https://doi.org/10.35336/VA-

THE POSSIBILITIES OF MONITORING THE EFFECTIVENESS OF ANTICOAGULANT THERAPY USING A THROMBODYNAMICS TEST IN PATIENTS WITH LEFT ATRIAL APPENDAGE THROMBOSIS WITH NON-VALVULAR ATRIAL FIBRILLATION: CLINICAL CASES

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Clinical observations of the possibility of using the thrombodynamics test (TD) in comparison with standard hemostasis tests in patients with non-valvular atrial fibrillation (AF) and detected thrombosis of the left atrial appendage against the background constant oral anticoagulants are presented. It has been shown that the transfer from one direct oral anticoagulant (DOACs) to another (with a different mechanism of action), as well as from DOACs to warfarin, can change the state of the blood plasma coagulation system towards both hyper- and hypocoagulation. Unlike standard hemostasis tests, TD can be used to assess the prothrombotic status of a patient with AF and personalized selection of effective anticoagulant therapy.

Key words: atrial fibrillation; thrombosis of the left atrial appendage; oral anticoagulants; thrombodynamics test

Conflict of Interest: none.
Funding: none.
Received: 09.11.2024 **Revision received:** 11.02.2025 **Accepted:** 27.02.2025
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For citation: Khorkova NYu, Gizatulina TP, Belokurova AV, Mamarina AV. The possibilities of monitoring the effectiveness of anticoagulant therapy using a thrombodynamics test in patients with left atrial appendage thrombosis with non-valvular atrial fibrillation: clinical cases. *Journal of Arrhythmology*. 2025;32(2): e1-e7. https://doi.org/10.35336/VA-1434.

Atrial fibrillation (AF) is a prognostically unfavourable cardiac arrhythmia, associated with a fivefold increase in the risk of thromboembolic events (TEEs) [1]. In non-valvular AF, left atrial appendage (LAA) thrombosis is the principal source of TEEs [2]. According to both European and national clinical guidelines, direct oral anticoagulants (DOACs) are preferred as first-line therapy over vitamin K antagonists for reducing thromboembolic risk in patients with non-valvular AF [1, 2]. However, even with continuous administration of appropriate anticoagulant therapy - including warfarin under strict international normalised ratio (INR) monitoring - the risk of thrombosis is not completely eliminated. Reported LAA thrombus detection rates range from 0.5% to 8.3% in the literature [3-5].

To explore potential mechanisms of thrombogenesis, it is of particular interest to assess haemostatic function during anticoagulant therapy, as hypercoagulability is one element of Virchow's triad. As is well known, warfarin dosing requires rigorous INR monitoring. In contrast, for DOACs, routine coagulation tests are not used for therapy monitoring or dose adjustment in everyday clinical practice [6, 7]. According to the European Practical Guide on the use of DOACs in patients with non-valvular AF, standard coagulation tests and drug-specific assays to determine DOAC plasma concentrations are recommended only in emergency situations (e.g. stroke, bleeding, surgery) [7].

A review of current literature indicates that changes in core laboratory parameters of plasma haemostasis during anticoagulant therapy remain insufficiently studied. In this context, a personalised approach to anticoagulant selection - based on efficacy monitoring - becomes particularly promising. This can be achieved using a novel global coagulation assay known as the thrombodynamics (TD) test [8]. Only a limited number of studies have explored the use of TD parameters in patients with AF under complex clinical circumstances requiring verification of anticoagulant efficacy - for instance, in cases of documented LAA thrombosis or previous transient ischaemic attack [9, 10].

Principle of the Thrombodynamics Test

The TD test assesses both the qualitative and quantitative characteristics of the coagulation state of plasma, enabling analysis of the spatiotemporal dynamics of fibrin clot formation in vitro [8].

The test is performed using the "Thrombodynamics T-2 Analyser" laboratory system. Prepared platelet-free plasma samples are introduced into two channels of a measuring cuvette, into which a special insert-activator is placed. The edges of this insert are coated with lipids and tissue factor. Upon contact between the plasma and the activator insert, coagulation is initiated, leading to the formation of a fibrin clot. The process is recorded by sequential digital photomicrography using a dark-field method (light scattering registration) over 30 minutes. The resulting series of images reveals the evolution of clot size, shape, and structure over time [11].

