

Atrial fibrillation and flutter – the state of the art. Part 2

Migotanie i trzepotanie przedsionków – aktualny stan wiedzy. Część 2

Agnieszka Janion-Sadowska, Łukasz Turek, Aneta Dudek, Jarosław Andrychowski, Marcin Sadowski

Institute of Medical Sciences, *Collegium Medicum*, Jan Kochanowski University, Kielce, Poland
Head of the Department: Prof. Beata Kręcisz MD, PhD

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Abstract

Despite constantly updating our knowledge on atrial fibrillation and flutter there are many questions and doubts about the nature and extent of arrhythmic and non-arrhythmic consequences of these arrhythmias. In part 1 of the state-of-the-art paper the diagnostic work-up of patients with the 2 arrhythmias was summarized. The management of patients with atrial fibrillation and flutter requires a multidisciplinary approach in the risk assessment (including stroke) and treatment strategy. Regardless of the type of antiarrhythmic or anticoagulant therapy, benefits must always surpass or at least offset potential adverse effects and drug toxicity. In part 2 of the state-of-the-art paper, current therapeutic strategies have been summarized.

Streszczenie

Mimo stałego poszerzania i aktualizowania wiedzy na temat nadkomorowych zaburzeń rytmu serca wiele pytań dotyczących natury i nasilenia arytmicznych oraz pozaarytmicznych konsekwencji migotania i trzepotania przedsionków pozostaje bez odpowiedzi. Stratyfikacja ryzyka ze szczególnym uwzględnieniem udaru mózgu oraz leczenie chorych z migotaniem lub trzepotaniem przedsionków wymaga zaangażowania wielodyscyplinarnego zespołu. Możliwe ryzyko wynikające z leczenia zarówno antyarytmicznego, jak i przeciwkrzepliwego zawsze powinno być mniejsze lub przynajmniej równoważone przez korzyści wynikające z tego postępowania. W części pierwszej niniejszego opracowania przedstawiono postępowanie diagnostyczne u pacjentów z migotaniem lub trzepotaniem przedsionków. W drugiej części opracowania podsumowano aktualne zasady postępowania terapeutycznego u chorych z tymi arytmiami.

Anticoagulation

Anticoagulant therapy is a milestone in the management of patients with atrial fibrillation (AF) and atrial flutter (AFL), resulting in a significant reduction of stroke and general mortality rates. Based on the Framingham study and subsequent clinical studies, which demonstrated that AF increased the risk of stroke, it has been discussed over several decades whether oral anticoagulation (OAC) can be used for stroke prophylaxis in patients with AF. A retrospective study in 134 patients with AF without rheumatic heart disease demonstrated that the incidence of thromboembolic disease was approximately 8 times higher in the period without anticoagulation than in the period of antithrombotic therapy [1]. The AFASAK study, published in *The Lancet* in 1989, carried out in a group of 1007 patients with AF without rheumatic heart disease demonstrated that the annual rate of thromboembolic complications was 2.0% (95% CI: 0.6–4.8%) in patients on warfarin and 5.5%

(95% CI: 2.9–9.4%) in those on aspirin and placebo [2]. The Stroke Prevention in Atrial Fibrillation (SPAF) study, published in *Circulation* in 1991, carried out in patients with AF showed that the rate of ischaemic stroke and systemic thromboembolism was markedly lower in patients receiving warfarin (2.3% annually) as compared with placebo (7.4% annually) ($p = 0.01$; RR by 67%; 95% CI: 27–85%). The Canadian Atrial Fibrillation Anticoagulation (CAFA) study revealed that the annual risk of stroke and thrombotic events in patients with AF receiving warfarin or placebo was 3.5% and 5.2%, respectively, with risk reduction of 37% (95% CI: 63.5–75.5%; $p = 0.17$) in the warfarin group as compared with the placebo group. Hart *et al.* [3] evaluated the efficacy of warfarin treatment in the prevention of brain ischaemia based on 29 randomized clinical studies including 28,044 patients with “nonvalvular” AF and found out that warfarin in tailored doses reduced the risk of stroke by 64% (95% CI: 49–74%) as compared with placebo, and in comparison with antiplatelet treatment, warfarin in

