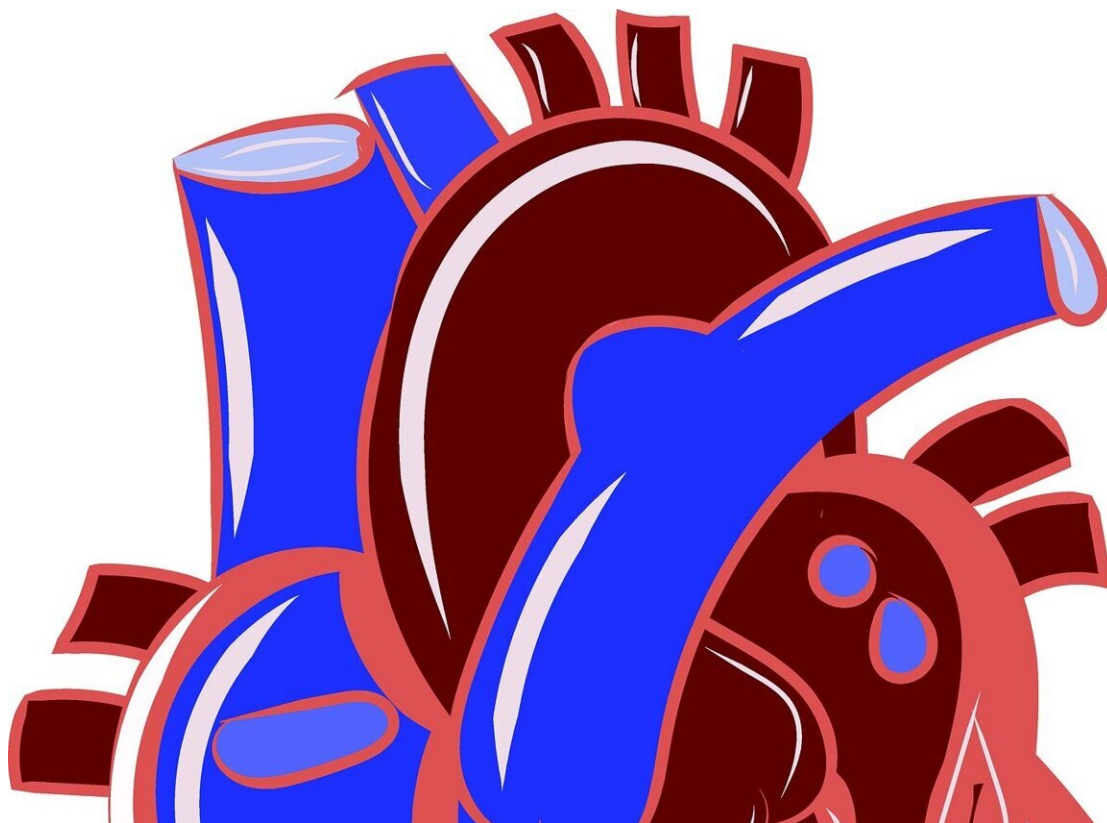


Abdominal aortic aneurysm: New treatment may reduce size; COVID infection may speed growth

May 11 2023



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The intravenous delivery of immune-modulating cells may someday slow the expansion of bulges in the aorta, known as abdominal aortic

aneurysms. A second study found evidence that a COVID-19 infection may promote the enlargement of these dangerous bulges. These preliminary studies were presented at the American Heart Association's [Vascular Discovery: From Genes to Medicine Scientific Sessions 2023](#). The meeting, held May 10–13, 2023, in Boston, is a premier global exchange of the latest advances in new and emerging scientific research in arteriosclerosis, thrombosis, vascular biology, peripheral vascular disease, vascular surgery and functional genomics.

The aorta is the body's largest artery, and the [abdominal aorta](#) is around 2 cm (0.79 inch) wide—roughly the width of a garden hose. The abdominal aorta leads away from the heart and carries oxygen-rich blood to the lower part of the body. An abdominal aortic [aneurysm](#) occurs when the aorta weakens and develops a bulge. When the bulge enlarges far beyond its normal size, it is extremely dangerous and potentially fatal.

According to the [American Heart Association's 2023 statistics](#), the 150,000 global deaths attributable to [aortic aneurysms](#) in 2020 represented a 26% increase from 2010, which was slightly higher in women compared with men. Rates of rupture were also higher among people who were smokers and women.

"Anyone who has ever over-inflated a balloon knows that too much pressure is likely to cause a rupture. In the aorta, this creates a true medical emergency, because approximately 70% of people will die before they reach the hospital, and 50% of those who make it to the hospital will die from blood loss before any intervention is possible," said Humraaz S. Samra, M.B.B.Ch., B.A.O., lead author of the study (abstract 111) and a resident in integrated vascular surgery at the Indiana University School of Medicine in Indianapolis.

Depending on its size, after an abdominal aortic aneurysm is diagnosed,

surgical repair may be recommended right away, or the aneurysm may be monitored over time, with intervention taking place before it reaches a rupture-prone size, according to researchers. When aneurysms are small, no medication has been proven to keep them from enlarging, however, these patients are advised to stop smoking and to take medications to manage [high blood pressure](#) if they have it, Samra explained.

Inflammation is increasingly thought to play a significant role in the development and early growth of abdominal aortic aneurysms. When there is a breakdown in the supportive structure of blood vessels (which evidence suggests is likely caused by smoking), proteins break down and their remnants are released into the bloodstream. The body recognizes these particles as foreign objects and activates the [immune system](#) to protect itself, promoting inflammation in the area.

