

IN BRIEF

VALVULAR DISEASE

Benefit of the MitraClip for mitral regurgitation

Transcatheter mitral valve repair improves outcomes in patients with heart failure and moderate-to-severe or severe secondary mitral regurgitation compared with medical therapy alone, according to data from the COAPT trial, presented at the 2018 TCT conference. A total of 614 patients were randomly assigned to receive a MitraClip device (Abbott) plus medical therapy or medical therapy alone. During 24 months of follow-up, the rate of the primary end point (hospitalizations for heart failure) was 35.8% per patient-year in the device group versus 67.9% per patient-year in the control group (HR 0.53, 95% CI 0.40–0.70, $P < 0.001$). The rate of the primary safety end point (freedom from device-related complication at 12 months) in the device group was 96.6%, which exceeded the prespecified objective performance goal of 88.0% ($P < 0.001$). All-cause mortality within 24 months was 29.1% and 46.1% in each group, respectively (HR 0.62, 95% CI 0.46–0.82, $P < 0.001$).

ORIGINAL ARTICLE Stone, G. W. et al. Transcatheter mitral-valve repair in patients with heart failure. *N. Engl. J. Med.* <https://doi.org/10.1056/NEJMoa1806640> (2018)

MYOCARDIAL INFARCTION

Survival not improved by defibrillator VEST

A wearable cardioverter–defibrillator does not significantly reduce the risk of arrhythmic death after a myocardial infarction (MI), according to the results of the VEST study. Implantable cardioverter–defibrillators are contraindicated until 40–90 days after MI, so a wearable defibrillator might reduce the rate of sudden death during this high-risk period. A total of 2,302 patients with acute MI and an ejection fraction $\leq 35\%$ were randomly assigned (2:1) to receive the wearable cardioverter–defibrillator LifeVest (ZOLL Medical) plus guideline-directed therapy or guideline-directed therapy alone. Participants in the device group wore the LifeVest for a median of 18 h per day. The rate of the primary end point (arrhythmic death) was 1.6% in the device group and 2.4% in the control group (relative risk (RR) 0.67, 95% CI 0.37–1.21, $P = 0.18$). All-cause mortality was 3.1% and 4.9% in each group, respectively (RR 0.64), and nonarrhythmic death occurred in 1.4% and 2.2% of patients in each group, respectively (RR 0.63). In the device group, 1.3% received an appropriate shock, 0.6% received an inappropriate shock, and 25% of the 48 patients who died were wearing the LifeVest at the time of death.

ORIGINAL ARTICLE Olgin, J. E. et al. Wearable cardioverter–defibrillator after myocardial infarction. *N. Engl. J. Med.* **379**, 1205–1215 (2018)

DIABETES

Cardiovascular benefit of albiglutide

The glucagon-like peptide 1 receptor agonist albiglutide is superior to placebo in preventing major adverse cardiovascular events in patients with type 2 diabetes mellitus. In the Harmony Outcomes trial, 9,436 patients with diabetes and cardiovascular disease were randomly assigned to a once-weekly subcutaneous injection of albiglutide (30–50 mg) or placebo, in addition to standard care. Over a median duration of 1.6 years, the rate of the primary end point (cardiovascular death, myocardial infarction or stroke) was 7.1% and 9.0% in the albiglutide and placebo groups, respectively (HR 0.78, 95% CI 0.68–0.90, $P = 0.0006$ for superiority). The rate of adverse events did not differ significantly between the groups.

ORIGINAL ARTICLE Hernandez, A. F. et al. Albiglutide and cardiovascular outcomes in patients with type 2 diabetes and cardiovascular disease (Harmony Outcomes): a double-blind, randomised placebo-controlled trial. *Lancet* [https://doi.org/10.1016/S0140-6736\(18\)32261-X](https://doi.org/10.1016/S0140-6736(18)32261-X) (2018)

GENETICS

GWAS identifies new blood lipid-associated genetic variants

The Million Veteran Program (MVP) is a large-scale multiethnic biobank launched in 2011 to investigate the role of genetic, behavioural and environmental factors in complex diseases. In a new study, Themistocles Assimes and his team used genetic and clinical data from 312,571 MVP participants to identify genetic variants associated with blood lipid levels; these findings could facilitate the emergence of new strategies for the prevention of atherosclerotic cardiovascular disease (CVD).

Previous genome-wide association studies (GWAS) have already linked variants to lipid levels. “Other groups have identified genetic variants and associations that influence lipids levels, many of which are under investigation as potential therapeutic targets. However, it was clear that there was room for additional discovery through the study of larger and more diverse populations,” says Assimes.

By performing a GWAS on the MVP cohort and combining the results with existing data, the investigators identified 826 lipid-associated variants across 118 novel and 268 previously identified loci. Some variants were shared among the African, European and Hispanic ethnicities, whereas novel coding variants were associated with lipid levels only in the non-European population. These new insights into the genetics of dyslipidaemia provide additional therapeutic targets to prevent CVD.

The investigators also identified new variants associated with the risk of coronary artery disease (CAD) in genes already targeted by pharmaceutical agents, including *ANGPTL4*, *LPL* and *PCSK9*. Interestingly, the mutation in *ANGPTL4* was also associated with a reduced risk of type 2 diabetes mellitus, and individuals carrying a



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loss-of-function mutation in *PCSK9* had a reduced risk of abdominal aortic aneurysm compared with individuals with the wild-type allele. “Through a focus on mutations predicted to result in a loss of gene function and a phenome-wide association study, we propose novel indications for pharmaceutical inhibitors of lipids that are either already on the market or under development,” explains study investigator Derek Klarin.

A loss-of-function variant in *PDE3B* was associated with lower plasma levels of triglycerides and a decreased risk of CAD. “To date, no pharmacotherapy has been clearly shown to reduce the risk of CAD by reducing triglyceride levels,” explains Klarin. Although studies have shown that treatment with cilostazol, an inhibitor of the phosphodiesterase encoded by *PDE3B*, reduces triglyceride levels in humans, the effects of the drug on the risk of CAD have not yet been investigated.

The investigators plan to explore further the possibility of repurposing cilostazol to prevent CAD. “If observational studies confirm our hypothesis, we may have enough evidence to launch a clinical trial to provide the ultimate proof of the clinical utility of the drug in this context,” concludes Assimes.

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ORIGINAL ARTICLE Klarin, D. et al. Genetics of blood lipids among ~300,000 multi-ethnic participants of the Million Veteran Program. *Nat. Genet.* <https://doi.org/10.1038/s41588-018-0222-9> (2018)