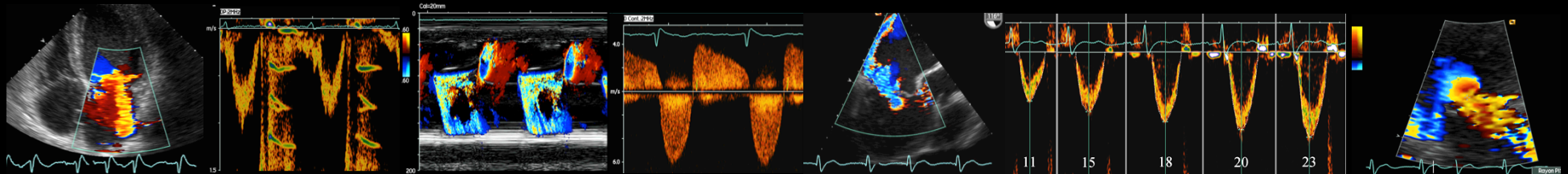# Early surgery for Asymptomatic AS :
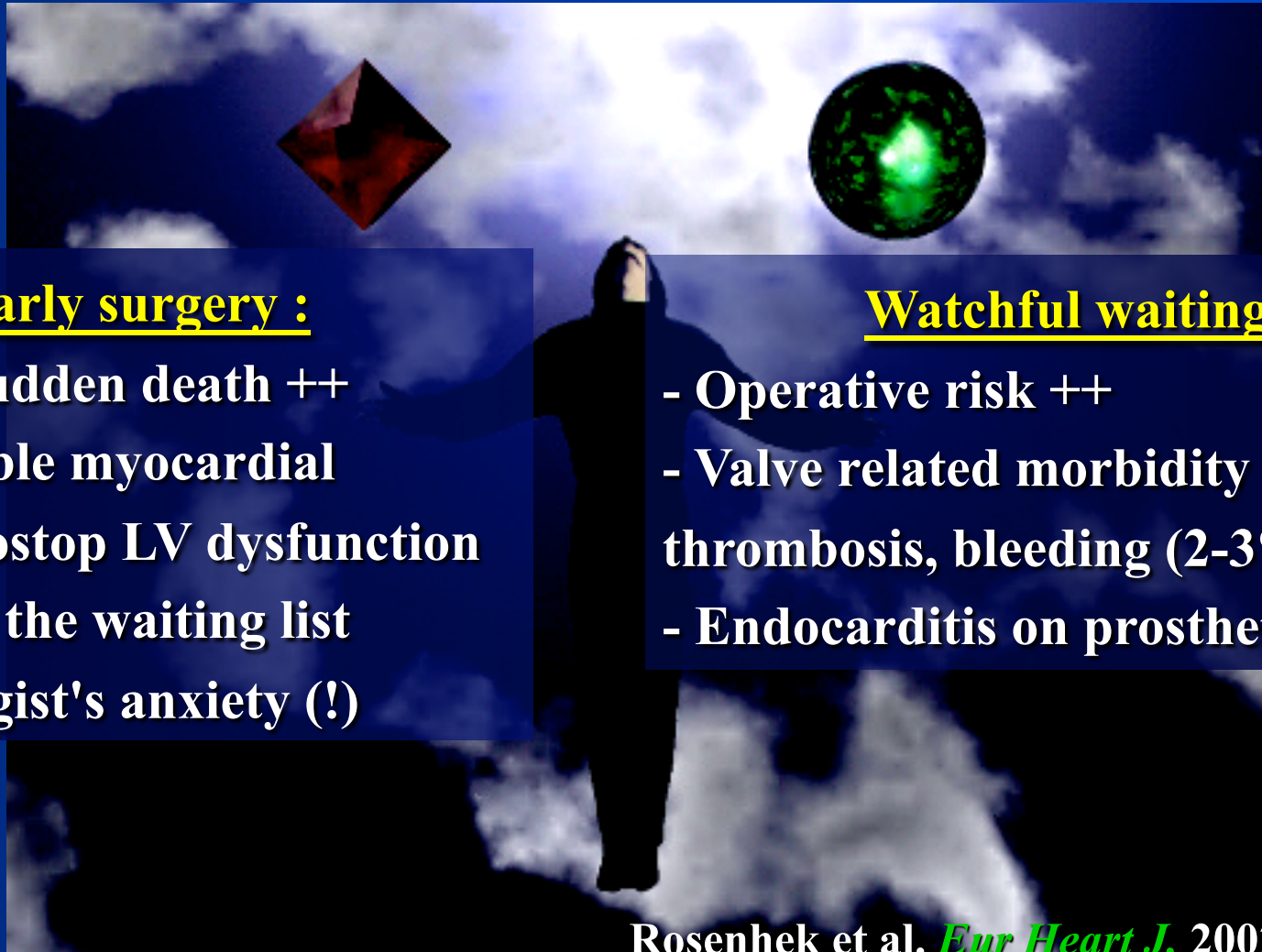# Is it reasonable ?

Réunion scientifique ECHOSUD
Nice, 05 janvier 2010

Jean-Luc MONIN. *Henri Mondor University Hospital* Créteil, FRANCE

Asymptomatic severe AS : the clinical dilemma

Early surgery :

- Risk of sudden death ++

- Irreversible myocardial

fibrosis/ Postop LV dysfunction

- Death on the waiting list

- Cardiologist's anxiety (!)

Watchful waiting :

- Operative risk ++

- Valve related morbidity :

thrombosis, bleeding (2-3%/ year)

- Endocarditis on prosthetic valve

Rosenhek et al. *Eur Heart J.* 2002;23:1417-21

When to Operate Asymptomatic AS

- **What is severe aortic stenosis ? Who are the patients at risk ?**

- **The risk of sudden death :**
        Are we racing into the wall ?

- **Exercise Testing/ Stress Echo / BNP**

- **Usefulness of Z_{va} or any Risk Score ?**

- **What about the Guidelines ?**

3

When to Operate Asymptomatic AS

• **What is severe aortic stenosis ? Who are the patients at risk ?**

• The risk of sudden death :
    Are we racing into the wall ?

•Exercise Testing/ Stress Echo / BNP

• Usefulness of Z_{va} or any Risk Score ?

• What about the Guidelines ?

4

What is severe Aortic Stenosis ? (Provided LV systolic function is preserved)

	Mild AS	Moderate AS	<u>Severe AS</u>
Peak V.	< 3.0 m/s	3.0-4.0 m/s	**> 4.0 m/s**
Mean P.G.	< 25 mm Hg	25-40 mm Hg	**> 40 mm Hg**
AVA	> 1.5 cm²	1.0-1.5 cm²	**< 1.0 cm²**
Indexed AVA	/	/	**< 0.6 cm²/m²**

ACC/ AHA Guidelines. *J. Am. Coll. Cardiol.* 2006;48: e1-148

Prospective study of asymptomatic AS : Peak aortic-jet velocity predicts outcome !

Eight deaths including 4 patients who refused surgery
**No occurrence of *de novo* sudden death**
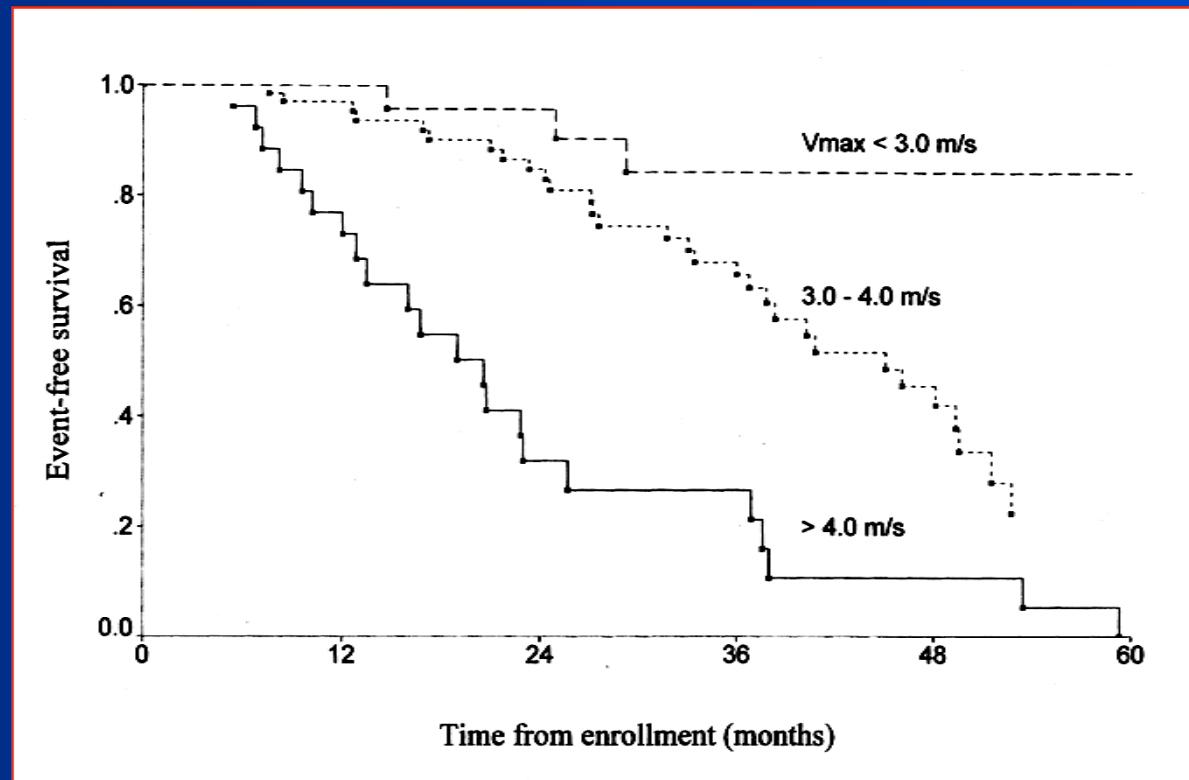
What is severe AS in terms of valve area : Why did we change from 0.7 to 1.0 cm²

Prospective study of asymptomatic AS : The Seattle Study
123 asymptomatic patients, Peak V > 2.5 m/sec, (1989-95)

- Age = 63±16 years (70% ♂)

- FU: 2.5 ±1.4 years, endpoints: death (CV), valve replacement

- Annual progression:

