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# ATRIAL FIBRILLATION AS A RISK FACTOR FOR STROKE

# ATRIJALNA FIBRILACIJA KAO RIZIK ZA MOŽDANI UDAR

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***Abstract:*** *Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia, occurring in 1–2% of the general population. AF confers a 5-fold risk of stroke, and one in five of all strokes is attributed to this arrhythmia. Ischemic strokes in association with AF are often fatal, and those patients who survive are left more disabled by their stroke and more likely to suffer a recurrence than patients with other causes of stroke. The prevalence of AF increases with age. Men are more often affected than women. AF is associated with a variety of cardiovascular conditions: valvular heart diseases, cardiomyopathies, including primary electrical cardiac diseases, which carry an increased risk for AF, especially in young patients. Atrial septal defect is associated with AF in 10–15%. This association has important clinical implications for the antithrombotic management of patients with a previous stroke or transient ischemic attack (TIA) and an atrial septal defect. AF may manifest initially as an ischemic stroke or TIA, and it is reasonable to assume that most patients experience asymptomatic, often self-terminating, episodes of arrhythmia, before AF is first diagnosed. Most patients with acute AF will require anticoagulation unless they are at low risk of thromboembolic complications (no stroke risk factors) and no cardioversion is necessary. Much earlier detection of the arrhythmia might allow the timely introduction of therapies to protect the patient, not only from the consequences of the arrhythmia, but also from progression of AF from an easily treated condition to an utterly refractory problem.*

***Key words****: atrial fibrillation, ischemic stroke, antithrombotic management*

***Sažetak:*** *Atrijalna fibrilacija (AF) je najčešća srčana aritmija sa prevalencom od 1-2% u opšto populaciji. Nosi petostruki rizik za moždani udar, i svaki peti moždani udar se pripisuje ovoj artimiji. Ishemijski moždani udar (IMU) zajedno sa AF je često fatalan, a oni pacijenti koji prežive imaju teže posledice i veću verovatnoću da dobiju recidiv nego bolesnici drugih uzroka moždanog udara. Prevalenca AF povećava se starenjem. Muškarci su češće pogođeni nego žene. AF je povezana sa različitim kardiovaskularnim stanjima, kao valvularnim bolestima srca i kardiomiopatijama, što sve povećava rizik za AF posebno u mladih bolesnika, dok je atrijalni septalni defekt povezan sa AF u 10-15% bolesnika. Ovo ima važne kliničke implikacije za upotrebu antitrombotskih lekova u bolesnika sa IMU ili tranzitornim ishemijskim atakom (TIA). AF se može registrovati u početku kod IMU ili TIA i zato je racionalno pretpostaviti da je većina pacijenata imala asimptomatsku AF koja je često spontano prestala. Većina pacijenata s akutnom AF će zahtevati antikoagulantnu terapiju, osim ako imaju nizak rizik od tromboembolijskih komplikacija i ne zahte-*

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*vaju kardiokonverziju. Rano otkrivanje aritmija može omogućiti pravovremeno uvođenje terapije kako bi zaštitili pacijenta, ne samo od posledica aritmije, već i za nastajanje hronične AF.*

***Ključne reči:*** *atrijalna fibrilacija, ishemijski moždani udar, antitrombocitna terapija*

## INTRODUCTION

The problem of early recognition of atrial fibrillation (AF) is greatly aggravated by the often 'silent' nature of the rhythm disturbance. In about one third of patients with this arrhythmia, the patient is not aware of the so-called "asymptomatic AF". Much earlier detection of the arrhythmia might allow the timely introduction of therapies to protect the patient, not only from the consequences of the arrhythmia, but also from progression of AF from an easily treated condition to an utterly refractory problem. AF confers a 5-fold risk of stroke, and one in five of all strokes is attributed to this arrhythmia. Ischemic strokes in association with AF are often fatal and those patients who survive are left more disabled by their stroke and more likely to suffer a recurrence than patients with other causes of stroke. In consequence, the risk of death from AF-related stroke is doubled and the cost of care is markedly increased (1-7). Most cases of atrial fibrillation can be attributed to diseases that affect the structure of the heart over many years, which is one of the main reasons why atrial fibrillation is most common in older adults. Disorders that can lead to atrial fibrillation include diseases of the heart valves (such as rheumatic heart disease), mitral stenosis, ischemic heart disease, diseases of the electrical conduction system of the heart (such as sick sinus syndrome) etc. Also, many other conditions can cause AF, such as hyperthyroidism. Atrial fibrillation can also be induced by emotional or physical stress, alcohol, nicotine, and caffeine. People with atrial fibrillation often report palpitation. For some, this rapid and disorganized heart beat may be so extreme that blood flow through the heart chambers is profoundly impaired. This may cause fainting, chest pain or even a temporary choking sensation (5-8).

