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The beat goes on: Highlights from the new American and European A-fib guidelines

With a prevalence of 37.57 million known cases globally, atrial fibrillation is one of the most commonly occurring cardiac arrhythmias.[1] Atrial fibrillation diminishes quality of life, is associated with poor long-term prognosis, and has a considerable socioeconomic impact on health systems worldwide.[2]

See related article, page 291

The updated American College of Cardiology (ACC), American Heart Association (AHA), American College of Chest Physicians (ACCP), and Heart Rhythm Society (HRS) 2023 guideline for the diagnosis and management of atrial fibrillation[3] and the recent 2024 European Society of Cardiology (European) guidelines for the management of atrial fibrillation[4] have been welcomed by cardiac societies. Recommendations in both guidelines stress the importance of a holistic patient-centered approach to atrial fibrillation and acknowledge that the increasing incidence of atrial fibrillation is linked to preventable risk factors in an aging population, such as heart failure, diabetes, hypertension, high alcohol consumption, physical inactivity, smoking, and obesity. The ACC/AHA/ACCP/HRS (American) guideline[3] recognizes the significance of preemptive treatment of risk factors in patients at risk of atrial fibrillation and highlights the need for integrative primary prevention as first-line therapy, as reflected by the introduction of atrial fibrillation stages such as "at risk of atrial fibrillation" and "pre–atrial fibrillation."

In this issue of the *Journal*, Campbell at al[5] provide a timely, expert review of the new American guideline for the diagnosis and management of atrial fibrillation.[3]

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The authors emphasize the new staging system and the inclusion of individuals at risk of atrial fibrillation, and acknowledge that atrial fibrillation is a "disease continuum." They also call attention to the need to incorporate lifestyle and risk-factor modification recommendations, including targeting obesity, encouraging reduced alcohol consumption, smoking cessation, and strict management of diabetes and hypertension, into clinical practice to reduce the risk of new-onset atrial fibrillation and the complications of clinically manifested atrial fibrillation. Further, the authors point out that the need for anticoagulation should be determined annually based on risk assessment of thromboembolic events.

PREVENTION CONSIDERATIONS

It is laudable that the European guidelines[4] recommend early intervention and aggressive treatment of cardiovascular risk factors to reduce progression and recurrence of atrial fibrillation and thereby prevent hospital admissions and exacerbations of symptoms. However, they stop short of strongly recommending preventive measures, despite results of trials such as RACE 3 (Routine Versus Aggressive Risk Factor Driven Upstream Rhythm Control for Prevention of Early Atrial Fibrillation in Heart Failure)[6] that showed early targeted therapy for underlying conditions helped maintain sinus rhythm in patients with persistent atrial fibrillation. This is particularly relevant for individuals with obesity, who, in a meta-analysis that included data from 587,372 patients in 16 studies, were found to have a 51% increased risk of new-onset atrial fibrillation, with no sex difference.[7] Progressive weight loss had a beneficial effect on long-term freedom from atrial fibrillation and arrhythmia-free survival in the LEGACY

(Long-Term Effect of Global Directed Weight Management in an Atrial Fibrillation Cohort) trial,[8] although this was only achieved if weight loss was 10% or more and maintained over time. In another study of patients with longstanding persistent atrial fibrillation undergoing ablation, weight loss had no impact on arrhythmia burden and long-term ablation outcome,[9] suggesting a possible point of no return. Further, atrial fibrillation incidence was noted to be risk-factor specific in several studies, with an increased risk of 50% for individuals with hypertension,[10] 20% for those with prediabetes, 28% for those with diabetes,[11,12] and 38% for heavy drinkers (≥ 21 alcoholic drinks per week).[13]

A study that used drug-target Mendelian randomization analyses suggested that lowering systolic blood pressure by 10 mm Hg with antihypertensive drugs had a preventive effect on atrial fibrillation development (odds ratio 0.64).[14] A recent meta-analysis found that treatment of diabetes with sodium-glucose cotransporter 2 inhibitors, glucagon-like peptide 1 receptor agonists, and dipeptidyl peptidase-4 inhibitors reduced the risk of new-onset atrial fibrillation by 23%, 28%, and 34%, respectively, compared with insulin.[15] Absolute abstinence from alcohol, but not reduced alcohol consumption, in chronically heavy drinkers showed the greatest effect, reducing incident atrial fibrillation by 63%.[16] Preventive measures need to address all risk factors individually to achieve cumulative success.

