Integrative Clinical Cardiology

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Review Article

Cerebrovascular Disorders of Arteriovenous Balance in Psychoneurology: Personalized Medical Process Management and Analytical Vascular IT-Technology in Quality-Management of Vascular Dyshemias

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Abstract

Review: Problems of effective correction and radical solving of cardiovascular disorders are not new. However, the statistic indexes of cardiovascular pathology are growing and they are considerably younger [1-6]; this testifies to lack of effective management strategy and tactics in fight against these diseases [7-13].

Today we can make a real estimation of achieved results: for the last 20-30 years many technologies are created for research of vascular system - USD of vessels, MRT in angiomode; devices for correction of cardiac disorders are widely used - from numerous technologies for estimation of the heart structure to coronarography and coronarshunting; new fields of radical medicine are successfully implemented, such as cardiac surgery, angiosurgery, phlebology [14-16].

And at the same time, regardless of the most up-to-date technologies for vascular diagnostics and angiosurgery cardiovascular diseases gets top ranking regarding morbidity and death rate [6,9,17,18].

It can be explained by the fact that development and introduction in medical practice of modern vascular technologies are behind a steady tendency to progress and cardiovascular diseases strike younger people.

This dissonance testifies to insufficient knowledge and analysis at the application of new technological potential of visualization of the cardiovascular system at structural (*in vitro and in vivo*) and functional level - in vivo [7,9,10,12,17].

Our 20-year-old experience of research of vascular disorders and successful attempts of their correction [19] has shown that

1) There is a huge layer of unexplored hemodynamic parameters, which are important in the personalized treatment processes. However, long neglecting biomechanics in medicine [20] resulted into excessive emphasis on endothelial dysfunction and cellular metamorphosis beneficial for promoting pharmacological business. As a result, doctors are not ready to think logically with categories of circulation mechanics and applied hydro- and hemodynamics [21].

2) Physicians and medical staff don't have enough knowledge in angiology, hemodynamics, hydrodynamics, analytical angiocorrection, angiotherapy, treatment management on evidential basis. Without understanding the depth of hemodynamic laws and logics of pathological and sanogenic transformations in blood supply for organs and regional reservoirs as closed system of vascular tubes - vascular blood flow, it is impossible to perform personalized adequate treatment and predict positive outcomes [8,10].

3) There is an urgent need in development of vascular monitoring technologies based on principles of evidential medicine [2,7,8,10].

Monitoring dynamic changes in any medical process management, doctors may correct on time the decline from sanogenic blood restoration in a particular regional reservoir and logic of blood redistribution in different vascular reservoirs in a patient's body.

Keywords: Personalized treatment, Hemodynamics, Cardiovascular diseases, Angiocorrection, Hydrodynamic conflicts, Brain edema, Biomarkers, Angiomarkers, Intracranial hypertension, Vascular screening, Angiotherapy

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Historical Aspect and Urgent Problems in Management of Vascular Disorders

In critical conditions for correction of the cardiovascular system physicians and medical staff currently use some hemodynamic parameters and technologies as arterial pressure, pulse pressure, pulsoximetry, cardiomonitoring, rare monitoring of emboli and that's all [22-25].

Emphasizing on atherosclerotic plaques, their sizes and localization for the last 30 years, general medical science got lost between three roads - arteries, veins and hydrodynamics. The venous system remains unattainable for understanding for many doctors and, therefore, it is often neglected or considered as non-predictable postoperative complications as a "phenomenon of reactive hyperemia" [24, 26-28].

And the microcirculation level is just ignored for blood supply estimation. Instead pharmaceutical business successfully develops the theme of endothelial dysfunction [29,30] and oxidative stress [31-33], mysteriously theorize this topic without real coverage of the dynamics of this process in vivo.

A new trend in the disease classification and assigning cardiovascular diseases to a group of non-infectious diseases only diverts attention of scientists and doctors from deep study and understanding of changes in the cardiovascular system in the pathogenesis of other diseases on the background of vascular dyshemias - infectious, degenerative diseases, fetal malformations and oncopathology [18,34-43]. However, there is a certain progress in statistics-a share of vascular disorders in genesis of vascular dementia has increased from 5% in 2005 to 65-80% in 2013.

Such attitude toward angiology and angiotherapy may be explained by deliberate distraction from understanding of the cardiovascular pathology, as there is a large gap between the information about cardiovascular system studied at medical institutions and the real state that can be explored using current medical technologies. They just need deep understanding of these processes of adequate blood supply in the organism, which actually holds the livelihoods of all living organisms [8,44-55].

Therefore, a postulate *"circulation is the basis of organism's vital activity"* should be explained for every doctor and medical staff as a dogma.

Angiology as a science is relatively young (it is only 40 years) and this may be related with the problem of hemodynamic system visualization in the last century. Perhaps in this regard, doctors have formed a certain stereotype that the metabolism is primary and vascularization is secondary. Although, the pathogenetic view is well known that the cardiovascular system provides blood supply to organs and systems and the arterial bloodstream delivers oxygen and nutrients to tissue and cellular metabolism, while the venous link takes out carbon dioxide and metabolic products [7,55].

And practitioners ignore how fast arterial blood moving in a reservoir, the signs of venous stasis and how it may be reflected on the velocity and quality of tissue oxygenation and metabolism [7,21,55-57].

The Positive Treatment Result as the Implementation of Proper Diagnostic and Predictive Personalized Medical Management at the Current Level of Vascular Medical Technology

Medicine as a science is constantly evolving. However, the human body is not yet fully known, and treatment of many diseases cannot find an adequate solution. This is explained by the fact that the patient's organism lives for some chaotic logics and the disease manifests by unpredictable certain reactions, often paradoxical, in vivo, but pathologically altered body.

For many years the medicine has introduced a postulate: *the final positive clinical result is a recovery or significant regression of the present clinical picture of the disease,* thus we may speak about correct strategic and tactic approach to a certain case.

When the pathology during treatment has been changed and the body has been recovered, we are talking about sanogenic treatment impact and that the pathogenetic approach was correct [56]. If such incidents are repeated at certain treatment tactics and in a specific nosological group - we have the courage to make assumptions about disease pathogenesis and treatment tactics. So compelling evidence of recovery in certain nosologies become a measure of knowledge and skills of a doctor in medical management and treatment art, and deep analysis of success stories to create new diagnostic and therapeutic algorithms.

Therefore, only a Cured Patient/a group of Patients is a True Arbiter for a Particular Theory in all Scientific Theoretical Considerations [2,52,56,57] due to Personalized and Preventive Treatment Measures [56,58,59].

This is the science progress and scientifically grounded approaches, when in practice we change some outdated views, using evidence-based medical science [14,18,33], instrumental monitoring of various processes, methods of mathematical modeling in living systems [51], get positive outcomes and we can use them in medical practice.

So today in medicine, personalized, predictive and preventive approach dominates based on the methods of evidence-based medicine [2,52,56-59].

On the other hand, the development of medical law and growing complaints of patients and their relatives to medical personnel on medical mistakes, evidence base is crucially important in arbitration of force majeure; when the patient's body has lost a certain level of health and unable to overcome certain critical situation, and the doctor and medical institution is charged with failure to resuscitate the patient, etc.

Evidence base of the patient's state at the time of admission to the clinic should be the starting point of consideration of force majeure and negligence of the patient to his/her own health as an intangible asset. These questions are extremely relevant today for insurers and for medical institutions. Therefore, modern diagnostic technologies and specific documentary facts should be an arbiter in the conflict of interests between patients and medical institutions.

Hydrodynamic Conflict as an Important Component in Medical Management of Cardiovascular Diseases

A so-called hydrodynamic conflict is in the basis of many circulatory problems. In general, it is terra incognita in comprehension even by the most advanced physicians. In particular, it can be a cause of origin of various edemata in the human organism, especially so dangerous - cerebral edema. Here we can remind the words of the famous Russian neurosurgeon Burdenko MN: "Who can own a key to treatment of cerebral edema, so will possess a key to life and death of a patient". This prominent doctor reached own experience to understanding such complicated interconnection, unfortunately, did not manage to form algorithms for its correction. Today theorizing proceeds around the theme of the swelling and the cerebral edema, but the real mechanisms for patients' recovery from these critical conditions aren't proposed [60-66].

The appearance of invasive sensors for measuring intracerebral pressure opens the evidence base for monitoring intracranial hypertension and the development of certain algorithms [67-71] for personalized approach to correction of intracranial hypertension.

Thus, even a cursory review of the current situation in medical management of cardiovascular diseases has showed that there are almost no smart technologies at the current stage of medical technology development that could serve as evidence base in personalized approach to medical management of cardiovascular disease. Existing standard approaches and pharmaceutical motivated treatment protocols have general symptomatic approach to population and do not take into account the depth and complexity of pathological alterations in the vascular system of an individual in particular.

Our Research Results

General characteristics of the examined patients

For 20 years the Clinic of Healthy Vessels and Istyna-Veritas Research Center have conducted research of blood supply in the brain at psychoneurological pathology combining examination of other regional vascular reservoirs.

In general, the structure of the studied patient's age range varied from 15 to 89 years, 63% were women, 37% of men. Differentiation by gender has showed females more frequently apply, which likely reflects the psycho-social feature of this group (diagram 1).

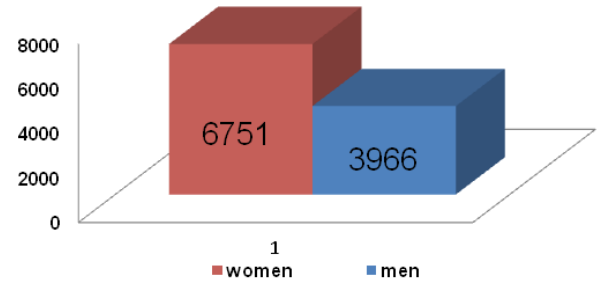

Diagram 1: Patients' arrangement by gender.

