Role of triple antithrombotic therapy in patients with atrial fibrillation and coronary artery stents

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Decisions regarding the use of triple therapy should take into account the balance between thromboembolism and bleeding risk in individual patients

The combined use of warfarin and dual antiplatelet therapy (aspirin plus clopidogrel) — so-called triple therapy — is a challenging management problem in patients with a coronary stent who also have an indication for oral anticoagulation. One of the most common clinical scenarios is a patient with atrial fibrillation (AF) who undergoes percutaneous coronary intervention with stenting. Guidelines for antithrombotic therapy recommend that patients with AF who are at high risk of stroke (ie, prior history of stroke or more than one of: age ⩾ 75 years, hypertension, diabetes, and congestive cardiac failure) receive warfarin;[1] and guidelines for percutaneous coronary intervention management recommend dual antiplatelet therapy in all stent patients to prevent stent thrombosis.[2] Both warfarin and clopidogrel increase the risk of bleeding in patients treated with aspirin, and combining all three drugs can be expected to further increase bleeding risk. However, the efficacy and safety of triple therapy have not been evaluated in randomised controlled trials.

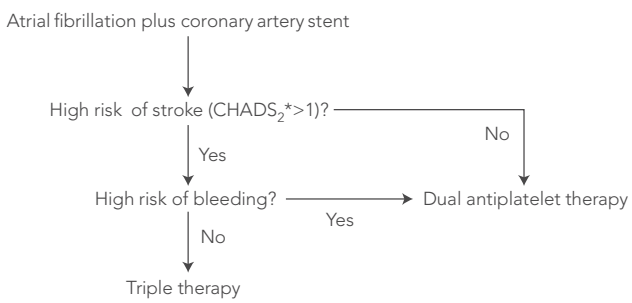
What is the evidence concerning the efficacy of anticoagulation or antiplatelet therapy in patients with AF who have recently received a coronary artery stent? In patients with AF who are at risk of stroke, warfarin compared with placebo or no treatment reduces the risk of stroke by about two-thirds, whereas aspirin reduces the risk by about one-fifth.[3] Adding clopidogrel to aspirin improves the effectiveness of antiplatelet therapy for stroke prevention,[4] but warfarin is substantially more effective than dual antiplatelet therapy.[5] In patients with a recent coronary artery stent, dual antiplatelet therapy compared with the combination of aspirin and warfarin reduces death or myocardial infarction by half.[6] Premature discontinuation of clopidogrel (less than 3 months of treatment for sirolimus-eluting stents; less than 6 months for paclitaxel-eluting stents) is the single most important risk factor for stent thrombosis.[7]

The efficacy and safety of triple therapy have been examined in multiple observational studies. Meta-analysis of 10 observational studies involving 1349 patients with AF who received triple therapy after stent insertion revealed a weighted mean incidence of major bleeding at 30 days of 2.2% (95% CI, 0.7%–3.7%).[8] Increasing the duration of triple therapy to longer than 6 months doubles the risk of major bleeding compared with 1 month of treatment.[9] The guidelines recommend at least 4 weeks of dual antiplatelet therapy for patients who receive a bare metal stent and at least 1 year for those who receive a drug-eluting stent.[2]

What is the optimum antithrombotic management of patients with AF who undergo coronary stent insertion? Decisions regarding the use of triple therapy should take into account the balance between thromboembolism and bleeding risk in individual patients. Dual antiplatelet therapy alone is likely to be adequate for stent patients with AF if they are at low or moderate risk of stroke ($CHADS_2$ stroke risk score [congestive heart failure, hypertension, age ⩾ 75 years, diabetes, 1 point each; previous stroke or transient ischaemic attack, 2 points[10]], 0–1), or if they are at high risk of stroke ($CHADS_2$ stroke risk score, > 1) and deemed to be at unacceptably high risk of bleeding with triple therapy. The most important risk factors for bleeding are older age (eg, > 75 years), severe renal dysfunction (eg, creatinine clearance < 30 mL/min), recent gastrointestinal bleeding (eg, within 6 months), previous stroke, and uncontrolled hypertension (eg, systolic blood pressure > 160 mmHg, diastolic blood pressure > 110 mmHg).[11] All other patients with AF who are at high risk of stroke ($CHADS_2$ stroke risk score, > 1) and have recently undergone coronary artery stenting should probably receive warfarin in addition to dual antiplatelet therapy (Box).[8]

Cardiologists and primary care physicians should communicate closely to optimise antithrombotic therapy and minimise the risk of bleeding in patients who may be candidates for triple therapy. Firstly, the duration of exposure to triple therapy should be limited where possible by selecting a bare metal stent, which requires a shorter duration of antiplatelet therapy than a drug-eluting stent.[2] Secondly, aspirin should be used at the lowest proven effective dose of 50–100 mg/day to minimise the risk of gastrointestinal bleeding.[12] Thirdly, in patients at high risk of gastrointestinal bleeding, consideration should be given to the use of acid-suppressive therapy, either with a histamine H2-receptor antagonist (eg, ranitidine) or a proton-pump inhibitor.[13] Retrospective analyses of administrative databases have suggested that the concomitant use of a proton-pump inhibitor (particularly omeprazole) reduced the efficacy of clopidogrel,[14,15] but subsequent analyses of data from randomised controlled trials indicated no loss of benefit of clopidogrel when the two were used in combination.[16] If a proton-pump inhibitor is used, it may be reasonable to avoid the use of omeprazole. Finally, warfarin therapy should,

Treatment decision algorithm for patients with atrial fibrillation and a coronary artery stent[8]



*$CHADS_2$ stroke risk score (congestive heart failure, hypertension, age ⩾ 75 years, diabetes, 1 point each; previous stroke or transient ischaemic attack, 2 points).[10] ◆

ideally, be monitored by an expert anticoagulation clinic to optimise the quality of international normalised ratio (INR) control (target INR, 2–3).[11]

What are the unresolved issues? Our recommendations for the use of triple antithrombotic therapy in patients with AF and a stent are based on observational studies[8] and extrapolations of evidence from randomised controlled trials of antithrombotic therapy for prevention of stent thrombosis and thromboembolism in patients with AF. Dedicated randomised studies are urgently needed to obtain more reliable estimates of the risks and benefits of triple antithrombotic therapy in patients with a coronary artery stent who have AF, as well as in stent patients with other indications for warfarin therapy, such as mechanical heart valves or recent venous thromboembolism.

Competing interests

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