DOI: https://doi.org/10.17816/rmmar625345

Diagnosis of hemostatic system disorders in patients with chronic heart failure using classical and integral methods

Maksim A. Lebedev[1], Mikhail B. Patsenko[1], Maksim I. Pugachev[1], Yuriy V. Ovchinnikov[1, 2], Larisa I. Mel'nichenko[1, 3], Marina A. Palchenkova[1]

[1] Military Medical Academy, Moscow, Russia;
[2] Industry Clinical Diagnostic Center of the Public Joint Stock Company "Gazprom", Moscow, Russia;
[3] N.E. Bauman City Clinical Hospital N. 29, Moscow, Russia

ABSTRACT

BACKGROUND: The state of the hemostatic system in patients with chronic heart failure (CHF) remains an insufficiently studied problem.

PURPOSE OF THE STUDY: to present the results of an original study of the coagulation system of patients with CHF using an integral technique — low-frequency piezothromboelastography (LPTEG).

MATERIAL AND METHODS: The study involved 90 patients with CHF due to hypertension and coronary artery disease aged 50–75 years. The subjects were divided into groups with CHF I–IIa (n = 30), CHF stages IIb–III (n = 60). All patients underwent a study of the hemostasis system using classical (coagulogram) and integral (NPTEG) methods before prescribing antiplatelet and anticoagulant therapy. The comparison group consisted of healthy patients of the same age group without CHF (n = 30).

RESULTS: In patients with CHF, a general blood test revealed a statistically significant decrease in the number of platelets (group 1 — 215; group 2 — 185) compared to the control group — 241. When analyzing the coagulogram, a decrease in the levels of prothrombin (group 1 — 89; group 2 — 86; control group 105), antithrombin-III (group — 76.5; group 2 — 73; control group — 91) and increased INR (group 1 — 1.03; group 2 — 1.12; control group 1.01) in patients in groups with CHF compared to the control group ($p < 0.05$). When using the NPTEG method in patients with CHF, a decrease in indicators characterizing the rate of clot polymerization (intensity of clot polymerization) and clot density (maximum amplitude) was determined when compared with the control group ($p < 0.05$).

CONCLUSION: In patients with CHF, changes in the hemostatic system are determined, characterized by a tendency to hypocoagulation, the frequency a severity of which increases with the progression of the stage of the disease.

Keywords: bleeding; chronic heart failure; coagulogram; hemostasis system; low-frequency piezothromboelastography; thrombosis; integral methods of studying the hemostasis system.

To cite this article

Lebedev MA, Patsenko MB, Pugachev MI, Ovchinnikov YuV, Mel'nichenko LI, Palchenkova MA. Diagnosis of hemostatic system disorders in patients with chronic heart failure using classical and integral methods. *Russian Military Medical Academy Reports*. 2024;43(2):141–150. DOI: https://doi.org/10.17816/rmmar625345

Received: 27.12.2023 **Accepted**: 03.05.2024 **Published**: 28.06.2024

УДК 616.1
DOI: https://doi.org/10.17816/rmmar625345

Диагностика нарушений системы гемостаза у пациентов с хронической сердечной недостаточностью с применением классических и интегральных методов

М.А. Лебедев[1], М.Б. Паценко[1], М.И. Пугачев[1], Ю.В. Овчинников[1, 2], Л.И. Мельниченко[1, 3], М.А. Палченкова[1]

[1] Военно-медицинская академия, Москва, Россия;
[2] Отраслевой клинико-диагностический центр публичного акционерного общества «Газпром», Москва, Россия;
[3] Городская клиническая больница № 29 им. Н.Э. Баумана, Москва, Россия

АННОТАЦИЯ

Актуальность. Состояние системы гемостаза у пациентов с хронической сердечной недостаточностью остается недостаточно изученной проблемой.

Цель исследования — представить результаты оригинального исследования свертывающей системы больных с хронической сердечной недостаточностью с применением интегральной методики низкочастотной пьезотромбоэластографии.

Материалы и методы. В исследовании приняли участие 90 пациентов с хронической сердечной недостаточностью на фоне гипертонической болезни и ишемической болезни сердца в возрасте 50–75 лет. Исследуемые были разделены на группы с хронической сердечной недостаточностью I–IIa (*n* = 30) и IIб–III стадии (*n* = 60). Всем больным проводилось исследование системы гемостаза классическими (коагулограмма) и интегральными (низкочастотная пьезотромбоэластография) методами до назначения антиагрегантной и антикоагулянтной терапии. Группу сравнения составили здоровые пациенты той же возрастной группы без хронической сердечной недостаточности (*n* = 30).

Результаты. У пациентов с хронической сердечной недостаточностью в общем анализе крови определялось статистически значимое уменьшение количества тромбоцитов (группа 1 — 215; группа 2 — 185) по сравнению с группой контроля — 241. При анализе коагулограммы выявлялось снижение уровней протромбина (группа 1 — 89; группа 2 — 86; группа контроля — 105), антитромбина-III (группа 1 — 76,5; группа 2 — 73; группа контроля — 91) и повышение международного нормализованного отношения (группа 1 — 1,03; группа 2 — 1,12; группа контроля — 1,01) у пациентов в группах с хронической сердечной недостаточностью по сравнению с группой контроля ($p < 0,05$). При применении метода низкочастотной пьезотромбоэластографии у пациентов с хронической сердечной недостаточностью определялось уменьшение показателей, характеризующих скорость полимеризации сгустка (интенсивность полимеризации сгустка) и плотность сгустка (максимальная амплитуда) при сравнении с группой контроля ($p < 0,05$).

Заключение. У пациентов с хронической сердечной недостаточностью определяются изменения системы гемостаза, характеризующиеся тенденцией к гипокоагуляции, частота встречаемости и выраженности которых увеличивается при прогрессировании заболевания.

Ключевые слова: интегральные методы исследования системы гемостаза; коагулограмма; кровотечения; низкочастотная пьезотромбоэластография; система гемостаза; тромбозы; хроническая сердечная недостаточность.

