ARTYKUŁ POGLĄDOWY / REVIEW PAPER
Otrzymano/Submitted: 20.08.2021 • Zaakceptowano/Accepted: 01.09.2021

Pathogenesis, diagnosis, treatment, and clinical implications of atrial fibrillation in the elderly

Patogeneza, diagnostyka, leczenie i implikacje kliniczne migotania przedsionków u osób starszych

Krzysztof Młodziński, Michał Świątczak, Grzegorz Raczak, Monika Chmielecka, Ludmiła Daniłowicz-Szymanowicz

II Klinika Kardiologii i Elektroterapii Serca, Gdański Uniwersytet Medyczny, Gdańsk, Polska

Streszczenie

Migotanie przedsionków to tachyarytmia nadkomorowa, charakteryzująca się nieskoordynowaną aktywnością przedsionków i przeważnie szybkim rytmem komorowym. 22,6% osób powyżej 65 roku życia cierpi na migotanie przedsionków, a częstość ta wzrasta wraz z wiekiem. Zakres objawów prezentowanych przez pacjentów z migotaniem przedsionków jest szeroki, od pacjentów całkowicie bezobjawowych po osoby niestabilne hemodynamicznie. Stosunkowo częsty brak objawów w tej grupie pacjentów sprawia, że choroba ta jest szczególnie niebezpieczna, gdyż znacząco zwiększa ryzyko powikłań zakrzepowo-zatorowych. Ryzyko to znacznie wzrasta, jeśli pacjent nie przyjmuje leków przeciwzakrzepowych, które są kluczowe w zapobieganiu udarom niedokrwiennym mózgu. Podstawową metodą diagnozowania arytmii jest EKG, a w celu zmniejszenia nasilenia objawów choroby konieczna jest właściwa kontrola rytmu komorowego. *Geriatria 2021; 15: 148-157. doi: 10.53139/G.20211518*

Słowa kluczowe: migotanie przedsionków; arytmia nadkomorowa; zaburzenia rytmu serca; osoby starsze

Abstract

Atrial fibrillation is a supraventricular tachyarrhythmia, characterized by uncoordinated atrial activity and predominantly rapid ventricular rhythm. 22,6% of people over 65 years of age suffer from atrial fibrillation, and the frequency increases with age. The range of symptoms presented by patients with atrial fibrillation is wide, from completely asymptomatic patients to hemodynamically unstable people. The relatively frequent absence of symptoms in the group of patients makes this disease particularly dangerous, as it significantly increases the risk of thromboembolic complications. The risk significantly increases if the patient is not taking anticoagulants, which are essential in preventing ischemic stroke. The primary method used to diagnose atrial fibrillation is an ECG. To reduce the severity of the symptoms of the disease the proper control of the ventricular rhythm is required. *Geriatria 2021; 15: 148-157. doi: 10.53139/G.20211518*

Keywords: atrial fibrillation; supraventricular arrhythmia; cardiac arrhythmia; elderly

Introduction

Atrial fibrillation (AF) is an example of a supraventricular tachyarrhythmia in which, due to uncoordinated atrial activity and predominantly rapid ventricular rhythm, there is a reduction in the filling of the ventricles with blood and, consequently, a reduction in cardiac output. AF, depending on its duration, is divided into diagnosed for the first time, paroxysmal, persistent, long-lasting and permament [1]. It is the most common arrhythmia, more common in men's population, the incidence increases with age, and is currently estimated to occur in approximately 2,9% of the adult population. Among people in the 60-69 age group, 4,2% of the population is affected, and among those in the 70-79 age group, 9,7%, and in the 80-89 age group – 13,4% [2]. According to the NOMED-AF study, as many as 22,6% of people aged ≥65 suffer from AF. It is estimated that by 2050 about 6-12 million people will suffer from AF in the US, while in Europe by 2060 it is predicted to be 17,9 million people [3]. One of the most important

modifiable factors in the development of AF Is the common arterial hypertension. The range of symptoms presented by patients with AF is very wide, from completely asymptomatic patients not experiencing arrhythmia, to hemodynamically unstable people requiring urgent hospitalization. The relatively frequent absence of symptoms in the group of patients makes this disease particularly dangerous, as it significantly increases the risk of thromboembolic complications, such as, for example ischemic stroke, the risk significantly increases if the patient is not taking anticoagulants. The primary method used to diagnose AF is an ECG.

The following paper aims to summarize the current knowledge on the management of AF with particular emphasis on the geriatric population.

Pathogenesis and risk factors of atrial fibrillation

There are many reasons which affect the development of AF. The most common risk factors include the following units: obesity, arterial hypertension, atrial fibrosis, hyperthyroidism or electrolyte disturbances [4,5].

