# Ten rules for oral anticoagulants prescription after a stroke



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*Every third or fourth ischemic stroke is cardioembolic. Prescribing oral anticoagulants can significantly reduce the risk of recurrent stroke, but this strategy requires the physician to have a firm orientation in the "efficacy – safety" coordinate system. We formulate 10 rules that should help any interested specialist (neurologist, cardiologist, therapist) to decide on the prescription of oral anticoagulants for cardioembolic stroke in daily clinical practice. We discuss issues of selection of an anticoagulant in atrial fibrillation, mitral stenosis and mechanical heart valves, the timing of prescription (also in haemorrhagic transformation of ischemic stroke and after intracerebral hemorrhage), the special features of anticoagulant prophylaxis in comorbid and "fragile" patients are discussed, the development of a stroke while taking an anticoagulant, the timing of discontinuation and resumption of therapy during surgical interventions, the choice of dose and peculiarities of therapy in cognitively impaired patients.*

***Keywords:*** *cardioembolic stroke; oral anticoagulants; apixaban.*
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***For reference:*** *Kulesh AA, Demin DA, Kucherenko SS. Ten rules for oral anticoagulants prescription after a stroke. Nevrologiya, neiropsikhiatriya, psikhosomatika = Neurology, Neuropsychiatry, Psychosomatics. 2024;16(4):111–121.* ***DOI:*** *10.14412/2074-2711-2024-4-111-121*

Cardioembolic stroke (CES) occupies $^1/_4$–$^1/_3$ in the etiological structure of ischemic stroke (IS) and often develops in elderly and senile patients [1]. The disease often leads to disabling neurological deficits, the need for constant care, and death. Previously, we discussed the clinical features of CES and the difficulties of its diagnosis [2]. This article focuses on secondary prevention, a measure that can reduce the risk of recurrent stroke by 66% [3]. As part of the article, we have formulated 10 rules for prescribing oral anticoagulants for CES, which can be used in everyday work by any interested clinician - a neurologist, cardiologist or therapist general practitioner.

**Rule 1.** ***In case of cardioembolic stroke due to atrial fibrillation, it is preferable to prescribe direct oral anticoagulants (DOACs).*** The difficulty of prescribing oral anticoagulants for CES against the background of atrial fibrillation (AF) is due to the need of finding a balance between two risks: the risk of early stroke recurrence (about 1% per day) [4] and the risk of hemorrhagic transformation (up to 60% in large cerebral infarctions) [5 ]. Both events can lead to worsening of neurological deficits, disability, and death. Any clinician involved in the selection of anticoagulant prophylaxis must confidently navigate the «efficacy-safety» coordinate system, the generalized measure of which is the net clinical benefit from prescribing the drug [6]. Randomized clinical trials (RCTs) RE-LY, ROCKET AF, ARISTOTLE and ENGAGE AF-TIMI 48 proved the advantages of DOACs over vitamin K antagonists (VKAs) in three aspects: reduction in the risk of stroke and systemic embolism (by 19%), the incidence of hemorrhagic stroke (by 51%) and mortality (by 10%) [7]. Among DOACs, only apixaban was superior to warfarin in four key risk reduction indicators: stroke, including recurrent stroke; systemic embolism; major bleeding and overall mortality [8]. Data from real clinical practice show that in the secondary prevention of CES, the use of apixaban is associated with a lower risk of intracranial hemorrhage (ICH) compared to warfarin and rivaroxaban [9, 10]. The safety of apixaban with respect to ICH does not differ from the safety of acetylsalicylic acid [11, 12], which makes the drug an ideal anticoagulant for the acute period of IS. Meta-analysis by Buckley et al. (2022) [13], including 38 studies (over 3.9 million patients in total), confirmed the greatest clinical benefit when prescribing apixaban compared to the use of other DOACs, which was also due to a reduction in the risk of IS and ICH. The priority of DOACs in the secondary prevention of CES should be considered undoubted, which is also reflected in the 2021 American Heart Association/American Stroke Association (AHA/ASA) recommendations for the secondary prevention of ischemic stroke [14] and the recommendations of the American College of Cardiology / American Heart Association (ACC/AHA) 2023 on AF, which states that «...It is recommended to prescribe DOACs instead of warfarin to reduce the risk of mortality, stroke, systemic embolism and ICH» [15]. Next, we need to look at a few exceptions to this rule.