A basic patient group was able-bodied and presented 48%, teenagers - 8%, other - 44% - adults and senior age (diagram 2,3).

We have analyzed the nosological structure of patients and found hemodynamic disturbances at the level of cerebral blood flow (Table 1 Diagrams 4,5).

Methods for diagnosis and evidence tool for monitoring angiotherapy process

All patients had general clinical examination, physical and psychiatric check-up, neurodynamic status and CT-MRI-verified pattern of brain damage.

The brain vascular system was studied by ultrasound scanning and dopplerography of extra- and intracranial segments of major arteries and veins in the head by the copyrighted method of UB Lushchyk [72-81] analyzing cardiovascular biomarkers - hemodynamic parameters of arterial and venous system, arteriovenous balance by USDG-patterns of intracranial hydrodynamic conflict and steal syndromes [10,40,52,53,56].

Microcirculation was studied using the method of smart optical capillaroscopy making quantitative and qualitative analysis of the capillaroscopic images from the nail bed of the fourth finger of both hands - the projection of cortical brain areas [82] (Figure 1). Analysis of the images held with the assessment of overall blood supply shortage percent, percent of structural and functional disorders of microangioarchitectonics and percent of hydrophilic perivascular tissue by means of vascular screening technology [54,83-86].

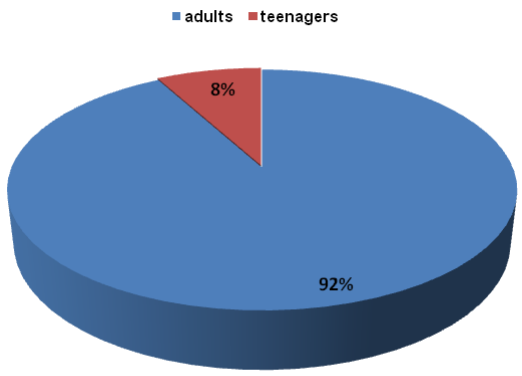

Diagram 2: Age range of the investigated patients.

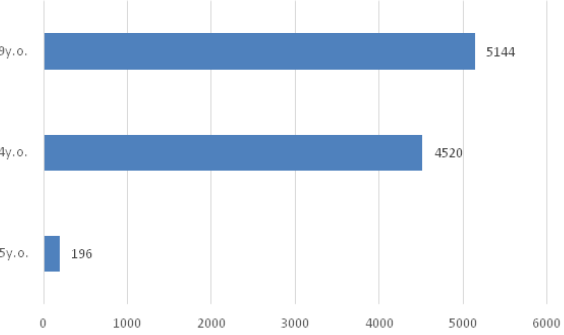

Diagram 3: Proportion of adult patients in terms of age involution .

Nosology	1996- 2000	2001-2005	2006-2010	2011-2015	Total
Dyscirculatory encephalopathy of different genesis (DE)					
1st stage	255	358	738	1901	3252
2nd stage	90	189	476	2554	3309
3rd stage	30	54	76	182	342
Apallic syndrome (vegetative status) AS (VS)	37	35	23	44	139
Transient disorders of cerebral circulation (TDoCC)	64	263	362	284	973
Post-traumatic encephalopathy (PTE)	82	342	574	662	1660
Other diseases of the nervous system (NS)	54	43	434	538	1069
Total	612	1284	2683	6165	10744

Table 1: Patients' structure by nosology.

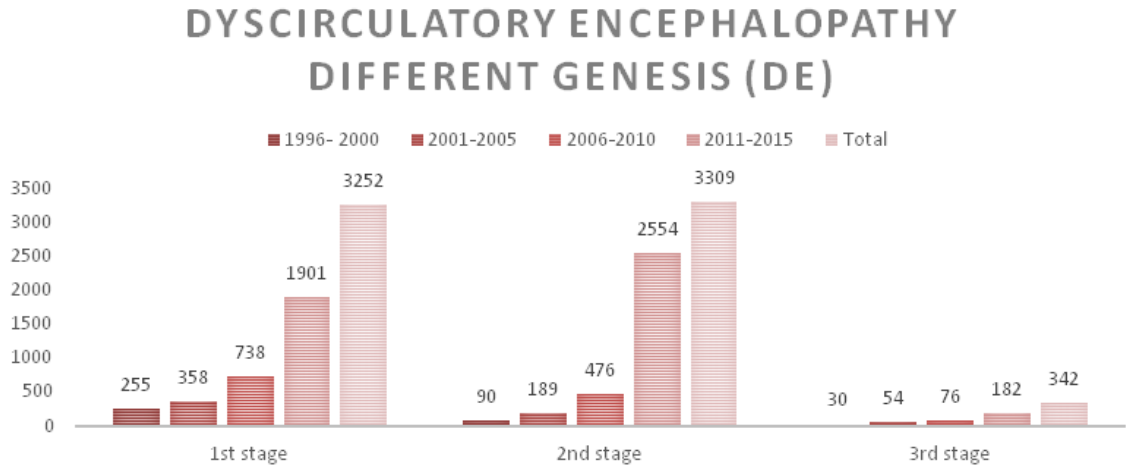

Diagram 4: Dyscirculatory encephalopathy of different genesis (DE)
The patients with symptoms of DE of 1-2 st. dominated in patient structure, their number gradually increased every year and especially increased since 2011. Recently DE-3 has increased reflecting patients with significant neurological deficits and requesting the effective treatment.
As the Table 1 shows all nosology groups has increasing number of examined and treated patients.

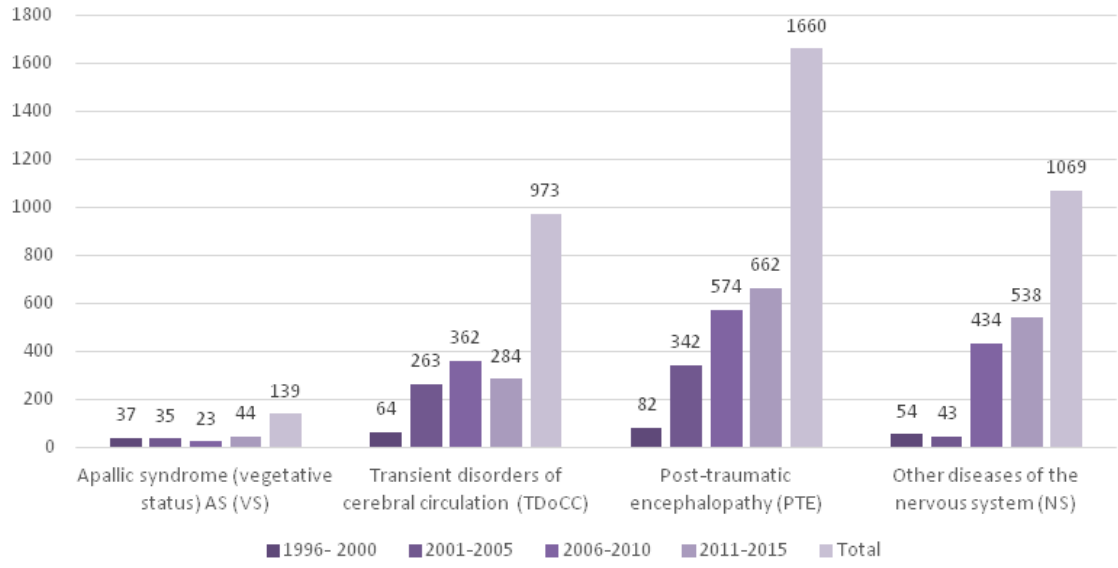

Diagram 5: Patients' structure by nosology
According to the diagram 3 the largest increase was observed in patients with TDoCC and posttraumatic encephalopathy. It should be emphasized that the proportion of patients with other diseases of the nervous system (vegetative, inflammatory, peripheral and degenerative diseases of the central nervous system) was also significant. All patients in this group were diagnosed vascular disorders in blood supply, which clearly influenced the course of the disease. This group of patients also received personlized pathogenetic treatment combined with correction of vascular disorders.