Previous studies indicate that AF arises from the development of local inflammation among atrial cardiomyocytes, which leads to their remodeling, changing their structure and electrical activity [4]. The most important inflammatory biomarkers associated with AF are C-reactive proteins (CRP), interleukins (IL) and miRNAs, the latter of which is attributed to the regulation of atrial remodeling [4,6,7]. The relationship between the increase in CRP protein concentration and the occurrence and the recurrence of AF after ablation or cardioversion has been shown [7,8]. In the case of interleukins, interleukin-6 (IL-6) has been shown to play the greatest role, its increase has been observed in people at increased risk of developing AF and also after ablation or cardioversion [7].

Atrial fibrosis

Atrial fibrosis is a significant factor in increasing the risk of AF. It may be caused by apoptosis of cardiomyocytes and the proliferation of fibroblasts at the site of damaged heart muscle cells, which then differentiate into myophybroblasts and produce extracellular matrix. This process ultimately slows down the conduction of excitation within the conductive system and increases the heterogeneity of the resulting impulses within the atrial muscle, which in return contributes to the development of the reentry wave and leads to the persistence of atrial fibrillation [7,9]. Fibroblast proliferation is regulated by extracellular calcium-dependent kinase (ERK), which increases the survival of fibroblasts and enhances fibrosis [10]. Additionally, fibroblasts show increased expression of potassium channels that lead to their hyperpolarization, increasing the influx of calcium ions into the cell and contributing to the promotion of the formation of new fibroblasts [9]. Atrial fibrosis may also develop in the course of comorbidities such as heart failure, hypertension or obesity and contribute to the development of AF. Many signaling pathways are involved in this process, several of them being the proinflammatory cytokine pathway, oxidative stress, TGF beta1 or the RAAS system [5,11]. Factors that inhibit or slow down this process are ACEI, statins or n-3 polyunsaturated fatty acids [5,12]. It has been shown that the degree of atrial fibrosis in magnetic resonance imaging using the late postcontrast enhancement technique (LGE-MRI) correlates with the incidence of AF as well as the incidence of risk factors for this disease [5,13]. The degree of fibrosis is defined by the ratio of the altered structure to the unvaried left atrium expressed as a percentage.

Obesity

Obesity is another important element in the development of AF. Three processes contribute to this. The first is the atrial fibrosis discussed above, the next is the increase in epicardial adipose tissue, and the last is the tendency of epicardial fat cells to infiltrate between the atrial myocytes. The epicardial adipose tissue undergoes hypoxia during accumulation and releases, among others, adipokines from the TGF beta family, and these in turn are one of the factors in the development of inflammation and, consequently, atrial fibrosis. The cause of the inflammatory reaction and the release of adipokines among obese people are factors such as the lack of a fascia between the fatty tissue of the heart and the muscle of this organ, and the shared blood supply to the muscle and adipose tissue. As a result, M1 macrophages penetrate into adipose tissue, which initiate the development of an immune reaction in the body, leading to the release of inflammatory mediators, which reach the atria, promoting the development of local inflammation and fibrosis of the atrial tissue [4,14]. This is evidenced by studies in which a higher activity of inflammation has been proven in people with AF than in healthy people [4,15]. In addition, adipocytes penetrating between the atrial cardiomyocytes contribute to their

isolation and the formation of unsynchronized stimuli, or even a reentry wave. Obesity is also associated with an increased concentration of free fatty acids in the body, which may accumulate in cardiomyocytes, leading to their apoptosis and fibrosis, increasing the risk of AF [4,16]. An important aspect of obesity is also dysfunction of the autonomic system associated with significant activity of epicardial adipose tissue, in which there are vagus nerve plexuses and sympathetic system plexuses. This tissue, due to the excessive release of inflammatory mediators, leads to the stimulation of both elements of the autonomic system, which in turn leads to a shortening of the impulse conduction time and an increase in the calcium current in the atrial muscle, which causes delayed post depolarization leading to arrhythmias [6]. It is noteworthy that epicardial adipose tissue deposits were determined as a predictor of AF of higher importance than left atrial weight or patient weight to height ratio [5,17].

Hypertension

Hypertension (HT) and AF often coexist. In the case of fresh cases of AF, approximately 20% of patients had already diagnosed HT, while in patients with chronic AF, hypertension was present in approximately 60-80% [18]. HT contributes to the thickening of the left atrial wall, its fibrosis and diastolic dysfunction, which leads to an increase in left atrial pressure. This results in a deterioration of the stroke volume of the left atrium to the left ventricle, ultimately leading to complete remodeling of the atrial structure and, consequently, to AF [19,20]. Two studies from Framingham were crucial to conclude HT as a risk factor of AF [21,22]. The first one showed that the deterioration of the left atrium function was more influenced by systolic than diastolic pressure. In the second case, it was proved that the risk of AF increases in direct proportion to the dimensions of the left atrium and its wall thickness, and inversely proportional to the decrease in left atrial stroke volume. It is unclear whether the risk of developing AF increases with increasing blood pressure (BP), but it has been observed that people with BP >150 mmHg have twice the risk of developing AF compared to people with BP between 120 and 129 mmHg [20]. On the other hand, paradoxically, within group of people with BP <120 mmHg there was increased risk of AF in contrary to participants with BP 140 to 149 mmHg where the risk was not significant [23]. Considering HT as a risk factor, one of the most common causes of primary arterial hypertension is primary aldosteronism, which increases the risk 12 times compared to people with secondary hypertension [24]. This process is caused by progressive atherosclerosis of the coronary arteries and, consequently, reduced blood supply to the heart muscle, atrial fibrosis and dysfunction of calcium channels in atrial cardiomyocytes, which results in electrical remodeling and electrical impulse conduction dysfunction in this part of the heart and thus the development of AF [25].