**Rule 2.** ***In patients with cardioembolic stroke due to moderate/severe mitral stenosis or mechanical heart valve, only vitamin K antagonists are used.*** Mitral stenosis (usually of rheumatic etiology) leads to progressive remodeling (dilatation) of the left atrium, its fibrosis and electrical dysfunction, which explains the high incidence of AF. According to a meta-analysis by Noubiap et al. (2020) [16], AF is detected in every third patient with mitral

stenosis, and its presence increases the likelihood of thromboembolism by 6 times. When choosing anticoagulant therapy for AF, moderate/severe mitral stenosis (mitral valve opening area ⩽1.5 $cm^2$) is taken into account) – in this case, it is possible to prescribe only VKA (warfarin) with a target INR level of 2.0–3.0, but not DOACs [17] (Fig. 1). The INVICTUS trial demonstrated that VKAs were associated with lower rates of death and stroke compared with rivaroxaban [18]. The presence of other pathology of native valves (for example, degenerative aortic stenosis, mitral regurgitation) is not a contraindication to the use of DOACs [19].

Also, the use of VKA has no alternative in the presence of mechanical prosthetic heart valves in any position [17]. Studies studying analyzing the use of DOACs in patients with mechanical prostheses (RE-ALIGN, PROACT Xa) confirmed the validity of this approach, demonstrating the benefits of VKAs in relation to the incidence of thromboembolic events [20, 21]. In the presence of biological prostheses and AF, the use of DOACs is possible for >3 months after implantation (VKAs are used in the first 3 months) [17, 19].

**Rule 3.** ***The timing of DOACs prescription after stroke is determined by the size of the cerebral infarction.*** Diener's clinical rule[1], which has long been used throughout the world to determine the timing of DOAC initiation in CES, is currently giving way to an infarction-based approach [2]. It is the size of the cerebral infarction that is the key determinant of the risk of hemorrhagic transformation (HT) [22], so deciding on the timing of DOAC prescription is impossible without visualizing the lesion, which often involves performing magnetic resonance imaging (MRI) of the brain. Obviously, in case of a transient ischemic attack, a DOAC should be prescribed immediately, since there is no cerebral infarction. Studies published over the past few years confirm the safety and effectiveness of early use of DOACs in patients with CES [23, 24]. The most significant arguments in favor of early anticoagulant prophylaxis were obtained in the ELAN (Early versus Late initiation of direct oral Anticoagulants in post-ischemic stroke patients with atrial fibrillation) RCT [25]. The study included 2013 patients with CES who were randomized into groups of early (the first 48 hours for «small» and «medium» stroke, 6–7 days for «large» stroke) and later (3–4 days for «small», 6–7 days for «medium» and 12–14 days for «large» stroke) the appointment administration of DOACs. Early initiation of DOACs resulted in a lower rate of stroke recurrence within the first month (1.4% vs. 2.5%) with the same risk of ICH (0.2%). Further meta-analyses, including, in addition to ELAN, data from the TIMING RCT, as well as observational studies, confirmed the advantage of early initiation of DOAC therapy in the form of a reduction in the risk of recurrent IS (by 29%) [26] without increasing the likelihood of ICH [27]. It is important to note that in the ELAN RCT, stroke severity was determined specifically by infarct size (Fig. 2). The effectiveness of secondary prevention was greatest in the subgroup of «large» infarcts (halving the odds of the combined primary outcome) without increasing the risk of HT [28]. Thus, in most patients, DOAC initiation should occur early, typically within the 1st week of stroke. However, the time window for DOAC initiation is quite wide (14 days) as outlined in the current 2021 AHA/ASA guidelines [14], providing the opportunity to individualize deadlines. Thus, the presence of high thromboembolic risk factors in patients (recurrent CES, systemic embolism, severe left atrial dilatation, spontaneous echo contrast or left atrial appendage thrombus) may justify earlier prescription of DOACs even in «large» infarctions [29]. On the other hand, detection of a dominant alternative cause of stroke (cerebral microangiopathy – CMA; extra- and especially intracranial atherosclerosis) may serve as a reason for a delayed start of DOACs (from the 2nd week) in order to maximize the potential of therapy aimed at a competing mechanism (for example, dual antiplatelet therapy; see Fig. 2) [30, 31].