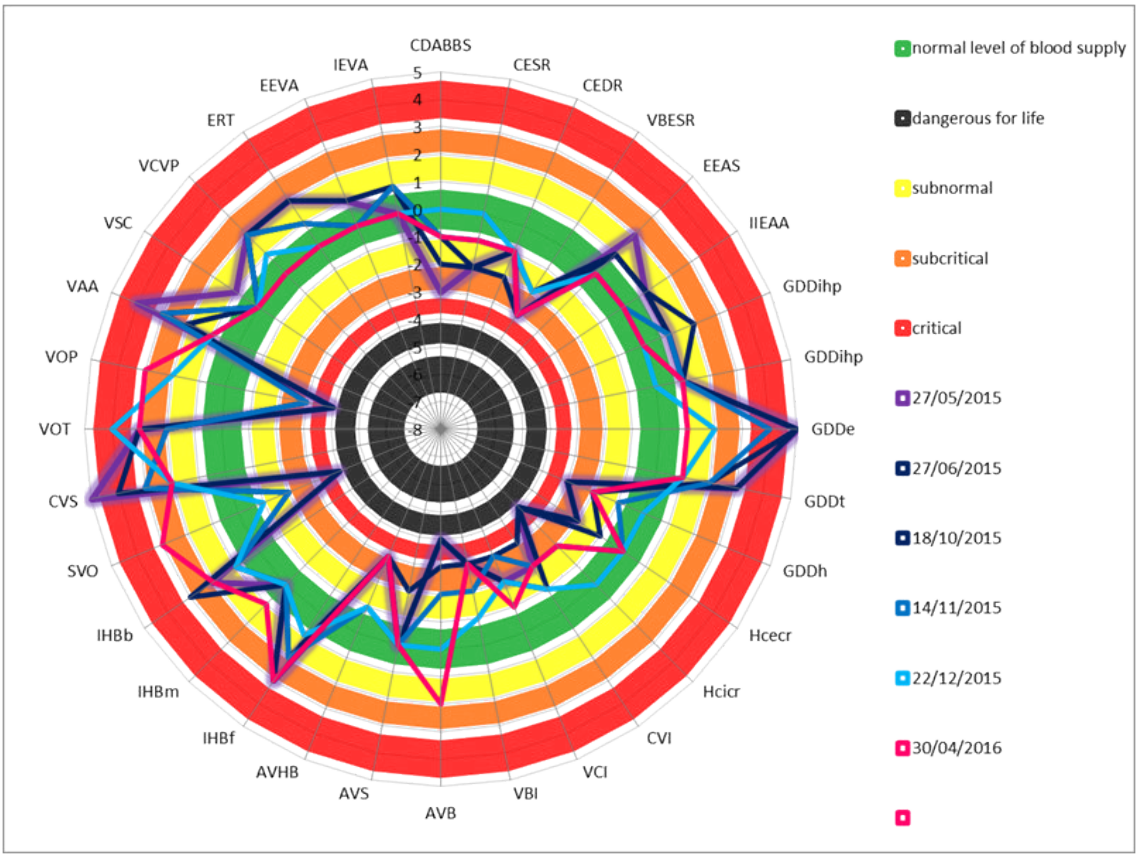

Figure 1: Sample analysis of changes in hemodynamic parameters in the main arteries and veins of the brain in angiotherapy dynamics.

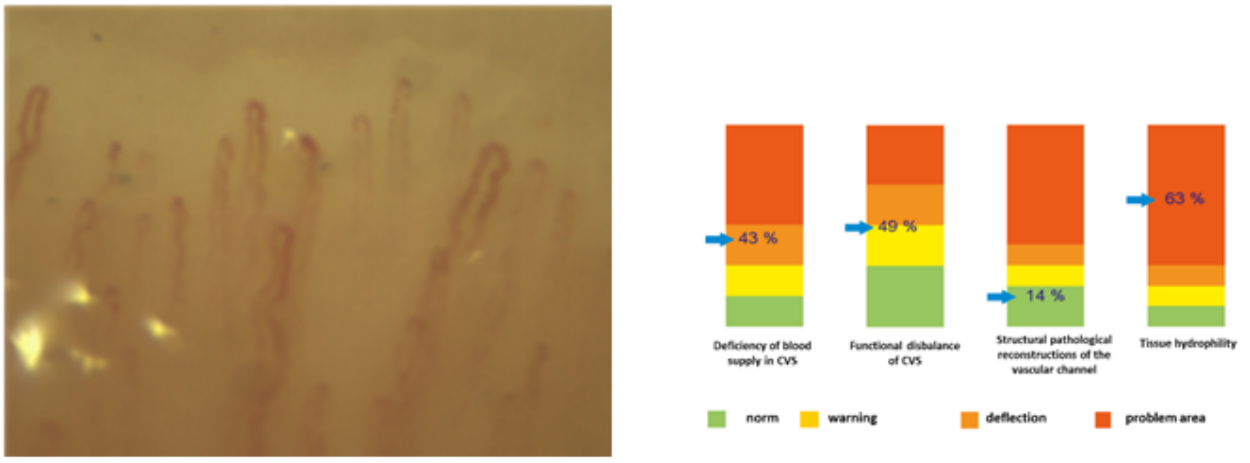

Figure 2: Evaluation results of microcirculation by means of vascular screening technology.

Analysis of the vascular dyshemias treatment

Based on the algorithm of the Clinic, after check-up all patients were offered treatment plan for the detected pathologies. However, some patients refused treatment and they were in the control group at correlation analysis in the case history (Figure 2).

We have divided patients who received treatment into 3 subgroups: 1) had standard treatment, 2) had periodic outpatient personalized treatment, 3) held periodic intensive personalized treatment of revealed hemodynamic changes with dynamic monitoring of detected pathological parameters of blood supply (Table 2).

In Diagram 6 2015 an index of specific gravity of patients, which got personalised treatment, reached 78% in the structure of all patients, who passed diagnostic check-up of vascular system.

Nosology	Total	one or periodic diagnostics without treatment	one or periodic diagnostics without treatment (%)	standard treatment	standard treatment (%)	periodic out-patient treatment лікування	periodic out-patient treatment (%)	Periodic intensive treatment	Periodic intensive treatment (%)
DE									
1 st.	3252	188	5.78%	348	10.70%	351	10.79%	2365	72.72%
2 st.	3309	63	1.90%	297	8.98%	132	3.99%	2817	85.13%
3 st.	342	21	6.14%	61	17.84%	95	27.78%	165	48.25%
AS (VS)	112	4	3.57%	42	37.50%	7	6.25%	59	52.68%
PBBSD	973	41	4.21%	201	20.66%	198	20.35%	533	54.78%
PTEP	1660	58	3.49%	231	13.92%	143	8.61%	1228	73.98%
Other diseases of NS	1069	34	3.18%	48	4.49%	55	5.14%	932	87.18%

Table 2: Patients' structure by the algorithm of receiving medical care.

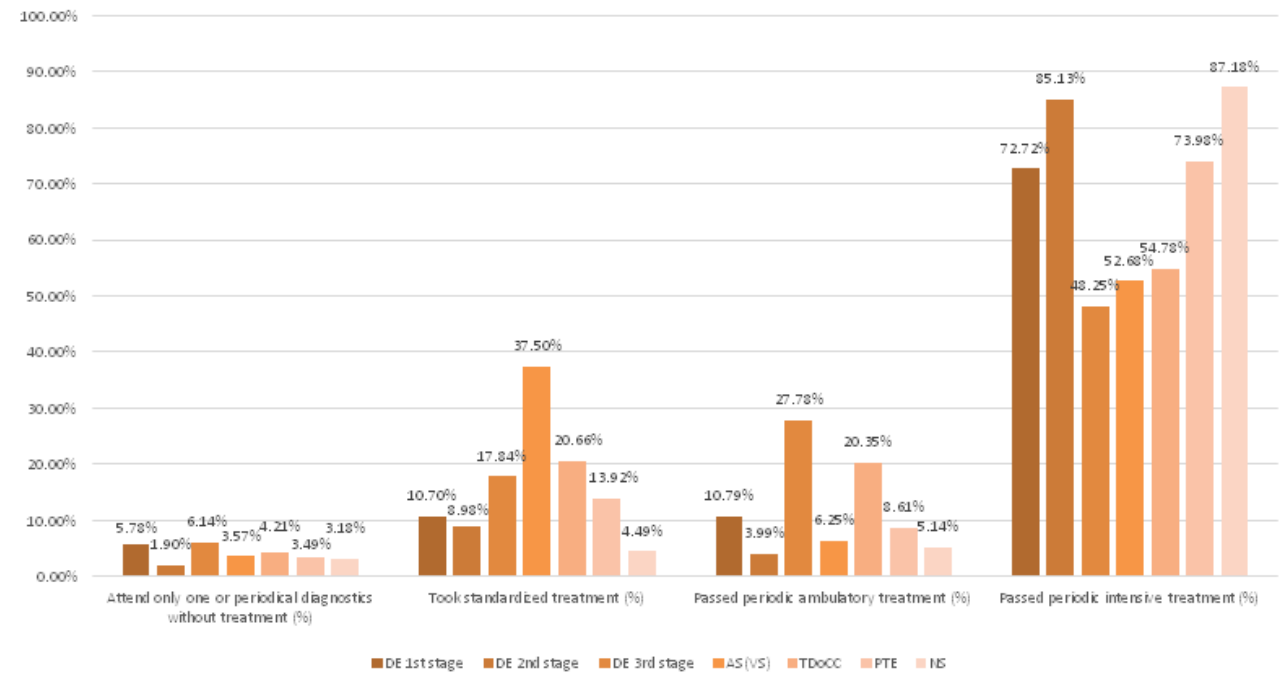

Diagram 6: Patients' structure by the algorithm of receiving medical care.

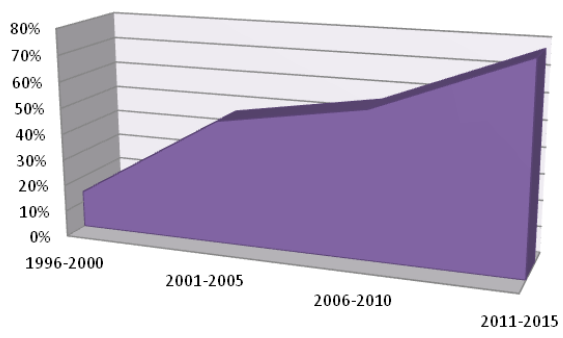

Diagram 7: Specific gravity of patients, who got personalized treatment (1996-2015)
The above-mentioned diagram shows the steady dynamics of increase of specific gravity of patients, which got personalized treatment in the Clinic of Healthy Vessels.

This testified to the increase of trust to the treatment method and efficiency of long treatment results (Diagram 7).

Table 3 and Diagram 8 show a generalized picture of the maximum result of the personalized approach on one hand and features of systemic reserves of restructuring in the body at specific nosologies with disorders in the nervous system.