Software analysis of the images generates curves

describing clot growth dynamics and spontaneous clot formation area over time. These data yield the following quantitative parameters of fibrin clot propagation: Lag time (Tlag) - delay before clot growth begins; Clot growth velocity (V); Initial clot growth rate (Vi); Steady-state growth rate (Vst); Clot size at 30 minutes (CS); Clot density (D) - based on light scattering intensity.

In addition, the test calculates the time to spontaneous clot formation (Tsp), defined as the time required for spontaneous clots to occupy 5% of the cuvette area away from the main clot front.

To assess anticoagulant efficacy, blood collection for the TD test is recommended at trough DOAC levels (i.e., shortly before the next dose). For warfarin users, the test is performed in the morning, not earlier than on the 7th day of continuous therapy.

The following clinical observations illustrate the potential of thrombodynamics testing - compared to standard haemostasis assays - for guiding anticoagulant therapy selection in patients with non-valvular AF and confirmed LAA thrombosis.

Clinical Case No. 1

Patient Sh., 42 years old, was admitted to the clinic in April 2024 with complaints of palpitations, shortness of breath when walking at a brisk pace, and general weakness. Medical history revealed a diagnosis of arterial hypertension established five years ago; however, the patient had not been taking antihypertensive medication regularly. His condition worsened in February 2024, when, for the first time upon arriving at his remote worksite, he experienced an episode of rapid and irregular heartbeat. ECG revealed atrial fibrillation with a ventricular rate (VR) of 110 bpm. The paroxysm resolved following bisoprolol intake. Subsequently, AF episodes recurred and reportedly transitioned into a persistent form approximately two months prior (AF with VR ranging from 100 to 116 bpm was consistently recorded on serial ECGs).

Transthoracic echocardiography (TTE) revealed hypokinesia of the inferior wall of the left ventricle (LV), with an asynergy zone area of 20%, dilation of both atria, an enlarged LA volume of 107 ml, and a reduced LV ejection fraction (LVEF) of 46%. Before hospital admission for coronary angiography (CAG) and evaluation for catheter ablation (CA), the patient was treated for one month with the following medications: metoprolol succinate 100 mg/day, perindopril 2 mg/day, apixaban 5 mg twice daily, rosuvastatin 20 mg/day, dapagliflozin 10 mg/day, and spironolactone 25 mg/day. CAG revealed no evidence of coronary artery stenosis. TEE showed marked spontaneous echo contrast in the LA and LAA, partial opacification of the LAA on colour Doppler imaging, a reduced LAA flow velocity of 30 cm/sec, and a soft, mobile, unorganised mural thrombus measuring 14 mm at the LAA ostium (Fig. 1a). Laboratory tests (complete blood count, biochemical panel, thyroid-stimulating hormone) showed no significant deviations from reference values.

Final clinical diagnosis: Hypertension, Stage III. Controlled arterial hypertension. Dyslipidaemia. Cardiovascular risk: very high (score 4). Target BP ≤130/70-79 mmHg. Complications: Atrial fibrillation, persistent form. CHA_2DS_2-VASc: 2, HAS-BLED: 1. Secondary atrial dilation. Soft mural thrombus at the LAA ostium. Chronic heart failure (CHF) IIA with moderately reduced ejection fraction (46%), NYHA functional class II.

