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How to improve long-term results of patients with atrial fibrillation of non-valvular ethiology after embolism to main arteries of the limbs

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ABSTRACT

BACKGROUND: In patients with atrial fibrillation, systemic thromboembolic complications dramatically worsen the long-term prognosis. There is currently no generally accepted treatment tactics for patients with atrial fibrillation of non-valvular ethiology after embolism to main arteries of the limbs. Objective: evaluate the efficacy of our approach for patients with atrial fibrillationof non-valvular ethiology who survived an embolism to main arteries of the limbs and acute limb ischemia.

MATERIALS AND METHODS: For the period from 1991 to 2022, in the Department of Vascular Surgery of our institution, emergency care due to embolism and acute limb ischemia was provided to 1816 patients. In 1425 (78.5%) patients, the main disease that led to arterial embolism was non-valvular atrial fibrillation. In the long-term period after discharge from our clinic, it was possible to trace the fate of 216 patients and determine the cause of death for 106 patients. The main causes of death in the long-term period were the decompensation of chronic diseases of the cardiovascular system in 73,6% of patients and the recurrence of systemic thromboembolic complications in 21.7%. Since 2012, at our department an integrated approach has been developed and implemented. It included a set of measures aimed at compensating for chronic cardiovascular pathology and preventing the recurrence of systemic thromboembolic complications. The whole set of measures all patients underwent during their current hospitalization after the elimination of life-threatening complications associated with acute limb ischemia and the stabilization of their general condition. They formed the main group (n = 50). The control group (n = 166) consisted of patients after embolism and acute limb ischemia discharged before 2012. Their cardiac pathology was treated after discharge from our department on an outpatient basis in a polyclinic at their place of residence. The overall comparative survival rate was analyzed. The survival function was evaluated using the Kaplan – Meyer method.

RESULTS: In the control group, long-term survival was low, and the median life expectancy was 24 months after discharge. In the main group, long-term survival improved significantly, and the median survival period was not reached during the observation time set. The differences in overall survival estimated using the likelihood ratio test were statistically significant (p = 0.001). When evaluating the groups, the risk of death in the main group was 2.2 times lower than in the control group for each month of follow-up (p = 0.003).

CONCLUSION: the set of measures implemented in our clinic over the last decade for patients with atrial fibrillation of non-valvular ethiology hospitalized with arterial embolism and acute limb ischemia has proved its efficacy and significantly (p = 0.003) improved the survival rate of patients with long-term follow-up after discharge from our department.

Keywords: atrial fibrillation; embolism of the main arteries of the limbs; long-term survival rate.

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Пути улучшения отдаленных результатов лечения больных с фибрилляцией предсердий неклапанной этиологии, перенесших эмболию магистральных артерий конечностей

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АННОТАЦИЯ

Актуальность. У больных с фибрилляцией предсердий системные тромбоэмболические осложнения существенно ухудшают отдаленный прогноз. Общепринятой системы, определяющей дальнейшую тактику лечения больных с фибрилляцией предсердий неклапанной этиологии, перенесших эмбологенную артериальную непроходимость, в настоящее время нет.

Цель — оценить эффективность проводимого лечения пациентов с фибрилляцией предсердий неклапанной этиологии, перенесших эмболию магистральных артерий конечностей.

Материалы и методы. За период с 1991 по 2022 год в отделении сердечно-сосудистой хирургии № 1 (ангиохирургия) СЗГМУ им. И.И. Мечникова оказана экстренная помощь 1816 больным с эмболиями магистральных артерий конечностей. У 1425 больных (78,5 %) основным эмбологенным заболеванием была фибрилляция предсердий неклапанной этиологии. В отдаленном периоде после выписки из отделения удалось проследить судьбу 216 пациентов и установить причину смерти у 106 пациентов. Основными причинами смерти в отдаленные сроки стали декомпенсация хронических заболеваний сердечно-сосудистой системы у 73,6 % больных и рецидивы системных тромбоэмболических осложнений у 21,7%. С 2012 года в клинике внедрен комплекс мер, направленных на компенсацию хронической сердечно-сосудистой патологии и предупреждение рецидивов системных тромбоэмболических осложнений. Весь комплекс мер проводился в текущую госпитализацию после устранения угрожающих жизни осложнений, связанных с острой ишемией конечности, и стабилизации общего состояния пациентов. Они составили основную группу (n = 50). Контрольную группу (n = 166) составили пациенты с эмбологенной артериальной непроходимостью, выписанные до 2012 г. Лечение кардиальной патологии после перенесенной эмбологенной артериальной непроходимости они получали амбулаторно в поликлинике по месту жительства. Проведен сравнительный анализ показателей общей выживаемости. Оценка функции выживаемости проводилась по методу Каплана – Мейера.