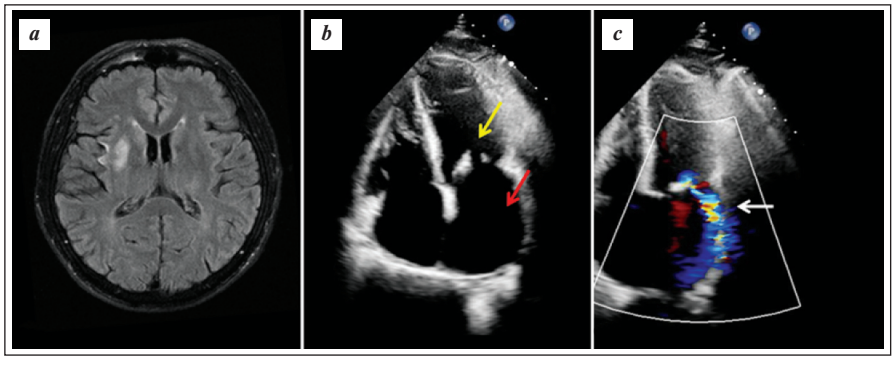


**Fig. 1.** *Clinical case No. 1. A 64-year-old man with anamnesis of an ischemic stroke in the territory of the right middle cerebral artery. FLAIR MRI (a) shows an insular infarction (characteristic of cardioembolism) with underlying subcortical region as a result of atrial fibrillation. According to transthoracic echocardiography, the mitral valve is thickened, indurated, partially fused along the commissures, its movement is restricted, unidirectional (b, yellow arrow), mitral valve stenosis with an opening area of 1 $cm^2$, an average gradient of 11 mm Hg. There is dilatation of the left atrium (b, red arrow) with a volume index of 48.7 $ml/m^2$ and grade II mitral regurgitation (c, white arrow). The patient therefore has severe rheumatic mitral stenosis; only a vitamin K antagonist (warfarin) can be used as anticoagulant therapy. The patient subsequently underwent heart surgery (mechanical prosthesis implantation) and then continued to take warfarin (target INR 2.5–3.5)*

**Rule 4.** ***The timing of DOAC prescription for hemorrhagic transformation is determined by its type.*** HT, according to the ECASS classification, is divided into hemorrhagic infarction (type 1 or 2, depending on the severity of petechial impregnation) and parenchymal hematoma (type 1 and 2, depending on the size and presence of mass effect). Hemorrhage is also isolated at a distance from the primary infarction (according to the Heidelberg classification) is also taken into account. When analyzing HT, the first step is to determine its symptomatology, i.e., its relationship correlation with neurological deterioration [32]. As a rule, type 2 parenchymal hematomas are symptomatic [33]. HT develops in the 1st week of stroke in 9% of patients ($^1/_3$ of them have parenchymal hematoma) [34]. Due to the widespread use of reperfusion therapy, clinicians are increasingly faced with the phenomenon of HT –

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for example, transformation occurs in $^1/_3$ of patients with CES who underwent intravenous thrombolysis [35], and parenchymal hematoma develops in 14% of patients after endovascular thrombectomy [36]. From this point of view, strict periprocedural blood pressure control (systolic blood pressure in the range of 140–180 mmHg) [37], aimed at reducing the risk of developing HT, is also a measure that facilitates the subsequent use of DOACs for secondary prevention. This is especially true for patients with CES admitted during the late therapeutic window and/or with developing cerebral infarction [38, 39]. Evidence-based medicine data regarding the timing of DOAC prescription for HT are insufficient. In the ELAN RCT, early initiation of DOACs for hemorrhagic infarctions was allowed at the discretion of the treating physician, so the issue can be considered resolved for this subtype of HT. The situation is more complicated with parenchymal hematomas during reperfusion: patients after intravenous thrombolysis and thrombectomy participated in the study (40% and 38%, respectively), but inclusion in it if a parenchymal hematoma developed, patients were not allowed to participate [25]. According to expert opinion, delayed administration of DOACs may be justified only in cases of severe parenchymal hematomas [1]. This point of view is confirmed by the results of a recent study (Japan), which included 111 patients with CES after thrombectomy. HT developed in every fourth patient (parenchymal hematoma in 11.7%). Prescription of DOACs in the first 14 days in the presence of a hematoma did not lead to progression of transformation. It is noteworthy that in the parenchymal hematoma group there was a trend toward a higher rate of recurrent CES (15.4% vs. 6.3% in hemorrhagic infarction), which confirms the importance of early prevention [40]. Thus, in most patients with HT, anticoagulant therapy can be initiated early; for type 1 parenchymal hematoma, some delay is advisable (1 week); the period of initiation for type 2 parenchymal hematoma is the most variable and depends on its severity, the presence of dislocation and dynamics according to computed tomography (CT; see Fig. 2).

**Rule 5.** ***Approaches to prescribing DOACs after hemorrhagic stroke are determined by its cause and blood pressure control.*** In patients with intracerebral hemorrhage (ICH) and AF, the risk of subsequent IS is higher than the risk of recurrent hemorrhage [41]. Observational studies have shown that the administration of an oral anticoagulant after ICH can reduce this risk without significantly increasing the likelihood of recurrent hemorrhagic stroke [42–44]. In accordance with the AHA/ASA recommendations (2022) for the treatment of patients with ICH, the issue a decision on resuming anticoagulants should be decided based on the assessment of the benefit-risk ratio, but clear criteria have not been developed [45]. First of all, it should be noted that the administration of DOACs after ICH is more effective and safer compared to the administration of warfarin [46, 47]. From a practical point of view, deciding whether to prescribe a DOAC is associated with determining the leading etiology of ICH: hypertensive CMA or cerebral amyloid angiopathy (CAA) [48, 49]. If only a CT scan of the brain is available in the diagnostic arsenal,

