



Asymptomatic patients with

..... Severe Aortic Stenosis

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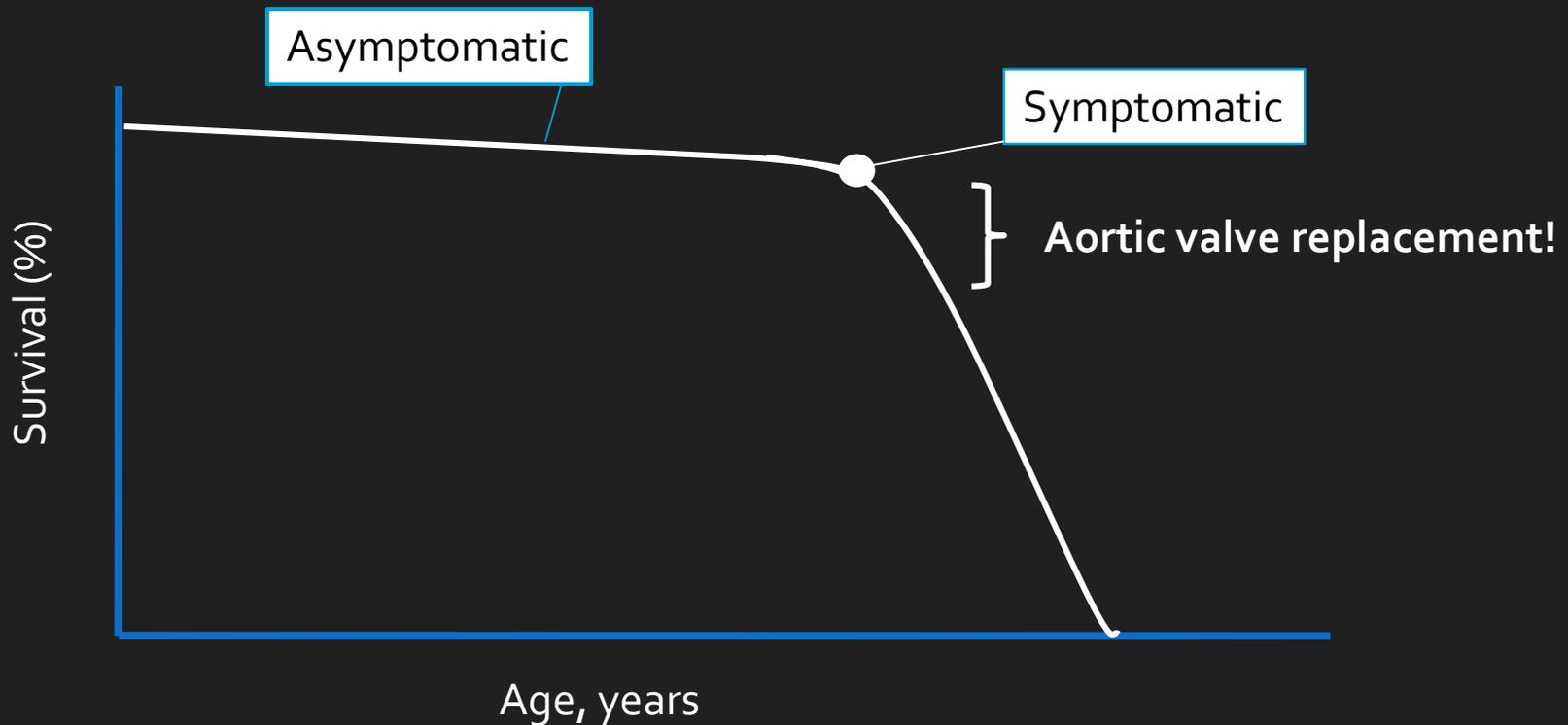
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Adverse Outcome