Как цитировать
Лебедев М.А., Паценко М.Б., Пугачев М.И., Овчинников Ю.В., Мельниченко Л.И., Палченкова М.А. Диагностика нарушений системы гемостаза у пациентов с хронической сердечной недостаточностью с применением классических и интегральных методов // Известия Российской военно-медицинской академии. 2024. Т. 43. № 2. С. 141–150. DOI: https://doi.org/10.17816/rmmar625345

Рукопись получена: 27.12.2023 **Рукопись одобрена:** 03.05.2024 **Опубликована:** 28.06.2024

ЭКО•ВЕКТОР

DOI: https://doi.org/10.17816/rmmar625345

应用经典方法和积分方法诊断慢性心力衰竭患者的止血障碍

Maksim A. Lebedev[1], Mikhail B. Patsenko[1], Maksim I. Pugachev[1], Yuriy V. Ovchinnikov[1, 2], Larisa I. Mel'nichenko[1, 3], Marina A. Palchenkova[1]

[1] Military Medical Academy, Moscow, Russia;
[2] Industry Clinical Diagnostic Center of the Public Joint Stock Company "Gazprom", Moscow, Russia;
[3] N.E. Bauman City Clinical Hospital N. 29, Moscow, Russia

摘要

论证。慢性心力衰竭患者的止血系统状况仍是一个研究不足的问题。
本研究旨在介绍利用低频压血流弹性成像整体技术对慢性心力衰竭患者凝血系统进行原创性研究的结果。

材料和方法。该研究涉及90名年龄在50-75岁之间的高血压和冠心病背景下的慢性心力衰竭患者。研究对象分为慢性心力衰竭 I-IIa 期（30 人）和 IIb-III 期（60 人）两组。所有患者在接受抗凝血和抗凝血治疗前，均通过经典（凝血图）和积分（低频压吸弹性成像）方法对止血系统进行了检查。对比组包括同年龄组无慢性心力衰竭的健康患者（30 人）。

结果。在慢性心力衰竭患者中，与对照组（241）相比，全血检测的血小板计数（第1组215；第2组185）有统计学意义的减少。凝血图分析显示，与对照组相比，慢性心力衰竭组患者的凝血酶原水平降低（第一组为 89；第二组为 86；对照组为 105），抗凝血酶-III 水平降低（第一组为 76.5；第二组为 73；对照组为 91），国际正常化比率上升（第一组为 1.03；第二组为 1.12；对照组为 1.01）（$p<0.05$）。与对照组相比，慢性心力衰竭患者的凝块聚合速率（凝块聚合强度）和凝块密度（最大振幅）表征指标降低（$p<0.05$）。

结论。慢性心力衰竭患者的止血系统会发生变化，其特点是容易出现凝血功能减退，随着病情的发展，发生的频率和严重程度都会增加。

关键词：止血系统研究的整体方法；凝血图；出血；低频压波弹性成像；止血系统；血栓形成；慢性心力衰竭。

To cite this article
Lebedev MA, Patsenko MB, Pugachev MI, Ovchinnikov YuV, Mel'nichenko LI, Palchenkova MA. 应用经典方法和积分方法诊断慢性心力衰竭患者的止血障碍. *Russian Military Medical Academy Reports*. 2024;43(2):141–150. DOI: https://doi.org/10.17816/rmmar625345

收到: 27.12.2023 **接受**: 03.05.2024 **发布日期**: 28.06.2024

BACKGROUND

Chronic heart failure (CHF) develops as a result of impaired filling and/or emptying ability of the heart. This occurs under conditions of imbalance of vasoconstrictor and vasodilating neurohormonal systems, accompanied by insufficient perfusion of organs and tissues [1]. CHF is the most urgent socio-economic problem and one of the main issues in clinical medicine [2, 3].

Studies on the functional state of the hemostasis system in patients with CHF are limited, and most of these studies date back to the early 2000s. These studies considered platelet properties, endothelial factors, coagulogram parameters, level of thrombosis risk, and bleeding in patients with CHF. Moreover, studies on platelet properties reported that platelet aggregation is increased in CHF patients [5–8]. In the studies by Shmeleva and Malchevsky, the values of screening indicators of the coagulogram did not deviate from the reference values [9, 10]. Moreover, in a study by Medvedeva, certain coagulogram parameters (i.e., prothrombin index [PTI], international normalized ratio [INR]) exhibited hypocoagulation, whereas other parameters (e.g., activated partial thromboplastin time, APTT) and Quick's prothrombin test demonstrated hypercoagulability [11]. The study of endothelial factors affecting hemostasis in patients with CHF demonstrated that nitric oxide synthesis inhibition is a viable mechanism. Furthermore, in patients exhibiting CHF symptoms, the von Willebrand factor expression was increased, indicating a reduction in anticoagulant properties of the endothelium in these patients [12–14]. The findings of these studies show that the hemostatic potential in patients with CHF may be inclined towards hypercoagulation. However, studies on thrombosis and bleeding risks in these patients did not provide definitive insights for understanding of the problem. Thrombosis and bleeding risks increased approximately equally and correlated with disease severity [15–19]. Furthermore, attempts to use direct oral anticoagulants to prevent venous thromboembolic complications in patients with CHF significantly increased hemorrhagic risks [20]. Hence, more sensitive methods should be used to study the hemostasis system in patients with CHF. Recent studies have shown that low-frequency piezoelectric thromboelastography (LFPTEG) can be used for the integral analysis of the hemostasis system, which allows a cumulative assessment of the interaction of all links of hemostasis [21].

This study is relevant owing to the need for frequent prescription of antiaggregant and anticoagulant therapy for coronary heart disease (CHD) in 60 % of patients with CHF [4] and atrial fibrillation (AF) in 40 % [22].

This study aimed to evaluate the state of hemostasis system in patients with CHF by classical (coagulogram) and integral (LEPTEG) methods.

MATERIALS AND METHODS

Study design

Two main groups of patients were recruited: group 1 with CHF stage I–IIa (30 patients) and group 2 with CHF stage IIb–III (60 patients). The control group included healthy individuals (30 patients without CHF).

The mean age of the patients with CHF was 70 years, and that of controls was 68 years. Among the patients with CHF, 26 had hypertension, 16 had CHD, and 48 had a combination of hypertension and CHD. AF was noted in 43 patients, 11 of whom were in sinus rhythm at the time of the study.

The study included patients who, for one reason or another, had not taken anticoagulant and antiaggregant therapy for at least 10 days prior to hospitalization (commonly because of poor compliance) to exclude the effect on the hemostasis system. At least a day after admission, patients were rigorously screened before administration of antiaggregant and anticoagulant therapy.

