

Aortic Stenosis: Pathophysiology, Diagnosis, and Treatment

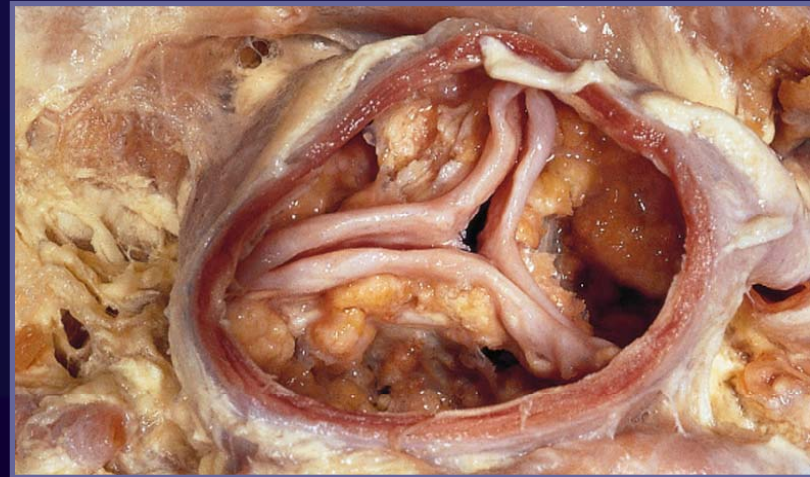
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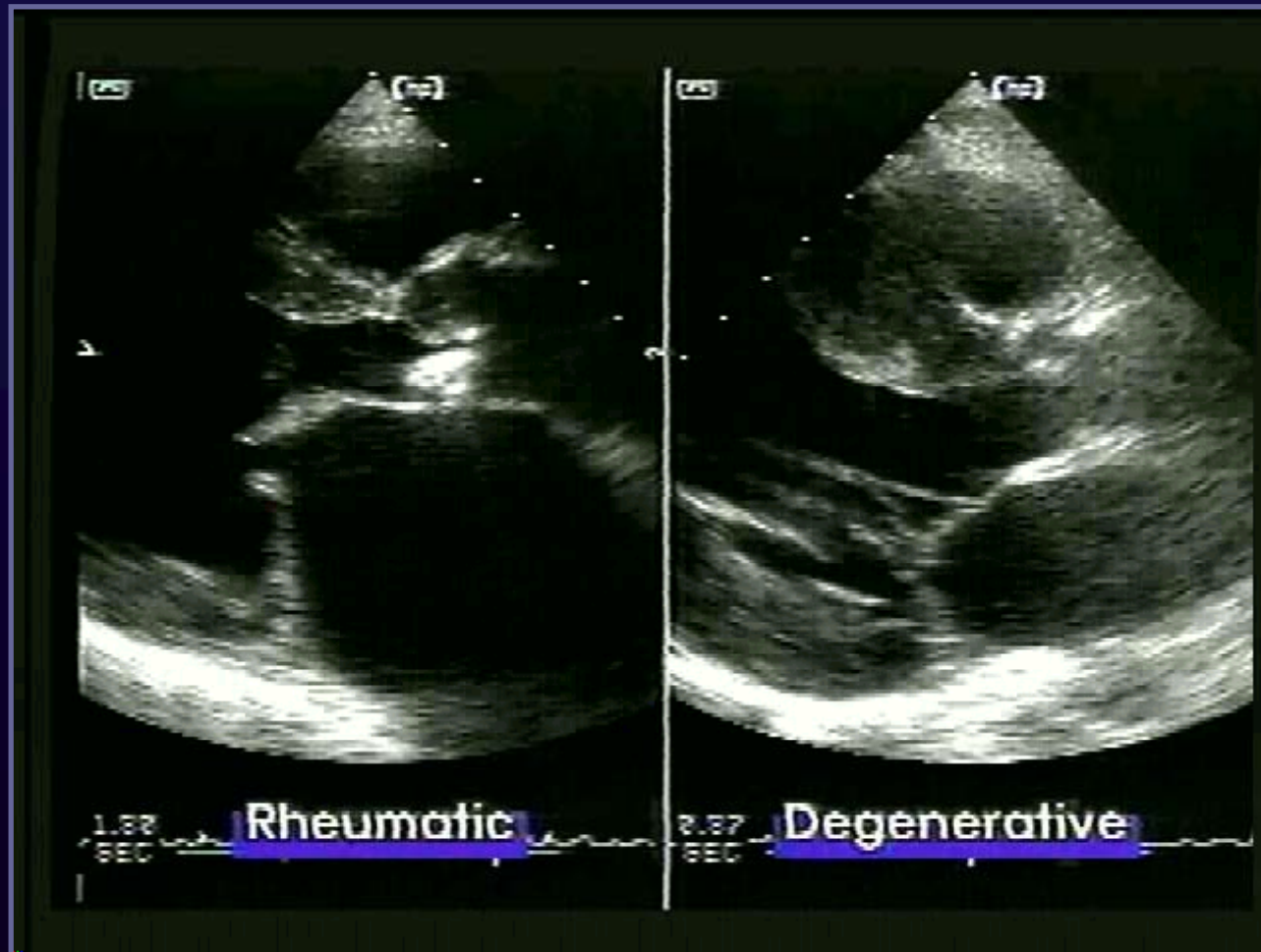
Aortic Stenosis

□ Etiology

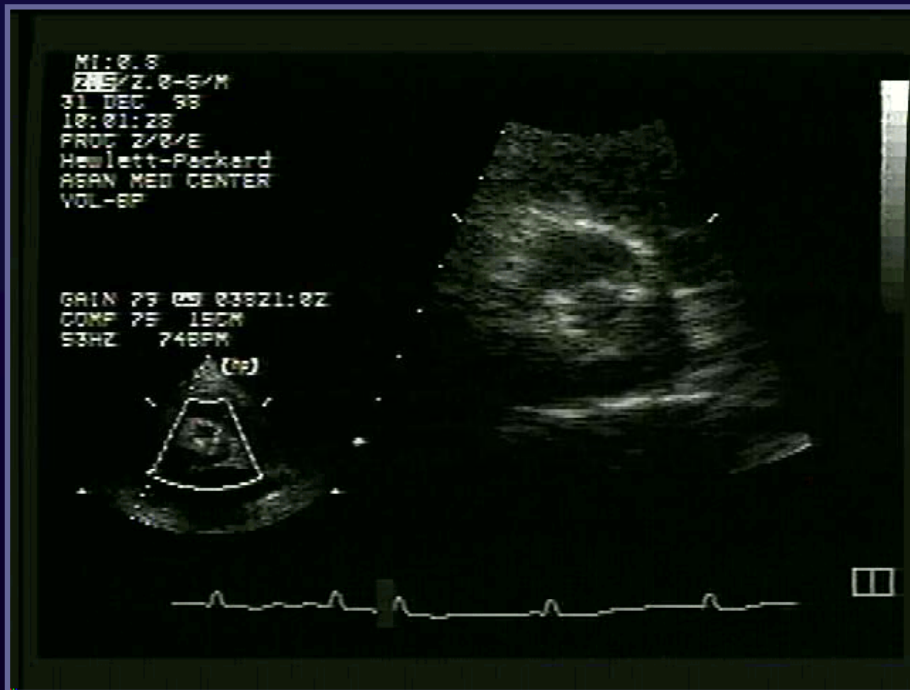
- Congenital
 - Bicuspid
- Acquired
 - Degenerative
 - Calcium deposition
 - AR : rare
 - DM, hypercholesterolemia
 - Smoking, HT, low HDL
 - Rheumatic
 - Commissure fusion
 - Cusp retraction & stiffening
 - MV involvement
 - AR : common



Aortic Stenosis



Aortic Stenosis



Rheumatic



Degenerative

Aortic Stenosis

□ Symptoms

▪ Angina

- 2/3 of tight AS
- 50% have associated coronary artery disease
- Increased oxygen demand & reduced oxygen delivery