To assess haemostatic status, the following tests were performed: activated partial thromboplastin time (aPTT),

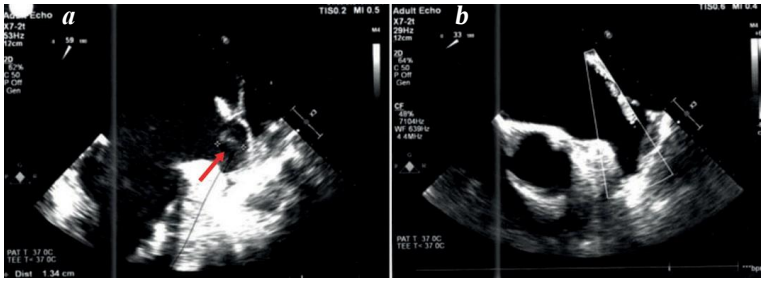

Fig. 1. Transoesophageal echocardiography (TEE) of patient Sh.: a - soft thrombus (indicated by arrow) in the ostium of the left atrial appendage (LAA) during apixaban therapy; b - no evidence of LAA thrombosis during dabigatran therapy.

Table 1.

Haemostasis Test Parameters in Patient Sh. During Apixaban and Dabigatran Therapy

Parameter	Reference Values	Apixaban 10 mg/day	Dabigatran 300 mg/day (3 days)	Dabigatran 300 mg/day (1 month)
Standard Haemostasis Tests				
aPTT, sec	26-36	34,8	49,1	-
PTI, %	80-120	90,6	85,3	-
INR	0,95-1,2	1,17	1,33	-
TT, sec	15-20	16,2	>250	-
Fibrinogen, g/L	2-4	3,76	3,54	-
Thrombodynamics Parameters				
Vi, μm/min	38-56	48,5	42,9	42,8
Vst, μm/min	20-29	27,3	25,1	25
Tlag, min	0,6-1,5	1,1	1,5	1,5
CS, μm	800-1200	1039	955	940
D, a.u.	15000-32000	25765	24163	17698
Tsp, min	none	none	none	none

Note: here and afetr: aPTT - activated partial thromboplastin time; INR - international normalized ratio; PTI - prothrombin index; TT - thrombin time; Vi - initial velocity; Vst - steady-state velocity; Tlag - growth delay; CS - clot size after 30 minutes; D - density; Tsp - time of spontaneous clot appearance.

prothrombin time (PT) expressed as prothrombin index (PI) and international normalized ratio, thrombin time (TT), fibrinogen, and thrombodynamics (TD) assay. Standard coagulation tests and TD analysis (Table 1) showed no abnormalities during apixaban therapy. However, TD parameters revealed no prolongation of clot growth lag time (Tlag), prompting a change in anticoagulant therapy: apixaban was replaced by a direct thrombin inhibitor - dabigatran, 300 mg/day. On day 3 of dabigatran therapy, aPTT and TT were elevated in standard coagulation tests, and TD results showed improvement - slower clot formation, reduced clot density, and prolonged Tlag. After one month of dabigatran therapy, TD parameters (Vst, Vi, Tlag, CS) remained stable, with clot density further reduced from 24,163 to 17,698 units.

