Elevated blood pressure is linked to increased risk of aortic valve disease

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People who have long-term raised blood pressure have an increased risk of aortic valve disease (AVD) - problems with the valve that controls how blood is pumped from the left ventricle of the heart out into the

main artery, the aorta.

In a study of 5.4 million adults in the UK, published in the *European Heart Journal* today (Thursday), researchers found that above a systolic blood pressure of 115 mmHg, every additional 20 mmHg was associated with a 41% higher risk of aortic stenosis (AS) and a 38% higher risk of aortic regurgitation (AR) later in life. Compared to people who had a systolic blood pressure of 120 mmHg or lower, those with systolic blood pressure of 161 mmHg or higher had more than twice the risk of being diagnosed with AS and were nearly twice as likely to be diagnosed with AR during follow-up.

The findings suggest that controlling blood pressure, even at levels below the threshold currently defined for hypertension of 140/90 mmHg, may be a way to prevent these conditions. "These findings collectively suggest that AS and AR might be partially preventable with potential implications on clinical practice guidelines for prevention of cardiovascular disease in general and valvular heart disease and hypertension in particular," write the authors of the EHJ paper.

AS is a condition in which the valve that opens and closes when blood is pumped out of the left ventricle becomes narrowed and stiff due to calcium building up. When this happens, the valve fails to work effectively, making it harder for the heart to pump blood to the rest of the body. AR occurs when the valve doesn't close properly, allowing some blood to leak back into the left ventricle.

During an average follow-up time of more than nine years, 20,680 (0.38%) of the 5.4 million patients in the study were diagnosed with AS alone and 6440 (0.12%) were diagnosed with AR alone. The average age at the time of diagnosis was 64 years and 57 years for AS and AR respectively.

Researchers, led by Kazem Rahimi, deputy director and associate professor of cardiovascular medicine at The George Institute for Global Health, University of Oxford, UK, analysed data from electronic health records for the UK Clinical Practice Research Datalink from January 1990 to December 2015. The CPRD database contains anonymised patient data from 674 general practices in the UK. The patients included in this analysis were aged between 30 and 90 years, and none had any known heart or blood vessel diseases at the time of their earliest blood pressure measurement.

An average of nearly seven blood pressure measurements per patient were taken during the study period, which helped to estimate the patient's actual blood pressure better. The ability to collect data over a long period of time, combined with the large number of patients, makes this the first study substantial enough to investigate the link between blood pressure and aortic valve disease and how it changes with age and with different blood pressure levels.

Professor Rahimi said: "The study shows that serious valvular heart diseases that are common at old age are not simply due to aging. Long-term exposure to higher blood pressure is a strong and potentially modifiable risk factor for aortic stenosis and regurgitation at every level of typical blood pressure, not only in those who are classified as having hypertension. Blood pressure should be considered as a major risk factor for aortic valve disease, much in the same way as we think of elevated blood pressure as a risk factor for atherosclerotic disease. The study suggests that the associations are causal, but this requires further confirmation."

Previous research has suggested that the mechanism involved in the link between blood pressure and AVD could be that higher blood pressure can cause cell damage leading to a loss of elasticity in the aorta and stiffening of the aortic valve.

Limitations of the study include the possibility that raised blood pressure may be an indication of an underlying problem with arterial stiffness that is caused by something else. To investigate this further, the researchers are carrying out a study that uses genetic indicators for higher blood pressure that are not affected by environmental factors. Another limitation is the use of data from a general practice registry, which might be prone to errors in measuring blood pressure, other factors that might affect the results, and patient outcomes.

In an editorial to accompany the research paper, Dr. Stefano Masi from the Department of Clinical and Experimental Medicine, Università di Pisa, Italy, and Dr. Alberto Giannoni from the Fondazione Toscana Gabriele Monasterio, Pisa, who were not involved with the research, write that the study "provides the first solid evidence supporting the need for a radical shift in the approach to AVD. Indeed, over the last few years, the research on valvular heart disease has been focused on improving treatment rather than prevention strategies.....Thus, the findings provided by Rahimi et al might be considered the first step towards a change in the management of AVD and likely to influence future clinical trials and guidelines. Current European guidelines for the management of arterial hypertension do not consider AVDs as manifestations of heart damage related to hypertension and, consequently, do not suggest accurate assessment of aortic valve function and structure in patients with arterial hypertension. Also, they might stimulate new lines of research, particularly imaging studies, with the scope of identifying early alterations of the aortic valve in patients with hypertension that might be highly predictive of future AVD".

The proportion of people living with AS is estimated to be around 0.4% of the population in the USA, although the prevalence increases with age; in the US, 0.02% of 18-44-year-olds have AS, but 2.8% of people aged 75 and over are diagnosed with it. For AR the corresponding prevalence in these age groups is estimated to be 0.2% and 2%

respectively, and the prevalence for AS and AR is similar in Europe. The number of people diagnosed with severe aortic valve disease has grown steadily in recent years and is expected to continue with the aging of populations.

More information: *European Heart Journal* (2018). DOI: 10.1093/eurheartj/ehy486