Peak V ↑ 0.3 ± 0.3 m/s

AVA ↓ 0.1 ± 0.2 cm²

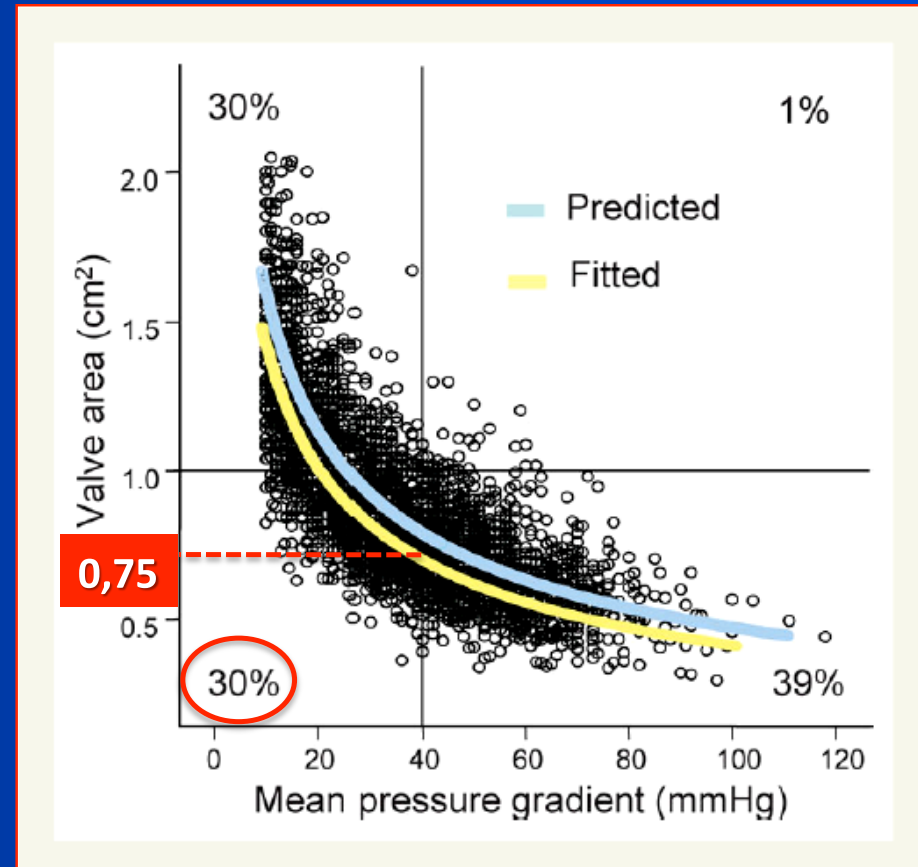Otto et al. *Circulation.* 1997;95: 2262
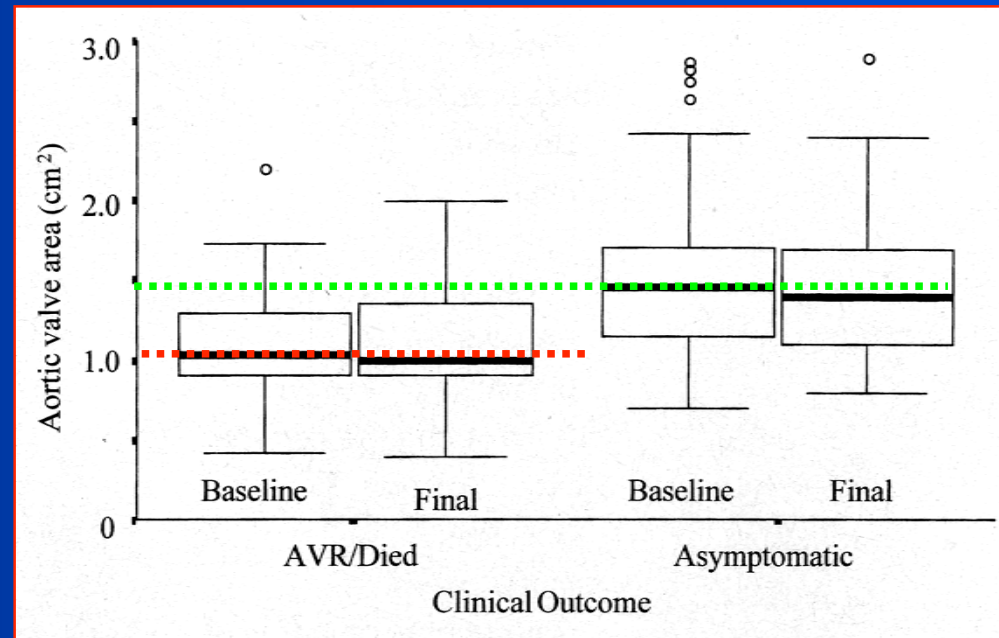
Inconsistencies of echocardiographic criteria for the grading of AS

Consistency of 3 criteria (AVA, Gradient, Peak Velocity) / Grading of AS

- **Analysis of 3483 Echo studies**

- **2427 patients, normal LV systolic function and AVA < 2.0 cm^2**

- **Gradient plotted vs. AVA**

- **Predicted curve: assuming CO = 6,0 L/min, HR = 80 BPM and SEP = 0.33 S**

- **Fitted curve : Actual data pairs**


Minners et al. *Eur Heart J.* 2008;29:1043-8

8

Inconsistencies of echocardiographic criteria for the grading of AS

Analysis of 3483 Echo studies in 2427 Pts normal LVEF / AVA < 2.0 cm²
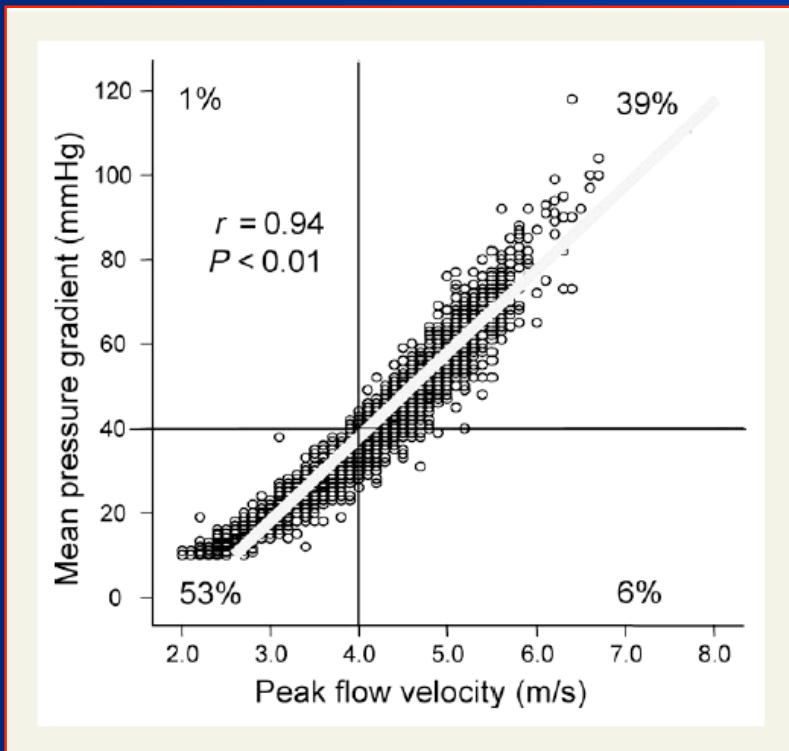
- **Peak Aortic-jet velocity plotted vs. AVA (Continuity Equation)**

- **Predicted curve: assuming LVOT diameter = 20 mm and LVOT peak velocity = 1,0 m/s**

- **Fitted curve : Actual data pairs**

9

Minners et al. *Eur Heart J.* 2008;29:1043-8

Henri Mondor
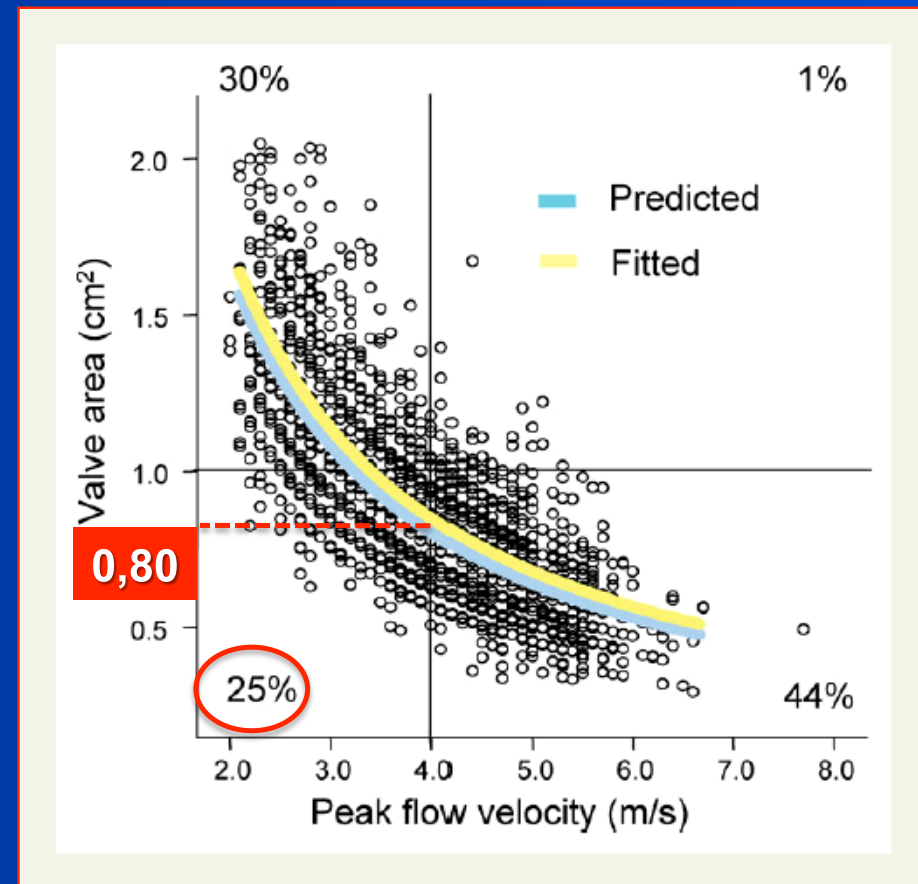
Inconsistencies of echocardiographic criteria for the grading of AS

Peak Aortic-jet velocity vs. Mean Pressure Gradient

Possible overestimation of AS severity according to AVA

Table 2 Percentage of patients diagnosed with severe aortic stenosis depending on which echocardiographic criterion was used

Guidelines/ recommendations	Parameter	Patients with severe stenosis
AHA/ACC[3]	AVA <1.0 cm^2	69%
ESC[2]	AVA/BSA <0.6 cm^2	76%
Otto[4]	$V_{max} >4.0$ m/s	45%
AHA/ACC[3]	$\Delta P_m >40$ mmHg	40%

AVA, aortic valve area; BSA, body surface area; V_{max}, peak flow velocity; ΔP_m, mean pressure gradient.