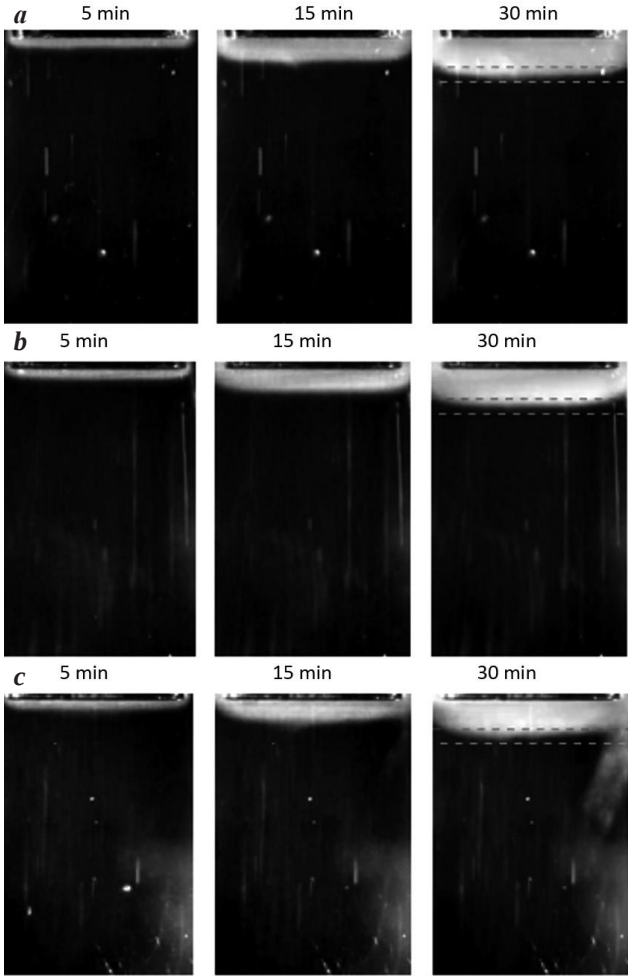

Fig. 2. Fibrin clot images obtained at 5, 15, and 30 minutes of the thrombodynamics (TD) test during apixaban and dabigatran therapy in patient Sh.: a - clot formation after 1 month of apixaban therapy; b - after 3 days of dabigatran therapy; c - after 1 month of dabigatran therapy. Images b and c demonstrate normocoagulation, with no spontaneous clotting, reflecting an optimal anticoagulant effect of the DOAC.

Follow-up TEE after one month showed full opacification of the LAA, mild residual SEC in the LA and LAA, improved LAA flow velocity (increased from 30 to 48 cm/sec), and no signs of thrombosis (Fig. 1b). ECG revealed spontaneous restoration of sinus rhythm. Follow-up TTE showed improvement in LVEF from 46% to 63%, and no residual asynergy zones were observed. Fibrin clot images from TD testing under apixaban and dabigatran therapy are presented in Fig. 2. This clinical case demonstrates the utility of the TD assay in monitoring the dynamics of a prothrombotic state following a change in anticoagulant therapy. The effectiveness of dabigatran was confirmed by the successful resolution of LAA thrombosis.

Clinical Case No. 2

Patient Ts., 64 years old, was admitted to the clinic in June 2022 with complaints of irregular heartbeat, dyspnoea during moderate physical exertion, general weakness, and fatigue. Medical history revealed a diagnosis of arterial hypertension established 15 years prior. The target blood pressure had been achieved through antihypertensive therapy. Approximately five months before admission, the patient experienced his first episode of palpitations, irregular heart rhythm, fatigue, and substernal discomfort not clearly associated with physical activity. AF was recorded on ECG. The patient independently discontinued the prescribed therapy (bisoprolol 10 mg/day, apixaban 10 mg/day, losartan 100 mg/day, atorvastatin 20 mg/day) due to a tendency toward hypotension and bradycardia (heart rate dropping to 50 bpm). He was hospitalised for CAG and further treatment planning.

CAG revealed no haemodynamically significant stenotic lesions of the coronary arteries. TTE showed aortic atherosclerosis, dilation of the left atrium (LA) with a volume of 70 ml (B-mode), dilation of the right atrium (volume 62 ml), and a slight reduction in left ventricular systolic function at rest (LVEF 51%). TEE showed no signs of LAA thrombosis, although moderate spontaneous echo contrast was observed in the LAA and LA cavity. The LAA flow velocity was reduced to 34 cm/sec. Given the absence of regular anticoagulant intake prior to hospitalisation and the presence of spontaneous echo contrast , which increases the risk of thromboembolic complications, the patient was discharged with a recommendation for continuous anticoagulant therapy with dabigatran 300 mg/day, followed by reassessment via TEE and consideration for CA.

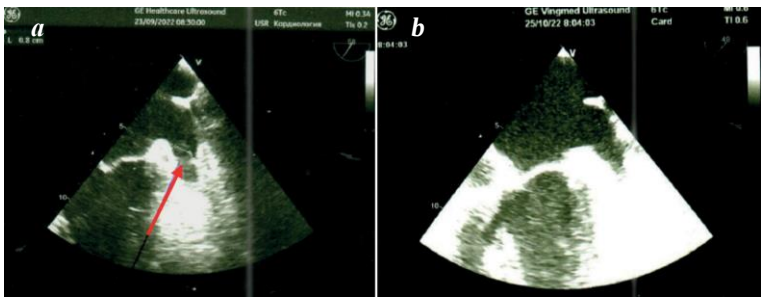

Fig. 3. Transoesophageal echocardiography (TEE) of patient Ts.: a - soft mural thrombus in the LAA (indicated by arrow) during dabigatran therapy; b - no evidence of LAA thrombosis during warfarin therapy.

