

Clinical Practice Guideline

Preventive Measures and Treatment Options for Atrial Fibrillation

Stephan Willems, Felix Wegner, Lars Eckardt

Cardiology and Internal Intensive Care Medicine, Asklepios Klinik St. Georg Hamburg, Germany: Prof. Dr. med. Stephan Willems

Department for Cardiology II: Electrophysiology, University Hospital Münster, Münster, Germany: PD Dr. med. Felix Wegner

Department for Cardiology II: Rhythmology, University Hospital Münster, Münster, Germany: Prof. Dr. med. Lars Eckardt

Summary

Background: With approximately 1.6 million people affected in Germany, atrial fibrillation (AF) is the most common arrhythmia. The management of AF, from prevention to treatment, including anticoagulation, is therefore of major clinical importance in terms of these patients' quality of life and their mortality.

Methods: This first German clinical practice guideline on AF was developed in accordance with the Regelwerk Leitlinien (rules for guidelines) of the Association of the Scientific Medical Societies in Germany (Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften e. V., AWMF). The available evidence on all relevant issues was retrieved by a systematic literature search and evaluated with the participation of many medical specialty societies.

Results: AF is classified on clinical grounds as paroxysmal, persistent, longstanding persistent, or permanent. It is associated with a 1.5- to 2-fold increase in mortality and a 4- to 5-fold increase in the risk of stroke. Nonetheless, general screening for AF is not currently recommended, as the data on this question are conflicting. Lifestyle interventions and the reduction of risk factors lessen the frequency of AF. Female sex is only a minor risk factor; the CHA₂DS₂-VA-Score is recommended to assess the risk of thromboembolic events. If it is 2 or higher, oral anticoagulation (OAC) is indicated, of a type that should be decided on an individual basis. In patients with cardiovascular risk factors, early rhythm control has

been shown to reduce prognostically relevant cardiovascular endpoints (3.9 versus 5.0 per 100 patient-years). Multiple studies have shown that catheter ablation is superior to drug-based antiarrhythmic therapy in patients with paroxysmal symptomatic AF as well as in those with heart failure and AF.

Conclusion: It is hoped that the recommendations contained in this guideline will lead to intensified measures for the prevention of AF, resulting in a lower prevalence of AF and its adverse sequelae. The available evidence supports the evaluation of the indications for OAC, early rhythm control, and the use of catheter ablation, especially in patients with paroxysmal AF or heart failure.

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Atrial fibrillation (AF) affects approximately 1.6 million people in Germany. It is the most common persistent cardiac arrhythmia and is associated with high morbidity (1) and, often, an impaired quality of life. AF is expected to become much more common because of the aging of the population and the rise in comorbidities (2, 3). Individualized treatment is needed, not just to treat the symptoms of AF, but also to prevent thromboembolism and heart failure, along with treatment of comorbid conditions (4–6). Thus, in recent years, a holistic approach to the treatment of AF has been widely adopted (Box). Moreover, the methods of managing AF have been expanded, across the spectrum from prevention and anticoagulation to rhythm control with an early intervention (Figure 1). This first-ever AF guideline of the Association of Scientific Medical Societies in Germany (*Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften e. V.*, AWMF) is intended to improve patient care on the basis of

the current scientific evidence. For specific questions and scenarios, the reader is referred to the text of the guideline itself (7).

Methods

The German clinical practice guideline on atrial fibrillation meets the requirements stated in the guideline regulations of the AWMF (8): it was issued by multidisciplinary panel comprising 15 medical-scientific societies and institutions and two patient organizations, conflicts of interest were dealt with transparently, evidence retrieved by a systematic search was evaluated according to the GRADE criteria ("Grading of Recommendations Assessment, Development and Evaluation"), and there was a structured, formal consensus process. 19 systematic searches on

Box

What is new?

- holistic approach with a strong emphasis on lifestyle-related measures for the primary and secondary prevention of atrial fibrillation (AF)
- recommendation of the use of the CHA₂DS₂-VA score for stroke prevention, with oral anticoagulation recommended for male or female patients with a score of 2 or above.
- recommendation to consider rhythm control in all patients with newly diagnosed AF
- emphasis on the value of catheter ablation for AF therapy, potentially for primary use in patients with paroxysmal and persistent atrial fibrillation and in patients with heart failure

specific interventions and cross-topic systematic reviews were conducted from April 2022 to December 2023. The searches were conducted in the following databases, depending on the topic: MedLine, Cochrane clinical trials (primary studies), Cochrane database of systematic reviews, Epistemonikos, as well as in the websites of the Institute for Quality and Efficiency in Health Care (IQWiG), the European Medicines Agency (EMA), the National Institute for Health and Care Excellence (NICE), and the Agency for Healthcare Research and Quality (AHRQ) for systematic reviews and regulatory documents. In the formulation of the recommendations, consideration was taken not only of the evidence retrieved by systematic search and its evaluation, but also of clinical expertise, aspects of care, and the perspective of patient representatives.