Minners et al. *Eur Heart J.* 2008;29:1043-8

Which hemodynamic index best accounts for clinical severity ?
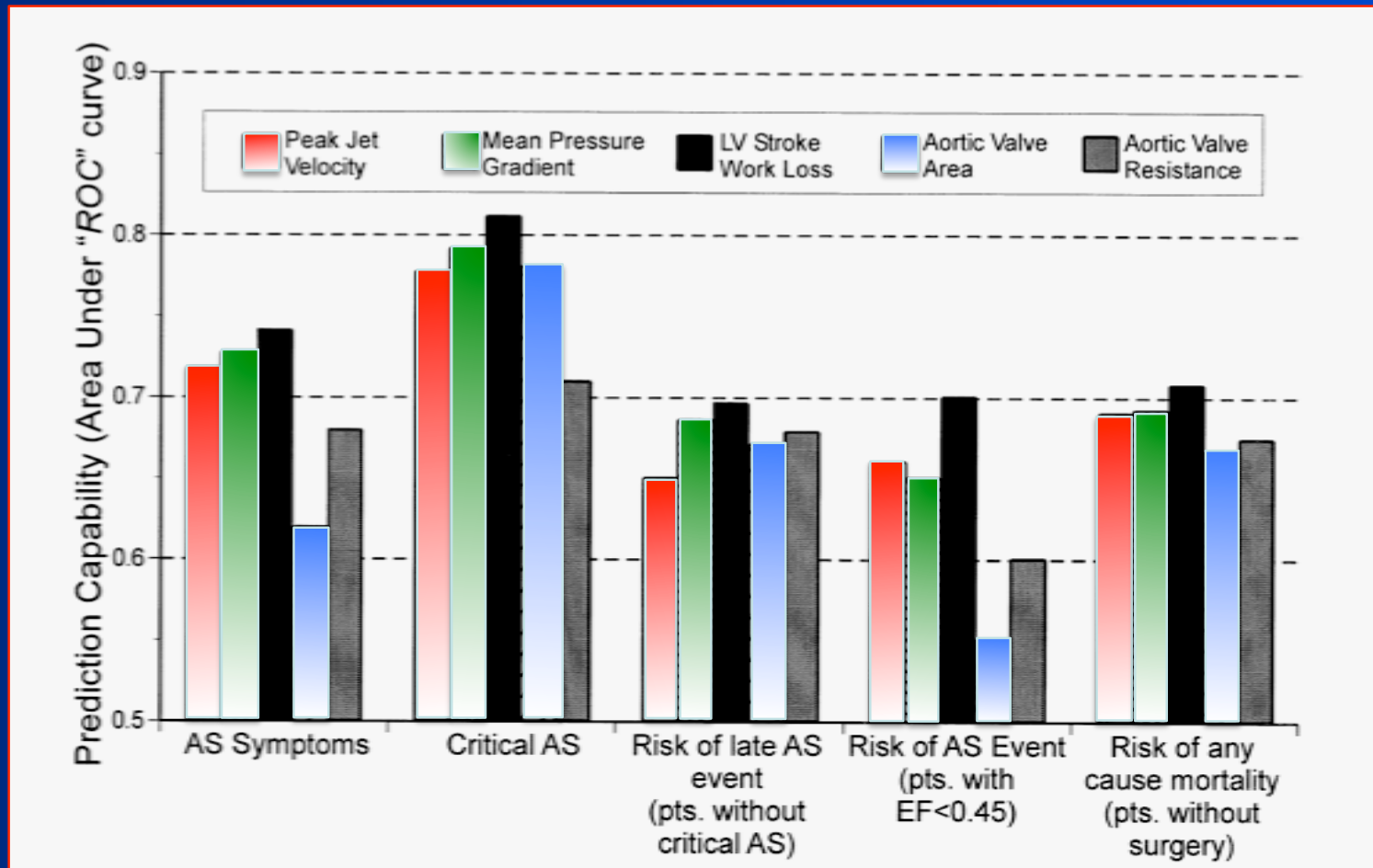
Risk score for predicting outcome in Asymptomatic AS (Prospective study)

107 patients (72 years [63-77]; 35 women), Vmax: 4.1 m/s [3.5-4.4], AVA: 0.9 cm² [0.8-1.1], MPG: 40 mm Hg [31-50]

Variable at baseline	Odds ratio	95% confidence interval	p value
Baseline serum BNP	3.9	1.8 - 8.1	0.0001
Baseline Peak-jet velocity	6.2	2.1 - 17.9	0.001
Female gender	5.2	1.5 - 18.6	0.012

Monin et al. *Circulation.* 2009; 120: 69-75

Natural History of very Severe AS :

Event-free Survival according to Peak Velocity

116 consecutive patients with asymptomatic AS and Vmax ≥ 5.0 m/s

P = 0.001

AV-Vel 5 to 5.5m/s

AV-Vel ≥ 5.5m/s

Event-free Survival (%)

Henri Mondor
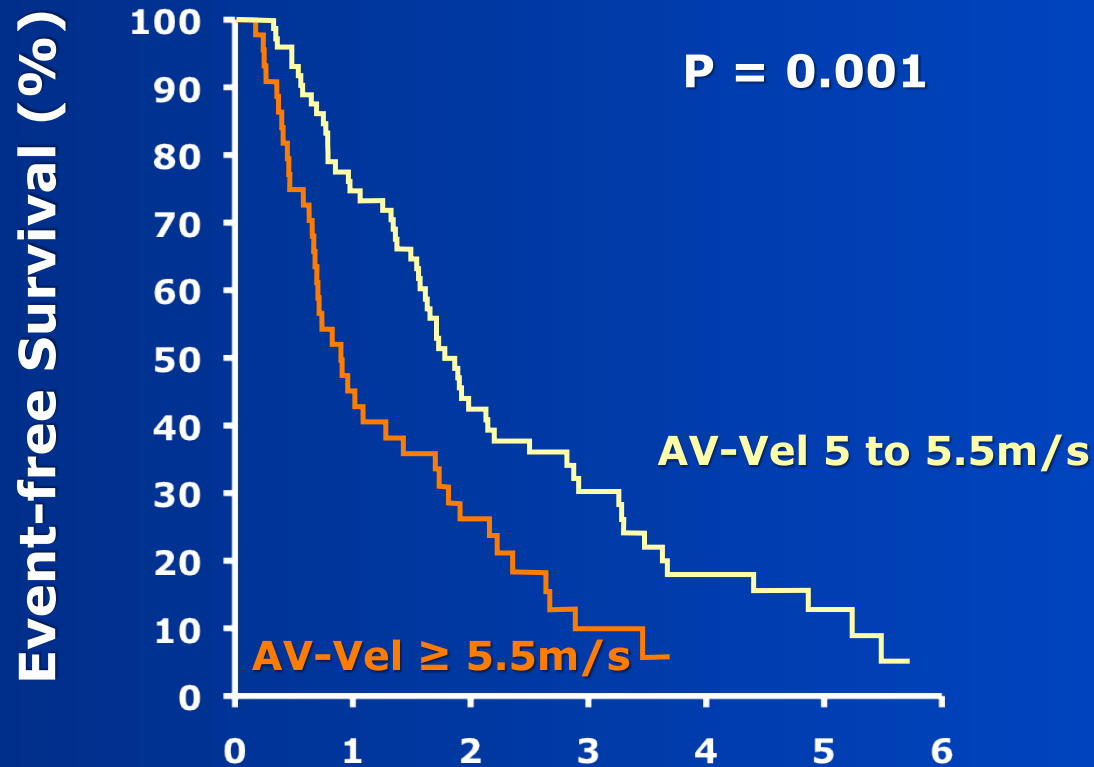
| Patients at risk: | 72 | 53 | 29 | 18 | 9 | 6 | 2 |
| Patients at risk: | 44 | 20 | 11 | 5 | 1 | | |

Rosenhek et al. *Circulation.* 2010; 121: 151-6

Natural History of very Severe AS :
Event-free Survival according to Valve Area

Henri Mondor

P = 0.12

Event-free Survival (%)

AVA ≥ 0.6 cm²

AVA < 0.6 cm²
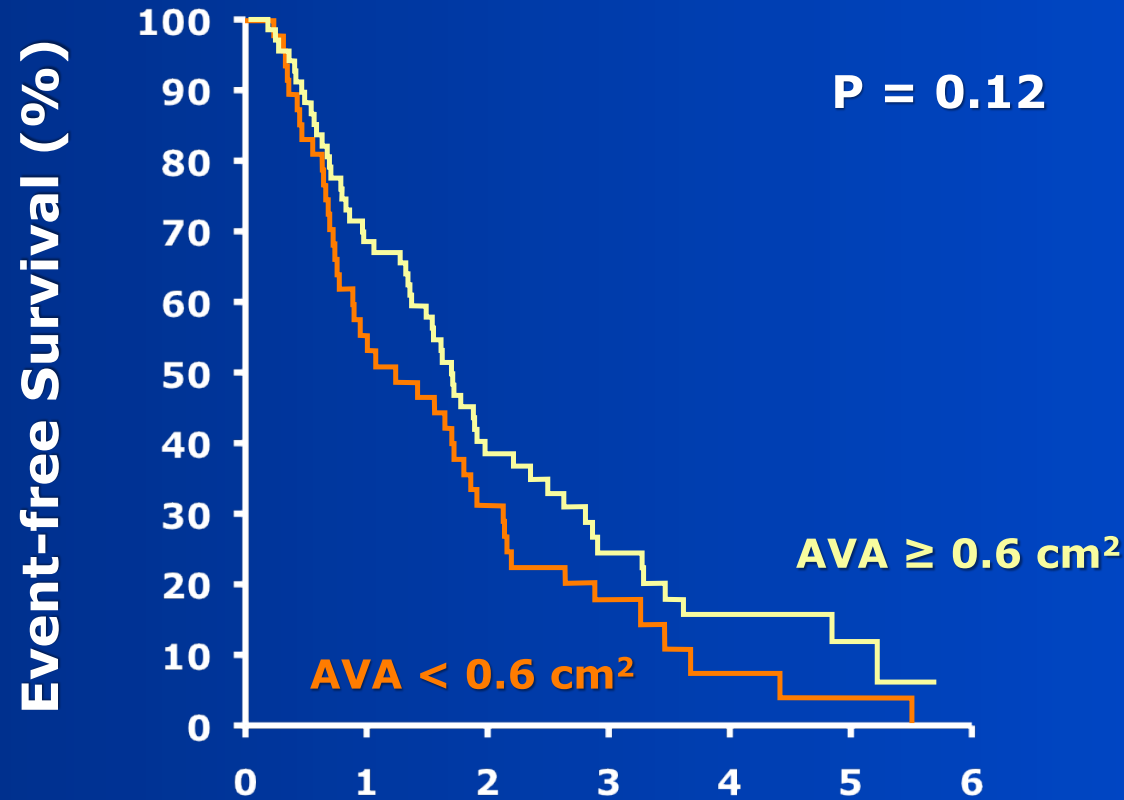
| Patients at risk: | 69 | 47 | 25 | 14 | 7 | 5 | 2 |
| Patients at risk: | 47 | 26 | 15 | 10 | 3 | 2 | 0 |

Rosenhek et al. *Circulation.* 2010; 121: 151-6

Assessment of valve calcification by TTE
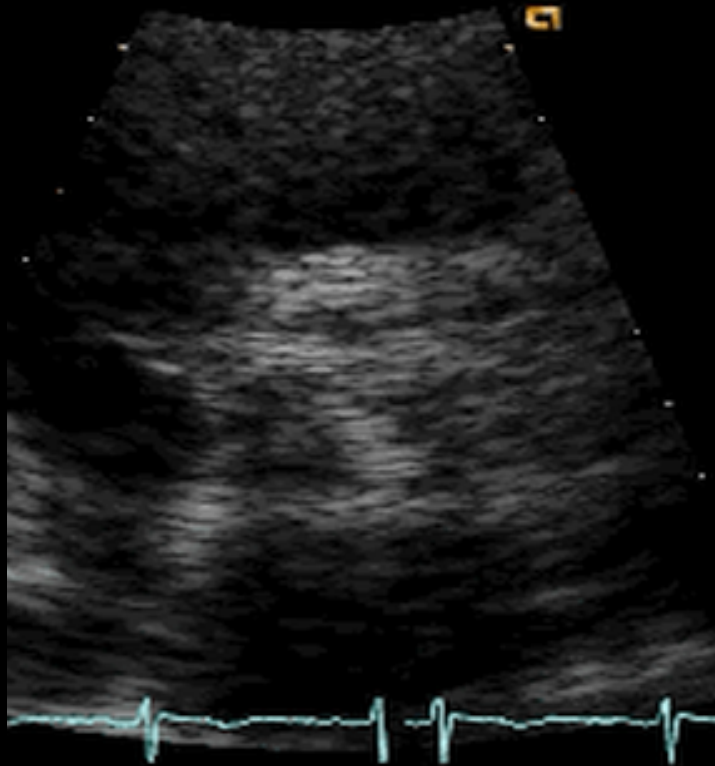
1/ No calcification

2/ Mildly calcified (isolated, small spots),

3/ Moderately calcified (multiple bigger spots)

4/ Heavily calcified (extensive thickening/ calcification of all cusps).

