Natural History of Aortic Regurgitation

Rheumatic Valvular AR

- Rheumatic fever remains a common cause of primary disease of the aortic valve that leads to regurgitation.
- The cusps become infiltrated with fibrous tissues and retract,a process that prevents cusp apposition during diastole;

Rheumatic Valvular AR

- this usually leads to regurgitation into the left ventricle through a defect in the centre of the valve.
- The associated fusion of the commissures may restrict the opening of the valve, resulting in combined AS and AR;
- some associated mitral valve involvement is also common.

Natural History of Chronic Aortic Regurgitation

- Depends on
  - AR severity,
  - aortic root pathology, and
  - adaptive response of LV.
- Mainly evolves in a slow and insidious manner
- with a very low morbidity during a long asymptomatic phase.

Natural History of Chronic Aortic Regurgitation

- While some patients with mild AR do not progress for decades,
- others exhibit progression of the regurgitant lesion
- with the gradual development of severe AR with subsequent left ventricular dilation, systolic dysfunction, and eventually heart failure

Natural History of Chronic Aortic Regurgitation

- Moderately severe or even severe chronic AR often is associated with a generally favourable prognosis for many years.

- Quantitative measures of AR severity predict clinical outcome,

- and LV size and systolic function also are strong predictors of clinical outcome.

Natural History of Chronic Aortic Regurgitation

- In chronic severe AR, the LV gradually enlarges while the patient remains asymptomatic.

- Symptoms of reduced cardiac reserve or myocardial ischemia develop, most often in the fourth or fifth decade of life

- usually only after considerable cardiomegaly and myocardial dysfunction have occurred.

Natural History of Chronic Aortic Regurgitation

- Exertional dyspnea, orthopnea, and PND—usually develop gradually.
- Angina pectoris prominent late in the course
- nocturnal angina occurs when rate slows and arterial diastolic pressure falls to extremely low levels.

Natural History of Chronic Aortic Regurgitation

- Patients with severe AR often complain of an uncomfortable awareness of the heartbeat, especially on lying down,

- thoracic pain caused by pounding of the heart against the chest wall.

- These complaints may be present for many years before symptoms of overt LV dysfunction develop.

Natural History of Chronic Aortic Regurgitation

- Once the patient becomes symptomatic,
- downhill course becomes rapidly progressive.
- Congestive heart failure, punctuated by episodes of acute pulmonary edema,
- sudden death may occur,in previously symptomatic patients who have considerable LV dilation.

Natural History of Chronic Aortic Regurgitation

- Gradual deterioration of LV function may occur even during the asymptomatic period,

- depressed LVEF is among the most important determinants of mortality after AVR,

- particularly when LV dysfunction is irreversible and does not improve after operation.

Natural History of Chronic Aortic Regurgitation

- LV dysfunction is more likely to be reversible if detected early,
- before ejection fraction becomes severely depressed, before the LV becomes markedly dilated, and before significant symptoms develop.
- important to intervene surgically before these changes have become irreversible.

STAGE	DEFINITION	VALVE ANATOMY	VALVE HEMODYNAMICS	HEMODYNAMIC CONSEQUENCES	SYMPTOMS
A	**At risk of AR**	Bicuspid aortic valve (or other congenital valve anomaly) Aortic valve sclerosis Diseases of the aortic sinuses or ascending aorta History of rheumatic fever or known rheumatic heart disease IE	AR severity none or trace	None	None
B	**Progressive AR**	Mild to moderate calcification of a trileaflet valve bicuspid aortic valve (or other congenital valve anomaly) Dilated aortic sinuses Rheumatic valve changes Previous IE	***Mild AR:*** Jet width <25% of LVOT vena contracta <0.3 cm RVol <30 mL/beat RF <30% ERO <0.10 cm^2 Angiography grade 1+ ***Moderate AR:*** Jet width 25%-64% of LVOT Vena contracta 0.3-0.6 cm RVol 30-59 mL/beat RF 30%-49% ERO 0.10-0.29 cm^2 Angiography grade 2+	Normal LV systolic function Normal LV volume or mild LV dilation	None

Stage C1 (asymptomatic AR with mildly to moderately increased LVESD)

- Asymptomatic patients with severe AR with LVEF >50 % **and** LVESD ≤45 to 50 mm (and an LV end-diastolic dimension <60 to 65 mm)
- are in a compensated phase associated with low risk of immediate progression to development of heart failure symptoms or LV dysfunction.