Результаты. В контрольной группе отдаленная выживаемость была низкой, медиана средней продолжительности жизни составила 24 мес после выписки. В основной группе отдаленная выживаемость значительно улучшилась, медиана средней продолжительности жизни увеличилась и за период наблюдения достигнута не была. Различия общей выживаемости, оцененные с помощью теста отношения правдоподобия, были статистически значимы (p = 0,001). При оценке групп сравнения риск наступления летального исхода в основной группе был ниже в 2,2 раза по сравнению с контрольной группой на каждый месяц наблюдения (p = 0,003).

Заключение. Внедренный в отделении сердечно-сосудистой хирургии № 1 (ангиохирургии) СЗГМУ им. И.И. Мечникова за последнее десятилетие комплекс мер по лечению пациентов с фибрилляцией предсердий неклапанной этиологии, госпитализированных с эмбологенной артериальной непроходимостью, показал свою эффективность и достоверно (p = 0,003) улучшил выживаемость пациентов с отдаленные сроки после выписки из нашего стационара.

Ключевые слова: фибрилляция предсердий; эмболия магистральных артерий конечностей; отдаленная выживаемость.

Как цитировать

Сотников А.В., Мельников М.В., Пышный М.В., Семенюта В.В. Пути улучшения отдаленных результатов лечения больных с фибрилляцией предсердий неклапанной этиологии, перенесших эмболию магистральных артерий конечностей // Cardiac Arrhythmias. 2023. Т. 3, № 4. С. 21–31. DOI: https://doi.org/10.17816/cardar625527

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ЭКО•ВЕКТОР

Nonvalvular atrial fibrillation (AF) is common among elderly and senile people in Russia [1]. Moreover, systemic thromboembolic complications (STEC) significantly worsen the immediate and long-term prognoses of patients with AF. Embolism of the main arteries of the extremities ranks second in incidence following cardioembolic strokes among STEC [2]. The survival rate of patients with embologenic arterial obstruction (EAO) is extremely low [3]. The main causes of high mortality in the long term have not been sufficiently studied. Currently, there is no generally accepted system that determines further treatment approach for patients with nonvalvular AF with a history of EAO.

This study aimed to evaluate the efficiency of a set of treatment measures for patients with nonvalvular AF with a history of EAO.

MATERIALS AND METHODS

Overall, 1816 patients with EAO received treatment in the Department of Cardiovascular Surgery No. 1 of Peter the Great Clinic of Mechnikov North Western State Medical University between 1991 and 2022; in 1425 (78.5%) of the patients, acute limb ischemia (ALI) developed in presence of nonvalvular AF. The collection, accumulation, and computer processing of clinical material was performed using the original program "Doctor's Scientific Archive — DSM", which was developed at Mechnikov North Western State Medical University and registered in the "Register of Computer Programs" of the Federal Service for Intellectual Property, Patents, and Trademarks (certificate of official registration of the computer program no. 2004611296; May 26, 2004).

Table 1 presents the clinical characteristics of the patients.

Among patients hospitalized with EAO due to AF, women predominated (67.9%), and 88.3% of patients were elderly and senile. All patients were urgently admitted with a clinical presentation of ALI. The degree of ischemia was assessed according to the classification by Zatevakhin et al. The severity of ALI manifestations upon admission to the clinic varied. Moreover, 470 (33.0%) patients were hospitalized with nonthreatening limb ischemia (degree I). The clinical manifestations of ALI were pain and paresthesia

Table 1. Clinical characteristics of patients with AF of non-valvular etiology hospitalized at our clinic with acute limb ischemia due to embolism
Таблица 1. Клиническая характеристика больных с фибрилляцией предсердий неклапанной этиологии, госпитализированных в отделении сердечно-сосудистой хирургии №1 (ангиохирургии) СЗГМУ им. И. И. Мечникова с эмбологенной артериальной непроходимостью

