Monotherapy for nonvalvular A-fib with stable CAD?

A meta-analysis found oral anticoagulant (OAC) monotherapy provided efficacy comparable to OAC plus single antiplatelet therapy—with lower bleeding risk.

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PRACTICE CHANGER

Recommend the use of a single oral anticoagulant (OAC) over combination therapy with an OAC and an antiplatelet agent for patients with nonvalvular atrial fibrillation (AF) and stable ischemic heart disease (IHD). Doing so may confer the same benefits with fewer risks.

STRENGTH OF RECOMMENDATION

A: Meta-analysis of 7 trials[1]

Lee SR, Rhee TM, Kang DY, et al. Meta-analysis of oral anticoagulant monotherapy as an antithrombotic strategy in patients with stable coronary artery disease and nonvalvular atrial fibrillation. *Am J Cardiol.* 2019;124:879-885. doi: 10.1016/j.amjcard.2019.05.072

ILLUSTRATIVE CASE

A 67-year-old man with a history of coronary artery stenting 7 years prior and nonvalvular AF that is well controlled with a beta-blocker comes in for a routine health maintenance visit. You note that the patient takes warfarin, metoprolol, and aspirin. The patient has not had any thrombotic or bleeding events in his lifetime. Does this patient need to take both warfarin and aspirin? Do the antithrombotic benefits of dual therapy outweigh the risk of bleeding?

Antiplatelet agents have long been recommended for secondary prevention of cardiovascular (CV) events in patients with IHD. The goal is to reduce the risk of coronary artery thrombosis.[2] Many patients with IHD also develop AF and are treated with OACs such as warfarin or direct oral anticoagulants (DOACs) to prevent thromboembolic events.

There has been a paucity of data to determine the risks and benefits of OAC monotherapy compared to OAC plus single antiplatelet therapy (SAPT). Given research that shows increased risks of bleeding and all-cause mortality when aspirin is used for primary prevention of CV disease,[3,4] it is prudent to examine if the harms of aspirin outweigh its benefits for the secondary prevention of acute coronary events in patients already taking antithrombotic agents.

STUDY SUMMARY

Reduced bleeding risk, with no difference in major adverse cardiovascular events

This study by Lee and colleagues[1] was a meta-analysis of 8855 patients with nonvalvular AF and stable coronary artery disease (CAD), from 6 trials comparing OAC monotherapy vs OAC plus SAPT. The meta-analysis involved 3 studies using patient registries, 2 cohort studies, and an open-label randomized trial that together spanned the period from 2002 to 2016. The longest study period was 9 years (1 study) and the shortest, 1 year (2 studies). Oral anticoagulation consisted of either vitamin K antagonist (VKA) therapy (the majority of the patients studied) or DOAC therapy (8.6% of the patients studied). SAPT was either aspirin or clopidogrel.

The primary outcome measure was ma-

jor adverse CV events (MACE). Secondary outcome measures included major bleeding, stroke, all-cause mortality, and net adverse events. The definitions used by the studies for major bleeding were deemed "largely consistent" with the International Society on Thrombosis and Haemostasis major bleeding criteria, ie, fatal bleeding, symptomatic bleeding in a critical area or organ (intracranial, intraspinal, intraocular, retroperitoneal, intra-articular, pericardial, or intramuscular causing compartment syndrome), or a drop in hemoglobin (≥ 2 g/dL or requiring transfusion of ≥ 2 units of whole blood or red cells).[5]

There was no difference in MACE between the monotherapy and OAC plus SAPT groups (hazard ratio [HR] = 1.09; 95% CI, 0.92-1.29). Similarly, there were no differences in stroke and all-cause mortality between the groups. However, there was a significant association of higher risk of major bleeding (HR = 1.61; 95% CI, 1.38-1.87) and net adverse events (HR = 1.21; 95% CI, 1.02-1.43) in the OAC plus SAPT group compared with the OAC monotherapy group.

This study's limitations included its low percentage of patients taking a DOAC. Also, due to variations in methods of reporting CHA_2DS_2-VASc and HAS-BLED scores among the studies (for risk of stroke in patients with nonrheumatic AF and for risk of bleeding in AF patients taking anticoagulants), this meta-analysis could not determine if different outcomes might be found in patients with different CHA_2DS_2-VASc and HAS-BLED scores.

This study strongly suggests that there is a large subgroup of patients with stable CAD for whom single antiplatelet therapy should not be prescribed as a preventive medication.

WHAT'S NEW

OAC monotherapy benefit for patients with nonvalvular AF

This study strongly suggests that there is a large subgroup of patients with stable CAD for whom SAPT should not be prescribed as a preventive medication: patients with nonvalvular AF who are receiving OAC therapy. This study concurs with the results of the 2019 AFIRE (Atrial Fibrillation and Ischemic Events with Rivaroxaban in Patients with Stable Coronary Artery Disease) trial in Japan, in which 2236 patients with stable IHD (coronary artery bypass grafting, stenting, or cardiac catheterization > 1 year earlier) were randomized to receive rivaroxaban either alone or with an antiplatelet agent. All-cause mortality and major bleeding were lower in the monotherapy group.[6]

This meta-analysis calls into question the baseline recommendation from the 2012 American College of Cardiology Foundation/American Heart Association (ACCF/AHA) guideline to prescribe aspirin indefinitely for patients with stable CAD unless there is a contraindication (oral anticoagulation is not listed as a contraindication).[2] The 2020 ACC Expert Consensus Decision Pathway[7] published in February 2021 stated that for patients requiring long-term anticoagulation therapy who have completed 12 months of SAPT after percutaneous coronary intervention, anticoagulation therapy alone "could be used long-term"; however, the 2019 study by Lee was not listed among their references. Inclusion of the Lee study might have contributed to a stronger recommendation.

Also, the new guidelines include clinical situations in which dual therapy could still be continued: "… if perceived thrombotic risk is high (eg, prior myocardial infarction, complex lesions, presence of select traditional cardiovascular risk factors, or extensive [atherosclerotic cardiovascular disease]), and the patient is at low bleeding risk." The guidelines state that in this situation, "… it is reasonable to continue SAPT beyond 12 months (in line with prior ACC/AHA recommendations)."[7] However, the cited study compared dual therapy (dabigatran plus APT) to warfarin triple therapy. Single OAC therapy was not studied.[8]

CAVEATS

DOAC patient population was not well represented

The study had a low percentage of patients taking a DOAC. Also, because there were variations in how the studies reported CHA_2DS_2-VASc and HAS-BLED scores, this meta-analysis was unable to determine if different scores might have produced different outcomes. However, the studies involving registries had the advantage of looking at the data for this population over long periods of time and included a wide variety of patients, making the recommendation likely valid.

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CHALLENGES TO IMPLEMENTATION

Primary care approach may not sync with specialist practice

We see no challenges to implementation except for potential differences between primary care physicians and specialists regarding the use of antiplatelet agents in this patient population. JFP

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