Stage C2 (asymptomatic with LV systolic dysfunction or moderate to severe LV dilation)

- Asymptomatic patients with severe AR with LV systolic dysfunction (an LVEF <50 percent **or** LV end-systolic dimension >50 mm)
- are in a decompensated phase with high risk of progression to development of heart failure symptoms requiring aortic valve surgery.

C	**Asymptomatic severe AR**	Calcific aortic valve disease Bicuspid valve (or other congenital abnormality) Dilated aortic sinuses or ascending aorta Rheumatic valve changes IE with abnormal leaflet closure or perforation	***Severe AR:*** Jet width ≥65% of LVOT Vena contracta >0.6 cm Holodiastolic flow reversal in the proximal abdominal aorta RVol ≥60 mL/beat RF ≥50% ERO ≥0.3 cm^2 Angiography grade 3+ to 4+ In addition, diagnosis of chronic severe AR requires evidence of LV dilation	*C1:* Normal LVEF (≥50%) and mild-to-moderate LV dilation (LVESD ≤50 mm) *C2:* Abnormal LV systolic function with depressed LVEF (<50%) or severe LV dilation (LVESD >50 mm or indexed LVESD >25 mm/m^2)	None; exercise testing is reasonable to confirm symptom status
D	**Symptomatic severe AR**	Calcific valve disease Bicuspid valve (or other congenital abnormality) Dilated aortic sinuses or ascending aorta Rheumatic valve changes Previous IE with abnormal leaflet closure or perforation	***Severe AR:*** Doppler jet width ≥65% of LVOT Vena contracta >0.6 cm Holodiastolic flow reversal in the proximal abdominal aorta RVol ≥60 mL/beat RF ≥50% ERO ≥0.3 cm^2 Angiography grade 3+ to 4+ In addition, diagnosis of chronic severe AR requires evidence of LV dilation	Symptomatic severe AR may occur with normal systolic function (LVEF ≥50%), mild-to-moderate LV dysfunction (LVEF 40% to 50%), or severe LV dysfunction (LVEF <40%) Moderate-to-severe LV dilation is present	Exertional dyspnea or angina, or more severe HF symptoms

- **Natural history of chronic aortic regurgitation mostly based upon data from nine series with a total of 593 patients followed for a mean of 6.6 years**

Asymptomatic patients with normal left ventricular (LV) systolic function	
Progression to symptoms and/or LV dysfunction	Less than 6 percent/year
Progression to symptoms, LV dysfunction, or death	
According to LV end-systolic dimension	
>50 mm	19 percent/year
40 to 50 mm	6 percent/year
<40 mm	0 percent/year
Progression to asymptomatic LV dysfunction	Less than 3.5 percent/year
Sudden death	Less than 0.2 percent/year
Asymptomatic patients with LV systolic dysfunction	
Progression to cardiac symptoms	More than 25 percent/year
Symptomatic patients	
Mortality rate	More than 10 percent/year