Definition, classification, and diagnosis

Atrial fibrillation is characterized by rapid and uncoordinated electrical activation of the atrial myocardium, resulting in limited or absent atrial contraction and thereby creating a risk of thrombus formation. In addition, the physiological coordination between the atria and the ventricles is disrupted. This typically leads to an irregular, often accelerated heartbeat, which has adverse hemodynamic effects and increases the risk of stroke (9–12). The diagnosis of AF is made by electrocardiography (EKG) (13, 14).

AF is called “subclinical” when it is detected in asymptomatic patients in whom AF has not previously been diagnosed by EKG. Subclinical AF can be detected by cardiac implantable electronic devices (CIEDs, such as pacemakers, defibrillators, and implantable event recorders) or wearable monitors (such as smartwatches), which is why the term “device-detected” AF (DDAF) has recently come into use.

The current classification mainly considers the phenotype of clinical AF in terms of the distribution pattern or duration of AF episodes. However, many patients with persistent AF do not differ from those with paroxysmal AF (PAF) with respect to the success of antiarrhythmic

therapy (9, 15). Epidemiological studies have shown that an estimated 15–30% of patients with PAF develop persistent AF within 1–3 years (16–18). Most patients with AF have symptoms such as palpitations, dyspnea, or reduced performance. The modified EHRA (European Heart Rhythm Association) score has been established as a measure of the limitation of everyday activities, the impairment of the quality of life, and the success of treatment (*eTable 1*). In patients with AF, it is recommended that risk factors should be identified (e.g., arterial hypertension, diabetes mellitus, sleep apnea syndrome, alcohol consumption) and that concomitant illnesses (such as heart failure) and psychosocial factors should be documented.

Screening

The systematic, population-wide AF screening programs that have tested to date prevent stroke less than previously expected (19–22), for multiple reasons. On the one hand, half of the people contacted in the population-based programs declined the invitation to be screened (20, 23). On the other hand, patients whose AF is detected by screening have a lower risk of stroke than those whose AF is detected by EKG in routine everyday clinical practice (21, 22). Systematic, population-based screening is therefore not recommended.

Prevention and lifestyle measures

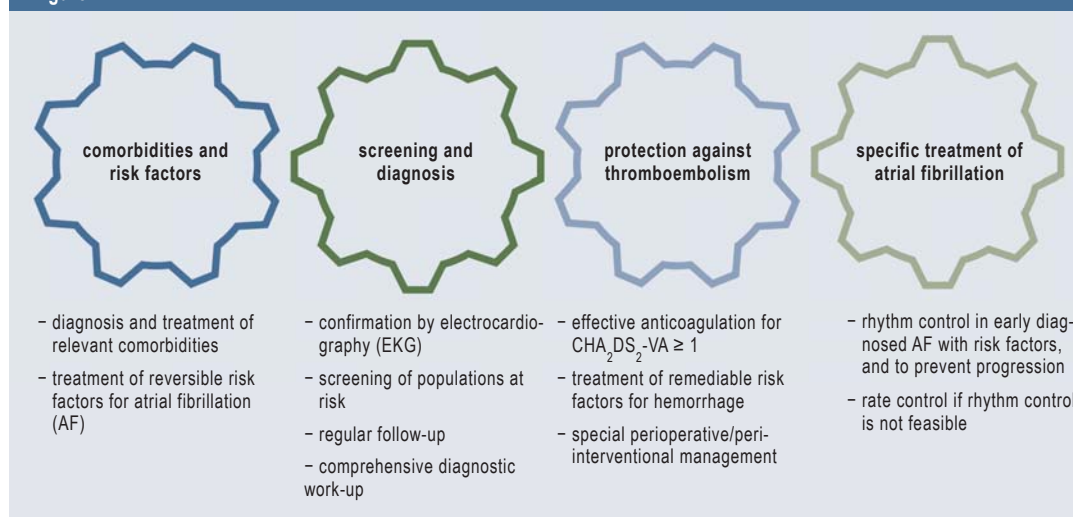
AF is clearly associated with obesity, hypertension, diabetes mellitus, sleep apnea, and physical inactivity (24), as well as with mental illnesses such as depression, anxiety disorders, and post-traumatic stress disorder and with lower socioeconomic status. Evidence from randomized, controlled trials suggests that lifestyle interventions reduce various risk factors for AF and lower its frequency.

