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IN BRIEF

GENETICS

HMGCR and *PCSK9* variants and cardiovascular risk

Genetic variation in *PCSK9* that results in the lowering of LDL-cholesterol levels has a similar effect on the risk of cardiovascular events and diabetes mellitus to that of genetic variation in *HMGCR* (which encodes the protein target of statins). This finding comes from a study involving 112,772 participants from 14 studies, who were grouped according to the number of LDL-cholesterol-lowering alleles they had inherited. For each 10 mg/dl decrease in LDL-cholesterol level, the risk of cardiovascular events was reduced to a similar degree by variants in *HMGCR* (OR 0.81, 95% CI 0.72–0.90) or *PCSK9* (OR 0.81, 95% CI 0.74–0.89). Individuals with these genetic variants and impaired fasting glucose levels were at increased risk of diabetes (OR 1.13, 95% CI 1.06–1.20 for *HMGCR*; OR 1.11, 95% CI 1.04–1.19 for *PCSK9*). Of note, "when present together, *PCSK9* and *HMGCR* variants had additive effects on the risk of both cardiovascular events and diabetes".

ORIGINAL ARTICLE Ference, B. A. *et al.* Variation in *PCSK9* and *HMGCR* and risk of cardiovascular disease and diabetes. *N. Engl. J. Med.* **375**, 2144–2153 (2016)

HEART FAILURE

Phase II trial results of omecamtiv mecarbil

Omecamtiv mecarbil is a selective cardiac myosin activator. In the phase II, pharmacokinetic COSMIC-HF study, this drug was associated with decreased ventricular diameters and improvements in cardiac function. A total of 148 patients with chronic heart failure and left ventricular ejection fraction ≤40% were randomly assigned to fixed-dose omecamtiv mecarbil (25 mg twice daily), omecamtiv mecarbil at a dose guided by pharmacokinetics (25 mg twice daily titrated to 50 mg), or placebo. After 20 weeks, the pharmacokinetic-guided group had increases in systolic ejection time (+25 ms) and stroke volume (+3.6 ml), and reductions in left ventricular end-systolic diameter (–1.8 mm), left ventricular end-diastolic diameter (–1.3 mm), heart rate (–3 bmp), and plasma N-terminal pro-B-type natriuretic peptide level (–970 pg/ml), compared with placebo. "Our findings support the hypothesis that directly and specifically improving cardiac function with a cardiac myosin activator results in favourable ventricular remodelling," conclude the investigators.

ORIGINAL ARTICLE Teerlink, J. R. *et al.* Chronic Oral Study of Myosin Activation to Increase Contractility in Heart Failure (COSMIC-HF): a phase 2, pharmacokinetic, randomised, placebo-controlled trial. *Lancet* http://dx.doi.org/10.1016/S0140-6736(16)32049-9 (2016)

ARRHYTHMIAS

Weight loss and reduced risk of atrial fibrillation

The risk of new-onset atrial fibrillation (AF) is reduced by weight loss after bariatric surgery. This finding comes from the SOS study conducted in Sweden. The prospective, matched cohort study involved 4,021 obese individuals in sinus rhythm and with no history of AF; 2,000 underwent bariatric surgery, and 2,021 received usual care. Bariatric surgery was associated with sustained weight reduction (18% weight loss after 20 years), whereas weight remained largely unchanged in the usual-care group. During the 19-year follow-up, new-onset AF occurred in 12.4% of the surgical group and 16.8% of the control group (HR 0.71, 95% CI 0.60–0.83, $P<0.001$). The risk reduction was greatest in young individuals and those with high diastolic blood pressure.

ORIGINAL ARTICLE Jamaly, S. *et al.* Bariatric surgery and the risk of new-onset atrial fibrillation in Swedish obese subjects. *J. Am. Coll. Cardiol.* **68**, 2497–2504 (2016)