- ~2-4% of elderly population
- High mortality once symptomatic



Asymptomatic
AoS

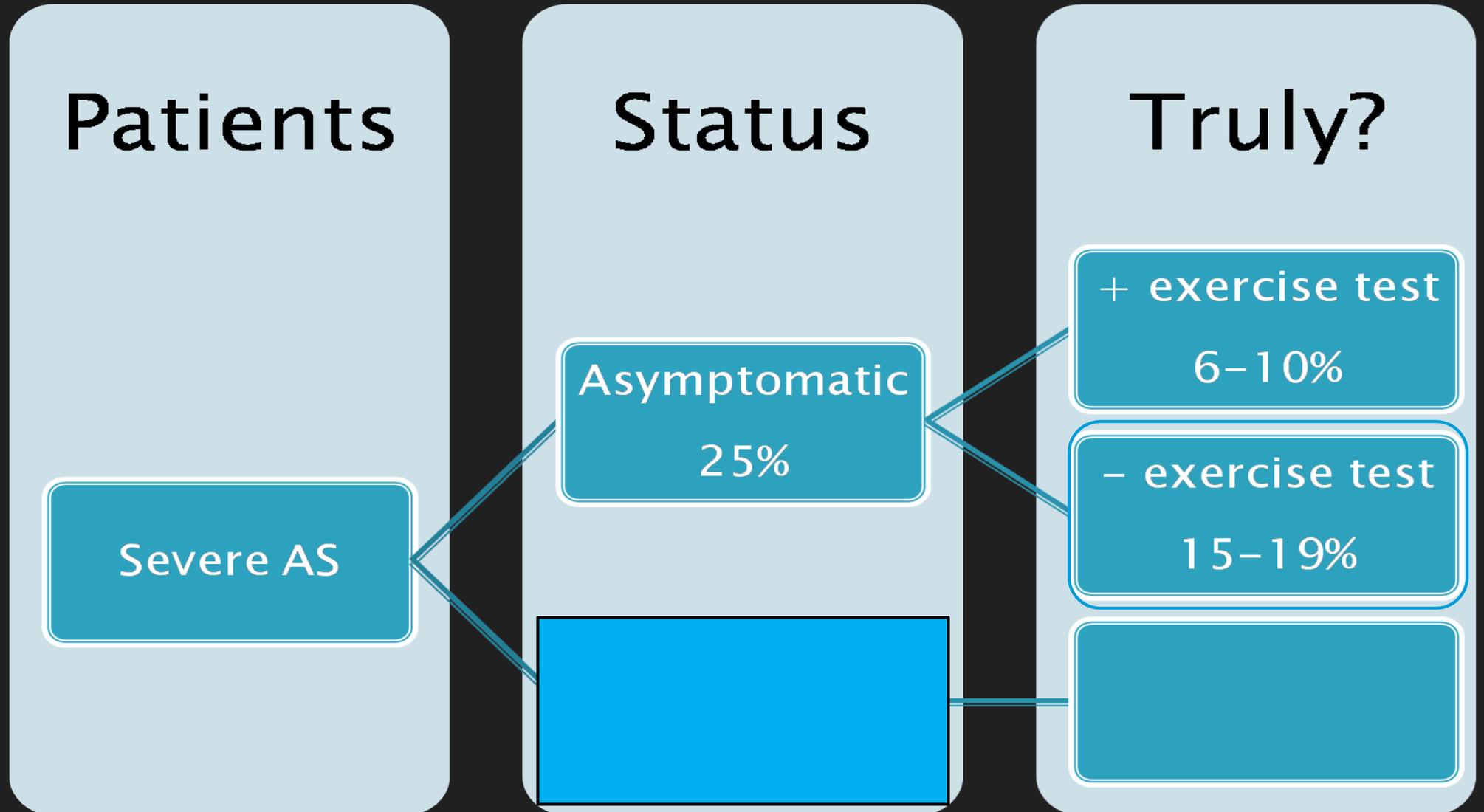
Predictors
Adverse outcome

Guidelines

Trial?