COMPARISON OF THE GUIDELINES

Campbell and colleagues[5] highlight the changes in recommendation class regarding shared decision-making between patient and clinician to determine the best course of action in atrial fibrillation management and the option of rhythm control as first-line treatment to evaluate the impact of atrial fibrillation on heart function—with the goal to prevent symptoms; improve quality of life; and reduce mortality, stroke, and hospitalization.[3]

Guidance on anticoagulation

Both the American and European guidelines[3,4] recommend using the CHA_2DS_2-VASc score (1 point given for congestive heart failure, hypertension, age 65 to 74 years, ≥ 75 years [doubled], diabetes mellitus, prior stroke, transient ischemic attack, or thromboembolism [doubled], vascular disease, female sex) for thromboembolic risk assessment and warn against using currently available bleeding scores in isolation to determine eligibility for anticoagulation. However, the European guidelines[4] discourage the use of sex to calculate the CHA_2DS_2-VASc score, seeing it as an age-related modifier and not a risk factor per se. Anticoagulation guidance for device-detected atrial high-rate episodes is appreciably more nuanced in the American guideline,[3] with clear cut-offs for duration of atrial high-rate episodes and clear guidance on anticoagulation management.

Treatment of life-threatening bleeds with specific antidotes for direct oral anticoagulants is designated a class 1 recommendation in the American guideline,[3] whereas the European guidelines acknowledge the limited availability of these agents in some healthcare environments, giving their use a class 2a recommendation.[4]

Left atrial appendage occlusion

Campbell et al[5] point out that the American guideline recommends that percutaneous placement of a left atrial appendage occlusion device is reasonable in patients experiencing atrial fibrillation with a moderate to high thromboembolic risk and contraindication to anticoagulation; this was upgraded to a class 2a recommendation owing to updated safety data on devices for left atrial appendage occlusion.[3] This remains a 2b recommendation by the European guidelines, citing the lack of "solid" randomized controlled trial data and need for continued postprocedure antithrombotic treatment.[4] Conversely, surgical left atrial appendage closure for all patients with atrial fibrillation undergoing cardiac surgery is recommended as an adjunct to oral anticoagulation to prevent ischemic stroke and thromboembolism,[4] while the American guideline[3] does not promote this technique for patients with a CHA_2DS_2-VASc score less than 2.

Catheter ablation

Catheter ablation with pulmonary vein isolation has a clear class 1 indication as first-line therapy when compared with antiarrhythmic drugs for select patients with paroxysmal and symptomatic atrial fibrillation who are younger and have fewer comorbidities.[3] This upgrade in recommendation has been partially adopted by the European guidelines, which do not limit the procedure to a specific ablation method or to select groups and give it class 2a status. Only when atrial fibrillation is proven to cause symptoms or drive heart failure does catheter ablation receive a class 1b recommendation. Anticoagulation following catheter and surgical ablation is advocated for 3 months in the American guideline[3] and at least 2 months in the European guidelines.[4]

Pharmacologic therapy

Further differences exist regarding pharmacologic treatment of atrial fibrillation. Unlike the European

guidelines,[4] the American guideline[3] does not recommend first-line digoxin for the treatment of acute and long-term atrial fibrillation in patients with preserved left ventricular ejection fraction, owing to its slower treatment response and subsequent longer hospital stays compared with diltiazem.[17]

Dronedarone is mentioned by both guidelines[3,4] for maintenance of sinus rhythm. The European guidelines[4] suggest using dronedarone for patients with heart failure with midrange and preserved ejection fraction and ischemic or valvular disease. The American guideline[3] warns against its use in patients with risk factors for cardiovascular events and recent history of symptoms or hospitalization due to heart failure, noting the results of ANDROMEDA (Antiarrhythmic Trial With Dronedarone in Moderate to Severe CHF Evaluating Morbidity Decrease),[18] which showed increased mortality in patients with severely symptomatic or recently decompensated heart failure.

