Antiplatelet and Antithrombotic Therapy in Patients with Atrial Fibrillation Undergoing Coronary Stenting

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KEYWORDS

• Atrial fibrillation • Stroke • Coronary artery disease • Acute coronary syndrome
• Percutaneous coronary intervention • Stenting • Oral anticoagulation • Antiplatelet therapy

KEY POINTS

- Prognosis in atrial fibrillation (AF) is determined by ischemic stroke risk, the prevention of which is the main priority.
- Many patients with AF have associated coronary artery disease (CAD) requiring percutaneous coronary intervention (PCI).
- The major challenge is how to balance risks of stroke, coronary ischemic events, and major bleeding in patients with AF referred for PCI.
- Different thrombotic mechanisms necessitate initial triple antithrombotic therapy with oral anticoagulation (OAC) plus dual antiplatelet therapy (DAPT) of shortest possible duration (depending on the clinical setting, CHA_2DS_2-VASc and HAS-BLED scores and the type of stent), followed by dual antithrombotic therapy of OAC plus single antiplatelet agent, followed by OAC alone after 12 months.
- For OAC, a lower intensity is recommended with either vitamin K antagonists or non–vitamin K OAC.

INTRODUCTION

Atrial fibrillation (AF) is the most prevalent sustained arrhythmia. Ischemic stroke is a devastating and debilitating complication of AF associated with a poor prognosis. Stroke prevention is therefore a major priority in the management of patients with AF. The vast majority have at least one additional stroke risk factor and therefore require chronic oral anticoagulation (OAC) as the only means of effective stroke prevention.[1]

Twenty percent to 35% of patients with AF also have coronary artery disease (CAD) that may cause AF. Furthermore, development of acute coronary syndrome (ACS) can be precipitated by AF paroxysms.[2] Percutaneous coronary

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intervention (PCI) with stenting is standard of care for patients with ACS and is also frequently used for myocardial revascularization in stable CAD. Prevention of recurrent cardiac ischemia and stent thrombosis necessitates DAPT that has to be administered for up to 12 months.[3]

The challenge is how to balance the risks of stroke and systemic embolism (SE), coronary ischemic events, and major bleeding. Increasing AF prevalence means that interventional cardiologist will encounter more patients with AF in the cardiac catheterization laboratory but there is little evidence from randomized controlled trials (RCTs) addressing antithrombotic management in this complex cohort, because patients with indications for chronic OAC were largely excluded from trials involving PCI.[4]

A joint consensus document of the European Society of Cardiology (ESC) Working Group on Thrombosis, European Heart Rhythm Association, European Association of Percutaneous Cardiovascular Interventions, and European Association of Acute Cardiac Care endorsed by the Heart Rhythm Society and Asia-Pacific Heart Rhythm Society was published, providing detailed recommendations on managing these patients based on best available data.[5]

THROMBOEMBOLIC RISKS IN ATRIAL FIBRILLATION

It has been widely acknowledged for decades that AF carries an increased probability of thromboembolic complications with the ischemic stroke considered to be the most devastating with respect to quality of life, hospitalizations, and survival. It is also known that not all patients with AF are similar in terms of their thromboembolic risk. The latter is characterized by the presence of comorbid conditions (eg, hypertension, heart failure with left ventricular dysfunction, diabetes mellitus, previous history of stroke or transient ischemic attacks [TIA], vascular disease including peripheral disease and also history of myocardial infarction [MI] or coronary revascularization) and patient-independent factors, such as increasing age and female gender. These factors were incorporated in the CHA_2DS_2-VASc (congestive heart failure, hypertension, age $\geq$75 years, diabetes, stroke, vascular disease, age 65-74 years, sex category) stroke score (Table 1), which provides the best discrimination between low stroke risk patients (ie, those without an additional stroke risk factor) and all the others (ie, those with at least one stroke risk factor).[6,7] The risk of stroke also may depend on other factors, such as left atrial size and function, inflammation and cytokines, fibrosis and ischemia, epicardial fat and endothelial dysfunction, AF burden, and obesity and obstructive sleep apnea, but these variables are not easily measured in routine clinical practice.[8–10]

According to current ESC guidelines, the presence of a single CHA_2DS_2-VASc stroke risk factor (apart from female gender that should appear in conjunction with one other stroke risk factor) mandates initiation of OAC, because stroke and SE rates are increased threefold[11] compared with those without additional risk factors (ie, CHA_2DS_2-VASc = 0 or 1 for male and female patients, respectively).[12,13] This was shown in a large Danish nationwide cohort study comprising 39,400 patients discharged with nonvalvular AF with a CHA_2DS_2-VASc, score of 0 or 1. Such patients had a stroke rate of 0.49 per 100 person-years at 1 year compared with 1.55 per 100 person-years in patients with one CHA_2DS_2-VASc risk factor beyond female gender if left untreated. An increase in mortality rate was also observed.[14] An analysis performed in the same cohort revealed a hazard ratio of 3.8 for stroke/TIA/SE embolism in patients with one or more risk factors compared with those with none.[15]

These differences in embolic event rate created the positive net clinical benefit seen with warfarin therapy compared with no treatment or aspirin (ie, risks of bleeding with warfarin are outweighed significantly by stroke prevention).[16] Of note, the American Heart Association/American College of Cardiology/Heart Rhythm Society (AHA/ACC/HRS) guidelines recommend that the choice of no treatment, aspirin, or OAC in patients with moderate stroke risk lies with the treating physician. This is in contrast to the ESC guidelines.[11,17]

The risk of major bleeding is a common reason for clinicians to withdraw OAC in cases in which it may be indicated despite accumulating evidence on effectiveness and safety of warfarin as well as non–vitamin K oral anticoagulants (NOACs) when appropriately controlled. There is a trend toward higher adherence to current guidelines, but OAC remains underused with significant proportion of patients with AF at stroke risk treated with aspirin.[18]

IMPACT OF ATRIAL FIBRILLATION ON CLINICAL COURSE OF CORONARY ARTERY DISEASE

CAD is the second (with arterial hypertension being the first) most common comorbidity in patients with AF. In the EURObservational Research Programme–Atrial Fibrillation Pilot

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