

groups for any individual component of the primary end point.

Differences in the design of the CIRT and the CANTOS trials and in the properties of the two antiinflammatory drugs could explain the contrasting results between the trials. Patients with stable atherosclerosis at high cardiovascular risk were enrolled in both trials, but the inclusion criteria for the CANTOS trial also included elevated plasma levels of C-reactive protein (CRP). Median baseline CRP levels among the participants of the CANTOS trial were 4.2 mg/l, compared with 1.6 mg/l in the CIRT trial, which indicates that patients in the CANTOS trial had a higher residual inflammatory risk.

In the CANTOS trial, canakinumab induced 35–40%

greater reductions in the plasma levels of IL-6 and CRP than placebo, whereas methotrexate therapy in the CIRT trial did not reduce plasma levels of IL-1β, IL-6 or CRP compared with placebo. The CIRT trial shows that selective inhibition of critical inflammatory pathways in atherosclerosis, such as the IL-1β, IL-6 or CRP pathways, might be essential to reduce the risk of adverse cardiovascular events. In the future, inexpensive and widely applicable agents that safely target these pathways should be identified and tested.

Alexandra Le Bras

ORIGINAL ARTICLE Ridker, P. M. et al. Low-dose methotrexate for the prevention of atherosclerotic events. N. Engl. J. Med. https://doi.org/10.1056/NEJMoa1809798 (2018)

of MI (HR 0.72, 95% CI 0.59–0.90), but had no effect on the rates of stroke, cardiovascular-related death or cancer. "The reduction in MI with n-3 fatty acids is consistent with previous observational research in primary prevention settings, but recent randomized trials in high-risk or secondary prevention patient populations have had disappointing results," remarks Manson. Indeed, the recent ASCEND trial showed that n-3 fatty acid intake did not reduce cardiovascular events in patients with diabetes mellitus.

Intake of vitamin D_3 also had no significant effects on the risk of cardiovascular disease or cancer, but a signal for reduction in cancer deaths (25% lower risk than with placebo) was observed over time.

Interestingly, subgroup analyses suggest that some people might particularly benefit from fish oil supplementation. Participants with low intake of fish (median of ≤1.5 servings per week) who took fish oil had a significant 19% lower risk of major cardiovascular events and a 40% lower risk of MI than those taking placebo, and African-American participants taking fish oil had a 77% reduction in the risk

of MI, irrespective of the level of fish intake. Nevertheless, Manson warns that these subgroup findings must be interpreted cautiously. "Additional research is needed to inform changes in clinical quidelines or public health recommendations," says Manson. "Our general guidance at this time is that, for patients who are already taking these supplements in doses similar to those tested by VITAL and doing well on them (or those who have clinical indications for taking these supplements), there is no clear reason to stop taking these supplements." For those with low fish consumption, Manson says they might want to check with their health-care provider about taking a supplement. For others, she recommends awaiting the findings from VITAL and other randomized trials to get a more complete picture of the benefits and risks before making a final decision.

Irene Fernández-Ruiz

ORIGINAL ARTICLES Manson, J. E. et al. Marine n=3 fatty acids and prevention of cardiovascular disease and cancer. *N. Engl. J. Med.* https://doi.org/10.1056/NEJMoa1811403 (2018) | Manson, J. E. et al. Vitamin D supplements and prevention of cancer and cardiovascular disease. *N. Engl. J. Med.* https://doi.org/10.1056/NEJMoa1809944 (2018)

RESEARCH HIGHLIGHTS

IN BRIEF

SURGERY

Endoscopic versus open vein-graft harvesting

The saphenous vein is frequently used in CABG surgery, notably because of its easy harvesting. Despite limited safety data, the less invasive endoscopic vein-graft harvesting is increasingly preferred to open harvesting for CABG surgery. A new trial to investigate the influence of vein-graft harvesting technique on long-term clinical outcomes of CABG surgery reveals no difference between endoscopic and open harvesting. A total of 1,150 patients were randomly assigned to either of the vein-graft harvesting techniques. After a median follow-up of 2.78 years, the primary outcome — a composite of major adverse events including death from any cause, nonfatal myocardial infarction, and repeat revascularization — occurred in 15.5% of the patients in the open-harvest group and 13.9% of the patients in the endoscopic-harvest group (HR 1.12, 95% CI 0.83-1.51). A longer follow-up is needed to confirm these findings, but with similar outcomes and a reduced rate of leg-wound complications, endoscopic harvesting should remain the preferred option for patients undergoing CABG surgery.

ORIGINAL ARTICLE Zenati, M. A. et al. Randomized trial of endoscopic or open vein-graft harvesting for coronary-artery bypass. N. Engl. J. Med. https://doi.org/10.1056/ NEJMoa1812390 (2018)

DEVICE THERAPY

No long-term benefit of IABP in cardiogenic shock

The results of the multicentre, open-label IABP-SHOCK II trial showed that intra-aortic balloon pump (IABP) counterpulsation did not reduce 30-day and 1-year mortality in patients with acute myocardial infarction (MI) and cardiogenic shock undergoing early revascularization. A new follow-up report of the study shows that IABP also did not reduce 6-year mortality in these patients. A total of 600 patients with acute MI and cardiogenic shock were randomly allocated to receive or not receive IABP support; analysis of the clinical outcomes of 591 of these patients at long-term follow-up revealed no between-group differences in all-cause mortality and in any other secondary outcome variables such as recurrent MI, stroke or new revascularization procedures. These data support the current quideline recommendations to not use IABP routinely.

ORIGINAL ARTICLE Thiele, H. et al. Intraaortic balloon pump in cardiogenic shock complicating acute myocardial infarction: long-term 6-year outcome of the randomized IABP-SHOCK II trial. Circulation https://doi.org/10.1161/CIRCULATIONAHA.118.038201

INTERVENTIONAL CARDIOLOGY

Long-term mortality benefit of CABG surgery over PCI in patients with diabetes mellitus

In the FREEDOM trial, revascularization with CABG surgery was superior to percutaneous coronary intervention (PCI) with drug-eluting stents in reducing the rate of major adverse cardiovascular events in patients with diabetes mellitus who have multivessel coronary artery disease (CAD). The FREEDOM Follow-On study, a 7.5 year-follow up report of 943 of the 1,900 patients of the FREEDOM trial, now shows that patients with diabetes who underwent CABG surgery have greater long-term survival than patients treated with PCI, with an all-cause mortality of 23.7% in the PCI group and 18.7% in the CABG surgery group. These results confirm the superiority of CABG surgery over PCI to treat patients with diabetes who have multivessel CAD, and support the current quidelines.

 $\label{lem:original_article} ORIGINAL\ ARTICLE\ Farkouh,\ M.\ E.\ et\ al.\ Long-term\ survival\ following\ multivessel\ revascularization\ in\ patients\ with\ diabetes\ (FREEDOM\ Follow-On\ Study).\ \textit{J.}\ Am.\ Coll.\ Cardiol.\ https://doi.org/10.1016/j.jacc.2018.11.001\ (2018)$