Supravalvular aortic stenosis

Supravalvular aortic stenosis (SVAS) is a heart defect that develops before birth. This defect is a narrowing (stenosis) of the large blood vessel that carries blood from the heart to the rest of the body (the aorta). The condition is described as supravalvular because the section of the aorta that is narrowed is located just above the valve that connects the aorta with the heart (the aortic valve). Some people with SVAS also have defects in other blood vessels, most commonly stenosis of the artery from the heart to the lungs (the pulmonary artery). An abnormal heart sound during a heartbeat (heart murmur) can often be heard during a chest exam. If SVAS is not treated, the aortic narrowing can lead to shortness of breath, chest pain, and ultimately heart failure.

The severity of SVAS varies considerably, even among family members. Some affected individuals die in infancy, while others never experience symptoms of the disorder.

Frequency

SVAS occurs in 1 in 20,000 newborns worldwide.

Causes

Mutations in the *ELN* gene cause SVAS. The *ELN* gene provides instructions for making a protein called tropoelastin. Multiple copies of the tropoelastin protein attach to one another and are processed to form a mature protein called elastin. Elastin is the major component of elastic fibers, which are slender bundles of proteins that provide strength and flexibility to connective tissue (tissue that supports the body's joints and organs). Elastic fibers are found in the intricate lattice that forms in the spaces between cells (the extracellular matrix), where they give structural support to organs and tissues such as the heart, skin, lungs, ligaments, and blood vessels. Elastic fibers make up approximately 50 percent of the aorta, the rest being primarily muscle cells called vascular smooth muscle cells that line the aorta. Together, elastic fibers and vascular smooth muscle cells provide flexibility and resilience to the aorta.

Most of the *ELN* gene mutations that cause SVAS lead to a decrease in the production of tropoelastin. A shortage of tropoelastin reduces the amount of mature elastin protein that is processed and available for forming elastic fibers. As a result, elastic fibers that make up the aorta are thinner than normal. To compensate, the smooth muscle cells that line the aorta increase in number, making the aorta thicker and narrower than usual. A thickened aorta is less flexible and resilient to the stress of constant blood flow and pumping of the heart. Over time, the wall of the aorta can become damaged. Aortic narrowing causes the heart to work harder to pump blood through the aorta, resulting in the signs and symptoms of SVAS.
Inheritance Pattern

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. However, some people who inherit the altered gene never develop features of SVAS. (This situation is known as reduced penetrance.)

In some cases, a person inherits the mutation from one parent who has the mutation. Other cases result from new mutations in the gene and occur in people with no history of the disorder in their family.

Other Names for This Condition

- aortic stenosis, supravalvular
- stenosis, aortic supravalvular
- stenosis, supravalvular aortic
- supravalvular stenosis, aortic
- SVAS

Diagnosis & Management

Genetic Testing Information

- What is genetic testing?
  /primer/testing/genetictesting

- Genetic Testing Registry: Supravalvar aortic stenosis
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0003499/

Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22supravalvular+aortic+stenosis%22+OR+%22Stenosis%2C+Aortic%22+OR+%22Aortic+Valve+Stenosis%22

Other Diagnosis and Management Resources

- Children's Hospital of Philadelphia
  https://www.chop.edu/conditions-diseases/aortic-stenosis

- Monroe Carell Jr. Children's Hospital at Vanderbilt
  https://www.childrenshospitalvanderbilt.org/medical-conditions/aortic-stenosis
Additional Information & Resources

**Health Information from MedlinePlus**

- Encyclopedia: Aortic Stenosis
  https://medlineplus.gov/ency/article/000178.htm
- Health Topic: Congenital Heart Defects
  https://medlineplus.gov/congenitalheartdefects.html

**Genetic and Rare Diseases Information Center**

- Supravalvular aortic stenosis
  https://rarediseases.info.nih.gov/diseases/743/supravalvular-aortic-stenosis

**Additional NIH Resources**

- National Heart Lung and Blood Institute: What is a Heart Murmur?
  https://www.nhlbi.nih.gov/health-topics/heart-murmur

**Educational Resources**

- Centers for Disease Control and Prevention: Congenital Heart Defects
  https://www.cdc.gov/ncbddd/heartdefects/
- Centers for Disease Control and Prevention: What Should You Know About Congenital Heart Defects?
  https://www.cdc.gov/ncbddd/heartdefects/
- March of Dimes: Congenital Heart Defects
  https://www.marchofdimes.org/complications/congenital-heart-defects.aspx
- Merck Manual Professional Version
  https://www.merckmanuals.com/professional/cardiovascular-disorders/valvular-disorders/aortic-stenosis
- Orphanet: Supravalvular aortic stenosis
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=3193

**Patient Support and Advocacy Resources**

- American Heart Association: Congenital Heart Defects
  https://www.heart.org/en/health-topics/congenital-heart-defects
- University of Kansas Resource List: Congenital Heart Defects
  http://www.kumc.edu/gec/support/conghart.html
Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Aortic+Stenosis,+Supravalvular%5BMAJR%5D%29+AND+%28supravalvular+aortic+stenosis%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- SUPRAVALVULAR AORTIC STENOSIS
  http://omim.org/entry/185500

Sources for This Summary

- Metcalfe K, Rucka AK, Smoot L, Hofstadler G, Tuzler G, McKeown P, Siu V, Rauch A, Dean J, Dennis N, Ellis I, Reardon W, Cytrynbaum C, Osborne L, Yates JR, Read AP, Donnai D, Tassabehji M. Elastin: mutational spectrum in supravalvular aortic stenosis. Eur J Hum Genet. 2000 Dec;8(12):955-63.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11175284

- Micale L, Turturo MG, Fusco C, Augello B, Jurado LA, Iuzzi C, Digilio MC, Milani D, Lapi E, Zelante L, Merla G. Identification and characterization of seven novel mutations of elastin gene in a cohort of patients affected by supravalvular aortic stenosis. Eur J Hum Genet. 2010 Mar;18(3):317-23. doi: 10.1038/ejhg.2009.181. Epub 2009 Oct 21.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19844261
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2987220/

- Rodriguez-Revenga L, Badenas C, Carrió A, Milà M. Elastin mutation screening in a group of patients affected by vascular abnormalities. Pediatr Cardiol. 2005 Nov-Dec;26(6):827-31.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15990952

- Tassabehji M, Urban Z. Congenital heart disease: Molecular diagnostics of supravalvular aortic stenosis. Methods Mol Med. 2006;126:129-56.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16930010

- Urbán Z, Riazi S, Seidl TL, Katahira J, Smoot LB, Chitayat D, Boyd CD, Hinek A. Connection between elastin haploinsufficiency and increased cell proliferation in patients with supravalvular aortic stenosis and Williams-Beuren syndrome. Am J Hum Genet. 2002 Jul;71(1):30-44. Epub 2002 May 6.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12016585
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC384991/

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