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NOACs Usually Preferable to Warfarin in Atrial Fibrillation: Guideline Update

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A new focused update to atrial fibrillation (AF) management guidelines from three North American societies explicitly prefers the latest generation of oral anticoagulants (OAC) over warfarin for stroke prevention in most appropriate cases.

Unlike the corresponding full 2014 AF guideline, the update allows lower thresholds for recommending OAC in women and men based on a more nuanced interpretation of CHA_2DS_2-VASc stroke-risk scores. In addition, it sharpens recommendations for combining OAC with antiplatelets in patients with both AF and acute coronary syndromes (ACS).

It also gives measured support to catheter ablation of AF in patients with heart failure and reduced ejection fraction (HFrEF), based foremost on the CASTLE-AF trial, and to percutaneous left-atrial appendage (LAA) occlusion as an alternative to OAC in some patients, based primarily on the PROTECT-AF and PREVAIL trials.

Although the update is in some ways playing catch-up with evolving clinical practice based on recent trials, or uses recent trial data to sharpen the societies' own previous recommendations, it also breaks some new ground. For example, it adds obesity to the traditional risk factors that should be targeted for controlling AF.

"For overweight and obese patients with AF, weight loss combined with risk-factor modification is recommended," the new document states. The class I recommendation is based on a B-R level of evidence, that is, on moderate-quality randomized trial evidence.

"Obesity has been recognized as a risk factor for atrial fib for a number of years, but what's new is evidence saying that weight loss actually can improve atrial fibrillation — evidence from clinical trials, not just observational," Craig T. January, MD, PhD, University of Wisconsin School of Medicine and Public Health, Madison, told *theheart.org | Medscape Cardiology*.

January chaired the writing group for the focused update, sponsored by the American Heart Association (AHA), the American College of Cardiology (ACC), and the Heart Rhythm Society (HRS) and published January 28 in their flagship journals *Circulation*, *Journal of the American College of Cardiology*, and *Heart Rhythm*, respectively.

OAC in "Nonvalvular" A

The updated recommendations lead off with the addition of edoxaban (*Savaysa*/*Lixiana*, Daiichi Sankyo) to the list of non-vitamin-K oral anticoagulants (NOACs) for stroke prevention in AF. The factor Xa inhibitor was approved for AF in the United States after the 2014 AF guideline, which had included the other NOACs, rivaroxaban (*Xarelto*, Bayer/Janssen Pharmaceuticals) and apixaban (*Eliquis*, Bristol-Myers Squibb/Pfizer), both factor Xa inhibitors, and dabigatran (*Pradaxa*, Boehringer Ingelheim), a direct thrombin inhibitor.

Next is a new class I, level-of-evidence-A recommendation to prefer any of the NOACs over warfarin "in NOAC-eligible patients with AF, except for those with moderate-to-severe mitral stenosis or a mechanical heart valve."

The guideline explicitly defines patients with AF lacking either of those two valve conditions as having "nonvalvular" AF; the term does not imply a lack of any heart valve disorder, it states.

The 2014 document treated warfarin and the NOACs as equal, January said. But, "data are steadily emerging that the newer drugs, at least some of them, probably have a reduced bleeding risk, compared with warfarin. Not by a lot, but by a little bit. And in some settings they may be more efficacious. We've been witnessing in the last several years a steady move away from warfarin toward NOACs, and we expect that to continue," he said.

However, "there are still selected patient populations where warfarin remains the preferred drug, and those specifically are patients with moderate to severe mitral stenosis, and patients with mechanical heart valves."

The update makes no recommendation of one NOAC over another. "We had some discussion within the committee about this," January said. "There are suspicions that some of the drugs may be slightly better than others, but the data aren't there to be definitive at this point."

The update preserves the use of CHA_2DS_2-VASc scores for stroke-risk assessment that was introduced in the 2014 AF guideline, he noted, but "we lowered the bar a little" on how they are used to recommend OAC for some patients.

Whereas OAC has had a class I-B recommendation for cutting stroke risk in patients with nonvalvular AF and a CHA_2DS_2-VASc score of at least 3 for women and at least 2 for men, the new document states that OAC "may be considered" for such patients with scores of 2 and 1, respectively.

The update rates the latter recommendation as IIb at a C-LD level of evidence, which implies the evidence is based on studies with design or execution limitations or physiologic or mechanistic studies in humans.

Device Therapy

Market approval of the Watchman (Boston Scientific) percutaneous LAA occluder for stroke-risk reduction in AF followed release of the 2014 AF guideline document, and so the device does not appear there. The new document allows for its use in patients "who are poor candidates for long-term oral anticoagulation because of the propensity for bleeding or poor drug tolerance or adherence."

It states that "percutaneous LAA occlusion may be considered in patients with AF at increased risk of stroke who have contraindications to long-term anticoagulation," a class IIb recommendation supported by a B-NR level of evidence (moderate quality evidence from well-designed and executed nonrandomized, observational, or registry studies).

The Center for Medicare and Medicaid Services, the focused update states, "has specified that patients should have a $CHADS_2$ score ≥2 or a CHA_2DS_2-VASc score ≥3 to be considered for the device," referring to Watchman.

Also new since the 2014 guideline: findings from the CASTLE-AF trial supporting the use of AF catheter ablation over rate- or rhythm-control medical therapy in patients with HFrEF and paroxysmal or persistent AF and an implanted cardiac rhythm device.

"The available data suggest that catheter ablation of atrial fib in heart failure patients may improve symptoms, they may be more likely to stay in sinus rhythm, and at least some data suggest it may improve mortality," January observed.

The result: a class IIb recommendation, level of evidence B-R, that ablation "may be reasonable in selected patients" with symptomatic AF and HFrEF "to potentially lower mortality rate and reduce hospitalization for HF."

The new document refers briefly to the recent CABANA trial, apparently as a moderating influence on their recommendation in HFrEF based on CASTLE-AF, showing catheter ablation as noninferior to drug therapy for the prevention of death and cardiovascular events in patients with new-onset or previously untreated AF and without heart failure.

But the focused update does not otherwise incorporate the CABANA results, because the trial has not yet been formally published, January said, referring to one of the writing committee's rules. "CABANA unfortunately did not show improved mortality, but we really couldn't talk about it."

Triple vs Double Antithrombotic Therapy

The update provides a warning about the extra bleeding risk associated with OAC in patients with AF who have undergone percutaneous coronary intervention (PCI) for ACS, who otherwise would also receive dual antiplatelet therapy (DAPT). Such "triple therapy" is usually best avoided, it emphasizes.

In patients with increased stroke risk (based on a CHA_2DS_2-VASc ≥2) who've had PCI for ACS, the update states, "double therapy" with $P2Y_{12}$ inhibitor antiplatelets plus a dose-adjusted vitamin-K antagonist, low-dose rivaroxaban, or 150 mg bid dabigatran "is reasonable to reduce the risk of bleeding compared with triple therapy." The recommendations are IIa, level of evidence B-R.

"The guideline acknowledges that if there's a need to put them on triple therapy, it should only be for a short period of time: 4 to 6 weeks, for example," January said. Following that early post-PCI period in which stent thrombosis is most likely, the patient should preferably be transitioned to double therapy.

"DAPT alone may be considered for patients with ACS who have AF and a CHA_2DS_2-VASc score of 0 to 1, with reconsideration of the indications for anticoagulation over time," the new document says.

January reported no conflicts. Disclosure information for all writing committee members and reviewers is in the report and tabulated separately online.

Circulation. Published online January 28, 2019. Report
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