$$\beta = \frac{2(\varepsilon - 1)}{\alpha - \varepsilon} \tag{7}$$

t_0 – time of pressure buildup in the feed system to the level of pressure in the elastic tube;

Δt_1 – time for elastic tube expansion within the pulse;

Δt_2 – time for elastic tube contraction within the pulse;

t – current time;

g – acceleration of gravity (g = 9,81 м/с²).

In conclusion it should be noted that the elastic tube functioning law (imposed by necessity to exercise in it the fluid motion in "third mode") imposes in its turn some specific requirements for the functioning of the supply system. Just this determines the volumes of fluid circulation.

With the knowledge of objective relationships described by equations (1) to (7), and applying the simple mathematical operations we can deduce the formulae required for calculation of the fluid flow volumetric parameters. Specifically, the following parameters can be defined:

- Q1: volume of fluid coming from the supply system and entering the elastic tube within the time of its expansion
- Q2: volume of fluid coming from the supply system and entering the elastic tube within the time of its contraction

• Q3: volume of fluid that fills the elastic tube internal space increment that appears during the tube expansion time. This volume is squeezed out (owing to elastic properties of the tube) when the tube is contracted. So, the elastic tube is functioning like the peristaltic pump.

Actually, the mathematical model of the effective and optimal hydraulic system for transportation of the multi-phase fluids (similar to blood) in the most effective "third" mode has been built.

Now, let us turn back to discussing the sanguimotion in blood vessels.

It needs to be ascertained if it is possible to use the described mathematical model for describing the transportation function of the blood circulatory system. For this purpose, we defined the set of parameters that can be used for characterization of the optimal and effective hydraulic system. Then, the same set of parameters has been defined in the blood circulatory system [35, 36].

As an instance, we can mention just some of the base attributes of the optimal hydraulic system:

• oscillating flow of fluid

• the tube open flow area expansion followed by contraction in each cycle

• flat and M-shaped fluid motion velocity profiles

• time-regulated three-phase structure of the fluid-flow cycle. The structure includes the phase of fluid flow acceleration to maximum speed, the phase of the tube open flow area extension and the phase of the tube open flow area contraction

• the volume vitro of the suspended particles in the liquid suspension shall not exceed the volume of the tube internal space filled with the fast-moving layers of fluid, i. e. 50 %.

The set of characteristics and criteria used for analysis was essentially wider.

Now, it is reasonable to highlight the similar features in the blood circulatory system:

• from blood circulation physiology science it is known, that the blood circulation in vessels forms a pulsating flow, the lumens of the blood vessels expand and then contract in every cardiocycle

• in recent years, a number of methods have been developed for blood velocity measuring in the arteries of animals (in vivo). This allowed to reveal (by experiments on animals) a lot of particularities of the blood circulation velocity shape. It was found out that the bloodstream velocity profile is always essentially flat along the whole length of aorta, and only near the very end of the aorta in the systole phase it assumes the M-shape [32]

• it is common knowledge that the cardiac cycle includes the specific time intervals (phases) [38, 39].

The systolic time interval includes the systolic tension period, rapid ejection phase and slow ejection phase. Also, the diastole has a phase structure.

• the blood is a suspension of formed elements (various blood cells) and specific liquid particles (chylomicrons) in plasma. In terms of volume the blood consists of 50% of water and 50% of formed elements, proteins and multiple organic and inorganic substances.

Aside from that, as noted above the third mode of liquid flow differs from the Poiseuille flow by essentially lower pressure loss due to friction (friction head). So, it satisfies the principle of optimality in biology science.

It follows from the represented analysis that the "third" mode of fluid flow can be applied to the blood circulation in blood vessels in vivo rather than Poiseuille flow laws [35, 36, 37]. This concept allows to widen the knowledge in the blood circulatory physiology.

In the "third" mode theory (related to fluid flow in elastic tube), the flow is characterized by basic parameters and by their derivatives. The following parameters are considered basic: sound speed in fluid, fluid density, acceleration of gravity and duration of three time intervals: pressure build-up phase duration in supply system, duration of the tube lumen expansion phase and duration of the tube lumen contraction phase. With the knowledge of these values and with using the mathematical formulas, one can calculate the values of the hydrodynamic parameters derivatives, particularly: the fluid flow speed, acceleration, volume of the pumped liquid.

