Up to eight percent of South Asians carry gene mutation that causes heart attacks

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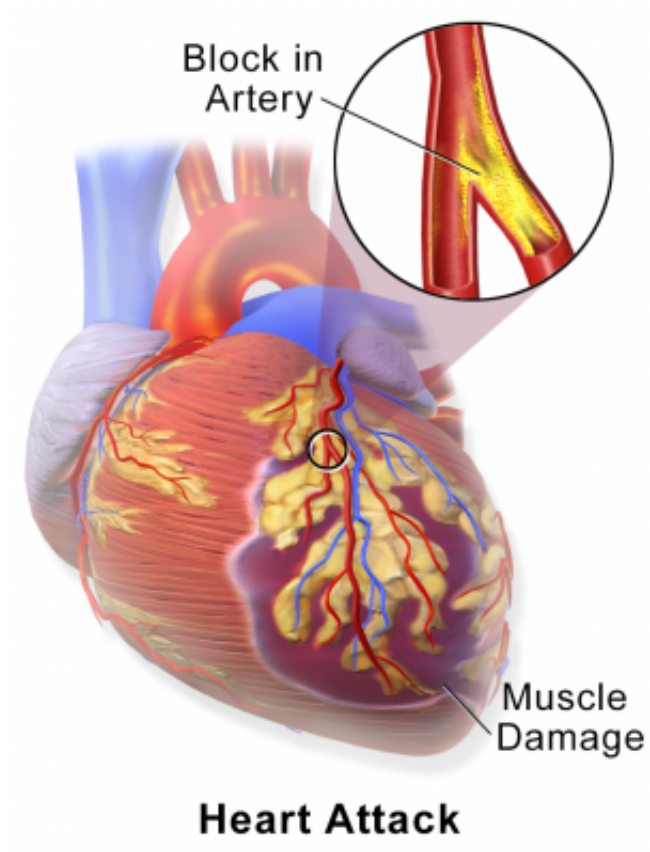

Myocardial Infarction or Heart Attack. Credit: Blausen Medical Communications/Wikipedia/CC-A 3.0

Up to 8 percent of people from India, Pakistan, Bangladesh and other South Asian countries carry a mutated gene that causes heart failure and potentially fatal heart attacks.

A new study demonstrates how this gene mutation impairs the heart's ability to pump blood. Results could point the way to eventual treatments and prevention strategies for an estimated 55 million people of South Asian descent worldwide, including 200,000 people in the United States, who carry the potentially fatal mutation.

The study, led by Sakthivel Sadayappan, PhD, MBA, of Loyola University Chicago Stritch School of Medicine, is published in the prestigious *Journal of Biological Chemistry*, a publication of the American Society for Biochemistry and Molecular Biology.

The mutation causes hypertrophic cardiomyopathy, the most common form of inherited cardiac disease and the leading cause of sudden cardiac death in young people. Previous studies by Dr. Sadayappan and other researchers have found that between 5 percent and 8 percent of South Asians carry the mutation. Carriers have about a 80 percent chance of developing heart failure after age 45. Dr. Sadayappan first reported the mutation in 2001 at the World Congress of the International Society for Heart Research, and has been studying it ever since. He said that, based on a report from one of his collaborators, the mutation likely arose in a single person roughly 33,000 to 55,000 years ago. The mutation then spread throughout South Asia.

The mutated gene encodes for a protein, called cardiac myosin binding protein-C (cMyBP-C), that controls cardiac muscle contractions and is critical for the normal functioning of the heart. In the mutated gene, 25 base pairs (DNA letters) are missing. As a result, the tail end of the protein is altered.

In his new study, Dr. Sadayappan and colleagues introduced the mutated gene into adult rat cardiomyocytes (heart muscle cells) in a petri dish. These cells were compared with cardiomyocytes that received a normal gene.

In cells with the mutant gene, the cMyBP-C protein was not incorporated into sarcomeres, the basic units of heart muscle. So rather than helping the sarcomeres contract properly, the mutant protein floated around the cell's cytoplasm, producing a toxic effect. The study showed, for the first time, that expression of the mutant protein is sufficient to

cause cardiac dysfunction.

The findings point the way toward future treatments that would remove the mutant protein from cells and introduce normal cMyBP-C protein. Researchers also hope to identify lifestyle and environmental risk factors that aggravate hypertrophic cardiomyopathy in people who carry the gene mutation.

Dr. Sadayappan and colleagues concluded that determining the disease mechanism will help in developing therapies, and is the "first priority to prevent the development of heart failure in millions of carriers worldwide."

More information: The study is titled "A hypertrophic cardiomyopathy-associated MYBPC3 mutation common in populations of South Asian descent causes contractile dysfunction."

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