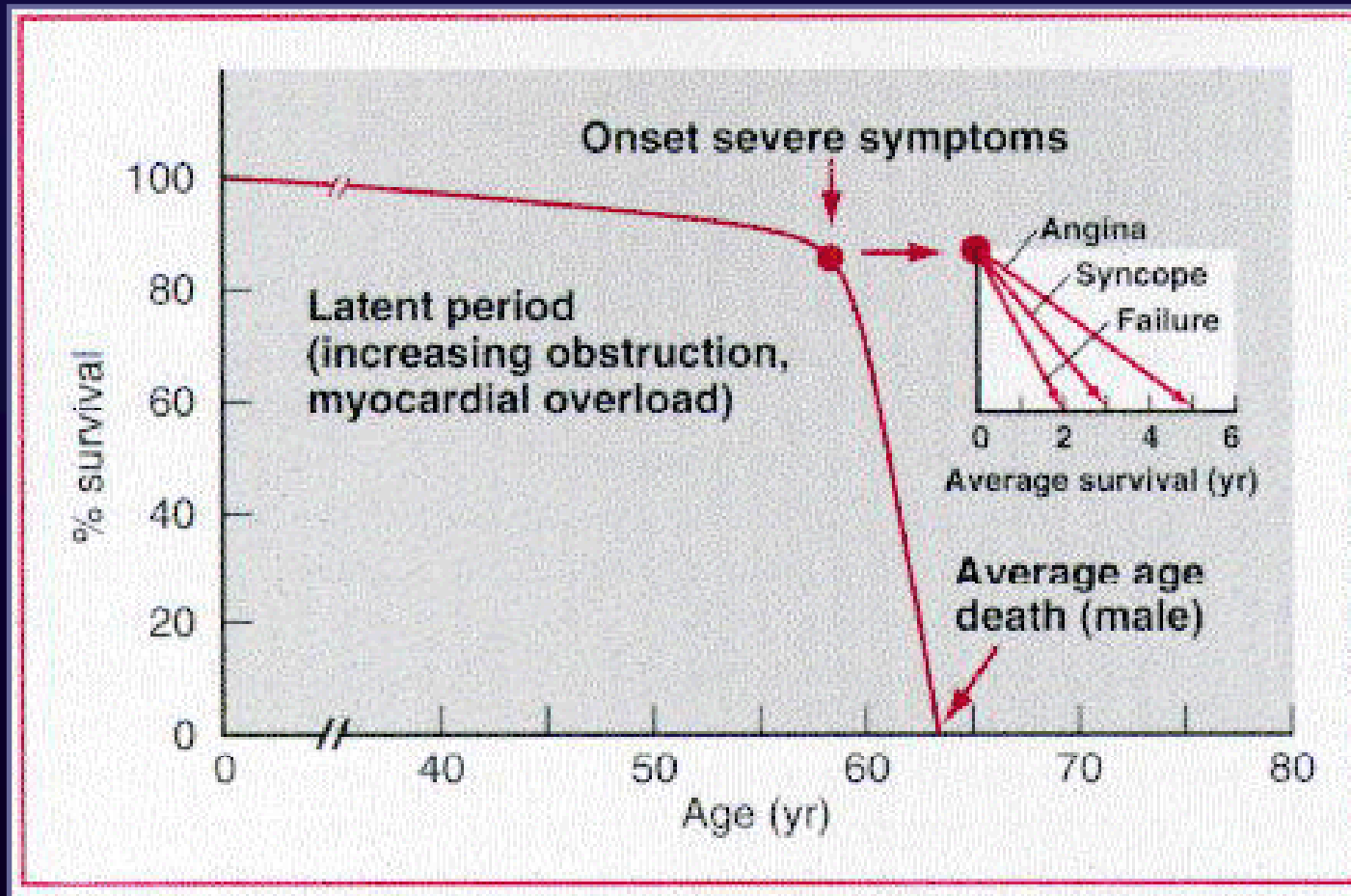
▪ Syncope

- Reduced cerebral perfusion during exertion
- Malfunction of the baroreceptor mechanism
- Vasodepressor response to elevated LV systolic pressure
- Transient Af
- Transient AV block
- Ventricular fibrillation

▪ Congestive heart failure

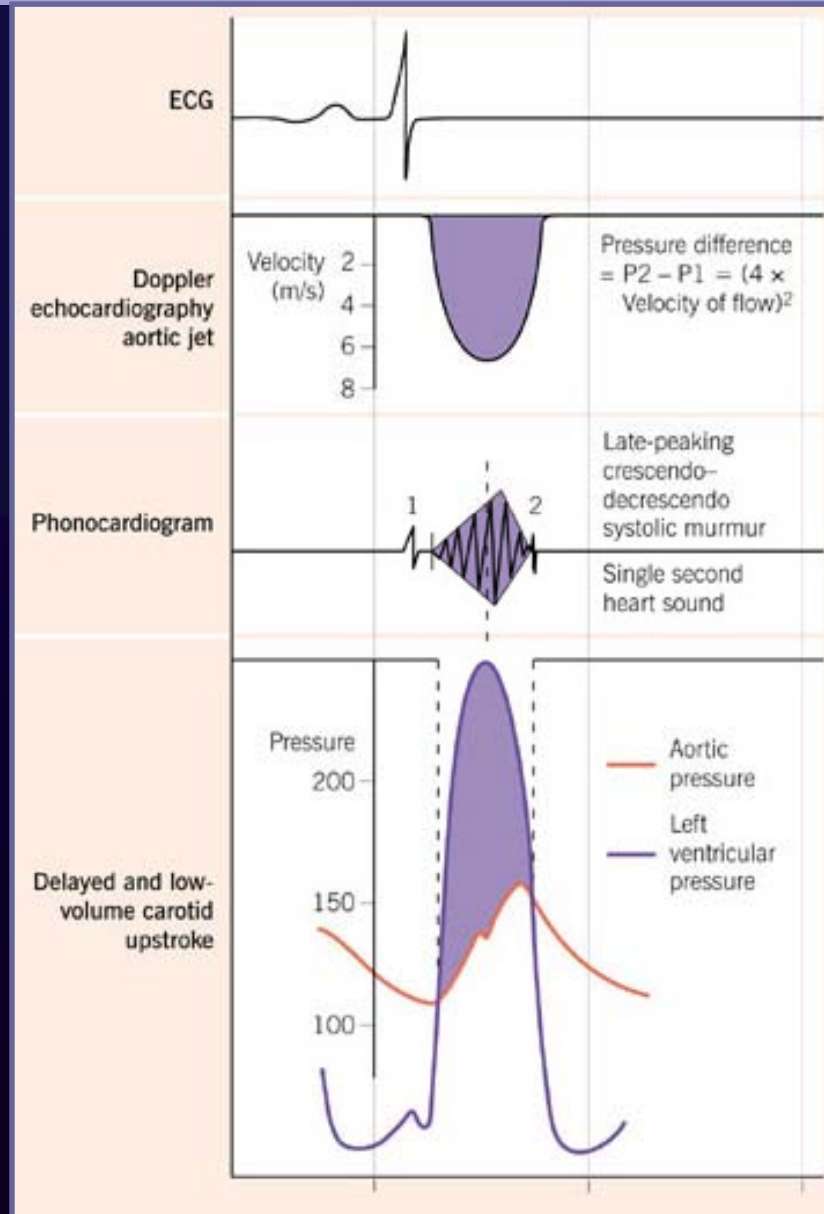
- Late symptom

Aortic Stenosis

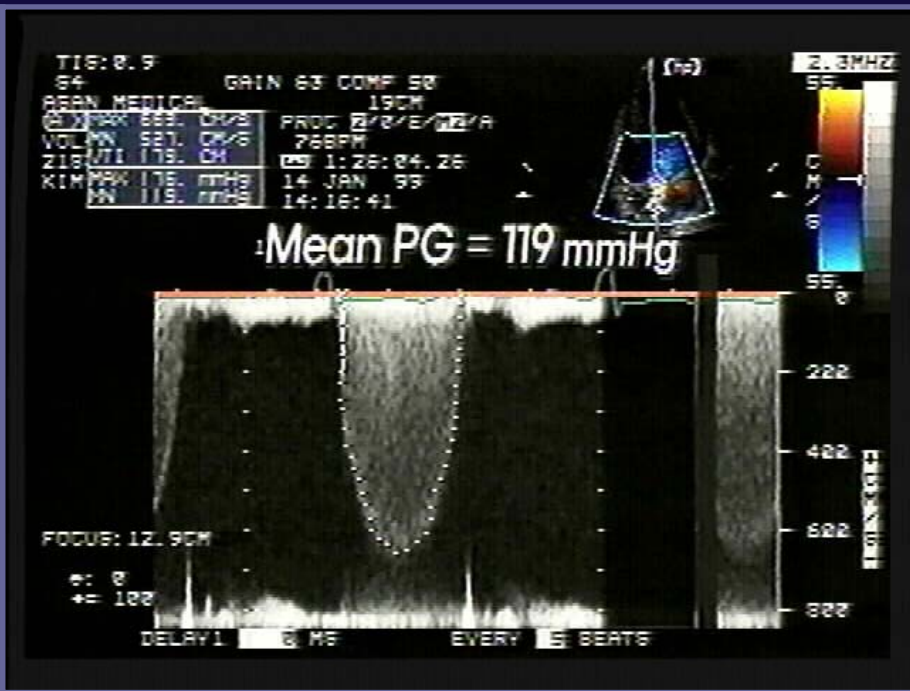
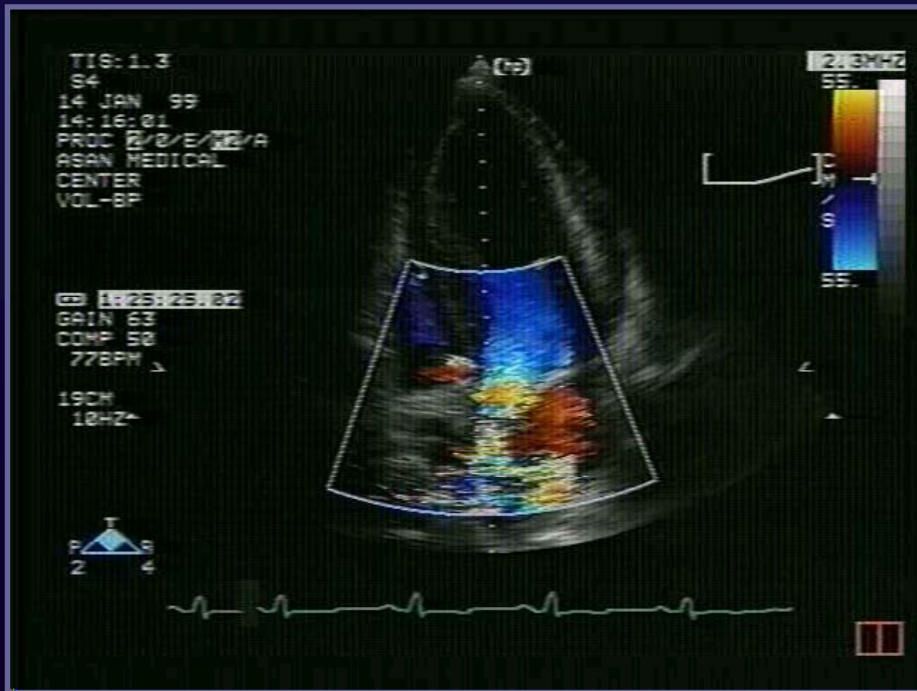


