

ATRIAL FIBRILLATION AND POSSIBILITIES OF STROKE PREVENTION

Milorad Žikić¹, Ognjen Novosel², Tamara Rabi Žikić³ and Marija Žarkov³

¹School of Medicine University of Novi Sad, Novi Sad, Serbia; ²“Novocard” Novosel, Health Institution Podgorica, Podgorica, Monte Negro; ³Department of Neurology, Clinical Center of Vojvodina, Novi Sad, Serbia

The morbidity and mortality associated with atrial fibrillation (AF) are related mainly to ischaemic stroke, and the prevention of thrombo-embolism is an important component of the patient management [1].

Hospital admissions caused by AF have increased by more than 60% in the last 20 years [2]. About 3% of the population over the age of 45, about 4% of the general adult populations and 6% over age 65 has AF. After the age of 55, and with other risk factors such as diabetes, high blood pressure, and underlying heart disease the incidence of AF increase to doubles with each decade of life [3], and the number of people with AF is expected to double by 2050 [4g].

One of the main complications of AF is stroke, which is 3 to 5 times greater than individuals without AF, and stroke cause by AF is typically hardest of the other podtype in all of ages groups [5].

It's estimated that AF is responsible for over 1500 strokes each year in Serbia, and 150 in Monte Negro, 1.5 times more frequently in males than in females.

Prevention of stroke related to AF has enormous important. AF is a major risk factor for cardioembolic stroke, and the most frequent cardial cause of stroke. Although AF is relatively hard to identification, stroke cause by AF is preventable. But, preventive measures are applied with a small number of patients. Up to three million people worldwide have a stroke related to AF every year, that is one person every 12 seconds! [6].

The different types of AF i.e. the classification system in the direction of ESC 2010 Guidelines for the management of patients with AF are: first detected - only one diagnosed episode, paroxysmal - recurrent episodes that self-terminate in less than 7 days, persistent - recurrent episodes that last more

than 7 days, require cardio-conversion, long-standing persistent - \geq 1 year duration, and permanent - an ongoing long-term episode, to take from patient and doctor [7].

Diagnosis of AF is based on factors such as: signs/symptoms, physical examination, and specific diagnostic studies that are used to confirm the presence of the condition. AF is diagnosed by the doctor using a stethoscope in the first instance. This will probably be followed by an ECG which will confirm the irregularity of the heartbeat.

Sometimes the patient wears a heart monitor for 24 hours or even more. This will

detect any abnormal heart beats that may be caused by AF by recording all heart activity over a prolonged period. It is not always possible to rely on the pulse beat felt in the wrist to detect AF as not only will the heart beat irregularly, many heartbeats which can be heard by listening to the heart cannot be distinguished at the wrist. They do not reach the wrist because the heart, contracting weakly, has not adequately filled with blood.

According to the Framingham Offspring Study 2040 asymptomatic patients (without clinical signs for stroke) had MRI signs for ischemic stroke. The minimum of 1 silent stroke was to find with 10.7% patients. The important numbers of silent stroke was become associated with AF [8]. A silent stroke increase risk for stroke and for dementia, therefore existance of silent ischemia (infarct or lesion in white masse): increase risk of stroke for over than 3 time, independent risk factors from the others, and increase risk of dementia 2,3 time, and become associated with higher damage of cognitive function [9].

AF is a worst prognostic sign for hard stroke and early die exit. Analyzed result of

85 patients with or without AF in the base of ischemic stroke after IV t-PA, after 7 and 90 days, group with AF was worst result - basic NIHSS was higher, having frequently of artery occlusion at the basic MRA, and 2,3% symptomatic ICH on AF patients after IV t-PA [10]. Except that, in one of the other study with 49 patients analyzed early recanalization after IV t-PA and neurological status (NIHSS): 51,3% patients no early recanalization, 0/18 patients with recanalization had worsening of neurologic status, 4/19 was without recanalization were worsening ($p=0,039$), and concluded that AF are an independent predictor for no recanalization [11].

Approximately 20% of all strokes are caused by embolism. If left untreated, AF can increase your stroke risk from 4 to 6 times. Long-term untreated AF can also weaken the heart, leading to potential heart failure [12].