Rosenhek et al. *N Engl J Med.* 2000;343:611

Predictors of outcome in severe asymptomatic Aortic Stenosis

P<0.001
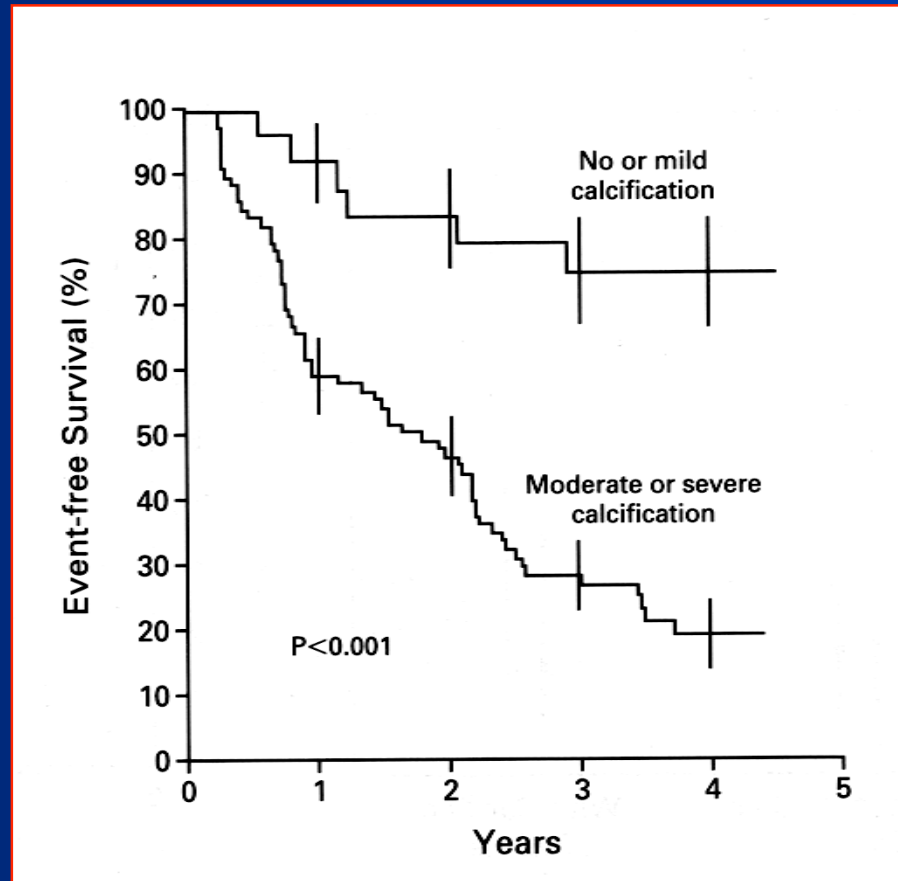
Univariate Analysis :

- Prognostic indicators : age, calcification, diabetes, CAD.

Multivariate Analysis:

1/ Valve Calcification ++

2/ Annual progression in Peak velocity ≥ 0.3 m/s

Who are the Patients at Risk ?

- High peak aortic-jet velocity at baseline: >4.0 m/s

- Highest velocity (>5.5 m/s) equals highest risk

- Rapid progression in jet velocity (>0.3 m/s within one year)

- Heavily calcified aortic valve

When to Operate Asymptomatic AS

- What is severe aortic stenosis ? Who are the patients at risk ?

- **The risk of sudden death :**
  Are we racing into the wall ?

- Exercise Testing/ Stress Echo / BNP

- Usefulness of Zva or Risk Score ?

- What about the Guidelines ?

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Outcomes in severe Asymptomatic AS

Mayo Clinic Database (1984-1995)/
Retrospective analysis:

- Patients ≥40 years
- Valvular AS
- Peak systolic V ≥ 4 m/s
- No other V. lesion
- No associated CAD
- Asymptomatic

Variable	n=622
Age (years)	72±11
Male gender, n (%)	384 (62)
Diabetes, n (%)	71 (11)
LVEF, %	64±7
Peak V (m/s)	4,4±0,4
AVA (cm²)	0,9±0,2
Mean PG, mm Hg	46±11

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Pellikka et al. *Circulation.* 2005;111:3290-5

Outcomes in severe <u>Asymptomatic</u> AS

80%

63%

25%
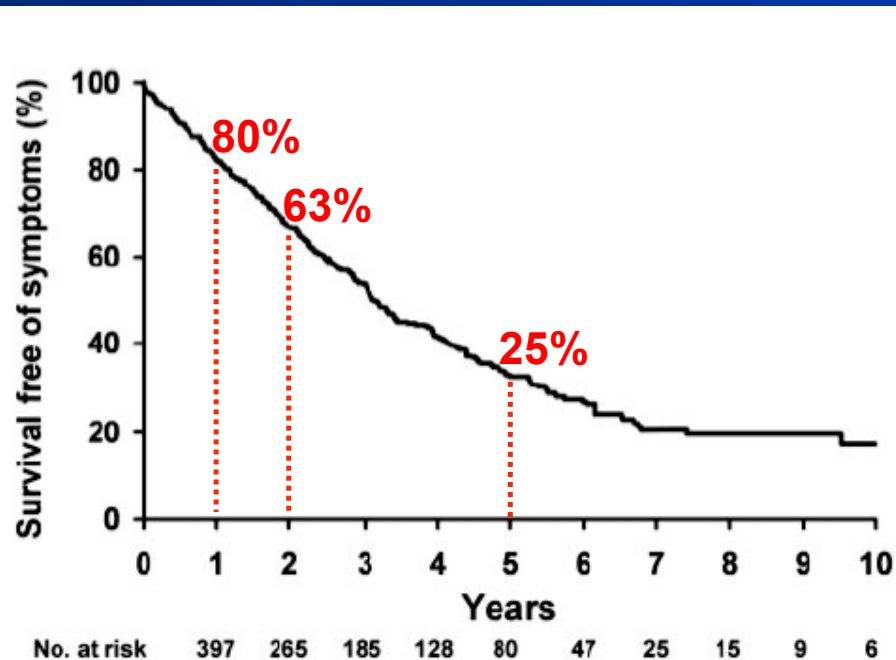
Figure 1. Survival free of symptoms censored at aortic valve surgery.

No. at risk: 397 265 185 128 80 47 25 15 9 6

TABLE 2. Predictors of Development of Symptoms Censored at Aortic Valve Surgery: 297 Events

	P	HR*	95% CI
Multivariate predictors			
Aortic valve area, cm^2	0.005	0.33	0.15–0.71
Left ventricular hypertrophy	0.04	1.39	1.02–1.89

TABLE 4. Predictors of All-Cause Mortality Censored at Surgery: 179 Events

	P	HR*	95% CI
Multivariate predictors			
Age, y	<0.0001	1.05	1.04–1.07
Chronic renal failure	0.004	2.41	1.33–4.35
Inactivity	0.001	2.00	1.32–3.04
Aortic valve velocity, m/s	0.03	1.46	1.03–2.08

20

Pellikka et al. *Circulation.* 2005;111:3290-5

Outcomes in severe Asymptomatic AS
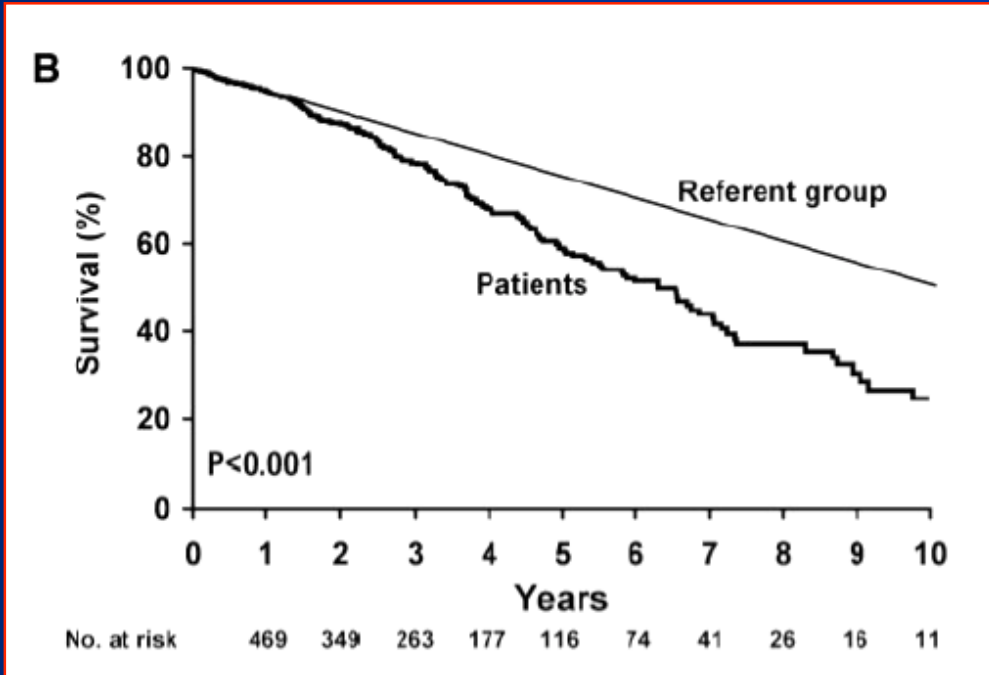
**Censoring Patients at
AVR including symptomatic Pts**
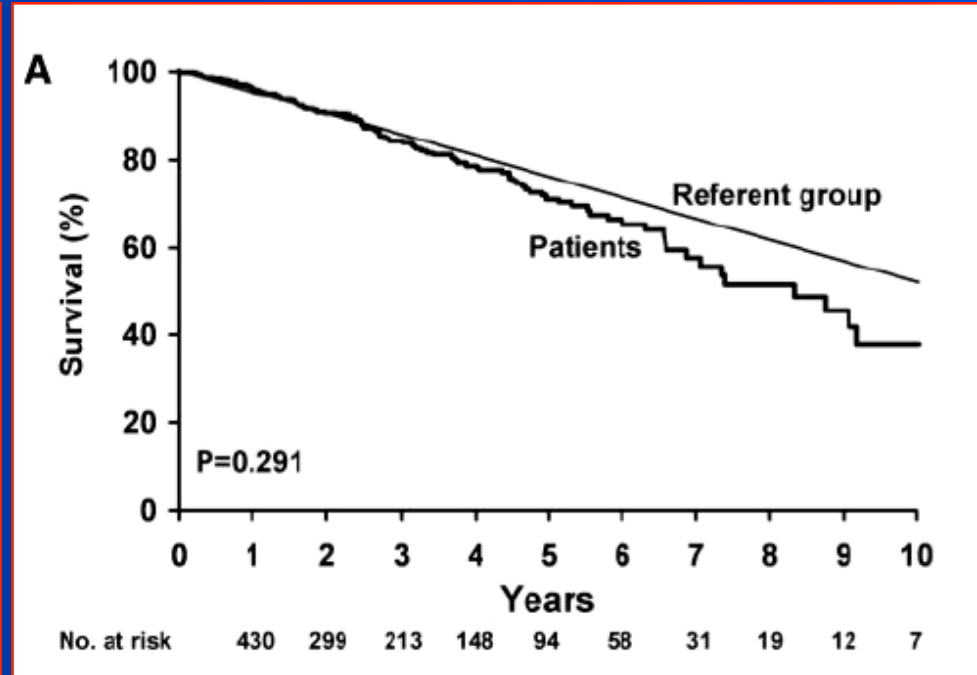
**Censoring Patients at
AVR or symptom onset**

21

What is the risk of sudden death Without preceding symptom ?

