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ПРЕДИКТОРЫ РАСТВОРЕНИЯ ТРОМБОВ В УШКЕ ЛЕВОГО ПРЕДСЕРДИЯ У БОЛЬНЫХ ПЕРСИСТИРУЮЩЕЙ НЕКЛАПАННОЙ ФИБРИЛЛЯЦИЕЙ ПРЕДСЕРДИЙ

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Predictors of Thrombus Dissolution in the Left Atrial Appendage in Patients with Persistent Nonvalvular Atrial Fibrillation

Резюме

Цель работы — выявить факторы, влияющие на вероятность растворения тромба в ушке левого предсердия у больных персистирующей неклапанной фибрилляцией предсердий. **Материал и методы**. Повторное чреспищеводное эхокардиографическое исследование выполнено 88 больным персистирующей неклапанной фибрилляцией предсердий, у которых при первом исследовании был выявлен тромб в ушке левого предсердия. **Результаты**. При повторном исследовании, которое выполнялось в среднем через 30,0 (22,0; 40,0) дня после первого, растворение тромба в ушке левого предсердия было констатировано у 60 (68,2%) из 88 включенных в исследование пациентов. Анализ многофакторной логистической регрессии показал, что шансы растворения выявленного в ушке левого предсердия тромба возрастают в 5,789 (1,907–17,568) раза при размере тромба не более 25 мм, в 5,318 (1,325–21,353) раза при скорости кровотока в ушке левого предсердия не менее 20 см/с и в 3,687 (1,229–11,059) раза в случае использования прямых оральных антикоагулянтов, а не варфарина. При сочетании двух и более из указанных факторов вероятность растворения тромба достигает 89,6%. **Заключение**. Вероятность растворения тромба в ушке левого предсердия у больных персистирующей неклапанной фибрилляцией предсердий возрастает при небольшом размере тромба, высокой скорости изгнания крови из ушка левого предсердия и использовании прямых оральных антикоагулянтов.

Ключевые слова: *персистирующая фибрилляция предсердий, чреспищеводная эхокардиография, тромбоз ушка левого предсердия, пероральные антикоагулянты*

Конфликт интересов

Авторы заявляют, что данная работа, её тема, предмет и содержание не затрагивают конкурирующих интересов

Источники финансирования

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Abstract

The aim of this study is to identify factors influencing the likelihood of the thrombus dissolution in the left atrial appendage in patients with persistent nonvalvular atrial fibrillation. **Material and methods.** A repeated transesophageal echocardiography was performed in 88 patients with persistent nonvalvular atrial fibrillation and with the left atrial appendage thrombus at the first transesophageal echocardiography. **Results.** The second transesophageal echocardiography was performed on average 30.0 (22.0; 40.0) days after the first one, the thrombus dissolution in the left atrial appendage was revealed in 60 (68.2%) patients. The multivariate logistic regression analysis showed that the chances of the thrombus dissolution increased by 5.789 (1.907–17.568) times with the thrombus size not more 25 mm, by 5.318 (1.325–21.353) times with the left atrial appendage emptying flow velocity not less 20 cm/s and 3.687 (1.229–11.059) times when prescribing the direct oral anticoagulants, and not warfarin. Combination of two or more factors give the probability of the thrombus dissolution of more than 89.6%. **Conclusion.** The probability of the thrombus dissolution in left atrial appendage in patients with persistent nonvalvular atrial fibrillation increases with a small thrombus size, a high the left atrial appendage emptying flow velocity, and if direct oral anticoagulants were prescribed.

Key words: *persistent atrial fibrillation, transesophageal echocardiography, left atrial appendage thrombosis, oral anticoagulants*

Conflict of interests

The authors declare no conflict of interests

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AF — atrial fibrillation, ACT — anticoagulant therapy, DOACs — direct oral anticoagulants, LAA — left atrial appendage, TEC — transesophageal echocardiography, TVA — Thrombus-Velocity-Anticoagulant prognostic scale

Introduction

According to current recommendations [1, 2], if transesophageal echocardiography (TEC) reveals a thrombus in the left atrial appendage (LAA) in a patient with persistent atrial fibrillation (AF), the planned cardioversion should be postponed for at least three weeks, during which the patient should receive adequate anticoagulant therapy (ACT, recommendation class I). Before cardioversion, repeated TEC should be considered to confirm thrombus dissolution (recommendation class IIa). This issue can be considered while relying only on the assessment of the probability of thrombus dissolution by the time of cardioversion. A high probability of thrombus dissolution may serve as a basis for cardioversion without repeated TEC, while a low probability indicates the need for such examination.