There seems to be a dose-dependent association between alcohol consumption and AF. A meta-analysis from 2022 showed a 6% increase in the incidence of AF in persons who drank one alcoholic drink per day (relative risk [RR] 1.06; 95% confidence interval [CI] [1.03; 1.08]). There are sex-specific differences; in men, the relationship between alcohol consumption and AF is linear (25). Prognostic studies (e.g., the Rotterdam study [26]) have also linked smoking to a higher risk of AF.

Stroke prevention

The risk of thromboembolic events, particularly strokes, is approximately four to five times higher in patients with AF, depending on their age and other risk factors. Stroke in AF patients also carries higher morbidity and mortality than stroke of other causes (27–30). The prevention of ischemic stroke and other thromboembolic events in AF patients is, therefore, very important. Sex affects the risk only weakly (31); the CHA₂DS₂-VA score is recommended as a risk estimator (*eTable 2*). The treating physician and the patient decide together whether, and how, to treat with oral anticoagulation, according to the principle of shared decision-making. If the CHA₂DS₂-VA score is 2 or higher, the benefits of oral anticoagulation outweigh the risk of bleeding, and anticoagulation is generally indicated (*eTable 3*). With a CHA₂DS₂-VA score of 1, the benefits and risks of oral anticoagulation are closely balanced,

Figure 1



Overview of the main recommendations given in this guideline for AF, including the management of accompanying conditions, detection and diagnostic work-up, stroke prevention, and specific treatment with either rhythm or rate control AF, atrial fibrillation; CHA₂DS₂-VA, a score for determining the risk of stroke in a patient with atrial fibrillation; EKG, electrocardiogram

and decisions whether to anticoagulate should be made on an individual basis (32).

The direct oral anticoagulants (DOACs) investigated in approval studies (33–36) were found to cause fewer hemorrhagic complications than warfarin, and, in particular, only half as many intracranial hemorrhages (37, 38). German healthcare data (e1–e7) indicate that the advantages demonstrated in randomized studies of DOAC compared to warfarin may be of lesser size when DOAC are compared to phenprocoumon. For example, the TTR (“time in therapeutic range,” INR 2–3) values were higher in both the intervention and the control groups (74% and 75%, respectively) than in the warfarin comparison group (TTR 55–65%) in the DOAC approval studies. Therefore, in contrast to other international guidelines (e8, e9), the German guideline group has decided not to recommend DOACs as first-line therapy for oral anticoagulation in AF. Instead, the decision on whether to use a DOAC or phenprocoumon should be left to the treating physician and the patient.

Interventional or surgical closure of the left atrial appendage can lower the risk of thrombus formation in the left atrial appendage and the risk of thromboembolism. Occlusion of the left atrial appendage performed during cardiac surgery can lower the rate of thromboembolism (attributable risk [AR] 4.8% vs. 7.0%; hazard ratio [HR] 0.67 [95% CI: 0.53–0.85]), provided that oral anticoagulation is given after the intervention (e10–e12).

Rhythm control

An overview of the recommendations for rhythm control is provided in Figure 2. In patients with unclear symptoms, cardioversion may be considered so the situation and any changes in left ventricular pump function can be evaluated again afterward in sinus rhythm (symptom-rhythm correlation). In patients who present as an emergency with acute symptoms, electrical cardioversion can also be used to terminate the current AF episode and alleviate symptoms (e13, e14). In hemodynamically stable patients with acute, symptomatic AF, one can wait 48

