

Animal Study: High-Fat, Ketogenic Diet May Prevent & Reverse Heart Failure *By Kim Stewart, Today's Practitioner*



An animal study from Saint Louis University finds that high fat or ketogenic diet could completely prevent, or even reverse heart failure caused by a metabolic process. The research team, led by Kyle S. McCommis, Ph.D., assistant professor in Biochemistry and Molecular Biology at SLU, looked at a metabolic process that seems to be turned down in failing human hearts. The findings, “Nutritional Modulation of Heart Failure in Mitochondrial Pyruvate Carrier-Deficient Mice” were published online in *Nature Metabolism*.

“Thus, these studies suggest that consumption of higher fat and lower carbohydrate diets may be a nutritional therapeutic intervention to treat heart failure,” McCommis said.

The heart’s myocardium requires vast amounts of chemical energy stored in nutrients to fuel cardiac contraction. To maintain this high metabolic capacity, the heart is flexible and can adapt to altered metabolic fuel supplies during diverse developmental, nutritional, or physiologic conditions. Impaired flexibility, however, is associated with cardiac dysfunction in conditions including diabetes and heart failure.

The mitochondrial pyruvate carrier (MPC) complex, composed of MPC1 and MPC2, is required for pyruvate import into the mitochondria. This study demonstrates that MPC expression is decreased in failing human and mouse hearts, and that genetic deletion of the MPC in mice leads to cardiac remodeling and dysfunction.

“Interestingly, this heart failure can be prevented or even reversed by providing a high-fat, low carbohydrate “ketogenic” diet,” McCommis said. “A 24-hour fast in mice, which is also “ketogenic” also provided significant improvement in heart remodeling.”

Diets with higher fat content, but enough carbohydrates to limit ketosis also significantly improved heart failure in mice lacking cardiac MPC expression.

“Our study reveals a critical role for mitochondrial pyruvate utilization in cardiac function, and highlights the potential of dietary interventions to enhance cardiac fat metabolism to prevent or reverse cardiac dysfunction and remodeling in the setting of MPC-deficiency,” McCommis said. Ongoing studies will seek to uncover the importance of ketone body versus fate metabolism in this process of improved cardiac remodeling.

Ketogenic Diet Study Take-aways

- Diets enriched with higher levels of fat but enough carbohydrate and protein to limit ketosis were also able to significantly improve or even prevent cardiac remodeling and dysfunction in a mouse model.
- These studies suggest that consumption of higher fat and lower carbohydrate diets may be a nutritional therapeutic intervention to treat heart failure.
- Like ketogenic diet, prolonged fasting increases the cardiac reliance on fatty acid oxidation and reduces ketolytic flux despite increased cardiac ketone body delivery. The 24-hour fast reduced blood glucose levels, and strongly enhanced plasma concentrations of non-esterified fatty acids and ketone bodies.
- Ketogenic diet consumption for only three weeks and the concordant increase in fat metabolism was associated with reverse remodeling of the failing hearts to essentially normal size.
- These results suggest that a ketogenic diet does not enhance cardiac ketone body metabolism, but rather stimulates fatty acid oxidation, which may be responsible for the improved cardiac remodeling and performance.

Conclusion/ Diets with higher fat content, but enough carbohydrate to limit ketosis, also improved heart failure, while direct ketone body provisioning provided only minor improvements in cardiac remodeling in CS-MPC2^{-/-} mice. An acute fast also improved cardiac remodeling. Together, our results reveal a critical role for mitochondrial pyruvate use in cardiac function, and highlight the potential of dietary interventions to enhance cardiac fat metabolism to prevent or reverse cardiac dysfunction and remodeling in the setting of MPC deficiency.

Source: McCommis, K.S., Kovacs, A., Weinheimer, C.J. *et al.* Nutritional modulation of heart failure in mitochondrial pyruvate carrier-deficient mice. *Nat Metab* (2020).
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