Information in the literature on the frequency of dissolution of thrombi in LAA by the time of repeated TEC is scarce and fairly contradictory. According to the X-TRA study and the CLOT-AF register [3], after 6–8 weeks of taking rivaroxaban, complete dissolution of thrombus is observed in 41.5% cases, and after 3–12 weeks of treatment with vitamin K antagonists — in 62.5% cases. However, in a study conducted by A. Hussain et al. [4], thrombus dissolution during repeated TEC performed on average 67 days after the first study was reported in 77% of patients treated with direct oral anticoagulants (DOACs) and in 74% of patients treated with warfarin. A study by Saaed M. et al. [5] demonstrated that after four weeks of taking warfarin, dissolution of thrombus in LAA was observed in 90% of cases. Discussing the effectiveness of ACT in patients with AF, the participants of the Delphi Panel Discussion concluded that there is still not enough information to make detailed recommendations for the management of patients with identified atrial thrombosis [6]. Given the above, we considered it appropriate to analyze and present our own data on the frequency of LAA thrombus dissolution by the time of repeated TEC in patients with persistent AF.

Objective of the study was to identify factors that affect the possibility of LAA thrombus dissolution in patients with persistent non-valvular AF.

Material and Methods

The material for a single-center, retrospective cohort study was the register of TECs performed before the planned cardioversion in patients with persistent AF

from 2011 to 2021 by one of the authors of this article. Examinations were performed on Vivid E9 and Vivid S70 (GE, USA) devices with a transesophageal matrix multiplane phased transducer (2D/3D/4D) 6VT-D. The LAA was scanned from the midesophageal access in sections from 0 to 180° with a stepwise interval of 10–30°. Thrombi in the LAA were defined as discrete echopositive masses with a density that differs from the endocardium and pectineal muscles [7]. Information was entered into the register after the operator performed 50 transesophageal examinations with results that could formally be considered unreliable.

At the time of analysis, the registry contained information on 963 patients with persistent AF; in 149 (15.5%), a thrombus in the LAA was detected during the first TEC performed before the planned cardioversion. The study included 88 patients who underwent at least one repeated TEC after thrombus detection.

At the time of thrombus detection, all patients received ACT [1, 2], in accordance with the recommendations for preparing patients with persistent AF for planned cardioversion. However, its duration exceeded three weeks in only 44 (50.0%) of them. After detection of a thrombus in the LAA, 39 (44.3%) patients started or continued taking warfarin at doses that maintain the INR at the level of 2–3 U, 21 patients (23.9%) — rivaroxaban 20 mg once a day, 14 patients (15.9%) — apixaban 5 mg twice a day and 14 patients (15.9%) — dabigatran at a dose of 150 mg twice a day. Repeated TEC was performed on average 30.0 (22.0; 40.0) days after the first examination. It should be noted that in all patients treated with warfarin, INR before both the first and repeated TEC was within the target range. However, the overall duration of maintaining optimal anticoagulation was unknown.

Statistical analysis was carried out using IBM SPSS Statistics 22 software. For intergroup comparisons of means, the Mann-Whitney test was used. Means were presented as a median and an interquartile interval — Me (P_{25}; P_{75}). When comparing sample rates, the χ^2 criterion with Yates correction was used. Multiple logistic regression analysis was used to identify factors influencing thrombus dissolution. To determine the cut-off points and to assess the prognostic value of these factors, ROC analysis was performed. The cut-off point was the value of the maximum sum of test sensitivity and specificity. Results were considered statistically significant if the alpha error probability was less than 5% ($p < 0.05$).