Circulation 1968;38[Suppl V]:61

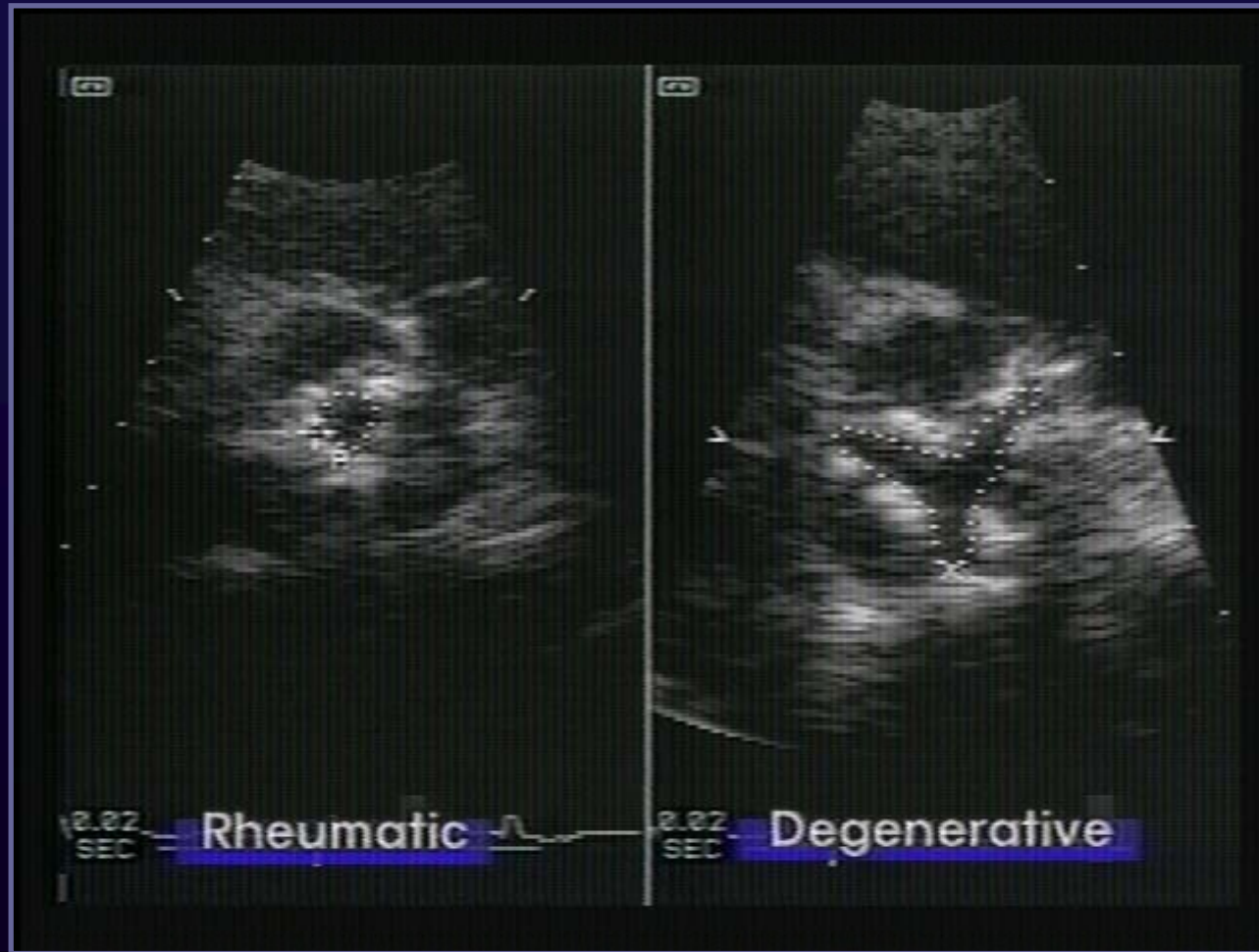
Aortic Stenosis



Aortic Stenosis

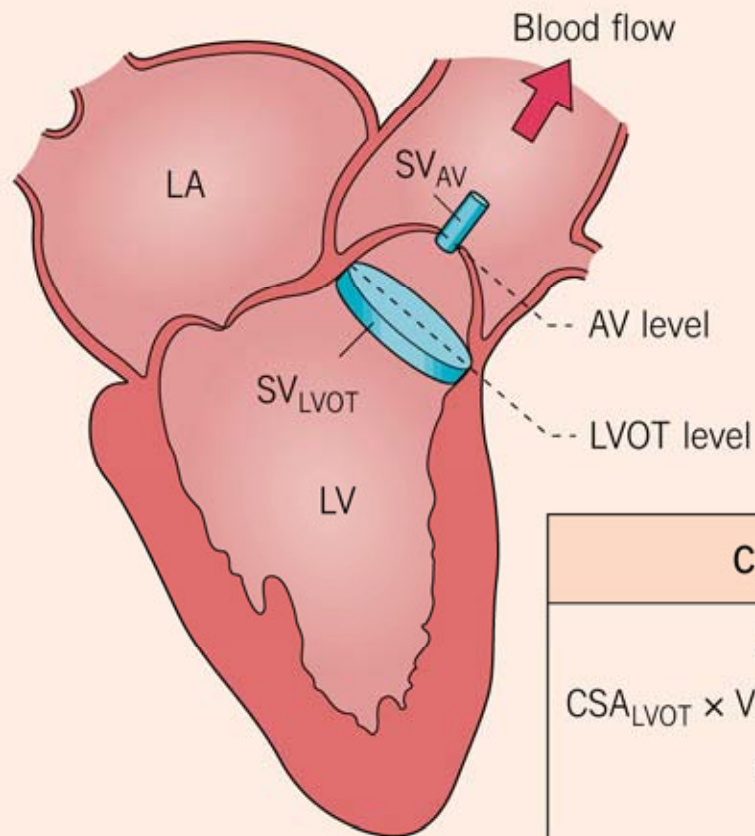



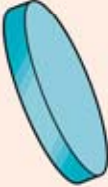
Aortic Stenosis



Aortic Stenosis

CONTINUITY EQUATION USED TO DETERMINE AORTIC VALVE AREA



SV_{AV}	Stroke volume at the level of the aortic valve
	
SV_{LVOT}	Stroke volume at the level of the left ventricle outflow tract
	

Continuity equation

$$SV_{LVOT} = SV_{AV}$$
$$CSA_{LVOT} \times VTI_{LVOT} = CSA_{AV} \times VTI_{AV}$$
$$CSA_{AV} = \frac{CSA_{LVOT} \times VTI_{LVOT}}{VTI_{AV}}$$