The most effective personalized treatment was in patients with DE of 1-2 stages as well as in patients with post-traumatic encephalopathy and TDoCC and reached 60-90% regression of neurological deficit.

It should be noted that the positive dynamics in psychoneurological status was occurred in less-curable patients with apallic syndrome and DE-3. However, such results reached mostly 20-40-50% in regression of neurological deficits and required more careful monitoring during angiocorrection,

because all the systems of autoregulation in various vascular reservoirs of the body were sharply unbalanced and in 93% of cases accompanied by pathological paradoxical types of vascular system response.

In 97% of patients with early signs of regression in the clinical picture of the disease were observed only after achieving hemodynamic parameters of 50% - and more of the physiological age level of cerebral blood flow. Patients with DE of 1-2 st. with the clinical picture of cerebral and cognitive symptoms had a tendency to decrease the intensity of symptoms and subjective improvement of feeling at increase of brain hemodynamics by 30-50%.

In some nosology, the so-called incurable and less curable (AS (VS), DE II, DE III), we can achieve better treatment results and get stabilized hemodynamic parameters on the achieved level of restored blood supply.

Nosology	Efficacy of treatment (degree of regression of pathological features) (persons)			
	20-30%	40-50%	60-80%	90-100%
DE 1st stage	213	476	1063	1500
DE 2nd stage	78	340	915	1976
DE 3rd stage	81	39	218	4
AS(VS)	44	13	50	5
TDoCC	171	92	563	147
PTE	345	280	612	423
NS	176	38	825	30
Total	1108	1278	4246	4085

Table 3: Close and remote results of efficiency of the personalised treatment by nosology units.

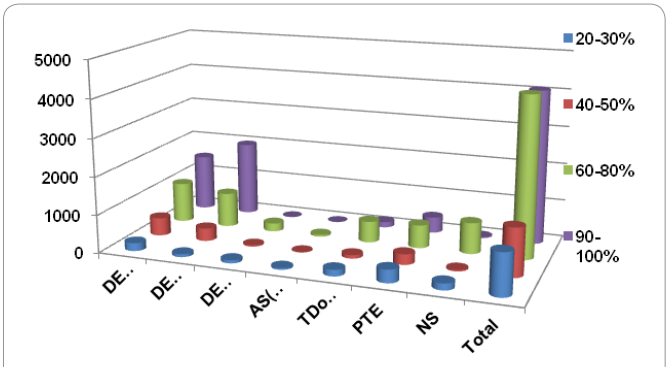

Diagram 8: Approximate and remote results of efficiency of the personalised treatment by nosology units.

However, further regression of rough neurological deficits with significant brain damage requires additional regular rehabilitation programs with the involvement of the relevant profile experts - psychologists, speech therapists, kinesitherapists etc. Rough brain injury need intensive neuroprotective therapy on a background of renewed blood supply to the brain, which we regarded as long ischemic-hypoxic brain damage on the background of various pathogenic factors.

Efficiency and stability of hemodynamics restoration with personalized approach differed in 2-8 times from the results obtained with standard approaches without the use of evidence-based personalized medicine.

Thus, the above-mentioned table 4 and diagram 9 present side reactions that were succeeded to level for 20 years owing to personalised treatment plan considering hemodynamic status, the results of mathematical modeling of the overall status of the body and plan to minimize risks. AS and TDoCC patients were observed more “side effects” of treatment. Due to these patient categories and analyze of critical conditions and paradoxical reactions in the period of 2000-2005, we were able to conclude the logics of reacting of extremely unbalanced body [7,51,74].

Therefore, since 2006 the ratio of acute patients has increased, and the side effects and critical state almost leveled during intensive personalized treatment under instrumental control of vascular technology. Overall results of intensive personalized treatment represent restoration of age-old physiology hemodynamic parameters at the level of 56-89% from the norm in most patients in the close time period and their stabilizing and maintenance during half-year-year in most patients (78%).

34% of patients, mainly due to the age-related group of 20-40 years, refused supporting treatment after completion of the first course of intensive medicinal correction of vascular system due to absence of their complaints on vascular reactions.

Currently our experience of conducting patients with apallic syndrome even in the case of the long duration of unconscious conditions (for some years) [66,72] enabled us to consider in a new way diagnostic and treatment problems of vascular disorders.

At an expected deficiency of blood supply to the brain, when the residual level of blood circulation in the main artery of the brain is at the level ranged from 5-10% from physiological age level, and the patient’s organism in unconscious state reacted mostly paradoxal even in small doses of preparations (95% of patients with apallic syndrome, 86% of patients with TDoCC, 99% of patients with DE-3), which required extra effort and

Nosology	Side effects of complex treatment (allergy, musculoskeletal system, digestive tract)								
	1996-2000	1996-2000 (%)	2001-2005	2001-2005 (%)	2006-2010	2006-2010 (%)	2011-2015	2011-2015 (%)	Total
DE 1st	6	40,00%	6	40,00%	3	20,00%	0	0,00%	15
DE 2nd st	5	38,46%	5	38,46%	2	15,38%	1	7,69%	13
DE 3rd st	2	66,67%	1	33,33%	0	0,00%	0	0,00%	3
AS(VS)	3	25,00%	5	41,67%	3	25,00%	1	8,33%	12
TDoCC	2	16,67%	7	58,33%	3	25,00%	0	0,00%	12
PTE	1	25,00%	1	25,00%	2	50,00%	0	0,00%	4
NS	2	33,33%	2	33,33%	1	16,67%	1	16,67%	6
Total	21	32,31%	27	41,54%	14	21,54%	3	4,62%	65

Table 4: Number of integrated treatment of adverse reactions (allergies, musculoskeletal system, digestive tract).

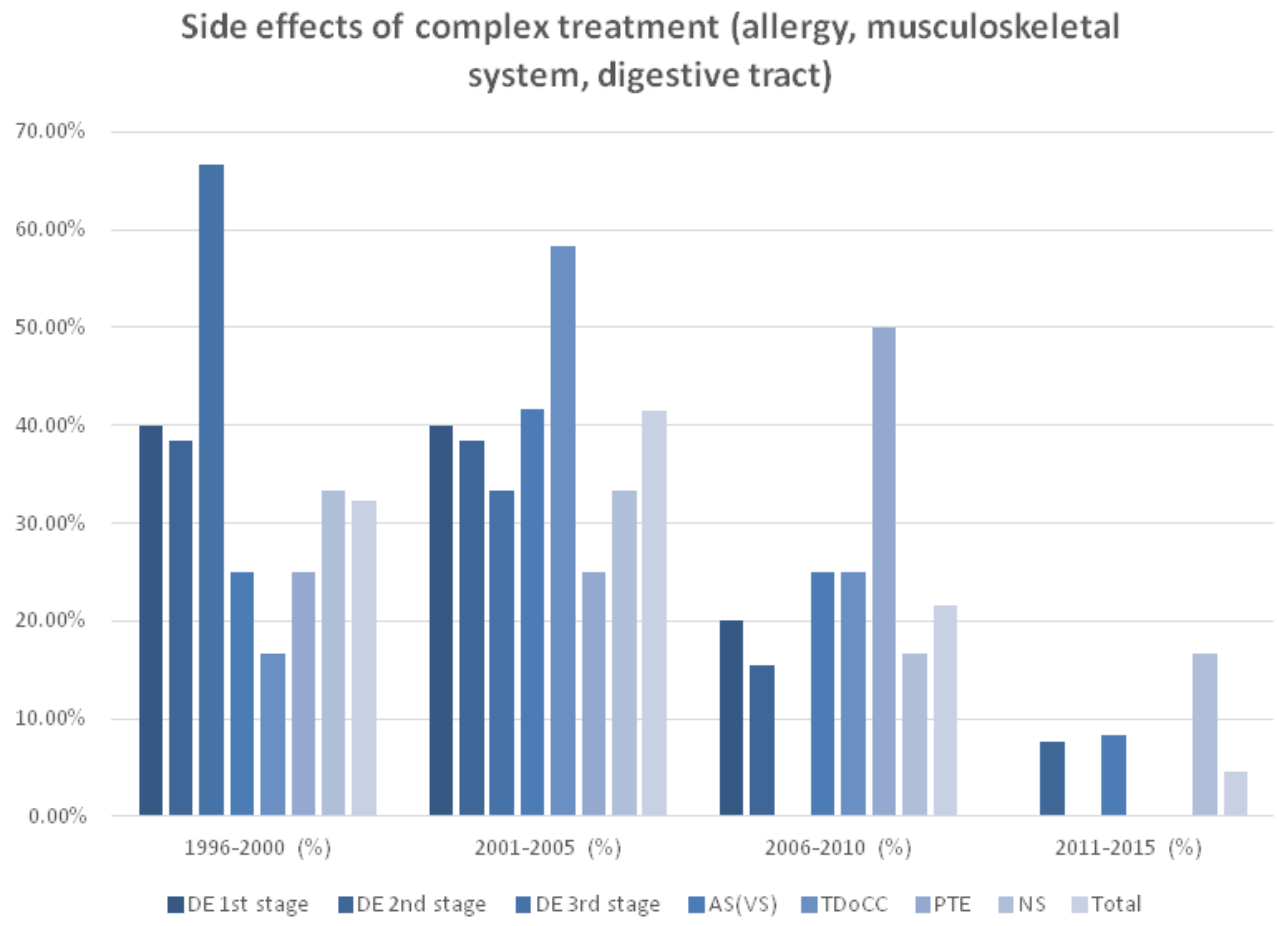

Diagram 9: Side effects of complex treatment (allergy, musculoskeletal system, digestive tract).

manpower, experienced doctors for supervision of the group of seriously ill patients and generally non-curable.