Results

Out of 88 patients with persistent non-valvular AF with a thrombus in the LAA detected during the first transesophageal examination, its dissolution was established during re-examination in 60 (68.2%) patients. The groups of patients who dissolved and did not dissolve thrombus in the LAA were comparable in age, gender, range of comorbidities and clinical assessment of stroke risk. There were no intergroup differences in the average duration of paroxysm, the proportion of individuals with atrial flutter and the time of re-examination (Table 1). However, in patients who dissolved a thrombus, its initial size was, on average, smaller, and blood flow velocity in the LAA was higher than in patients with an undissolved thrombus. Also, the majority of patients who dissolved the thrombus received DOACs, and the majority of patients with an undissolved thrombus received warfarin. Therefore, thrombus size, blood flow velocity, and ACT features can be considered as potential predictors of thrombus dissolution by the time of echocardiographic re-examination.

All three variables were included in the multiple logistic regression analysis, with thrombus length and LAA flow velocity presented both in numerical terms and in binary form. According to ROC analysis, the points of separation of patients with a dissolved and undissolved thrombus are thrombus length of 26 mm and blood flow velocity of 20 cm/s. Data presented in Table 2 indicate that an increase in thrombus size by 1 mm is associated with a decrease in the chances of its dissolution by 1.098 times, and an increase in the velocity of blood ejection from the LAA by 1 cm/s is accompanied by an increase in the chance of thrombus dissolution by 1.084 times. The small size of thrombus (no more than 25 mm) increases the chances of its dissolution by 5.789 times, and the velocity of blood ejection from the LAA over 20 cm/s increases it by 5.318 times. Regardless of these factors, DOACs rather than warfarin increase the chances of thrombus dissolution by 3.687 times.

It should be noted that small thrombus size, high blood flow velocity in the LAA, and the use of DOACs have approximately the same effect on the chances of thrombus dissolution in the LAA, making it possible to assess the presence of any of these factors in a patient with 1 point. In this case, the minimum score that a patient can receive on the TVA scale (Thrombus ≤25 mm, Velocity ≥20 cm/s, Anticoagulant = DOAC) will be 0, and the maximum is 3.

According to the data presented in Figure 1, an increase in the total score on the TVA scale is accompanied by an increase in the number of cases of thrombus dissolution, and with a score of 2 or more, thrombus dissolution is observed in the overwhelming majority of patients. The area under the characteristic curve of the assessment on the TVA scale is greater than the area under the characteristic curves of all predictors included in this scale, although these differences do not reach the level of statistical significance (Fig. 2).

Data presented in Table 3 indicate that 1 point on the TVA scale does not statistically significantly affect the chance of thrombus dissolution compared to a zero

score on this scale. However, at 2 points, the chances of thrombus lysis increase by 18 times, and at 3 points — by 57 times.

Sensitivity of the TVA ≥2 criterion in relation to the dissolution of thrombus in the LAA is 71.7%, specificity is 82.1%, the predictive value of a positive and negative result is 89.6 and 57.5%. Therefore, the probability of thrombus dissolution in the LAA after 4–5 weeks of ACT is close to 90% if at least two of the following three conditions are met: thrombus size is not more than 25 mm, blood flow velocity in the LAA is not lower than 20 cm/s, a patient is taking DOACs.