At repeat hospitalisation in August 2022, the patient was adhering to the prescribed regimen: dabigatran 300 mg/day, losartan 50 mg/day, amlodipine 5 mg/day, and rosuvastatin 20 mg/day. Repeat TEE revealed persistence of moderate SEC in the LAA and LA cavity. The LAA flow velocity had further decreased to 24

cm/sec. A soft, irregularly shaped mural thrombus measuring 8 × 14 mm was visualised on the trabeculae of the LAA (Fig. 3).

The final clinical diagnosis was: Hypertensive heart disease, Stage III. Controlled arterial hypertension. Dyslipidaemia. Cardiovascular risk: very high (score 4). Target BP ≤130/70-79 mmHg. Complications: Atrial fibrillation, persistent form. CHA_2DS_2-VASc: 2, HAS-BLED: 1. Soft mural thrombus in the LAA. CHF IIA, NYHA functional class II.

Standard haemostasis tests revealed significant prolongation of TT to 143 sec, indicating thrombin inhibition by dabigatran. TD testing showed signs of hypercoagulation, specifically an increase in the stationary clot growth velocity to 29.6 sec (Table 2, Fig. 4a). The prolongation of Tlag confirmed inhibition of the clot initiation phase by dabigatran. However, the rate of fibrin clot formation did not decrease and, on the contrary, had increased.

Given the presence of LAA thrombus on TEE and TD indicators of hypercoagulability, the patient was switched to warfarin with close INR monitoring, aiming to maintain values within the therapeutic range of 2.5-3.0. During outpatient follow-up, INR was monitored weekly, and the time in therapeutic range was 70%. TD testing during warfarin therapy revealed hypocoagulation, with reduced initial and stationary clot growth rates and decreased clot density (Table 2, Fig. 4b). Repeat TEE after two months of warfarin therapy (October 2022) showed no evidence of thrombosis or SEC in the LAA (Fig. 3b), which enabled referral of the patient for catheter ablation. This clinical case illustrates a discrepancy between standard coagulation test results (prolonged TT) and thrombodynamics indicators (signs of hypercoagulation) during dabigatran therapy. Warfarin therapy, under tight INR control and guided by TD testing, was associated with hypocoagulation parameters and subsequent thrombus resolution in the LAA as confirmed by TEE.

DISCUSSION

Haemostasis is a complex cascade system comprising the vascular-platelet and coagulation components, as well as the anticoagulant and fibrinolytic systems. Among local haemostasis tests used in clinical practice, the most commonly applied are activated aPTT, PT/INR, TT, which respectively reflect the intrinsic and extrinsic coagulation pathways, and the polymerisation of fibrinogen into fibrin in the presence of fibrinolytic agents and natural anticoagulants.

In recent years, DOACs have increasingly been used in clinical practice for both prevention and treatment of thromboembolic events. Unlike vitamin K antagonists, DOACs have a rapid onset of action, are administered in fixed doses without routine coagulation monitoring, owing to their more predictable pharmacokinetics and pharmacodynamics. Although the absence of regular laboratory monitoring is considered an advantage of DOACs, the assessment of anticoagulant effect or drug concentration can be valuable in certain clinical scenarios, such as thrombosis, bleeding, or surgical interventions [6]. The detection of a thrombus in the LAA during adequate anticoagulant therapy [4] also supports the need for haemostasis monitoring in routine practice.