Aortic Stenosis

□ Severity

■ Mild

- Mean PG < 25 - 30 mmHg
- AVA > 1.5 cm²

■ Severe

- Mean PG > 40 - 50 mmHg
- Vmax > 4.0 - 4.5 m/s
- AVA < 0.75 - 1.0 cm²

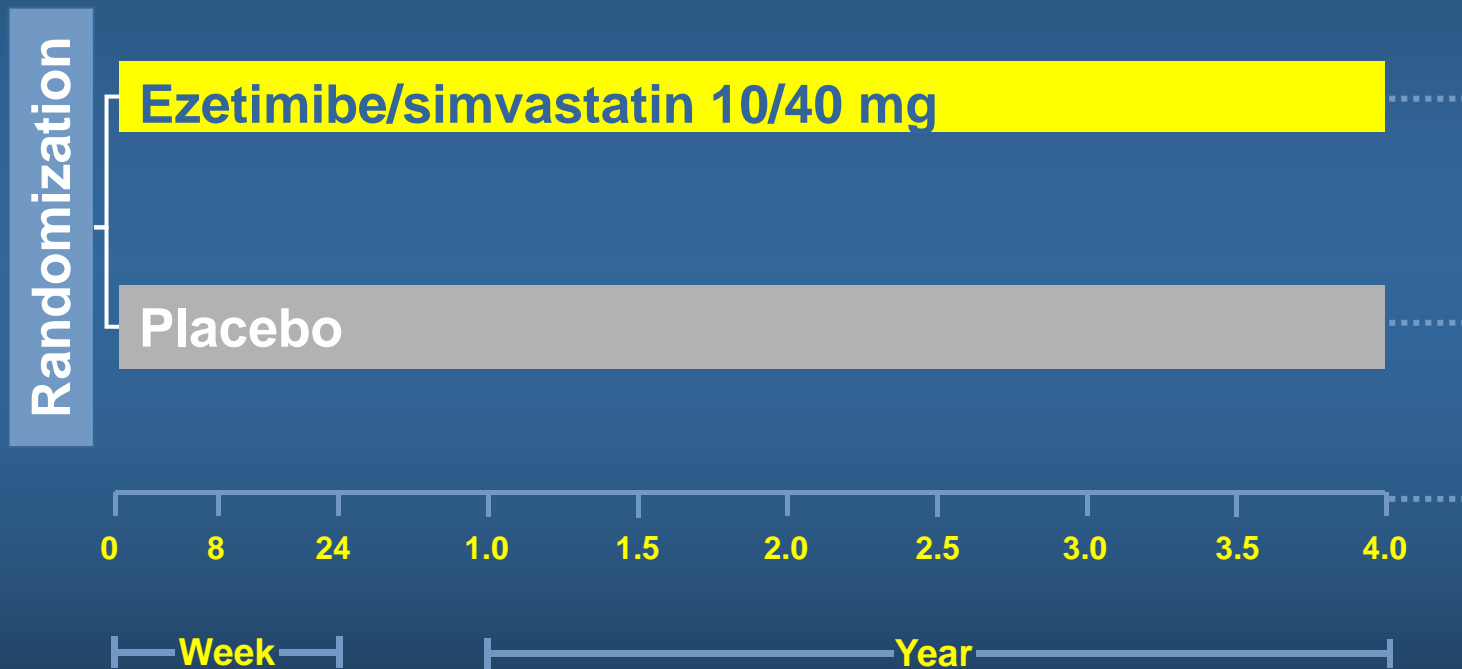
Aortic Stenosis

- Medical management
 - Limited value
 - Angina
 - Beta-blocker
 - Nitrates
 - Congestive heart failure
 - Diuretics
 - Atrial fibrillation
 - Digitalis
 - Cardioversion
 - ACE inhibitors
 - HMG CoA reductase inhibitors

Simvastatin and Ezetimibe in Aortic Stenosis (SEAS)

Sample size: **1873 patients**

173 Centers: Norway, Sweden, Denmark, Finland, Germany, UK, Ireland

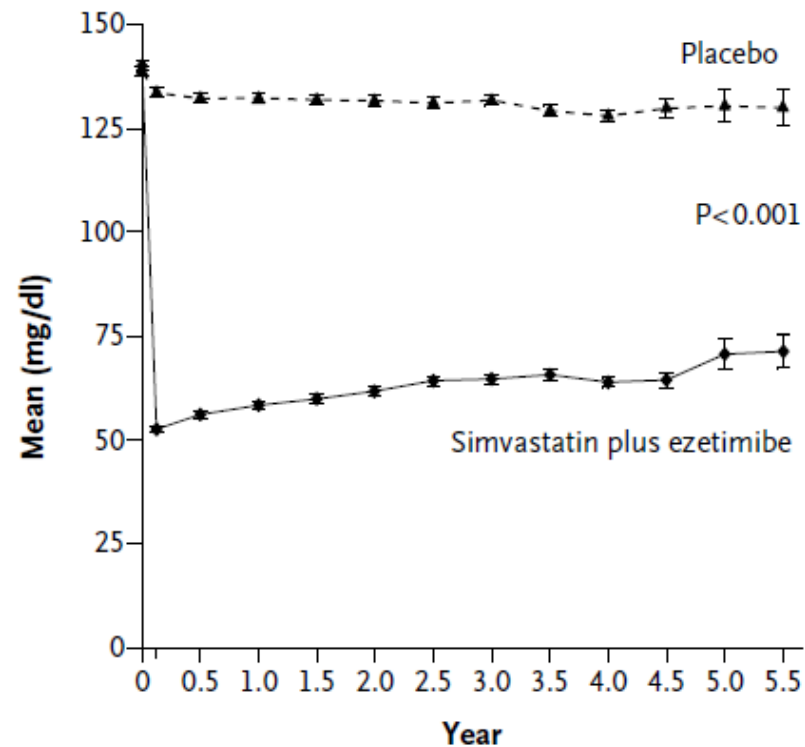


Minimum follow-up: 4 years (all patients)

