

Ketone Body Supplementation—A Potential New Approach for Heart Disease

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As consumer and scientific interest in the very low-carbohydrate, high-fat ketogenic (“keto”) diet continues to boom, some cardiovascular researchers are turning their attention to ketone bodies. The liver converts stored fatty acids into these metabolites—which various organs then use for extra fuel—during conditions including carbohydrate restriction, prolonged fasting, or extreme exercise. Ketone bodies are the body’s main energy source during the fat-burning state of ketosis that ketogenic dieters aim to achieve.

But ketone bodies could have benefits beyond [weight loss and blood sugar management](#). Researchers have discovered that the failing heart uses them for energy. A recent [review](#) in the *Journal of the American College of Cardiology* considered this and other emerging evidence that could support ketone body supplementation as a novel cardiovascular disease (CVD) treatment.

The Backstory

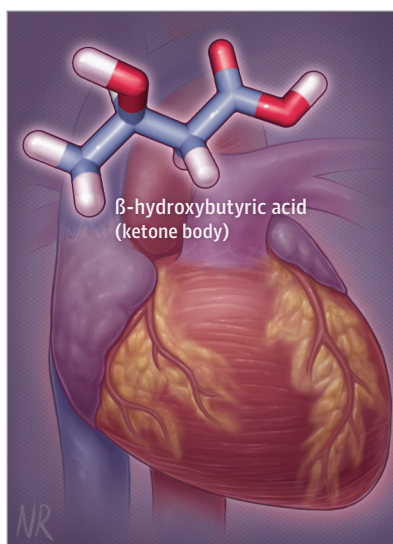
The healthy heart mainly uses fatty acids for fuel. In patients with early indications of heart failure, the organ switches to less reliance on fatty acids with an increase in glucose metabolism. As the disease progresses, the organ’s ability to use glucose also appears to be disrupted, starving it of energy and further worsening heart failure. According to the review’s authors, supplemental ketones could help this fuel starvation problem.

What We’ve Learned

Five years ago, 2 independent research teams showed that, in [patients](#) and [mice](#) with heart failure, the organ increasingly relies on ketone bodies for fuel. An uptick in circulating ketones and cardiac ketone use has now been demonstrated in additional patients with [heart failure](#), as well as individuals with [diabetes](#) and an inherited disorder called [arrhythmogenic cardiomyopathy](#), which suggests that “the keto-

genic shift is a universal cardiac response to stress,” the review’s authors wrote. What’s more, preclinical [research](#) suggests that the [heart failure benefits](#) of sodium-glucose cotransporter 2 inhibitors depend on ketone bodies. Animal experiments and early clinical studies, some using the ketogenic diet, have also demonstrated benefits of ketones on:

- Endothelial function
- Oxidative stress and mitochondrial function
- Inflammation
- Cardiac remodeling
- Cardiovascular risk factors including blood pressure, body weight, blood glucose, and lipids



Why Supplements?

There’s also evidence that the more ketones circulating in the body, the more the heart can and will use, regardless of whether a person has heart failure. Boosting ketones, therefore, could prove beneficial for patients who have CVD or are at risk for it, according to the reviewers.

One way to do so is with the [ketogenic diet](#) but, like all diets, adherence is a challenge. And falling off the keto wagon can have particularly rapid and dramatic conse-

quences. One sugar splurge or even too much protein can kick an individual out of ketosis for days.

“From a pharmacological point of view this is a nightmare,” said B. Daan Westenbrink, MD, PhD, the review’s senior author and a cardiologist and clinical pharmacologist at the University of Groningen in the Netherlands. In contrast, he noted in an email, “Exogenous ketones are poised to have predictable pharmacokinetics, making state of the art clinical trials possible.”

Achieving Nutritional Ketosis

In fact, over-the-counter ketone supplements already exist. Some amateur athletes consume drinks containing ketone esters or ketone salts to improve exercise performance. Ketone salts are higher in sodium, one reason why Westenbrink is more interested in esters. He recently showed that ketone esters help [prevent and treat](#) heart failure in rodent models and he’s now testing their effects on energy production in the leg muscle during exercise among patients with heart failure.

“We have reason to believe that a daily dose of 75-100 grams of ketone esters would be required to achieve steady state ketosis in patients,” he wrote. “This is not possible to put in a pill. So, in the near future, it will probably remain drinks or food supplements.”

However, Westenbrink called the taste of commercially available ketone drinks “daunting”—a problem that would have to be remedied for long-term clinical use.

The Next Steps

In Westenbrink’s view, the approach is promising for heart failure, both acute and chronic with preserved as well as reduced ejection fraction. Ketones also may have cardioprotective effects after STEMI (ST-segment elevation myocardial infarction), he said.

For now, more mechanistic studies involving patients with various forms of heart



Although some amateur athletes use ketone supplements to improve their exercise performance, research indicates that exogenous ketones might help patients with heart failure.

disease are needed, as well as clinical studies with single doses of ketones, focused on tangible outcomes such as exer-

cise performance. Then, "We need to define the safety and tolerability of chronic administration of ketones in various dis-

eases as well as the effect of a ketogenic diet," Westenbrink wrote.

A Caveat

Despite the research so far, Westenbrink cautioned that little is known about the safety of the ketogenic diet or ketone supplements for patients with CVD. He noted that their interactions with diabetes medications could cause [ketoacidosis](#). "We need to do the research before I would recommend it to anyone," Westenbrink noted in regard to ketone supplementation.

The Bottom Line

"Ketones hold great promise as an ancillary fuel for the failing heart, but their potential extends far beyond cardiac energetics," Westenbrink wrote. "Whether these benefits may help to improve the lives of patients with CVD should be addressed in future clinical trials." ■

Note: Source references are available through embedded hyperlinks in the article text online.