

Non-vitamin K oral anticoagulants (NOACs) in patients with stroke and atrial fibrillation

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Summary

Patients with atrial fibrillation who had a previous transient ischemic attack or ischemic stroke had a significantly high risk of stroke recurrence and the introduction of oral anticoagulants should be mandatory. However, the long-term use of oral anticoagulants increases the risk of developing all types of intracranial hemorrhages. The advantages of non-vitamin K oral anticoagulants (NOACs) compared to warfarin are that they have a significantly lower risk for hemorrhagic stroke. They are preferred in elderly patients, those with small vessel disease, or those with previous intracerebral hemorrhage. The time of NOACs introduction after an ischemic stroke depends on its severity and the rule “1-3-6-12” days should be applied. The reintroduction of NOACs in patients with atrial fibrillation and previous intracerebral hemorrhage depends on its etiology and should be after about 4-8 weeks if the cardioembolic risk is high and the risk for intracranial hemorrhage small.

Keywords: ischemic stroke, intracranial hemorrhage, non-vitamin K oral anticoagulants, atrial fibrillation

Introduction

Secondary prevention of an ischemic stroke (IS) depends on its cause. Aspirin is a drug of choice in the early phase of acute IS, which should be introduced within 48 hours of stroke onset. In the further course, antiplatelet or oral anticoagulant therapy is continued, depending on whether it is a cardioembolic or non-cardioembolic type of IS. Cardioembolic IS accounts for about 20-30% of all stroke patients (1). The most common cardiogenic cause of IS is atrial fibrillation (AF), which carries a high risk of developing the first IS, and even higher in patients who already had IS (2). The introduction of oral anticoagulants (OAC) in patients with AF reduces their risk of developing first IS by 67%, and in secondary prevention by 66% (3,4). However, the fact is that some patients experience IS during an unregistered AF paroxysm which subsequent detection may be delayed, and thus the use of OAC is also delayed. Another important fact is that OACs carry a significant risk of hemorrhagic complications and that their long-term use is supported only when the cardioembolic cause of IS is confirmed. These facts raise two important questions. One is how to recognize cardioembolic IS, and the other is whether long-term anticoagulant therapy is safe.

Cardioembolic stroke

Cardioembolic IS is usually associated with a severe neurological deficit because the embolus is most often lodged in the proximal segments of the middle cerebral artery (ACM) or its branches (5). Cardioembolism is the cause of about 50% of all malignant ACM occlusions with a high mortality rate, in 34% ACM branches occlusion and in 41% of all cortical infarcts (5,6). Very rarely, cardioembolism is the cause of lacunar infarcts or transitory ischemic attacks (TIA) (5,7). Interestingly, cardioembolic IS is not only localized in the anterior circulation, but also in the posterior circulation areas to a much greater extent than originally thought. The cerebellum, bilateral thalamus, and other multifocal infarcts in the posterior cranial fossa are the typical localization of infarcts in the posterior circulation (6). An important feature of cardioembolic infarcts is the presence of hemorrhagic transformation (HT) which is detected in as many as 71% of cases (6,7). The typical clinical presentation of cardioembolic IS implies a large neurological deficit that develops rapidly with the punctum of clinical symptoms at the beginning of the disease, possible initial disturbance of consciousness, but also the possibility of rapid recovery of symptoms as a sign of spontaneous lysis of thrombus (5,7,8). The neuroimaging often shows multiple infarcts of different ages in distinct vascular areas or cortical infarcts in the distal branches of large arteries, often with signs of HT (6).