Hyperthyroidism

Hyperthyroidism is another predisposing factor to the development of AF. The prevalence of AF in people with hyperthyroidism ranged from 10% to 25%, of which only 5% were under 60 [26]. In such patients, the persistent form is more common than the paroxysmal one [26]. Patients aged ≥60 years should be regularly examined for changes in thyroid hormones due to the significant risk of developing AF in people with subclinical hyperthyroidism compared to those without this disease (28% vs 11%) [27]. The mechanism of AF development in people with hyperthyroidism is complex and may be associated with increased left atrial pressure, increased left ventricular mass and deterioration of its diastolic function, decreased blood supply to the heart muscle due to an increase in resting heart rate or an increase in ectopic activity in the atria [26].

Electrolyte disturbances

Electrolyte disturbances can also cause AF. In elderly patients, they are caused by two factors. The first is the impairment of the feeling of thirst, which increases with age, and contributes to the dehydration of the patient. The second reason is the chronic use of medications, which often contribute to the development of these disorders [28]. Additionally, in the elderly, the number of potassium channels in the atrial cardiomyocytes increases and the activity of L-type calcium channels decreases, which increases the risk of developing AF [29]. The imbalance of the electrolyte balance between both parts of the cell leads to a disturbance of the coherence of the depolarization and repolarization phases, which lowers the threshold for arrhythmia, ultimately contributing to its persistence [30].

Symptoms of atrial fibrillation

In most cases, AF is asymptomatic, it may be due to slower ventricular frequency and degenerative changes

in the stimulatory system [29]. In symptomatic AF, patients most often report heart palpitations, exertional dyspnea, dizziness, decreased exercise tolerance, chest pain, sleep disturbance or syncope.

The severity of the symptoms of AF is assessed according to the EHRA scale, which takes into account 6 symptoms, i.e. palpitations, fatigue, dizziness, dyspnea, chest pain and anxiety (Table I). Depending on their presence and influence on daily functioning, the severity of symptoms is assessed.

4S-AF Scheme

As AF is a disease of complex etiology, it is currently suggested to use the 4S-AF regimen for people with clinically diagnosed AF. This regimen is intended to assist in deciding on anticoagulant therapy, the choice between pharmacological and interventional therapy, and the treatment of concomitant cardiovascular diseases and risk factors for AF development. It highlights the risk of stroke, symptoms, the severity of AF burden and cardiovascular disease, and risk factors for the development of AF [31]. The stroke risk is determined by the number of points scored on the CHA_2-DS_2-VASc scale (Table II). Symptoms are scored by the number of points scored on the EHRA scale. The severity of AF burden is estimated by the duration of the AF and whether it resolves spontaneously. The last S letter of the 4S-AF regimen (substrate) is comorbidities, assessed by the presence of associated cardiovascular risk factors and atrial cardiomyopathy [31]. Despite the limitations of using this scale, such as the lack of information about the risk of bleeding or the number of cardioversion or ablations performed so far, it allows faster and easier communication among healthcare professionals to determine the appropriate treatment required by the patient.

Table I. Classification of AF-related symptoms (EHRA Score)

EHRA SCORE	EXPLANATION
EHRA I	No symptoms
EHRA II	Mild symptoms: normal daily activity not affected
EHRA III	Severe symptoms: normal daily activity affected
EHRA IV	Disabling symptoms: normal daily activity discontinued

AF – atrial fibrillation

Complications of atrial fibrillation

The most common complications of AF are ischemic stroke, chronic heart failure, deterioration in quality of life, tachyarrhythmic cardiomyopathy and depression [32]. Of the listed complications in the elderly, the first three are dominant.

Ischemic stroke

Ischemic stroke occurs 5 times more often in people with AF due to the nature of the arrhythmia that reduces blood flow from the atria to the ventricles, leading to stagnation of blood in the atria, resulting in the formation of clots which, when localized in the left atrium, flows along with the bloodstream, they reach narrower and narrower cerebral vessels, leading to ischemia of specific regions of the brain [33,34]. Patients who have already had an episode of ischemic stroke or transient ischemic attack (TIA) with a narrow left venous outlet or after prosthetic valve implantation are particularly vulnerable [35]. In such patients, another stroke significantly increases the risk of disability, a higher risk of recurrence and a 30-day mortality [2]. The CHA2-DS2-VASc scale is used to assess the risk of stroke in patients with non-valvular AF, which is used to determine the need for anticoagulation in these patients.