Standard haemostasis tests, including aPTT, PT/INR, and TT, are readily available and may serve as first-line tools for qualitative evaluation of DOAC effects. TT is particularly used to assess the anticoagulant effect of dabigatran. This test is highly sensitive to dabigatran activity - even low plasma concentrations (≥25 ng/mL) can prolong TT. High-sensitivity tests for dabigatran measurement, such as diluted TT and ecarin clotting time (ECT) using mass spectrometry, exist [6], but they are not accessible in routine clinical settings.

Rivaroxaban prolongs PT in a concentration-dependent manner, but the effect varies significantly depending on the thromboplastin reagent used, due to differing sensitivities to the drug. Rivaroxaban may also increase aPTT, although this test is less sensitive than PT and is not recommended for patients on rivaroxaban [6]. There are even fewer published studies on laboratory monitoring of apixaban compared to rivaroxaban.

In general, standard coagulation tests such as PT and aPTT have limited sensitivity to the effects of apixaban, and thus are not recommended for assessing its anticoagulant activity. Currently, anti-Xa chromogenic assays calibrated specifically for each factor Xa inhibitor are used to quantify their effects. However, the lack of certified calibrators for rivaroxaban and apixaban limits their routine use in clinical settings.

Recent studies have investigated the correlation between DOAC concentrations (apixaban, rivaroxaban) and anti-Xa assay results using low-molecular-weight heparin

Table 2.

Haemostasis Test Parameters in Patient Ts. During Dabigatran and Warfarin Therapy

Parameter	Reference Values	Dabigatran 300 mg/day	Warfarin 6.25 mg/day (2.5 months)
Standard Haemostasis Tests			
aPTT, sec	26-36	32,5	-
PTI, %	80-120	80,1	-
INR	0,95-1,2	1,23	2,3
TT, sec	15-20	143	-
D-dimer, μg/mL	0-0,5	0,3	-
Fibrinogen, g/L	2-4	3,77	-
Antithrombin III, %	75-140	94,6	-
Thrombodynamics Parameters			
Vi, μm/min	38-56	42,7	36,3
Vst, μm/min	20-29	29,6	18,6
Tlag, min	0,6-1,5	2,2	1
CS, μm	800-1200	1041	753
D, a.u.	15000-32000	23855	23412
Tsp, min	none	none	none

(LMWH) calibrators. These studies suggest that anti-Xa assays may detect subtherapeutic DOAC concentrations, but their utility appears restricted to emergency situations, such as bleeding risk assessment before invasive procedures [12, 13].

Our findings demonstrate that TT is a viable test for evaluating dabigatran activity, but in Clinical Case No. 1, local haemostasis tests were not sensitive to apixaban, in line with published literature [6].

Classical local haemostasis tests assess isolated components of the haemostatic system and have limited sensitivity to hypercoagulable states. This highlights the importance of a novel global method for diagnosing plasma coagulation disorders - the TD test - which is designed to identify thrombotic risk in cardiovascular patients and to monitor anticoagulant therapy effectiveness.

The TD test is based on video registration of fibrin clot growth from a simulated damaged vessel wall. Changes in TD parameters correlate closely with the mechanism and concentration of anticoagulants in plasma. Specific diagnostic parameters reflect distinct phases of fibrin clot formation, allowing comprehensive qualitative and quantitative assessment of how different anticoagulants impact the haemostatic system of an individual patient.