In this study, Samra and colleagues investigated whether immune-modulating cells, called mesenchymal stromal cells, a type of stem cell, from a healthy donor administered to a patient with a small abdominal aortic aneurysm might create a less-inflammatory environment and slow the growth of the aneurysm.

"We believe that a defect in the expression of an anti-inflammatory immune cell called interleukin (IL)-10 is a key event in the formation of abdominal aortic aneurysms. We have confirmed in lab studies that mesenchymal stromal cells have the potential to turn into cells that are profoundly anti-inflammatory and secrete copious amounts of IL-10 when under the right experimental circumstances," Samra said.

The researchers enrolled 28 adults with small abdominal aortic aneurysm (average age of 66 years; all men) in the study. Six participants were given a low concentration of mesenchymal stromal cells, the low-dose group; 10 patients received a higher concentration of mesenchymal

stromal cells, the high-dose group; and 12 patients received a placebo. For four weeks after the intravenous administration of the mesenchymal cells or placebo, the researchers tracked changes in levels of immune cells and the ratio of a few select types of highly inflammatory immune cells (T-helper 17, or Th17) to another immune cell (T regulatory type 1, or Tr1), which secretes large amounts of anti-inflammatory signaling molecules called IL-10s. Changes in abdominal aortic aneurysm size were calculated one year after treatment.

The analysis found:

- The mesenchymal stromal cells were safe, causing no allergic reactions in any of the study participants.
- Seven days after treatment, there was a significant increase in the concentration of anti-inflammatory IL-10 among participants in both the high- and low-dose mesenchymal stromal cell groups compared with the placebo group.
- At day 14, there was a significant decrease in the percentage of inflammatory Th17 cells in both the high- and low-dose mesenchymal stromal cell groups compared with the placebo group.
- At day 30, there was a significant improvement in the ratio of anti-inflammatory to pro-inflammatory cells in the high-dose mesenchymal stromal cells group compared with the placebo group; however, the difference between the high-dose and the low-dose mesenchymal stromal cell group did not reach statistical significance.
- At one year, there was a decrease in aneurysm size among the participants in the high-dose mesenchymal stromal cell group compared with the placebo group, however, the difference did not reach statistical significance.

"These data are very promising but still early. We hope to obtain more

data to develop clinical trials and hopefully change treatment paradigms, more research needs to be done but we have an exciting start!" Samra said.

In a separate study also to be presented at the meeting (abstract 280), another group of researchers explored whether COVID-19 infection might influence the growth of abdominal aortic aneurysms. They evaluated the yearly growth rate of abdominal aortic aneurysms in 175 adults (average age of 77 years; 80% male; 67% white; 78% past or present smokers) who had at least two measurements of their aortic diameter taken in 2020 to 2021 and recorded in the Stanford Research Repository Database.

Researchers compared 26 people who had previously tested positive for COVID-19 with 149 people who had not had COVID-19. Two aortic imaging/diameter measurements were performed in both groups. Prior COVID-19 infection timing varied from weeks to months before the tests were completed.

The analysis found:

- Participants who reported a previous COVID-19 infection were 9.7 times as likely to have rapid abdominal aortic aneurysm growth (higher growth than the average of 2.7 mm per year). The average size of the abdominal aorta is 2 cm (0.79 inch).
- Factors that appeared to increase the risk of rapid abdominal aortic aneurysm growth to a lesser degree were chronic kidney disease (3.8 times as likely) and having ever been a smoker (twice as likely).

In addition to these findings in people, the research team administered spike protein 1 (a protein the COVID-19 virus uses to enter cells) to standard mice and transgenic mice, which are genetically modified mice

and widely used as a model for COVID-19 infection in humans. They found that abdominal aortic aneurysms grew significantly in both types of mice when infected with the COVID-19 virus.

"People who have risk factors for developing abdominal aortic aneurysms, and those already known to have abdominal aortic aneurysms who are having their progression monitored, should know that COVID-19 infection may potentially alter the natural course or outcome of [abdominal aortic aneurysms](#)," said Baohui Xu, M.D., Ph.D., senior research scientist in the department of surgery at the Stanford University School of Medicine in Stanford, California.

The study is limited by only having information on whether a person had previously tested positive for COVID-19, so researchers were unable to examine whether symptomatic COVID-19 or severe cases of COVID-19 had different influences on abdominal aortic aneurysm growth. In addition, because the data was from 2020 and 2021 when there were earlier variants of the COVID-19 virus, the study's findings may not be applicable to the omicron variant or any other COVID-19 variants.

"Large, multi-center studies are needed to validate our findings. We previously confirmed that pneumonia associated with the flu also increased the prevalence of abdominal aortic aneurysm, and other research has found an increased abdominal aortic aneurysm risk in people with HIV infection. Thus, it would be interesting to see whether rapid enlargement of [abdominal aortic aneurysm](#) in people with COVID-19 infection is specific to COVID-19 or to respiratory viral infections in general," Xu said.

Provided by American Heart Association

Citation: Abdominal aortic aneurysm: New treatment may reduce size; COVID infection may

speed growth (2023, May 11) retrieved 25 April 2024 from
<https://medicalxpress.com/news/2023-05-abdominal-aortic-aneurysm-treatment-size.html>

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