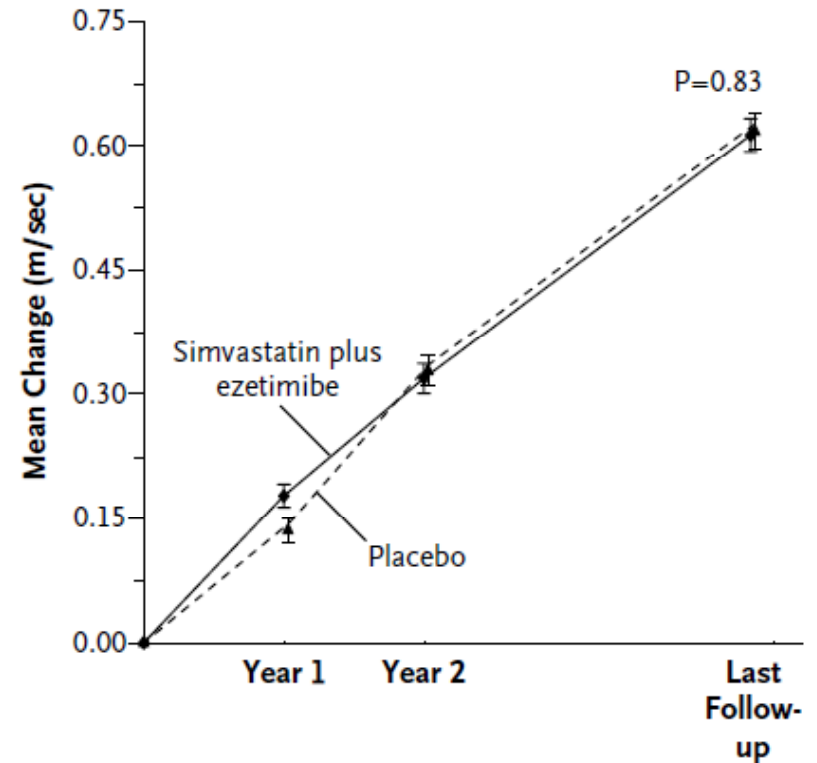
Median follow-up: 52.2 months

SEAS Disease Progression

A Serum LDL Cholesterol



B Peak Aortic-Jet Velocity



SEAS Clinical Events

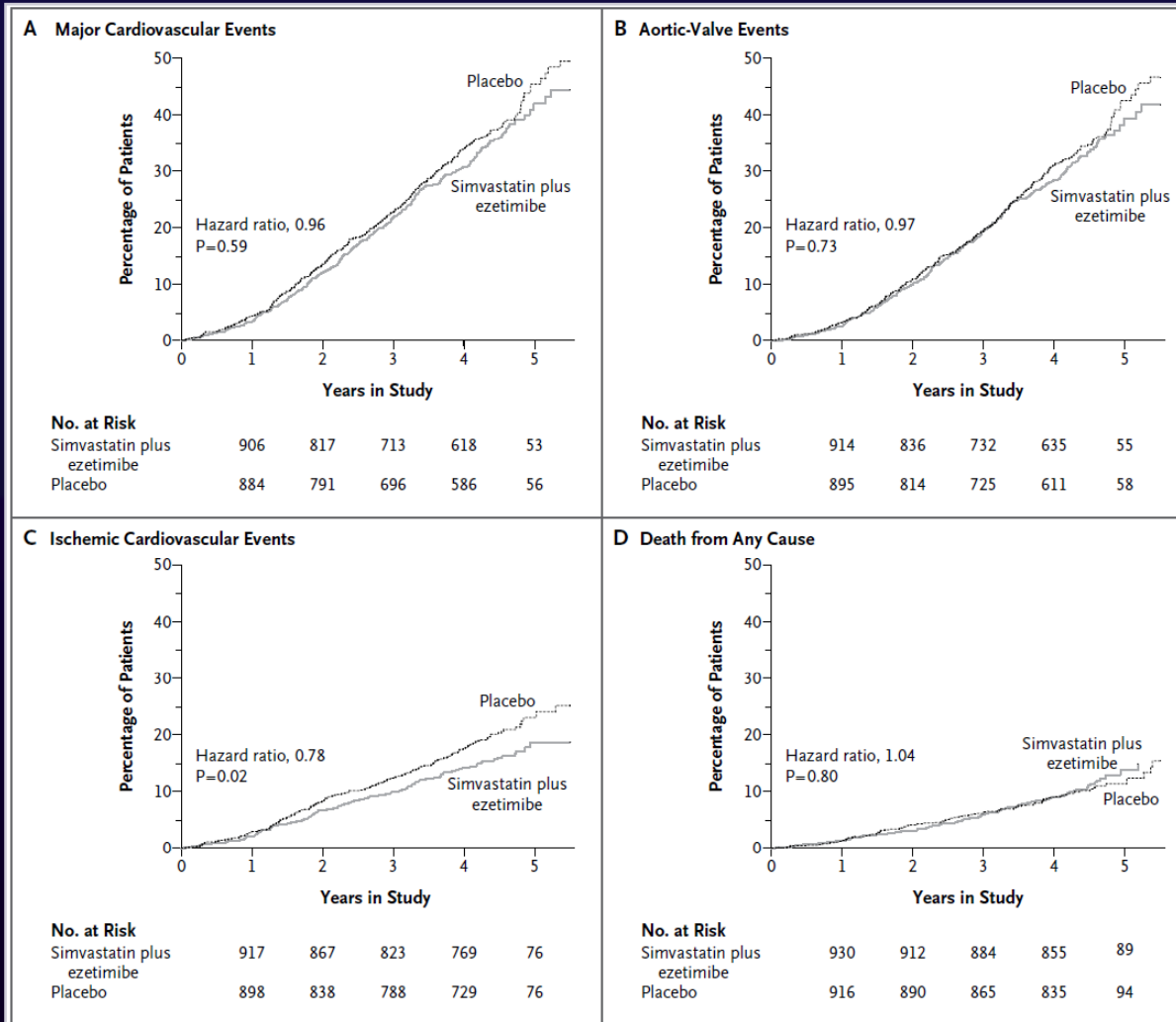


Figure 3. Kaplan–Meier Curves for Primary and Secondary Outcomes and Death.

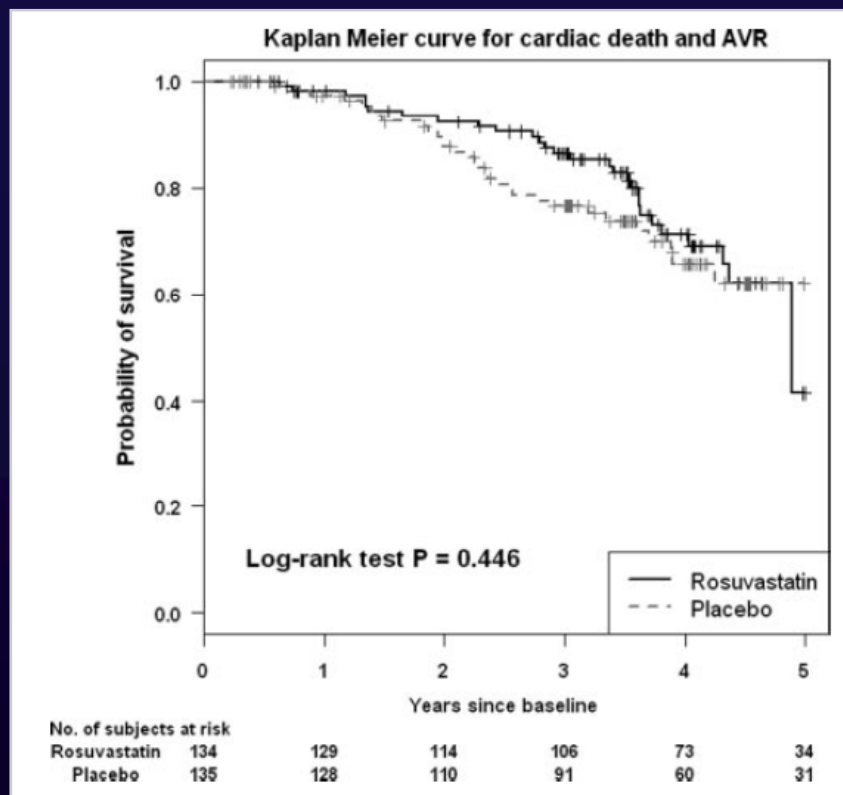
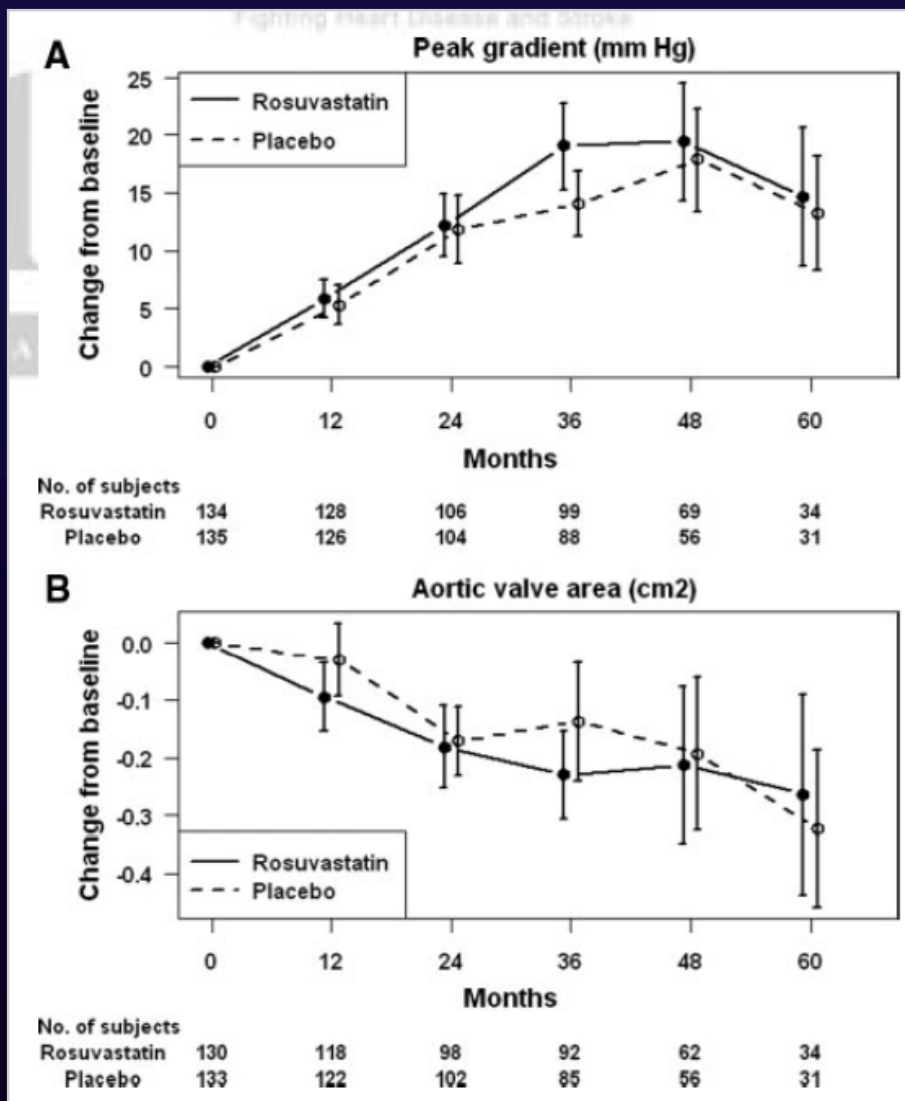
The primary outcome was a composite of major cardiovascular events, including death from cardiovascular causes, aortic-valve replacement, nonfatal myocardial infarction, hospitalization for unstable angina pectoris, heart failure, coronary-artery bypass grafting, percutaneous coronary intervention, and nonhemorrhagic stroke (Panel A). Secondary outcomes were events related to aortic-valve stenosis (Panel B) and ischemic cardiovascular events (Panel C). There was no difference between the study groups in overall mortality (Panel D).

