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IN BRIEF

BIOMARKERS

Lymphocyte GRK2 levels predict HF prognosis

Myocardial G protein-coupled receptor kinase 2 (GRK2) levels are upregulated in patients with heart failure (HF), and directly correlate with levels found in peripheral lymphocytes. To evaluate whether lymphocyte GRK2 levels can be used to predict clinical outcomes in patients with HF, Rengo and colleagues performed a prospective study which included 257 patients with HF with mean left ventricular ejection fraction (LVEF) of 31.4 ± 8.5%. Numerous clinical variables, as well as lymphocyte GRK2 levels, were measured at time of enrolment. After a follow-up period of 37.5 ± 20.2 months, 39.7% of patients had died from cardiovascular-related causes. Age, LVEF, NYHA class, and lymphocyte GRK2 levels were all independent predictors of cardiovascular-related mortality in patients with HF. Importantly, the study investigators reported that "GRK2 levels showed an additional prognostic and clinical value over demographic and clinical variables".

ORIGINAL ARTICLE Rengo, G. *et al.* Prognostic value of lymphocyte G protein-coupled receptor kinase-2 protein levels in patients with heart failure. *Circ. Res.* http://dx.doi.org/10.1161/CIRCRESAHA.115.308207

HEART FAILURE

Gut-derived metabolite is a predictor in acute HF

Trimethylamine *N*-oxide (TMAO), a gut-derived metabolite, has been linked to risk of death in patients with chronic heart failure (HF), but its association with acute HF remains unclear. Suzuki and colleagues measured TMAO levels in plasma samples from 972 patients with acute HF. TMAO improved risk stratification for in-hospital mortality when assessed together with clinical scorings (OR ≥1.13, P ≤0.014). Furthermore, the investigators report that "elevated levels [of TMAO] were associated with poor prognosis at 1 year, and combination of TMAO and [N-terminal pro-B-type natriuretic peptide] provided additional prognostic information". TMAO was an independent predictor of death, and death and HF, until adjusted for renal confounders.

ORIGINAL ARTICLE Suzuki, T. *et al.* Trimethylamine *N*-oxide and prognosis in acute heart failure. *Heart* http://dx.doi.org/10.1136/heartjnl-2015-308826

CEREBROVASCULAR DISEASE

Pioglitazone reduces risk of stroke or MI

Insulin resistance is present in >50% of patients without diabetes who have had an ischaemic stroke or a transient ischaemic attack (TIA). The IRIS trial investigators hypothesized that pioglitazone, an insulin-sensitizing agent, could reduce rates of stroke and myocardial infarction (MI) after ischaemic stroke or TIA in patients without diabetes who have insulin resistance. In total, 3,876 patients who had a recent ischaemic stroke or TIA were randomly assigned to receive pioglitazone or placebo. After a median follow-up of 4.8 years, stroke or MI occurred in 9.0% and 11.8% of each group, respectively (HR 0.76, 95% CI 0.62–0.93, P = 0.007). The rate of progression to diabetes was significantly lower in the pioglitazone group than in the placebo group (HR 0.48, 95% CI 0.33–0.69, P <0.001). Consistent with previous studies, pioglitazone use was associated with weight gain, oedema, and bone fracture requiring surgery or hospitalization. According to the IRIS investigators, these "findings suggest that the administration of pioglitazone in 100 patients similar to those in our trial for about 5 years could prevent three patients from having a stroke or MI".

ORIGINAL ARTICLE Kernan, W. *et al.* Pioglitazone after ischemic stroke transient ischemic attack. *N. Eng. J. Med.* http://dx.doi.org/10.1056/NEJMoa1506930