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ANTIPLATELET THERAPY

Risks and benefits of extended DAPT after stenting

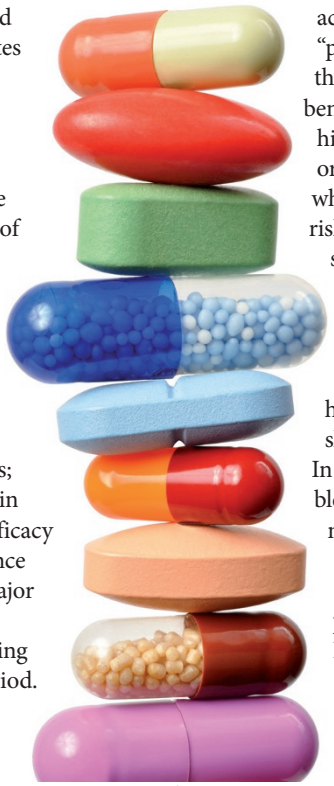
In patients who received coronary drug-eluting stents, continuation of dual antiplatelet therapy beyond 1 year after stent placement, compared with aspirin therapy alone, is associated with reduced thrombotic risk and major adverse cardiac events. These findings were reported by investigators of the Dual Antiplatelet Therapy (DAPT) study, and were presented at the AHA Scientific Sessions 2014 in Chicago, IL, USA and published in *The New England Journal Of Medicine*.

Current guidelines recommend the use of dual antiplatelet therapy for 6–12 months after stenting for the prevention of coronary stent thrombosis. Until now, little evidence has been reported to support the benefit of dual antiplatelet therapy beyond 1 year. The DAPT study is the first international, multicentre, randomized, placebo-controlled trial sufficiently powered to determine the risks and benefits of prolonged dual antiplatelet therapy after stent placement.

The investigators enrolled patients who were candidates for dual antiplatelet therapy after treatment with an FDA-approved drug-eluting coronary stent. After stenting and the standard 12-month course of thienopyridine antiplatelet therapy (clopidogrel or prasugrel) and aspirin, a total of 9,960 patients were randomly assigned to continue antiplatelet therapy or receive placebo for an additional 18 months; all patients continued aspirin therapy. The co-primary efficacy end points were the incidence of stent thrombosis, and major adverse cardiovascular and cerebrovascular events during the extended treatment period.

Patients who continued thienopyridine therapy, when compared with patients receiving placebo, had a significant reduction in the rate of stent thrombosis (0.4% versus 1.4%, HR 0.29, 95% CI 0.17–0.48; $P<0.001$) and major adverse cardiovascular and cerebrovascular events (4.3% versus 5.9%, HR 0.71, 95% CI 0.59–0.85; $P<0.001$). Furthermore, patients in the thienopyridine treatment group had a lower rate of myocardial infarction compared with those receiving placebo (2.1% versus 4.1%, HR 0.47; $P<0.001$). According to the DAPT investigators, this "reduction in the risk of ischemic events was consistent across stent type and specific thienopyridine drug used and was evident regardless of the risk of stent thrombosis".

The clinical benefit derived from prolonged dual antiplatelet therapy compared with placebo was accompanied by an increased risk of moderate or severe bleeding (2.5% versus 1.6%, HR 1.61, 95% CI 1.21–2.16; $P=0.001$). In light of these findings Antonio Colombo and Alaide Cheiffo highlight in an accompanying editorial that "prolonged dual antiplatelet therapy is most likely to be of benefit in patients who are at high risk for stent thrombosis or myocardial infarction, but who are also at relatively low risk for bleeding." Although some patients treated with a drug-eluting stent might have benefited from extended dual antiplatelet therapy, "the potential harm with this approach should not be overlooked." In addition to increased risk of bleeding, the rate of death from noncardiovascular causes was higher in the thienopyridine group compared with the placebo group (1.1% vs 0.6%; HR 1.80, $P=0.04$).



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In a separate study, to assess the effect of extended dual antiplatelet therapy on all-cause, cardiovascular, and noncardiovascular mortality, Elmariah *et al.* performed a meta-analysis of 14 trials, including the DAPT study, which examined the effect of long-term versus no or short duration dual antiplatelet therapy on mortality. In this study published in *The Lancet*, extended dual antiplatelet therapy, compared with aspirin alone or short-term dual antiplatelet therapy (≤6 months), was not associated with an increase in all-cause mortality (HR 1.05, 95% credible interval 0.96–1.19, $P=0.33$) or cardiovascular and non-cardiovascular mortality.

One limitation inherent in randomized trials such as the DAPT study is the enrolment of a highly selected population. To address this, Yeh *et al.* compared the clinical characteristics of patients in the DAPT trial to other patients undergoing percutaneous coronary intervention in the CathPCI Registry. Those patients enrolled in the DAPT study were not different from patients in the CathPCI registry, with respect to ethnicity, sex, and comorbidities such as hypertension; however, DAPT study participants had a lower prevalence of chronic cardiovascular disease.

Taken together, these studies indicate that dual antiplatelet therapy beyond 1 year of stenting might be beneficial across the population of patients requiring a drug-eluting coronary stent. The optimal duration of dual antiplatelet therapy remains uncertain, and should be individualized according to bleeding risk.

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Original articles Mauri, L. *et al.* Twelve or 30 months of dual antiplatelet therapy after drug-eluting stents. *N. Engl. J. Med.* doi:10.1056/NEJMoa1409312 | Colombo, A. & Chieffo, A. Dual antiplatelet therapy after drug-eluting stents—how long to treat? *N. Engl. J. Med.* doi:10.1056/NEJMe1413297 | Elmariah, S. *et al.* Extended duration dual antiplatelet therapy and mortality: a systematic review and meta-analysis. *Lancet* doi:10.1016/S0140-6736(14)62052-3 | Yeh, R. W. *et al.* Evaluating the generalizability of a large streamlined cardiovascular trial: Comparing hospitals and patients in the Dual Antiplatelet Therapy Study versus the National Cardiovascular Data Registry. *Circ. Qual. Outcomes* doi:10.1161/CIRCOUTCOMES.114.001239