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Study finds possible link between diabetes and increased risk of heart attack death

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Having diabetes doubles a person's risk of dying after a heart attack, but the reason for the increased risk is not clear. A new University of Iowa study suggests the link may lie in the over-activation of an important heart enzyme, which leads to death of pacemaker cells in the heart, abnormal heart rhythm, and increased risk of sudden death in diabetic mice following a heart attack.

"Many studies have shown that patients with diabetes are at especially high risk for dying from a myocardial infarction (heart attack). Our study provides new evidence that this excess mortality could involve a pathway where oxidized CaMKII enzyme plays a central role," says Mark Anderson, M.D., Ph.D., UI professor and chair and executive office of internal medicine, and senior author of the study published Feb. 15 in the Journal of Clinical Investigation.

Diabetes affects more than 8 percent of the U.S. population, and heart attack is the most common cause of death in people with diabetes. Diabetes also causes increased oxidative stress – a rise in the level of so-called reactive oxygen species (ROS) that can be damaging to cells.

In 2008, Anderson's lab showed that CaMKII (calcium/calmodulin-dependent protein kinase II) is activated by oxidation. The new study links oxidative stress caused by diabetes to increased death risk after a heart attack through the oxidation-based activation of the CaMKII enzyme.

"Our findings suggest that oxidized CaMKII may be a 'diabetic factor' that is responsible for the increased risk of death among patients with diabetes following a heart attack," says lead study author Min Luo, D.O., Ph.D., a cardiology fellow in the UI Department of Internal Medicine.

Luo and her colleagues used a mouse model of diabetes to probe the link between the disease and an increased risk of death from heart attack.

The study showed that heart rates in the diabetic mice slowed dramatically and, like humans with diabetes, the mice had double the death rate after a heart attack compared to non-diabetic mice.

Evidence from the diabetic mice suggested that the excess deaths following heart attack was due to heart rhythm abnormalities, prompting the team to investigate the heart's pacemaker cells, which control heart rate.

Looking at the diabetic mice, the team found that pacemaker cells had elevated levels of oxidized CaMKII enzyme and more cell death than pacemaker cells in non-diabetic mice. The levels of oxidation and cell death were further increased in the diabetic mice following a heart attack.

When the team blocked oxidation-based activation of the enzyme, fewer pacemaker cells died, and the diabetic mice maintained normal heart rates and were protected from the increased death risk following a heart attack.

The findings suggest that preventing or reducing activation of the CaMKII enzyme in specific heart cells may represent a new approach for reducing the risk of death due to heart attack in patients with diabetes.