Author (year)	N pts	FU (years)	AS Severity	« De novo » Sudden death
Horstkotte (1988)	378	"years"	AVA = 0,8-1,5 cm^2	3
Pellikka (1990)	113	1,7	$V_{max} > 4,0$ m/s	0
Otto (1997)	123	2,5	$V_{max} = 3,6 \pm 0,6$ m/s	0
Rosenhek (2000)	128	4	$V_{max} > 4,0$ m/s	1
Pellikka (2005)	622	5	$V_{max} > 4,0$ m/s	11

22   Risk of sudden death ≈ 0.5% /year *vs.* Operative risk ≈ 2-15%

Indications for AVR: Class III

AVR is not indicated for the prevention of sudden death in asymptomatic patients with severe AS <u>without</u> :
LV dysfunction, abnormal exercise test, other cardiac surgery, etc.

(Level of Evidence: B)

When to Operate Asymptomatic AS

- What is severe aortic stenosis ? Who are the patients at risk ?

- The risk of sudden death :
        Are we racing into the wall ?

- **Exercise Testing/ Stress Echo / BNP**

- Usefulness of Zva or Risk Score ?

- What about the Guidelines ?

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What is the role of exercise testing ?

Exercise Testing in Asymptomatic AS

Positive Test if:

- Dyspnea, Angina, near syncope

- < 80% maximal predicted heart rate

- Elevation in SBP <20 mm Hg

- ST segment depression > 3 mm

- Complex ventricular arrhythmias

Iung et al. *Eur Heart J.* 2002;23: 1253

Risk stratification in asymptomatic AS : The role of exercise testing

- 125 asymptomatic patients (85 ♂), aged 65 [56-74] years

- Baseline AVA = 0,9 ± 0,2 cm²

Modified Bruce Protocol

- Abnormal if : Any symptom, **Fall in SBP > 20 mm Hg,** ST depression> 5 mm, **3 consecutive PVB**

AIMS OF THE STUDY:

• To assess the accuracy of exercise testing (Modified Bruce protocol) in <u>predicting symptom onset within 12 months</u>

• To establish **the best criteria** that define a positive test.

Das et al. *Eur Heart J.* 2005;26: 1309

Exercise Testing to Stratify Risk in AS

	Symptoms < 12 months n=36	Asymptomatic n=89	P
Age (ans)	70 (56-75)	67(56-73)	0,43
Peak V (m/s)	4,1±0,6	3,7±0,8	0,0004
Mean PG (mm Hg)	43±15	33±16	0,002
AVA (cm²)	0,7±0,2	0,9±0,3	<0,0001
Ex. duration (min)	9,1±3,7	11,6±3,5	0,001
Symptoms	26 (72%)	20 (22%)	<0,0001
Δ SBP (mm Hg)	13±20	22±19	0,002

Das et al. *Eur Heart J.* 2005;26: 1309

Only independent predictor of symptom onset: Limiting symptoms during exercise

Table 3 Univariate and multivariate logistic regression analyses to predict symptom-onset within 12 months

	Multivariate analysis		
	OR	95% CI (OR)	P-value
Exercise time (min)	1.00	(1.00, 1.00)	0.17
Limiting symptoms (yes/no)	7.73	(2.79, 21.39)	<0.001
Abnormal blood pressure response (yes/no)	1.02	(0.98, 1.05)	0.34
Peak velocity (m/s)	1.01	(0.98, 1.05)	0.41
Effective orifice area (cm^2)	0.99	(0.96, 1.02)	0.66
ST depression ≥ 2 mm (yes/no)	0.97	(0.95, 1.02)	0.51

**46 patients stopped exercise because of limiting symptoms :
Breathlessness (28), chest tightness (12) or dizziness (6)**

Das et al. *Eur Heart J.* 2005;26: 1309

Risk stratification in asymptomatic AS : The role of exercise testing

66 asymptomatic Patients,
Aged 50±15 years; AVA : 0,6±0.2 cm²; Peak gradient : 83±33 mm Hg

Amato et al. *Heart.* 2001;86: 381

Risk stratification in asymptomatic AS : The role of exercise testing

66 asymptomatic Patients,
aged 50±15 years; AVA : 0,6±0.2 cm²; Peak gradient : 83±33 mm Hg

31

Amato et al. *Heart*. 2001;86: 381
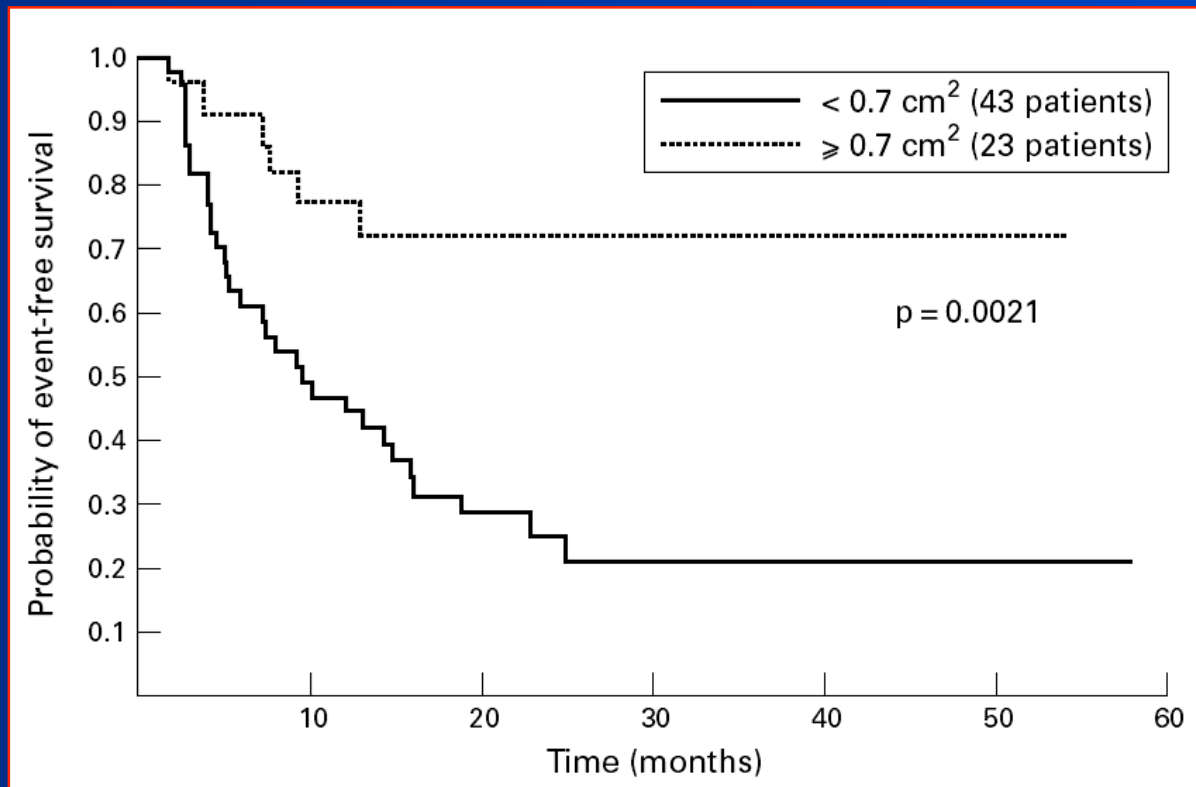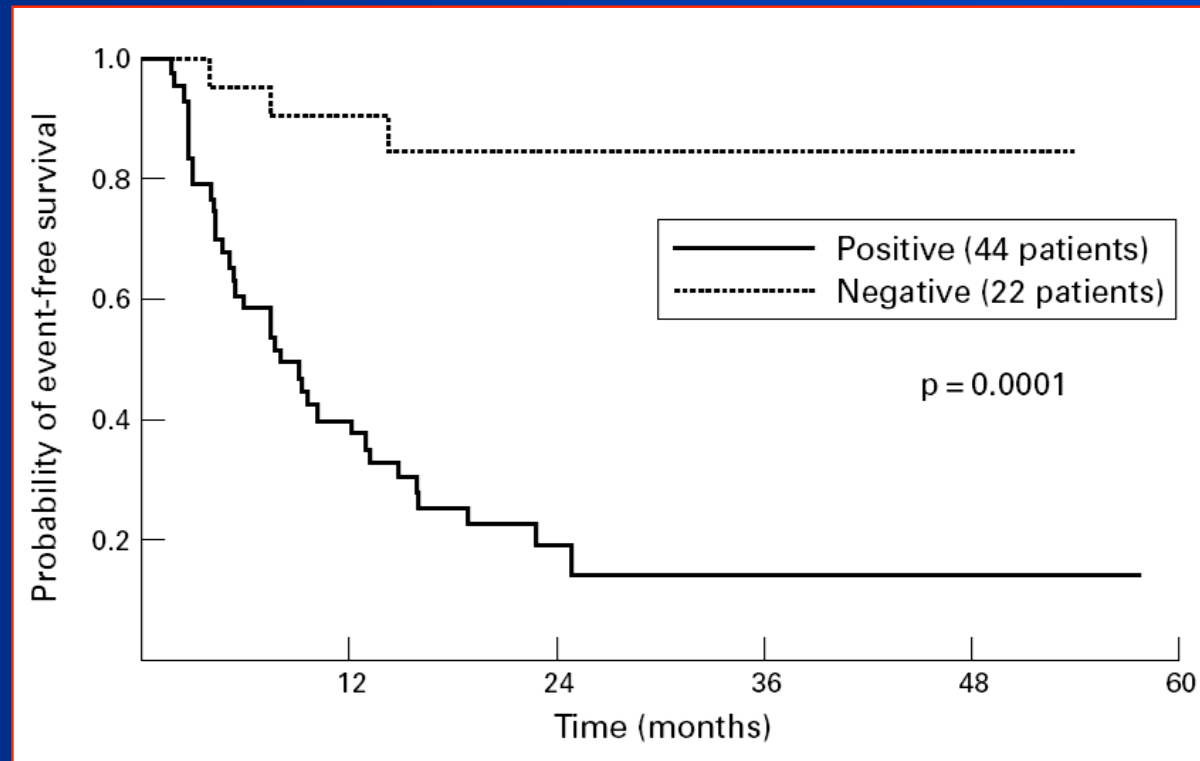
Risk of sudden death in AS : The role of exercise testing

Among 66 "asymptomatic" patients : 4 sudden deaths (6%)

Table 3   Characteristics of patients who experienced sudden death (n = 4)

| Sex | Age (years) | Valve area (cm^2) | Gradient (mm Hg) | Exercise testing | | | Follow up (Δ days) |
				Symptom	ST (mm)	Δp	
Male	41	0.38	110	Angina	1.5	10	130
Female	59	0.60	80	Angina	–	0	482
Male	49	0.49	136	–	3.5	10	180
Male	48	0.48	99	Angina	2.0	0	140

Δp, change in systolic blood pressure from baseline in mm Hg; ST, ST segment depression 0.08 seconds after J point.