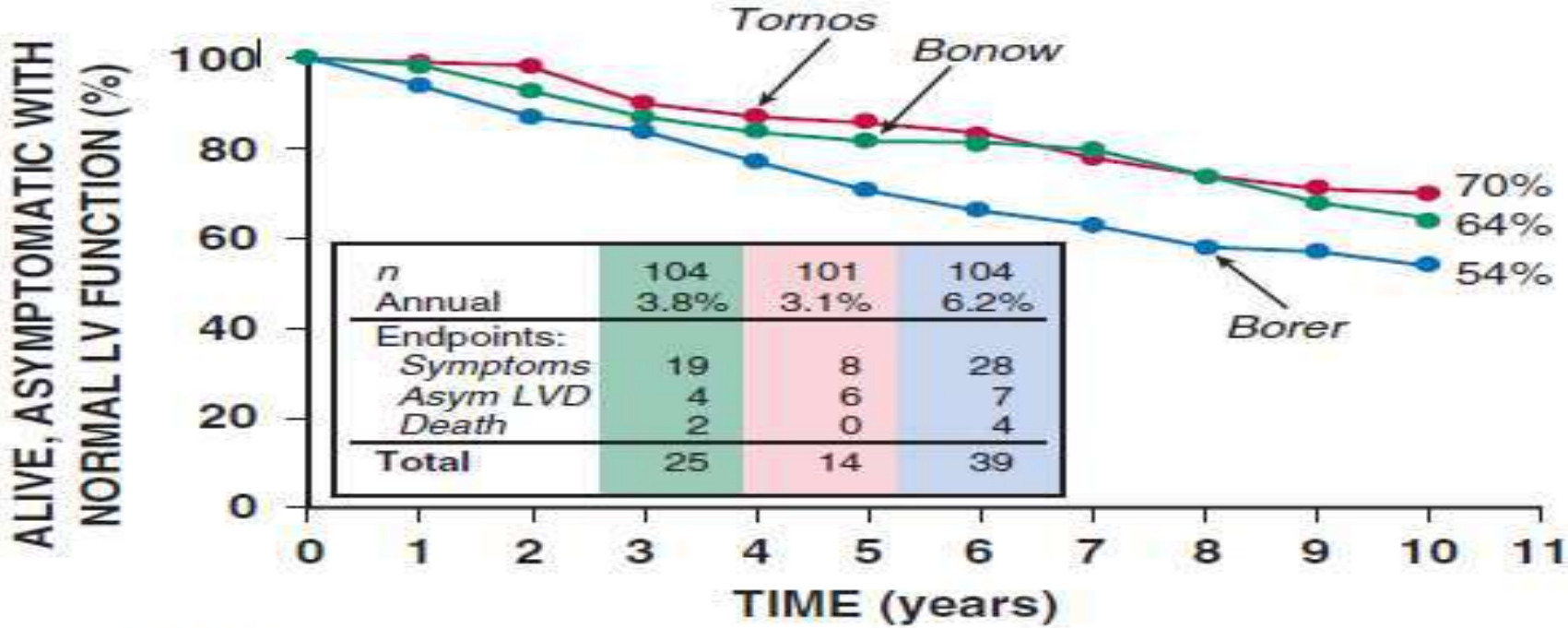


FIGURE 63-16 Three series examining the natural history of chronic asymptomatic AR in patients with normal LV ejection fraction at rest, each comprising more than 100 patients. At 10 years, 54% to 70% of patients remained asymptomatic with normal LV function, such that the risk of developing symptoms, LV dysfunction (LVD), or death is approximately 3% to 6%/year. The endpoints encountered in these series are indicated. Most patients who deteriorated developed symptoms leading to aortic valve replacement. However, 25% to 30% of the endpoints, either asymptomatic LVD (Asymp LVD) or death, occurred without warning symptoms. *(From Bonow RO: Chronic mitral regurgitation and aortic regurgitation: Have indications for surgery changed? J Am Coll Cardiol 61:693, 2013. Data modified from Bonow RO, Lakatos E, Maron BJ, et al: Serial long-term assessment of the natural history of asymptomatic patients with chronic aortic regurgitation and normal left ventricular systolic function. Circulation 84:1625, 1991; Tornos MP, Olona M, Permanyer-Miralda G, et al: Clinical outcome of severe asymptomatic chronic aortic regurgitation: A long term prospective follow up study. Am Heart J 130:333, 1995; and Borer JS, Hochreiter C, Herrold EM, et al: Prediction of indications for valve replacement among asymptomatic and minimally symptomatic patients with chronic aortic regurgitation and normal left ventricular performance. Circulation 97:525, 1998.)*