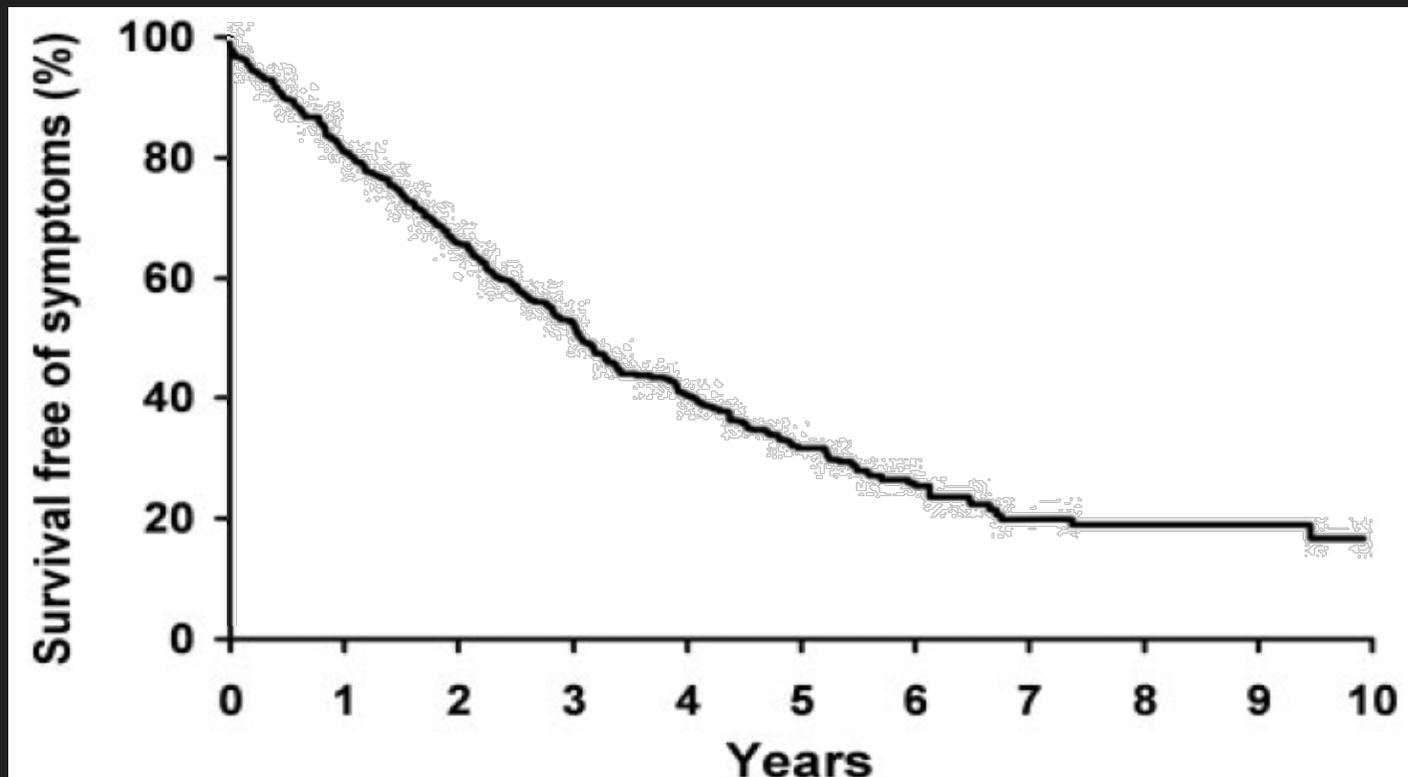


Patient population (*of total*)



Asymptomatic patients

- Risk of sudden death ~0.5–3% per year
- Death or AVR occur early in follow-up



Outcome of Asymptomatic Significant Aortic Stenosis During Follow-Up

Cardiac Deaths	Surgery	No surgery
Congestive heart failure	3.4	13.0
Myocardial infarction	2.8	4.8
Aortic stenosis		6.7
Sudden death	1.7	4.1
Perioperative	1.4	
Cardiac catheterization		1.5
Prosthetic valve failure	0.5	
Myocarditis	0	0.4

Life expectancy
Surgery

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LV hypertrophy

- Very common in AS → up to 90% of patients*
- Independent predictor of mortality after AVR
 - Persistence of LVH after surgery†
- Correlates little with symptomatic status
 - asymptomatic patients 48% with very high LV mass‡
- Perform early AVR *before* LVH is irreversible!?
 - Better LV remodeling
 - No LV dysfunction and conduction disturbances
 - Improved quality of life

*Seiler et al *Heart* 1996

†Beach et al *JTCVS* 2013

‡Mihaljevic et al *JTCVS* 2008

Hemodynamics

- LV remodeling and mass regression is influenced by valve hemodynamics
 - Prosthesis-patient mismatch*
 - No regurgitation
- Bovine pericardium preferred over porcine
 - At 1 and 5 years: better hemodynamics, improved LV remodeling, and better survival in RCT†
 - Predictor of 15-year survival: HR=0.88; 0.77-1.00‡

*Head et al *Eur Heart J* 2012

†Dalmau et al *EJCTS* 2011

‡Grunkemeier et al *JTCVS* 2012

Ventricular hypertrophy and left atrial dilatation persist and are associated with reduced survival after valve replacement for aortic stenosis

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Objectives: We sought to understand the factors modulating left heart reverse remodeling after aortic valve replacement, the relationship between the preoperative symptoms and modulators of left heart remodeling, and their influence on long-term survival.