Indicators	Categories	Number of cases (*n* = 1425)	Proportion, %	95% Confidence interval
Sex	Women	968	67.9	65.4–70.3
	Men	457	32.1	29.7–34.6
Age, years	30–39	3	0.2	0.0–0.6
	40–49 years old	36	2.5	1.8–3.5
	50–59 years old	128	9.0	7.5–10.6
	60–69 years old	314	22.0	19.9–24.3
	70–79 years old	518	36.4	33.8–38.9
	Over 80 years old	426	29.9	27.5–32.3
Degree of acute limb ischemia (according to Zatevakhin [4])	I	470	33.0	30.5–35.5
	IIa	480	33.7	31.2–36.2
	IIb	277	19.4	17.4–21.6
	IIc	99	6.9	5.7–8.4
	IIIa	9	0.6	0.3–1.2
	IIIb	90	6.3	5.1–7.7
Duration of limb ischemia before hospitalization	Up to 6 hours	447	31.4	29.0–33.8
	6–12 hours	563	39.5	37.0–42.1
	12–24 hours	150	10.5	9.0–12.2
	24–48 hours	73	5.1	4.0–6.4
	Over 48 hours	192	13.5	11.7–15.4
Atrial fibrillation	Paroxysmal or persistent form	470	33.0	30.5–35.5
	Permanent form	939	65.9	63.4–68.4
	Permanent form, PPM	16	1.1	0.6–1.6

End of the table 1

Indicators	Categories	Number of cases (*n* = 1425)	Proportion, %	95% Confidence interval
Ischemic heart disease	Chronic IHD without a history of myocardial infarction	669	46.9	44.8–49.1
	Postinfarction cardiosclerosis	205	14.4	12.6–16.3
	Acute period of myocardial infarction	43	3.0	2.2–4.0
Arterial hypertension	Degree I	77	5.4	4.3–6.7
	Degree II	1223	85.8	83.9–87.6
	Degree III	125	8.8	7.4–10.4
Chronic heart failure	Not expressed	59	4.1	3.2–5.3
	Stage 2	1291	90.6	89.0–92.1
	Stage 3	75	5.3	4.2–6.6
Concomitant disease	Atherosclerosis of peripheral arteries	256	18.0	16.0–20.1
	Diabetes mellitus	283	19.9	17.8–22.0
	Chronic nonspecific lung diseases	229	16.1	14.2–18.1
	Chronic kidney and/or liver diseases	63	4.4	3.4–5.6
	Others	23	1.6	1.0–2.4
History of acute disturbances in arterial blood supply	Acute cerebrovascular accident	179	12.6	10.9–14.4
	Embologenic arterial obstruction	126	8.8	7.5–10.4

Note: IHD — ischemic heart disease; PPM — permanent pacemaker; AF — atrial fibrillation.

Примечание: ИБС — ишемическая болезнь сердца; ПЭКС — постоянный электрокардиостимулятор; ФП — фибрилляция предсердий.

in the ischemic limb. Majority of the patients (856 cases; 60.1%) were hospitalized with manifestations of threatening ALI (degrees IIA–IIB). In addition to pain, the main clinical presentation was sensory and motor disorders in the ischemic limb, namely, paresis and paralysis. The most severe condition was noted in 99 (6.9%) patients hospitalized with irreversible acute ischemia (IIIa and IIIb), that is, distal or total contracture of the limb. Moreover, 588 (41.3%) patients had acute ischemia of the upper limb and 803 (56.3%) had the lower limbs affected, including 27 (1.9%) patients with acute ischemia of both lower limbs caused by embolism associated with aortic bifurcation. Multiple embolisms with simultaneous damage to two or three arterial territories of the extremities was diagnosed in 34 (2.4%) patients.

In all patients included in this study, AF was the major cause of EAO. Paroxysmal or persistent AF was detected in 470 (33.0%) patients, whereas the permanent form of AF was observed in 939 (65.9%) patients, and a permanent pacemaker had been previously implanted in 16 of these patients.