Amato et al. *Heart.* 2001;86: 381

Exercise Testing in Asymptomatic AS: American Guidelines

ACC/AHA Task Force Report. *JACC*. 2006;48: e1-148

• **Exercise testing should <u>not be performed in symptomatic patients with AS</u>;** *(Class III)*

• **Exercise testing may be considered in asymptomatic patients with AS to elicit exercise-induced symptoms or abnormal blood pressure responses.** *(Class IIb)*

• **AVR may be considered for Severe asymptomatic AS and abnormal response to exercise;** *(Class IIb)*

European Guidelines : Indications for Surgery in AS

Asymptomatic patients with severe AS and Abnormal   (I) exercise test showing *symptoms on Exercise*

Asymptomatic patients with severe AS and Abnormal   (IIa) exercise test showing *fall in blood pressure below baseline*

Asymptomatic patients with severe AS and Abnormal   (IIb) exercise test showing *complex ventricular arrhythmias*
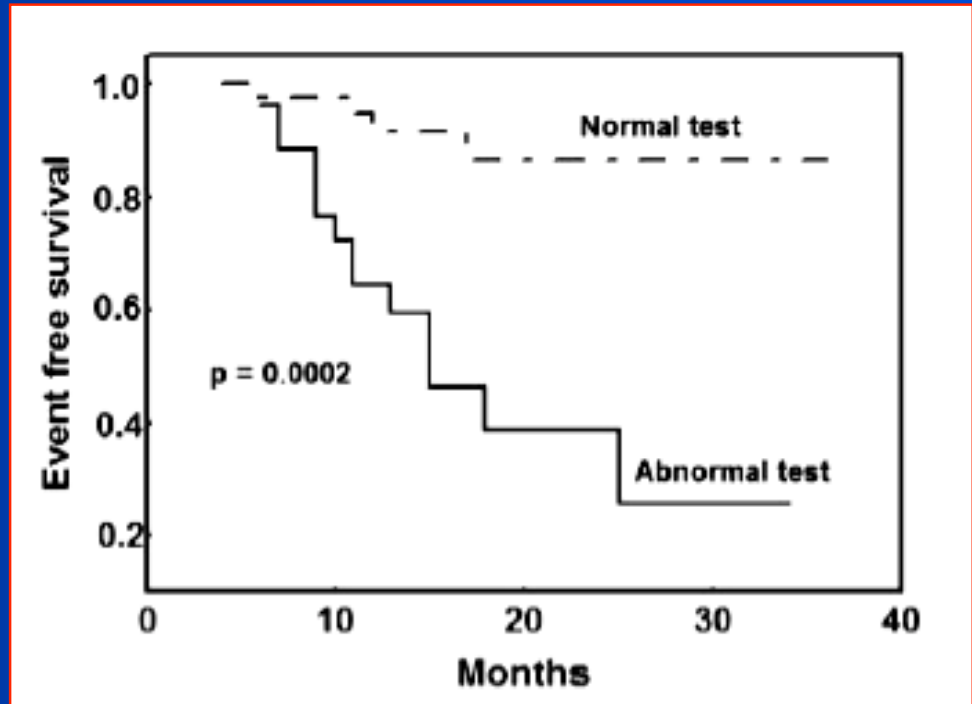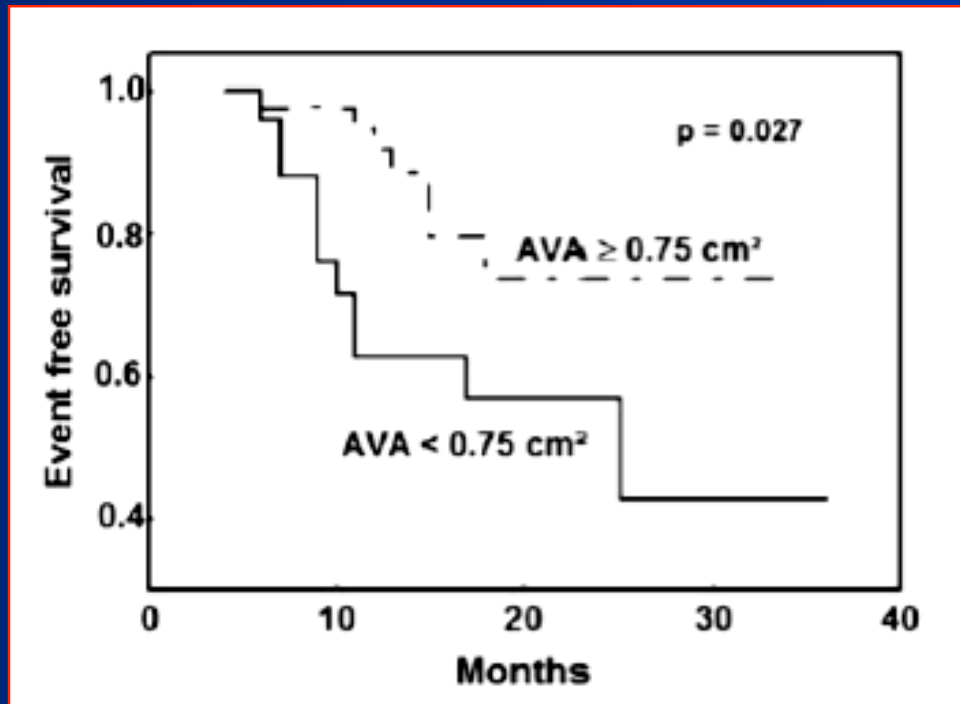
ESC Guidelines /Task Force Report. *Eur Heart J.* 2007;28:230-68.

What about Exercise Echo ?

Exercise Echo in Asymptomatic AS

N= 69 asymptomatic Pts, AVA: 0.8±0.2 cm², normal LVEF, FU: 15±7 months

Lancellotti et al. *Circulation*. 2005;112[Suppl I]: I-337

Exercise Echo in Asymptomatic AS

N= 69 asymptomatic Pts, AVA: 0.8±0.2 cm², normal LVEF, FU: 15±7 months
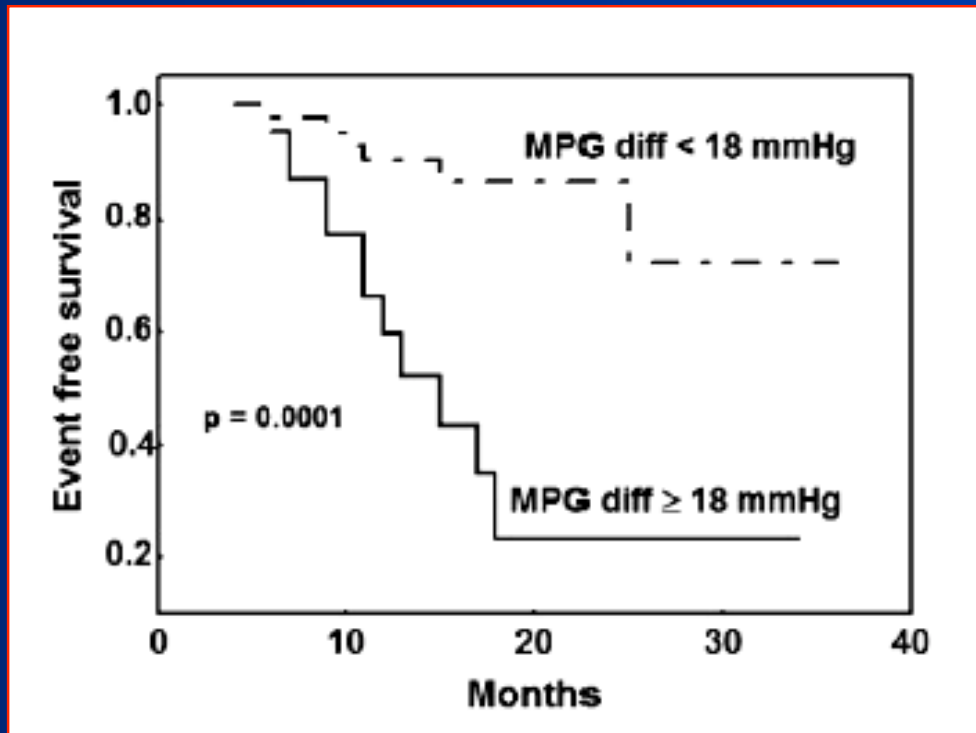
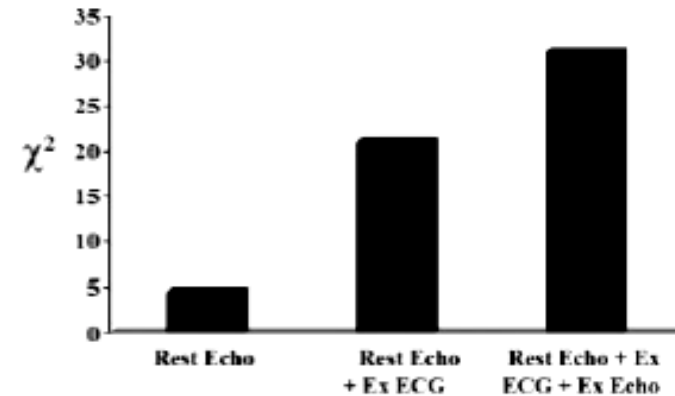Figure 3. Incremental prognostic value of exercise Doppler echocardiography over resting echocardiographic and exercise electrocardiographic parameters. Ex indicates exercise; Echo, echocardiography.

Incremental prognostic value of Stress Doppler parameters

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Lancellotti et al. *Circulation*. 2005;112[Suppl I]: I-337

Left Ventricular Response to Exercise in AS: An Exercise Echocardiographic Study

- Semi-supine Ex-Echo in 50 patients (AVA <1.0 cm^2, LVEF > 50%)

- Prospective FU during 11 (2-40) months

RESULTS

- Normal response in 30 Pts: LVEF increased from 62±7 to 70±8%

- Abnormal response to exercise in 20 Pts : LVEF decreased from 64±10 to 53±12%

- Symptoms during exercise: 27% vs. 80% (p< 0.001)

ΔLVEF≥0%

ΔLVEF<0%

Log rank = 4.65, p = 0.03

Figure 1. *Event-free survival according to the LV response to exercise.*

Limitation: Valve replacement not necessitated by symptoms in most cases

38

Maréchaux et al. *Echocardiography.* 2007; 24: 955-9.