Our experience has shown that less-curable patients are patients with extremely unbalanced structure of administrative management and with practically no autoregulation reaction. Therefore, in medical practice medical staff tries to avoid their supervision. But the fact of the possibile treatment of such acute patients and even achieving successful result requires new approaches to the economic valuation of such personalized comprehensive multidisciplinary medical and rehabilitation services for algorithm price-quality value.

Patients' recovery from the unconscious state to the level of self-service, and single patients to the level of social and professional rehabilitation, allowed asserting that there are mechanisms of restoration of the damaged brain by means of restoration of the physiology level of blood supply of cerebral tissue [51, 66, 73] and further second stage of functional recovery of damaged brain, which testifies about primary state of vascular dyshemias and secondary state of ischemic and metabolic disorders.

Long intensive drug treatments (lasting from six months to several years) and associated personalized monitoring of hemodynamic and neurodynamic changes in treatment and rehabilitation of acute patients of psychiatric profile enabled us to radically change the generally accepted postulates of the last century about the secondary vascular dyshemias at neuropsychiatric disorders. Individual authors also consider the essential role of vascular factors in the genesis of neuropsychiatric pathology [9]. We just tried to verify these facts and put them on the evidence basis thanks to advanced vascular technologies.

It is generally considered that a positive result in treatment testifies to the correct approaches, about innovative technologies, and the unusual results forces to change conservative positions in medicine and at the same time to refute out-of-date axioms about atrophy and brain death [8,37,66].

Studies and results of patients' recovery with postresuscitation diseases, in apallic syndrome, with vascular dementia allowed to analyse the tactics of conducting such patients and applied points of influence on alive and "not very" living system, which has lost capacity for self-control and autoregulation [51,74].

Thus, our experience of medicinal correction and renewal of the capacity of vascular system led to the necessity in consideration of efficiency of treatment process in management of cardiovascular pathology and quality control of therapeutic and surgical treatment methods of cardiovascular illnesses [75,76].

Results' Discussion

Theory of blood supply as the basis of logic hemodynamic alterations at vascular dyshemias

The theory of vascular blood flow lays in the basis of our algorithm concerning correction of blood supply to the brain [7,8,21] allowing to approximately simulate the cardiovascular system and to identify the most affected segments in a particular regional reservoir with displacement of arteriovenous balance applying biomarkers, based on the methodology of obtaining information by means of ultrasound dopplerography [7,8,77] and smart optical capillaroscopy [78,79,86].

We model each case by analyzing histograms of vascular biomarkers-angiomarkers of extra and intracerebral arteriovenous bed and histograms from vascular screening with analysis of microcirculatory pattern in a nail bed. The combination of the situation analysis regarding blood supply in major and microcirculatory levels enabled to model functional and structural reconstructions of the cardiovascular system, which had sanogenic or abnormal paradoxical features. Taking into account models of vascular circulation allowed to analyze not only the arterial and venous level of cerebral regional reservoirs, but also take into account the characteristics of hydrodynamic intracranial conflict and the phenomenon of intracellar hypertension, a condition of hydrophilic tissue at microcirculation, consider the ratio of total deficit of brain blood supply, and make details in vascularization areas of ACA, MCA, PCA and BA.

It should be stressed that almost all nosology groups had the hemodynamic picture with a high degree of reliability - 95-99%, but specificity of parameters was low - within 50-60% for each nosology. This suggests that vascular pathology should be considered individually, creating specific matrix of functional and structural lesions of various segments in the cardiovascular system, and then moderate various situations that could lead to sanogenic reconstructions in the blood flow, minimize all the risks, avoiding critical conditions and adverse reactions during medical treatment. [7]. In fact, today it should be recognized that there can't be a narrow specificity of vascular pathology in certain nosology, because we are dealing with a global system that works on the principles of gradient redistribution of pressure and blood volume in a closed system of connecting tubes and is unique in the organism because it provides vital functions for all living organism [8].

Applied aspects of hemodynamic laws application in the personalized angiotherapy

Personalized angiotherapy requires an analytical approach to angiocorretion and angiotherapy. During first years of our medical center (further the Clinic of Healthy Vessels) on the basis of Istyna-Veritas Research Center, we found out that conventional treatment regimens were insufficient to obtain the desired result to restore adequate blood supply and minimize neurologic deficit. Surgical treatment has not always given stable long-term results.

So our search for the optimal treatment strategy and treatment of patients with cerebrovascular disease continued in the direction of an individual acute pharmaceutical test, monitoring hemodynamic changes and duration study of angiotherapy side effects [7]. Gradually, applying personalized approach and monitoring the hemodynamic changes during treatment, we were able to trace a number of reconstructions in the arteriovenous bed, obtain the phenomenon of arteriovenous balance [77,81,83].

The above-mentioned data represent that at first we adhered to the generally accepted approach in treatment of patients as ambulatory treatment according to the classic treatment scheme. Gradually the nosology structure of patients was changed due to an appeal of many serious patients that stipulated a requirement in the search of individual algorithms of accompainment and treatment of such patients (cerebral palsy, epilepsy, autism, apallic syndrome, multiple sclerosis, post traumatic encephalopathy etc.). Identifying signs of vascular disorders and dyshemias in such patients, we tried to correct these abnormal restructuring regarding our experience of personalized angiocorrection and angiotherapy controlled by instrumental diagnostic methods using ultrasound dopplerorgaphy and capillaroscopy.

By this reason, specific gravity of such patients, which required the personalized treatment scheme and intensive course of angiotherapy grew to 63% in the structure of all patients, who got diagnostics in 2014 as compared to 18% in 1996.

Thus, conducting the analysis of catamnesis of our patients, which were examined in Istyna-Veritas Research Centre for the last 15 years, we got the data represented in the Table 5.

Some anatomical and functional levels of cardiovascular, nervous system, musculoskeletal and mental spheres had also features of recovery, which previously were not clinically detected. Thereby we clarify some important relationships and interdependt intersystem restructuring during angiotherapy.

Wholly in the treatment dynamics we examined the planned treatment courses, applying personalized treatment and regular periodic dynamic control of changes in a vascular system depending on the treatment process and achieved stability of hemodynamic parameters (Tables 6 and 7).

Nosology	Likely first signs of positive dynamics bypair (sub) systems of the organism during 1st personalized intensive angiotherapy course together with rehabilitation		
	10 days	20 days	30 days
Multiple sclerosis	macrocirculation, microcirculation	movements, sensitivity	coordination, emotions
AS (VS)	macrocirculation, microcirculation	vegetatics, sensitivity	muscles, internal organs
Parkinson's disease	macrocirculation, microcirculation	vegetatics, psychosphere	movements, coordination
Cerebral palsy	macrocirculation, microcirculation	vegetatics, psychosphere	movements, coordination
Autism	macrocirculation, microcirculation	movements, attantion	character, speech
Epilepsy	macrocirculation, microcirculation	convulsions, vegetatics	emotions, intelligence
Stroke	macrocirculation, microcirculation	vegetatics, movements	coordination, emotions

Table 5: Dynamics of the first positive changes in the disease course during 1st course of angiotherapy together with personalized neurorehabilitation at some less-curable nosology units. Table 5 highlights the role of monitoring (routine diagnosis) of the organism's systems at the 1st treatment course finding the most sensitive to vascular treatment of subsystems (0.75 ±0.2).

Nosology	Integrated personalized neurorehabilitation with hemodynamic recovery effect on 60-100%			
	Duration of 1 course, (days)	amount of courses	Intercourse period, (days)	Next visit
DE				
1 st.	25-30	1-2	30-60	1 year
2 st.	30	2	30	1 month-1 year
3 st.	30	3	20-30	Every month
AS (VS)	30-40	30-35	15-20	1 month-2 years
PBBSD	30	2-3	20-30	2 months
Stroke	30	3-5	20-30	1 month-1 year

Table 6: Structure of the treatment course duration and average duration of period of the life quality renewal of patients prior to the secondary visit.

	Conceptual therapeutic approaches to the treatment of cardiovascular diseases								
	Non-conventional medicine (Ayurveda)			Under standard protocol			Personalized		
Nosoogy	No effect	Average affect	Good effect	No effect	Average affect	Good effect	No effect	Average affect	Good effect
DE 1st.	**85-90%**	10-15%	0%	0%	**40-50%**	40-50%	0%	0-20%	**80-100%**
DE 2 st.	**100%**	0%	0%	0%	**40-50%**	40-50%	0%	0-20%	**80-100%**
DE 3 st.	**100%**	0%	0%	0%	**40-50%**	40-50%	0%	0-20%	**80-100%**
AS (VS)	**100%**	0%	0%	0%	**75-80%**	20-25%	0%	40-50%	**50-60%**
PBBSD	**100%**	0%	0%	80-100%	0-20%	0%	0%	0-10%	**90-100%**
Stroke	**100%**	0%	0%	60-80%	20-40%	0%	0%	30-40%	**60-70%**

Table 7: Dynamics of the disease course at different approaches to diagnostics and treatment of the investigated patients

When comparing different treatments, we settled on 3 approaches: popular today Ayurveda, standard outpatient methods and intensive personalized treatment.

Actually Ayurveda methodology had relaxation sanogenic treatment and positive impact on patients with only minor cognitive deficits and slight general cerebral symptoms.

Patients of neuropsychiatric profile, who had standard treatment achieved mostly moderate effect in average of 40-50% of patients. Maybe prior neurological patients often claimed that neurologists diagnosed well, but badly treated.

We believe that a significant treatment effect and significant improvement in the clinical picture of studied patients, who received personalized treatment with instrumental monitoring, allows reaching 70-80% level in regression of neuropsychiatric symptoms even in less-curable patients.