The source of cardioembolism should be specified as follows: thrombus formation in the left ventricle (i.e. after large myocardial infarction, in the left ventricular aneurysm, cardiomyopathies), infective endocarditis, thrombosis of artificial valves, paradoxical embolism (patent foramen ovale, atrial septal defect), aortic plaque embolization, and

most frequently left atrial appendage thrombosis in atrial fibrillation and/or rheumatic valvule disease. However, the most common cause of cardioembolic IS with about 50% prevalence is AF (9). It is a major risk factor for IS, as one out of five patients with AF develops IS and one out of four over the age of 80 (9). The early recurrences of IS in patients with AF are registered in about 12% of patients (7). The presence of AF at the onset of acute IS is associated with significantly higher mortality compared with patients without AF. Thus, the 30-day mortality of IS with AF is 32.5%, and for those without AF 16.2% (10).

The permanent AF carries a high risk of developing IS, but it is confirmed that the risk is also significant in paroxysmal AF. The paroxysmal AF is found as a cause of IS in about 6.2%, and in patients with cryptogenic stroke in 13.4% of cases (11). The detection of paroxysmal AF in patients with previous IS increases with the duration of monitoring. Thus, with continuous ECG monitoring within the first 24-72 hours after the onset of IS, paroxysmal AF can be detected in 2.4 to 8.3%, with subsequent 24-hour Holter ECG in 3-5%, and with repeated or prolonged Holter ECG in up to 14% of IS patients (11-13). In patients with cryptogenic IS, paroxysmal AF is detected by implantable ECG recorders over 36 months in about 30% (14).

Anticoagulant therapy in the secondary prevention of IS in patients with AF

The patients with IS and AF have a high risk of early recurrence of stroke, and therefore it would be prudent to introduce anticoagulants immediately after its onset. On the other hand, the frequent occurrence of HT in the presence of anticoagulant therapy increases the risk of developing symptomatic intracerebral hemorrhage (ICH), and it should be cautious with the introduction of OAC in the early phase of acute IS. Also, the long-term use of OAC in patients with the previous IS increases the risk of developing ICH, especially in those with small vessel disease (SVD). The CHADS₂VASc and HASBLED scores are not of great importance in a risk assessment in patients with previous IS. In both scores, recent stroke increases the risk for either hemorrhagic stroke or recurrence of IS, and they do not consider other significant risk factors such as the presence of ischemic leukoencephalopathy or leukoaraiosis. The risk of developing symptomatic ICH is increased in the presence of major infarction, HT, uncontrolled hypertension, conditions with a hemorrhagic tendency (e.g. thrombocytopenia), previous hemorrhagic strokes, in combined antithrombotic therapy or non-steroidal anti-platelet therapy (15). The HASBLED score is always a great tool to evaluate a patient's risk for hemorrhagic complications, including intracranial hemorrhage. Therefore, in each patient with IS, his or her risk of recurrence of IS or developing hemorrhagic stroke should be balanced and then decide whether or not to use OAC.

For decades, vitamin K antagonists (VKA) have been unique and highly effective medications used in the primary and secondary prevention of IS in patients with AF, but

with some limitations such as a narrow therapeutic window, the need for frequent laboratory monitoring, and numerous food and drug interactions. To overcome these limitations of VKA medications, new direct non-vitamin K oral anticoagulants (NOACs) have been developed in recent decades. The NOACs could be considered ideal because they do not interact with food, have few interactions with other drugs, and have a predictable therapeutic response (16). Dabigatran acts on thrombin and apixaban, rivaroxaban and edoxaban on factor Xa.

Efficacy and safety of NOACs in the secondary prevention of IS in patients with AF

The efficacy and safety of NOACs in secondary prevention of IS have not been investigated in special randomized controlled trials (RCS), but significant information was provided by the subanalysis of patients with previous IS or TIA from RE-LY, ROCKET-AF and ARISTOTLE studies, which introduced these medications in practice (17-19). In all these studies, patients with a previous TIA or IS had a significantly higher risk of stroke recurrence, regardless of whether they were on NOACs or warfarin.