tailored doses reduced the risk of brain ischaemia by 39% (95% CI: 22–52%). Moreover, the study demonstrated that all-cause mortality in the tailored warfarin group was reduced by 26% (95% CI: 3–43%) as compared with placebo. Currently, first-choice drugs for pharmacological anticoagulation in patients with AF and AFL include non-vitamin K oral anticoagulants (NOACs), i.e., dabigatran (direct thrombin inhibitor) or apixaban, rivaroxaban, and edoxaban (direct factor Xa inhibitors), whereas vitamin K antagonists (VKA), i.e., warfarin or acenocoumarol, are prescribed as a second choice. However, there is one exception, i.e., patients with AF/AFL and mechanical valve prostheses and patients with AF/AFL and at least moderate mitral stenosis (MS), in whom VKA remains the only therapeutic option [4]. Unfortunately, there are no “head-to-head” double-blind randomized studies that directly compare various NOACs to evaluate differences in the rate of stroke and systemic thromboembolic events. In contrast, there are prospective and randomized studies assessing the efficacy of NOACs in preventing stroke and peripheral thromboembolic events in comparison with warfarin. The risk of brain ischaemia or peripheral thromboembolism was lowest in patients receiving dabigatran 150 mg twice daily (RE-LY study) [5] and apixaban (ARISTOTLE study) [6]. The RE-LY study and a meta-analysis by Yu *et al.* [7] did not find any significant differences in the rate of brain ischaemia and systemic thromboembolism between patients receiving dabigatran 110 mg twice daily and those on warfarin. As for rivaroxaban (ROCKET AF) [8] and edoxaban (EMANAGE AF-TIMI 48) [9], they were not found to be worse than warfarin. Summing up, NOACs appear to be more efficacious than warfarin, but drugs in this class can be compared only indirectly. It is also worth mentioning that the trial populations were not similar – there were differences in the clinical characteristics of the patients participating in the studies. Well controlled, randomized clinical studies in patients with AF receiving long-term anticoagulant therapy have shown that the average annual rate of stroke and annual mortality is approximately 1.5% and 3%, respectively [4]. In patients with AF or AFL referred for cardioversion, warfarin has been routinely used periprocedurally. Periprocedural prophylaxis of stroke and systemic thromboembolism in patients with AF undergoing cardioversion was evaluated in post hoc analyses for such retrospective studies as RE-LY, ARISTOTLE, ROCKET AF, and EMANAGE AF-TIMI 48 [10–13] and in several prospective and randomized clinical studies, i.e., X-VerT – on rivaroxaban [14], EMANATE – on apixaban [15], ENSURE-AF – on edoxaban [16]. The findings of these studies confirm that NOACs are a safe and efficacious alternative to warfarin in periprocedural prevention of stroke in patients with AF without MS and without mechanical valve prostheses

undergoing cardioversion [17]. All interventions and clinical studies in patients with AF and AFL are undertaken because both pharmacological and electrical cardioversion are associated with a significant risk of periprocedural stroke and systemic thromboembolism. If the relevant safety requirements are observed, the rate of direct current cardioversion (DCC)-related complications, including thromboembolic complications, is very low. In the population of patients with AF without adequate anticoagulation therapy cardioversion is associated with a 5–7% periprocedural rate of stroke and systemic thromboembolic events [18]; however, the risk may be reduced to 0.3–1.9% using appropriate anticoagulation therapy [19–23]. Periprocedural risk of stroke and systemic thromboembolic events is highest immediately after cardioversion; 82% of these complications occurs within 72 h, and 98% within 10 days after cardioversion [24]. Long-term OAC to prevent thromboembolic events may be considered in patients at risk for stroke with postoperative AF after cardiac surgery and it should be considered in patients at risk for stroke with postoperative AF after non-cardiac surgery [25].

In haemodynamically stable patients with AF and AFL lasting > 48 h OACs should be started \geq 3 weeks before cardioversion and continued for at least 4 weeks after the procedure (indications for chronic OAC depend on the evaluation of stroke risk according to CHA₂DS₂-VASc score) [4]. An alternative for 3-week anticoagulation therapy before cardioversion in haemodynamically stable patients with AF and AFL is transoesophageal echocardiography (TEE) performed to exclude intracardiac thrombi [4, 17]. TEE as compared with intraprocedural evaluation of the left atrium (LA) is characterized by a sensitivity of 100%, specificity of 99%, positive predictive value of 86%, and negative predictive value of 100% in detecting atrial thrombi [26] and has become the gold standard in diagnosing left atrial thrombus (LAT) and left atrial appendage thrombus (LAAT). Moreover, TEE is regarded as a safe procedure associated with a low rate of complications. In a single-centre study that involved evaluating 10,000 consecutive TEE scans, there were only 3 cases of oesophageal perforation [27].