In most patients, AF-associated background cardiac pathology manifested as hypertension, ischemic heart disease (IHD), and atherosclerotic cardiosclerosis. Degree I arterial hypertension was detected in 77 (5.4%) patients, and degree II was found in 1223 (85.8%) patients. Arterial hypertension severity was correlated with chronic heart failure (CHF) severity. In most of the patients (1291 cases; 90.6%), clinical manifestations corresponded to stage IIa–b CHF. Other predisposing factors of AF included IHD such as stable effort angina without a history of acute myocardial infarction (AMI) in 669 (46.9%) patients, postinfarction cardiosclerosis in 205 (14.4%) patients, and an acute period of myocardial infarction in 43 (3.0%) patients. Concomitant noncardiac pathology was significant in the development of AF in several patients: diabetes mellitus in 283 (19.9%) patients and chronic nonspecific lung diseases in 229 (16.1%) hospitalized patients. In 256 (18.0%) patients, ALI coexisted with stage 2 chronic arterial insufficiency caused by peripheral atherosclerosis.

A crucial characteristic of the studied group of patients was their CHA2DS2-Vasc scale score [5]. More than 97% of the patients had a high or extremely high risk of STEC (Table 2).

The adherence to prescribed oral anticoagulant therapy during the prehospital stage of patients hospitalized in the past 10 years in the Department of Cardiovascular Surgery No. 1 (Angiosurgery) of Mechnikov North Western State Medical University was approximately 12%. In earlier cases, systemic antithrombotic therapy in patients admitted with EAO was limited to acetylsalicylic acid.

In most cases, medical approach in relation to ALI in the Department of Cardiovascular Surgery No. 1 (Angiosurgery) of Mechnikov North Western State Medical University included open surgical treatment aimed at restoring arterial blood supply to the limb. Moreover,

Table 2. Values of CHA2DS2-Vasc scores in patients hospitalized at our clinic with acute limb ischemia due to embolism
Таблица 2. Значения баллов по шкале CHA2DS2-Vasc у госпитализированных в отделение сердечно-сосудистой хирургии № 1 (ангиохирургии) СЗГМУ им. И.И. Мечникова пациентов с эмбологенной артериальной непроходимостью

Value on the CHA2DS2-Vasc scale	Number of cases (n = 1425)	Proportion, %	95% Confidence interval
2 points	5	0.4	0.1–0.8
3 points	31	2.2	1.5–3.1
4 points	151	10.6	9.0–12.3
5 points	290	20.4	18.3–22.5
6 points	385	27.0	24.7–29.4
7 points	380	26.7	24.4–29.0
8 points	158	11.1	9.5–12.8
9 points	25	1.8	1.1–2.6

Note: CHA2DS2-Vasc is a scale for assessing the risk of systemic thromboembolic complications in patients with atrial fibrillation [5].
Примечание: CHA2DS2-Vasc — шкала оценки риска системных тромбоэмболических осложнений у больных с фибрилляцией предсердий [5].

1241 (87.1%) patients underwent emergency surgery, and another 74 (5.2%) patients received surgical treatment within 24 h of admission. Operational activity was 92.3%. In 1239 (86.9%) patients, limb revascularization was performed using direct or indirect embolectomy with a balloon catheter. In 76 (5.8%) patients, because of irreversible ischemia, primary amputation of the limb was conducted within well-vascularized tissues.

Revascularization resulted in restoration of the main arterial blood supply in 892 (65.5%) patients, with complete ALI regression and peripheral pulse restoration. In 333 (25.3%) patients, the arterial blood supply to the limb was reestablished following surgery without restoring the pulsation of the distal limb arteries. The required limb perfusion was not achieved in 14 (1.0%) patients after the intervention. In 73 (5.1%) patients with nonthreatening ALI (grade I), arterial blood supply was restored through conservative treatment. Hospital mortality was 12.2%; 174 patients died. The main causes of in-hospital lethal outcomes were the initial terminal condition in 37 (2.6%) patients and postoperative complications, including ischemic intoxication, decompensation of the initial cardiac and other concomitant pathologies, and STEC relapses in 137 (9.6%) patients. Additionally, 1183 (83%) patients were discharged with a salvaged limb.

Furthermore, 216 patients were available for analysis of long-term treatment results. The follow-up period ranged from 1 to 12 years. The causes of lethal outcomes in long-term follow-up were established in 106 patients, that is, decompensation of CHF in 52 (49.1%) patients, AMI in 26 (24.5%), recurrent STEC in 23 (21.7%), and other causes in 5 (4.7%) (Fig. 1). Summarizing the causes of the high long-term mortality of patients discharged from the Department of Cardiovascular Surgery No. 1 (Angiosurgery) of Mechnikov North Western State Medical University, after treatment for EAO, the most significant links in thanatogenesis in the long term were decompensation of chronic cardiovascular disease in 73.6% of the patients and relapse of systemic thromboembolic events in 21.7%.