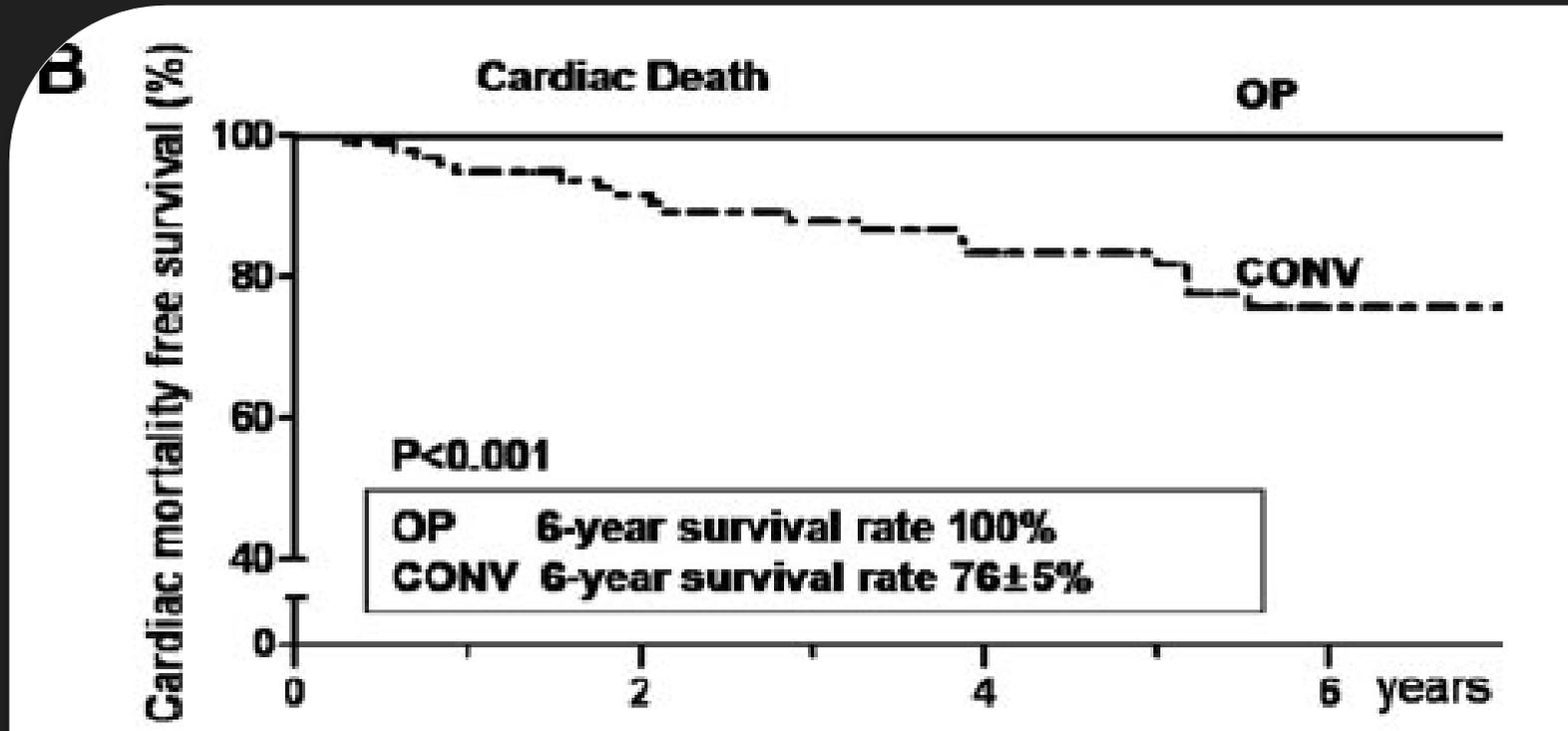
Methods: From October 1991 to January 2008, 4264 patients underwent primary aortic valve replacement for aortic stenosis. Changes in the time course of left ventricular reverse remodeling were assessed using 5740 postoperative transthoracic echocardiograms from 3841 patients.