The paramount therapeutic goal of OAC in patients with AF and AFL is prophylaxis of brain ischaemia and systemic thromboembolism at an accepted risk of haemorrhagic complications. In this clinical context the actual significance of LAAT in patients with AF and AFL on chronic OAC is not clear. It cannot be excluded that thrombi in such patients do not constitute a real health hazard to justify treatment modification, including modification of anticoagulation therapy in order to eliminate the clot. It is not clear whether LAAT in patients with AF or AFL on OAC therapy may be regarded as a substitute marker of stroke and systemic thromboembolic events in or-

der to evaluate the efficacy of a given anticoagulation therapy at an acceptable risk-benefit ratio. Regardless of doubts about LAT and/or LAAT, anticoagulation therapy should not be the only component of stroke prophylaxis in patients with AF and AFL, but only part of the whole process of care [2, 3, 28–30]. One should not forget either that anticoagulation therapy means not only benefits but also risk of adverse effects, including bleeding. Because of all these risks, patients with AF and AFL should not be perceived collectively; it is recommended to take an individualized approach in order to define the actual health hazard in order to choose optimal treatment. It is always recommended that complete and reliable evaluation of stroke risk be performed, taking into account both clinical characteristics and additional parameters such as left ventricular wall motion abnormalities, atherosclerotic plaque in the aorta, intracardiac thrombi, spontaneous echo contrast in cardiac cavities, left atrial appendage emptying velocity reduced below 20 cm/s, and lower values of strain rate in the left lateral ridge, i.e., imaging parameters that measure the risk of brain ischaemia [31].

Pharmacological cardioversion

Stroke risk in patients referred for cardioversion to restore sinus rhythm and control heart rate may not be reduced, and it may even increase transiently. Furthermore, such patients will have additional health risks associated with the procedure of cardioversion and antiarrhythmic therapy side effects, with no guarantee of longer maintenance of sinus rhythm. In light of the foregoing, a reasonable decision, preferably with patient participation, should be made between a rate control strategy and a rhythm control strategy. Rate control is an integral part of AF management and is often sufficient to improve AF-related symptoms. The optimal heart rate target in AF patients is unclear. In the RACE II trial of permanent AF patients, there was no difference in a composite of clinical events, New York Heart Association (NYHA) class, or hospitalizations between the strict (target heart rate < 80 beats per minute at rest and < 110 beats per minute during moderate exercise) and lenient (heart rate target < 110 beats per minute) arm [32, 33], similar to an analysis from the AFFIRM and RACE trials [34]. Therefore, lenient rate control is an acceptable initial approach, regardless of heart failure (HF) status (with the exception of tachycardia-induced cardiomyopathy), unless symptoms call for stricter rate control [25]. Pharmacological rate control can be achieved with β -blockers, digoxin, diltiazem, and verapamil, or combination therapy. Other antiarrhythmic drugs also have rate-limiting properties (i.e., amiodarone, dronedarone, sotalol), but generally they should be used only for rhythm control. The choice of rate control drugs depends on symptoms, comor-

bidities, and potential side-effects [25]. It should be mentioned that the prognostic benefit of β -blockers seen in HF with reduced ejection fraction patients with sinus rhythm has been questioned in patients with AF [35]. In the case of suboptimal rate control by medication, worsening of symptoms or quality of life, and ineligible for rhythm control by catheter ablation, atrioventricular node ablation should be considered to control heart rate in AF patients, accepting that these patients will become pacemaker-dependent and, in this case, the choice of pacing therapy (right ventricular or biventricular pacing) will depend on patient characteristics [25].