Eligibility criteria

Inclusion criteria:

1) Age 50–75 years

2) Diagnosis of CHF confirmed by laboratory and instrumental studies

3) Presence of CHD, hypertension, or their combination (according to medical history and laboratory tests)

Exclusion criteria:

1) Acute coronary syndrome within 2 months prior to the examination

2) Coronavirus infection (or vaccination) within the last 6 months

3) Autoimmune diseases, cancer, acute inflammatory diseases, and chronic inflammatory diseases in acute stage

4) Chronic liver disease

5) Chronic pulmonary and bronchial diseases

6) Hereditary and acquired coagulopathies and thrombocytopathies and chronic hematologic diseases.

Setting

The study was conducted in 2021–2023 at the Vishnevsky Central Military Clinical Hospital of the Russian Ministry of Defense (Moscow Region, Novy Village) and Bauman State Clinical Hospital No. 29 of the Moscow City Health Department.

Study duration

The study lasted 36 months. Patients were enrolled upon admission to the hospital and followed throughout their stay.

Methods for recording outcomes

Verification of the diagnosis of CHF and assessment of the stage of the disease were based on complaints, data from the patient's objective examination, laboratory data (e.g., NT-proBNP level), instrumental

studies (e.g., ECHO-CG, ECG), and functional exercise tests (e.g., 6-minute walk test).

The hemostasis system was assessed by standard laboratory (i.e., INR, APTT, PTT, PTI, fibrinogen, D-dimer, antithrombin-III) and instrumental (i.e., LFPTEG) methods. LFPTEG allows for the comprehensive assessment of the hemostasis system, including the process of fibrinogenesis. In the present study, whole unstabilized blood was collected without the use of a tourniquet using a disposable three-component siliconized syringe with a volume of 1 ml. Subsequently, the obtained sample was positioned within a disposable cuvette of 0.45 ml (Mednord, Russia), situated within the thermostat of the MEDNORD hardware–software complex (piezoelectric thromboelastograph).

LFPTEG is a standardized test based on the observation of changes in the studied aliquot of whole, unstabilized venous blood during its transformation from a pre-gel (liquid) to a post-gel (solid-elastic) state. The kinetics of hemocoagulation is determined by changes in the aggregate state of the studied aliquot, as illustrated in the integrated curve shown in Figure 1. Each point (Ai) on the curve represents the state of the system at a specific time point (ti).

Statistical analysis

The sample size was not pre-calculated.

Statistical analysis was performed using Microsoft Excel and Statistica 10.0. Based on the formalized examination maps, summary tables were generated in Microsoft Excel. The obtained variation series were subjected to a series of tests to ascertain their normality of distribution. These tests included the calculation of asymmetry and kurtosis and Shapiro–Wilk test. All data are presented as mean with standard error ($M \pm m$) or median with 25 % and 75 % quartiles, depending on the normality of the distribution of random variables. The Mann–Whitney U test was used to examine the differences between groups. The differences were considered reliable at a significance level of $p < 0.05$.

Ethical review

On December 29, 2021, the Ethics Committee of Vishnevsky Central Military Clinical Hospital of the Russian Ministry of Defense approved the submitted documents and authorized the research involving human participants.

RESULTS

Comparison of platelet levels between patients with CHF and controls

In patients with CHF who were experiencing disease progression, no notable decline was observed in platelet levels. A significant difference was found between the groups under investigation ($p < 0.05$). A comparison of the studied groups with the control group revealed

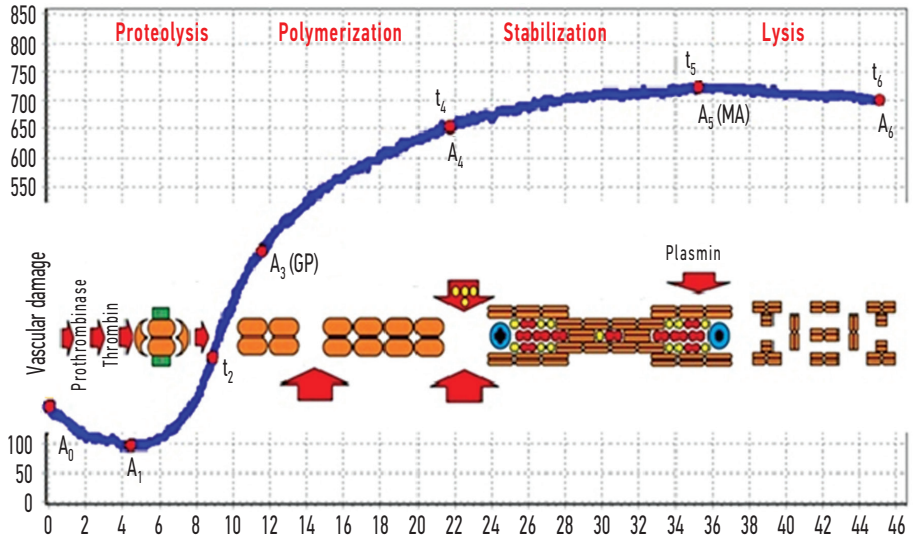

Fig. 1. Dynamics of the wound process in the study groups. A_0 is the initial amplitude value at time t_0, min; A_1 — max decrease in amplitude during time t_1 (reaction period), min.; t_2 — time to reach amplitude A_2 NPTEG, min; A_3 is the amplitude of the NPTEG at the gelation point, r.u.; A_4 is the value of the NPTEG amplitude 10 minutes after reaching the gelation point, r.u.; A_5 — maximum amplitude of NPTEG recorded for 10 min, r.u.; t_5 — time to reach the maximum amplitude of NPTEG (A_5) (time of formation of the fibrin-platelet structure of the clot), min; A_6 — value of the amplitude of the NPTEG 10 minutes after reaching the maximum amplitude, r.u.