Figure 2

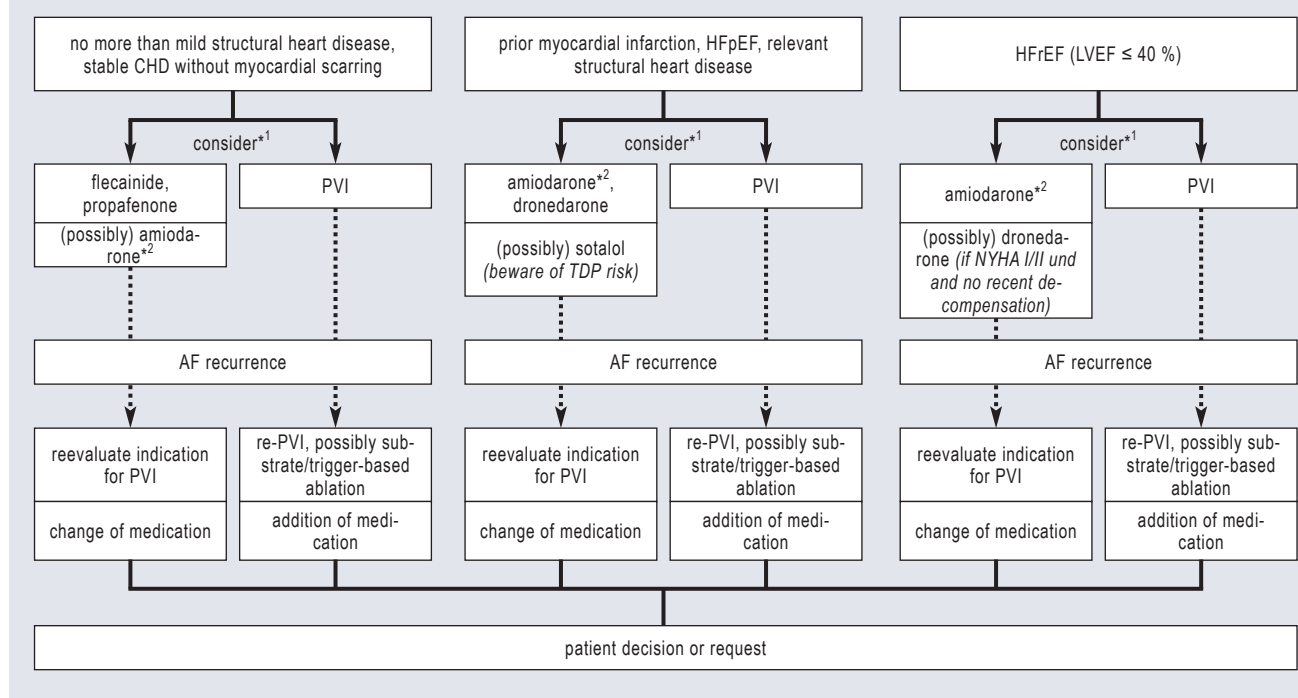
- The indication for early rhythm control in newly diagnosed AF should be assessed.
- Patients with AF-induced cardiomyopathy should be treated with rhythm control.
- Catheter ablation should be performed in younger, symptomatic patients without relevant comorbidities to lessen the frequency of AF episodes and hospitalization.
- Catheter ablation should be recommended to symptomatic patients with persistent AF to lessen the frequency of AF episodes, hospitalization, and cardioversion.
- Early rhythm control should be recommended in patients with newly diagnosed AF, cardiovascular risk factors, advanced age, or comorbidities (CHA₂DS₂-VA score ≥ 2), regardless of symptoms.
- Rhythm control should be considered in patients with AF and severe heart failure, in addition to guideline-based treatment for heart failure.
- Rhythm control should be recommended in paroxysmal AF and when indicated to hinder progression to persistent AF.
- In symptomatic patients with longstanding persistent AF and a dilated left atrium, a hybrid procedure (epi- and endocardial ablation) should be considered after interdisciplinary evaluation.
- Rhythm control is no longer recommended in asymptomatic patients with persistent AF of at least two years' duration and dilated atria.
- Long-term amiodarone therapy for rhythm control should be avoided.

Overview of recommendations in the guideline concerning the indications for rhythm control in patients with paroxysmal and persistent atrial fibrillation, which vary depending on the potential underlying disease. Green: rhythm control should be performed; yellow: rhythm control may be performed; rhythm control is not recommended. AF, atrial fibrillation

hours at first to see whether sinus rhythm returns without cardioversion (e15). When cardioversion is planned, a long-term treatment plan should be established as well, as the recurrence rate without concomitant antiarrhythmic therapy is 30% at 3 months 50–70% at one year (e16, e17).

After cardioversion of AF lasting longer than 24 hours, there is a higher risk of a thromboembolic event. All such patients, therefore,

Figure 3



Overview of the options for antiarrhythmic treatment to achieve rhythm control in patients with paroxysmal or persistent atrial fibrillation.

*¹ Consideration on an individual basis taking into account the AWMF recommendations, the risks and benefits, and the patient's wishes. NYHA I/II refers to the New York Heart Association classification of heart failure. Patients with NYHA I have no limitation of physical performance, while those with NYHA II have a mild slight limitation.

*² Long-term treatment with amiodarone should be avoided if possible.

CHD, coronary heart disease; HFrEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced left ventricular ejection fraction; LVEF, left ventricular ejection fraction; PVI, pulmonary vein isolation; TDP, torsade de pointes (a specific type of ventricular tachycardia)

whatever their estimated annual risk of such an event, should be orally anticoagulated for three weeks, or else an intracardiac thrombus should be ruled out before cardioversion, generally by echocardiography (e18, e19, e20). Whatever the risk profile, oral anticoagulation is always recommended for at least 4 weeks after electrical cardioversion. The individual stroke risk (CHA₂DS₂-VA score) determines whether it should be continued thereafter (e18).

