

Why does diabetes cause heart failure?

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Men with diabetes are 2.4 times more likely than non-diabetics to suffer heart failure and women are five times more likely.

A new Loyola University Chicago Stritch School of Medicine study reveals how, on a cellular level, diabetes can cause heart failure. The



findings could lead to medications to treat and perhaps prevent heart failure in <u>diabetes patients</u>, researchers said.

The study from the lab of Jonathan A. Kirk, Ph.D., is published in the American Society for Clinical Investigation journal *JCI Insight*. Dr. Kirk is an assistant professor in the Department of Cell and Molecular Physiology of Loyola University Chicago Stritch School of Medicine.

In a healthy heart, microscopic lattice-like structures called myofilaments cause heart muscle cells to contract. The cells work in concert to make the heart contract and relax with each beat. In patients suffering from heart failure, heart muscle cells become weaker, and consequently, the heart does not pump enough blood to meet the body's needs. The patient experiences symptoms such as shortness of breath, fatigue and swelling in the legs. Heart failure ultimately can be fatal.

In the Loyola study, researchers focused on a molecule called methylglyoxal. When the body transforms food into chemical energy, waste products are generated, including methylglyoxal. Normally, the body does an efficient job clearing out methylglyoxal. But the cleansing process does not work as well in diabetics, allowing methylglyoxal to accumulate. Methylglyoxal attaches to key building blocks of proteins, which can affect how the proteins function.

Researchers examined heart tissue from three groups: people without heart failure, people with heart failure who also had diabetes and people with heart failure who did not have diabetes. The study found that methylglyoxal modifies the cardiac myofilament more in diabetic heart failure patients than it does in people who either don't have heart failure or have heart failure without diabetes. Researchers further found that the modifications caused by methylglyoxal weakened heart muscle cells by interfering with how the molecular motor works.



"This little molecule, methylglyoxal, builds up in heart <u>cells</u> during diabetes and gums up the myofilaments so they cannot contract as well," said lead author Maria Papadaki, Ph.D., a post-doctoral fellow at Loyola University Chicago Stritch School of Medicine.

The findings suggest a new approach to treating patients with diabetes who are at risk of developing heart failure. This approach involves developing drugs that would counter the effects of methylglyoxal by fine-tuning the myofilament motors.

Dr. Kirk speculates that the effects of methylglyoxal, as identified in the study, may be a key early step in how <u>diabetes</u> induces <u>heart failure</u>. This discovery could provide an effective therapeutic target for preventing <u>heart failure</u> in the growing population of diabetics.

More information: Maria Papadaki et al. Diabetes with heart failure increases methylglyoxal modifications in the sarcomere, which inhibit function, *JCI Insight* (2018). DOI: 10.1172/jci.insight.121264

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