	PROGRESSION TO SYMPTOMS, DEATH, OR LV DYSFUNCTION			PROGRESSION TO ASYMPTOMATIC LV DYSFUNCTION			
STUDY	No. of Patients	Mean Follow-Up (years)	Rate/ year (%)	No. of Patients	Rate/ year (%)	Mortality (No. of Patients)	COMMENTS
Bonow et al, 1983, 1991	104	8.0	3.8	4	0.5	(2)	Outcome predicted by LV ESD, EDD, change in EF with exercise, rate of change in ESD and EF at rest with time
Scognamiglio et al, 1986	30	4.7	2.1	3	2.1	0	Three patients developing asymptomatic LV dysfunction initially had lower PAP/ESV ratios and trend toward higher LV ESD and EDD and lower FS
Siemienczuk et al, 1989	50	3.7	4.0	1	0.5	0	Patients included those receiving placebo and medical dropouts in a randomized drug trial; included some patients with NYHA FC II symptoms; outcome predicted by LV ESV, EDV, change in EF with exercise, and end-systolic wall stress
Scognamiglio et al, 1994	74	6.0	5.7	15	3.4	0	All patients received digoxin as part of a randomized trial
Tornos et al, 1995	101	4.6	3.0	6	1.3	0	Outcome predicted by pulse pressure, LV ESD, EDD, and EF at rest
Ishii et al, 1996	27	14.2	3.6	—	—	0	Development of symptoms predicted by systolic BP, LV ESD, EDD, mass index, and wall thickness; LV function not reported in all patients
Borer et al, 1998	104	7.3	6.2	7	0.9	(4)	20% of patients in NYHA FC II; outcome predicted by initial FC II symptoms, change in LV EF with exercise, LV ESD, and LV FS
Tarasoutchi et al, 2003	72	10	4.7	1	0.1	0	Development of symptoms predicted by LV ESD and EDD; LV function not reported in all patients
Evangelista et al, 2005	31	7	3.6	—	—	(1)	Placebo control group in 7-year vasodilator clinical trial
Detaint et al, 2008	251	8.0	5.0	17	2.1	(33)	10-year actuarial survival free of AVR: 92% ± 4% with mild AR (RV ≪30 mL and ERO ≪0.1 cm^2) 57% ± 5% with moderate AR 20% ± 5% with severe AR (RV ≥60 mL and ERO ≥0.3 cm^2)
Pizzaro et al, 2011	294	3.5	10%		2.8%	1.7%	Adverse outcomes associated with BNP >130 pg/mL, RVol, EROA, ESD index, EDD index, ESV index, and EDV index
Olsen et al, 2011	35	1.6	14.3%			0%	Disease progression associated with reduced myocardial systolic strain, systolic strain rate, and early diastolic strain rate

Dujardin KS, et al. Circulation 1999; 99: 1851-1857.

- 246 patients with moderate-severe AR,
- mean follow-up 7 years
- Ten-year mortality rate 34%
- Independent predictors of survival were age, functional class, comorbidity index, atrial fibrillation, LVESD, and LVEF