Connection between heart failure and atrial fibrillation

AF increases the risk of heart failure 5-fold, and with subsequent classes of heart failure according to the NYHA scale, the risk of AF increases (<5% of the population in the case of NYHA I and approximately 50% in the case of NYHA IV) [2]. Symptoms related to AF, such as fainting or dizziness, significantly increase the risk of falling in this group of patients, which in the geriatric population may have serious complications. Due to the frequent occurrence of osteoporosis in the elderly population, a fall can fracture the femoral neck, immobilizing the patient for a long time, which can lead to a range of complications, pressure ulcers, infections and muscle wasting, which can prevent the elderly from recovery from before the fall.

Reduction of the quality of life

The deterioration of the quality of life occurs most often due to the reduced tolerance of physical effort, frequent recurrences of arrhythmias and symptoms, and the need for further hospitalizations. Taking medi-

cations, in particular anticoagulants, is often associated with patient anxiety about treatment complications such as hemorrhage, which contributes to the development of depression and anxiety disorders in the elderly.

Atrial fibrillation and valvular diseases

It is also worth noting that among patients with AF, mitral valve defects are relatively common, with mitral stenosis being much more common than mitral regurgitation [36]. However, valvular disease occurs independently of AF, and only 30% of patients with AF have an echocardiographic detection of a valvular defect [37].

Influence of atrial fibrillation on myocardial ischemia

AF also increases the risk of myocardial ischemia 3 times compared to healthy people, and the risk of a heart attack in people with AF is higher when the patient does not suffer from hypertension, diabetes, has never suffered an ischemic stroke or does not suffer from lipid metabolism disorders [38].

Diagnosis of atrial fibrillation

The diagnosis of AF is performed based on ECG, where P waves are absent replaced by fibrillatory waves characterized by low, irregular amplitudes. Additionally, a fast (usually 90-170/min.), and irregular frequency of ventricular rate is observed. In addition to confirming the diagnosis, the 12-lead ECG will allow us to assess the presence of other cardiac arrhythmias, ischemia, or structural features of heart disease. In a paroxysmal AF, a useful diagnostic method is the monitoring of the heart rhythm with the use of Holter-ECG, sometimes even for several days.

In search of the causes of AF, apart from ECG, it is necessary to perform laboratory tests to assess the function of the kidneys, thyroid gland, electrolyte levels, and complete blood count. In each patient with AF, transthoracic echocardiography (TTE) should be performed to exclude the presence of disturbances in the structure of the heart muscle, which may be the cause of the arrhythmia.

Due to the frequent asymptomatic nature of patients with AF, quick diagnosis of the disease is often difficult. Therefore, the recommendations of the European Society of Cardiology from 2020 suggest that every person ≥65 years of age should have either heart rate assessed or performed an ECG as part of a clinical evaluation performed with other reasons (evidence rating: Ia) [39]. Regular screening in this group of patients allows for early initiation of appropriate treatment, significantly reduces the risk of serious complications, such as ischemic stroke.

Treatment of atrial fibrillation

Treatment of patients with AF should begin with patient education. They should be informed about the importance of taking regular medications, especially anticoagulants, and the complications that untreated AF can cause. Additionally, these patients should take an active part in establishing the therapeutic plan, and their treatment preferences should be taken into account by a doctor when selecting the appropriate therapy. Proper patient education and involving them in the diagnostic and therapeutic process significantly increases the chances of their compliance with the recommendations.

Currently, to conduct proper therapy of patients with AF, an integrated ABC model has been developed - "A": anticoagulation / avoid stroke, "B": better symptom management, "C": cardiovascular and comorbidity optimization. This pathway is characterized by a lower frequency of cardiovascular events, lower mortality, and a lower percentage of strokes and major bleeding compared to the standard model of care for this group of patients [39].

„A" – Anticoagalotion/Avoid stroke

AF significantly increases the risk of stroke, so it is essential to initiate appropriate anticoagulant therapy promptly to reduce the risk of this potentially fatal complication.

Before starting this type of treatment, it is crucial to properly assess the risk of a stroke in this group of patients. For this purpose, widely available and commonly used in clinical practice CHA2DS2-VASc scale is used, which takes into account the following risk factors that increase the risk of ischemic stroke: congestive heart failure, hypertension, age ≥75 years, diabetes, history of stroke, vascular disease, age 65-74 years, and gender (Table II). Age is a significant factor in increasing the chance of stroke in patients with AF. The risk increased already from the age of 65, and new studies presenting data from Asia suggest that the risk increases as early as 50-55 years of age [40,41]. It is also worth noting that women without other risk factors (CHA_2DS_2-VASc Score: 1) have a low risk of stroke, as are men without other burdens (CHA_2DS_2-VASc Score: 0).