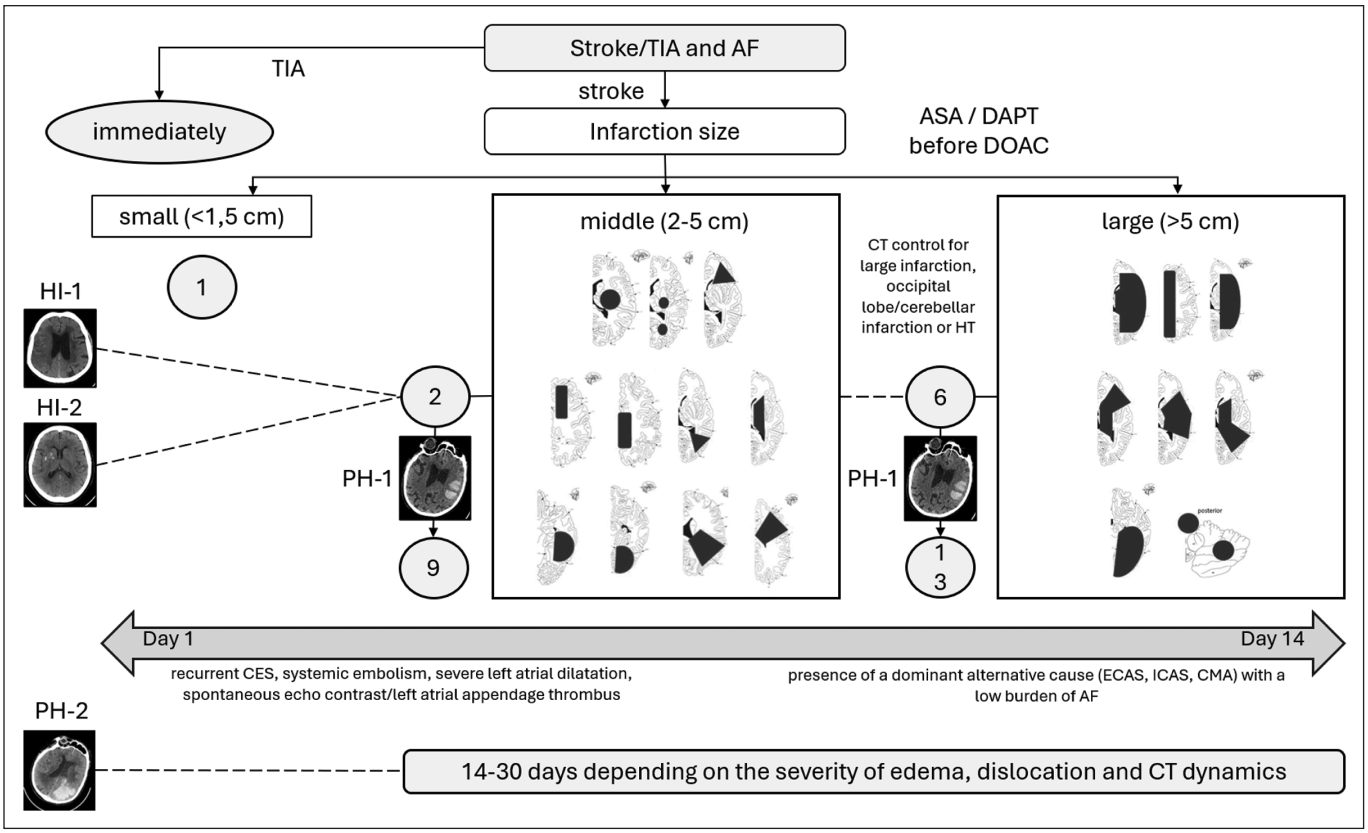


**Fig. 2.** *Time of prescription of direct oral anticoagulants (DOACs) after cardioembolic stroke*
*HI – hemorrhagic infarction; PH – parenchymal hematoma; ASA – acetylsalicylic acid; DAPT – dual antiplatelet therapy; ECAS – extracranial atherosclerosis; ICAS – intracranial atherosclerosis; CMA – cerebral microangiopathy*

