Long-term antiplatelet monotherapy after stenting is safe but does not improve outcomes

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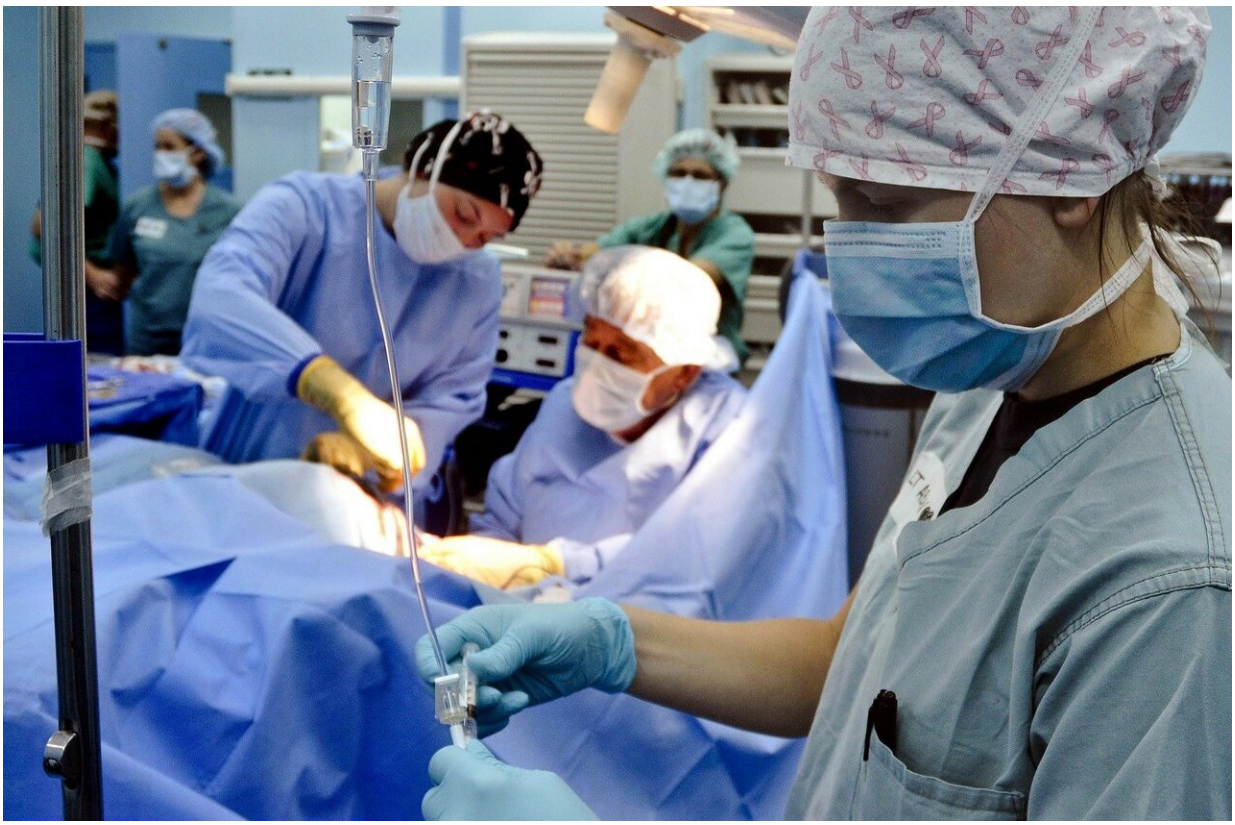

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Long-term antiplatelet monotherapy after stenting is safe but does not reduce the risk of death or heart attack compared to standard dual

antiplatelet therapy, according to late breaking results from the GLOBAL LEADERS trial presented today in a Hot Line Session at ESC Congress 20181 and published in *The Lancet*.

Ischaemic heart disease is the top global cause of death.3 In this condition, arteries supplying oxygen-rich blood to the heart become narrowed due to the build-up of fatty material. Treatments include medication, surgery to bypass the arteries, and keyhole surgery to open clogged arteries by inserting a stent (percutaneous coronary intervention; PCI).

Among patients undergoing PCI, dual antiplatelet therapy (aspirin plus a P2Y12 inhibitor) reduces the risk of blood clots and heart attacks but also increases the risk of bleeding.4-8 A shorter duration of dual antiplatelet followed by single antiplatelet therapy with a P2Y12 inhibitor might reduce adverse events with no increase in bleeding.9

GLOBAL LEADERS is the largest trial to date testing one month of dual antiplatelet therapy versus the standard of more prolonged dual antiplatelet therapy after drug eluting stent implantation.10 The trial enrolled 15,991 patients scheduled to undergo PCI for stable coronary artery disease or acute coronary syndromes. Patients were recruited from 130 centres in 18 countries in Europe, North and South America, and Asia Pacific.

Patients underwent PCI with a drug-eluting stent, were treated with the direct thrombin inhibitor bivalirudin, and then randomly assigned in a 1:1 ratio to the experimental or standard treatment arm.

The experimental arm received one month of dual antiplatelet therapy with aspirin plus the P2Y12 inhibitor ticagrelor, followed by ticagrelor monotherapy for 23 months. The standard treatment arm received 12 months of dual antiplatelet therapy with aspirin plus a P2Y12 inhibitor

(clopidogrel for patients with stable coronary artery disease, ticagrelor for those with acute coronary syndromes), followed by aspirin monotherapy for 12 months.

Patients were followed up for the primary endpoint of all-cause death or non-fatal myocardial infarction at two years. Myocardial infarction diagnoses were confirmed by a central committee that examined electrocardiograms (ECGs) at discharge, three and 24 months. The secondary endpoint was the rate of moderate or severe bleeding (grade 3 or 5 on the Bleeding Academic Research Consortium scale) within two years.

At two years the primary endpoint had occurred in 304 (3.8 percent) patients in the monotherapy group and 349 (4.4 percent) in the standard treatment group (rate ratio [RR] 0.87, 95 percent confidence interval [CI] 0.75–1.01, p=0.073). All-cause mortality occurred in 224 (2.8 percent) patients in the monotherapy group and 253 (3.2 percent) in the standard treatment group (RR 0.88, 95 percent CI 0.74–1.06, p=0.186), and the incidence of non-fatal myocardial infarction was 1.0 percent versus 1.3 percent, respectively (RR 0.80, 95 percent CI 0.60–1.07, p=0.142). Rates of moderate or severe bleeding were 2.0 percent versus 2.1 percent, respectively (RR 0.97, 95 percent CI 0.78–1.20, p=0.766).

Professor Patrick Serruys, principal investigator, Imperial College London, UK, said: "Ticagrelor, in combination with aspirin for one month, followed by ticagrelor alone was not superior to one-year standard dual antiplatelet therapy followed by aspirin alone for reducing deaths or heart attacks during the two years after stenting."

Professor Serruys noted that the trial was not designed to assess non-inferiority, meaning that further studies are needed to confirm that monotherapy is not less effective than extended dual antiplatelet therapy. But he said: "The risk of monotherapy compared to extended dual

therapy was 0.75–1.01, suggesting that monotherapy is relatively safe."

More information: Pascal Vranckx et al. Ticagrelor plus aspirin for 1 month, followed by ticagrelor monotherapy for 23 months vs aspirin plus clopidogrel or ticagrelor for 12 months, followed by aspirin monotherapy for 12 months after implantation of a drug-eluting stent: a multicentre, open-label, randomised superiority trial, *The Lancet* (2018). DOI: 10.1016/S0140-6736(18)31858-0

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