Major studies on AF have shown no real difference in mortality between rhythm- and rate-control strategies. However, a rhythm-control strategy is sometimes needed to help control symptoms. Recent data from clinical trials and registries suggest that agents with both rhythm- and rate-controlling properties are effective at maintaining sinus rhythm, avoiding cardiac and extracardiac side effects and improving quality of life [13].

Until recently, vitamin K antagonists (VKAs) and aspirin were the only agents available for the prevention of AF related stroke. However, many patients eligible for anticoagulant therapy simply did not receive it. In addition, maintaining patients on VKAs within their target international normalized ratio range can be challenging in real-world practice. Recently, results have been reported for RE-LY and ROCKET-AF trials of novel oral anticoagulant agents in the prevention of AF related stroke. These agents offer the promise of addressing many of the challenges in VKA therapy with the hope of improving patient care (14).

For the patients with AF diagnosis it's a necessary education about AF in order to improve diagnosis and management. Education AF patients about stroke signs, as well as to plan eventual transport in emergency to the nearest stroke unit in order to receive acute stroke treatment, preparing food workshops based on warfarin diet information and safe recipes [15].

The choice of optimum antithrombotic therapy for a given patient depends on the risk of thromboembolism, and the assessment of thrombo-embolic risk using validated stratification schemes, such as the CHADS2 score, is a critical step. Improved stratification schemes are needed that take into account the risk of intracerebral haemorrhage, which is the most worrisome complication of anticoagulant therapy. The pattern of AF (paroxysmal, persistent, or permanent) should not influence the selection of antithrombotic treatment. Similarly, successful rhythm control is not a sound basis for withdrawing antithrombotic treatment, and whether this situation differs after successful catheter ablation of AF has not been established. At present, oral vitamin K antagonists alone are recommended for patients with AF at moderate-to-high risk of stroke. A combination of anticoagulant and antiplatelet drugs is necessary in patients with AF undergoing percutaneous coronary intervention and stent implantation, but the optimal therapeutic management of these patients has not been defined. The development of new antithrombotic agents that are easier to use and have a superior benefit-to-risk ratio will extend treatment to a greater proportion of the AF population at risk. The large number of phase III trials currently investigating specific inhibitors of thrombin or factor Xa that do not require laboratory monitoring suggests that this goal is within reach (1).

Frequent of illness, and structure of the patients in the Serbian Experience with Thrombolysis in Ischemic Stroke (SETIS) were as follow: patients with AF participate with 18% (425 patients - 75 with AF), 29 females in group with AF vs 119 in the others diagnostic categories, and 46 males with AF vs 231 with others diagnosis ($\chi^2 0,59$; $p < 0,1$), averages age 65,12 in group with AF vs 56,66 in the others diagnostic categories ($t 6,61$; $p < 0,0001$). Initial indicators, and early course of disease in the field of initial clinical status for basic NIHSS were 14,9 among patients with AF, and 12,9 for the others ($t 3,29$; $p 0,0012$), initial radiologic status with ASPECTS were 9,05 among patients with AF vs 9,52 for the others ($t -3,42$; $p 0,0009$), the time to begin of the threatment were 161 minutes among AF patients, and 166 minutes for the others ($t -0,78$; $p 0,43$). Finally, early course of the treatment were with NIHSS after 24 hours 10,68 in the AF group, and 8,33 in the others diagnostics cat-

egories (t 2,17; p 0,032). Among complications haemorrhage was important frequently on patients with AF (χ^2 8.61; $p < 0.01$), asymptomatic haemorrhage 9 in the AF group vs 32 in the others (χ^2 0.57; $p > 0,1$), and symptomatic haemorrhage 11 in the AF group vs 14 in the others (χ^2 12.65; $p < 0,001$). Die exit were in 19% with AF patients vs 12% in the group with others diagnostic categories (χ^2 2.81; $p > 0,05$). State after three months e.i. recovery after 90 days were in AF group in 47% favorable vs 53% unfavorable, and in the group with the others diagnostic categories in 56% favorable vs 44% unfavorable results (χ^2 2.16; $p > 0,1$).

In conclusion notes it's can says that thrombolysis in patients with AF is equal

efficasse as in the others patients from SETIS base. In addition, thrombolysis in patients with AF is less safe in relation on the others patients, to take into consideration important bigger number of symptomatic ICH, which isn't brought to higher lethality after 90 days. Reasons for less safety of thrombolize in patients with AF can be come from facts: that patients with AF and stroke are important older, and they have important basic neurologic deficit, and bigger brain infarct [16].