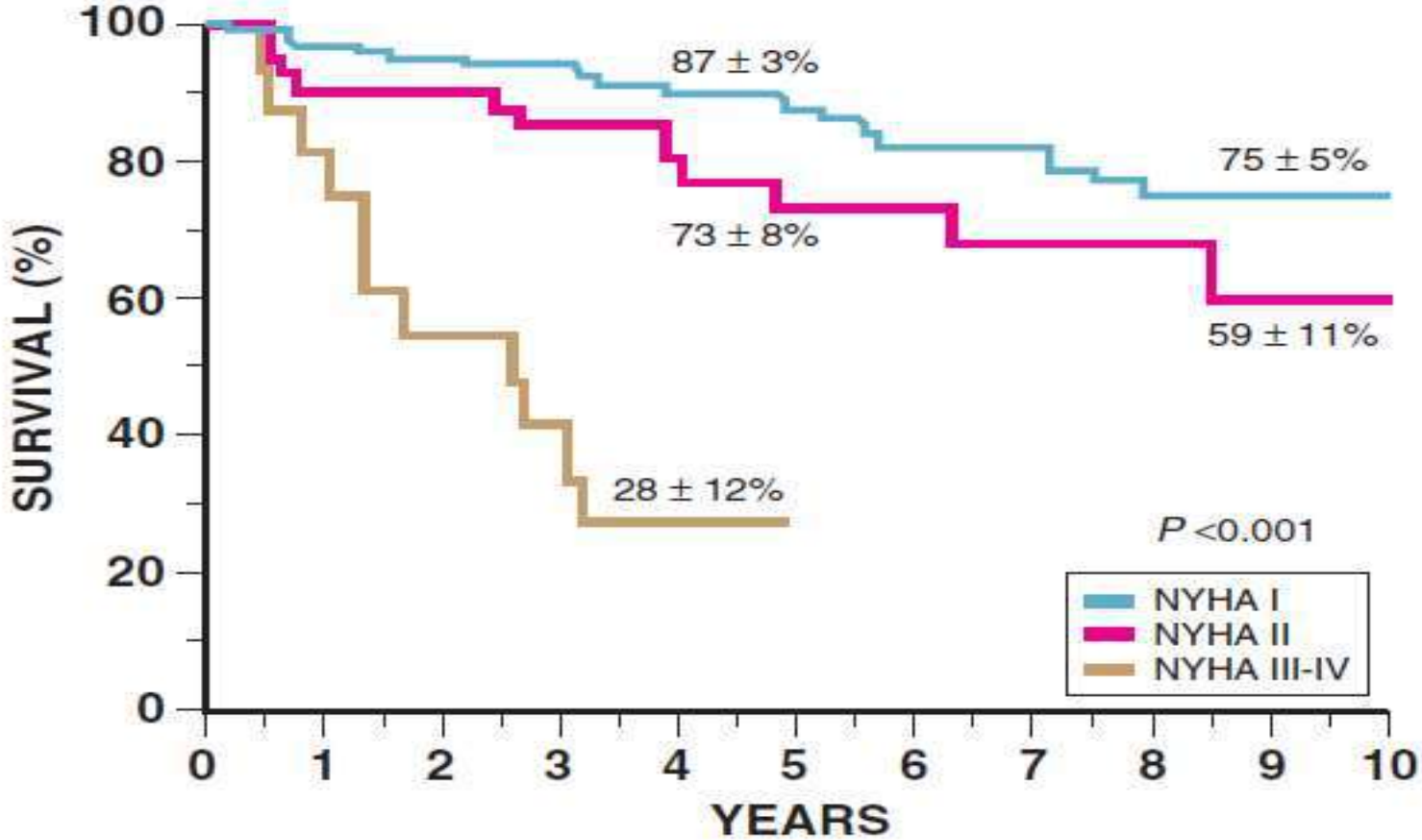


FIGURE e63-1 Survival without surgery in 242 patients with chronic AR, demonstrating the importance of symptoms in determining outcome. Patients with NYHA class III or IV symptoms had a survival of only 28% at 4 years. By contrast, the 10-year survival in patients in class I was 75%, which was identical to that for an age-matched normal population. *(From Dujardin KS, Enriquez-Sarano M, Schaff HV, et al: Mortality and morbidity of aortic regurgitation in clinical practice: A long-term follow-up study. Circulation 99:1851, 1999.)*