Table 1. *Characteristics of patients with persistent nonvalvular AF*

Indicator	Total n = 88	LAA thrombus dissolved n = 60	LAA thrombus not dissolved n = 28	p
Age, years	62,5 (56,0; 67,0)	63,0 (56,5; 67,0)	61,0 (54,0; 65,5)	0,284
Men	48 (54,5)	36 (60,0)	12 (42,9)	0,203
Idiopathic AF	15 (17,0)	12 (20,0)	3 (10,7)	0,439
Hypertension	63 (71,6)	41 (68,3)	22 (78,6)	0,461
Coronary heart disease	12 (13,6)	9 (15,0)	3 (10,7)	0,832
Myocardial infarction history	8 (9,1)	5 (8,3)	3 (10,7)	0,972
DCMP	6 (6,8)	3 (5,0)	3 (10,7)	0,592
Heart failure	25 (28,4)	20 (33,3)	5 (17,9)	0,213
Diabetes	20 (22,7)	11 (18,3)	9 (32,1)	0,244
Stroke history	6 (6,8)	5 (8,3)	1 (3,6)	0,711
CHA_2DS_2-VASc, scores	2,00 (1,00; 3,00)	2,00 (1,00; 3,00)	2,00 (2,00; 3,00)	0,619
High stroke risk	53 (60,2)	36 (60,0)	17 (60,7)	0,865
ACT more than three weeks	44 (50,0)	29 (48,3)	15 (53,6)	0,819
Atrial flutter	11 (12,5)	8 (13,3)	3 (10,7)	1,000
Paroxysm, days	53,0 (30,0; 90,0)	49,5 (30,5; 72,5)	53,0 (27,5; 90,5)	0,542
Thrombus length, mm	18,8 (13,0; 27,0)	16,2 (12,0; 22,4)	27,0 (19,4; 29,0)	0,001
LAA emptying flow velocity, cm / s	15,5 (10,0; 20,0)	18,5 (11,0; 22,0)	12,5 (4,00; 18,0)	0,001
LAA area, cm^2	4,75 (4,22; 6,02)	4,70 (4,10; 5,88)	5,21 (4,40; 6,20)	0,233
Warfarin therapy	39 (44,3)	21 (35,0)	18 (64,3)	0,020
Rivaroxaban therapy	21 (23,9)	18 (30,0)	3 (10,7)	0,088
Apixaban therapy	14 (15,9)	10 (16,7)	4 (14,3)	0,978
Dabigatran therapy	14 (15,9)	11 (18,3)	3 (10,7)	0,551
Treatment time, days	30,0 (22,0; 40,0)	30,0 (22,0; 41,0)	31,5 (23,5; 35,5)	0,733

Note: Data are presented as median (25^{th}; 75^{th} percentiles) or as absolute and relative numbers — n (%)
ACT — anticoagulant therapy, DCMP — dilated cardiomyopathy, DOAC — direct oral anticoagulants, LAA — left atrial appendage, AF — atrial fibrillation, CHA_2DS_2-VASc — clinical stroke risk assessment scale

Table 2. *Some factors influence on the chances of a LAA thrombus dissolution*

Factor	OR	95% CI	p
Thrombus, mm	0,911	0,855–0,972	0,005
Flow velocity, cm/s	1,084	1,011–1,162	0,024
Thrombus ≤25 mm	5,789	1,907–17,568	0,002
Flow velocity ≥20 cm/s	5,318	1,325–21,353	0,018
Receiving DOAC	3,687	1,229–11,059	0,020

Note: CI — confidence interval, OR — odds ratio, DOAC — direct oral anticoagulants

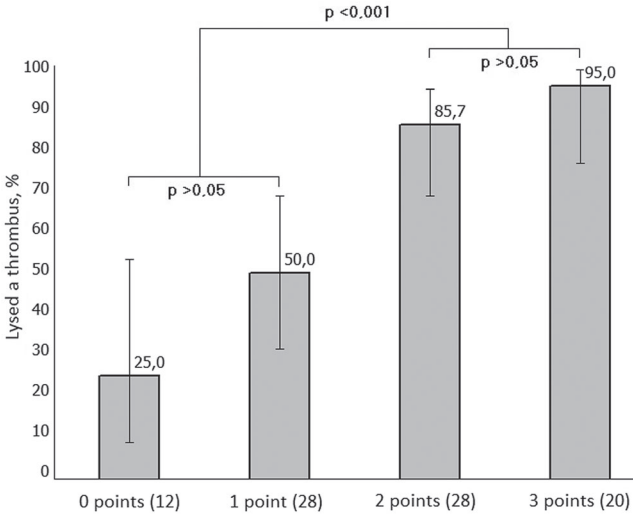

Figure 1. *Frequency of the left atrial appendage thrombus dissolution in patients with different sum of points on the TVA scale (Thrombus, Velocity, Anticoagulant). The number of patients with different sum of points is indicated in parentheses*