Stress-Echo in Asymptomatic AS: Guidelines

ACC/AHA Task Force Report. *JACC*. 2006;48: e1-148

(…)

ESC Guidelines. *Eur Heart J*. 2007;28:230-68.

" Exercise stress echocardiography has been proposed for risk stratification in asymptomatic severe AS but more data are necessary to determine its role. "

What about Natriuretic Peptides?

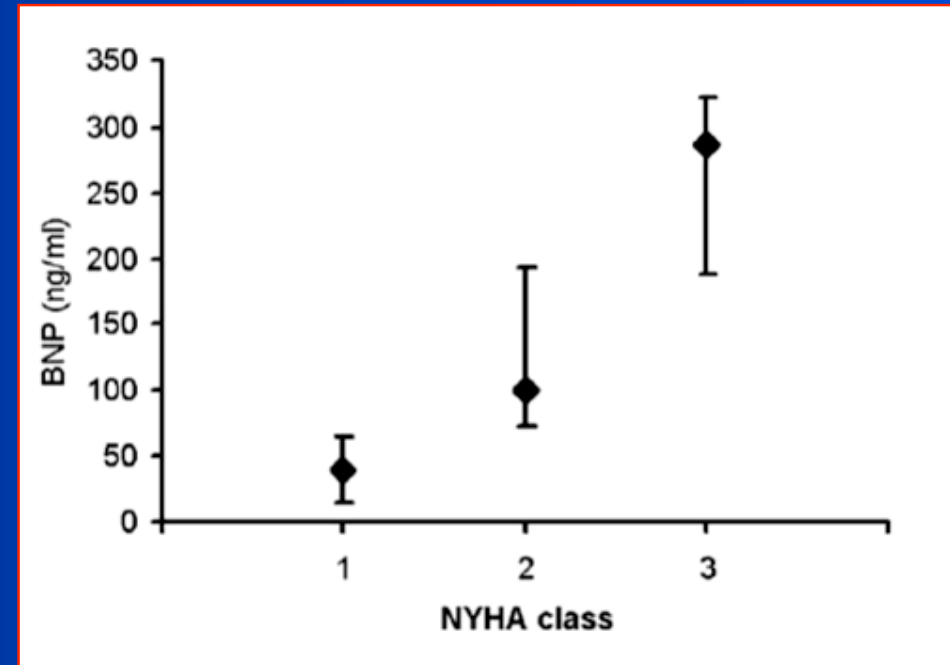# B-Type Natriuretic Peptide in severe AS:

70 patients, aged 74 years (62-82), AVA: 0,7 cm² (0,6-0,8), MPG: 48 mm Hg (36-60), FS: 38% (32-43)
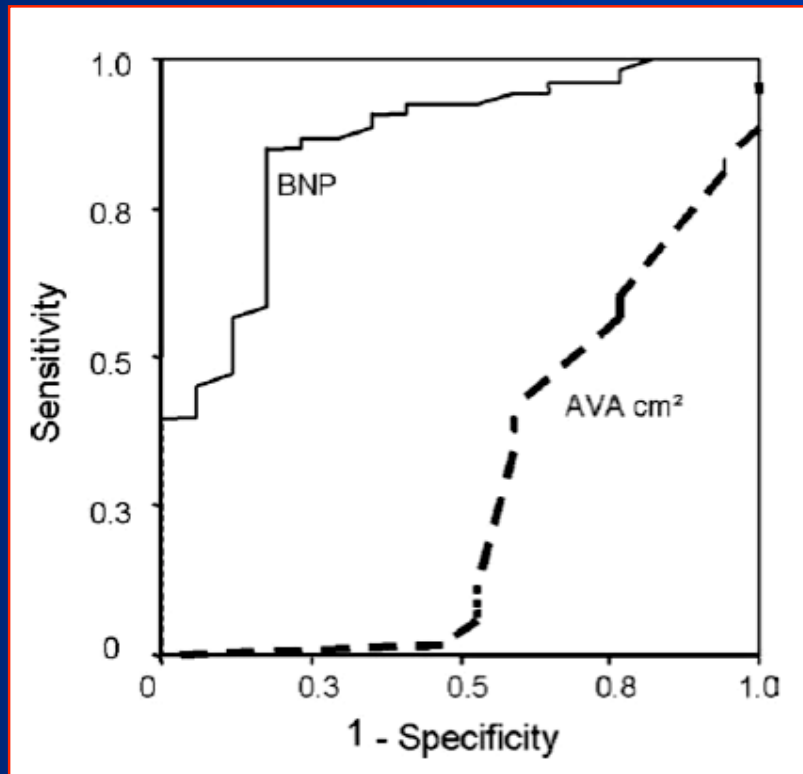
41 **Asymptomatic patients**

Lim et al. *Eur Heart J* 2004;25:2048

Predictors of Outcome in severe AS: Role of B-Type Natriuretic Peptide
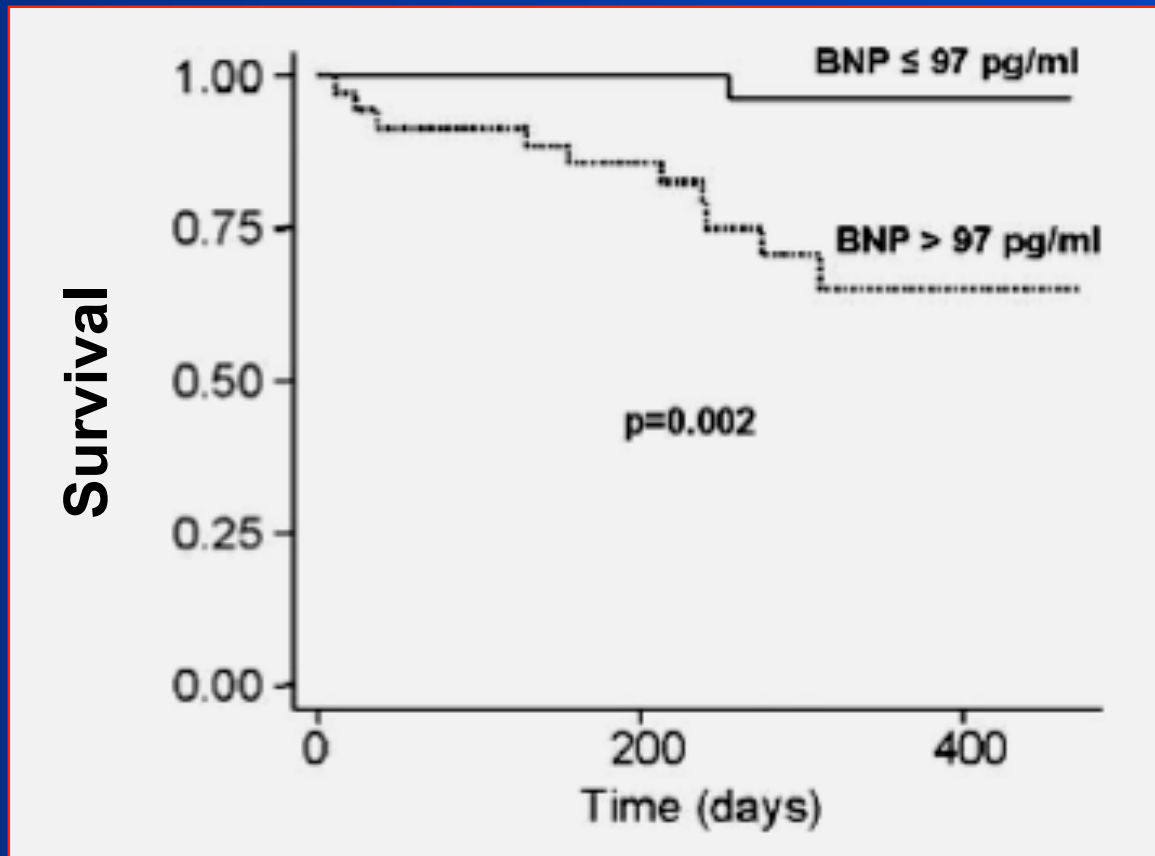
Lim et al. *Eur Heart J* **2004;25:2048**

When to Operate Asymptomatic AS

• What is severe aortic stenosis ? Who are the patients at risk ?

• The risk of sudden death :
    Are we racing into the wall ?

•Exercise Testing/ Stress Echo / BNP

• **Usefulness of Zva or Risk Score ?**

• What about the Guidelines ?

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Outcomes in asymptomatic AS: Usefulness of Valvulo-arterial Impedance

Retrospective analysis of 544 patients with at least moderate AS (V_{max} >2.5 m/s)

Valvulo-arterial impedance: Z_{va} = (SAP + MPG) / SVI: Global LV afterload

| Table 2 Doppler Echocardiographic and Systemic Arterial Indexes of Valvular Load, Arterial Load, and Global LV Hemodynamic Load According to the Level of Z_{va}			
Group	Low Z_{va} (n = 172)	Medium Z_{va} (n = 192)	High Z_{va} (n = 180)	p Value
Valvular load				
Aortic valve area, cm^2	1.2 ± 0.2	1.0 ± 0.3*	0.8 ± 0.2*†	<0.0001
Aortic valve area index, cm^2·m^{-2}	0.66 ± 0.13	0.56 ± 0.15*	0.45 ± 0.12*†	<0.0001
Energy loss index, cm^2·m^{-2}	0.78 ± 0.18	0.65 ± 0.23*	0.51 ± 0.15*†	<0.0001
Peak gradient, mm Hg	44 ± 16	46 ± 20	56 ± 26*†	<0.0001
Mean gradient, mm Hg	25 ± 10	27 ± 12	34 ± 17*†	<0.0001
Vascular load				
Systolic arterial pressure, mm Hg	122 ± 16	135 ± 19*	145 ± 23*†	<0.001
Diastolic arterial pressure, mm Hg	68 ± 9	73 ± 10*	78 ± 10*†	<0.0001
Systemic arterial compliance, ml·m^{-2}·mm Hg^{-1}	0.94 ± 0.24	0.69 ± 0.18*	0.57 ± 0.18*†	<0.0001
Systemic vascular resistance, dyne·s·cm^{-5}	1,303 ± 287	1,605 ± 361*	1,824 ± 398*†	<0.001
Global LV hemodynamic load				
Valvuloarterial impedance, mm Hg·ml^{-1}·m^2	3.1 ± 0.4	4.0 ± 0.3*	5.2 ± 0.9*†	<0.0001

Outcomes in asymptomatic AS: Usefulness of Valvulo-arterial Impedance

Retrospective analysis of 544 patients with at least moderate AS (V_{max} >2.5 m/s)