Рис. 1. Схема этапов формирования гемостатического потенциала, аппроксимированная на показатели НПТЭГ цельной крови. A_0 — начальное значение амплитуды в момент времени t_0, мин; A_1 — max снижение амплитуды за время t_1 (период реакции), мин.; t_2 — время достижения амплитуды A_2 НПТЭГ, мин; A_3 — величина амплитуды НПТЭГ в точке желирования, о. е.; A_4 — значение амплитуды НПТЭГ через 10 мин после достижения точки желирования, о. е.; A_5 — максимальная амплитуда НПТЭГ, регистрируемая в течение 10 мин, о. е.; t_5 — время достижения максимальной амплитуды НПТЭГ (A_5) (время формирования фибрин-тромбоцитарной структуры сгустка), мин; A_6 — значение амплитуды НПТЭГ через 10 мин после достижения максимальной амплитуды, о. е.

significant differences ($p < 0.05$), thereby confirming the relationship between an increase in the functional class of CHF and the degree of platelet count reduction (Fig. 2).

Coagulation parameters in patients with CHF and in controls

In patients with CHF, hypocoagulation tendency was noted in both studied groups, which was expressed as decreased prothrombin and antithrombin-III and increased INR, correlated with the severity of heart failure manifestations and statistical differences among themselves ($p < 0.05$) and with the control group ($p < 0.05$) (Fig. 3; Table 1).

The increase of indicators such as the prothrombin time and APTT was observed in the studied groups compared to the control group ($p < 0.05$); no differences were found between the studied groups ($p > 0.05$). Regarding fibrinogen and D-dimer levels, a difference was observed between group 2 and controls and group 1 ($p < 0.05$). No significant differences were found between group 1 and the control group ($p > 0.05$) (Table 2).

LEPTEG parameters in patients with CHF and in controls

In patients with CHF in both study groups, no differences were observed in some LFPTEG parameters compared to the control group and to each other ($p > 0.05$): T1 time (time from the beginning of the study to the attainment of the minimum amplitude of the LFPTEG curve), thrombin activity constant, contact phase coagulation intensity (characterizing the activity of the proliferation and amplification phases of fibrinogenesis); T3 time (transition from liquid state (sol) to elastic-solid state (gel)), T5 time (indicator evaluating the time of clot formation of maximum density), and clot lysis retraction intensity (indicator evaluating clot lysis) (Table 3).

However, the most crucial LFPTEG indicators for assessing the hemostasis system are clot polymerization intensity (CPI) and maximum amplitude (MA). CPI evaluates the polymerization stage of the hemocoagulation phase III and rate of cross-linked fibrin formation, whereas MA characterizes the maximum clot density resulting from platelet activity; the qualitative characteristics of cross-linked fibrin exhibited significant differences ($p < 0.05$)

Table 1. Coagulogram parameters (INR, antithrombin III) in patients with CHF and in the control group
Таблица 1. Показатели коагулограммы (МНО, антитромбин III) у пациентов с ХСН и в контрольной группе

Indices (group)	*Me*	Lower quartile	Upper quartile	*p*
INR in group 1	1.03	1.0	1.07	<0.05#*
INR in group 2	1.12	1.05	1.20	<0.05#*
INR in the control group	1.01	0.96	1.02	<0.05
Antithrombin-III in group 1	76.5	73	81	<0.05#*
Antithrombin-III in group 2	73	69	76	<0.05#*
Antithrombin-III in the control group	91	88	93	<0.05

*Note: *,* when comparing between groups 1 and 2; #, when comparing with the control group.
Примечание. * — при сравнении между 1 и 2 группой; # — при сравнении с группой контроля.

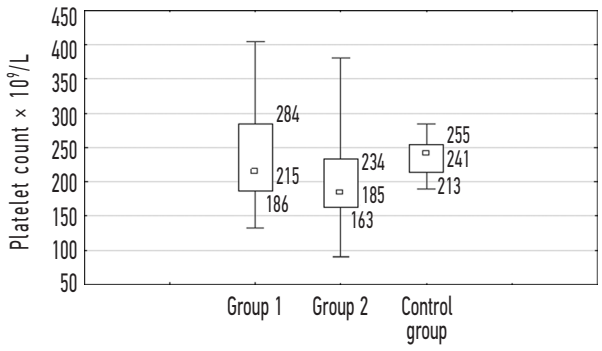

Fig. 2. Platelet count in patients with CHF and individuals in the control group
Рис. 2. Количество тромбоцитов у пациентов с ХСН и лиц в контрольной группе

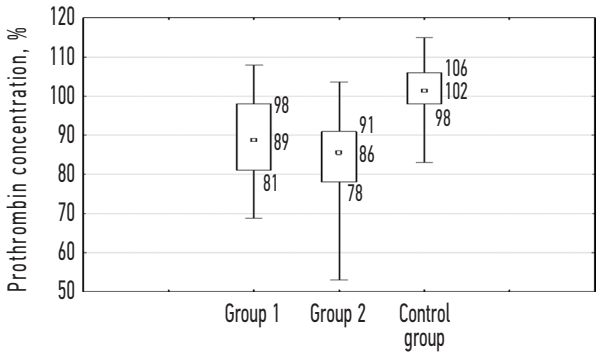

Fig. 3. Prothrombin concentration in patients with CHF and individuals in the control group
Рис. 3. Концентрация протромбина у пациентов с ХСН и лиц в контрольной группе

Table 2. Indicators of coagulogram and fibrinolysis system (Fibrinogen, PTT, APTT, D-Dimer) in patients with CHF and in the control group
Таблица 2. Показатели коагулограммы и системы фибринолиза (фибриноген, ПТВ, АЧТВ, D-Димера) у пациентов с ХСН и в контрольной группе

Indices (group)	*Me*	Lower quartile	Upper quartile	*p*
Fibrinogen in group 1	3.25	2.8	3.6	>0.05* <0.05#
Fibrinogen in group 2	3.4	3.05	3.7	>0.05#*
Fibrinogen in the control group	3.5	3.5	3.8	<0.05 >0.05
Prothrombin time in group 1	11.9	10.9	12.3	>0.05* <0.05#
Prothrombin time in group 2	12.1	11.25	12.8	>0.05* <0.05#
Prothrombin time in the control group	10.6	10.1	11	<0.05
APTT in group 1	29.6	26.2	32.3	>0.05* <0.05#
APTT in group 2	29	27.35	31.15	>0.05* <0.05#
APTT in the control group	27	26.4	27.8	<0.05
D-dimer in group 1	139	112	210	<0.05* >0.05#
D-dimer in group 2	284	222	432	<0.05#*
D-dimer in the control group	135	110	183	>0.05 <0.05

*Note: *,* when comparing between groups 1 and 2; #, when comparing with the control group.
Примечание. * — при сравнении между 1 и 2 группой; # — при сравнении с группой контроля.