Table II. The CHA2DS2-VASc Score

LETTER	RISK FACTOR	SCORE
C	Congestive heart failure	1
H	Hypertension	1
A2	Age ≥ 75	2
D	Diabetes mellitus	1
S2	Stroke/TIA	2
V	Vascular disease[a]	1
A	Age 65 – 74	1
Sc	Sex category (female[b])	1

[a] a history of myocardial infarction; atherosclerosis; atherosclerotic plaque in the aorta
[b] increases the risk in the presence of ≥1 other risk factor

Another element that needs to be assessed before conducting anticoagulation therapy is the potential risk of bleeding in patients with AF. Selecting patients at high risk of bleeding is essential in determining the appropriate treatment strategy because it is taken into account in the case of the need for surgery, and therapy planning. To evaluation of the risk of bleeding, the HAS-BLED scale is used, which takes into account the following risk factors: uncontrolled hypertension, abnormal kidney, and liver function, recent stroke, history of bleeding/predisposition to bleeding, unstable international normalized ratio (INR), old age (>65 years of age), medication or excessive alcohol consumption (Table III). In long-term therapy is recommended to periodic monitoring of the risk of stroke and bleeding risk to proper modification of the treatment.

Table III. The HAS-BLED Score

RISK FACTOR	SCORE
Hypertension (SBP > 160 mmHg)	1
Abnormal renal and liver function	1 or 2
Stroke	1
Bleeding	1
Labile INRs	1
Age > 65	1
Drugs and alcohol	1 or 2
≥ 3 points = high risk of bleeding	

One point is awarded for each of the following: abnormal liver function, abnormal kidney function, drug use, and alcohol abuse.

Stroke prevention

Vitamin K antagonists (VKA)

The most commonly used drugs from this group are warfarin and acenocoumarol. They achieve their anticoagulant effect by inhibiting the activity of clotting factors: II, VII, IX, and X, as well as proteins C and S. Caution should be exercised when treating with these drugs that they acquired their anticoagulant effect after 3-5 days, so if you need to obtain a rapid result, it should apply initially with heparin or fondaparinux.

VKAs are characterized by a narrow therapeutic window. Therefore, require regular monitoring of INR levels and appropriate dose modifications. The INR level in patients with AF should be in the range of 2.0-3.0 [42]. Reaching the proper therapeutic range (TTR; >70%) over an appropriate time makes VKAs an effective and safe method of preventing stroke. Hart et al. in their work showed that the proper use of VKA reduces the risk of stroke by 64% and mortality by 26% compared to the control group [43].

The effectiveness of VKA is affected by many factors. Therefore, in the elderly, patients with a high risk of bleeding, women, or people with low body weight, the dose of the drug may need to be reduced. However, in the case of obese people, it may be necessary to increase the dose of the medication.

Non-vitamin K antagonist oral anticoagulants (NOACs)

NOACs are a relatively new group of anticoagulants. There are factor Xa inhibitors (rivaroxaban, apixaban, edoxaban) and factor IIa inhibitors (dabigatran). The use of NOAC is associated with a 19% reduction in the risk of systemic embolism, a 51% reduction in the risk of hemorrhagic stroke, and a similar reduction in the risk of ischemic stroke compared to VKA [39]. NOACs were also associated with a significant decrease in the risk of all-cause mortality – 10%.

The kidneys are largely involved in the elimination of the drug from the body, 80% for dabigatran, 50% for edoxaban, 35% for rivaroxaban, and 27% for apixaban. Therefore, in the case of chronic kidney disease, the dose of the drug may need to be reduced. The decision has to be made after the determination of creatinine clearance (CrCl). Dabigatran dose reduction should be considered with CrCl values in the range of 30-49 ml/min., edoxaban 15-50 ml/min., rivaroxaban 15-49 ml/min., and apixaban 15-29 ml/min.. In patients

over 75 years of age with normal CrCl values, frequent verification of kidney function is suggested.

Drug dose reduction may also be necessary for: patients over 75-80 years of age, patients with low body weight, patients with thrombocytopenia, and additionally treated with an antiplatelet drug [44].

Surgical closure of the left atrial appendage (LAA)

Surgical closure of the LAA is performed to reduce the probability of a thrombus forming within the LAA. It limits the slow flow of blood through this structure, resulting in a reduced risk of thrombus formation.

LAA closure is usually performed during cardiac surgery for other reasons, and the most common indication for this procedure is a high risk of bleeding or contraindications to the use of oral anticoagulants [45].

It should be emphasized that the residual LAA flow or its incomplete closure makes the risk of ischemic stroke persist increased [46].

„B" – Better symptom managment

This step of management relates to the proper control of the heart rhythm to keep it within a range that is well tolerated by the patient and results in a reduction in the severity of symptoms associated with AF. There are no clearly defined targets of ventricular rhythm ranges that should be achieved while treating patients with AF. Each case should be considered individually, taking into account the tolerability of treatment and the effect on the reduction of symptoms of arrhythmia. Ventricular rhythm control in AF can be achieved in several ways using pharmacological and non-pharmacological agents.