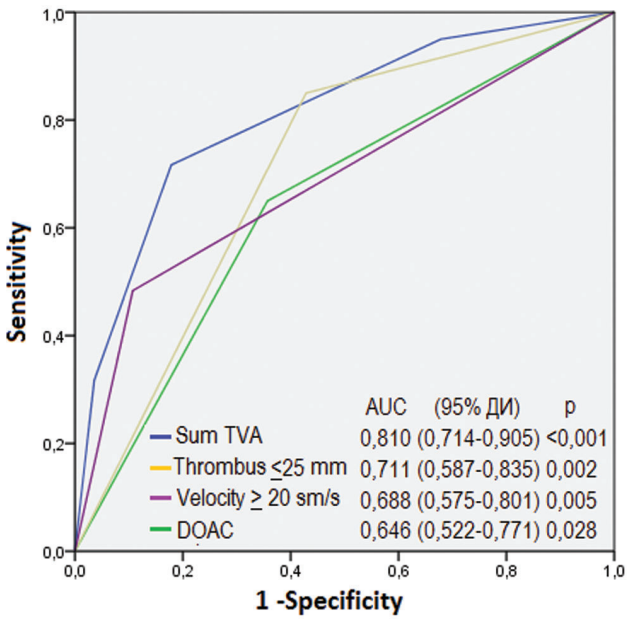

Figure 2. *Characteristic curves of the sum of points on the TVA scale and each predictor. TVA — Thrombus, Velocity, Anticoagulant, DOAC — direct oral anticoagulants, AUC — area under the characteristic curve*

Discussion

In the present study, three factors were identified that have an effect on the possibility of thrombus dissolution in the LAA in patients with persistent AF — thrombus size, blood flow velocity in the LAA, and the nature of anticoagulant therapy (warfarin or DOACs). Of 63 thrombi, the length of which did not exceed 25 mm, 51 (81.0%) had dissolved by the time of repeated TEC, and of the 25 larger thrombi — only 16 (36.0; p < 0.001). Therefore, the small size of the thrombus increases the chances of its dissolution by 5.789 (1.907–17.568) times.

We were unable to find published data on the effect of the size of the atrial thrombus on the probability of its dissolution. However, such data are available for thrombi in LV. A study conducted by B. Lattuca et al. [8] demonstrated that an increase in the area of a left ventricular thrombus reduces the probability of its dissolution (OR 0.66; 95% CI 0.45–0.96; p = 0.031). J.K. Oh et al. [9] reported the dissolution of the left ventricular apical thrombus in 23 (29.9%) of 77 examined patients one month after starting anticoagulant therapy. The initial size of the dissolved thrombi was less than that of the preserved thrombi: 10.7 ± 4.2 vs. 12.1 ± 5.5 mm, p = 0.046. According to the logistic regression analysis, an increase in the size of the apical thrombus by 1 mm reduces the chances of its dissolution by 1.06 (0.99–1.14) times, that is, by 6.2% (p = 0.053). According to the present study, an increase in the size of a thrombus in the LAA by 1 mm reduces the chances of its dissolution by 1.098 (1.029–1.170) times, that is, by 2.9–17.0% (p = 0.005). Therefore, the data obtained in this study on the effect of the LAA thrombus size on its dissolution are fully consistent with the data presented in the literature on the probability of dissolution of the left ventricular thrombi.

The effect of blood flow velocity in the LAA on the possibility of thrombus development and the risk of developing thromboembolic complications was first demonstrated in the SPAF-III study [10] and later confirmed in several other studies [11–14]. A decrease in the blood flow velocity in the LAA to 20 cm/s or less is considered critical for the development of a thrombus [10, 15, 16]. According to our data, at such a velocity of blood ejection from the LAA, the chances of thrombus dissolution decrease by 5.318 (1.325–21.353) times (p = 0.018). Of 32 patients with blood flow velocity in the LAA of at least 20 cm/s, thrombus dissolution was observed in 29 (90.6%) patients, and out of 56 patients with a lower

Table 3. *Changes in the chances of a thrombus dissolution depending on the TCA score*

TCA score	OR	95% CI	p
1 point	3,000	0,668–13,472	0,152
2 points	18,000	3,349–96,734	0,001
3 points	57,000	5,181–627,138	0,001

Note: CI — confidence interval, OR — odds ratio

blood flow velocity in the LAA — in 31 (55.4%, p = 0.002). The coincidence of critical blood flow velocity in the LAA, which predetermines the development and dissolution of a thrombus, is not accidental since these processes occur simultaneously, and the "fate" of a thrombus depends on the predominance of one of them.