So, the sound speed in blood, blood density, acceleration of gravity and duration of cardiac cycle phases are the main parameters of the blood circulatory system. The other parameters, such as sanguimotion speed, volumetric hemodynamic parameters, etc., are referred to as arbitrary parameters. The direct measurement methods are used for measuring the main parameters. The mathematical model of the third mode can be used for calculation of values of the derived hemodynamic parameters based on basic parameters.

From what has been said one can deduce that the phase structure of the cardiac cycle is the basis of the cardiovascular system hemodynamic processes. Among other factors, it enables and regulates the blood circulation and supports the sanguimotion structure.

The practical application of the theoretical results proved that the sanguimotion volumetric parameters can be measured based on linear values, such as duration of the cardiac cycle phases, volume of circulating blood.

2.2 Indirect measurement of hemodynamics parameters: stroke, minute and phase volumes of blood

The pumping ability of blood circulatory system is characterized by cardiac output: minute volume, stroke volume and phase volume. That is why the information about the blood volume extruded by heart or entering the heart within the definite time is of great interest for physiological, clinical and diagnostical examination. It is necessary for objective assessment and monitoring of the cardiovascular system in normal and pathological state.

By now, a great number of invasive and non-invasive methods for determination of the minute and stroke volumes of blood is available. We do not review these methods in the present paper because in many papers the philosophy of the complicated biological processes modelling was analyzed, and the currently existing methods of the hemodynamic parameters characterization were described [35, 37, 40].

It only should be noted that of all the existing direct methods for blood minute volume determination, the Fika oxygen method and the indicator-dilution methods are considered by the majority of investigators to be the most accurate. And what is more, they are regarded as the reference standards.

One would think, that the problem is solved and the methods for the most accurate determination of minute blood circulation volume is worked out. But for application of these methods it is necessary to perform the cardiac cavities and great vessels catheterization which makes the procedure much more complicated and very unpleasant for the patients. Moreover, the procedure itself can cause the abrupt changes in the hemodynamics parameters, thus stimulating the errors in the cardiac minute volume determination. So, it is possible to draw the conclusion that Fica methods and the indicator-dilution methods themselves materially affect the hemodynamic processes. They do not ensure the accurate determination of the minute blood volume, and, it follows that they can't be used for monitoring and check of the data obtained through other methods.

Aside from that, these methods do not afford the cardiac output values (stroke volume) in each cardio cycle, all the more about the phase volume of the blood. This statement is true for the most of the existing methods. Knowing only the volume of blood per minute, it is not feasible to evaluate adequately the pump function of the cardio-vascular system. At times even the considerable changes in its functional state are not accompanied with the significant variations in this most integrative parameter values. Even in serious pathological conditions, the organism will keep the minute blood circulation volume within the normal range by using the available compensatory mechanisms. The more objective assessment of the heart pumping ability can be obtained through a complex analysis of the minute, stroke and phase volumes of blood. This provides the understanding of the efforts required to ensure the minute cardiac output appropriate for the needs of the organism.

The medical books provide only the single bits of information about the blood volume values correlation when the human health is in norm, as proved by the results of M-mode echocardiography. But it is necessary to keep in mind that these data are very discrepant. That is, the same blood volume values obtained in result of various types of investigation differ essentially from each other.

That is why it is extremely difficult to determine the range of the normal values of the phase hemodynamic volume parameters.

From these considerations, one can draw a conclusion that it is necessary to develop the methods for the complex determination of volumetric parameters that characterize the blood circulatory system functioning.

It might be very useful to invent the indirect method applicable for the cardiovascular system functional state investigation that would enable the obtaining of full range of the hemodynamic parameters. At that, the method should be simple and easy to implement without using the expensive equipment, not requiring the specially trained personnel, and would be not burdensome for patients.

Precisely this method has been developed based on the philosophy of the "third mode" of the in-vivo-sanguimotion in vessels. Below, the problem solution algorithm is given in more details:

1. The mathematical model of the optimum fluid power system [35] has been used as a theoretical basis. The model includes the mathematical patterns of the fluid flow in elastic tube in the third mode as described by equations (1)÷(7). In fact, these are the basic hemodynamic equations. Depending on duration of the process selected for the test, one can obtain in result the mathematical model either for systole, for diastole or for the atrial systole. The model can be also used for determination of the blood flow characteristics in any selected vessel, it is only required to measure the time parameters of the process.

2. This mathematical model has been also applied to the process of determination of the characteristics of blood flowrate in vessels. In result, the mathematical relationships of the cardiac pumping function volumetric parameters to duration of the cardiac cycle phases were deduced.