attention should be paid to the location of the hematoma: with CMA, the typical location is in the putamen, thalamus, and pons; CAA is characterized by lobar hematomas [50–52]. However, for nonspecific localization of hemorrhage (subcortical white matter, cerebellum), CT will not be enough to determine the cause of ICH. We believe that patients with ICH and AF must undergo MRI of the brain with the SWAN/SWI sequence: it will allow not only to establish the pathogenetic subtype, but also, if CAA is detected, to identify its most «aggressive» variant. Thus, CMA is characterized by a deep location of lacunae, dilated perivascular spaces and cerebral microbleeds hemorrhages (CMBs) [53], while CAA is characterized by cortical CMBs, expansion of perivascular spaces in the area of the centrum semiovale and spots of white matter hyperintensity [54]. The MRI marker pathognomonic for CAA is cortical superficial siderosis; the presence of this phenomenon significantly increases the risk of ICH recurrence [55]. At the same time, siderosis marks a high risk of hemorrhagic stroke even with a small number of CMBs [56]. Currently, there is insufficient data to support the use of MRI markers to guide decisions about anticoagulant therapy after ICH. It is known that in the secondary prevention of IS, the presence of multiple CMBs (⩾11) or cortical superficial siderosis leads to a significant increase in the risk of ICH, which neutralizes the effect of preventing ischemic events only with the use of dual antithrombotic therapy (anticoagulant and antiplatelet) [57, 58]. Expert opinions regarding the prescription of oral anticoagulants for CAA vary from the impossibility of their use [59] to their inapplicability in the presence of the hemorrhagic phenotype of the disease (siderosis) [60]. An analysis of data from the Swedish national registry (n=2619; 2017) showed that the optimal time interval for resuming anticoagulant use after ICH is 7–8 weeks [61]; this period formed the basis of the AHA/ASA recommendations in 2022. Other observational studies have demonstrated the effectiveness and safety of prescribing the drug at an earlier time – as early as 2–4 weeks after ICH [62–64]. In our opinion, the optimal interval is 4–8 weeks, as specified in the 2023 ACC/AHA recommendations (Fig. 3). In the presence of a very high thromboembolic risk (rheumatic heart disease or mechanical valve), warfarin is prescribed after 1–2 weeks [15]. At an earlier date, A DOAC can be prescribed earlier if the cause of the ICH is eliminated (for example, an aneurysm or malformation is excluded from the bloodstream). Due to the previously discussed high safety of apixaban, it is the drug of choice in patients with AF and a history of ICH [9, 10]. The most important condition for resuming anticoagulant therapy is achieving and maintaining target blood pressure (<130/80 mmHg). In situations when anticoagulation therapy is contraindicated, left atrial appendage occlusion should be considered as an alternative to long-term anticoagulation [45].

**Rule 6.** ***When prescribing DOACs after stroke, comorbidity should be taken into account.*** The «silver tsunami», i.e., global population aging, is leading to an increase in the proportion of «frail» elderly patients (Fig. 4). Every third patient with AF has this geriatric syndrome, and its presence is associated with an increased incidence of adverse events, including mortality [65]. According to a meta-analysis by Desai et al. (2022) [66], including 880,464 «frail» patients with AF (mean age 79.6 years),