*Rossebø AB, et al.
NEJM 2008;359*

Statins for Aortic Stenosis

- Aortic Stenosis Progression Observation: Measuring Effects of Rosuvastatin (**ASTROMER**) trial
 - Asymptomatic patients with mild to moderate AS and no clinical indications for cholesterol lowering.
 - A total of 269 patients were randomized
 - 134 patients to rosuvastatin 40 mg daily
 - 135 patients to placebo

ASTROMER



ACC/AHA Guidelines

□ Aortic valve replacement (AVR)

▪ Class I

- Symptomatic patients with severe AS
- Severe AS undergoing CABG
- Severe AS undergoing surgery on the aorta or other valves
- Severe AS with LV dysfunction (EF < 50%)

▪ Class IIa

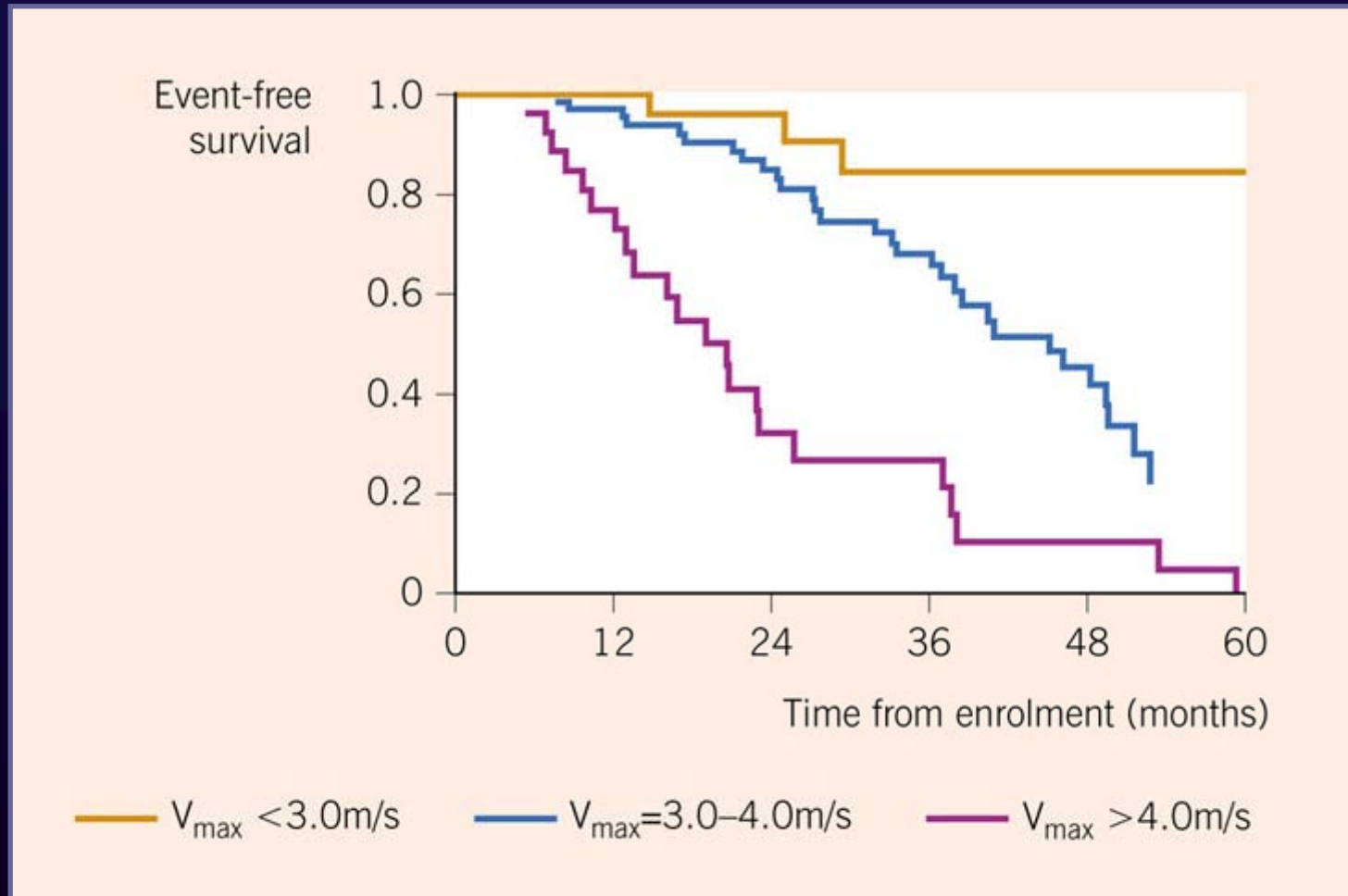
- Moderate AS undergoing CABG or surgery on the aorta or other valves

Circulation. 2008;118:e523-e661

Asymptomatic Severe AS

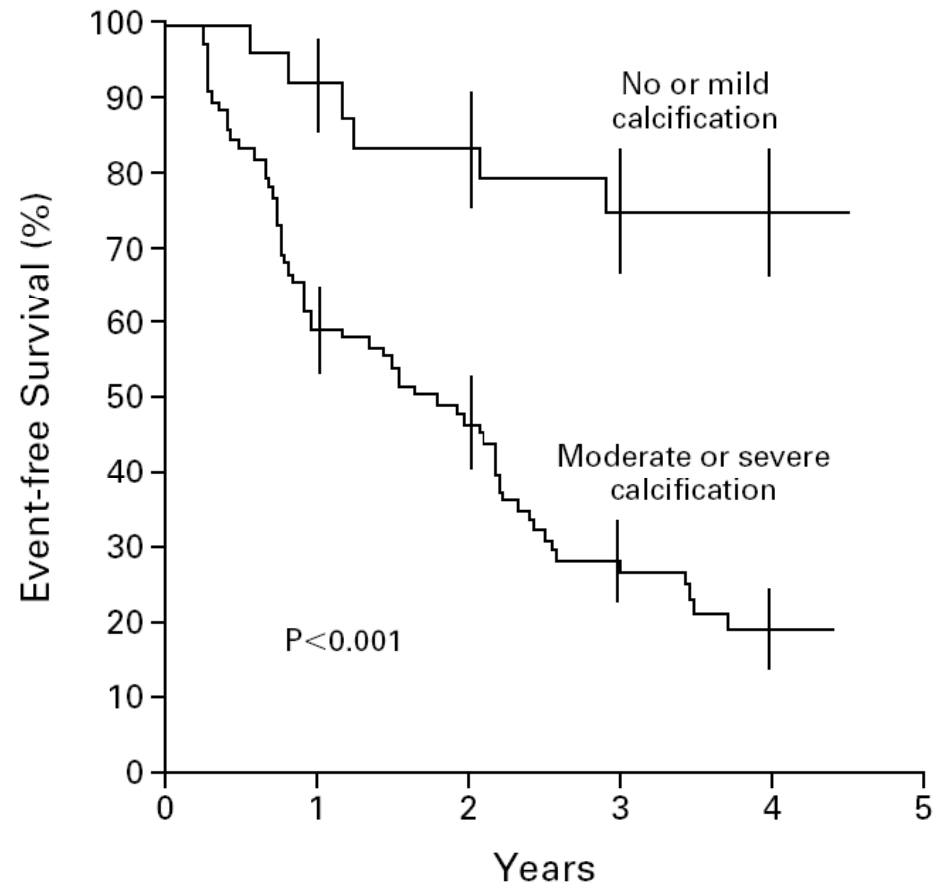
- **AVR** : **not** generally recommended
 - Sudden death
 - < 1%/year without symptom
 - Can occur after AVR
 - Perioperative mortality
 - 3.2%
 - Morbidity caused by prosthetic valve
 - 2-3%/year
 - Infective endocarditis
 - Anticoagulation
 - Prosthetic valve failure