3. Based on these relationships, the formulas were deduced that allow to calculate the systolic and diastolic stroke volume indices of the cardiac pumping function.

4. Electrocardiography was used as a technique for the determination of the cardiac cycle phase structure.

Accordingly, the duration of waves and segments on the cardiogram are the base values for calculation of the hemodynamic volumetric parameters, specifically:

QRS – duration of complex from the origin of the wave Q to the end of S wave

RS – duration of complex from the top of R wave to the end of S wave

QT – duration of Q – T interval measured from the origin of the Q wave to the end of T wave

PQ – duration of P – Q segment measured from the end of P wave to the origin of Q wave

TT –cardiac cycle duration measured from the end of T wave to the end of the next T wave.

This type of the cardiac cycle duration measuring is critical when we mean the determination of the hemodynamics volumetric parameters. It is rightful to join the diastole with the succeeding systole.

The regular patterns represented by the equations (1) to (7) are fundamental and lay the basis for the sanguimotion mathematical model building and for developing the method of the hemodynamics volumetric parameters determination based on the cardiac cycle phases duration.

As is known, the pumping ability of the heart and of large blood vessels is implemented by means of the systole and diastole alternation.

The cardiac and vessels activity during the systole is characterized by the following hemodynamic parameters:

SV – stroke volume of blood (ml)

MV – minute volume of blood (l/m) PV3 – volume of blood ejected by the ventricle in rapid ejection phase (ml)

PV4 – volume of blood ejected by the ventricle in slow ejection phase (ml)

PV5 – volume of blood pumped by ascending aorta during the systole, when it functions as a peristaltic pump (ml)

Further on, represented is the algorithm for systolic volumetric hemodynanamic parameters determinating based on the cardiac cycle phases duration measured on ECG.

1. Let us consider the vessel section at the level of the ascending aorta.

S_0 is the aorta section area (cm^2), determined by the nomogram or using any other method.

2. Duration t_0 is determined as:

$$t_0 = RS \text{ (s)}$$

3. Systole duration (including t_{01}) equals to:

$$t_2 = QT - QRS + RS \text{ (s)}$$

4. Heart rate equals to:

$$HR = 60 / TT \text{ (BPM)}$$

5. Formulae for calculating the nondimensional parameters:

$$\alpha = \left(\frac{t_2}{t_0}\right)^{0,2} \qquad \varepsilon = \frac{3\alpha + 2}{5} \qquad \beta = \frac{2(\varepsilon - 1)}{\alpha - \varepsilon}$$

$$f_1(\varepsilon,\alpha,\beta) = \frac{5}{12}\varepsilon^2\left(2+\beta\right)^2\left(\alpha^3 - \varepsilon^3\right) - \frac{5}{8}\varepsilon\beta\left(2+\beta\right)\cdot\left(\alpha^4 - \varepsilon^4\right) + \frac{1}{4}\beta^2\left(\alpha^5 - \varepsilon^5\right)$$

$$f_2\left(\varepsilon\right) = \varepsilon^5 - \frac{5}{3}\varepsilon^3 + \frac{2}{3}$$

6. Maximum blood velocity per impulse:

$$U_0 = \frac{36787{,}5t_0\left[(5\varepsilon-2)^3 - 27\right]}{\left(5\varepsilon-2\right)^5 - 243} \quad \text{(cm/s)}$$

7. Volume of blood ejected by the cardiac ventricle in rapid ejection phase:

$$PV3 = S_0U_0t_0(\varepsilon^5 - 1) \quad \text{(ml)}$$

8. Volume of blood ejected by cardiac ventricle in slow ejection phase:

$$PV4 = S_0U_0t_0\left[f_1\left(\varepsilon,\alpha,\beta\right) - f_2\left(\varepsilon\right)\right] \quad \text{(ml)}$$

9. Volume of blood pumped by ascending aorta during the systole, characterizes the aorta tonus:

$$PV5 = S_0U_0t_0f_2(\varepsilon) \quad \text{(ml)}$$

10. Stroke volume of blood:

$$SV = PV3 + PV4 \quad \text{(ml)}$$

11. Blood circulation minute volume:

$$MV = \frac{SV \cdot HR}{10^3} \quad \text{(l)}$$

12. Specific stroke volume per unit of the ascending aorta lumen area:

$$SSV = \frac{SV}{S_0} \quad \text{(ml/cm}^2\text{)}$$

This indicating parameter shall be required for determination of the diastolic phase volumes of blood.