β-adrenolytics

They are the first-line drugs for the control of ventricular rhythm in patients with AF due to their rapid effect and high efficacy. The preparations recommended in the treatment of elderly patients are nebivolol, carvedilol, bisoprolol, and metoprolol. It should be noted that β-blockers also have an antihypertensive effect. Therefore, when they are included in treatment in the elderly, it is worth increasing the frequency of blood pressure control to exclude hypotension and reduce the risk of falls in this group of patients. β-blockers are indicated in patients with heart failure [42]. β-blockers should be used with caution in patients with a history of bronchial asthma due to the risk of inducing bronchospasm.

Nondihydropyridine calcium antagonists (NDCC)

This group of drugs is often used to control ventricular rhythm in patients with AF, and their effectiveness in reducing arrhythmia symptoms is comparable to that of β-blockers. The most commonly used medicaments are diltiazem and verapamil. In the case of renal and hepatic dysfunction, these drugs should be used in reduced doses. Additionally, they are contraindicated in patients with left ventricular ejection fraction <40% [42]. Verapamil and diltiazem are both contraindicated in individuals with an accessory pathway in the heart.

Digoxin

In addition to affecting the ventricular rhythm, it also has a positive inotropic effect, increasing left ventricular ejection fraction. Therefore, it is recommended for people with heart failure. It must be used with caution in patients with impaired renal function, since the increase in its serum concentration is associated with the risk of serious complications, such as cardiac arrhythmias. The therapeutic concentration of digoxin is 0.5-0.9 ng/ml. Like verapamil and diltiazem, digoxin is contraindicated in people with an accessory pathway in the heart.

Amiodarone

It is a drug that has many side effects. It can lead, among others, to abnormal thyroid function, symptomatic bradycardia, or acute liver dysfunction. Therefore, it is used when other drugs are ineffective. Due to the presence of iodine in its molecule, amiodarone is contraindicated in patients with thyroid dysfunction.

Other methods of controlling the ventricular rhythm and restore sinus rhythm

Electrical cardioversion (ECV)

ECV is one of the non-pharmacological methods of restoring sinus rhythm. The procedure is performed under short-term general anesthesia, often with midazolam or propofol. It is based on the use of the electrical impulse generated by the defibrillator in the synchronization mode transmitted to the heart through electrodes located on the patient's chest. The electric discharge occurs at the apex of the R wave. During and after the procedure blood pressure, and oxygen saturation should be controlled.

Newly diagnosed AF, lasting more than 48 hours, or failure to take the appropriate dose of anticoagu-

lants by the patient 3 weeks before the ECV, requires excluding the presence of thrombus in the LAA. Transesophageal echocardiography is the method of choice.

Pharmacological cardioversion

In the case of hemodynamically stable patients, it is possible to attempt to restore sinus rhythm through the use of pharmacological agents. In patients without organic heart disease, propafenone and flecainide are the preferred agents. In the case of using antiarrhythmic drugs belonging to the IC class, an atrioventricular node blocking agent should be used concomitantly to prevent the arrhythmia from converting to 1:1 ventricular flutter [39]. In patients with heart failure, amiodarone should be administered.

Catheter ablation

Transcatheter ablation of AF is a satisfactory method of preventing the recurrence of arrhythmias. Its main effect is the reduction of symptoms related to AF. Indication for transcatheter ablation is a failure of pharmacological treatment [39]. Pulmonary vein isolation (PVI) is the most commonly used method. The tissues around pulmonary veins orifices are damaged, which leads to the destruction of the starting point of arrhythmia. In some cases, the procedure is more extensive.

"C": Cardiovascular and Comorbidity optimization

It is an integral part of the modern treatment of patients with AF. Cardiovascular and comorbidity optimization depends on proper identification and control of risk factors for the development of AF. Uncontrolled risk factors and untreated comorbidities significantly increase the risk of developing AF. Part C of the "ABC" model of AF treatment is assumed to promote a healthy lifestyle by increasing the physical activity of patients, reducing excess body weight, and limiting the consumption of alcohol and caffeine. In addition, it also draws attention to targeting the appropriate treatment of comorbidities, such as arterial hypertension, diabetes, or heart failure.

Summary

The incidence of AF increases with age. This arrhythmia is often asymptomatic, and regular screening of the elderly population significantly increases the probability of early diagnosis. Appropriate anticoagulant therapy is essential in the treatment of AF because it remarkably reduces the risk of ischemic stroke and reduces mortality in this group of patients. An important factor in reducing the symptoms of the disease is the proper control of the ventricular rhythm, both by pharmacological methods and by invasive procedures such as transcatheter ablation. Proper control of risk factors and lifestyle modification significantly reduces the risk of developing AF.