Results: Left ventricular hypertrophy rapidly declined after surgery, from 137 ± 42 g/m² preoperatively to 115 ± 27 by 2 years and remained relatively constant but greater than the upper limit of normal. The most important risk factor for residual left ventricular hypertrophy was greater preoperative left ventricular hypertrophy ($P < .0001$). Other factors included a greater left atrial diameter (reflecting diastolic dysfunction), a lower ejection fraction, and male gender. An increased postoperative transprosthesis gradient was associated with greater residual left ventricular hypertrophy; however, its effect was minimal. Preoperative severe left ventricular hypertrophy and left atrial dilatation reduced long-term survival, independent of symptom status.

Conclusions: Severe left ventricular hypertrophy with left atrial dilatation can develop from severe aortic stenosis, even without symptoms. These changes can persist, are associated with decreased long-term survival even after successful aortic valve replacement, and could be indications for early aortic valve replacement if supported by findings from an appropriate prospective study. (J Thorac Cardiovasc Surg 2013; ■ :1-8)

Asymptomatic patients:

- Prevent sudden death
- No trials... but prospective study showed:



Conclusions—Compared with the conventional treatment strategy, early surgery in patients with very severe aortic stenosis is associated with an improved long-term survival by decreasing cardiac mortality. Early surgery is therefore a therapeutic option to further improve clinical outcomes in asymptomatic patients with very severe aortic stenosis and low operative risk. (*Circulation*. 2010;121:1502-1509.)

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European guideline recommendations for patients with Asymptomatic AoS

	Class	Level	Ref
<u>Indicated</u> if <i>LVEF <50%</i> due to AS	I	C	
<u>Indicated</u> if <i>symptoms on exercise</i> test due to AS	I	C	
<u>Considered</u> if <i>blood pressure fall on exercise</i> test	IIa	C	
<u>Considered</u> if none of above, low surgical risk, and ≥ 1 of: - <i>peak velocity >5.5 m/s</i> - severe calcification + <i>velocity progression ≥ 0.3 m/s p/y</i>	IIa	C	
<u>May be considered</u> if none of above, and ≥ 1 of: - <i>Elevated BNP levels</i> on repeated measurements - <i>>20 mmHg mean gradient increase</i> with exercise - <i>Excessive LV hypertrophy</i> without hypertension	IIb	C	

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AoS

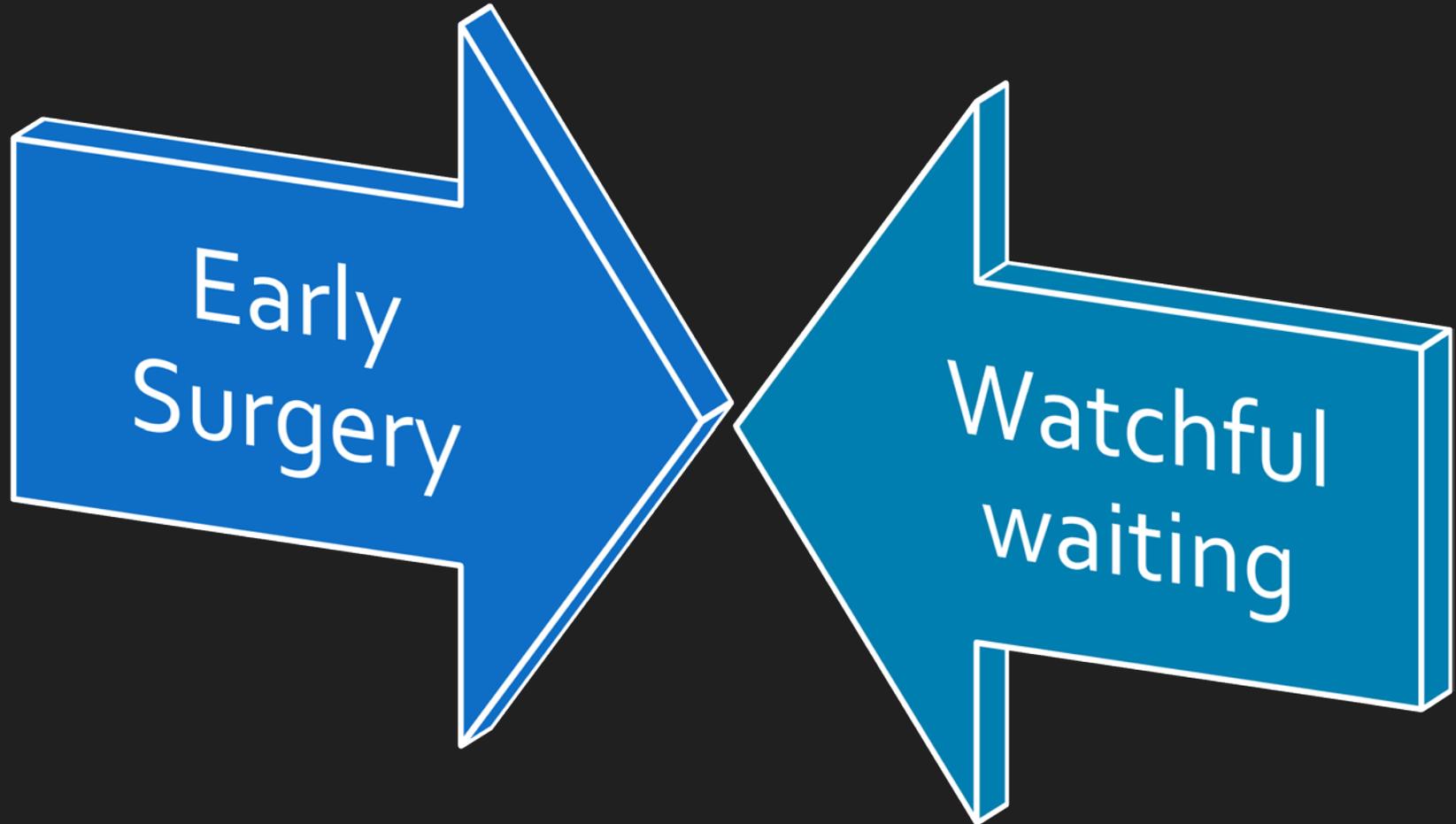
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Compare 2 groups