The most recent raport about treatment with the 150-mg twice daily dose of dabigatran etexilate is equally safe and effective in patients with permanent, persistent, and paroxysmal atrial fibrillation, according to a new subgroup analysis of the Randomized Evaluation of Long-Term Anticoagulant Therapy (RE-LY) trial. The results were presented at the American College of Cardiology (ACC) 2011 Scientific Sessions at the begining of April 2011.

Like the overall results from the 18 000-patient study, dabigatran 150 mg twice daily was more effective than warfarin for reducing the risk of stroke or systemic embolism, with a comparable risk of bleeding, compared with the older anticoagulant.

Investigators did observe slightly different responses among patients treated with the 110-mg twice-daily dose, however, with dabigatran most effective in patients with paroxysmal AF and less so in patients with permanent AF.

Among patients with permanent AF treated with the lower dose of dabigatran, the hazard ratio for the risk of stroke/systemic embolism was 1.13 (95% CI 0.81-1.57), while there was a significant 40% rela-

tive reduction in risk among paroxysmal-AF patients treated with dabigatran 110 mg twice daily [17].

References

1. HOHNLOSER SH, et al. Prevention of stroke in patients with atrial fibrillation: current strategies and future directions. *Eur Heart J Suppl* 2008; 10 (suppl H) : H4-H10.
2. FRIBERG J, et al. Rising rates of hospital admissions for atrial fibrillation. *Epidemiology* 2003; 14:666-72.
3. LAKSHMINARAYAN K, et al. Atrial fibrillation and stroke in the general medicare population: a 10-year perspective (1992 to 2002). *Stroke* 2006;37:1969-74.
4. MIYASAKA Y, et al. Secular trends in incidence of atrial fibrillation in projections for future prevalence. *Circulation* 2006; 114:119-125.
5. DULLI DA, et al. Atrial fibrillation is associated with severe acute ischemic stroke. *Neuroepidemiology* 2003;22:118-23
6. Media Fact Sheet: 1 Mission 1 Million – Getting to the Heart of Stroke <http://search.incredimail.com/> (available April 14. 2011, 15:56)
7. ESC 2010 Guidelines for the Management of Patients with Atrial Fibrillation. *European Heart Journal* doi: 10.1093/eurheart/ehq278
8. DAS RR, et al. Prevalence and correlates of silent cerebral infarcts in the Framingham offspring study. *Stroke* 2008; 39(11):2929-35.
9. JAE-SUNG L AND HYUNG-MIN K. Risk of “silent stroke” in patients older than 60 years: risk assessment and clinical perspectives. *Clin Interv Aging*. 2010; 5: 239–251.
10. ŠANAK D. et al. Is atrial fibrillation associated with poor outcome after thrombolysis? *J. Neurol.* 2010; 257 (6):999-1003.
11. KIMURA K, et al. Atrial fibrillation as an independent predictor for no early recanalization after IV-t-PA in acute ischemic stroke. *J Neurol Sci* 2008;267(1):57-61.
12. Website: www.BISociety.org Brain Injury Society Bikur Cholim (available April 14. 2011, 14:45)
13. The heart.org Realizing the Burden of AF: A Hard Look at Quality of Life and Hospitalization. <http://www.theheart.org/article/> (available April 14. 2011, 14:54)
14. The heart.org A Multidisciplinary Approach to AF-Related Stroke:Building a Consensus to Improve Patient Care <http://www.theheart.org/documents/> (available April 14. 2011, 15:01)
15. Mayo Clinic. Atrial Fibrillation. <http://www.mayoclinic.org/atrial-fibrillation/rsttreatment>.(available April 14. 2011, 15:15)
16. ŽARKOV M. Trombolysis and atrial fibrillation - is the cause has influence at the exit. 4th Symposium of CVD, Belgrade 26-28. Oct 2010. Authorized invited lecture.
17. Multidisciplinary Approach to AF-Related Steoke. Dabigatran 150 mg twice daily effective in all types of AF; lower dose and cost issues questioned. <http://www.theheart.org/article/> (available April 18. 2011, 01:35)