GENETICS

**TTR AND HF IN
BLACK AMERICANS**

A valine-to-isoleucine substitution in the *TTR* gene, which encodes transthyretin and is carried by ~3–4% of black individuals in the USA, is associated with an increased incidence of heart failure (HF), but not death. This finding was described in a paper published in the *New England Journal of Medicine*.

The investigators used data from the prospective, observational Atherosclerosis Risk in Communities study, which includes 15,792 participants from four different communities in the USA recruited between 1987 and 1989. From this cohort, the team identified 3,856 black individuals with genotype-status data for the V122I *TTR* variant rs76992529. Overall, 3% of this group had the V122I mutation; by comparison, only two out of 10,893 non-black participants (<0.1%) were carriers of this variant.

After a median follow-up of 21.5 years, no significant difference was seen in mortality between the two groups—41 participants with the V122I variant died compared with 1,382 deaths among noncarriers (33% versus 37%). However, those carrying the V122I variant had a 47% higher risk of developing incident HF than noncarriers (age-adjusted and sex-adjusted HR 1.47, 95% CI 1.03–2.10, $P=0.04$). No interaction between carrier status and sex for either death or HF was observed. Carriers of V122I had worse systolic and diastolic cardiac function, and significantly higher levels of N-terminal pro-B-type natriuretic peptide than noncarriers (127 pg/ml, interquartile range 69–349 pg/ml versus 92 pg/ml, interquartile range 44–188 pg/ml; $P=0.03$).

The V122I variant has also been associated with late-onset restrictive amyloid cardiomyopathy. Although amyloidosis leads to structural alterations in the heart, only three patients (7%) with the V122I variant in this study had thickening of the left ventricular wall and features consistent with infiltrative amyloidosis. This rate was significantly higher than the rate in noncarriers (1%; $P=0.01$), but the investigators conclude “these data suggest that amyloidosis associated with the V122I *TTR* variant may be more benign than previously thought, although elderly persons who carry this variant may be at modestly increased risk [of] heart failure.”

Tim Geach

Original article Quarta, C. C. et al. The amyloidogenic V122I transthyretin variant in elderly black Americans. *N. Engl. J. Med.* 372, 21–29 (2015)