It is essential to note that ascending aorta lumen area S_0 (which is taken into account in the calculation of the volume values) is defined empirically as a mean value for adult people, since this value can't be calculated theoretically. It should be kept in mind that the application of the empirical values introduces some error in calculations. In this particular case, the ascending aorta lumen area represents the constant factor. This effect the absolute values of the minute output and stroke output volumes, but it has no influences on the time history of these parameters variations depending on the internal and external factors.

Farther, let us consider the algorithm for the determination of diastolic volume parameters in hemodynamics.

Diastole has a defining function in formation of the cardiac output to systole. As a matter of fact, there is neither auricular contraction nor diastole without the heart and systole relaxation.

Nevertheless, though the diastolic activity is very important from the physiological point of view, it remains still less investigated than systolic activity. That is why the development of the methods for diastole phasic-volumetric structure determination is of current interest now.

To solve this problem, again the same mathematical model of optimal hydraulic system (applied to description of the heart and vessels systolic activity) has been used.

The diastole is considered as two processes (or otherwise as two successive systoles) in the course of which the blood leaves the atrium and enters the ventricle.

The first process includes the fast and slow ventricular filling with blood and is considered similarly to fast and slow ejection during the systole. The volumes of blood (entering during the fast and slow ejection phases) have been joined in one volume corresponding to the early diastole phase.

The second process includes the auricular systole and is considered along the similar lines as a rapid ejection during the systole.

The cardiac activity and the activity of conjugated vessels during diastole are characterized by the following hemodynamic parameters:

PV1: volume of blood coming to cardiac ventricle in the early diastole phase. It characterizes the sucking function of the ventricle, (ml).

PV2: volume of blood coming to cardiac ventricle during the auricular systole. It characterizes the atrial transport function, (ml).

In result of the mathematical transformations, the formulas have been deduced for the determination of the diastolic phase volumes, specifically of the blood volumes PV1 and PV2 that enter the cardiac ventricle during the early diastole and the auricular systole.

The meridian at the level of mitral valve cusps is considered.

1. There is no possibility to determine the given meridian (section) area for the particular patient. It is only possible to determine the blood volume per unit of mitral valve lumen area, or the volume expressed in percentage of the total filling volume.

2. The durations of t01 and t02 are determined theoretically based on the assumption that the structure of moving blood is retained at the moment of the transition from the early diastole to auricular systole. It was proved, that this assumption is met provided that:

$$t_{01}=t_{02}$$

3. The early diastole period duration (including t_{01}):

$$t_{21} = T_1T_2 - QT - PQ$$

4. The auricular systole period duration (including t_{02}):

$$t_{12} = t_{02} + PQ = t_{01} + PQ$$

5. The nondimensional parameters calculation formula:

$$\alpha_1=\left(\frac{t_{21}}{t_{01}}\right)^{0,2} \qquad \varepsilon_1=\frac{3\alpha_1+2}{5}$$

$$\beta_1=\frac{2(\varepsilon_1-1)}{\alpha_1-\varepsilon_1} \qquad \varepsilon_2=\left(\frac{t_{12}}{t_{01}}\right)^{0,2}$$

$$f_1(\varepsilon_1,\alpha_1,\beta_1)=\frac{5}{12}\varepsilon_1^2(2+\beta_1)^2\left(\alpha_1^3-\varepsilon_1^3\right)-$$

$$-\frac{5}{8}\varepsilon_1\beta_1(2+\beta_1)\left(\alpha_1^4-\varepsilon_1^4\right)+\frac{1}{4}\beta_1^2\left(\alpha_1^5-\varepsilon_1^5\right)$$

$$f_2(\varepsilon_1)=\varepsilon_1^5-\frac{5}{3}\varepsilon_1^3+\frac{2}{3}$$

6. Maximal speeds U_{01} for the early diastole period, and U_{02} for the auricular systole:

U_{02} speed value is calculated by the same formula

$$U_{01}=\frac{36787{,}5t_{01}\left[(5\varepsilon_1-2)^3-27\right]}{(5\varepsilon_1-2)^5-243} \quad \text{(cm/s)}$$

when $\varepsilon = \varepsilon_2$.