In the RE-LY study, there were 3623 (20%) patients with a previous IS or TIA (17). Dabigatran 110 mg and 150 mg were as effective as warfarin in reducing the risk of stroke recurrence or systemic embolism (Table I). A lower dose of dabigatran had a 30% significantly lower all-cause mortality compared to warfarin, an 80% lower relative risk of intracranial hemorrhage, and lower major bleeding by about 34%. A higher dose of dabigatran reduced the relative risk for intracranial hemorrhage by 59% but carried an increased risk for gastrointestinal (GI) bleeding (Table II).

Table I The efficacy of NOACs versus VKA in secondary stroke prevention in patients with atrial fibrillation

Tabela I Efikasnost NOAK u poređenju sa VKA u sekundarnoj prevenciji moždanog udara kod bolesnika sa atrijalnom fibrilacijom

	RE- LY 110 OR (95%CI)	RE-LY 150 OR (95%CI)	ROCKET -AF OR (95%CI)	ARISTOTLE OR (95%CI)
Stroke or SE	0.84 (0.58-1.21)	0.75 (0.52-1.09)	0.94 (0.77-1.17)	0.76 (0.56-1.03)
Stroke	0.89 (0.61-1.31)	0.76 (0.52-1.13)	0.98 (0.79-1.22)	0.71 (0.52-0.97)*
Ischemic or unknown stroke	1.28 (0.84-1.94)	1.02 (0.66-1.57)	1.04 (0.82-1.31)	0.86 (0.60-1.23)
Fatal or invalidating stroke	0.81 (0.52-1.27)	0.72 (0.46-1.13)	0.93 (0.69-1.24)	0.87 (0.57-1.34)

NOACs non-vitamin K oral anticoagulants, VKA vitamin K antagonists,
SE systemic embolism

* Statistically significant ($p < 0.05$ or $p < 0.01$)

In the ROCKET-AF study, as many as 52% of patients had previous TIA or IS with a large number of vascular risk factors (18). A subanalysis of these patients showed that rivaroxaban was as effective as warfarin in reducing the risk of stroke, systemic embolism, or death (Table I). Rivaroxaban in this group of patients with previous TIA/IS had the same safety profile as warfarin, with the same risk of intracranial hemorrhage, ICH, or major bleeding, but with a significant reduction in the relative risk of fatal bleeding for about 46% compared to warfarin (Table II).

Table II Safety of NOACs versus VKA in secondary stroke prevention in patients with atrial fibrillation

Tabela II Bezbednost NOAK u poređenju sa VKA u sekundarnoj prevenciji moždanog udara kod bolesnika sa atrijskom fibrilacijom

	RE- LY 110 OR (95%CI)	RE-LY 150 OR (95%CI)	ROCKET -AF OR (95%CI)	ARISTOTLE OR (95%CI)
All-cause mortality	0.79 (0.52-0.95)*	0.98 (0.74-1.29)	0.97 (0.82-1.14)	0.88 (0.69-1.12)
Intracranial hemorrhage	0.26 (0.13-0.50)*	0.43 (0.24-0.79)*	0.73 (0.47-1.13)	0.40 (0.24-0.68)*
Hemorrhagic stroke	0.20 (0.08-0.48)*	0.31 (0.14-0.70)*	0.73 (0.42-1.25)	0.42 (0.23-0.77)*
Major hemorrhage	0.65 (0.48-0.90)*	1.02 (0.76-1.36)	0.96 (0.76-1.19)	0.74 (0.55-0.99)*
GI hemorrhage	1.00 (0.61-1.63)	1.68 (1.11-2.57)*	NA	0.84 (0.45 - 1.57)

NOACs non-vitamin K oral anticoagulants, VKA vitamin K antagonists, GIT gastrointestinal, NA not available

* Statistically significant ($p < 0.05$ or $p < 0.01$)

In the ARISTOTLE study, there were 3436 (19%) patients with previous TIA/IS and apixaban was shown to be more effective than warfarin in this patient population in reducing the risk of recurrence of any type of stroke by about 29% and even by about 60% risk reduction for hemorrhagic stroke (19) (Table I). Compared to warfarin, apixaban has a 27% lower risk of major bleeding and a 63% lower risk of intracranial hemorrhage (Table II).

