Study identifies 18 proteins linked to heart failure, frailty

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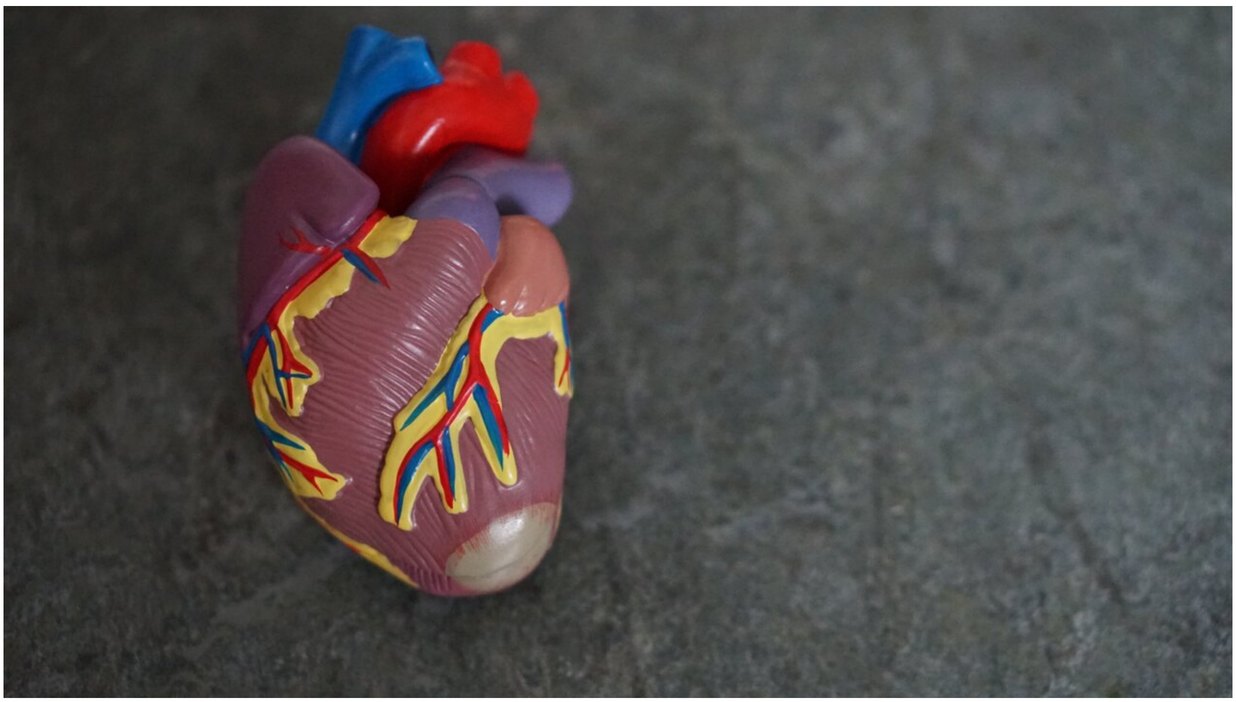

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An analysis of blood samples from thousands of study participants, led by researchers at UT Southwestern Medical Center, revealed 18 proteins associated with both heart failure and frailty, conditions that commonly develop in late life. Their findings, published in *JAMA Cardiology*, could lead to new strategies to jointly predict risk, administer preventive approaches, or treat these conditions, which often occur together.

"Our findings support shared biological pathways underlying both heart failure and frailty, suggesting interventions to prevent or treat one outcome may help decrease the burden of the other," said study leader Amil Shah, M.D., M.P.H., Professor of Internal Medicine in the Division of Cardiology and in the Peter O'Donnell Jr. School of Public Health at UT Southwestern.

As the world's population ages, so do the prevalence and incidence of heart failure and frailty, disorders that tend to occur in the seventh decade of life and beyond. Heart failure is characterized by an inability of the heart to keep up with the body's demands; symptoms of frailty are a general loss of physical function, with features often including unintentional weight loss, physical exhaustion, and low physical activity. Frailty occurs in up to half of people with heart failure, and the risk of heart failure increases in people with frailty.

Although inflammation has been implicated in both of these multisystem disorders, whether heart failure and frailty share molecular pathways has been unknown.

To answer this question, Dr. Shah and colleagues across the country used data from the Atherosclerosis Risk in Communities (ARIC) study, an ongoing longitudinal study initiated in the late 1980s at sites in North Carolina, Mississippi, Minnesota, and Maryland. Originally meant to investigate factors that influence atherosclerosis risk in study participants over a series of visits, ARIC has expanded its scope over the past four decades, including an assessment of frailty at study visits five, six, and seven between 2011 and 2019.

Using medical records, the researchers searched for hospitalizations for heart failure in 10,630 ARIC participants who submitted blood samples earlier in the study. They then compared almost 5,000 proteins present in the blood samples of participants who experienced heart failure and those who didn't, turning up 83 proteins that seemed to be associated with heart failure that occurred both in midlife and late life.

After searching for proteins in participants who developed frailty in late life (by visit six), they narrowed the list to 18 proteins that seemed to be associated with both heart failure and frailty. The same 18 proteins also were associated with both disorders among 3,189 participants in a different study, the Cardiovascular Health Study.

Not surprisingly, several of these proteins play known roles in inflammation. However, others appear to be involved in fibrosis (thickening and scarring of tissue), lipid metabolism, and cell death. A separate genetic analysis suggested five of the proteins could be causative for both conditions.

Future research will build on these findings by delving into the mechanisms of how the proteins might contribute to heart failure and frailty or result from their occurrence, Dr. Shah said. By building a better understanding of the 18 proteins, he added, researchers may eventually be able to develop drugs to concurrently prevent or treat both conditions.

Other UTSW researchers who contributed to this study were first author Diego Ramonfaur, M.D., M.Sc., M.P.H., Research Associate, and Victoria Lamberson, Ph.D., Data Scientist II.

More information: Diego Ramonfaur et al, High Throughput Plasma Proteomics and Risk of Heart Failure and Frailty in Late Life, *JAMA Cardiology* (2024). DOI: 10.1001/jamacardio.2024.1178

Provided by UT Southwestern Medical Center

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