Asymptomatic Severe AS



Otto et al. Circulation 1997;95:2262-70

Asymptomatic Severe AS

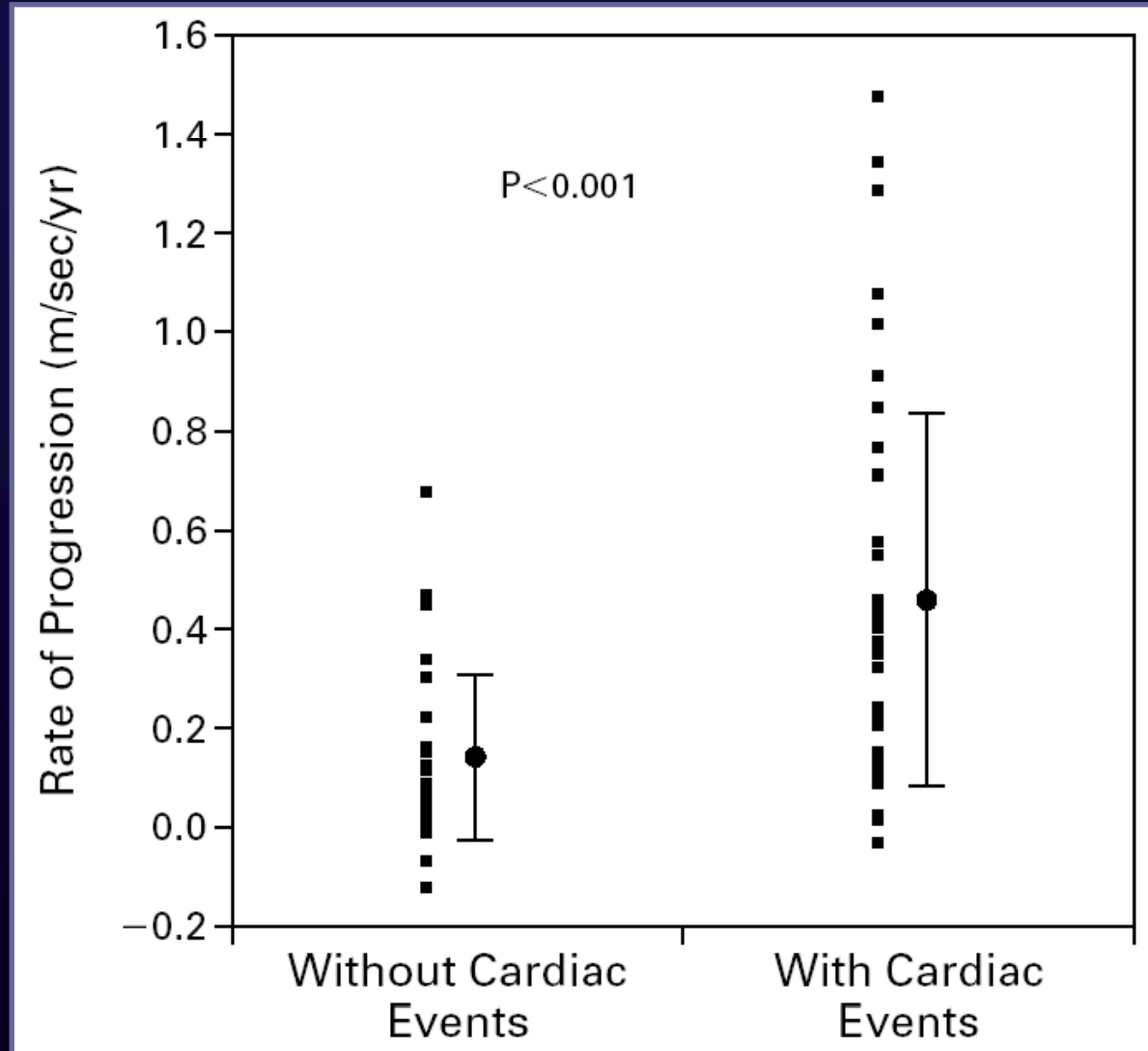


NO. OF PATIENTS AT RISK

No or mild calcification	25	23	20	17	9
Moderate or severe calcification	101	48	38	21	7

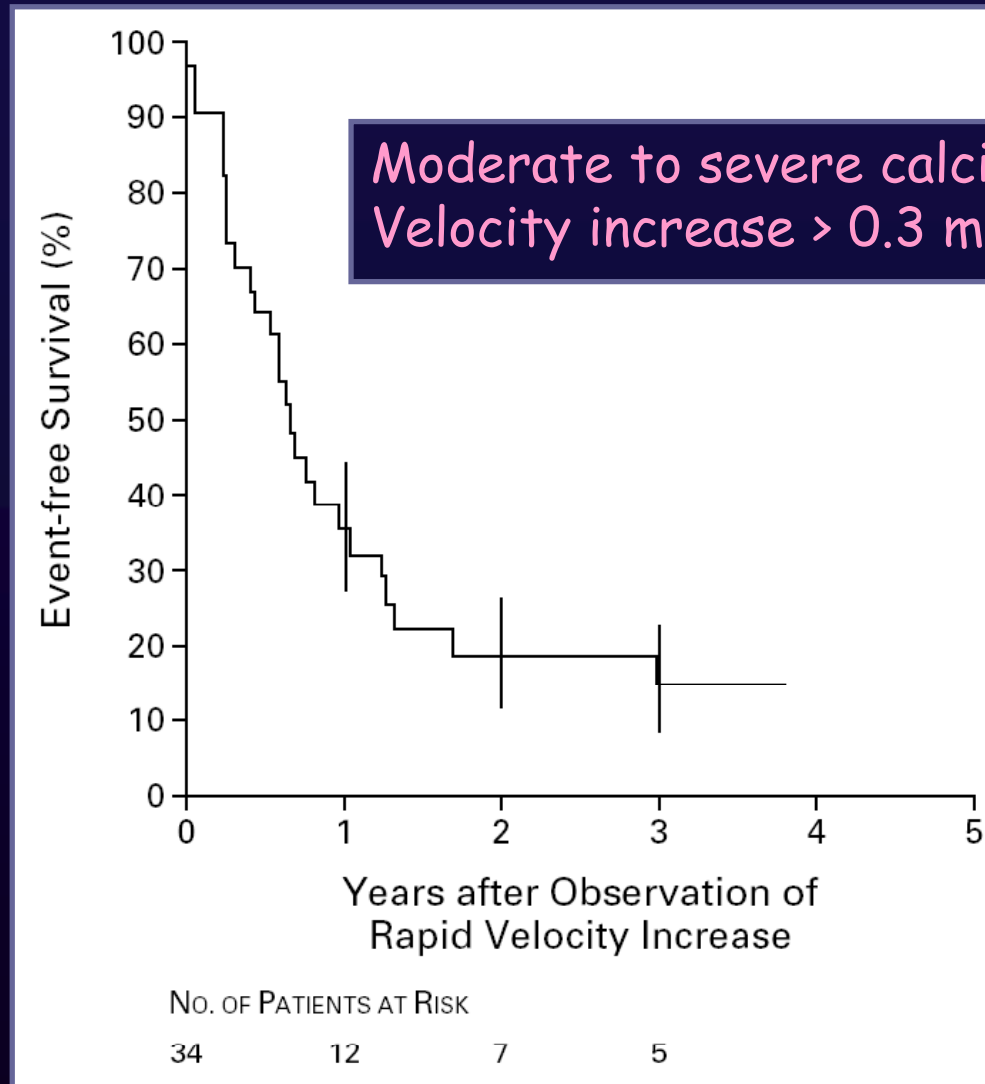
N Engl J Med 2000;343:611-7

Asymptomatic Severe AS



N Engl J Med 2000;343:611-7

Asymptomatic Severe AS



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Asymptomatic Severe AS

□ Aortic Valve Replacement

▪ Class IIb

- AVR may be considered for asymptomatic patients with severe AS and **abnormal response to exercise**.
- AVR may be considered for adults with severe asymptomatic AS if there is a high likelihood of **rapid progression** (age, calcification, and CAD) or if **surgery might be delayed** at the time of symptom onset.
- AVR may be considered for asymptomatic patients with **extremely severe AS** (aortic valve area less than 0.6 cm^2 , mean gradient greater than 60mmHg, and jet velocity greater than 5.0 m per second) when the **patient's expected operative mortality is 1.0% or less**.

Circulation. 2008;118:e523-e661

ESC Guidelines

□ Aortic valve replacement (AVR)

▪ Class I

- Symptomatic severe AS
- Severe AS undergoing coronary artery bypass surgery, surgery of the ascending aorta, or on another valve
- Asymptomatic patients with severe AS and systolic LV dysfunction (LVEF <50 percent) unless due to other cause
- Asymptomatic patients with severe AS and abnormal exercise test showing symptoms on exercise