7. The time interval t_{01} is determined based on the certain condition. For calculation of the diastole phase volumes, the value of t_{01}, that satisfies the following equation, shall be used:

$$SSV-t_{01}\left\{U_{01}\left[\varepsilon_1^5-1+f_1(\varepsilon_1,\alpha_1,\beta_1)-f_2(\varepsilon_1)\right]+U_{02}\left(\varepsilon_2^5-1\right)\right\}=0$$

8. Blood volume RV1, entering the ventricle of heart in the early diastole phase in terms of percent of the filling volume:

$$RV1=\frac{100\cdot U_{01}\left[\varepsilon_1^5-1+f_1(\varepsilon_1,\alpha_1,\beta_1)-f_2(\varepsilon_1)\right]}{U_{01}\left[\varepsilon_1^5-1+f_1(\varepsilon_1,\alpha_1,\beta_1)-f_2(\varepsilon_1)\right]+U_{02}\left(\varepsilon_2^5-1\right)} \text{(\%)}$$

9. Blood volume RV2, entering the ventricle of heart in the auricular systole phase and expressed in percent of the filling volume:

$$RV2 = 100 - RV1 \qquad \text{(\%)}$$

10. On the assumption of keeping the balance between the blood supply in diastole and the blood outflow in systole, the condition of equality of the blood filling volume and blood ejection volume can be assumed. Then, knowing the value of the stroke volume (SV) in the specific cardiac cycle, it is possible to determine the absolute values of phase volumes (in ml) in the early diastole PV1 and of the auricular systole PV2 in accordance with the obtained percentage ratio.

$$PV1=\frac{SV\cdot RV1}{100} \quad \text{(ml)}$$

$$PV2=\frac{SV\cdot RV2}{100} \quad \text{(ml)}$$

Accordingly, the described method enables the determination of the basic volumetric parameters of hemodynamics that characterize the pumping function of the blood circulatory system: seven blood volumes ejected by heart and entering the heart in various phases of the cardiac cycle. They are: stroke volume (SV), minute volume (MV), two diastolic phase volumes (PV1 and PV2), two systolic phase volumes (PV3 and PV4), and the blood volume (V5) that characterizes the pumping function of aorta.

In the course of investigation, the relative phasic blood volumes (RV1 ÷ RV5) have been calculated. They represent the phase blood volume-to-stroke volume percentage ratio for each phase. These parameters illustrate the contribution of each phase to formation of the stroke volume. The hemodynamic parameters (whose values are represented in per cent of the stroke volume) give a more clear idea on how the cardiac output is formed, than the absolute values. Thus, the percentage ratio of diastolic phase volumes (RV1 and RV2) gives an idea of how the heart is filled, specifically of the atriums and ventricles contribution to the filling of the heart in diastole. Volume RV5 characterizes the participation of aorta in process of the blood ejection from the cardiac ventricle during the systole.

It is essential to note that the developed algorithms are also applicable to the right ventricle of the heart. In this case, the durations of the systolic and diastolic phases of the pulmanory heart are applied as the input variables.

The diastola is one of the most complex and vulnerable processes of the cardiac activity. For example, the slow, delayed and incomplete relaxation of the myocardium during the diastole is the fundamental precursory symptom of the cardiac muscle pathology.

Also, the data are available that prove that the cardiac muscle relaxation process is more sensitive to the action of the main natural regulatory forces then the contraction process. The diastolic activity abnormality may be a premonitory symptom of the nascent cardiovascular pathology.

The cardiac rate acceleration is the human organism protection measure aimed to support the adequate blood supply to the organs and tissues in high load conditions. In it's turn, this results in the alternations in the cardiac cycle internal structure and in atriums, ventricles and large blood vessels functions redistribution in the course of the cardiac output formation. The investigations carried out by our working group showed that in these conditions the diastole phase volumes correlation is changed sufficiently: PV2 blood volume increases and the load on the cardiac muscle of atrium increases essentially. When the pulse frequency is very high, the ventricles filling with blood occurs essentially only during the systole of atriums. It is a very important compensatory mechanism.

That is why a particular attention should be given to analysis of the diastolic function of the heart. At that, the volumes PV1 and PV2 ratio shall be considered as the diagnostic criterion. The person has a sufficient compensatory potential if the cardiac ventricles feeling with blood (in motionless condition) takes place mainly in the early diastole.

For the effective practical application of this method potential, it is necessary to develop (based on this method) the diagnostic criteria of various pathological conditions. It is of the utmost importance to evaluate the deviation of the obtained values of the hemodynamic volumetric parameters from the normal values. In this particular case, the normal limits of the hemodynamic parameters have been obtained through calculations.

