

# TTR V122I variant linked to adverse cardiac mechanics in middle-aged Black Americans

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*Journal*

JAMA Cardiology

Reuters Health - 04/01/2021- Echocardiographic screening of middle-aged U.S. Blacks revealed a significant association between the V122I transthyretin amyloidosis genetic variant (TTR V122I) and worse cardiac structure and function, possibly portending symptomatic heart failure later in life, researchers suggest.

About 4% of Black Americans have the TTR V122I variant, and "early identification in individuals and families may inform closer monitoring via echocardiography and potentially change treatment strategies for blood pressure lowering," Dr. Sadiya Khan of Northwestern University Feinberg School of Medicine in Chicago told Reuters Health by email.

"Many direct-to-consumer testing companies are returning this result to consumers, and clinicians need to be prepared with an approach to evaluate, screen family members, and address other risk factors for heart failure, like high blood pressure," she said. "New therapies that target TTR offer the potential to stop irreversible cardiac damage before it happens, with early identification."

"It is known that the V122I variant is not enriched in non-US Black populations," she added. "But there are other TTR variants that are present in different populations and further research is needed to know if similar cardiac manifestations may be present earlier in life."

As reported in JAMA Cardiology, Dr. Khan and colleagues analyzed data on 875 Black participants in the Coronary Artery Risk Development in Young Adults cohort. Recruitment from four centers was completed in 1985-1986, and follow-up examinations were conducted 25 and 30 years later.

Analyses were adjusted for age, sex, echocardiography quality, genetic ancestry, and field center.

Among the 875 participants (mean age at year 25, 49.4; 62% women), 31 were heterozygous and one, homozygous, for the V122I TTR variant; 24 with the variant were included in the comparative analyses.

Among all participants who had an echocardiogram at year 25, rates of hypertension (46%), diabetes (15%), and current smoking (19%) were not significantly different between those with or without V122I TTR. Further, there was no difference in left ventricular (LV) circumferential strain, longitudinal strain, or LV structure.

However, at year 30, those who carried V122I TTR had significantly lower absolute LV circumferential strain (mean, 12.4 vs. 13.7 percentage units) and significantly higher LV mass index values (mean, 97.5 g/m<sup>2</sup> vs. 83.7 g/m<sup>2</sup>).

Summing up, the authors state, "Carrier status for the V122I TTR variant is associated with subclinical cardiac abnormalities in middle age (worse LV systolic function and higher LV mass) that have been associated with increased risk of incident HF. Midlife screening of individuals who carry V122I TTR with echocardiography may prognosticate risk of symptomatic HF and inform prevention strategies."

Interventional cardiologist Dr. Richard Gumina, Associate Division Director for Research in the Division of Cardiovascular Medicine at the Ohio State Wexner Medical Center in Columbus, commented in an email to Reuters Health, "The study includes a small sample size of only 24 participants with the V122I variant. This small number did not allow for analysis of the interaction of the V122I genotype and cardiovascular risk factors."

"Additionally," he noted, "while the reported measures are statistically significant, the standard deviations

would make interpretation at an individual patient data level difficult."

"However," he said, "the findings do speak clearly of the need for a prospective study in Black patients that is appropriately powered to examine if early imaging changes are a harbinger for the progression to heart failure and if early treatment could impact these changes."

Meanwhile, he noted, "the results suggest that in patients with the TTR V122I genotype, cardiac changes occur earlier than previously thought (and) if you don't think of it, you can't diagnose and treat it."

"In Black patients presenting with heart failure symptoms in mid-life, TTR V122I cardiac amyloidosis should be tested for and treated," Dr. Gumina concluded.

SOURCE: <https://bit.ly/2X8DLvZ> JAMA Cardiology, online December 23, 2020.

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