

Enlarged hearts in women shrink faster than those in men after aortic valve replacement

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Heart enlargement caused by narrowed aortic valves regresses faster in elderly women than in men after aortic valve replacement, according to research reported in a surgical supplement of *Circulation: Journal of the American Heart Association*.

Men's slower heart-size regression times may be attributable to [genetic differences](#) that cause the [heart](#) to develop more fibrous tissue after surgery because of narrowed [heart valves](#), a condition known as aortic stenosis.

"We show for the first time that elderly women and men differ in their gene expression related to fibrous [heart tissue](#)," said Vera Regitz-Zagrosek, M.D., study co-author and director of the Institute of Gender in Medicine at Charite University of Medicine in Berlin. "We hypothesize that women with aortic stenosis develop a different form of the same disorder."

Aortic stenosis, which limits blood flow through the aortic valve, has several causes, including a congenital defect in the valve. The most common form results from the calcification of the flaps that control the flow of blood through the valve. The development of high blood pressure in patients with aortic stenosis causes fibrous tissue growth and enlargement of the heart.

Regitz-Zagrosek and her colleagues began their 92-patient study following laboratory experiments that showed female mice with induced

aortic stenosis fare better after surgery than male mice and that the genders demonstrated different adaptations of the heart to the increased load and different gene expression patterns for generating cardiac fibrous material.

"We wanted to see if we could find comparable differences in humans," she said.

There were 53 women (average age 72) and 39 men (average age 67) in the study.

Rates of overweight, diabetes and [high blood pressure](#) were comparable in both groups.

Among other study findings:

- Women had a higher frequency of increased left ventricular mass before surgery than men. After treatment the prevalence of left ventricular hypertrophy fell more in women (86 percent to 45 percent) than in men (56 percent to 36 percent).
- Shortly after surgery, the left ventricle decreased in size at the end of heart relaxation in both genders but more in women. Women, but not men, had a decrease in the ventricle's size at the end of contraction.
- Biopsies revealed higher expression of the collagen I and III and metalloproteinase-2 and -3 genes, well in agreement with higher levels of fibrous tissues in the hearts of men compared to women. Women did not show increased fibrous tissue gene expression.

- In a separate experiment in rats, cardiac fibroblasts (the cells that form fibrous tissue) from male and female animals were treated with E2, a female sex hormone. Male cells showed increased collagen I and III expression while collagen expression decreased in female cells.
- More women than men had thyroid disorders, 34 percent to 8 percent. The researchers cannot exclude that low thyroid levels may have contributed to impaired heart growth in women because the thyroid hormone is known to stimulate heart growth.
- The number of patients in the study is still small. However, the German team plans to increase numbers in a follow-up study and is collaborating with researchers conducting two larger trials to further investigate genetic mechanisms to explain their findings.

If confirmed, these results may lead to the development of strategies to slow the increase of cardiac fibrous tissue in both men and women with aortic stenosis. The findings might also provide at least one prognostic tool. Failure of a woman's enlarged heart to regress quickly after surgery could be an ominous sign.

"It is important to study gender differences in elderly patients," Regitz-Zagrosek said. "Many think that when people don't have sex hormones or have low levels, women and men are the same. This is untrue. To develop optimal treatment for both, we need studies that pre-specify gender differences as an endpoint and that have enough statistical power to look at the differences between women and men."

Provided by American Heart Association

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