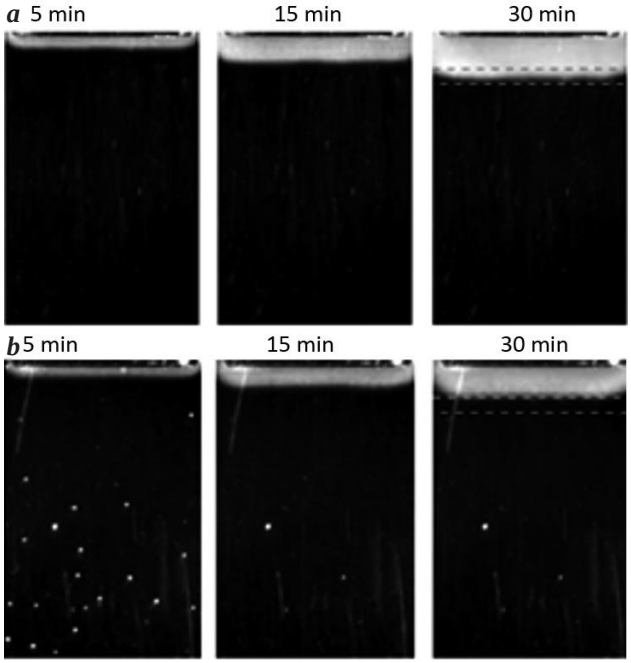

Fig. 4. Fibrin clot images obtained at 5, 15, and 30 minutes of the thrombodynamics (TD) test during dabigatran (a) and warfarin (b) therapy in patient Ts. Dabigatran therapy was associated with hypercoagulation (increased Vst of the fibrin clot), with no spontaneous clotting observed. Warfarin therapy resulted in hypocoagulation, demonstrated by a moderate reduction in the dynamic parameters of clot formation (Vst, Vi, clot size), indicating an adequately selected dose of the anticoagulant.

In limited clinical studies, TD has demonstrated higher sensitivity to anticoagulant therapy (e.g., heparins, warfarin) compared to aPTT and other global coagulation tests such as thrombin generation test and thromboelastography [14, 15]. TD sensitivity was also comparable to that of anti-Xa activity assays [15]. However, similar data for DOACs are not yet available.

Generally, DOACs primarily increase Tlag (indicating inhibition of the clot activation phase) and reduce the clot growth rate V. In 2022, Z.E. Gebekova et al. reported TD parameters in AF patients without prior thrombotic or bleeding events receiving various DOACs [8]. The TD parameters mostly remained within reference ranges, reflecting an optimal anticoagulant effect. These data support the safety and efficacy of DOACs, even with residual drug concentrations.

Our clinical observations showed that in some patients, DOAC use was associated with increased fibrin clot growth rate and density in TD, suggesting a possible reduced sensitivity to certain DOACs. Switching from one DOAC to another (with a different mechanism of action) or from a DOAC to warfarin can markedly alter the coagulation profile - towards either hypercoagulation or hypocoagulation.

Numerous studies have investigated predictors of LAA thrombosis in patients with non-valvular AF [4, 5], but there are still no clear algorithms for anticoagulant management when LAA thrombus is already present. According to national guidelines, a change in anticoagulant is recommended when a thrombus is detected in the LAA prior to cardioversion [2]. However, there remains uncertainty regarding the preferred oral anticoagulant and the optimal timing for follow-up TEE to assess thrombus status.

In this context, the key issue becomes evaluating both the efficacy and safety of the prescribed anticoagulant.

The clinical cases presented suggest that the TD test may be a valuable additional tool for early assessment of the coagulation status and for personalised selection of effective anticoagulant therapy aimed at LAA thrombus resolution - an area warranting further research.

CONCLUSION

The detection of left atrial appendage thrombosis despite adequate anticoagulant therapy highlights the necessity of laboratory monitoring of the coagulation system. The presented clinical cases have demonstrated the advantages of the thrombodynamics test over standard haemostasis assays in assessing the patient's prothrombotic status and in the personalised selection of effective anticoagulant therapy in patients with atrial fibrillation and LAA thrombosis**.**

REFERENCES

1. Hindricks G, Potpara T, Dagres N, et al. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS). *European Heart Journal.* 2021;42(5): 373-498. https://doi.org/10.1093/eurheartj/ehaa612.

2. Arakelyan MG, Bockeria LA, Vasilieva EYu, et al. 2020 Clinical guidelines for Atrial fibrillation and atrial flutter. *Russian Journal of Cardiology.* 2021;26(7): 4594. (In Russ.). https://doi.org/10.15829/1560-4071-2021-4594.