DCC as part of a rhythm control treatment strategy most often is performed on an urgent basis in haemodynamically unstable patients or electively in haemodynamically stable patients after optimal patient preparation for the procedure. In the former case, an emergency DCC is considered when the patient has severe haemodynamic disorders related to AF or AFL, i.e., hypotension, cardiogenic shock, syncope, angina pain, and signs of pulmonary congestion. Currently, DCC is considered more effective than pharmacotherapy for restoring sinus rhythm in patients with AF and AFL; furthermore, it is associated with lower risk of proarrhythmia, and shorter procedure duration as compared with pharmacological cardioversion [36–39]. In haemodynamically unstable patients with postoperative AF, emergency electrical cardioversion (or intravenous administration of amiodarone or vernakalant, if consistent with the clinical situation) is indicated. In a recent randomized controlled trial of postoperative AF patients after cardiac surgery, neither rate nor rhythm control showed a net clinical advantage over the other [40]. Hence, rate or rhythm control treatment decisions should be based on symptoms, and non-emergency cardioversion should follow the principles of peri-cardioversion anticoagulation guidelines [25]. Quinidine was advocated by Lewis in order to terminate and prevent atrial fibrillation, after Wenckebach had demonstrated in 1914 that quinine, another alkaloid of the cinchona tree, could terminate this arrhythmia [41]. Within the next 50 years pharmacological cardioversion was the only means of restoring sinus rhythm in patients with AF. The current guideline on AF recommends flecainide, propafenone, amiodarone, vernakalant, ibutilide, and dofetilide for pharmacological cardioversion. The choice of a specific drug is based on the type and severity of associated heart disease. Flecainide and propafenone indicated in patients without significant left ventricular hypertrophy, left ventricular systolic dysfunction, or ischaemic heart disease results in prompt (3–5 h) and safe restoration of sinus rhythm in > 50% of patients, while intravenous amiodarone, mainly indicated in patients with severe heart failure, has a limited and delayed effect but can slow the heart

rate within 12 h [25]. Moreover, chronic administration of amiodarone has been associated with multiple systemic adverse effects, including bradycardia, hypo- or hyperthyroidism, pulmonary toxicity, ocular deposits, and liver function derangements [42]. Intravenous vernakalant is the most rapidly cardioverting drug, including patients with mild HF and ischaemic heart disease, and it is more effective than amiodarone or flecainide. Dofetilide is not used in Europe and is rarely used outside Europe. Ibutilide is effective for conversion of AFL to sinus rhythm. An atrioventricular node-blocking drug should be added in patients treated with flecainide or propafenone to avoid transformation to AFL with 1 : 1 conduction. In Poland, antazoline is also used for pharmacological cardioversion, although it is not included in the current guidelines [25].

Direct current cardioversion

Eskin and Klimov carried out pioneering studies on external defibrillation in the 1950s. In 1959, under the supervision of Lown, a monophasic waveform defibrillator was developed. The first clinical use and documented electrical cardioversion using the monophasic waveform defibrillator was made in Boston in 1961 in an elderly woman with heart rhythm disorders induced by myocardial infarction [43, 44]. The first electrical cardioversion protocols with monophasic current required high energy, which caused significant post-defibrillation cardiomyocyte and local skin injury. In order to minimize the injuries external defibrillators were improved. In the early 1990s the biphasic truncated exponential (BTE) waveform was developed, and from 2000 defibrillators use rectilinear biphasic (RLB) waveforms. The superiority of biphasic over monophasic defibrillation is supported by a marked decrease in the frequency of post-defibrillation/post-cardioversion heart injuries and skin burns and increased efficacy in restoring sinus rhythm. Additionally, biphasic defibrillators compensate transthoracic impedance by electronically adjusting the waveform magnitude and duration [45–49]. During defibrillation the delivered shock is not synchronized with the ECG, in contrast to electrical cardioversion, where the delivered shock is automatically synchronized with the ECG in the ventricular refractory period (the descending limb of the R wave). Such synchronization prevents overstimulation by delivery of shocks on the T wave, otherwise ventricular fibrillation could be induced [50–52]. An electric current flowing through the heart muscle rapidly depolarizes most cardiomyocytes, and the sinus node is capable of capture and imposing normal pacemaker function. The effectiveness of an external direct current in AF and AFL is related to the intensity of the current travelling through the chest, which is directly dependent on transthoracic impedance – the magnitude of elec-