ESC Guidelines

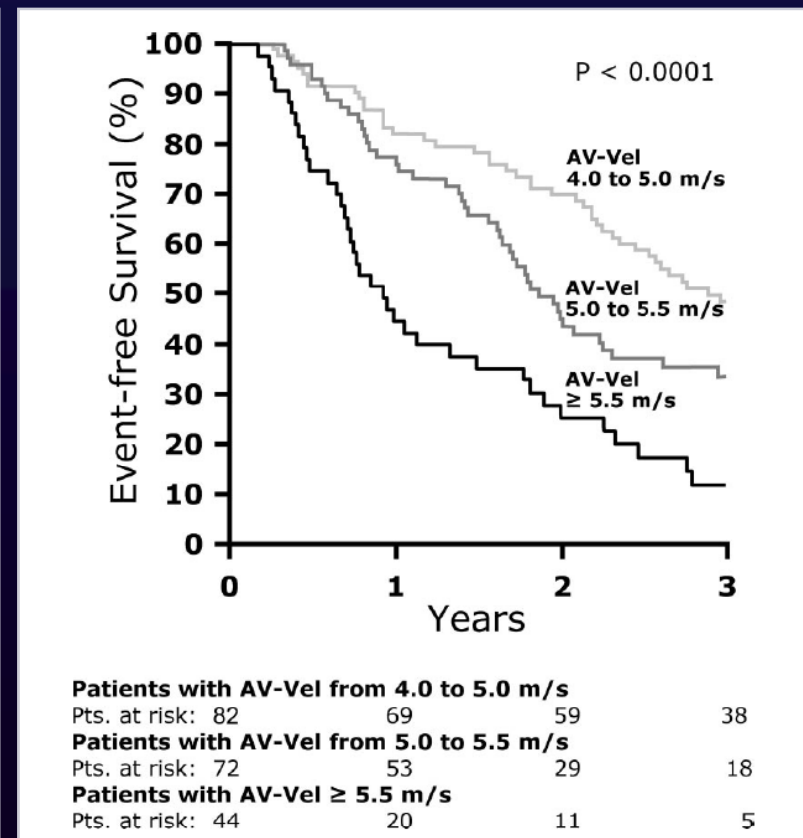
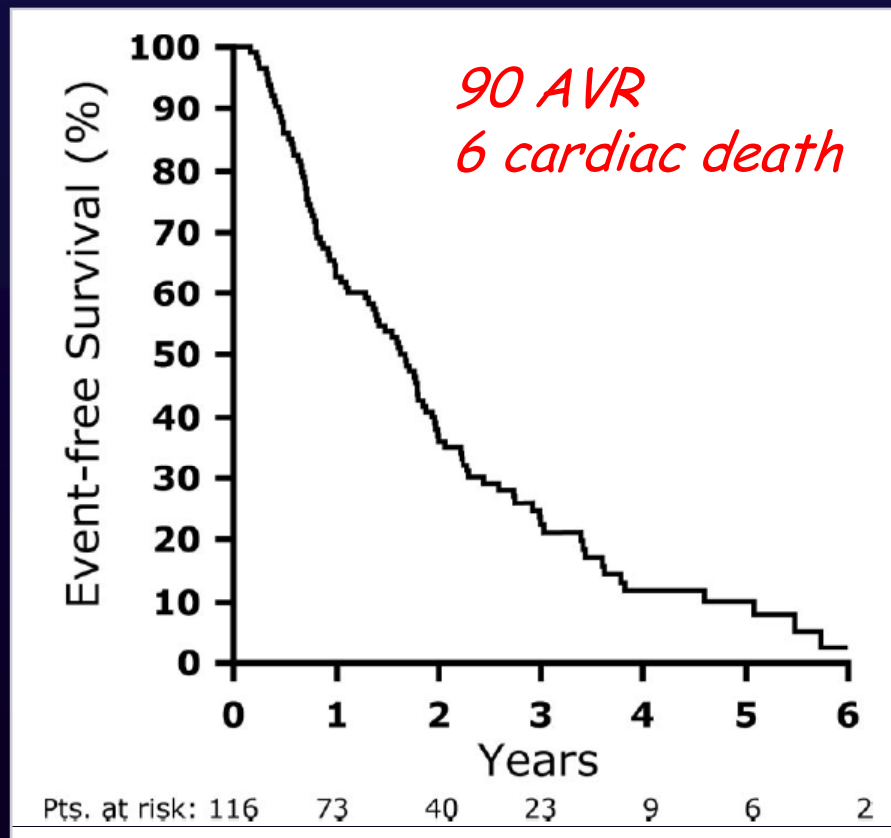
□ Aortic valve replacement (AVR)

▪ Class IIa

- Asymptomatic patients with severe AS and abnormal exercise test showing fall in blood pressure below baseline
- Moderate AS undergoing coronary artery bypass surgery, surgery of the ascending aorta or another valve
- Asymptomatic patients with severe AS and moderate-to-severe valve calcification, and a rate of peak velocity progression ≥ 0.3 m/s per year
- AS with low gradient (< 40 mmHg) and LV dysfunction with contractile reserve

Asymptomatic Very Severe AS

- 116 consecutive asymptomatic patients with very severe isolated AS (AV-Vel > 5.0 m/s)



Circulation. 2010;121:151-156

Asymptomatic Very Severe AS

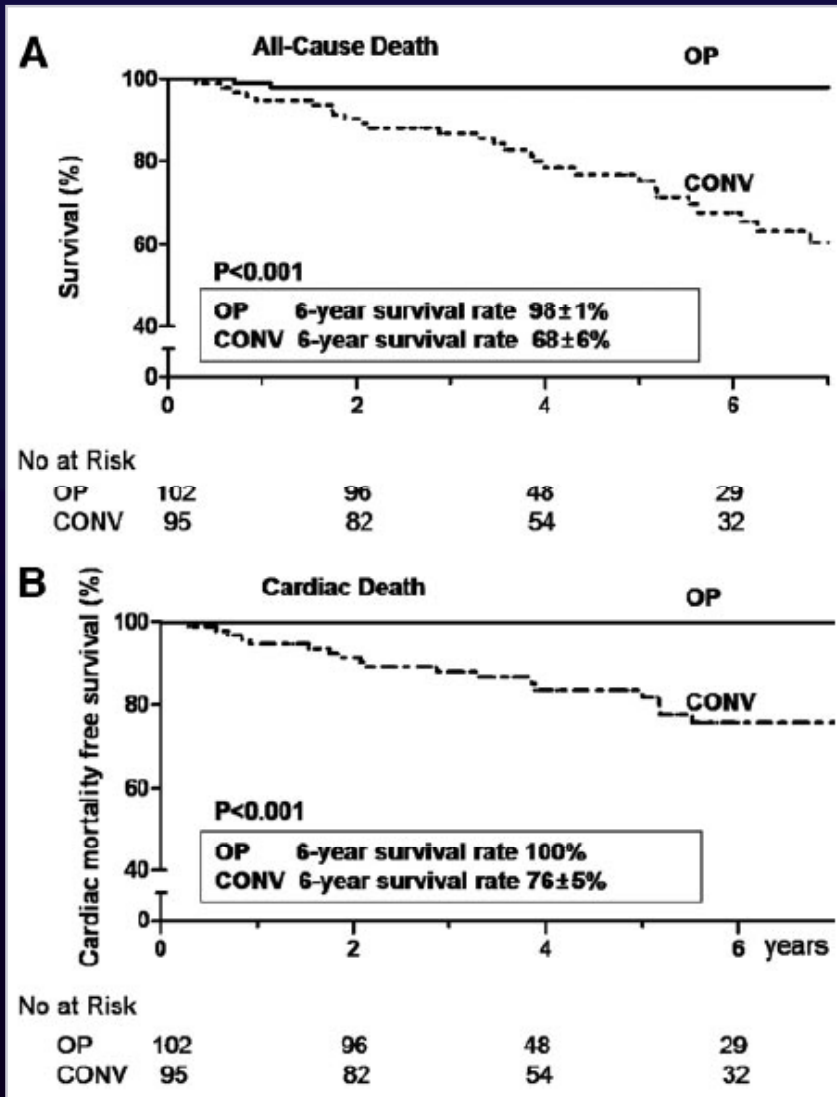
Table 2. Event-Free Survival: Univariate and Multivariate Analyses of Clinical and Echocardiographic Explanatory Variables

Variable	Univariate Analysis		Multivariate Analysis	
	<i>P</i>	HR (95% CI)	<i>P</i>	HR (95% CI)
Age >70 y	0.93	1.02 (0.68–1.54)	0.88	1.04 (0.66–1.62)
Female sex	0.43	1.17 (0.78–1.76)	0.57	1.14 (0.72–1.81)
Coronary artery disease	0.87	1.04 (0.64–1.64)	0.80	0.94 (0.55–1.55)
Hypertension	0.87	0.97 (0.65–1.45)	0.16	0.70 (0.43–1.15)
Diabetes mellitus*	0.016	1.47 (1.07–2.02)	0.0025	1.84 (1.24–2.73)
Hypercholesterolemia	0.14	1.39 (0.89–2.13)	0.043	1.68 (1.02–2.75)
Aortic valve area <0.6 cm ²	0.12	1.38 (0.92–2.07)	0.36	1.25 (0.77–2.02)
Aortic valve peak velocity ≥5.5 m/s	0.001	2.0 (1.31–3.03)	0.0069	1.88 (1.19–2.96)

HR indicates hazard ratio; CI, confidence interval.

*Because a time-dependent effect of diabetes mellitus was observed after testing interactions with the log of time (univariate, $P=0.023$; multivariate, $P=0.030$), HRs obtained by a weighted Cox regression analysis are provided for this variable.²⁰

Asymptomatic Very Severe AS



*AVA ≥ 0.75 cm² &
(Vmax ≥ 4.5 m/s or
mean PG ≥ 50 mm Hg)*

KangDH, Circulation. 2010 ;121:1502-9.

Octogenarians

□ Outcomes after AVR in octogenarians

- Higher frequency of NYHA functional class III or IV: 86% versus 36% ($p < 0.001$)
- Early mortality rate: 14% versus 4% ($p = 0.045$)
- 2-year survival rate: 73% versus 90% ($p = \text{NS}$)
- The duration of respirator support, intensive care and the total duration of the hospital stay did not differ significantly between groups.
- Symptomatic improvement

Octogenarians

□ Outcomes after AVR in octogenarians

- 171 consecutive patients aged 80 to 91 years
- The overall 30-day early mortality: 17.5%
 - 5.2% for patients with AVR only
 - 27.7% for those with concomitant surgical procedures
- Predictors of operative mortality
 - LV EF < 45%, hypertension, and concomitant surgical procedures
- The overall actuarial survival at 1, 3, and 5 years was 90.8%, 84.2%, and 76.0%.

Circulation 1993 Nov;88(5 Pt 2):II11-6