A meta-analysis of 14527 patients with previous TIA/IS in these three RCT showed that the introduction of NOACs significantly reduced the incidence of stroke or systemic embolism by about 15% compared with warfarin (20). The use of NOACs was associated

with a significantly lower risk of major bleeding (by ~ 14%), mainly due to a reduction in the risk of hemorrhagic stroke (by 56%) (20).

Having in mind all the advantages of NOACs in relation to warfarin, above all their safety profile, and the fact that they reduce the risk of hemorrhagic stroke and intracranial hemorrhage to which are particularly predisposed patients with previous IS, the recommendation of the European Society of Cardiology (ESC) and the European Stroke Organization (ESO) is that the NOACs should have preference over warfarin or aspirin in patients with AF and previous IS (21,22).

The NOACs in specific groups of patients with previous IS and AF

In RCT subanalyses that compared the efficacy and safety of NOACs against VKA, it was not shown that the use of NOACs has a different effect in the *elderly population* compared to younger people (17-19). The ESO Guideline gives preference to NOACs over VKA in the elderly population, although there is currently no data on whether there are differences between older and younger patients with previous IS and AF (22).

There are currently no data on the use of OAC in *patients with previous cognitive deficits*. The introduction of OAC in these patients should consider the degree of cognitive decline, ability to understand, quality of life and life expectancy, the possibility of poor therapeutic adherence, and higher risks of hemorrhagic complications. The ESO Guideline gives preference to NOACs over VKA in the secondary prevention of IS in patients with AF and cognitive deficits (22).

There are currently no studies comparing the use of NOACs with VKA in patients with previous IS who have mild or moderate *renal insufficiency*. In the secondary prevention of IS, the use of NOACs is recommended in these patients in adjusted doses as well as in primary prevention (22).

The NOACs in patients with SVD

The SVD is a spectrum of changes occurring in the small blood vessels of the brain and is manifested by the presence of small multiple lacunar infarcts, white matter hyperintensities (WMH), or cerebral microbleeds (CMB). They account for about 25% of the causes of IS and 80% of the causes of ICH (23,24). The fact that SCD is associated with the occurrence of ICH often makes neurologists hesitant to introduce OACs in these patients or to refrain from their introduction. The WMH changes and CMB that carry an increased risk of developing ICH, are present with significant frequency among patients with AF (25). A CROMIS-2 study of patients with previous IS and AF treated with VKA or NOACs showed that the presence of CMB increased the risk of developing symptomatic ICH by 3.7 times, compared with patients in whom CMB was not detected (26). Given these facts, having detected the SVD neuroimaging markers could be useful to clinicians in predicting the risk of introducing long-term OAC in patients with previous

IS and AF. However, it is necessary to wait for ongoing studies to provide solid recommendations on this issue. Theoretically, NOACs may have an advantage over VKA in patients with SVD and previous AF (22).

The NOACs in an embolic stroke of unknown source (ESUS)

Secondary prevention of stroke depends on timely and adequate detection of the stroke mechanism. Namely, in cardioembolic stroke, the therapy of choice in secondary stroke prevention is anticoagulant therapy, because aspirin is not effective enough. About 25% of all IS are cryptogenic and antiplatelet therapy is recommended for secondary prevention. However, the fact is that based on clinical and neuroimaging criteria, the cardioembolic mechanism of cryptogenic stroke can be assumed, as well as that it can be paroxysmal AF. For these reasons, the Embolic Stroke of Undetermined Source (ESUS) has emerged as a separate entity among cryptogenic strokes in recent years (27). According to available data, as much as 14-30% of ESUS may be due to paroxysmal AF (11-14). The criteria for the diagnosis of ESUS are the presence of non-lacunar IS on head CT/MRI, the absence of extra/intracranial atherosclerosis narrowing the lumen > 50% in the irrigation area of ischemia, the absence of high-risk cardioembolic cause or other specific causes of IS (arteritis, dissection, vasospasm, etc.) (27). In order to confirm the ESUS, it is necessary to conduct a detailed etiological diagnosis of IS (head CT/MRI, ECG, transthoracic echocardiography, ECG monitoring > 24h with automatic rhythm detection, neurovascular imaging of extra and intracranial blood vessels).