Statistical analysis was performed using StatTech v. 4.0.4 (Stattech, Russia).

Until 2012, in the Department of Cardiovascular Surgery No. 1 (Angiosurgery) of Mechnikov North Western State Medical University, after eliminating life-threatening complications associated with ALI and stabilizing the general condition, majority of the patients were discharged on days 5–7 for outpatient treatment under the supervision of a therapist at the primary healthcare facility. Patients available for contact in the long term after discharge (n = 166) formed the control group (CG) of follow-up.

The involvement of a cardiologist among the staff of our department in 2012 enabled the implementation of the main (cardiological) part of the rehabilitation. Since then, the cardiologist of the Department of Cardiovascular

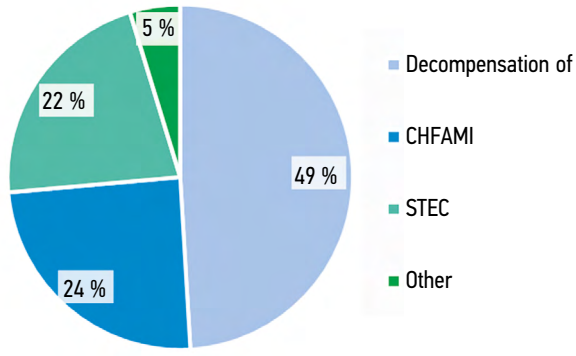


Fig. 1. The main causes of death of patients with AF in the long term follow-up discharged from our clinic after treatment for acute limb ischemia due to embolism. AMI — acute myocardial infarction; STEC — systemic thromboembolic events; AF — atrial fibrillation; CHF — chronic heart failure
Рис. 1. Основные причины смерти пациентов с ФП в отдаленные сроки, выписанных из отделения сердечно-сосудистой хирургии № 1 (ангиохирургии) СЗГМУ им. И. И. Мечникова после лечения по поводу эмбологенной артериальной непроходимости. ОИМ — острый инфаркт миокарда; СТЭО — системные тромбоэмболические осложнения; ФП — фибрилляция предсердий; ХСН — хроническая сердечная недостаточность

Surgery No. 1 (Angiosurgery) select directly and prescribe anticoagulants, antihypertensives, and cardiotropic therapy for patients of the main group (MG) according to current clinical recommendations, coordinate the treatment of concomitant noncardiac pathology, resolve the issue of further treatment strategies for AF ("rhythm control" or "rate control"), determine indications for consultation with an arrhythmologist, verify myocardial ischemia, identify indications for coronary angiography and the need and timing of myocardial revascularization, establish the significance of structural heart pathology and indications for consultation with a cardiac surgeon, and determine indications for alternative methods of preventing STEC such as implantation of an occluder of the left atrial appendage. Patients discharged after 2012 and who were available for contact in the long term after discharge were included in the MG (n = 50).

A cross-sectional and observational study was conducted in MG, whereas a retrospective analysis was performed in CG.

RESULTS

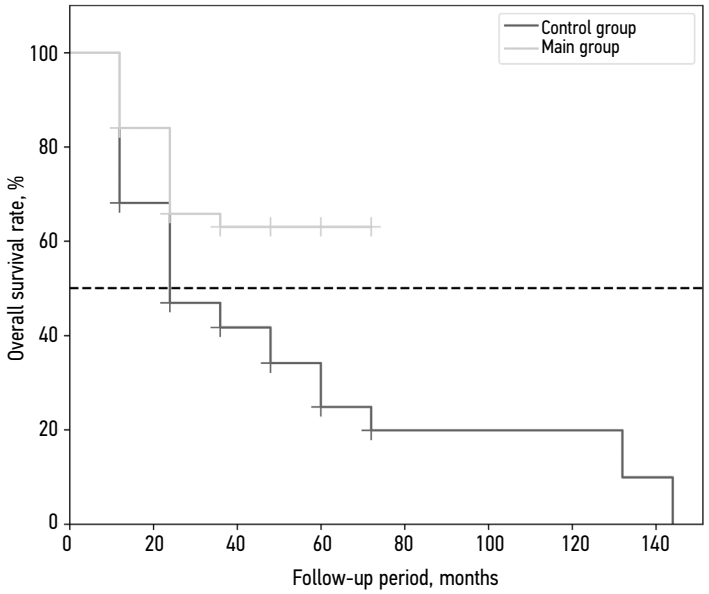
Analysis of the overall survival in the study participants was performed depending on the comparison groups. The survival function of patients was assessed using the Kaplan – Meier method (Fig. 2).

