Hypertension, aortic stenosis, and aortic regurgitation

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Submitted Oct 27, 2017. Accepted for publication Nov 15, 2017.

doi: 10.21037/atm.2017.11.30

View this article at: http://dx.doi.org/10.21037/atm.2017.11.30

The prevalence of hypertension (1) and of valvular aortic stenosis (2) increase with age, and both hypertension (3,4) and valvular aortic stenosis (5) cause left ventricular hypertrophy. Both hypertension (1,3) and valvular aortic stenosis (2,6) are also associated with an increased incidence of cardiovascular events and mortality. Hypertension (either a systolic blood pressure of 140 mmHg and higher or a diastolic blood pressure of 90 mmHg and higher) was present in 132 of 180 persons (73%), mean age 82 years, with mild valvular aortic stenosis (7), in 1,238 of 1,720 persons (72%), mean age 67 years, with asymptomatic mild-to-moderate valvular aortic stenosis (8), and in 153 of 225 patients (68%), mean age 68 years, with severe valvular aortic stenosis (9). Hypertension is a risk factor for aortic stenosis (7,10,11) and is associated with progression of aortic stenosis (7). Hypertension is also associated with aortic valve calcification (10-13). In a study of 3.39 million hospital discharges in Ireland, hypertension was associated with aortic stenosis with an odds ratio of 4.0 (14). At 4.3-year follow-up of 1,656 patients, mean age 67 years, with asymptomatic mild-to-moderate valvular aortic stenosis, in Cox regression analyses, each 15 g/m higher baseline left ventricular mass index predicted increases of 12% for major cardiovascular events, of 28% for ischemic cardiovascular events, of 34% for cardiovascular mortality, and of 23% for combined total mortality and hospitalization for heart failure independent of confounders (15). A progressive increase in left ventricular mass index during follow-up of each 15 g/m increase was consistently associated with a 13% to 61% increase in cardiovascular events independent of other variables (15).

The American College of Cardiology/American Heart Association valvular heart disease guidelines (16) and the European Society of Cardiology/European Association for Cardio-Thoracic Surgery valvular heart disease guidelines (17) recommend the treatment of hypertension in patients with valvular aortic stenosis with antihypertensive drug therapy but do not specify which antihypertensive drugs should be used. These guidelines recommend treatment of hypertension with aortic stenosis of any severity with emphasis on careful titration and blood pressure monitoring (16,17). In the absence of randomized controlled clinical trial data, on the basis of expert medical opinion, this author recommends reducing the blood pressure in patients with valvular aortic stenosis to less than 130/80 mmHg with an emphasis on careful titration and blood pressure monitoring.

Systemic hypertension in low-gradient severe valvular aortic stenosis with a preserved left ventricular ejection fraction causes increased left ventricular filling pressure and pulmonary hypertension with development of dyspnea. Treatment of hypertension in these patients with vasodilator therapy caused a reduction of left ventricular afterload with a lowering in left ventricular filling pressure and pulmonary artery pressure (18).

There are limited data on randomized controlled trials of treating hypertension in patients with valvular aortic stenosis. The Symptomatic Cardiac Obstruction-Pilot Study of enalapril in Aortic Stenosis (SCOPE-AS) randomized 56 patients with symptomatic severe valvular aortic stenosis to enalapril or to double-blind placebo (19). Enalapril was started at a dose of 2.5 mg twice daily which was increased to a dose of 10 mg twice daily. Enalapril was tolerated without syncope or hypotension when the left ventricular ejection fraction was preserved. The patients who tolerated enalapril had a significant improvement in New York Heart Association functional class, in the Borg dyspnea index, and in the 6-minute walk distance at 4 and 12 weeks (19).

A prospective, double-blind, placebo-controlled trial randomized 100 patients with asymptomatic moderate or severe valvular aortic stenosis to ramipril 10 mg daily or to placebo for 1 year (20). The primary endpoint of left ventricular mass at 1-year follow-up was significantly reduced by enalapril with a reduction of 3.9 g in patients treated with ramipril and an increase of 4.5 g in patients treated with placebo (20). At 1 year, the aortic valve area was not changed in patients treated with ramipril and was reduced 0.2 cm^2 in patients treated with placebo. Systolic blood pressure was reduced by 5.5 mmHg at 1 year in patients treated with ramipril and by 2.9 mmHg in patients treated with placebo. The change in peak tissue Doppler systolic velocity at 1 year was 0.03 m/s for patients treated with ramipril and 0.12 m/s for patients treated with placebo. There was no significant difference in major adverse cardiac events between the ramipril group and the placebo group (20).

A study was performed in 123 patients who had 2 serial electron beam computed tomographic scans for determining the rate of change in volumetric aortic valve calcium scores during a mean interval of 2.5 years (21). Eighty of the 123 patients (65%) were treated with angiotensin-converting enzyme inhibitors. Progression of aortic valve calcium was 71% significantly lower in the patients who were treated with angiotensin-converting enzyme inhibitors (21).

Of 2,117 patients, mean age 73 years, with aortic stenosis, 699 (33%) were treated with angiotensin-converting enzyme inhibitors or angiotensin receptor blockers (22). At 4.2-year mean follow-up, patients treated with angiotensin-converting enzyme inhibitors or angiotensin receptor blockers had a significant reduction in all-cause mortality of 24% and a significant reduction in cardiovascular events of 23% (22).

There are no clinical trials comparing the use of different antihypertensive drugs in the treatment of hypertension in patients with valvular aortic stenosis. On the basis of the available data, it is reasonable to use angiotensin-converting enzyme inhibitors or angiotensin receptor blockers in the treatment of hypertension in patients with valvular aortic stenosis. I would use beta blockers in these patients if they have a prior myocardial infarction, angina pectoris, a reduced left ventricular ejection fraction, ventricular arrhythmias, or supraventricular arrhythmias. Diuretics should be used very cautiously if there are small left ventricular chamber dimensions.

There are no clinical trials comparing the use of different antihypertensive drugs in the treatment of hypertension in patients with aortic regurgitation. Antihypertensive drug therapy should be used in these patients with drugs used that do not slow the ventricular rate. One study that randomized 143 asymptomatic patients with severe aortic regurgitation and normal left ventricular systolic function to nifedipine 20 mg twice daily or to digoxin 0.25 mg daily demonstrated that use of nifedipine reduced or delayed the need for aortic valve replacement (23). However, another study of 95 patients with asymptomatic severe aortic regurgitation and normal left ventricular ejection fraction randomized to nifedipine 20 mg every 12 hours, enalapril 20 mg daily, or to no treatment demonstrated at 7-year mean follow-up that long-term treatment with enalapril or nifedipine did not reduce or delay the need for aortic valve replacement in these patients (24).

Acknowledgements

None.

Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

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Cite this article as: Aronow WS. Hypertension, aortic stenosis, and aortic regurgitation. Ann Transl Med 2018;6(3):43. doi: 10.21037/atm.2017.11.30