Assessing the indication for rhythm control

Progression of AF is known to be associated with the development of an arrhythmogenic substrate in the left atrium (e.g., through progressive atrial fibrosis) (e21, e22). Early (first-line) catheter ablation of PAF can prevent progression from paroxysmal to persistent AF (e23, e24). In the EAST-AFNET-4 trial (EAST, "early treatment of atrial fibrillation for stroke prevention"), the presence of sinus rhythm after one year was the most important predictor of reduction in the primary endpoint (stroke, death from cardiovascular disease, hospitalization due to heart failure or acute coronary syndrome) (e25, e26). In the group with early rhythm control, 86% of participants had sinus rhythm on EKG at one year ($p < 0.001$), compared with 66% in the control group. Thus, early and effective rhythm control should be considered in all patients with newly diagnosed AF (Figure 2).

To date, rhythm control treatment for AF has been reserved primarily for symptomatic patients. However, with growing evidence that rhythm control also lessens hospitalization and mortality (e25), it is now recommended for asymptomatic persons as well. In a subgroup analysis of the EAST-AFNET-4 trial, early rhythm control

therapy was shown to have a benefit on cardiovascular endpoints in patients aged 70 and above with relevant cardiovascular risk factors, whether or not they had symptoms (e27).

Tachycardia- or arrhythmia-induced cardiomyopathy (AiCM) (e28, e29) lessens the left ventricular ejection fraction, but this can be reversed by the restoration of a stable sinus rhythm. In cases of newly diagnosed, primarily tachycardic AF with impaired left ventricular pump function, arrhythmia-induced cardiomyopathy (AiCM) should be considered as a possible diagnosis (e28).

Rhythm control in AF and heart failure

AF and heart failure due to structural heart disease are known to reinforce each other (e30–e37). For the diagnosis of AF-related cardiomyopathy, rhythm control can be attempted first, followed by re-evaluation of left ventricular function in sinus rhythm with echocardiography in 3–6 months. If the suspicion is confirmed by an improvement of the ejection fraction, permanent rhythm control is recommended (e38–e40). Current evidence suggests that rhythm control therapy improves on left ventricular function, with reverse remodeling (e41). Catheter ablation is recommended for long-term rhythm control (Figures 2 and 3) (e18, e42). The findings of recent randomized trials suggest that patients

suffering from these two conditions benefit from rhythm control by catheter ablation (e43, e44). (e43, e44).

Catheter ablation for rhythm control

Randomized trials (e45, e46) have shown that catheter ablation, compared to pharmacotherapy, yields more frequent freedom from arrhythmia (53% vs. 32.2%), fewer hospitalizations, and improved quality of life in patients with symptomatic, paroxysmal AF who have not previously been treated with antiarrhythmic drugs (number needed to treat [NNT], 5). Catheter ablation is therefore recommended as first-line therapy for symptomatic, paroxysmal atrial fibrillation (PAF) (Figures 2 and 3). Studies have also shown that catheter ablation of PAF can prevent progression to persistent AF (e23, e24). Catheter ablation is, moreover, associated with a reduction in recurrence rates, hospital stays, and the need for cardioversion in patients persistent AF (e47). The available evidence on how persistent AF should be treated with interventions beyond pulmonary vein isolation is not determinative (e48–e50). There is evidence suggesting that some patients with persistent AF may benefit from substrate ablation in the left atrium (e51).

Although rhythm control and the presence of sinus rhythm are important in the treatment of AF, there are patient groups in whom rhythm control is not expected to succeed over the long term because of disease progression and can therefore be dispensed with. For example, left atrial dilatation is associated with less successful rhythm control and a higher AF recurrence rate (e52–e54). The LA volume should be used as a measure of left atrial dilatation (e55, e56). The upper bound of normal LA volume is 34 ml/m² for both sexes; this should be used as the cut-off value for a dilated left atrium, according to the EHRA recommendation (e57).