Therefore, the relationship between the probability of thrombus dissolution and its size and blood flow velocity in the LAA revealed in this study is confirmed by literature data; the same cannot be said about the third of the identified predictors of successful thrombus dissolution, i.e. the use of DOACs. At present, there is no evidence in the literature of the advantage of DOACs over warfarin in dissolving thrombi in the LAA. The only randomized trial on this issue (X-TRA) demonstrated that rivaroxaban can be used to dissolve atrial thrombi but is not superior to warfarin [3]. Several non-randomized studies found no differences between DOACs and vitamin K antagonists in terms of the effectiveness of LAA thrombus dissolution [4, 5, 17]. In the present study, thrombus dissolution during repeated TEC was found in 21 (53.8%) of 39 patients treated with warfarin and in 39 (79.6%) of 49 patients treated with DOACs (p = 0.020). Given the non-randomized nature of this study, the relatively small number of patients enrolled, and the lack of data on the duration of the target range of INR in warfarin-treated patients, additional evidence is required for the greater effectiveness of DOACs in dissolving thrombi in the LAA.

Any of the predictors identified in this study enables us to predict the probability of thrombus dissolution by the time of repeated TEC. However, the combination of these predictors has the greatest prognostic value. If the patient has at least two of them, the probability of thrombus dissolution reaches 89.6%, which allows following clinical recommendations [1, 2] and avoiding control TEC before cardioversion.

Conclusion

In patients with persistent non-valvular AF, the chances of dissolution of a thrombus detected in the LAA in connection with ACT increase by 5.789 (1.907–17.568) times with a thrombus size of not more than 25 mm, by 5.318 (1.325–21.353) times with blood flow velocity in the LAA of at least 20 cm/s and by 3.687 (1.229–11.059) times with DOACs rather than warfarin. When two or more of these factors are combined, the probability of thrombus dissolution by the time of repeated TEC is 89.6%.

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All the authors contributed significantly to the study and the article, read and approved the final version of the article before publication

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Список литературы / References:

1. Аракелян М.Г., Бокерия Л.А., Васильева Е.Ю., и др. Фибрилляция и трепетание предсердий. Клинические рекомендации 2020. Российский кардиологический журнал. 2021; 26(7): 4594. doi:10.15829/1560-4071-2021-4594.
Arakelyan M.G., Bockeria L.A., Vasilieva E.Yu., et al. 2020 Clinical guidelines for Atrial fibrillation and atrial flutter. Russian Journal of Cardiology. 2021; 26(7): 4594. doi:10.15829/1560-4071-2021-4594 [In Russian].
2. Hindricks G., Potpara T., Dagres N., et al. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with EACTS. Eur Heart J 2020; 00: 1–125. doi: 10.1093/eurheartj/ehaa612.
3. Lip G.Y.H., Hammerstingl C, Marin F. et al. Left atrial thrombus resolution in atrial fibrillation or flutter: Results of a prospective study with rivaroxaban (X-TRA) and a retrospective observational registry providing baseline data (CLOT-AF). American Heart Journal. 2016; 178: 126-34. doi:10.1016/j.ahj.2016.05.007.
4. Hussain A., Katz W.E., Genuardi M.V., et al. Non-vitamin K oral anticoagulants versus warfarin for left atrial appendage thrombus resolution in nonvalvular atrial fibrillation or flutter. Pacing Clin Electrophysiol. 2019; 42(9): 1183–1190. doi: 10.1111/pace.13765.
5. Saeed M., Rahman A., Afzal A., et al. Role of transesophageal echocardiography guided cardioversion in patients with atrial fibrillatio, previous left atrial thrombus and effective anticoagulation. Int J Cardiol. 2006; 113(3): 401–405. doi: 10.1016/j.ijcard.2006.03.036.
6. Mumoli N., Amellone C., Antonelli G., et al. Clinical discussions in antithrombotic therapy management in patients with atrial fibrillation: a delphi consensus panel. CJC Open. 2020; 2: 641–651. doi:10.1016/j.cjco.2020.07.016.
7. Hahn R.T., Abraham T., Adams M.S., et al. Guidelines for Performing a Comprehensive Transesophageal Echocardiographic Examination:

