NEWS in Brief

Investigational anti-platelet Ticagrelor in stenting for acute coronary syndromes.

Of patients with acute coronary syndromes who had planned stenting, those who received ticagrelor (an investigational anti-platelet agent) had fewer cardiovascular events than those who received Clopidogrel. This was a finding from a subset analysis of the Study of Platelet Inhibition and Patient Outcomes (PLATO) trial (multi-centre, double-blind) published in *The Lancet*. Ticagrelor is a direct-acting adenosine diphosphate receptor P2Y12 inhibitor.

The trial randomised patients to Clopidogrel (300 to 600mg loading dose, then 75mg), or Ticagrelor (180mg loading dose, then 90mg twice daily). Patients were followed for 12 months. The study analysed data from a subset of 13,408 patients who had planned stenting, prior to randomisation to Ticagrelor or Clopidogrel. For every 1,000 patients admitted to the hospital for planned stenting, the use of Ticagrelor (instead of Clopidogrel) for 12 months resulted in 11 fewer deaths, 13 fewer myocardial infarctions (MIs), and 6 fewer stent thrombosis. At 12 months, there was a 16% relative risk reduction (P = 0.0025) for the primary endpoints of cardiovascular death, MI, or stroke (10.7% of Clopidogrel patients, versus 9.0% of Ticagrelor patients). One of the researchers from Brigham and Women's Hospital, Boston, stated that "treating 59 patients with Ticagrelor instead of Clopidogrel for one year would prevent one cardiovascular death, MI, or stroke. Treating just 88 patients would save one life in one year." The authors said that the mechanisms of the mortality benefit could be defined from the study, but they speculated that it might relate to the reduction in an ischaemic event without an increase in bleeding (there was no increase in major bleeding with Ticagrelor and no need for transfusions). Dyspnoea was reported as a troublesome side effect.

A commentary in *The Lancet* stated that the "compelling results support Ticagrelor as a new standard of care in acute coronary syndromes." But the commentary warned that there should be a personalised approach to drug selection, weighing risk of ischaemia versus bleeding.

The majority of patients in PLATO were from Europe, the Middle East, and Africa. Patients from North America (1% of the total) did not appear to benefit from Ticagrelor. The authors put this down to a function of trial design (fewer North American patients), rather than a "real" finding.

Ticagrelor has a fast on-off mechanism. If a patient missed an evening dose, the patient might be almost completely unprotected by morning, when thrombi are more likely to form, with serious implications after stenting. The commentary stated that Clopidogrel might still be the drug of choice for selected patients at low risk of major bleeding, and for whom non-compliance (with Ticagrelor) was a concern.

The PLATO trial was funded by AstraZeneca, which produces Ticagrelor.

Sources: (1) Cannon CP, et al. Comparison of Ticagrelor with Clopidogrel in patients with a planned invasive strategy for acute coronary syndromes (PLATO): a randomised double-blind study. Lancet 2009; DOI:10.1016/S0140-6736(09)62191-7. (2) Stone GW. Ticagrelor in ACS: redefining a new standard of care? Lancet 2009; DOI:10.1016/S0140-6736(10)60070-0.

Novel platelet-rich plasma injection to tendon may offer no benefit over exercise.

According to Dutch researchers from Erasmus University Medical Center, Rotterdam, an experimental drug-and-exercise therapy (platelet-rich plasma or PRP injections combined with eccentric exercise) for chronic Achilles tendinopathy does not work.

The researchers said that PRP injection was gaining popularity based on limited studies and its apparent connection to use by professional athletes, most notably golfer Tiger Woods, who reportedly received PRP injections to speed up recovery after knee surgery. (The theory of PRP injections is that platelets release growth factors that assist tissue repair.) They thus conducted the first randomised, placebo-controlled trial of the therapy.

They enrolled 54 patients being treated for chronic tendinopathy, 2 to 7cm above the Achilles tendon insertion. The patients were randomly assigned to receive PRP injections (derived from their own venous blood) or a saline placebo. This was combined with 12 weeks of eccentric exercises. The Victorian Institute of Sports Assessment-Achilles (VISA-A) questionnaire (which evaluates pain score and activity level) was used to assess the primary endpoint change from baseline (at 6, 12, and 24 weeks). The fluid was injected through 3 ultrasound-guided punctures in the tendon (5 small depots in each puncture site).

Based on the questionnaire, both groups improved significantly from baseline through 24 weeks. Patients receiving PRP improved by 21.7 points; those receiving placebo improved by 20.5 points. There was no significant difference between the groups at 24 weeks or at any other evaluation time point. The researchers attributed improvement in both groups to the exercise programme, and partly to placebo effect.

The researchers said that the main limitation of the study was that the quantity of platelets and quantity of growth factors in the injections was not known. Also, it was not clear how long growth factors remained in the tendon (there is a possibility that they may diffuse away rapidly). SMA

Source: De Vos RJ, et al. Platelet-rich plasma injection for chronic Achilles tendinopathy: A randomized controlled trial" JAMA 2010; 303(2): 144-49.