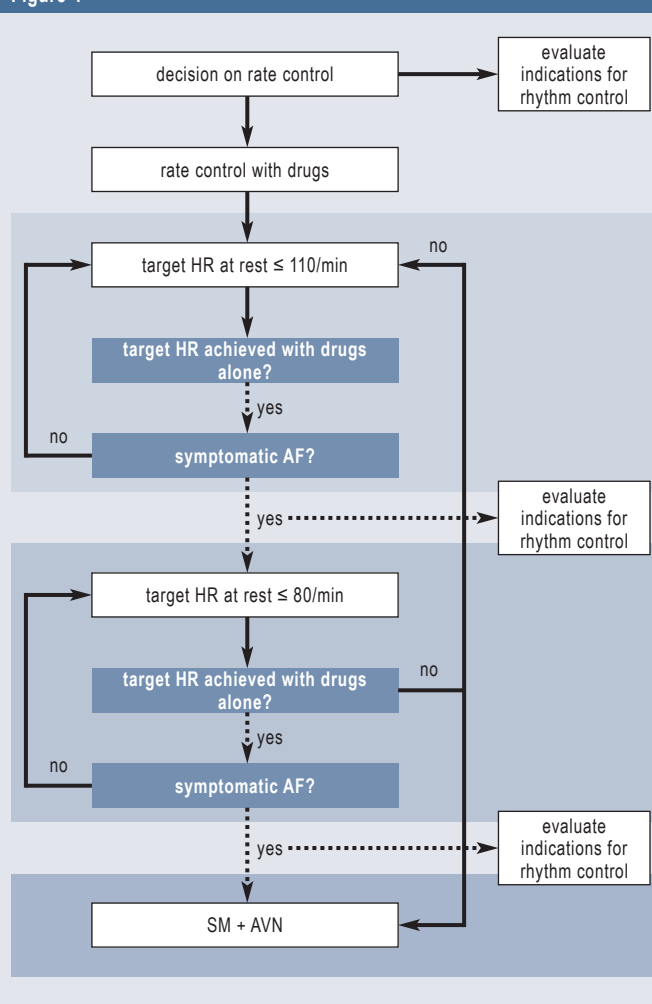
Rhythm control with drugs

Class IC antiarrhythmic drugs (flecainide and propafenone) are an important pharmacotherapeutic option for rhythm control (Figure 4). They are effective in early rhythm control and have a low risk profile (e58). Unlike amiodarone, they should only be used in patients with a structurally healthy heart; where indicated, they can be used only as needed and, if necessary, as medication on demand (e59, e60) (Figure 3). Of all the available antiarrhythmic drugs, amiodarone is the most effective, but also the most prone to side effects (e61, e62). Its wide-ranging side effects can affect, e.g., the thyroid, lungs, and liver; as it can also have proarrhythmic effects, safety considerations and close therapeutic monitoring are needed (e63–e68). Since alternative therapies such as catheter ablation are available, the guideline group, after weighing the risks and benefits, recommends against long-term amiodarone treatment for most patients.

Longstanding atrial fibrillation

The success rates of catheter ablation as a sole treatment are much lower in longstanding AF (≥ 12 months) than in paroxysmal or persistent AF. Hybrid procedures with catheter ablation followed by surgical ablation were found, in a meta-analysis, to lower the AF recurrence

Figure 4



Simplified flowchart of staged strategies for appropriate rate control with moderate and strict stages and, if necessary, AV node ablation combined with pacemaker therapy AF, atrial fibrillation; BIV, biventricular stimulation/cardiac resynchronization; CSP, conduction system pacing; HR, heart rate; LV-EF, left ventricular ejection fraction; SM + AVN, pacemaker therapy plus AV node ablation

rate (e69, e70). When rhythm control is indicated in a symptomatic patient in the context of cardiac surgery, simultaneous intraoperative AF ablation is recommended, as it has been found to lower the rate of atrial tachyarrhythmias from 51.0 to 24.1% (e71).

Rate control

If rhythm control therapy is not used, adequate rate control can reduce the exacerbation of heart failure and the occurrence of tachycardia-induced cardiomyopathy and, above all, ameliorate symptoms and improve in exercise capacity and quality of life (e72–e77) (Figure 4).

If rhythm control therapy is not used, adequate rate control can minimize the likelihood of exacerbation of heart failure and tachycardia-induced cardiomyopathy. Above all, it can lead to a reduction in symptoms and an improvement in exercise capacity and the quality of life (e72–e77) (Figure 4).

In general, a three-step treatment algorithm is recommended for rate control (Figure 4). In the first step, moderate rate control is used.

If AF-related symptoms persist, stricter rate control is implemented. A third option is pacemaker therapy with AV node ablation (e72–e77).