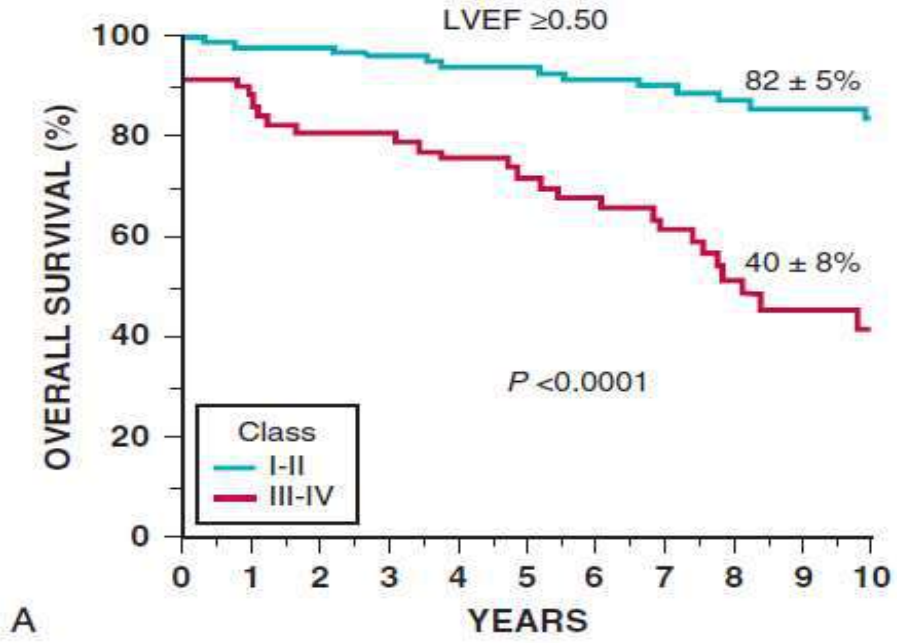
Dujardin KS, et al. Circulation 1999; 99: 1851-1857.

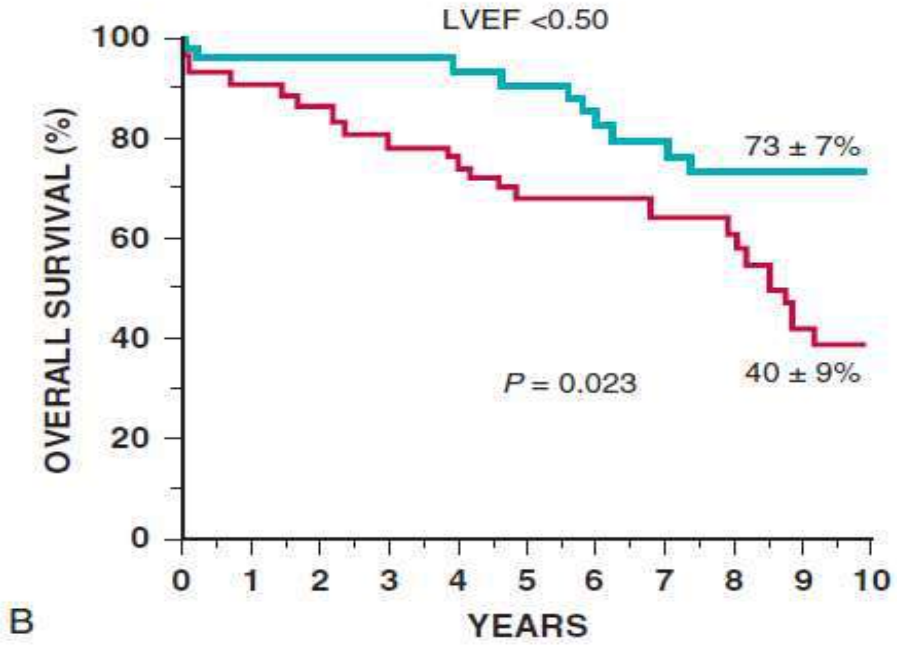
- The mortality rate for patients with severe AR with NYHA Class II symptoms is 6%/year and

- 25% / year for patients with NYHA Class III or IV symptoms

Bonow RO, et al. Circulation 1991; 84: 1625-1635.

- 104 asymptomatic patients with severe AR and normal LVEF
- Death, symptoms, or asymptomatic LV dysfunction was < 5%/year over 11-year F/U
- Rate of sudden death- 0.4%/year
- At 11 years, 58% remained asymptomatic and had normal LV systolic function.
- Serial changes in LV systolic function/ LV dilatation important to clinical outcome in AR and potential reasons for AVR.





Long-term postoperative survival in patients with AR, stratified according to the severity of preoperative symptoms and preoperative LVEF.

Patients with NYHA class III or IV symptoms experienced significantly worse survival than those with class I or II symptoms whether LVEF was higher than 0.50 **(A)** or less than 0.50 **(B)** without associated coronary artery disease.

(From Klodas E, Enriquez-Sarano M, Tajik AJ, et al: J Am Coll Cardiol 30:746, 1997.)