The introduction of the ESUS concept intended to examine whether the introduction of NOACs in this particular group of patients is more effective in secondary prevention than antiplatelet therapy, which is currently the only recommended antithrombotic therapy in cryptogenic IS. The preterm completed NAVIGATE ESUS study did not show a higher efficacy of rivaroxaban compared to aspirin in patients with ESUS, while the risk of major bleeding in the rivaroxaban group was significantly higher, especially for intracranial hemorrhages (28). Neither dabigatran compared to aspirin did not show its advantage in patients with ESUS, but there was no difference in the risk of major bleeding between the two groups of patients (29). Given the results of these two studies, aspirin remains the only recommended therapy in patients with ESUS. It is possible that in selected groups of patients with ESUS, the NOACs may be effective. Thus, the sub-analysis of NAVIGATE ESUS showed that rivaroxaban was significantly more effective in patients with ESUS and PFO compared with aspirin (30). The ongoing studies compare the efficacy of apixaban with aspirin in patients with cryptogenic IS and atrial cardiopathy (ARCADIA) or their effectiveness in preventing the occurrence of new ischemic lesions on MRI over a period of 12 months (ATTICUS) (31,32).

When is the right time to introduce NOACs after acute IS?

The answer to this question is not easy to give, because in all RCT (RE-LY, ROCKET-AF, ARISTOTLE) the exclusion criterion for entering the study was TIA or IS in the previous 7-14 days, and in some of them the exclusion criterion was a severe stroke in the previous 3-6 months (17-19). Data from observational studies, as well as of control groups in RCT, indicate a high risk for early recurrence of stroke among patients with AF within the first 14 days, which is around 0.5 – 1.3% per day (22,33). On the other hand, in this early period, after large IS such as those in patients with AF, there is a high risk of HT which would be further increased with the introduction of therapeutic doses of anticoagulants (34).

The HAEST study did not show the superiority of dalteparin in the first 14 days from the onset of IS compared with aspirin in terms of preventing recurrence of IS, but there were no major hemorrhagic complications (35). A meta-analysis of subgroups of patients with AF in whom heparin was administered within the first 48 hours after the onset of IS did not show a significant reduction in the risk of stroke recurrence but did confirm the existence of a significantly increased risk of intracranial hemorrhage (36). However, one recent meta-analysis of 7 prospective cohort studies with 4912 patients with acute IS and AF showed that early introduction of NOACs (median 5 days) carries a significantly lower risk for ICH compared to VKA and this effect is present both in those with small (NIHSS ≤ 3) or severe neurological deficit (NIHSS > 15), older than 80 years or those treated with recanalization therapy (37).

There are expert opinions that in *patients with TIA or minor stroke* (< 1.5 cm) the introduction of NOACs should be similar to those of warfarin, and that they can be safely introduced after about 24 to 48 hours from the onset of TIA/IS (22). Their position is supported by the results of two small studies with early introduction of rivaroxaban and dabigatran in patients with minor stroke (38,39). In the study of Hong et al. no significant difference in the incidence of stroke recurrence or symptomatic hemorrhage was found between rivaroxaban and warfarin when administered within 5 days of the onset of minor IS (median NIHSS 2) (38). In the DATAS II study, there was no significant difference in the incidence of symptomatic parenchymal ICH when administering aspirin or dabigatran within the first 72 hours in patients with the previous minor IS (NIHSS < 9) (39). In patients with minor IS, prior administration of aspirin was not required given the results of an AVERROES study showing that apixaban was more effective than aspirin (40). Also, there is no need for overlap with low molecular weight heparins (LWH), because their use in the early phase of IS in patients with AF carries an increased risk of HT and they have a worse outcome compared to those in which only OAC is given (41).