The analysis showed that the 75th percentile of life expectancy in CG was 12 (12–12) months from the start of monitoring, the median was 24 (24–48) months, and the 25th percentile was 60 (48–144) months. In the study group, the 75th percentile of life expectancy was 24 (12 – ∞) months, and the median and 25th percentiles for the entire follow-up period were not reached (Fig. 2). Differences in overall survival, which was assessed using the likelihood ratio test, were statistically significant (p = 0.001).

To determine the key factors that influenced the risk of lethal outcome, a multivariate Cox proportional hazards regression analysis was performed. Following multifactorial stepwise selection, only the factor of attitude toward the group was statistically significantly associated with the event occurrence. The final proportional hazards model was as follows:

$$h_i(t) = h_o(t) \times \exp(-0{,}801 \times X_{\text{Comparison groups : MG}})$$

where $h_i(t)$ is the predicted risk of the deceased for the i-th follow-up element (%), $h_o(t)$ is the basic risk of the deceased for a certain time period t (%), and $X_{\text{Comparison groups : MG}}$ — $X_{\text{Comparison groups : Main group}}$ (Table 3, Fig. 3).



Control group								
Cases	166	87	22	5	2	2	2	1
Censored	0	26	59	69	71	71	71	71
Events	0	53	85	92	93	93	93	94
Main group								
Cases	50	37	17	2	0	0	0	0
Censored	0	5	16	31	33	33	33	33
Events	0	8	17	17	17	17	17	17

Fig. 2. The overall survival curve depending on the comparison groups
Рис. 2. Кривая общей выживаемости в зависимости от групп сравнения

Table 3. Values of the basic risk of death for different periods for the general sample of the patients
Таблица 3. Значения базового риска смерти для разных временных периодов для общей выборки пациентов

Time periods, months	Base risk values $h_o(t)$, %
12	32.37
24	66.15
36	76.907
48	90.406
60	110.965
72	127.921
132	177.921
144	277.921

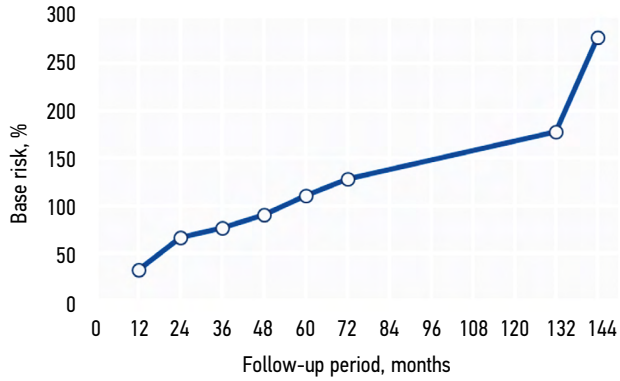


Fig. 3. The curve of the basic risk for the entire follow-up period for the general sample of the patients
Рис. 3. Кривая базового риска смерти на весь период наблюдения для общей выборки пациентов

The relative risk of MG was 0.449 (0.267–0.755; $p = 0.003$). Accordingly, the risk of lethal outcome in MG was 2.227 times lower than that in CG for each month of follow-up. This is equivalent to a 26.7-fold reduction in the risk of death for each year since the start of treatment.

DISCUSSION

The study results showed the advantages of developing a scheme for further conservative treatment of AF patients with a history of EAO during the current hospitalization compared with rehabilitation conducted at the outpatient stage.

The study was cross-sectional and observational in nature; therefore, full coverage of discharged patients was not expected. The study patients were mostly elderly and of low social status; thus, even at the end of year 1, contact with most of them was complicated. Data from the most compliant patients are presented, and the results showed a significantly increased survival rate of patients in long-term follow-up. The immediate causes of lethal outcomes of patients in the long-term period were mostly established according to information provided by relatives, since most of the patients died at home or in different hospitals in the city. More than two-thirds of the deaths were due to the decompensation of chronic cardiovascular diseases, and in a quarter of patients, sudden severe neurological symptoms indicated a relapse of STEC (Fig. 1).