Both American and European guidelines recommend that low-dose amiodarone is reasonable for long-term maintenance of sinus rhythm if other rhythm-control strategies are ineffective or contraindicated.[3,4] Further reversal of trigger factors and concomitant treatment of risk factors and comorbidities is encouraged as part of a complementary atrial fibrillation care pathway for patients with first-time atrial fibrillation.

Both cardiac and noncardiac surgery can trigger new-onset, incidental, acute, and recurrent atrial fibrillation, but evidence regarding preventive or therapeutic pharmacologic measures appears to be contradictory. The American guideline[3] understandably argues that evidence on pretreatment of patients at high risk of atrial fibrillation is not clear due to mixed results in prior trials, with no clinical advantage seen between rate- and rhythm-control strategies in a randomized controlled trial of 2,109 patients looking at the length of hospitalization and rates of new-onset persistent atrial fibrillation after cardiac surgery.[19]

In comparison, the European guidelines[4] introduced pretreatment with amiodarone (class 1) before cardiac surgery if prophylaxis is desired, owing to its ability to reduce the incidence of postoperative atrial fibrillation by 51% compared with placebo, with no difference in effect between pre- or postoperative initiation.[20] Conversely, pretreatment with beta-blockers is discouraged[4] owing to a lack of efficacy prior to cardiac surgery and a recorded increase in mortality in noncardiac surgery, according to a review of 23 meta-analyses comprising 89 randomized controlled trials (19,211 patients).[21]

Guidance on treatment of postoperative atrial fibrillation is similar for both guidelines[3,4] and has not changed, with rhythm and rate control equally recommended, taking into account the hemodynamic status of the patient.

Both guidelines[3,4] note that atrial fibrillation that occurs both during and after surgery has an up to 50% risk of recurrence, putting patients at high risk of stroke, heart failure, and mortality, thereby necessitating an upgrade in recommendations regarding long-term anticoagulation (class 2a). The American guideline recommends initial treatment for 60 to 90 days followed by reassessment of thromboembolic risk and rate-control strategy at 90 days, with the possibility of lifelong anticoagulation. This is mirrored in the European guidelines.

Concomitant posterior left pericardiotomy during cardiac surgery reduces pericardial effusion postoperatively and decreases risk of postoperative atrial fibrillation (odds ratio 0.49, 95% confidence interval 0.38–0.61),[22] which is similar to the reductions seen with treatment with amiodarone but without the adverse effects.

Guideline writing process

The American guideline[3] was written by the ACC- and AHA-appointed Joint Committee on Clinical Practice Guidelines, which summarizes the evidence and formulates the recommendations that are then peer reviewed, approved by the governing bodies of the ACC and AHA, and endorsed by the ACCP and HRS. European guidelines are written by consensus of an appointed clinical practice guidelines committee after all evidence is reviewed.[23] Patient-reported outcomes and experiences are also measured and evaluated. The guidelines are reviewed by all national cardiac societies, at which time revisions can be incorporated.

Considerations regarding cost-effectiveness of treatment of atrial fibrillation also differ between committees. Local multidisciplinary teams evaluate cost efficiencies for the European guidelines owing to the vast differences in healthcare provision in Europe.[4] The American guideline,[3] on the other hand, acknowledges that affordability is limited for some patients in the United States due to lack of healthcare insurance and no national consensus on cost-effectiveness.[24] They advise taking affordability into account when recommending treatment options such as warfarin in nonvalvular atrial fibrillation if direct oral anticoagulants are unaffordable for the individual.[3] These differences in procedure might explain some weighting differences in the recommendations between societies.

CONCLUSION

Both recently published guidelines represent a strong shift toward preventive medicine and a holistic patient-centered approach to the diagnosis and management of atrial fibrillation. Further clinical trials are warranted to address gaps in evidence relating to the optimal timing, technique, and target patient groups for catheter ablation, as well as uncertainty regarding anticoagulation strategies in patients with device-detected atrial fibrillation.

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Dr. Howell has disclosed receiving fellowship funding from EBR Systems. Dr. Liew has disclosed being a coinvestigator for a trial sponsored by Boston Scientific. Dr. Rinaldi has disclosed receiving research fellow funding from Abbott and consulting, teaching and speaking, and receiving research funding from EBR Systems.

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