Summary

The high prevalence and incidence of AF and the highly variable quality of treatment at present call for stepped-up efforts to improve the care of patients with this condition. The authors of the German clinical practice guideline on atrial fibrillation hope to bring about improvement in the following ways:

- by supporting participatory decision-making and strengthening the role of patients
- by improving treatment adherence by fostering the communication and adoption of shared treatment goals
- by lowering the incidence of AF with evidence-based primary prevention measures
- by promoting beneficial lifestyle changes
- by improving management, including thromboembolism prevention
- by promoting a paradigm shift from rate control to early rhythm control.

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These guidelines could not have been produced without the continuous collaboration of the entire team (see eBox 2). Special thanks are due to the staff of the ÄZQ, Corinna Schaefer, Katrin Pieper, and Peggy Prien. In particular, we would like to thank Ms. Schaefer for her tireless commitment, even after the ÄZQ was dissolved.

Conflict of interest statement

SW refers to the declaration of his conflicts of interest to the AWMF. He also states that the German Society of Cardiology reimbursed his travel expenses.

FW states that he has received lecture honoraria from Abbott and reimbursement of travel expenses from Boston Scientific and Bayer. He is a member of the DGK, ESC, and EHRA and reports that he is engaged in clinical scientific activities on supraventricular arrhythmias, thromboembolism in atrial fibrillation, and cardiac implantable devices.

LE refers to the declaration of his conflicts of interest to the AWMF. He reports that he has given lectures for various companies in the pharmaceutical and medical technology industries. He also states that he has received reimbursement of travel expenses and meeting participation fees in connection with his participation in numerous national and international studies in various capacities. He is a member of the DGK, ESC, and EHRA, and reports in this context: committee work in the umbrella organizations; research on rhythmology, pathophysiology of rhythm disorders, atrial fibrillation, and ventricular tachycardia; clinical work in cardiology/rhythmology, electrical device therapy, catheter ablation, atrial fibrillation, and ventricular tachycardia; and participation in continuing education/training: member of the planning group of the DGK "Academy."

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Clinical practice guidelines in the *Deutsches Ärzteblatt*, as in many other journals, are not subject to a peer review process, since clinical practice (S3 level) guidelines are texts which have already been evaluated, discussed, and broadly agreed upon multiple times by experts (peers).

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Corresponding author

Prof. Dr. med. Stephan Willems
s.willems@asklepios.com

Supplementary material

Complete list of full references, eReferences, eTables, eBoxes:
www.aerzteblatt-international.de/m2025.0082

Additional material to accompany the article

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eTable 1		
Modified European Heart Rhythm Association (EHRA) scoring system, adapted from Van Gelder, et al., European Heart Journal 2024		
Score	Symptoms	Description
1	none	Asymptomatic atrial fibrillation.
2a	mild	There are symptoms of AF that do not impair the patient's everyday activities.
2b	moderate	There are symptoms of AF that do not impair the patient's everyday activities but nevertheless cause worry to the patient.
3	severe	There are symptoms of AF that impair the patient's everyday activities.
4	disabling	Normal everyday activities are no longer possible.

eTable 2		
CHA ₂ DS ₂ -VA score for estimating the risk of thrombo-embolic events in patients with atrial fibrillation		
Letter	Feature	Point(s)
C	congestive heart failure	1
H	hyperension	1
A ₂	age 75 or above	2
D	diabetes	1
S ₂	stroke / TIA	2
V	vascular disease	1
A	age 65–74	1

eTable 3

The effect of anticoagulation in one year, depending on the prior stratification of stroke risk (modified from NICE 2021)

CHA ₂ DS ₂ -VA score	Number of patients (per thousand) who have a stroke in one year if not anticoagulated	Number of patients (per thousand) who have a stroke in one year if anticoagulated
0	2	1
1	6	2
2	25	9
3	37	13
4	55	19
5	84	29
6	114	39

eBox 1

Participating specialty societies

Guideline issued by

German Society of Cardiology (DGK), <https://dgk.org/>

with the participation of

Drug Commission of German Pharmacists (AMK), www.abda.de

Drug Commission of the German Medical Association (AkdÄ), www.akdae.de

Federal Working Group on Self-Help (BAG Selbsthilfe), www.bag-selbsthilfe.de/

German Society for General Medicine and Family Medicine (DEGAM), www.degam.de

German Society for Anesthesiology and Intensive Care Medicine (DGAI), www.dgai.de

German Society for Geriatrics (DGG), www.dggeriatrie.de/

German Society for Internal Medicine (DGIM), www.dgim.de/

German Society for Medical Intensive Care and Emergency Medicine (DGIIN), www.dgiin.de/

German Society for Neurology (DGN), www.dgn.org

German Society for Pediatric Cardiology and Congenital Heart Defects (DGPK), www.dgpk.org/