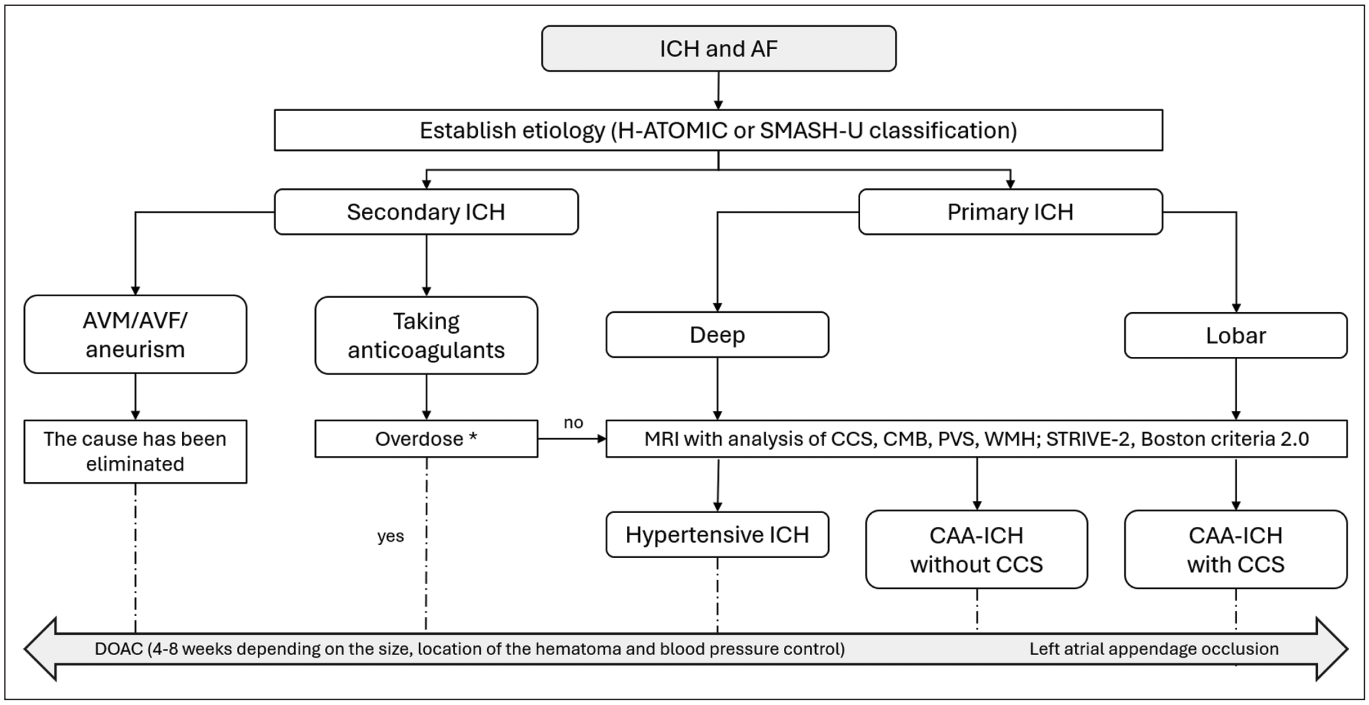


**Fig. 3.** *Prescription of DOACs after intracerebral hemorrhage*
**Overdose means: INR >3 when taking warfarin; standard doses of DOACs when there are indications for their dose reduction; drug interactions leading to increased concentrations of DOACs (systemic use of ketoconazole/itraconazole, ritonavir); overdosing duplicate by mistake*
*AVM – arteriovenous malformation; AVF – arteriovenous fistula; CSS – cortical superficial siderosis; WMH – white matter hyperintensity; PVS – perivascular spaces*

DOACs were associated with a lower likelihood of stroke/systemic embolism compared with VKAs (odds ratio 0.74); with In this case, the lowest risk was observed when apixaban was prescribed (odds ratio – 0.62). In a large (n = 71,638) nationwide cohort study by Grymonprez et al. (2024) [67], apixaban also demonstrated a lower risk of major bleeding (including intracranial and gastrointestinal) than other DOACs and VKAs in patients with AF and frailty syndrome. Also, the presence of «fragility» increases the risk of falls, which is especially important in the context of vascular neurology (stroke as a risk factor for falls, risk of traumatic subdural hematomas). Prescribing DOACs to patients with a history of falls/risk of falls reduces the risk of ICH by half compared with the use of VKAs [68].

Considering Given the fact that all DOACs are eliminated to varying degrees through the kidneys (dabigatran - by 80%, rivaroxaban - by 35%, apixaban - by 27%), all patients require an assessment of creatinine clearance (Cockcroft-Gault formula). With clearance <15 ml/min (or dialysis), the use of DOACs is contraindicated (only VKAs are used); with a clearance of 15–29 ml/min, reduced doses of apixaban (2.5 mg 2 times a day) and rivaroxaban (15 mg once a day) may be prescribed, while, according to the EHRA recommendations for the use of DOACs (2021), apixaban is preferable in these conditions. It should be noted that when prescribing rivaroxaban, dose reduction should be carried out starting with a creatinine clearance of 49 ml/min [19]. Also, the level of creatinine is assessed during the standard selection of the dose of apixaban - the «ABC rule»: it is necessary to take into account age (A) i80 years, body weight (B) I60 kg, creatinine (C) i133 μmol/l and in the presence of at least two of these criteria the dose of apixaban should be reduced to 2.5 mg 2 times a day (see table).

The impact of chronic kidney disease on anticoagulant therapy was studied in the large (n = 285,292) observational study of real-world clinical practice ARISTOPHANES (2018), in which all DOACs were associated with lower rates of stroke or serious adverse events compared with warfarin. However, apixaban [hazard ratio (RR) 0.58] and dabigatran (RR 0.73) showed a lower risk of major bleeding. Taking into account the presence of renal insufficiency, apixaban showed benefit when controlling for renal impairment over rivaroxaban and dabigatran in relation to both the risk of stroke and the risk of major bleeding [69].

The use of DOACs in elderly patients (over 75 years of age) was analyzed by the Spanish multidisciplinary expert group of the ACONVENIENCE study (2022). Three blocks of complex clinical scenarios were identified: specific situations («frailty», low body weight, stage IV chronic kidney disease, etc.), cardiac conditions (chronic coronary syndrome, peri-infarction AF, intraventricular thrombus and AF, bioprostheses, etc.) and high risk of bleeding (anemia, thrombocytopenia, risk of gastrointestinal bleeding, etc.). In 14 of 16 clinical situations, experts identified apixaban as the drug of choice. Only in two cases another anticoagulant was more preferable: in case of left ventricular thrombus - warfarin, in case of risk of drug-drug interactions - edoxaban (not used in Russia) [70].