The Personalized Approach in Medical Management of Vascular Disorders

Vascular blood supply theory as a basis for personalized and predictive approach to angiocorrection of vascular disorders

The cardiovascular system is a single mechanism of interconnected closed tubes (vessels), which provides the purposeful streams of continuous blood motion in a living organism - arterial blood into the heart (pulse pump) to the capillaries of organs and tissues and, accordingly, returning back of venous blood (suction function of the myocardium of the right heart sections and the diaphragm) from capillaries to the heart.

Actually in case of the vascular pathology the renewal of such ideology of blood supply is the mission of our individual correction of vascular bed – angiotherapy on evidence instrumental base [14].

Appropriately, that the individual approach [2,9,11,23,51] requires certain indicative parameters, which would allow representing background pathological changes in the vascular system in the moment of treatment beginning and during the treatment process. Some classic parameters have been mentioned at the beginning of the article. The practice has shown that these parameters are not sufficient for forming of the objective view to diagnostic and treatment results [9,14].

Viability of the vascular system can be presented by a control of changes in the structure of the cardiovascular system, taking into account new additional parameters, related to such concepts as angioarchitectonics, caliber, branching types, valvular vehicle, elasticity and tonus, firmness of the framework of vessels to external and internal influences, change of form of transversal section of vessels, extravasal conflicts, intravascular conflicts [7,9,14,81,83].

However, all problems in blood supply and vascular critical conditions (hypertensive crises, absences, collapse, drop-attacks, stroke, heart attack and other) take place exactly at the level of derangement of functional ability of the vascular system - in the regular blood supply in an organ at the level of regional vascular reservoir or at system level. Rapid development of acute ischemia is a cause for sudden vascular crises and related clinical picture.

Such approach to the cardiovascular system explains that critical vascular conditions develop suddenly as a display of derangement of compensation or decompensation in the functional capacity of vascular blood-duct for providing regular and adequate blood circulation - blood flow and blood supply for organs and tissues.

Therefore, vascular diagnostics and treatment requires control parameters adequate to the technology and control days for monitoring pathological or sanogenic reconstructions in the vascular bed in the process of medical management-angiotherapy [51,76,78,79].

The chart represents the control process of quality changes in dynamic treatment at chronic vascular disorders

The Figure 3 represents that blind out-of-control usage of

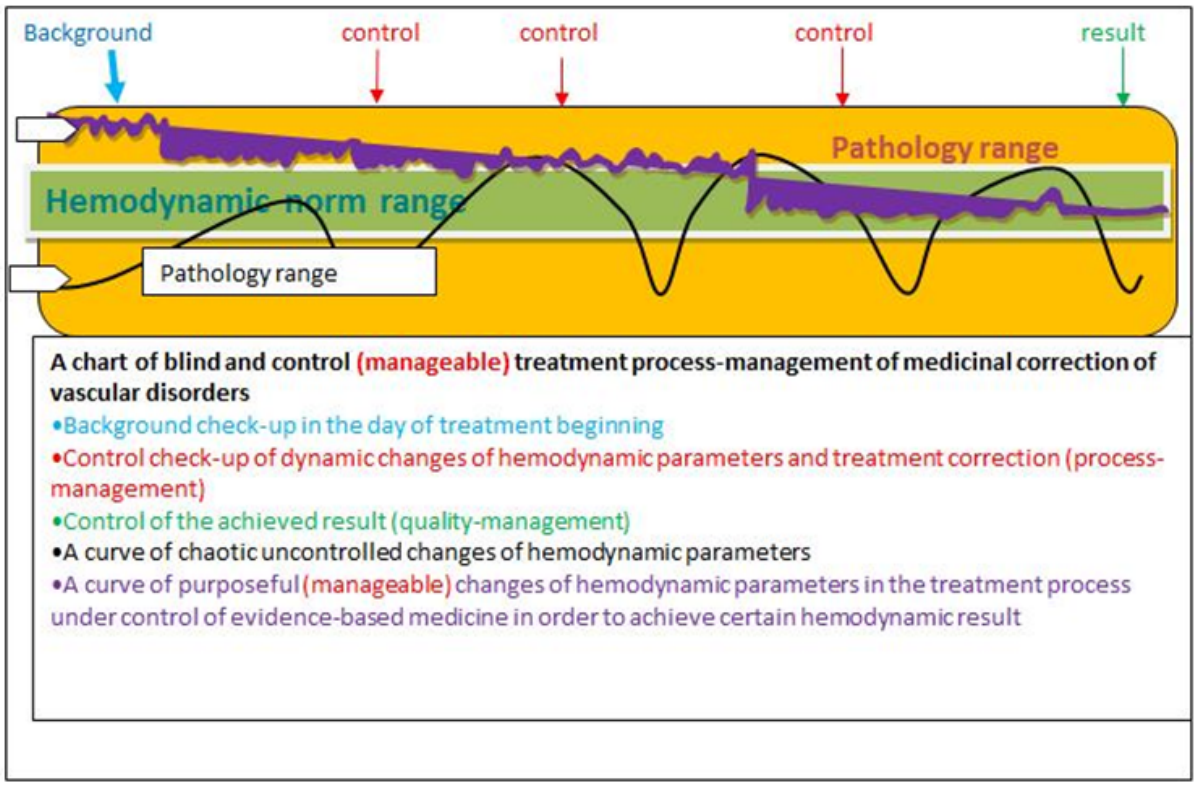

Figure 3: A chart of blind and control (manageable) treatment process-management of medicinal correction of vascular disorders.

medicines does not allow monitoring the treatment process and the vector of hemodynamic changes in the vascular system. Applying methods of evidential medicine and periodic monitoring of dynamic changes of hemodynamic parameters – personalized monitoring of hemodynamic indicative parameters - it is possible to model hemodynamic picture, predict the treatment course, hold risk-management of possible critical states, purposefully conduce the cardiovascular system to the selected purpose, control achieved results and to estimate quality of the completed medical process according to the estimated model of restoration of hemodynamic parameters in individual patients [76].

We apply in our angiotherapy practice the personalized preventive and predicative approach based on the knowledge of hemodynamic disorders and hemodynamic changes [2,8,23,80] (Figure 4,5).

Personalized treatment management according to strategy, tactics and quality of achieved results in treatment of cardiovascular diseases and cerebrovascular pathology

Examining medical process from positions of management bases, it follows conditionally to distinguish certain stages of this process:

1. A strategic stage with vision of end-point - complete renewal of CVS, partial renewal, selective correction of the most precarious hemodynamic parameters, prophylactic correction etc.
2. According to the expected result, we form a treatment strategy - radical, palliative, soft or aggressive, stage-by-stage or one-moment etc.
3. A tactical stage, where we form a treatment plan and treatment tactics - operative, medicinal, combined, mixed, stage-by-stage course with daily sessions or with certain interruptions and etc.
4. Distinguish risk factors and predict possible critical indicative parameters for monitoring dynamics of changes in the living organism.
5. Create a mathematical model for medical process with prognostication of all risks and searching ways for their minimization.

Such approach to every patient with vascular disorders enables to personalize all hemodynamic and structural disorders, to reveal level of disorder in the vascular system and try to find the optimal client-oriented solution for patient's problems and detected objective changes in clinical-hemodynamic status of the patient.

Only possessing certain wealth of knowledge and experience, a physician will be able to predict results of the treatment of a certain patient and aim to work for the cherished dreamed result.

Appropriately, it is not a routine and even not an ordinary case in the work of a doctor. It is an expert-level of work of a specialist of new profession, which is only arising, - *angiotherapist*. Such specialists need deep knowledge in vascular diagnostics, medicinal and surgical correction and other contiguous areas of angiology, hydrohemodynamics, clinic of local regional dyshemias and system disorders in the cardiovascular system.