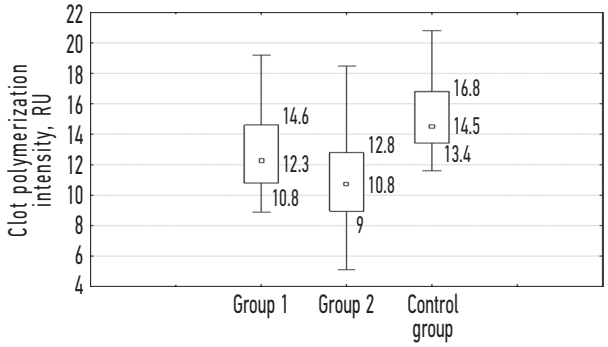

Fig. 4. The indicator of low-frequency piezothromboelastography is the intensity of clot polymerization (IPS)
Рис. 4. Показатель НПТЭГ — интенсивность полимеризации сгустка (ИПС)

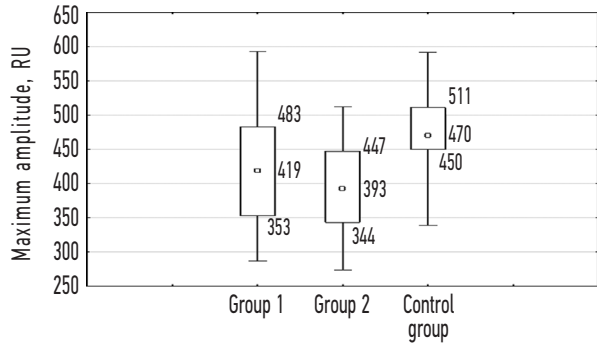

Fig. 5. The indicator of low-frequency piezothromboelastography is maximum amplitude (MA)
Рис. 5. Показатель НПТЭГ — максимальная амплитуда (МА)

between the studied groups (groups 1 and 2) and control group. These differences were more pronounced when comparing group 2 to the control group ($p < 0.01$) (Figs. 4 and 5).

A comparison of the coagulogram parameters to those of LFPTEG (Table 4) reveals that, despite significant differences between the groups, the coagulogram parameters do not exceed the reference values and thus are of minimal clinical significance.

In turn, LFPTEG parameters exhibit significant differences between the groups, with values exceeding the reference range in patients with CHF. These deviations are more pronounced in patients with stage IIb–III of the disease. Therefore, the LFPTEG method can be regarded

Table 3. Indicators of low-frequency piezothromboelastography
Таблица 3. Показатели НПТЭГ

Indices (group)	*Me*	Q1	Q3	*p*
T1 time in group 1	0.85	0.1	1.2	>0.05#*
T1 time in group 2	0.9	0.3	1.55	>0.05#*
T1 time in the control group	0.75	0.1	1.3	>0.05
Contact phase coagulation intensity (CCI) in group 1	8.2	0.0	13.8	>0.05#*
CCI in group 2	8.4	2.9	19.45	>0.05#*
CCI) in the control group	4	0.0	20.0	>0.05
Thrombin activity constant (TAC) in group 1	43.6	33.3	66.7	>0.05* <0.05#
TAC in group 2	42.65	21.5	55.6	>0.05#*
TAC in the control group	32.8	27	40.0	<0.05 >0.05
T3 time in group 1	7.3	3.5	8.4	>0.05#*
T3 time in group 2	7.65	5.2	10.8	>0.05#*
T3 time in the control group	6.95	5.7	8.8	>0.05
T5 time in group 1	31.0	26.7	38.0	>0.05#*
T5 time in group 2	30.6	26.1	35.25	>0.05#*
T5 time in the control group	28.25	25.8	36.8	>0.05
Clot lysis retraction intensity (CLRI) in group 1	0.67	0.28	0.88	>0.05#*
CLRI in group 2	0.69	0.29	1.5	>0.05#*
CLRI in the control group	0.65	0.44	1.37	>0.05

*Note: **, when comparing between groups 1 and 2; #, when comparing with the control group.
Примечание. * — при сравнении между 1 и 2 группой; # — при сравнении с группой контроля.

Table 4. Comparison of coagulogram and NPTEG parameters
Таблица 4. Сравнение показателей коагулограммы и НПТЭГ

Indices (reference values)	Groups		
	Group 1 (median)	Group 2 (median)	Control group (median)
Coagulation indices			
INR (0.8–1.2).	1.03	1.12	1.01
Prothrombin (70%–120%)	89	86	101
Prothrombin time (10–15 s)	11.9	12.1	10.6
APTT (25.4–36.9 s)	29.6	29	27
Fibrinogen (2.0–4.0 g/L)	3.25	3.4	3.5
Antithrombin-III (66%–124%)	76.5	73	91
D-dimer (<243 ng/mL)	139	284	135
LFPTEG indicators			
CPI (15.4–22.5 RU)	12.25	10.75	14.5
MA (450–650 RU)	419	393	470
TCR (14–18.1 RU)	12.8	12.7	16

as a more sensitive diagnostic tool for hemostasis system disorders in patients with CHF.

Adverse events

No adverse events were noted.

DISCUSSION

In patients with CHF, changes in hemostasis system characterized by a hypocoagulation tendency are observed. This phenomenon is directly correlated with the CHF stage and affects the platelet and plasma components of the coagulation system. A reduction in platelet levels has been observed during CHF progression. This may be attributed to splenomegaly, which can lead to hypersplenism and stasis in the great circle of blood circulation [23]. Additionally, according to some studies, a possible cause of platelet count reduction may be a decrease in thrombopoietin production due to liver and kidney damage in patients with CHF [24].

Furthermore, the study on standard coagulogram parameters showed a hypocoagulation tendency in patients with CHF, apparently due to congestion in the systemic circulation, which leads to impaired hepatic microcirculation, involving the processes of hepatic fibrosis [25–27], and impaired synthesis of plasma coagulation factors.

In this case, the changes in the hemostatic system in patients with CHF are confirmed by an integral research method, namely, LFPTEG, which allows for the assessment of the patient's hemostatic potential considering the interaction of all parts of the coagulation system. Indicators assessing clot density, rate of clot formation, and qualitative characteristics of cross-linked fibrin significantly change in the direction of decrease of hemostatic potential in patients transitioning to more severe stages of heart failure.