**Rule 7.** ***The presence of cognitive impairment influences the choice of DOACs.*** Stroke is often accompanied by cognitive impairment, both transient (in the acute period of the disease) and persistent and even progressive (within the continuum of cerebrovascular pathology or mixed dementia) [71, 72]. On the other hand, dementia occurs in 8% of patients with AF aged 65 years or older. Its causes are cerebral micro- and macroembolization (AF-associated factor), as well as coexisting pathology (CMA, Alzheimer's disease and other neurodegenerative diseases) [73]. In this category of patients, the use of apixaban is associated with the lowest risk of major bleeding and ischemic stroke compared to the use of other oral anticoagulants [74]. An analysis of a national Belgian cohort (more than 237 thousand patients) showed that the use of DOACs is associated with a lower risk of dementia (vascular and unspecified) compared to VKAs; this effect is associated with the use of apixaban and edoxaban (not used in Russia) [75]. To prevent stroke, it is not enough to prescribe a DOAC; it is important to ensure its regular use, which is especially difficult in a cohort of patients with cognitive impairment. In addition to prescribing basic therapy for dementia (cholinesterase inhibitors, memantine), pill boxes with an alarm reminder function or daily monitoring of drug intake by relatives/caregivers can be used to increase adherence in patients with cognitive impairment [76].

**Rule 8.** ***If an ischemic stroke develops while taking a DOACs, its cause must be carefully analyzed.*** Violations of the DOAC regimen (omission/refusal or unreasonably reduced dose) in a patient with AF are the most obvious cause of IS. Thus, in the RENo study, an unreasonably reduced DOAC dose increased the risk of cerebral ischemic events by 3 times [77]. However, every third stroke in AF may have a non-cardioembolic etiology; more often, this role is played by it is an atherothrombotic stroke against the background of extra- or intracranial stenosis or lacunar infarction against the background of CMA [78, 79]. Thus, with IS against the background of DOACs, a detailed assessment of the infarction focus is required (correspondence to lacunar infarction, diagnosis of CMA according to the STRIVE criteria) and mandatory vascular imaging (usually CT angiography) to identify stroke-related stenosis and, accordingly, planning carotid revascularization - carotid endarterectomy or stenting.

*Contraindications for use and conditions for reducing the dose of DOACs*

| DOACs are contraindicated | DOACs are used at a reduced dose |
|---|---|
| • Mechanical prosthetic heart valves<br>• Moderate/severe rheumatic mitral stenosis<br>• Chronic kidney disease stage V (creatinine clearance <15 ml/min or hemodialysis)<br>• Liver failure (Child-Pugh class C, rivaroxaban is also contraindicated in class B)<br>• Thrombocytopenia <20 thousand/μl (at 20–50 thousand/μl – with caution, consider half the dose of DOAC)<br>• Antiphospholipid syndrome<br>• Pregnancy | • *Apixaban* (2.5 mg 2 times a day): creatinine clearance 15–29 ml/min or at least two of three criteria: age ⩾80 years, body weight ⩽60 kg, creatinine ⩾133 μmol/l<br>• *Dabigatran* (110 mg twice daily): age >80 years, concomitant use of verapamil, dose reduction may be considered if age 75–80 years, creatinine clearance 30–49 ml/min, high risk of gastrointestinal bleeding<br>• *Rivaroxaban* (15 mg once daily): creatinine clearance 15–49 ml/min |

If there are no alternative causes of stroke, and the patient regularly takes an adequate dose of DOACs, the issue of changing the antithrombotic therapy regimen is discussed. In a study by Ip et al. (2023) [79] three approaches were analyzed: switching from DOACs to warfarin; switching from one DOAC to another; addition of an antiplatelet drug, but none of these strategies reduced the risk of recurrent ischemic events. At the same time, the retrospective observational study ATHENS (2024) showed that replacing apixaban with rivaroxaban was associated with a higher risk of stroke/systemic embolism (RR 1.99) and major bleeding (RR 1.80) than continuing its use reception. However, switching patients from rivaroxaban to apixaban was not associated with an increased risk of stroke and major bleeding [80].

**Rule 9.** ***The timing of discontinuation and resumption of DOACs during surgery is determined by the type of surgical treatment based on the risk of bleeding.*** The perioperative period is a time of increased vulnerability for patients with AF, since discontinuation of the anticoagulant increases the risk of thromboembolism, and continued use increases the risk of surgical bleeding. Moreover, within 2 years, every fourth patient with AF needs to temporarily discontinue DOACs due to planned interventions [81]. In vascular neurology, drug support for the perioperative period during carotid surgery is most relevant. According to the EHRA recommendations (2021), operations with a high risk of bleeding (including carotid endarterectomy) and low risk (including carotid stenting) are distinguished. For high-risk surgery, it is necessary to discontinue DOACs 2 days before surgery (for apixaban, rivaroxaban – regardless of creatinine clearance; for dabigatran - with clearance ⩾80 ml/min) and resume taking it 2 days after surgery. In low-risk operations, it is possible to perform surgical treatment without discontinuing DOACs (or skipping the evening dose on the eve of surgery) and restarting either on the day of surgery (after 6 hours or more with reliable hemostasis) or the next day [19].