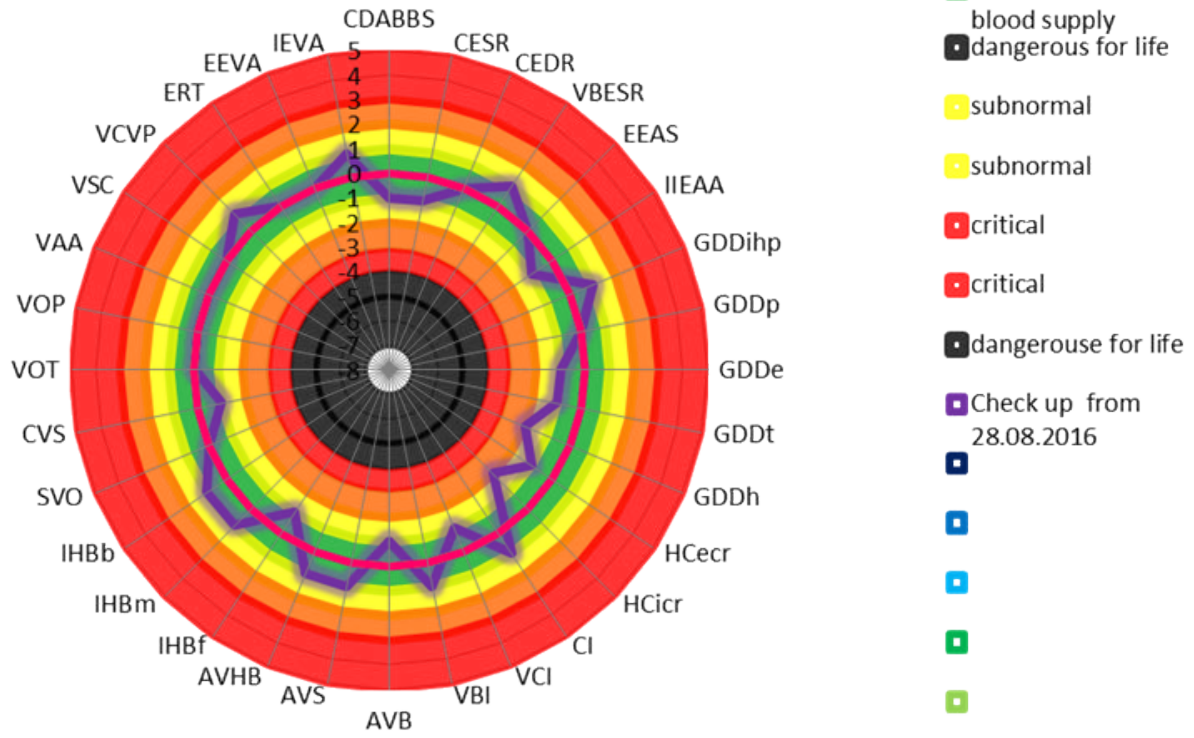

Figure 4: Norm

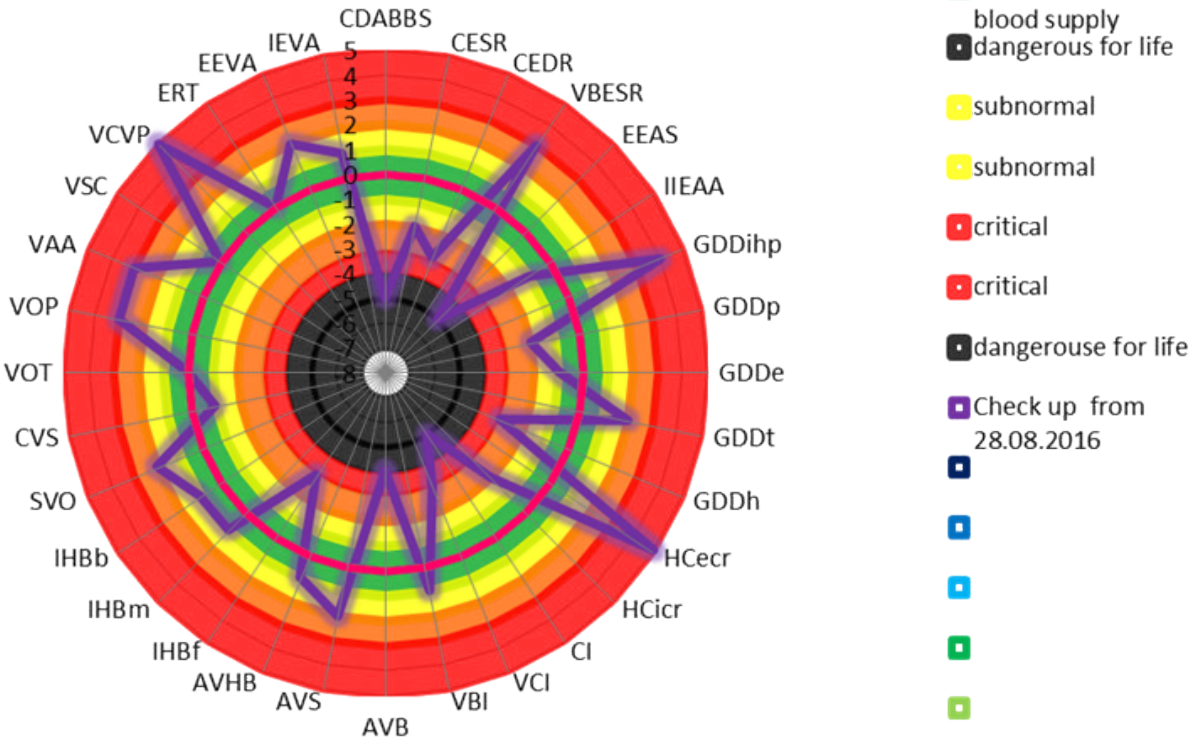

Figure 5: Pathology.

The experience of application of vascular screening has shown that changes in the vascular bed at the microcirculation level took place prior to development of vascular critical conditions and this period of time can be measured by days, weeks or years.

Our previous study about signs of Flammer syndrome in top-managers suggested that early changes occur in the bloodstream long before the disease signs (prior to 1-3-4 years) and had preclinical nature depending on the degree of psycho-emotional, mental and physical activity of workers in constant stressful environment and high responsibility for decisions [10,40,51,53] (Diagram 10).

Pathohemodynamic patterns of forming vascular dyshemias

Summarizing the results of the study and analyzing dynamic of personalized angiotherapy and angiocorrection, we tried to analyze the hemodynamic parameters that cause vascular dyshemias and were key to imbalance in the whole vascular system of a certain patient (Figure 6).

In general, analyzing the hemodynamic situation, we used 30 hemodynamic parameters that reflect the state of arterial, venous, arteriolar and venular links of vascular system and state of hydrophyly of perivascular tissue and intracranial hydrodynamic conflict significantly influenced the shift of arteriovenous balance in one direction or another.

Patients with vascular dyshemia, who started timely treatment, during the year shifted from the state of the pre-disease and / or illness onset (yellow-orange range in the diagram) to the group of persons with normal vascular status (green), which were 29 in 1 year of treatment, in the next year - 115 persons.

Untreated patients (orange range) completed the group of CVD patients and the critical state (red-violet range) during the year. However, CVD patients and patients with vascular crisis in 1-2 years of treatment practically displaced into groups with corrected hemodynamics (yellow-orange range).

The analysis of dynamic changes of the vascular status has showed that with sufficient adequate correction of vascular system the psycho-neurological signs of CVD can be significantly reduced and neurological deficits can be minimized, which greatly improves the quality of life and minimize cardiovascular critical condition.

We tried to analyze the dynamics of changes of hemodynamic parameters in the vascular status of these patients and received an interesting matrix of dynamics of imbalanced hemodynamic parameters during increasing of vascular dyshemias without timely adequate medical correction (Table 8).

Within 5 years there were developing of complete imbalance of all hemodynamic parameters and vascular system losing leverage of autoregulation and chances for self sanogenic reconstrcutions, the chaos appeared in the vascular system that corresponds to 3rd, the highest phase of chaotic imbalance. It should be noted that patients of young and middle age had more radical changes, as the pathological chain included paradoxical angiospastic and dystonic disorder in adequate work of vascular wall, which increases the blood supply shortage.

If there are 5 abnormal hemodynamic parameters, the cardiovascular system lost adequate levers and launched a mode of moderate chaos (1 of 3 degrees of chaos), which launched a cascade of pathological changes in the entire vascular system with redistribution of blood volume in different vascular regional

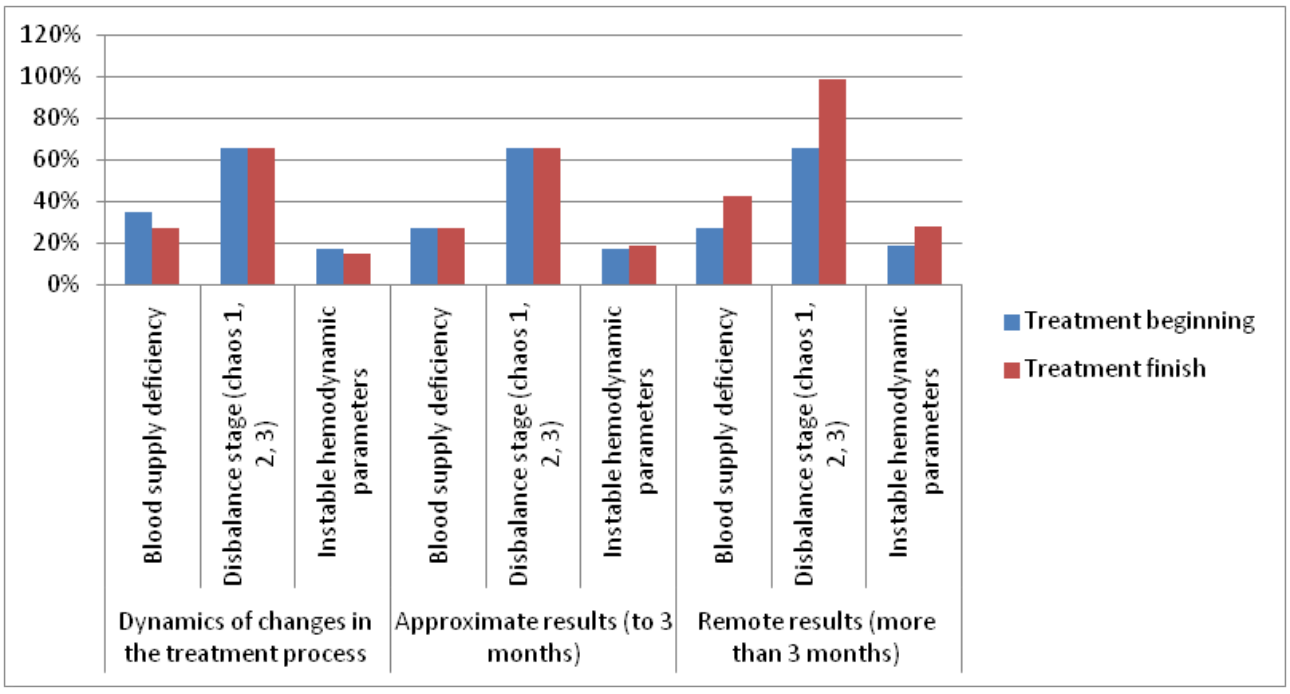

Diagram 10: The dynamics of the course of vascular disorders in top-managers
Thus, personalized angiotherapy with monitoring of changes was the most effective to get the desired result of vascular dyshemia correction and stabilization of the result to the nearest and remote periods.