The data on normal (proper) values of the waves, intervals and segments on the ECG of the adult person have been obtained from the medical sources and are as follows:

1. Upper and lower limits of QRS complex value:

$$QRS_{max} = 0.1\ (s);\ QRS_{min} = 0.08\ (s)$$

2. Upper and lower limits of RS complex value:

$$RS_{max} = 0.05\ (s);\ RS_{min} = 0.035\ (s)$$

3. Normal value of Q–T interval in each specific cardiac cycle is determined based on the Bazett formula:

$$QT = 0{,}37 \cdot TT^{0{,}5} \quad (s)\ (\text{for males})$$

$$QT = 0{,}4 \cdot TT^{0{,}5} \quad (s)\ (\text{for females})$$

4. Normal value of P–Q segment is determined by the following formula:

$$PQ = \frac{1}{638{,}44 \cdot \frac{HR^2}{10^6} + 9{,}0787} \quad (s)$$

The calculation formula has been deduced through the approximation of the known values of the P – Q segment depending on the heart rate (HR).

These values are used as the source data for the calculation of the individual range of the normal volumetric hemodynamic parameters of the particular patient.

Although the theoretical basis is rather complicated, a new indirect method of the hemodynamic phase volumes determination is very simple from the point of view of its implementation in practice. The mathematical model of G.Poedinzev – O.Voronova makes the basis of this method. The model describes the blood circulation in vessels. The method includes a number of formulae for volumetric hemodynamic parameters calculation. The durations of the cardiac cycle phases measured through the ECG form the source information used for the calculation. The rheogram can be recorded simultaneously with the cardiogram, thus enabling the more sufficient quantity of obtained information.

The method developed by the authors of the present paper enables to obtain the full line of values of the hemodynamic volume and phase parameters. Not only the numerical values of the hemodynamic phase volumetric parameters, but also the qualitative estimates of the functional/structural and hemodynamic changes in the various parts of the cardiovascular system can be obtained.

The hemodynamic volume and phase parameters are the most informative functional characteristic of the blood circulatory system. They represent the joint work of the heart and vessels. With the knowledge of their relationship and after the correlation with the heart and vessels anatomic features and functional condition, it is possible to make a highly reliable diagnostics of the blood circulatory system functional state and reveal the pathological conditions. The described method can be successfully used for estimation of the remedial measures and preventive treatment effectiveness.

2.3 Comparative clinical analysis of the cardiometrical method, thermodilution and Fick method

2.3.1 Fick method

The Fick method is based on measuring the difference between the degree of oxygen in venous (dark-red) blood and in arterial (bright-red) blood, with the subsequent use of the result for the calculation of minute volume of blood (liter per minute).

In classical Fick method, the respirable oxygen is used as a substance delivered into the bloodstream. To measure the difference in oxygen concentration in arteria and in vena ($AVDO_2$, ml/100 ml), they make use of the blood portions taken from the pulmonary artery during the cannulation of the right heart, and the blood taken form aorta or left ventricle during the cannulation of the left heart.

The oxygen consumption by blood in lungs per unit of time (VO_2, ml/min) can be defined with certainty only using the spirometer. In practice, this parameter most often is calculated based on the empirical formula depending on the body surface area (KO, m^2) and the age of the patient. At that, the body surface area is determined based on the special nomographic table which is calculated based on Du Bois formula depending on the patient body height and weight. This introduces the error in the determination of the minute volume VO_2.

The procedure of the minute volume of blood determination using Fick technique includes the following steps:

- Sampling of blood from the pulmonary artery to determine the oxygen saturation of pooled venous blood.
- Blood sampling from the left ventricle or from aorta to determine the oxygen saturation of arterial blood.
- Determination of oxygen saturation in both samples with allowance for the packed cell volume (Hb, g/dl).

Since one gram of hemoglobin takes up 1.34 ml of oxygen, the Hb index is multiplied by 1.34 (Hufner number).