trical resistance is inversely related to the magnitude of current delivered to the heart [53, 54]. Moreover, the effectiveness of DCC depends on the type and duration of arrhythmia [55, 56]. In DCC of AF transthoracic impedance has been shown to increase with increased body mass index (BMI), chest size [56], and haemoglobin concentration; moreover, higher electrical resistance has been found in women and during inhalation. In contrast, transthoracic impedance is decreased in patients with lower BMI, lower left ventricular ejection fraction (LVEF), in patients with HF, with lower haemoglobin levels, larger LA size, higher creatinine levels, lower estimated glomerular filtration rate (eGFR) levels, and in men [57]. One of the studies not relating directly to transthoracic impedance demonstrated that patients with eGFR < 60 ml/min/1.73 m² by MDRD study equation had less chance of sinus rhythm return after DCC of AF. Unfortunately, the study did not attempt to elucidate this relationship and did not provide the size of the population with body surface area other than 1.73 m² [58]. Resuming the topic of transthoracic impedance, studies on atrial fibrillation showed that transthoracic impedance decreased with each sequential shock delivered by the external defibrillator, probably due to the activation of acute inflammatory response. The phenomenon is linear in character, which means that the larger the number of shocks, the greater the reduction of transthoracic impedance, which indicates that decreased thoracic impedance is reversible in this case. Thoracic impedance is also dependent on size, position, and distance between defibrillator electrodes, type of defibrillator electrodes, contact pressure on the chest, chemical properties of electrode gels used during cardioversion/defibrillation, and skin reaction [56, 59–61]. In AF the effectiveness of DCC ranges from 75% to 94% in restoring sinus rhythm and is inversely related to AF duration and transthoracic impedance [38, 46, 57, 59, 62–67]. Moreover, the effectiveness of DCC may be increased after amiodarone (initiating the treatment a few weeks before DCC), sotalol, ibutilide, or vernakalant and probably after flecainide and propafenone [4, 51]. In patients with AFL direct current cardioversion can restore sinus rhythm more frequently and using lower energy than in patients with AF [66, 68, 69]. During defibrillation or cardioversion, the electrodes are placed in the anterior left lateral position or antero-posterior position, so that the heart lies between the 2 defibrillation electrodes. The most effective electrode position in monophasic devices is the antero-posterior position [70]. Biphasic defibrillators have been shown not only to have higher effectiveness of cardioversion at lower energy [46, 49, 71–73], but also with this technology electrode positioning and geometry of energy transfer are of lesser importance [38, 74, 75]. In patients with implantable pacemakers or defibrillators, external defibrillator electrodes should be placed > 8 cm from the device

pocket and preferably in the antero-posterior position [76]. Despite the long history of using external defibrillators optimal shock energy both for monophasic and biphasic defibrillators has not been established yet [45]. Reisinger *et al.*, when using biphasic external defibrillators, recommend an initial shock energy of 100 J in patients with AF < 48 h and 150 J in patients with long-term AF, whereas a low energy of 50 J should be initially selected for DCC in patients with AFL [69]. In a study by Wozakowska-Kaplon *et al.* in patients with AF undergoing biphasic cardioversion the cumulative delivered energy of 350 J was much more effective than 50 J or 150 J. The investigators suggested initiating cardioversion at 200 J in patients with AF of longer duration, whereas in patients with AF of shorter duration the initial shock energy for cardioversion should be lower [77]. In patients with atrial fibrillation biphasic direct current cardioversion is frequently performed with increasing shock energy starting at 100–150 J and, if unsuccessful, increasing the shock energy maximally to 360 J. In a prospective and randomized study published in 2019, maximum-fixed energy shocks (360-360-360 J) and low escalating energy shocks (125-150-200 J) were compared for cardioversion in AF patients. The study demonstrated that maximum fixed-energy shocks significantly increased chances of DCC success. Furthermore, there were no significant differences between the 2 groups in any endpoint regarding safety, i.e., proarrhythmic action, skin burns, pain after cardioversion, and myocardial damage measured by high-sensitivity troponin I [78]. Despite numerous studies, it is not clear which DCC model is most appropriate in AF. DCC is performed under general anaesthesia. Depending on the position of defibrillation electrodes, cardioversion may be transthoracic, transoesophageal, intracardiac, or epicardial. Contraindications to DCC include lack of patient consent, over-digitalization, and intracardiac thrombi. The complications related to DCC can be divided into local damage associated with direct application of electric current, i.e., mainly skin burns and generalized complications such as brain ischaemia and embolic events or complications related to general anaesthesia.