Conflict of interest
none

Correspondence address
Michał Świątczak
II Department of Cardiology
Medical University of Gdańsk, Poland
7 Dębinki St., 80-211, Gdańsk
☎ (+48 58) 349 39 10
e-mail: michal_swiatczak@gumed.edu.pl

References

1. Jankiewicz-Błoch A, Zawadzki J, Kustrzycki W, Sławuta A. Leczenie farmakologiczne napadów migotania przedsionków. Folia Cardiologica, 2018;13(4):331-7.
2. Karaś-Głodek M, Styczeń A, Wysokiński A, Zapolski T. Migotanie przedsionków–najczęstsza arytmia w starszym wieku. Odrębności leczenia antykoagulacyjnego Atrial fibrillation–the most common arrhythmia in older age. Differences of anticoagulation treatment. Gerontol Pol 2018;26:201-8
3. Lippi G, Sanchis-Gomar F, Cervellin G. Global epidemiology of atrial fibrillation: An increasing epidemic and public health challenge. Int J Stroke. 2021;16(2):217-21.
4. Hu YF, Chen YJ, Lin YJ, Chen SA.: Inflammation and the pathogenesis of atrial fibrillation. Nat Rev Cardiol. 2015;12(4):230-43.
5. Lau DH, Schotten U, Mahajan R, Antic NA et al. Novel mechanisms in the pathogenesis of atrial fibrillation: practical applications. Eur Heart J. 2016;37(20):1573-81
6. Komal S, Yin JJ, Wang SH, et al. MicroRNAs: Emerging biomarkers for atrial fibrillation. J Cardiol. 2019;74(6):475-82.

7. Noubiap JJ, Sanders P, Nattel S, Lau DH. Biomarkers in Atrial Fibrillation: Pathogenesis and Clinical Implications. Card Electrophysiol Clin. 2021; 13(1):221-233.
8. Jiang Z, Dai L, Song Z, Li H et al. Association Between C-Reactive Protein and Atrial Fibrillation Recurrence After Catheter Ablation: A Meta-analysis. Clin Cardiol, 2013;36(9):548-54.
9. Nattel S. Molecular and Cellular Mechanisms of Atrial Fibrosis in Atrial Fibrillation. JACC Clin Electrophysiol. 2017;3(5):425-35.
10. Thum T, Gross C, Fiedler J, et al. MicroRNA-21 contributes to myocardial disease by stimulating MAP kinase signalling in fibroblasts. Nature. 2008;456(7224):980-4.
11. Mahajan R, Lau DH, Sanders P. Impact of obesity on cardiac metabolism, fibrosis, and function. Trends Cardiovasc Med 2015;25:119–26
12. Shiroshita-Takeshita A, Brundel BJ, Burstein B, et al. Effects of simvastatin on the development of the atrial fibrillation substrate in dogs with congestive heart failure. Cardiovasc Res 2007;74:75–84
13. Daccarett M, Badger TJ, Akoum N, et al. Association of left atrial fibrosis detected by delayed-enhancement magnetic resonance imaging and the risk of stroke in patients with atrial fibrillation. J Am Coll Cardiol 2011 57:831-38.
14. Zhou X, Dudley SC Jr. Evidence for Inflammation as a Driver of Atrial Fibrillation. Front Cardiovasc Med. 2020;7:62.
15. Packer DL, Mark DB, Robb RA, et al. Effect of Catheter Ablation vs Antiarrhythmic Drug Therapy on Mortality, Stroke, Bleeding, and Cardiac Arrest Among Patients With Atrial Fibrillation: The CABANA Randomized Clinical Trial. *JAMA*. 2019;321(13):1261-74.
16. Poirier P, Giles TD, Bray GA, et al. American Heart Association; Obesity Committee of the Council on Nutrition, Physical Activity, and Metabolism. Obesity and cardiovascular disease: pathophysiology, evaluation, and effect of weight loss: an update of the 1997 American Heart Association Scientific Statement on Obesity and Heart Disease from the Obesity Committee of the Council on Nutrition, Physical Activity, and Metabolism. Circulation. 2006;113(6):898-918.
17. Batal O, Schoenhagen P, Shao M, et al. Left atrial epicardial adiposity and atrial fibrillation. Circ Arrhythm Electrophysiol. 2010;3(3): 230-6.
18. Nabauer M, Gerth A, Limbourg T, et al. The Registry of the German Competence NETwork on Atrial Fibrillation: patient characteristics and initial management. Europace. 2009;11(4):423-34.
19. Dzeshka MS, Shantsila A, Shantsila E, Lip GYH. Atrial Fibrillation and Hypertension. Hypertension. 2017;70(5):854-61.
20. Verdecchia P, Angeli F, Reboldi G. Hypertension and Atrial Fibrillation: Doubts and Certainties From Basic and Clinical Studies. Circ Res. 2018;122(2):352-68.
21. Vaziri SM, Larson MG, Benjamin EJ, Levy D. Echocardiographic predictors of nonrheumatic atrial fibrillation. The Framingham Heart Study. Circulation. 1994;89(2):724-30.
22. Vaziri SM, Larson MG, Lauer MS, et al. Influence of blood pressure on left atrial size. The Framingham Heart Study. Hypertension. 1995;25(6):1155-60.
23. Thomas MC, Dublin S, Kaplan RC, et al. Blood pressure control and risk of incident atrial fibrillation. Am J Hypertens. 2008;21(10): 1111-6.
24. Milliez P, Girerd X, Plouin PF, et al. Evidence for an increased rate of cardiovascular events in patients with primary aldosteronism. J Am Coll Cardiol. 2005;45(8):1243-8.
25. Seccia TM, Caroccia B, Adler GK, et al. Arterial Hypertension, Atrial Fibrillation, and Hyperaldosteronism: The Triple Trouble. Hypertension. 2017;69(4):545-50.
26. Osuna PM, Udovcic M, Sharma MD. Hyperthyroidism and the Heart. Methodist Debakey Cardiovasc J. 2017;13(2):60-3.
27. Delitala AP, Fanciulli G, Maioli M, Delitala G. Subclinical hypothyroidism, lipid metabolism and cardiovascular disease. Eur J Intern Med. 2017;38:17-24.
28. Mziray M, Siepsiak M, Żuralska R, et al. Woda istotnym składnikiem pokarmowym diety osób w wieku podeszłym. Problemy Higieny i Epidemiologii, 2017;98(2):118-124.
29. Hakim FA, Shen WK. Atrial fibrillation in the elderly: a review. Future Cardiol. 2014; 10(6):745-58.
30. Mielczarek W. Arytmie u osób w podeszłym wieku Część I. Migotanie przedsionków Cardiac arrhythmias in the elderly Part I. Atrial fibrillation. Geriatria 2018;12:213-21
31. Potpara TS, Lip GYH, Blomstrom-Lundqvist C, et al. The 4S-AF Scheme (Stroke Risk; Symptoms; Severity of Burden; Substrate): A Novel Approach to In-Depth Characterization (Rather than Classification) of Atrial Fibrillation. Thromb Haemost. 2021;121(3):270-8.
32. Fumagalli S, Said SAM, Laroche C, et al. Age-Related Differences in Presentation, Treatment, and Outcome of Patients With Atrial Fibrillation in Europe: The EORP-AF General Pilot Registry (EURObservational Research Programme-Atrial Fibrillation). JACC Clin Electrophysiol. 2015;1(4):326-34.
33. Savelieva I, Bajpai A, Camm AJ. Stroke in atrial fibrillation: update on pathophysiology, new antithrombotic therapies, and evolution of procedures and devices. Ann Med. 2007;39(5):371-91.
34. Tu HT, Campbell BC, Christensen S, et al. Pathophysiological determinants of worse stroke outcome in atrial fibrillation. Cerebrovasc Dis. 2010;30(4):389-95.
35. Sominka D, Kozłowska M, Kozłowski D, et al. Leczenie migotania przedsionków u osób w podeszłym wieku Treatment of the atrial fibrilation in the elderly. Geriatria 2008;2:344-48
36. Fauchier L, Philippart R, Clementy N, et al. How to define valvular atrial fibrillation?. Archives of cardiovascular diseases, 2015;108(10): 530-9.

