

IN BRIEF

SURGERY

Radial-artery versus saphenous-vein grafts

The majority of patients undergoing CABG surgery receive a saphenous-vein graft, but a new study provides evidence that use of radial-artery grafts improves clinical outcomes after CABG surgery compared with use of saphenous-vein grafts. A total of 1,036 patients were included in this analysis of six randomized controlled trials that compared radial-artery grafting (534 patients) with saphenous-vein grafting (502 patients). At 5 years of follow-up, the risks of myocardial infarction (HR 0.72; $P = 0.04$) and of repeat vascularization (HR 0.50; $P < 0.001$) were significantly lower in the radial-artery graft group than in the saphenous-vein graft group. Use of radial-artery grafts was also associated with a lower risk of occlusion. These findings support the current guidelines, which recommend the use of arterial grafts for CABG surgery.

ORIGINAL ARTICLE Gaudino, M. et al. Radial-artery or saphenous-vein grafts in coronary artery bypass surgery. *N. Engl. J. Med.* <https://doi.org/10.1056/NEJMoa1716026> (2018)

GENETICS

Genetic variation explains residual CHD risk with statin therapy

Statins decrease the incidence of coronary heart disease (CHD) by reducing the levels of plasma LDL cholesterol (LDL-C), but some individuals still have CHD events despite receiving statin therapy. New research provides a genetic explanation to this inter-individual variability. Genotyping of 3,099 individuals with CHD events and 7,681 individuals without CHD events, both groups on statin therapy, identified seven single nucleotide polymorphisms (SNPs) that were associated with CHD and were located in the *LPA* gene, which encodes apolipoprotein(a) (Lp(a)). The SNP rs10455872 showed the strongest association with CHD, and individuals carrying this risk variant had a 58% increased risk of CHD events compared with non-carriers. This association was independent of LDL-C changes in response to statin therapy and persisted in individuals with LDL-C ≤ 70 mg/dl. A previous study also showed that rs10455872 is associated with increased plasma Lp(a) levels, an indicator of high risk of CHD. Thus, strategies to lower Lp(a) levels might reduce CHD incidence in patients receiving statin therapy.

ORIGINAL ARTICLE Wei, W.-Q. et al. LPA variants are associated with residual cardiovascular risk in patients receiving statins. *Circulation* <https://doi.org/10.1161/CIRCULATIONAHA.117.031356> (2018)

PHARMACOTHERAPY

TANNylated proteins target the heart

Delivery of therapeutics directly to the heart remains challenging. According to a new study, the modification of proteins with tannic acid (TA) can improve their ability to target specifically cardiac tissue, because of the affinity of TA for macromolecules such as collagen and elastin, which are abundant in heart tissues. TA-modified (TANNylated) green fluorescent proteins (GFPs) intravenously injected in mice were detected mainly in the heart after 6 h, whereas un-TANNylated GFPs accumulated in the liver. Injection of TANNylated fibroblast growth factor (FGF) in mice after myocardial infarction reduced the infarct size to 16.3% of the whole heart size compared with a 50.5% infarct size with no treatment and 30.5% with un-TANNylated FGF treatment. TANNylated FGF also improved cardiac function, validating the therapeutic potential of TANNylated-based strategies for heart diseases.

ORIGINAL ARTICLE Shin, M. et al. Targeting protein and peptide therapeutics to the heart via tannic acid modification. *Nat. Biomed. Eng.* **2**, 304–317 (2018)

VALVULAR DISEASE

Computer modelling to personalize bioengineered heart valves

Computational modelling improves the design of tissue-engineered heart valves (TEHVs) and consistently predicts valve tissue remodelling and long-term functionality in a large-animal model. These findings suggest that integrating computational simulation into tissue engineering approaches can lead to more successful and predictable clinical outcomes.

With the increasing use of aortic valve implantation in young patients with aortic valve disease, device durability has gained importance. Current artificial or bioprosthetic valves have limited longevity and growth capacity; therefore, new approaches have focused on developing TEHVs with self-repair, remodelling, and regeneration capacity. However, these processes are complex and highly variable, and can lead to valve failure as a result of uncontrolled remodelling such as

leaflet shortening, thereby limiting the clinical translation potential of these bioengineering approaches. To address these limitations, Emmert and colleagues used computational modelling to design TEHVs and predict in vivo tissue remodelling, long-term performance, and the differences in outcomes between the TEHVs.

Computer-designed TEHVs were generated from polymer scaffolds seeded with vascular cells that deposited extracellular matrix constituents during 4 weeks of in vitro culture. The TEHVs were then decellularized and implanted as pulmonary valve replacements in adult sheep. The investigators monitored the TEHVs for 1 year using multimodal in vivo imaging and tissue remodelling assessments in the explanted valves. Computational modelling

ATHEROSCLEROSIS

Chronotherapy for atherosclerosis

Increasing evidence suggests that circadian rhythms influence cardiovascular physiology and pathology, notably by modulating systemic mediators such as immune cells. A study now reveals that myeloid cells are recruited to atherosclerotic lesions in a circadian fashion and that timed inhibition of leukocyte invasion can reduce atherosclerosis.

The role of the circadian clock in leukocyte recruitment has previously been described in the microcirculation, but not in the arterial wall. *Apoe*^{-/-} mice were housed on a 12-h light–dark cycle (lights on at 07:00 h refers to zeitgeber time 0 (ZT0); lights off at 19:00 h refers to ZT12) and fed with a high-fat diet for 4 weeks. The investigators measured leukocyte recruitment to the carotid artery for 24 h, which revealed an oscillatory pattern, with a peak at ZT1 and a minimum at ZT13.

Plasma levels of C-C motif chemokine 2 (CCL2) — a factor that promotes the migration of myeloid cells into atherosclerotic lesions — and myeloid expression levels of its receptor, C-C chemokine receptor type 2 (CCR2), were higher at ZT1 than at ZT13, which suggests that the CCL2–CCR2 axis is involved in the circadian regulation. *Apoe*^{-/-} mice with myeloid-specific deletion of *Bmal1* (also known as *Arntl*), a gene that encodes a core clock protein, showed no circadian fluctuations in myeloid-cell adhesion or in CCL2 plasma levels. Pharmacological blockade of CCR2 in *Apoe*^{-/-} mice at ZT0 reduced arterial leukocyte recruitment at ZT1 to a level similar to that at ZT13, whereas leukocyte recruitment in the microcirculation was not affected. “The arterial recruitment pattern is 12-h phase shifted compared with that in the microcirculation, thus permitting the