### Epidemiology, patophysiology and clinical picture

AF is the most common sustained cardiac arrhythmia, occurring in 1–2% of the general population. Over 6 million Europeans suffer from this arrhythmia, and its prevalence is estimated to at least double in the next 50 years as the population ages (1-8). In patients with acute stroke systematic electrocardiographic (ECG) monitoring would identify AF in 1 in 20 subjects. AF may long remain undiagnosed (silent AF), and many patients with AF will never present to hospital. Hence, the "true" prevalence of AF is probably closer to 2% of the population (1-8). The prevalence of AF increases with age, from 0.5% at 40–50 years, to 5–15% at 80 years. Men are more often affected than women. AF is associated with increased rates of death, stroke and other thromboembolic events, heart failure and hospitalizations, degraded quality of life, reduced exercise capacity and left ventricular dysfunction. Death rates are doubled by AF, independently of other known predictors of mortality. Only antithrombotic therapy has been shown to reduce AF-related deaths. Stroke in AF is often severe and results in long-term disability or death. Approximately every fifth stroke is due to AF, furthermore, undiagnosed "silent AF" is a likely cause of some cryptogenic strokes (1-12). Paroxysmal AF carries the same stroke risk as permanent or persistent AF. Hospitalizations due to AF account for one-third of all admissions for cardiac arrhythmias. Cognitive dysfunction, including vascular dementia, may be related to AF. Some observational studies suggest that asymptomatic embolic events may contribute to cognitive dysfunction in AF patients in the absence of an overt stroke (4,11,12). Quality of life and exercise capacity are impaired in patients with AF. Patients with AF have a significantly poorer quality of life compared with healthy controls, the general pop-

ulation, or patients with coronary heart disease in sinus rhythm. Conditions associated with AF are also markers for global cardiovascular risk and/or cardiac damage rather than simply causative factors. Ageing increases the risk of developing AF, possibly through age-dependent loss and isolation of atrial myocardium and associated conduction disturbances. Heart failure can be both a consequence of AF and a cause of the arrhythmia due to increased atrial pressure and volume overload, secondary valvular dysfunction, or chronic neurohumoral stimulation. While rheumatic AF was a frequent finding in the past, it is now relatively rare in Europe. Atrial septal defect is associated with AF in 10–15% of patients. This association has important clinical implications for the antithrombotic management of patients with previous stroke or transient ischemic attack (TIA) and an atrial septal defect. AF is defined as a cardiac arrhythmia with the following characteristics: the surface ECG shows absolutely irregular RR intervals (AF is therefore sometimes known as arrhythmia absoluta), RR intervals that do not follow a repetitive pattern. There are no distinct P waves on the surface ECG. Any episode of suspected AF should be recorded by a 12-lead ECG of sufficient duration and quality to evaluate atrial activity. Occasionally, when the ventricular rate is fast, atrioventricular nodal blockade during the Valsalva maneuver, carotid massage, or intravenous adenosine administration can help to unmask atrial activity. An irregular pulse should always raise the suspicion of AF, but an ECG recording is necessary to diagnose AF. Any arrhythmia that has the ECG characteristics of AF and lasts sufficiently long for a 12-lead ECG to be recorded, or at least 30 s on a rhythm strip, should be considered as AF.

## Management of atrial fibrillation and risk of stroke

AF may manifest initially as an ischemic stroke or TIA, and it is reasonable to assume that most patients experience asymptomatic, often self-terminating, arrhythmia episodes before AF is first diagnosed. AF can present as symptomatic or asymptomatic as well as paroxysmal, persistent, long-standing and permanent atrial fibrillation (4,9). Paroxysmal AF is self-terminating, usually within 48 hours. Although AF paroxysms may continue for up to 7 days, the 48-hour time point is clinically important - after this the likelihood of spontaneous conversion is low and anticoagulation must be considered. Persistent AF is present when an AF episode either lasts longer than 7 days or requires termination by cardioversion, either with drugs or by direct current cardioversion (DCC). Long-standing persistent AF has lasted for ≥1 year when it is decided to adopt a rhythm control strategy. Permanent AF is said to exist when the presence of the arrhythmia is accepted by the patient (and physician). Hence, rhythm control interventions are, by definition, not pursued in patients with permanent AF. Should a rhythm control strategy be adopted, the arrhythmia is redesignated as 'longstanding persistent AF'. This classification is useful for clinical management of AF patients, especially when AF-related symptoms are also considered. Silent AF (asymptomatic) may manifest as an AF-related complication (ischemic stroke or tachycardiomyopathy) or may be diagnosed by an opportunistic ECG. Silent AF may present as any of the temporal forms of AF (4,9,10). In patients with suspected AF, a 12-lead ECG is recommended as the first step to establish the diagnosis, and 24-hour ECG monitoring (Holter recording) should be considered (4,9,10). Clinical evaluation should include determination of the European Heart Rhythm Association (EHRA) score, for estimation of stroke risk, and search for conditions that predispose to AF and for complications of the arrhythmia. EHRA score provides a simple clinical tool for assessing symptoms during AF, divided in four classes (EHRA I-IV: no, mild, severe, and disabling symptoms). A very similar scale has been validated by the Canadian Cardiovascular Society. The EHRA score only considers symptoms that are attributable to AF and reverse or reduce upon restoration of sinus rhythm or with effective rate control. The time of onset of the arrhythmia episode should be established to define the type of AF. Most patients with AF 48 h in duration can be cardioverted on low-molecular-weight heparin (LMWH) without risk for stroke. If AF duration is 48 h or there is doubt about its duration, transthoracic echocardiography or transesophageal echocardiography may be used to rule out intracardiac thrombi prior to cardioversion, although it can be difficult in patients in acute distress and may not be available in emergency settings. Patients should be assessed for risk of stroke. Most patients with acute AF will