Experience in the Department of Cardiovascular Surgery No. 1 (Angiosurgery) of Mechnikov North Western State Medical University provided evidence on the extremely low adherence of hospitalized EAO patients to lifelong oral anticoagulant therapy, which should have been performed on an outpatient basis. Among EAO patients admitted to our hospital, the overall adherence to this type of treatment was approximately 12%. Moreover, this trend has not improved over the past decade. The lack of anticoagulant therapy was often associated with insufficient patient awareness of the risks associated with AF, or the arrhythmia was first identified during hospitalization. The lack of continuous anticoagulation therapy could be one of the main factors in the development of EAO. Low adherence to oral anticoagulant treatment among AF patients hospitalized for STEC has been noted among those admitted with embolism of the main arteries [6] and acute cerebrovascular accident (ACVA). Thus, 6.9%–17.5% of AF patients hospitalized for ACVA in 2014–2015 took anticoagulants regularly and in an adequate dose [7].

This type of treatment is critical for the study patients, considering their CHA2DS2-Vasc score (Table 2).

The selection and prescription of an oral anticoagulant for lifelong use should be performed during the current hospitalization, immediately after limb revascularization, and stabilization of the condition during inpatient treatment. Currently, the main oral medications for patients with AF are indirect anticoagulants (warfarin) and new oral anticoagulants (NOACs). According to current clinical guidelines, NOACs are the drugs of choice in patients with nonvalvular AF for the prevention of STEC; however, warfarin may also be considered [8]. In 2011–2016, the Department of Cardiovascular Surgery No. 1 (Angiosurgery) of Mechnikov North Western State Medical University prescribed NOACs to MG patients in every third case; in the remaining cases, the warfarin dose was selected according to the international normalized ratio (INR). In recent years, NOACs have been prescribed to most patients, and the prescription of indirect anticoagulants has become an exception.

In this study, patient adherence to anticoagulant therapy in the long term after EAO and discharge from the Department of Cardiovascular Surgery No. 1 (Angiosurgery) of Mechnikov North Western State Medical University was significantly higher than that before hospitalization, which was facilitated by regular follow-up of patients by an angiosurgeon and cardiologist. During the follow-up period, the average adherence of MG to this type of treatment prescribed upon discharge among patients available for contact was 52.0% (26 patients). The main drugs taken were NOACs. No relapses of hospitalizations were observed in MG patients with EAO in the Department of Cardiovascular Surgery No. 1 University over the past decade. Among newly admitted patients, a decrease in the frequency of EAO relapses during hospitalization was not noted (26 patients in MG (8.8%) versus 100 patients in CG (8.8%)).

Despite the convenience of using NOACs, warfarin may have advantages for treating some patients after EAO. First is the low cost (orders of magnitude less than NOAC drugs), which enables elderly patients, even those with low income, to provide themselves with this drug in case of difficulties with free provision of NOACs. Second is the constant availability of warfarin in pharmacies in various regions of Russia since it is produced in Russia. Finally, despite the safety of using NOACs, we believe that a drawback is the lack of an accessible method for monitoring the regularity of their intake. Upon detailed questioning of patients taking NOACs, evidence of errors in the regularity of administration was repeatedly revealed, which could affect the final efficiency. Over the years of monitoring, we identified only one patient in whom EAO occurred while taking warfarin in presence of target INR values. Thus, the choice of an anticoagulant drug for lifelong use in patients with AF who have undergone EAO requires a differentiated approach.

The next mandatory step for treating patients with AF who have undergone EAO is normalization of blood pressure. This component of therapy should be identified and implemented in the current hospitalization as soon as the patient's condition has stabilized. The data from our study indicate that all hospitalized patients had hypertensive disease (HD), with only 5.4% of patients having initial forms such as degree I arterial hypertension (AH). In the rest, degrees II and III AH were determined. The wide prevalence of HD among patients with nonvalvular AF in Russia is confirmed by literature data [1]. This emphasizes the leading role of chronic AH in the development of AF. Uncontrolled AH in patients with AF leads to increased CHF incidence, increased risk of STEC, and increased risk of hemorrhage during lifelong use of oral anticoagulants [9]. Therefore, the selection of effective antihypertensive therapy at the stage of inpatient rehabilitation after EAO, in addition to the selection of oral anticoagulants, is critical. Repeated studies have confirmed improved long-term survival of patients with AF when arterial normotension is achieved [10, 11].