In *patients with moderate to severe IS* and AF, the risk of developing ICH outweighs the benefit of anticoagulants in the first days after stroke onset. Most experts and guidelines state that NOACs should be started within 4 - 14 days from the onset of

IS, considering the degree of neurological deficit and the size of the infarction (21,22,41,42). In the absence of data from the RCT, a consensus was reached on the introduction of NOACs after IS in AF patients illustrated by the "1-3-6-12 day" rule (43) (Table III). In severe and disabling forms of IS, the use of NOACs can be delayed even after 2 weeks, with low dose aspirin given until their introduction (21,22,33). In deciding when to introduce NOACs, it may help to repeat head CT after about 5 - 7 days. If there is no HT, aspirin can be stopped and NOAC may be introduced, and in case of its presence, the use of NOACs is postponed and other risk factors for HT are considered.

Table III Time of NOACs introducing after acute ischemic stroke

Tabela III Vreme uvođenja NOAK posle akutnog ishemijskog moždanog udara

Severity of IS	Time of NOACs introduction
TIA	1 day, immediately after neuroimaging excludes ICH
Minor IS (NIHSS < 8)	3-5 days after stroke onset
Moderate IS (NIHSS 8-16)	5-7 days after stroke onset
Severe IS (NIHSS > 16)	After 2 weeks of stroke onset

NOACs non-vitamin K oral anticoagulants, TIA transient ischemic attack, IS ischemic stroke, ICH intracerebral hemorrhage

The of intravenous thrombolysis in the treatment of IS in patients on NOACs

The patients with acute IS are candidates for intravenous thrombolysis (IVT) in the first 4.5 hours of stroke onset. In patients on previous VKA therapy, IVT is recommended if the INR is less than 1.7 (42). However, in patients on NOACs there is no reliable quantitative coagulation test that would allow IVT to be used when its values are below a safe limit. In patients on dabigatran, prolonged aPTT of any value precludes the use of IVT. The specific tests of the anticoagulant effect of some NOACs take a long time for performing them, they are not routinely available, and some are qualitative tests. Only the complete absence of the anticoagulant effect of NOAC in these tests can enable the use of IVT.

Since the half-life of NOACs is between 8 and 17 hours, IVT administration could be safe after 24 hours and quite safe after 48 hours from the last dose of NOAC (2-4 times the half-life) (43-45). For patients with renal insufficiency, this period should be longer, up to 96 hours. In patients who have previously been on dabigatran, it is possible to use idarucizumab before IVT, if mechanical thrombectomy is not possible (45).

The NOACs and intracranial hemorrhage

The long-term use of OAC increases the risk of developing all types of intracranial hemorrhage (46). The greatest risk of developing intracranial hemorrhage is with older age, earlier IS, and concomitant use of antiplatelet therapy. Most of them are ICH and subdural hematomas, and less often they are subarachnoid hemorrhages or post-traumatic epidural hematomas (47). The use of NOACs in comparison with warfarin reduces the risk of intracranial hemorrhage by 33 - 70% depending on the medication and its dose (17-19). The NOACs-ICH compared to those induced by VKA have a smaller volume, a smaller initial neurological deficit with a lower incidence of severe ICH, have lower mortality, and a better functional outcome (48).

The initial approach in patients who developed intracranial hemorrhage during the use of NOACs implies an assessment of the effect of the drug, i.e. laboratory evaluation of their effect. Normal values of aPTT (dabigatran) or anti-Xa activity (apixaban, rivaroxaban) should question whether NOACs are the cause of intracranial hemorrhage. The efficacy and safety of the recommended measures in the event of major bleeding associated with NOACs are questionable when it comes to intracranial hemorrhage. The use of activated or inactivated prothrombin complex concentrate or with the significantly delayed effect fresh frozen plasma is recommended (21,49). If available, the use of idarucizumab as a specific reversing agent in dabigatran is recommended and haemodialysis may be useful (21).