require anticoagulation unless they are at low risk of thrombo-embolic complications (no stroke risk factors) and no cardioversion is necessary (e.g. AF terminates within 24–48 h). After the initial management of symptoms and complications, underlying causes of AF should be sought. Management of AF patients is aimed at reducing symptoms and at preventing severe complications associated with AF. These therapeutic goals need to be pursued in parallel, especially upon the initial presentation of a newly detected AF. Prevention of AF-related complications relies on antithrombotic therapy, control of ventricular rate, and adequate therapy of concomitant cardiac diseases. These therapies may already alleviate symptoms, but symptom relief may require additional rhythm control therapy by cardioversion, antiarrhythmic drug therapy, or ablation therapy (11-26). Extensive evidence was used to monitor the usage of antithrombotic therapy, anticoagulants and LMWH (12-32). Also, risk stratification for stroke and thrombo-embolism is necessary. The simplest risk assessment scheme is the $CHADS_2$ score (9). The $CHADS_2$ calculates the following: the presence of cardiac failure, hypertension, age, diabetes, and stroke. It is a point system where each figure is assigned as one point except stroke, which is assessed double. Thus, the $CHADS_2$ stroke risk stratification scheme should be used as an initial, rapid, and easy-to-remember means of assessing stroke risk. The original validation of this scheme classified a $CHADS_2$ score of 0 as low risk, 1–2 as moderate risk, and 2 as high risk. In patients with a $CHADS_2$ score ≥2, chronic oral anticoagulant therapy with a vitamin K antagonists (VKA) is recommended in a dose-adjusted approach to achieve an international normalized ratio (INR) target of 2.5 (range, 2.0–3.0), unless contraindicated. This risk factor-based approach for patients with non-valvular AF can also be expressed as an acronym, $CHA_2DS_2$-VASc (congestive heart failure, hypertension, age ≥75 /doubled/, diabetes, stroke /doubled/, vascular disease, age 65–74, and sex category/female/). This scheme is based on a point system in which 2 points are assigned for a history of stroke or TIA, or age ≥75 and 1 point each is assigned for age 65–74 years, a history of hypertension, diabetes, recent cardiac failure, vascular disease (9). Guidelines suggest that if one 'major' risk factor or >2 'clinically relevant non-major' risk factors are present (score > 2) oral anticoagulant therapy (OAC) is recommended. If one 'clinically relevant non-major' risk factor (score 1) is present, either OAC or aspirin 75-325 mg daily is recommended, however OAC is preferred rather than aspirin. If no risk factors are present (score 0) either aspirin 75-325 mg daily or no antithrombotic therapy is recommended, however, no antithrombotic therapy is preferred to aspirin (9). In all cases where oral anticoagulant therapy is considered, a discussion with the patient is obligatory, concerning evaluation of the risk of bleeding complications and patient's ability to safely sustain adjusted chronic anticoagulation. In patients with AF and an acute TIA, OAC therapy should be considered as soon as possible in the absence of cerebral infarction or hemorrhage. In some patients with one 'clinically relevant non-major' risk factor, e.g., female patients aged <65 years with no other risk factors, aspirin may be considered rather than OAC therapy. When surgical procedures require interruption of OAC therapy for longer than 48 h in high-risk patients, unfractionated heparin or subcutaneous LMWH may be considered. In patients with AF who sustain ischemic stroke or systemic embolism during treatment with usual intensity anticoagulation with VKA (INR 2.0–3.0), raising the intensity of the anticoagulation to a maximum target INR of 3.0–3.5 may be considered, rather than adding an antiplatelet agent (9).

## CONCLUSION

Atrial fibrillation is the most common sustained cardiac arrhythmia. Ischemic stroke in association with AF is often fatal and those patients who survive are left more disabled by their stroke and more likely to suffer a recurrence than patients with other causes of stroke. Permanent search for atrial fibrillation as well as estimation of risk factors for our patients is mandatory, in order to prevent complications and provide adequate therapy.

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