CONCLUSIONS

1. In patients with CHF, changes in the hemostasis system are evident, manifesting as hypocoagulation tendency.

2. Changes in the coagulation system are associated with disease severity and are most pronounced in patients with CHF stage IIb–III.

3. LFPTEG confirms hemostasis disorders detected by standard laboratory methods (e.g., platelet count, coagulogram indices) and may be considered a more sensitive method for use in clinical practice in patients with CHF.

ADDITIONAL INFORMATION

Funding source: No funding was provided for this study.

Conflict of interest: The authors declare that there are no obvious and potential conflicts of interest related to the publication of this article.

Ethical review: The study was approved by the Ethical Committee Vishnevsky Central Military Clinical Hospital of the Russian Ministry of Defense on December 29, 2021.

Authors' contribution: M.A. Lebedev, primary collection of materials, analysis of scientific data, writing the text; M.B. Patsenko, author of the idea and objectives of the study; M.I. Pugachev, methodological control over the processing of scientific data, writing the text; Y.V. Ovchinnikov, concept and design of the study; L.I. Melnichenko, collection, systematization and analysis of scientific data; M.V. Palchenkova, collection and processing of materials, literature review, translation of foreign articles. All authors made a significant contribution to the research and preparation of the article and read and approved the final version before publication.

REFERENCES

1. Tereshchenko SN, Galyavich AS, Uskach TM, et al. Chronic heart failure. Clinical recommendations 2020. *Russian Journal of Cardiology*. 2020;25(11):311–374. (In Russ.) EDN: LJGGQV doi: 10.15829/1560-4071-2020-4083

2. Dunlay SM, Roger VL, Redfield MM. Epidemiology of heart failure with preserved dejection fraction. *Nat Rev Cardiol*. 2017;14(11): 591–602. doi: 10.1038/nrcardio.2017.65

3. 3.Tsao CW, Aday AW, Almarzooq ZI, et al. Heart Disease and Stroke Statistics-2022 Update: A Report From the American Heart Association. *Circulation*. 2022;145(8):153–639. doi: 10.1161/CIR.0000000000001052

4. Polyakov DS, Fomin IV, Belenkov YuN, et al. Chronic heart failure in the Russian Federation: what has changed over 20 years of follow-up? Results of the EPOCH-CHF study. *Kardiologiia*. 2021;61(4):4–14. (In Russ.) EDN: WSZNFS doi: 10.18087/cardio.2021.4.n1628

5. Mongirdienė A, Laukaitienė J, Skipskis V, at al. Platelet Activity and Its Correlation with Inflammation and Cell Count Readings in Chronic Heart Failure Patients with Reduced Ejection Fraction. *Medicina (Kaunas)*. 2021;57(2):164–176. doi: 10.3390/medicina57020176

6. Altieri P., Brunelli C., Garibaldi S., et al. Metalloproteinases 2 and 9 are increased in plasma of patients with heart failure. *Eur J Clin Invest*. 2003;33(8):648–656. doi: 10.1046/j.1365-2362.2003.01187.x

7. Gurbel P.A., Bliden K.P., Hayes K.M., Tantry U. Platelet activation in myocardial ischemic syndromes. *Expert Rev Cardiovasc Ther*. 2004;2(4):535–545. doi: 10.1586/14779072.2.4.535

8. Ueland T, Aukrust P, Yndestad A, et al. Soluble CD40 ligand in acute and chronic heart failure. *Eur J Clin Invest*. 2005;26(11): 1101–1107. doi: 10.1093/eurheartj/ehi132

9. Shmeleva VM, Semenova ON, Papayan LP, Yagashkina SI. Activation of the hemostatic system in patients with chronic heart failure. *Vestnik of Saint Petersburg University. Series 11. Medicine*. 2009;(1):37–43. (In Russ.) EDN: KVNIQB

10. Mal'chevskiy YuE. Rheological properties of blood in patients with chronic heart failure in applying of plasmapheresis. *Heart failure*. 2014;15(4(85)):238–242. (In Russ.) EDN: KQOTXR
11. Medvedeva KA. Indicators of hematology and hemostasis in decompensated heart failure. *Scientist*. 2023;(2(24)):17–25. (In Russ.) EDN: YQNUWM
12. Vila V, Martínez-Sales V, Almenar L, et al. Inflammation, endothelial dysfunction and angiogenesis markers in chronic heart failure patients. *Int J Cardiol.* 2008;130(2):276–277. doi: 10.1016/j.ijcard.2007.07.010
13. Cugno M, Mari D, Meroni PL, et al. Haemostatic and inflammatory biomarkers in advanced chronic heart failure: role of oral anticoagulants and successful heart transplantation. *Br J Haematol*. 2004;126(1):85–92. doi: 10.1111/j.1365-2141.2004.04977.x
14. Song J, Liu Y, Huang G. Predictive value of von Willebrand factor for venous thrombosis in patients with chronic heart failure complicated with atrial fibrillation after anticoagulant therapy. *BMC Cardiovasc Disord*. 2023;23(1):349. doi: 10.1186/s12872-023-03167-1
15. Tang L, Wu YY, Lip GY, et al. Heart failure and risk of venous thromboembolism: a systematic review and meta-analysis. *Lancet Haematol*. 2016;3(1):30–44. doi: 10.1016/S2352-3026(15)00228-8
16. Shantsila E, Lip GY. Thrombotic complications in heart failure: an underappreciated challenge. *Circulation*. 2014;130(5):387–389. doi: 10.1161/CIRCULATIONAHA.114.011353
17. Vereina NK, Agasyan DG, Chulkov VS. The risk of venous thromboembolism in patients with heart failure. *Russian Journal of Cardiology*. 2020;25(1):9–13 (In Russ.) EDN: MIQSET doi: 10.15829/1560-4071-2020-1-3678
18. Siniarski A, Gąsecka A, Borovac JA, et al. Blood Coagulation Disorders in Heart Failure: From Basic Science to Clinical Perspectives. *J Card Fail*. 2023;29(4):517–526. doi: 10.1016/j.cardfail.2022.12.012
19. Karaban K, Słupik D, Reda A, et al. Coagulation Disorders and Thrombotic Complications in Heart Failure With Preserved Ejection Fraction. *Curr Probl Cardiol*. 2024;49(1 Pt C):102127. doi: 10.1016/j.cpcardiol.2023.102127
20. Vinogradova NG, Zhirkova MM, Polyakov DS, et al. Anticoagulant therapy and prognosis in patients with CHF and AF in the setting of real-life clinical practice. *Kardiologiia*. 2017;57(S4):4–10. (In Russ.) EDN: YKUOVW doi: 10.18087/cardio.2430
21. Tyutrin II, Udut VV. *Low-frequency piezothromboelastography of whole blood: algorithms for diagnosis and correction of hemostasiological disorders*. Tomsk: Publishing House of Tomsk State University; 2016. 170 p. (In Russ.)
22. Gagloeva DA, Mironov NYu, Layovich LYu, et al. Atrial fibrillation and chronic heart failure: interrelationship and approaches to treatment. *Kardiologicheskiy vestnik*. 2021;16(2):5–14. (In Russ.) EDN: SEAZWQ doi: 10.17116/Cardiobulletin2021160215
23. Voitsekhovsky VV, Goborov ND. Splenomegaly in clinical practice. *Amur Medical Journal*. 2019;26(2):61–77. EDN: XAKEUS doi: 10.22448/AMJ.2019.2.61-77
24. Mazurov AV. *Physiology and pathology of platelets.* Moscow: Litterra Publishing House; 2011:196–206. (In Russ.)
25. Fortea JI, Puente Á, Cuadrado A, et al. Congestive Hepatopathy. *Int J Mol Sci.* 2020;21(24):9420. doi: 10.3390/ijms21249420
26. Lemmer A, VanWagner LB, Ganger D. Assessment of Advanced Liver Fibrosis and the Risk for Hepatic Decompensation in Patients With Congestive Hepatopathy. *Hepatology.* 2018;68(4):1633–1641. doi: 10.1002/hep.30048
27. Kobalava ZhD, Villeval'de SV, Solov'yova AE. Cardiohepatic syndrome in heart failure: prevalence, pathogenesis, prognostic significance. *Kardiologiia*. 2016;56(12):63–71. (In Russ.) EDN: XIMOCZ doi: 10.18565/cardio.2016.12.63-71