Trial endpoint – Survival?

- In asymptomatic patients:

Weighted meta-analysis of 12 studies with 8986 patient-years:

- *Risk of sudden death = 0.85% per patient p/y*
- *Risk of death due to CHF = 0.99% per patient p/y*
- *Combined = 1.48% per patient p/y*

- After surgery in general (1- and 4-year)

STS Score	65-69 yrs	70-79 yrs	≥80 yrs
0-5	95.3% and 88.4%	93.4% and 83.3%	90.5% and 75.1%
5-10	79.7% and 56.1%	80.0% and 55.8%	80.7% and 57.6%
>10	60.7% and 37.9%	65.0% and 34.7%	62.9% and 40.0%

Inclusion criteria

- Severe aortic stenosis
- Absence of symptoms: absence of subjective limitations of exercise capacity or complaints expressed by the patient and confirmed by the cardiologist
- Patients should be fit for surgery

Exclusion criteria

- Class I or IIa indication for surgery according to the ESC / EACTS guidelines
- Symptoms
- Ejection fraction $<50\%$ and left ventricular end-systolic dimension >45 mm

Trial endpoint – days alive outside the hospital*?

- Surgery is 'behind' watchful waiting because of the initial procedural hospitalization
- However, AVR during follow-up in 'watchful waiting' will balance this out over a longer trial duration (*~15% per year*)
- Advantages of early surgery:
 - *Lower risk at time of operation*: asymptomatic, younger, 'more healthy' → complications and LOS ↓
 - *Preservation of LVEF* → lower procedural risk and postoperative hospitalizations for heart failure
 - *No progression of disease* → less hospitalizations and sudden death

Sample size calculation

Survival without hospitalization for cardiovascular events

- Power of 80%, alpha = 0.05
 - Sudden death or CHF = 3% per yr
 - Death or CHF after AVR = 2.0% per yr
 - Non-cardiovascular death = 1.5% per yr
 - AVR mortality = 1% in asympt. and 1.5% in sympt.

 - Primary endpoint at 2 years
 - 7% versus 9.1% → 5,300 patients
- Primary endpoint at 4 years
 - 15.0% versus 24.0% → 1050 patients

Demonstrate superiority in “days alive outside the hospital”

- Unfortunately there is no good data
- One can assume that the reduction in event rate is around 3% which can reduce the sample size to around 850 patients

Asymptomatic AoS

- Follow asymptomatic patients carefully
- Surgery if low EF or symptomatic on exercise
- Treat when symptoms occur
- More data needed from prospective randomized trial