The effectiveness of the standardized approach was proven in the PAUSE study (2019), including 3007 patients with AF and planned surgical interventions ($^1/_3$ had operations with a high risk of bleeding). The study assessed the safety of discontinuing DOACs 1–4 days in advance (depending on the risk of hemorrhagic complications and creatinine clearance) and resuming its use 1–2 days after surgery. The risk of developing thrombotic and hemorrhagic complications did not exceed the predicted values. The incidence of thromboembolic complications (within 30 days) was 0.16%, major bleeding – 1.35%. Arterial thromboembolism was observed in 0.16% of patients in the apixaban group, 0.37% in the rivaroxaban group and 0.6% in the dabigatran group [82].

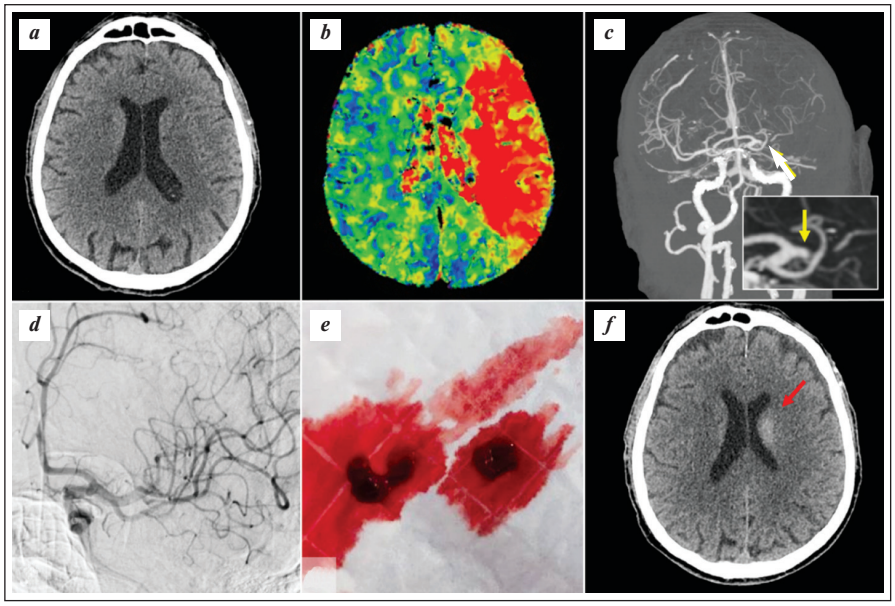


**Fig. 4.** *Clinical case No. 2. A "frail" elderly man, 88 years old, with persistent atrial fibrillation, not taking DOACs. While gardening, suddenly felt weakness in right limbs and disturbed speech. He was admitted to the hospital 1.5 hours after the onset of symptoms with global aphasia and right-sided hemiplegia, NIHSS – 21 points. CT scan of the brain (a – no early ischemic changes, ASPECTS score 10), CT perfusion (b – extensive area of hypoperfusion in the territory of the left middle cerebral artery) and CT angiography (c – occlusion of the M1 segment of the left middle cerebral artery, yellow arrows) were performed. Endovascular thrombectomy was performed and complete recanalization was achieved (d). The thromboemboli are shown in Fig. 4, e. Immediately after reperfusion therapy, the patient began to regain movement in the right limbs; within 24 hours, the patient was able to move independently across the room, speech disorders regressed (modified Rankin scale – 1 point). A control CT scan of the brain one day later showed a hemorrhagic transformation resembling a haemorrhagic infarction type 2 in the deep areas of the left hemisphere, without a brain infarction becoming visible (f, red arrow). On the 2nd day, apixaban was prescribed at a dose of 5 mg twice daily (body weight – 68 kg, creatinine – 92 μmol/l, creatinine clearance – 46 ml/min)*

**Rule 10.** ***Most patients are indicated for A full dose of DOAC is indicated for most patients.*** A meta-analysis of 11 studies showed that the use of inappropriately reduced doses of DOACs is associated with an increased risk of not only stroke and systemic embolism, but also death [83]. According to the hospital registry of the RSC City Clinical Hospital No. 4 in Perm (unpublished data), only 8% of surviving patients with CES have indications for reducing the dose of apixaban. Incorrect dosing of DOACs is associated with an increased risk of death from any cause, highlighting the need for responsible dosing of anticoagulants by physicians of different specialties [84]. Conditions for prescribing reduced doses of DOACs are indicated in the table.

## Conclusion

Thus, compliance with the rules discussed in the article will allow individualizing anticoagulant therapy and achieving maximum clinical benefit in each patient with AF-associated IS. Considering the characteristics of patients with CES, apixaban can be regarded as the drug of choice in most clinical situations due to the optimal balance of efficacy and safety.

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Received/Reviewed/Accepted
29.04.2024/15.07.2024/16.07.2024

**Conflict of Interest Statement**

The investigation has not been sponsored. There are no conflicts of interest. The authors are solely responsible for submitting the final version of the manuscript for publication. All the authors have participated in developing the concept of the article and in writing the manuscript. The final version of the manuscript has been approved by all the authors.

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