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IN BRIEF

HYPERTENSION

Lifestyle offsets genetic risk of hypertension

Adopting a healthy lifestyle has beneficial effects on lowering blood pressure (BP) and cardiovascular risk, regardless of an individual's genetic predisposition to raised BP. In a study involving 277,005 individuals from the UK Biobank, investigators scored the participants according to both lifestyle factors (BMI, diet, alcohol consumption, smoking status, sodium excretion, and sedentary behaviour) and a genetic risk score involving 314 loci associated with high BP. A healthy lifestyle was strongly and inversely correlated with systolic and diastolic BP levels and with incident cardiovascular disease ($P < 10^{-320}$ for each). Participants with a healthy lifestyle had approximately 3.5 mmHg lower systolic BP and 30–33% lower risk of cardiovascular disease across the low, medium, and high genetic risk groups compared with those with an unfavourable lifestyle. "Given the importance of population-wide lifestyle modification, the use of genetic information for risk stratification merits careful evaluation before it is routinely implemented in clinical practice," conclude the researchers.

ORIGINAL ARTICLE Pazoki, R. *et al.* Genetic predisposition to high blood pressure and lifestyle factors: association with midlife blood pressure levels and cardiovascular events. *Circulation* **137**, 653–661 (2018)

HEART FAILURE

Histone deacetylases and diastolic dysfunction

Heart failure with preserved ejection fraction (HFpEF), which is characterized by left ventricular diastolic dysfunction, currently has no approved drug treatment. According to preclinical studies, the histone deacetylase inhibitor ITF2357 (givinostat) might be a therapeutic option. In two rodent models of HFpEF (induced by hypertension in Dahl salt-sensitive rats and by ageing in normotensive mice), ITF2357 blocked the development of diastolic dysfunction. The drug did not affect blood pressure, fibrosis, hypertrophy, or titin or myosin isoform expression, but instead ameliorated the impairment of cardiac myofibril relaxation. Relaxation of cardiac myofibrils from patients with HFpEF was also found to be impaired. "Agents, such as histone deacetylase inhibitors, which target myofibrils to improve relaxation, should be evaluated for clinical efficacy in patients with HFpEF," summarize the investigators.

ORIGINAL ARTICLE Jeong, M. Y. *et al.* Histone deacetylase activity governs diastolic dysfunction through a nongenomic mechanism. *Sci. Transl Med.* **10**, eaao0144 (2018)

TRANSPLANTATION

Sirolimus after heart transplantation

Long-term outcomes after heart transplantation are better with immunosuppression with sirolimus than with calcineurin inhibitor. Patients who underwent heart transplantation were treated either with calcineurin inhibitor alone ($n = 134$) or were switched from calcineurin inhibitor to sirolimus ($n = 268$) after assessment of their primary immunosuppression. Switching to sirolimus therapy was associated with a significant reduction in plaque volume and plaque index ($P < 0.0001$ for each). During follow-up (mean 8.9 years), sirolimus therapy was associated with fewer events related to cardiac allograft vasculopathy (adjusted HR 0.35, 95% CI 0.21–0.59, $P < 0.0001$) and lower all-cause mortality (adjusted HR 0.47, 95% CI 0.31–0.70, $P = 0.0002$) compared with calcineurin inhibitor therapy. Earlier conversion to sirolimus therapy (≤2 years after transplantation) was associated with better outcomes than later conversion.

ORIGINAL ARTICLE Asleh, R. *et al.* Long-term sirolimus for primary immunosuppression in heart transplant recipients. *J. Am. Coll. Cardiol.* **71**, 636–650 (2018)