Introduction of NOACs after intracranial hemorrhage

The reintroduction of OAC in a patient with AF and previous ICH depends on its etiology. Thus, if the intracranial hemorrhage was the result of a condition that can be controlled and treated (e.g. hypertensive hemorrhage), the reintroduction of OAC should be considered. On the other hand, in conditions with a continuously increased risk of bleeding (e.g. amyloid angiopathy), the indications for the reintroduction of OAC should be carefully weighed.

A retrospective analysis of patients with OAC - ICH showed that the reintroduction of OAC significantly reduced the risk of ischemic events by 3 times and did not increase the risk of hemorrhagic complications (50). The same analysis showed that patients in whom OAC were reintroduced have significantly greater long-term survival. These results were confirmed by a meta-analysis involving 7 studies with 2452 AF patients who had previously experienced intracranial hemorrhage associated with OAC (51). This analysis showed that OAC reintroduction carried a significantly lower risk of developing IS over 6 weeks to a year, without increasing the risk for ICH, compared to patients without antithrombotic therapy or those on antiplatelets (51). Another meta-analysis of approximately 1012 patients with ICH showed that the reintroduction of OAC significantly reduced the risk of death and the occurrence of IS regardless of whether it

was a lobar or non-lobar hematoma and that there was no significant increase in the risk of ICH recurrence in either of the two types of a hematoma (52).

The ESO guideline states that the reintroduction of OAC after ICH should be considered with a prior careful risk-benefit assessment (22.) The ESC guideline recommends reintroduction of OAC in patients with AF and previous OAC - ICH after about 4-8 weeks if the cardioembolic risk is high and the risk for intracranial hemorrhage small (21). The refrain of the OAC reintroduction in patients with previous intracranial hemorrhage and AF should stand when bleeding has occurred at adequate doses of OAC, in the elderly, in the presence of uncontrolled hypertension, lobar hematomas, an increasing number of CMB on MRI, chronic alcohol consumption, or the need for concomitant antiplatelet therapy (21). Although there are currently no studies comparing the reintroduction of VKA or NOAC after previous intracranial hemorrhage, the opinion of experts is that the less risky NOACs should be the choice in such cases (22).

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Ne-vitamin K oralni antikoagulansi (NOAK) kod bolesnika sa moždanim udarom i atrijskom fibrilacijom

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Kratak sadržaj

Bolesnici sa atrijskom fibrilacijom koji su preležali tranzitorni ishemijski atak ili ishemijski moždani udar imaju značajno povećan rizik za recidiv moždanog udara, zbog čega je neophodno uvesti oralne antikoagulanse. Ipak, dugotrajna primena oralnih antikoagulanasa povećava rizik od nastanka svih vrsta intrakranijalnih hemoragija. Prednost ne-vitamin K oralnih antikoagulanasa (NOAK) u odnosu na varfarin je da nose značajno manji rizik za hemoragijski moždani udar. Oni imaju prednost kod starijih osoba, kod bolesnika sa bolešću malih krvnih sudova mozga i kod pacijenata sa ranijom intracerebralnom hemoragijom. Vreme uvođenja NOAK posle ishemijskog moždanog udara zavisi od njegove težine i veličine i predloženo je da se upotrebljava pravilo “1-3-6-12” dana. Ponovno uvođenje NOAK kod bolesnika sa atrijskom fibrilacijom i prethodnom intracerebralnom hemoragijom zavisi od njenog uzroka i treba ih uvesti posle 4-8 nedelja ukoliko je kardioembolijski rizik velik, a rizik za intracerebralnu hemoragiju mali.

Ključne reči: ishemijski moždani udar, intrakranijalna hemoragija,
ne-vitamin K oralni antikoagulansi, atrijska fibrilacija
