

# Family history doubles aortic stenosis risk

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The risk of aortic stenosis doubles when a first degree relative had the disease, according to research presented at ESC Congress 2013 today by Dr. Mattis F. Ranthe from Denmark. The study of 4.2 million people from Danish registers also found that aortic stenosis risk increased by eight-fold in patients with ischemic heart disease and family history.

Aortic stenosis is the most common heart valve disease in the elderly. It is associated with congenital [bicuspid aortic valve](#) and previous [rheumatic heart disease](#), but is also often caused by calcification of a normal valve. Calcification of a normal valve may be associated with atherosclerotic changes in the portion of the [aorta](#) closest to the valve.

Dr Ranthe said: "Genetic factors may play a role in the development of aortic stenosis. A [single nucleotide polymorphism](#) in the lipoprotein(a) locus has been associated with aortic valve calcification and aortic stenosis.<sup>1</sup> Elevated [lipoprotein\(a\)](#) is a risk factor for atherosclerosis, including ischaemic heart disease, which is known to aggregate in families. Our aim was to discover whether aortic stenosis also aggregates in families."

The study used information from national Danish registers and included the 4.2 million Danes born in or after 1920. The cohort was followed for more than 73 million person-years, starting in 1977 (the year the Danish Hospital Discharge Register began) and ending in 2012. Cases of aortic stenosis were recorded when they occurred at age 35 years or older.

Patients with any registration of a [congenital heart defect](#) and those with cardiovascular disease diagnosed at 35 years. Of those, 193 had a first degree relative with aortic stenosis and the relative risk was 2.04 (95% confidence interval [CI] 1.77-2.35). Dr Ranthe said: "The risk of aortic stenosis roughly doubled when patients had a first degree relative with the disease. In addition, aortic stenosis occurred earlier in life in patients with a

family history of the condition."

The impact of family history differed between patients with and without ischaemic heart disease. Family history increased the risk of aortic stenosis by 2-fold in patients without ischaemic heart disease. The risk of aortic stenosis was increased by 8-fold in patients with ischaemic heart disease and a family history of aortic stenosis compared to those with no family history and no ischaemic heart disease.

Dr Ranthe said: "Family history confers a 2-fold increased risk in all patients. Ischaemic heart disease alone is also a strong risk factor for aortic stenosis, increasing the risk of aortic stenosis by 4-fold in patients with no family history. This 4-fold risk increase is doubled, i.e. to 8-fold, in those with both ischaemic heart disease and family history."

The researchers conducted a robustness analysis with aortic valve replacement as an endpoint and found similar results. In a similar cohort they identified 130 patients with a family history of aortic stenosis out of 12,690 patients undergoing the procedure. The relative risk by family history was 2.18 (95% CI 1.79-2.65).

Dr Ranthe concluded: "We found significant and robust associations indicating that aortic stenosis clusters in families. Although epidemiologic studies cannot directly infer causality, our results suggest the existence of a familial component to the disease. Our results suggest that patients with ischaemic heart disease and a family history of aortic stenosis have a high relative risk of [aortic stenosis](#)."

**More information:** 1 Thanassoulis G, et al. Genetic associations with valvular calcification and aortic stenosis. *N Engl J Med.* 2013;368(6):503-512.

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