СПИСОК ЛИТЕРАТУРЫ

1. Терещенко С.Н., Галявич А.С., Ускач Т.М., и др. Хроническая сердечная недостаточность. Клинические рекомендации 2020 // Российский кардиологический журнал. 2020. Т. 25, № 11. С. 311–374. EDN: LJGGQV doi: 10.15829/1560-4071-2020-4083
2. Dunlay S.M., Roger V.L., Redfield M.M. Epidemiology of heart failure with preservedejection fraction // Nat. Rev. Cardiol. 2017. Vol. 14, N 11. P. 591–602. doi: 10.1038/nrcardio.2017.65
3. Tsao C.W., Aday A.W., Almarzooq Z.I., at al. Heart Disease and Stroke Statistics 2022. Update: A Report From the American Heart Association // Circulation. 2022. Vol. 145, N 8. P. 153–639. doi: 10.1161/CIR.0000000000001052
4. Поляков Д.С., Фомин И.В., Беленков Ю.Н., и др. Хроническая сердечная недостаточность в Российской федерации: что изменилось за 20 лет наблюдения? Результаты исследования ЭПОХА-ХСН // Кардиология. 2021. Т. 61, № 4. С. 4–14. EDN: WSZNFS doi: 10.18087/cardio.2021.4.n1628
5. Mongirdienė A., Laukaitienė J., Skipskis V., at al. Platelet Activity and Its Correlation with Inflammation and Cell Count Readings in Chronic Heart Failure Patients with Reduced Ejection Fraction // Medicina (Kaunas). 2021. Vol. 57, N 2. P. 164–176. doi: 10.3390/medicina57020176
6. Altieri P., Brunelli C., Garibaldi S., at al. Metalloproteinases 2 and 9 are increased in plasma of patients with heart failure // Eur. J. Clin. Invest. 2003. Vol. 33, N 8. P. 648–656. doi: 10.1046/j.1365-2362.2003.01187.x
7. Gurbel P.A., Bliden K.P., Hayes K.M., Tantry U. Platelet activation in myocardial ischemic syndromes // Expert Rev. Cardiovasc. Ther. 2004. Vol. 2, N 4. P. 535–545. doi: 10.1586/14779072.2.4.535
8. Ueland T., Aukrust P., Yndestad A., at al. Soluble CD40 ligand in acute and chronic heart failure // Eur. J. Clin. Invest. 2005. Vol. 26, N 11. P. 1101–1107. doi: 10.1093/eurheartj/ehi132
9. Шмелева В.М., Семенова О.Н., Папаян Л.П, Ягашкина С.И. Активация системы гемостаза у пациентов с хронической сердечной недостаточностью // Вестник Санкт-Петербургского университета. Серия 11. Медицина. 2009. № 1. С. 37–43. EDN: KVNIQB
10. Мальчевский Ю.Е. Реологические свойства крови больных хронической сердечной недостаточностью при применении плазмафереза // Сердечная недостаточность. 2014. Т. 15, № 4 (85). С. 238–242. EDN: KQOTXR
11. Медведева К.А. Показатели гематологии и гемостаза при декомпенсации хронической сердечной недостаточности // Scientist (Russia). 2023. № 2 (24). С. 17–25. EDN: YQNUWM
12. Vila V., Martínez-Sales V., Almenar L., at al. Inflammation, endothelial dysfunction and angiogenesis markers in chronic heart failure patients // Int. J. Cardiol. 2008. Vol. 130. N 2. P. 276–277. doi: 10.1016/j.ijcard.2007.07.010