German Society for Nursing Science (DGP), www.dg-pflegewissenschaft.de

German Society for the Prevention and Rehabilitation of Cardiovascular Diseases (DGPR), www.dgpr.de/

German Society for Thoracic, Cardiac, and Vascular Surgery (DGTHG), www.dgthg.de/

German Heart Foundation, www.herzstiftung.de/

German Interdisciplinary Association for Intensive Care and Emergency Medicine (DIVI), www.divi.de/

German Stroke Society (DSG), www.dsg-info.de/

Coordination and project lead

Prof. Dr. Lars Eckardt, German Society of Cardiology (DGK)

Prof. Dr. Stephan Willems, German Society of Cardiology (DGK)

Methodological support

Corinna Schaefer, Katrin Pieper, and Peggy Prien for the Agency for Quality in Medicine (ÄZQ)

PD Dr. med. Felix Wegner Clinic for Cardiology II – Rhythmology, Universitätsklinikum Münster

eBox 2

Contributors to the guideline (collaborators)

Dr. Sebastian Adamowicz, German Society for Anesthesiology and Intensive Care Medicine (DGAI)
 Prof. Dr. Philipp Attanasio, German Society of Geriatrics (DGG)
 Prof. Dr. Leif Hendrik Boldt, German Society of Cardiology (DGK)
 Hans Brink, Federal Working Group on Self-Help (BAG Selbsthilfe)
 Prof. Dr. Hans-Jörg Busch, German Interdisciplinary Association for Intensive Care and Emergency Medicine (DIVI)
 Prof. Dr. Thomas Deneke, German Society of Cardiology (DGK)
 Andreas Dirksen, German Society for Nursing Science (DGP)
 Prof. Dr. Nicolas Doll, German Society for Thoracic, Cardiac, and Vascular Surgery (DGTHG)
 Prof. Dr. Lars Eckardt, German Society of Cardiology (DGK)
 Dr. Natascha Einhart, Drug Commission of the German Medical Association (AkdÄ)
 Prof. Dr. Klaus Gröschel, German Society of Neurology (DGN)
 Dr. Melanie Anuscha Gunawardene, German Society of Cardiology (DGK)
 Dr. Jörg Haasenritter, German Society of General Medicine and Family Medicine (DEGAM)
 Prof. Dr. Roland Hardt, German Society for Geriatrics (DGG)
 Prof. Dr. Karl Georg Häusler, German Stroke Society (DSG)
 Prof. Dr. Gerhard Hindricks, German Society for Cardiology (DGK)
 Prof. Dr. Uwe Janssens, German Interdisciplinary Association for Intensive Care and Emergency Medicine (DIVI)
 Dr. Ilja Karl, German Society for General Medicine and Family Medicine (DEGAM)
 Prof. Dr. Gunter Kerst, German Society for Pediatric Cardiology and Congenital Heart Defects (DGPK)
 Prof. Dr. Erich Kilger, German Society for Anesthesiology and Intensive Care Medicine (DGAI)
 Prof. Dr. Paulus Kirchhof, German Society for Cardiology (DGK)
 Prof. Dr. Thomas Klingenheben, German Society for Cardiology (DGK)
 Prof. Dr. Karl-Heinz Kuck, German Society for Cardiology (DGK)
 Dr. Eike Langheim, German Society for the Prevention and Rehabilitation of Cardiovascular Diseases (DGPR)
 Prof. Dr. Pia Lebiez, German Society for Medical Intensive Care and Emergency Medicine (DGIIN)
 Prof. Dr. Frederik Mader, German Society for General Medicine and Family Medicine (DEGAM)
 Prof. Dr. Thomas Meinertz, German Heart Foundation
 Prof. Dr. Christian Andreas Perings, German Society of Cardiology (DGK)
 PD Dr. Andreas Rillig, German Society of Cardiology (DGK)
 PD Dr. Sascha Rolf, German Society for Cardiology (DGK)
 Dr. Andre Said, Drug Commission of German Pharmacists (AMK)
 Prof. Dr. Birke Schneider, Drug Commission of the German Medical Association (AkdÄ)
 Prof. Dr. Martin Schulz, Drug Commission of German Pharmacists (AMK)
 Prof. Dr. Philipp Sommer, German Society of Cardiology (DGK)
 Prof. Dr. Christoph Starck, German Society for Thoracic, Cardiac, and Vascular Surgery (DGTHG)
 Prof. Dr. Daniel Steven, German Society of Cardiology (DGK)
 PD Dr. Felix Ulbrich, German Society for Anesthesiology and Intensive Care Medicine (DGAI)
 Prof. Dr. Stephan Willems, German Society for Cardiology (DGK)