

**Response to Journal of American Medical Association
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By Elizabeth Owings, MD**

I have been asked by numbers of people to comment on articles and blogs that suggest that L-Arginine is a nutrient that should not be taken by people who have suffered from heart attacks.

These blogs or articles refer to a specific article in the medical literature.ⁱ These articles assume that the original article was based on perfect research. These articles also assume that broad generalizations can be made to anyone who has ever had a heart attack in their entire lives. Wrong on both counts!

I conducted an in-depth review of the original article and its corresponding research protocols, structure and methodology. On the one hand, it is laudable to study natural supplements with the same rigor that pharmaceuticals are studied. On the other hand, it appears they did not utilize all the information available to them. The concept was a good one: treat everybody exactly the same, with one change, and see what happens. This is a great philosophy, and works in the kitchen. But people are not cakes, and medicine is not a cookbook. You must use all the information available to you in order to design a study worthy of testing on humans.

To summarize the study briefly, the researchers took test subjects who had just had a heart attack, and randomized them to receive either up to 9 grams of L-Arginine daily, or a placebo. The study was stopped early because people in the L-Arginine group were found more likely to die than people in the placebo group.

In my opinion, the researchers made 3 serious errors in giving L-Arginine to patients. 1) They gave it without L-Citrulline. 2) They gave it without antioxidants. 3) They gave it without B vitamins to process and metabolize the additional homocysteine the patient's body might be making.

The final conclusions were that people who had *just had a heart attack* (within days to weeks) did not have improvement in their elasticity and might have an increased risk of

death after L-Arginine supplementation. The study does not refer to people who had heart attacks 6 months before or even 10 years before.

What happens to L-Arginine in the body? L-Arginine is made into nitric oxide by the body. Nitric oxide tells the blood vessels to relax. This helps support blood flow. But nitric oxide goes away in seconds. THEN WHAT?

ANTIOXIDANTS

Lou Ignarro, PhD, Nobel Laureate, talks in his book called “NO More Heart Disease,” about how important antioxidants and L-citrulline are in conjunction with L-Arginine. He says that the combination of L-Arginine plus antioxidants is completely different from either alone. (p. 100) Antioxidants not only make nitric oxide last longer, but also helps prevent any damage that nitric oxide might cause in certain situations (high oxidant situations like you might find right after a heart attack). In my opinion, it is irresponsible to give L-Arginine without giving antioxidants, but that is what they did in this study.

L-CITRULLINE

L-citrulline is important because it gives the body something ELSE to make L-Arginine and then nitric oxide out of. Remember, nitric oxide was Nobel-Prize winning science because it took decades to discover. It took decades to work out the identity of the molecule because it goes away in seconds. Imagine what happens when a person takes L-Arginine, and the body makes nitric oxide and the vessels open up somewhat. The cells and organs fed by the blood vessels expect that flow, they start working better, possibly even increasing demand. Then the body runs out of L-Arginine and the vessels begin to tighten up. Suddenly, there is demand but no supply. “Oxidant stress” increases, and damage may be done. With L-citrulline, there is a continuous, steady slow supply of L-Arginine to continue to make nitric oxide with—so the supply of nitric oxide can remain fairly stable.

Multiple experiments with combination supplements show improvement.^{ii iii} This was confirmed in humans by randomization to “long-term” (6 month) supplementation with L-Arginine or placebo. The result was an astounding 150% increase in coronary blood flow under test conditions.^{iv}

The number of studies demonstrating the efficacy and safety of L-Arginine is staggering. It disappoints me that a single study, with obviously flawed mechanics, was hailed as the

final, complete answer. It was picked up by every major website and newspaper. If speech is truly free in America, why didn't these same venues comment on the other multiple studies which showed benefit? There are other serious flaws in the study. For a more complete critique of this study, check out the following link:

<http://www.thorne.com/altmedrev/.fulltext/11/2/91.pdf>

Personally, if I had a heart attack, I would drink a balanced L-Arginine product containing antioxidants and L-Citrulline getting at least 10 grams of L-Arginine daily, and up to 20 grams daily. If people you care about are still concerned that L-Arginine after a heart attack is dangerous, then ask them to wait 6 months before they start.

ⁱ L-Arginine therapy in acute myocardial infarction: the Vascular Interaction With Age in Myocardial Infarction (VINTAGE MI) randomized clinical trial. Schulman SP, Becker LC, Kass DA, Champion HC, Terrin ML, Forman S, Ernst KV, Kelemen MD, Townsend SN, Capriotti A, Hare JM, Gerstenblith G. JAMA. 2006 Jan 4;295(1):58-64.

Click here:

<http://jama.ama-assn.org/cgi/content/full/295/1/58>

ⁱⁱ Long-term combined beneficial effects of physical training and metabolic treatment on atherosclerosis in hypercholesterolemic mice. Napoli C, Williams-Ignarro S, De Nigris F, Lerman LO, Rossi L, Guarino C, Mansueto G, Di Tuoro F, Pignalosa O, De Rosa G, Sica V, Ignarro LJ. Proc Natl Acad Sci U S A. 2004 Jun 8;101(23):8797-802. Epub 2004 May 28.

ⁱⁱⁱ Physical training and metabolic supplementation reduce spontaneous atherosclerotic plaque rupture and prolong survival in hypercholesterolemic mice. Napoli C, Williams-Ignarro S, de Nigris F, Lerman LO, D'Armiento FP, Crimi E, Byrns RE, Casamassimi A, Lanza A, Gombos F, Sica V, Ignarro LJ. Proc Natl Acad Sci U S A. 2006 Jul 5;103(27):10479-84. Epub 2006 Jun 26.

^{iv} Long-term L-Arginine supplementation improves small-vessel coronary endothelial function in humans. Lerman A, Burnett JC Jr, Higano ST, McKinley LJ, Holmes DR Jr. Circulation. 1998 Jun 2;97(21):2123-8.