3. Zhan Y, Joza J, Rawahi M, et al. Assessment and management of the Left Atrial Appendage Thrombus in Pa-

tients with Nonvalvular Atrial Fibrillation. *Canadian Journal of Cardiology*. 2018;34(3): 252-261. https://doi.org/10.1016/j.cjca.2017.12.008.
4. Krivosheev YS, Bashta DI, Krasilnikova SY, et al. Left atrial appendage thrombosis in atrial fibrillation - current status of the problem. *Journal of Arrhythmology*. 2019;26(4): 13-20 (In Russ.). https://doi.org/10.35336/VA-2019-4-13-20.
5. Khorkova NYu, Gizatulina TP, Belokurova AV, et al. Additional factors of thrombosis of the left atrial appendage in nonvalvular atrial fibrillation. *Journal of Arrhythmology*. 2020;27(2): 26-32. (In Russ.). https://doi.org/10.35336/VA-2020-2-26-32.
6. Ten Cate H, Henskens YM, Lancé MD. Practical guidance on the use of laboratory testing in the management of bleeding in patients receiving direct oral anticoagulants. *Vasc Health Risk Management*. 2017;13: 457-467. https://doi.org/ 10.2147/VHRM.S126265.
7. Steffel J, Collins R, Matthias Antz M, et al. 2021 European Heart Rhythm Association Practical Guide on the Use of Non-Vitamin K Antagonist Oral Anticoagulants in Patients with Atrial Fibrillation. *Europace*. 2021;23: 1612-1676. https://https://doi.org/10.1093/eurheartj/ehy136.
8. Gebekova ZA, Ivanov II., Asambayeva A, et al. Thrombodynamics Test in Assessing the Risk of Thrombus Formation in Patients with Atrial Fibrillation Taking Direct Oral Anticoagulants. *Rational Pharmacotherapy in Cardiology*. 2022;18(5): 544-552 (In Russ.). https://https://doi.org/10.20996/1819-6446-2022-09-07.
9. Gebekova ZA, Ivanov II, Kudrjavtseva AA, et al. New prospects for assessing the hemostasis system in atrial fibrillation and left atrial appendage thrombosis. *Atherothrombosis*. 2022;12(2): 103- 112. (In Russ.). https://doi.org/10.21518/2307-1109-2022-12-2-103-112.
10. Vuimo T, Belikov E, Litinskaya O, Davtyan K. Efficiency of Thrombodynamics for Analysis of Hemostasis in Case of Transitory Ischemic Attack after Radiofrequency Ablation in a Patient with Paroxysmal Atrial Fibrillation. *Am J Med Case Reports*. 2015;3: 333-337. https://https://doi.org/10.12691/ajmcr-3-10-8.
11. Balandina AN, Koltsova EM, Shibeko AM, et al. Thrombodynamics: a new method to the diagnosis of hemostasis system disorders. *Pediatric hematology/oncology and immunopathology*. 2018;17(4): 114–126 (In Russ.). https:// doi.org/10.24287/1726-1708-2018-17-4-114-126.
12. Titaeva EV, Dobrovolsky AB. Chromogenic anti-Xa test: the ratio between heparin activity units and concentration of apixaban and rivaroxaban. *Aterotromboz = Atherothrombosis*. 2020;(2): 96-104. (In Russ.). https://doi.org/10.21518/2307-1109-2020-2-96-104.
13. Billoir P, Barbay V, Joly LM, et al. Anti-Xa Oral Anticoagulant Plasma Concentration Assay in Real Life: Rivaroxaban and Apixaban Quantification in Emergency with LMWH Calibrator. *Ann Pharmacother*. 2019;53(4): 341-347. https:// doi.org/10.1177/1060028018811657.
14. Gracheva MA, Urnova ES, Sinauridze EI, et al. Thromboelastography, thrombin generation test and thrombodynamics reveal hypercoagulability in patients with multiple myeloma. *Leuk. Lymphoma*. 2015;56(12): 3418-25. https://doi.org/10.3109/10428194.2015.1041385.
15. Balandina AN, Serebriyskiy II, Poletaev AV, et al. Thrombodynamics - a new global hemostasis assay for heparin monitoring in patients under the anticoagulant treatment. *PloS One*. 2018;13(6): e0199900. https://doi.org/10.1371/journal.pone.0199900.