Recommendations from the American Society of Echocardiography and the Society of Cardiovascular Anesthesiologists. J Am Soc Echocardiogr. 2013; 26: 921-64. doi: 10.1016/j.echo.2013.07.009
8. Lattuca B., Bouziri N., Kerneis M. et al. Antithrombotic Therapy for Patients With Left Ventricular Mural Thrombus. J Am Coll Cardiol 2020; 75: 1676–85. doi: 10.1016/j.jacc.2020.01.057
9. Oh J.K., Park J-H., Lee J-H., et al. Shape and Mobility of a Left Ventricular Thrombus Are Predictors of Thrombus Resolution. Korean Circ J. 2019; 49(9): 829-837. doi: 10.4070/kcj.2018.0346.
10. Goldman M.E., Pearce L.A., Hart R.G., et al. Pathophysiologic Correlates of Thromboembolism in Nonvalvular Atrial Fibrillation: I. Reduced Flow Velocity in the Left Atrial Appendage (The Stroke Prevention in Atrial Fibrillation [SPAF-III] Study). Journal of American Society of Echocardiography. 1999; 12: 1080–1087. doi:10.1016/s0894-7317(99)70105-7.
11. Lee J.M., Shim J., Uhm J.S., et al. Impact of Increased Orifice Size and Decreased Flow Velocity of Left Atrial Appendage on Stroke in Nonvalvular Atrial Fibrillation. American Journal of Cardiology. 2014; 113: 963-969. doi: 10.1016/j.amjcard.2013.11.058.
12. Cresti A., Garcia-Fernandez M.A., De Sensi F., et al. Prevalence of auricular thrombosis before atrial flutter cardioversion: a 17-year transoesophageal echocardiographic study. Europace 2016; 18: 450–456. doi:10.1093/europace/euv128
13. Lee J.M., Kim J-B., Uhm J-S. et al. Additional value of left atrial appendage geometry and hemodynamics when considering anticoagulation strategy in patients with atrial fibrillation with low CHA2DS2-VASc scores. Heart Rhythm 2017; 14(1): 297–1301. doi: 10.1016/j.hrthm.2017.05.034
14. Голухова Е.З., Громова О.И., Аракелян М.Г. и др. Предикторы тромбоза ушка левого предсердия и тромбоэмболических осложнений у больных с фибрилляцией предсердий без сопутствующей клапанной патологии и ишемической болезни сердца. Креативная кардиология. 2017; 11(3): 262-72. doi: 10.24022/1997-3187-2017-11-3-262-272.
Golukhova E.Z., Gromova O.I., Arakelyan M.G. et al. Risk factors of left atrial thrombus and/or thromboembolism in patients with nonvalvular, nonishemic atrial fibrillation. Kreativnaya Kardiologiya (Creative Cardiology). 2017; 11(3): 262-72. doi: 10.24022/1997-3187-2017-11-3-262-272 [in Russian].
15. Beigel R., Wunderlich N.C., Ho S.Y. et al. The Left Atrial Appendage: Anatomy, Function, and Noninvasive Evaluation. Journal of American College of Cardiology: Cardiovascular Imaging. 2014; 7(12): 1251-65. doi:10.1016/j.jcmg.2014.08.009.
16. Zateyshchikov D.A., Brovkin A.N., Chistiakov D.A., et al. Advanced age, low left atrial appendage velocity, and Factor V promoter sequence variation as predictors of left atrial thrombosis in patients with nonvalvular atrial fibrillation. Journal of Thrombosis and Thrombolysis. 2010; 30: 192-199. doi: 10.1007/s11239-010-0440-1.
17. Niku A.D., Shiota T., Siegel R.J., et al. Prevalence and Resolution of Left Atrial Thrombus in Patients with Nonvalvular Atrial Fibrillationand Flutter with Oral Anticoagulation. Am. J. Cardiol. 2019; 123: 63–68. doi: 10.1016/j.amjcard.2018.09.027