Moreover, it is crucial to select cardiotropic therapy to compensate for the manifestations of CHF in accordance with current clinical recommendations. Optimization of this type of treatment during the current hospitalization, according to MG results, had advantages compared with delayed administration. The relevance of this type of treatment for patients was due to the high prevalence of high-grade CHF among hospitalized patients. Manifestations of chronic circulatory failure were at stage IIa–b in 90.6% of patients and at stage III in 5.3% of cases. In addition to significant limitations of physical activity and decreased quality of life, CHF decompensation was the leading cause of lethal outcomes in the long term after discharge in almost 50% of the patients. According to current clinical recommendations, the composition of drugs for optimal drug therapy for CHF should include angiotensin-converting enzyme inhibitors, beta-blockers, mineralocorticoid receptor antagonists, and dapagliflozin [12]. Effective drug therapy improves long-term survival rates in patients with AF (CHARM 2006, ANTIPAF 2012, GISSI-AF 2009, EMPHASIS-HF 2012 studies). Furthermore, it aims to normalize coronary circulation in chronic forms of IHD. In the study group, 46.9% of patients had chronic IHD without a history of myocardial infarction, and another 14.4% of patients had postinfarction cardiosclerosis.

In addition to optimizing anticoagulant and cardiotropic therapy, patients with AF who underwent EAO during their current hospitalization required treatment for concomitant pathology, primarily diabetes mellitus (DM). The recommended composition of optimal drug therapy for the treatment of CHF includes the hypoglycemic drug dapagliflozin, even in the absence of DM, with recommendations class I and level of evidence A [12]. Notably, the prevalence of DM among hospitalized patients was 19.9%. The increased risk of thrombotic complications in DM is associated with an increase in the level of blood coagulation factors and inhibition of fibrinolysis, which is associated with chronic hyperglycemia [13]. Strict control of glucose levels and stable normoglycemia can reduce the risk of STEC in patients with AF [14].

When considering a treatment strategy for AF ("rhythm control" or "rate control") after EAO, most patients required a "rate control" strategy, i.e., achieving normosystole without attempting to restore the sinus pacemaker. This is due to the fact that most of the patients were elderly (66.3% of patients were over 70 years old) and that in 67.0% of cases, AF was permanent. The appropriateness of choosing the "rhythm control" strategy with this combination was controversial. In some cases of paroxysmal AF and high life expectancy, the "rhythm control" approach was chosen; however, these cases were rare. Therefore, conclusions about long-term efficiency require data accumulation.

A promising direction that can make a positive contribution to improving the long-term survival of patients with AF with a history of EAO in MG is endovascular implantation of an occluder of the left atrial appendage. This procedure is as effective as warfarin in preventing STEC in patients with contraindications to oral anticoagulants, as demonstrated in the PROTECT AF trial [15]. In the Department of Cardiovascular Surgery No. 1 (Angiosurgery) of Mechnikov North Western State Medical University, endovascular implantation of left atrial appendage occluders has been performed since 2019. The long-term results of this treatment type in patients with a history of EAO are currently being analyzed.

Optimization of conservative treatment during the current hospitalization in AF patients with a history of EAO improved long-term survival. We believe that the most significant difference was the normalization of anticoagulant therapy. However, the clinical role of the remaining links cannot be overestimated. The relatively small number of patients available for long-term follow-up did not enable to identify the most crucial among these links; therefore, continued research in this direction has been planned. This study primarily aimed to evaluate the influence of the optimization of cardiotropic therapy on long-term survival in EAO patients during the current hospitalization. We have not come across any publications in the available literature on the prospects for improving long-term results of treatment of patients with nonvalvular AF with a history of EAO.

CONCLUSION

The absence of a generally accepted system that determines further treatment approach for patients with nonvalvular AF with a history of EAO reduces long-term survival. Optimization of conservative treatment during rehabilitation after EAO during the current hospitalization led to a monthly reduction in the risk of lethal outcome by 2.2 times ($p = 0.003$).

ADDITIONAL INFORMATION

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