13. Cugno M., Mari D., Meroni P.L., at al. Haemostatic and inflammatory biomarkers in advanced chronic heart failure: role of oral anticoagulants and successful heart transplantation // Br. J. Haematol. 2004. Vol. 126. N 1. P. 85–92. doi: 10.1111/j.1365-2141.2004.04977.x
14. Song J., Liu Y., Huang G. Predictive value of von Willebrand factor for venous thrombosis in patients with chronic heart failure complicated with atrial fibrillation after anticoagulant therapy // BMC Cardiovasc. Disord. 2023. Vol. 23, N 1. P. 349. doi: 10.1186/s12872-023-03167-1
15. Tang L., Wu Y.Y., Lip G.Y., at al. Heart failure and risk of venous thromboembolism: a systematic review and meta-analysis // Lancet Haematol. 2016. Vol. 3, N 1. P. 30–44. doi: 10.1016/S2352-3026(15)00228-8
16. Shantsila E., Lip G.Y. Thrombotic complications in heart failure: an underappreciated challenge // Circulation. 2014. Vol. 130, N 5. P. 387–389. doi: 10.1161/CIRCULATIONAHA.114.011353
17. Вереина Н.К., Агасян Д.Г., Чулков В.С. Риск венозных тромбоэмболических осложнений у пациентов с хронической сердечной недостаточностью // Российский кардиологический журнал. 2020. Т. 25, № 1. С. 9–13. EDN: MIQSET doi: 10.15829/1560-4071-2020-1-3678
18. Siniarski A., Aleksandra G., Josip A. B., et al. Blood Coagulation Disorders in Heart Failure: From Basic Science to Clinical Perspectives // J. Card. Fail. 2023. Vol. 29, N 4. P. 517–526. doi: 10.1016/j.cardfail.2022.12.012
19. Karaban K., Słupik D., Reda A., et al. Coagulation Disorders and Thrombotic Complications in Heart Failure With Preserved Ejection Fraction // Curr. Probl. Cardiol. 2024. Vol. 49, Issue 1, Part C, 2024. Art. 102127. doi: 10.1016/j.cpcardiol.2023.102127
20. Виноградова Н.Г., Жиркова М.М., Поляков Д.С., и др. Антикоагулянтная терапия и прогноз у пациентов с ХСН и ФП в условиях реальной клинической практики // Кардиология. 2017. Т. 57, № S4. С. 4–10. EDN: YKUOVW doi: 10.18087/cardio.2430
21. Тютрин И.И., Удут В.В. Низкочастотная пьезотромбоэластография цельной крови: алгоритмы диагностики и коррекции гемостазиологических расстройств. Томск: Издательский Дом Томского государственного университета, 2016. 170 с.
22. Гаглоева Д.А., Миронов Н.Ю., Лайович Л.Ю. и др. Взаимосвязь фибрилляции предсердий и хронической сердечной недостаточности. Современные подходы к лечению // Кардиологический вестник. 2021. Т. 16, № 2. С. 5–14. EDN: SEAZWQ doi: 10.17116/Cardiobulletin2021160215
23. Войцеховский В.В., Гоборов Н.Д. Спленомегалия в клинической практике // Амурский медицинский журнал. 2019. Т. 26, № 2. С. 61–77. EDN: XAKEUS doi: 10.22448/AMJ.2019.2.61-77
24. Мазуров А.В. Физиология и патология тромбоцитов. М.: Литтерра, 2011. С. 196–206.
25. Fortea J.I., Puente Á., Cuadrado A. et al. Congestive Hepatopathy // Int. J. Mol. Sci. 2020. Vol. 21, N 24. Art. 9420. doi: 10.3390/ijms21249420
26. Lemmer A., VanWagner L.B., Ganger D. Assessment of Advanced Liver Fibrosis and the Risk for Hepatic Decompensation in Patients With Congestive Hepatopathy // Hepatology. 2018. Vol. 68, N 4. P. 1633–1641. doi: 10.1002/hep.30048
27. Кобалава Ж.Д., Виллевальде С.В., Соловьева А.Е. Сердечно-печеночный синдром при сердечной недостаточности: распространенность, патогенез, прогностическое значение // Кардиология. 2016. Т. 56, № 12. С 63–71. EDN: XIMOCZ doi: 10.18565/cardio.2016.12.63-71

AUTHORS' INFO

***Maxim A. Lebedev,** address: 7, Malaya Cherkizovskaya str., Moscow, Russia, 111020; ORCID: 0000-0002-9536-6683; eLibrary SPIN: 4775-9499; e-mail: vmeda-nio@mil.ru

Mikhail B. Patsenko, MD, Cand. Sci. (Medicine), Associate Professor; ORCID: 0000-0001-8391-1691; eLibrary SPIN: 5681-3603; e-mail: vmeda-nio@mil.ru
Maxim I. Pugachev, MD, Cand. Sci. (Medicine); ORCID: 0000-0001-5523-8233; eLibrary SPIN: 1549-6552; e-mail: vmeda-nio@mil.ru
Yury V. Ovchinnikov, MD, Dr. Sci. (Medicine), Professor; ORCID: 0000-0003-1843-087X; eLibrary SPIN: 6965-6407; e-mail: vmeda-nio@mil.ru
Larisa I. Mel'nichenko, MD, Cardiologist; ORCID: 0009-0004-8275-9009; e-mail: vmeda-nio@mil.ru
Marina V. Palchenkova, MD, Cand. Sci. (Medicine), Associate Professor; ORCID: 0000-0001-6885-9610; eLibrary SPIN: 7567-9650; e-mail: vmeda-nio@mil.ru

ОБ АВТОРАХ

***Максим Александрович Лебедев,** адрес: 111020, Россия, г. Москва, ул. Малая Черкизовская, д. 7; ORCID: 0000-0002-9536-6683; eLibrary SPIN: 4775-9499; e-mail: vmeda-nio@mil.ru
Михаил Борисович Паценко, канд. мед. наук, доцент; ORCID: 0000-0001-8391-1691; eLibrary SPIN: 5681-3603; e-mail: vmeda-nio@mil.ru
Максим Игоревич Пугачев, канд. мед.наук; ORCID: 0000-0001-5523-8233; eLibrary SPIN: 1549-6552; e-mail: vmeda-nio@mil.ru
Юрий Викторович Овчинников, докт. мед. наук, профессор; ORCID: 0000-0003-1843-087X; eLibrary SPIN: 6965-6407; e-mail: vmeda-nio@mil.ru
Лариса Игоревна Мельниченко, врач-кардиолог; ORCID: 0009-0004-8275-9009; e-mail: vmeda-nio@mil.ru
Марина Владимировна Палченкова, канд. мед. наук, доцент; ORCID: 0000-0001-6885-9610; eLibrary SPIN: 7567-9650; e-mail: vmeda-nio@mil.ru

* Corresponding author / Автор, ответственный за переписку