DCC is one of the main components of the rhythm control strategy in patients with AF. However, it should be emphasized that the multicentre clinical studies such as AFFIRM, RACE, STAF, PIAF, and HOT CAFE have not shown differences in mortality and cardiovascular complications between the rate control and rhythm control strategy, although many post-hoc analyses have revealed advantages of sinus rhythm maintenance, taking into account so-called soft endpoints such as improved physical capacity or improved humoral profile [79–88]. The CABANA trial in the intention-to-treat analysis failed to support the hypothesis that catheter ablation for the purpose of

suppressing AF is superior to medical therapy in improving the primary composite endpoint of death, disabling stroke, serious bleeding, or cardiac arrest. However, the primary endpoint was analysed according to the intention-to-treat principle, which means that patients in either group remained on the initial randomization, regardless of whether they had crossed over to the other group in the course of the trial, and the treatment effect of catheter ablation in this trial might have been affected by the cross-over rates in both directions and the lower-than-expected event rate in the drug arm [89]. In fact, according to the “as treated” analyses, catheter ablation of atrial fibrillation would have demonstrated superior efficacy compared to medical therapy regarding mortality [90]. The results of this trial are different from other similar trials such as CABANA, AFFIRM, and RACE. One difference is the population enrolled – recent onset (within 12 months) in EAST-AFNET 4 versus more sustained AF in the other trials. There was also a reasonably high rate of AF ablation (8% at enrolment, 20% by 5 years) in the EAST-AFNET 4 trial, and the results of this trial indicate that a rhythm-control strategy is superior to usual care (rate control in most cases) in improving cardiovascular (CV) outcomes at 5 years among patients with recent diagnosis of AF and concomitant CV conditions. Significant reductions were noted for the primary composite endpoint, as well as for CV death and stroke in this trial [91]. In addition, the results of the CASTLE-AF trial indicate that catheter ablation for AF in patients with HF was associated with a significantly lower rate of a composite endpoint of death from any cause or hospitalization for worsening HF than was medical therapy [92]. The outcomes of the AATAC trial indicate that among patients with persistent AF and HF, catheter ablation was superior to amiodarone therapy. In that study catheter ablation was associated with an improvement in freedom from AF. Other benefits of catheter ablation included improvement in LVEF, 6-minute walking distance, and hospitalization at 2 years [93].

Sinus rhythm maintenance

DCC is very effective in terminating AF and AFL, but unfortunately modern medicine does not offer tools that equally effectively maintain sinus rhythm and guarantee survival without arrhythmia recurrences. Nowadays, antiarrhythmic drug therapy is the most frequent approach to maintain sinus rhythm after successful DCC of AF and AFL. Unfortunately, antiarrhythmic agents have only moderate efficacy in maintaining sinus rhythm after successful DCC of AF/AFL, and only 20–61% of patients maintain sinus rhythm within the first year after cardioversion, regardless of the type of prophylactic antiarrhythmic treatment [55, 94–97]. Furthermore, antiarrhythmic agents do not decrease mortality [98], and unfortu-

nately they may show proarrhythmic activity leading to adverse organ effects. For this reason, when making decisions about antiarrhythmic treatment one should pay more attention to therapy safety and patient preferences than to the expected efficacy of antiarrhythmic drug therapy [4, 17]. A list of antiarrhythmic agents for heart rhythm control is short. Amiodarone, flecainide, propafenone, sotalol, and dronedarone are used in chronic therapy [4]. Of them, amiodarone, appears most efficacious in preventing recurrences of AF and AFL, but multiple possible adverse effects limit its long-term use. Despite these inconveniences, according to the EORP-AF registry, amiodarone has been the most frequently used antiarrhythmic agent for rhythm control in patients with AF [99]. A meta-analysis by Lafuente-Lafuente demonstrated that metoprolol also decreased AF recurrences, but its antiarrhythmic efficacy was lower as compared with amiodarone and IC class drugs [100] but did not differ significantly from class IA agents and some antiarrhythmic drugs from class III [94]. In the DAPHNE study comparing sotalol with metoprolol and atenolol and in a study by Plewan *et al.* comparing sotalol and bisoprolol there were no significant differences between beta-adrenolytic drugs and sotalol in preventing AF recurrences [101, 102]. According to the guidelines of the European Society of Cardiology (ESC) and recommendations of the Polish Cardiac Society (PTK) beta-adrenolytic drugs should not be considered for secondary prevention of recurrent AF [4], although in the European registry published in 2013 these drugs were regarded as first-choice treatment for secondary prevention of AF recurrences, followed by other substances such as amiodarone, sotalol, flecainide, propafenone, and dronedarone [103]. The antiarrhythmic effectiveness of interventions undertaken in patients with AF and AFL is not exclusively related to a given type of antiarrhythmic drugs, but it may also depend on additional clinical factors. Advanced age, concomitant heart disease, long duration of arrhythmia, previous cardioversion, and, in addition to these, the markers of mechanical remodelling of LA, i.e., LA enlargement, low left atrial emptying fraction, low blood flow velocity through the mitral valve, abnormal strain or strain rate of LA and LAA, low left atrial appendage emptying velocity, and low left atrial appendage wall motion velocity have been identified as potential predictive factors for AF/AFL recurrence after cardioversion. Calcium channel antagonists may reduce the likelihood of recurrence [96, 97, 104].