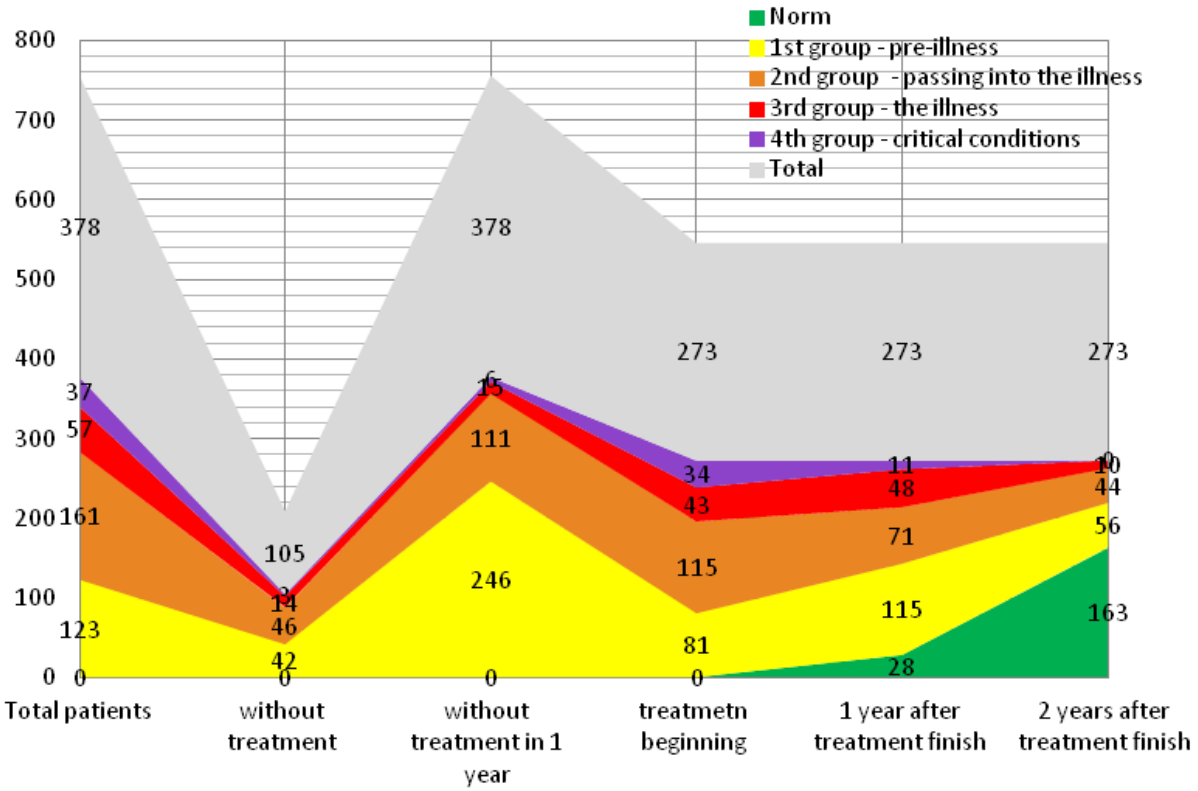

Figure 6: Dynamics of development of vascular dyshemias in the patient group, which did not receive treatment
As seen from the histogram, a group of patients in a stage prior to disease - yellow color (i.e. have moderate signs of vascular dyshemias) within a year without treatment increased in 5 times (from 42 to 246 persons) at the time of treatment they decreased in three times (from 246 to 81 patients).

reservoirs. Naturally, all additional external and internal stimuli of cardiovascular system at the background chaos of 3rd degree could not adequately respond to changes in meteorological situation, emotions, especially in the physical and mental overload, which resulted in vascular catastrophe – stroke or heart attack, pathogenetic nature - ischemia or hemorrhage was not the matter. Vascular blood flow was blocked in one or another way in 83% of untreated patients with imbalance of over half from 30 hemodynamic parameters of blood flow [10,40,51,53].

For the last 20 years we have developed clinical angiology and clinical interpretation of vascular dyshemias, aiming to analyse every patient, to predict probable treatment result, to model possible variants of angiocorrection and to monitor achieved changes during angiotherapy, to analyse the predicted and real risks during treatment.

Conclusions

1. The cardiovascular system is an extraordinarily compound living system by an analogy of a vascular blood duct with plenty of dynamically changeable and simultaneously synchronized hemodynamic parameters, that limits doctors' ability to objectify and radically change the hemodynamic parameters of blood supply for organs and systems in required direction. Successful treatment of cardiovascular and cerebrovascular diseases requires technology for noninvasive monitoring of these parameters in vivo, for analyzing about 30-50 hemodynamic parameters simultaneously.
2. The successful treatment management of CVD based on evidence medicine requires new medical smart-technology for analytical diagnosis and treatment of vascular dyshemia that help to detect early changes in the vascular system, predict risks, model pathohemodynamic situations and monitor sanogenic alterations in hemodynamics to minimize or eliminate existing problems in CVS.
3. The treatment management of cardiovascular diseases must be oriented to the positive result – renewing quality of life, minimization of patients' complaints, stabilizing hemodynamic parameters of blood supply and autoregulation in the baseline and reserve modes of the organism's functioning. Only personalized approach allows us to achieve positive results and to stabilize the hemodynamic parameters of the cardiovascular system.
4. Mortality and morbidity of cardiovascular diseases can be reduced provided forming of the personalized mathematical models of vascular diagnostics, vascular monitoring and personalized predictive medical process- and quality-management.
5. Preventive vascular technologies must be actively used in medical practice to prevent vascular dyshemias in the

dynamic changes of hemodynamic parameters

	norm	1 year	2 year	3 year	4 year	5 year
		preclinical signs of vascular dyshemias				
hemodynamic parameter						
norm	30	25	22	15	4	0
deviation of hemodynamic prameters from the norm at vascular dyshemias (norm 30)	2	5	8	15	26	30
chaos (1-3 sdegree of CVS disbalance)	0	1	2	3	3	3
expressed vascular disorders: (1-3 degree of expressiveness)						
deficiency of blood supply (1-3 degree of deficiency)	0	1	1	2	3	3
tonus disorder	1	1	1	2	3	3
elasticity disorder	0-1	0-1	1-2	1-3	1-3	1-3
structural changes of microcirculation	0-1	1-3	2-3	2-3	3	3
stcutural changes of macrocirculation	0	0-1	0-2	1-3	1-3	1-3
peripheric resistance	0	0-1	0-2	0-3	0-3	2-3
hydodynamic conflict	0	0-3	0-3	1-3	1-3	1-3
blood viscosity	0	0	1	1	1-2	1-3
capillary distonia	0-1	0-2	0-3	0-3	0-3	0-3
arteriolar spasm	0-1	1 - 2	1 - 2	1-3	2-3	2-3
reactivity of vascular system (-3 to +3 degree of disbalance)	-1 - 0 - +1	-1 - 0 - +2	-2 - 0 - +2	-2 - 0 - +3	-3 - 0 - +2	-3 - 0 - +1

Table 8: Pathohemodynamic patterns of forming of cardiovascular disease and vascular dyshemias from norm to hemodynamic crisis.
The first signs of dyshemias based on disorders of vascular tonus with the gradual forming of serious pathohemodynamic pattern with deviation from norm of 5 indexes for 2-3 years, then these

early stages, when abnormalities in the cardiovascular system are minimal and changes have functional disregulatory character on the background of the saved autoregulatory compensation mechanisms.

6. Today providing quality in medical management there are effective technologies of indicative control of hemodynamic parameters and their purposeful return to the physiology level in the dynamics of personalized angiotherapy.

7. Introduction in healthcare practice of analytical vascular technologies and mathematical models for correction of vascular disorders is a precondition of successful primary and secondary prophylaxis of CVD and prevention of vascular critical conditions. This approach can stop the epidemy of noncontagious cardiovascular disease.

8. Vascular biomarkers are the real decision for the early prevention of CVD.

9. Biomarkers of vascular disorders are an innovative technology, which is able to find early functional and structural problems in vascular system of the whole human body.

10. Personalized angiotherapy requires innovative technologies of evidential medicine - technology for vascular screening, angiomarker of arterial and venous bed – with the purpose of instrumental monitoring of dynamics of sanogenic or pathological reconstructions in the vascular bed and transfer of expert knowledge in the prepared programmed technological solutions on principles of intellectual property.

11. At the time of legal relationship between patients and doctors, new program for fixing data and analytical support of doctor's work are essential for medical establishments for evidence of the treatment process correctness and fixing force majeure conditions caused by lack of health cult in patients and bring their organism to critical state.

Abbreviations

AS - Apallic syndrome

ACA- anterior cerebral artery

BA - basilar artery

CVD – cardiovascular diseases

CVS – cardiovascular system

DE - Discirculatory encephalopathy

MCA – middle cerebral artery

TDoCC - Transient disorders of cerebral circulation

PCA – posterior cerebralartery

PTEP - Posttraumatic encephalopathy

VS - Vegetative state

Authors' contributions

UL is an initiator of the vascular angiopsychoneurology, proposed and developed principles for the arteriovenous balance in the human cardiovascular system and mathematical models of the hemodynamics in living systems, analyzed the efficiency of the applied technologies, and designed and drafted the manuscript. VN was engaged in modeling of biophysical processes in the human organism and modeling of biomechanics of the cardiovascular system. IB, NL, IL carried out the diagnostics and treatments according to the proposed approaches. TI, ChO conducted the instrumental functional diagnostics and helped draft the manuscript. All authors read and approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

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