37. Kirchhof P, Benussi S, Kotecha D, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Eur J Cardiothorac Surg. 2016;50(5):e1-e88.
38. Lee HY, Yang PS, Kim TH, et al. Atrial fibrillation and the risk of myocardial infarction: a nation-wide propensity-matched study. Sci Rep. 2017;7(1):12716
39. Hindricks G, Potpara T, Dagres N, et al. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC [published correction appears in Eur Heart J. 2021 Feb 1;42(5):507] [published correction appears in Eur Heart J. 2021 Feb 1;42(5):546-547]. Eur Heart J. 2021;42(5):373-498.
40. Lip GY, Clementy N, Pericart L, et al. Stroke and major bleeding risk in elderly patients aged ≥75 years with atrial fibrillation: the Loire Valley atrial fibrillation project. Stroke. 2015;46(1):143-50.
41. Kim TH, Yang PS, Yu HT et al. Age Threshold for Ischemic Stroke Risk in Atrial Fibrillation. Stroke. 2018;49(8):1872-9.
42. Sawicka M, Kalarus Z. Managment of atrial fibrillation in the elderly patients. Choroby Serca i Naczyń. 2017;14(5):248-57
43. Hart RG, Pearce LA, Aguilar MI. Meta-analysis: Antithrombotic Therapy to Prevent Stroke in Patients Who Have Nonvalvular Atrial Fibrillation. Ann Intern Med.2007;146:857-867. [Epub ahead of print 19 June 2007].
44. Kasprzak JD, Dąbrowski R, Barylski M et al. Doustne antykoagulanty nowej generacji — aspekty praktyczne. Stanowisko Sekcji Farmakoterapii Sercowo-Naczyniowej Polskiego Towarzystwa Kardiologicznego. Folia Cardiologica 2016;11(5):377-393
45. Boersma LV, Ince H, Kische S, et al. Efficacy and safety of left atrial appendage closure with WATCHMAN in patients with or without contraindication to oral anticoagulation: 1-Year follow-up outcome data of the EWOLUTION trial. *Heart Rhythm*. 2017;14(9):1302-8.
46. Aryana A, Singh SK, Singh SM, et al. Association between incomplete surgical ligation of left atrial appendage and stroke and systemic embolization. *Heart Rhythm*. 2015;12(7):1431-7.