- Calculating the arteriovenous oxygen difference ($AVDO_2$).
- Determination of oxygen quantity/volume (VO_2) absorbed by the blood in lungs using the empirical formulas with allowance for the body surface area and age of the patient:

$$VO_2 = KO\ (161 - 0.54 \cdot age)\ (male)$$
$$VO_2 = KO\ (147.5 - 0.47 \cdot age)\ (female)$$

Minute volume of blood (MV) value is calculated by formulae:

$$MV = VO_2/10 \cdot AVDO_2\ (l/min)$$

Notwithstanding the fact that Fick method is in use for a long time and is taken to be one of the most accurate procedures for determination of the minute volume of blood, there are a good few of factors that can lead to measurement errors. In particular [28]:

1. Application of empirical formulas with a lot of conditional coefficients (namely KO), nomographic chart data, and other coefficients carries a risk of obtaining the erroneous results.
2. Using this method only the MV integral value can be measured. The method does not allow measuring the value in each cardiac cycle.

3. This method can't be used for treatment of the patients having the severe lung illnesses leading to the disturbance of oxygen diffusion in lungs.

4. The direct principle of Fick can not be used for determination of the minute volume in the presence of the intracardiac shunts, because

in this case some amount of blood does not enter the pulmonary circuit, that also leads to error.

5. The Fick method is the most precise method when we deal with the low minute volume and high arteriovenous difference in oxygen value. At the same time, with the high values of the minute volume the error of method can be higher.

2.3.2 Thermodilution

The Fick principle made the basis for the thermodilution method. But in this case instead of using the oxygen in the function of indicator, they use the solution cooled to the temperature lower than the body temperature (for example, the isotonic sodium chloride solution or the five-percent glucose solution).

Below is given the description of the minute volume of blood determination using the thermodilution method:

- Standard quantity of the cooled fluid is injected into the right atrium, and using the thermally sensitive resistor (set in the pulmonary artery) record the blood temperature decrease curve (similar to indicator-dilution curve). For this purpose, the multisection balloon catheters are used. Through one section of the catheter with the lumen located on the right atrium level, the temperature indicator is introduced, the other section is used for passing the wire of the thermally sensitive resistor (set in the pulmonary artery).
- The variations in temperature of blood running through the pulmonary artery are recorded in the form of the curve. The area under the curve is inversely proportional to the pulmonary blood flow. At that, the minute blood volume can be calculated only if the perfect curve is available. If it is unstable, it should be ignored in calculations.
- To measure the area under the temperature curve, it shall be automatically integrated.
- The blood minute volume (MV) is calculated using the simplified Stewart – Hamilton formula:

$$MV = \frac{K\,V_I\left(t_H - t_I\right)}{S}$$

where:

– V_I is the volume of the temperature indicator

– t_H is the blood temperature

– t_I is the indicator temperature

– K is an empirical coefficient that allows for the blood and indicator specific density and heating capacity

– S is the area under dilution curve.

Both the Fick method (based on oxygen) and the thermodilution method have the factors that give rise to the blood minute volume measuring error [28], namely:

1.Nonuniform (jump-like) insertion of indicator, as well as too rapid or too slow (> 4 sec) insertion of indicator, that can result in the non-uniform mixing with blood in the right atrium and in the right ventricle.

2.Extrasystole in the course of measuring.

3.In contrast to Fick method, the thermodilution gives the high error when the minute volume of blood is less than 3.5 l/min.

2.3.3 Cardiometry method

The theoretical foundations of the cardiometrical method and the system of equations used for the hemodynamic parameters calculation based on the cardiac cycle phases duration periods are represented in section 2.2 in details.

Functional relationship between the blood stroke volume SV, minute volume of blood MV and the cardiac cycle phase duration can be represented as follows:

$$SV = f\,(a,\, g,\, S_0,\, QRS,\, QS,\, QT)\ \ (ml)$$

$$MV = \frac{0.06\ SV}{TT} \qquad (1)$$

Sources of potential errors occurring in the minute volume of blood measurement using the cardiometrical procedures:

1. The ascending aorta lumen area, S0, for adults is determined empirically as a mean value. But in this case, it is used in calculations as a constant factor. By this, the error can be introduced in measuring the absolute values of the blood minute volume and blood stroke volume, but it shall have no influence on the dynamic of these parameters changing with time under the influence of the internal and external factors.

2. The method provides the high-quality accuracy of the cardiac cycle phases measuring, but at the same time it is characterized with the high sensitivity and fast response. It registers the slightest alternations in the cardio-vascular system of the patient, including the variations in the emotional state of the patient that have an effect on the hemodynamics. Anxiety, worry, abrupt movement, cogged-wheel breathing can lead to the distortion of the recorded signals. In connection with this it is required to calm/sooth the patient in order to obtain the true values and indices in hemodynamic profile typical for usual baseline state of the patient.