Catheter ablation is emerging as a superior alternative to drugs. Several studies have shown that catheter ablation is associated with better maintenance of sinus rhythm and symptom relief than currently available antiarrhythmic drugs. However, it should be noted that the cross-recurrence of AFL and AF is a very frequent phenomenon, and even the most effective ablation one of these arrhythmias does not guarantee arrhythmia-

free survival. In the CAPTAF trial in patients with paroxysmal or persistent AF, who failed to maintain sinus rhythm on at least one antiarrhythmic drug, catheter ablation was associated with improvement in quality of life compared with optimized drug therapy [105]. In the AATAC and CABANA trials, catheter ablation was associated with an improvement in freedom from AF compared with medical therapy [89, 93].

Conclusions

Atrial fibrillation and flutter are arrhythmias that constitute a serious clinical, social, and economic problem. Stroke remains one of the main issues related to AF and AFL. Apparently, the stroke risk stratification in patients with AF or AFL is not a simple arrhythmia-related derivative but represents a more complicated issue. The current guidelines on AF recommend the CHA₂DS₂-VASc scoring system to define the risk of stroke and thromboembolic complications in patients with both arrhythmias; however, that system was not validated in patients with AFL. LAAT is regarded as the stroke risk factor in patients with AF or AFL, but the real health risk associated with this pathology in AF or AFL patients under chronic anticoagulant therapy is unknown. Depending on the study group, the incidence of LAAT in patients with AF administering oral anticoagulation varies from 0.6% to 8.2%. AF-related and AFL-related thrombogenesis is a complex process and is thought to be more intense in structurally abnormal hearts. Several bodies of evidence suggest that the stroke risk stratification in AF or AFL patients with LAAT under OAC is not only the result of LAAT presence, but also their clinical impacts may depend on the left atrial appendage morphology, thrombus age, or types of cardio-logical treatments and procedures (i.e., conservative treatment, cardioversion, ablation). It is known that the restoration of sinus rhythm in patients with AF or AFL increases the stroke risk; however, the stroke mechanism in patients in these clinical conditions can be difficult to establish. Proper anticoagulation decreases the stroke risk in AF and AFL patients undergoing cardioversion. In accordance with the Atrial Fibrillation Better Care (ABC) pathway and ESC guidelines on AF, we are obliged to prevent stroke and provide better symptom management, optimal cardiovascular, and comorbidity management in patients with both AF and AFL. There are 2 therapeutic strategies in AF and AFL patients: a rhythm control strategy and a heart-rate control strategy. The aim of the rhythm control strategy is the maintenance of sinus rhythm to eliminate arrhythmia-related symptoms and in highly selected patients with AF to improve CV outcomes. DCC for AF and AFL is performed as part of the rhythm-control treatment. Many factors predict a successful electrical cardioversion, long-term maintenance of sinus rhythm, and the risk of AF and

AFL recurrence. The duration of AF and AFL, the size of cardiac chambers and their function, and BMI are among the most commonly recognized risk factors. The current guidelines recommend antiarrhythmic drugs for the prevention of AF and AFL recurrence; however, they reduce the AF/AFL recurrence of the AF rate rather than prevent it, and they can be associated with serious adverse effects. Therefore, the antiarrhythmic treatment should be individualized and guided by its safety rather than its efficacy.

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Conflict of interest

The authors declare no conflict of interest.

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Address for correspondence:

Assoc. Prof. **Marcin Sadowski**
 Institute of Medical Sciences
Collegium Medicum
 Jan Kochanowski University
 Kielce, Poland
 Phone: +48 606906454
 E-mail: emsad@o2.pl