2.3.4. Main findings

For comparative analysis of Fick, thermodilution and cardiometric methods, the Bland-Altman's statistical procedures and Spearman's grade correlation method have been applied (Fig. 4, 5, 6).

For the grade correlation, the following coefficients of correlation are used:

- less than 0.3 for low correlation
- 0.4 to 0.7 for moderate correlation
- more than 0.7 for high correlation.

The comparative analysis of three methods showed the following results:

One may make a following conclusion: the blood MV measured by cardiometrical method falls within the range of moderate correlation with the Fick and thermodilution methods.

When estimating the difference in MV values, it is necessary to keep in mind that the direct methods do not allow the direct measuring of the blood flow. The blood flow is measured in the same way as in indirect method. At that, the various empirical coefficients are applied. Moreover, there are much more of them than in cardiometry method, and they are of variable character. This results in more errors in MV measuring using the direct methods.

Furthermore, to determine the blood MV value via the thermodilution and Fick methods, required are the special conditions, moreover the patient preparation for the procedure will take some hours. The procedure itself is properly speaking a surgery and can result in complication of treatment.

The cardiometrical method allows to perform the procedure without special preparation of the patient. It allows to obtain the blood minute vol-

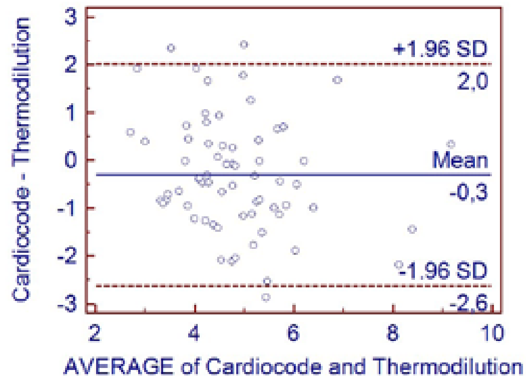

Fig. 4. Cardiometric method – Thermodilution. Spearman's correlation coefficient 0.388…..0.511

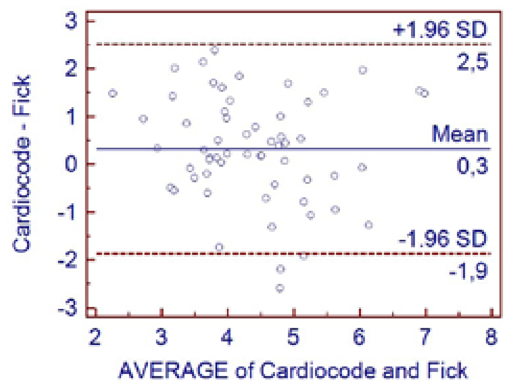

Fig. 5. Cardiometrical method – Fick method. Spearman correlation coefficient 0.333 ... 0.514

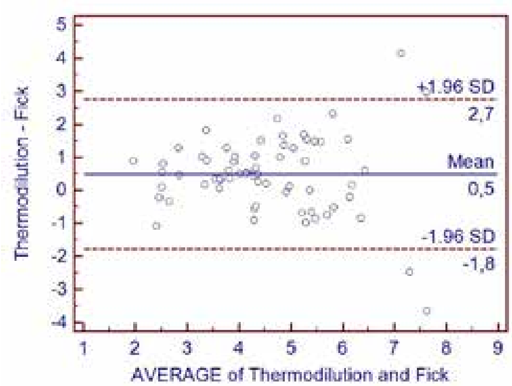

Fig. 6. Thermodilution – Fick method. Spearman correlation coefficient 0.814

ume and other hemodynamic parameters even “in-field”, and just in some seconds. At that, any complicating diseases are excluded.

The cardiometry method has a lot of important advantages. It is user-friendly, cost-effective, easy-to-operate, informative procedure.

It is essential to bring to notice one more fact. Thermodilution and Fick methods provide only a value of the blood minute volume per each cycle of a patient investigation. Within the same period, the cardiometry procedure allows the comprehensive set of the hemodynamic parameters per each cardio cycle (stroke, minute and phase blood volumes).

The cardiometry method offers the feasibility to monitor the cardio-vascular system state in real-time conditions and immediately to obtain the information about the CVS state. It also makes feasible to obtain the CVS functioning time-history depending on the internal and external factors.

The indirect cardiometry method allows not only to obtain the numerical values of parameters, but also to evaluate the quality of the cardio-vascular system basic functions.