Study endpoint: overall mortality, regardless of the performance of AVR

| Table 1	Baseline Clinical Characteristics of the Patients According to the Level of Z_{va}			
Group	Low Z_{va} (n = 172)	Medium Z_{va} (n = 192)	High Z_{va} (n = 180)	p Value
Age, yrs	66 ± 15	70 ± 12*	73 ± 13*†	<0.001
Female sex	69 (40)	73 (38)	82 (46)	NS
Body surface area, m²	1.8 ± 0.2	1.8 ± 0.2	1.8 ± 0.2	NS
Body mass index, kg/m²	27 ± 6	27 ± 5	28 ± 5	NS
Obesity	39 (23)	53 (27)	55 (31)	NS
Hypertension	96 (56)	138 (72)*	128 (71)*	0.02
Hypercholerolemia	93 (54)	109 (57)	76 (42)	NS
Diabetes	39 (23)	40 (21)	34 (19)	NS
Coronary artery disease	96 (56)	128 (67)	106 (59)	NS
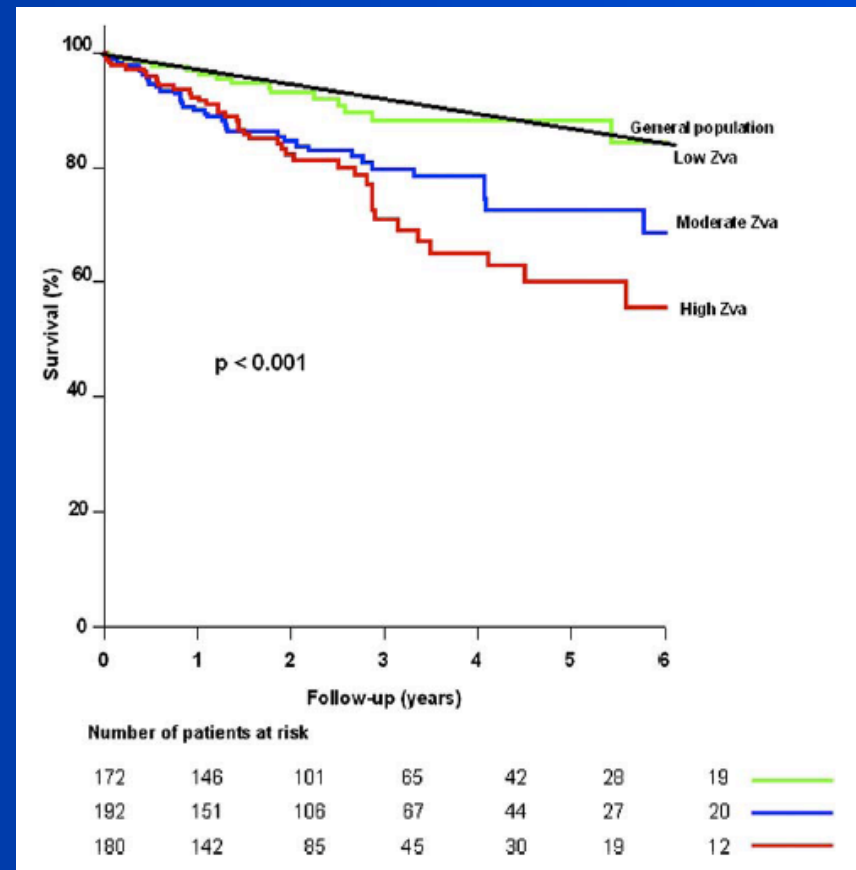
Hachicha et al. *J Am Coll Cardiol.* 2009;54: 1003

Outcomes in asymptomatic AS: Usefulness of Valvulo-arterial Impedance

Overall mortality was 17% (91 patients) after a mean FU of 2.5 years

AVR performed in respectively:

31%   30%   36%

20%   46%   76%

p < 0.001

Hachicha et al. *J Am Coll Cardiol.* 2009;54: 1003-11
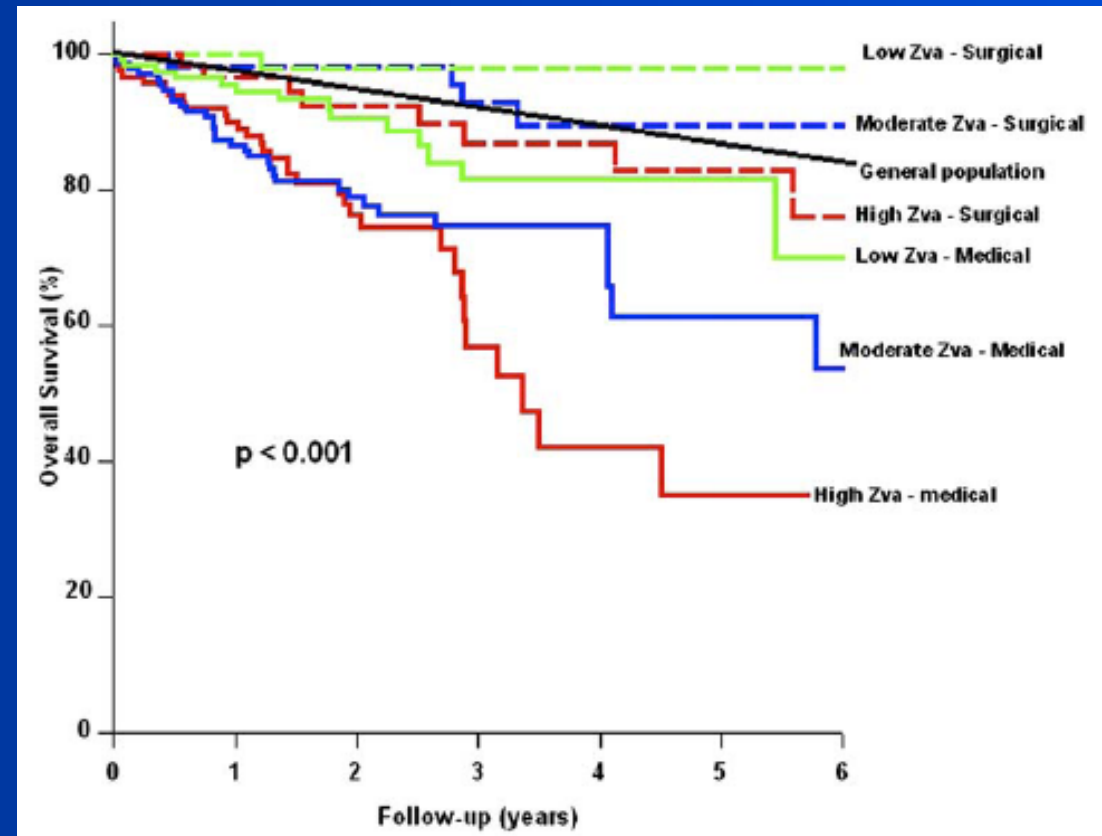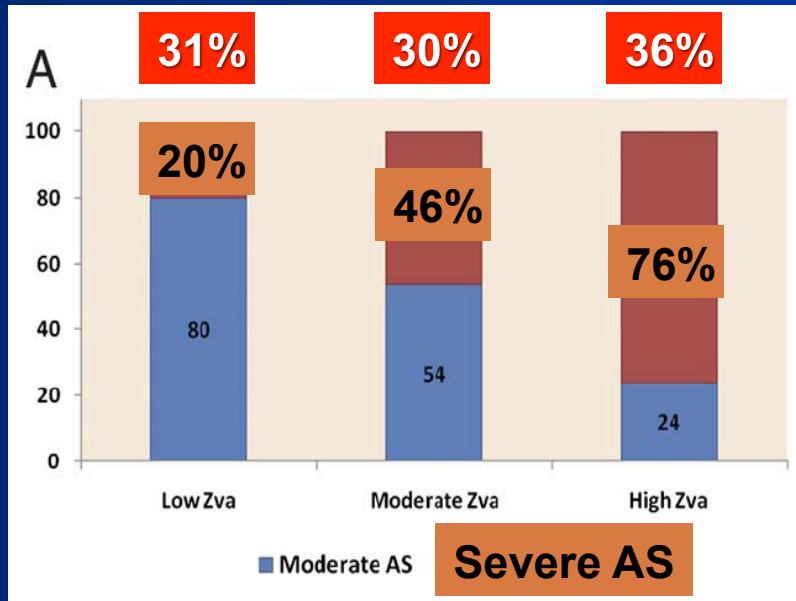
Valvulo-arterial Impedance : Do we need a new Concept ?

Study limitations

No information was available regarding:

1/ Timing of symptom onset

2/ Proportion of patients with severe symptomatic AS who were not operated

3/ Primary reason that motivated AVR

4/ Cause of death in all cases

Clinical implications

- Z_{va} does not account separately for the valvular vs. arterial component

- High Z_{va} may reflect either:

  1/ Moderate AS with severe hypertension, requiring Blood pressure control

  2/ Severe AS requiring valve replacement

- In current practice, we can continue to rely on recommended measures of AS severity, as long as we also consider blood pressure and cardiac output

H. Baumgartner & CM. Otto. *J Am Coll Cardiol.* 2009;54: 1012-3

Risk Score for Predicting Outcome in Patients with Asymptomatic Aortic Stenosis

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Conflicts of Interest: None

Patients and methods : Development cohort (Créteil, France)

- 107 asymptomatic patients (aged 72 years [63-77]; 35 women) with moderate / severe AS were prospectively included (March 2001 to June 2006)

Inclusion criteria:

- Baseline AVA ≤ 1.5 cm² and/ or peak velocity ≥ 3.0 m/s

- Sinus rhythm, LVEF > 50%, without segmental WMA, serum creatinine ≤ 160 µmol/L

Evaluation at baseline:

- Clinical evaluation, comprehensive TTE, BNP serum level and exercise test (Bicycle, n= 89, 83%)

Follow-up / Predefined endpoints

Follow-up

• Clinical evaluation, TTE, BNP and exercise test (if applicable) every 6 months (severe AS) to 12 months (moderate AS)

Predefined endpoints (within 24 months):

• Death from any cause

• Symptom development: dyspnea, chest pain, syncope

• Positive exercise test according to ESC guidelines

(Iung et al. *Eur Heart J.* 2002;23: 1253)

Development cohort:
Clinical outcomes

- **Three preoperative deaths: CHF, endocartitis and cancer**

Valve replacement (n=59) necessitated by:

- Symptoms development: n=37 patients, average interval of
10 [7-16] months : Dyspnea (n=32), angina (n=3) or syncope (n=2)

- Positive exercise test at baseline (n=11) or during follow-up (n=7,
 after 7-14 months)

- Aneurysm of the ascending aorta (52 mm) in one female patient
 with a bicuspid AV

Monin et al. *Circulation.* 2009; 120: 69-75

Development cohort : Patients characteristics vs. Outcome

Variable at baseline	Whole population (n= 104)	Remained asymptomatic (n= 42)	Endpoint ≤ 24 months (n=62)	P value
Age (years)	72 [63-77]	70 [53-77]	74 [63-78]	0.16
Women, n (%)	35 (34)	9 (21)	26 (42)	0.03
LVEF, %	67 [62-72]	68 [65-72]	66 [60-70]	0.08
Peak velocity, m/s	4.1 [3.5-4.4]	3.6 [3.2-4.0]	4.3 [3.9-4.6]	0.0001
MPG, mm Hg	40 [31-50]	33 [24-40]	47 [36-55]	0.0001

Monin et al. *Circulation.* 2009; 120: 69-75

Development cohort :
Patients characteristics vs. Outcome (2)

Variable at baseline	Whole population (n= 104)	Remained asymptomatic (n= 42)	Endpoint ≤ 24 months (n=62)	p value
Calcification score ≥3, n (%)	72 (69)	24 (57)	48 (77)	0.01
Valve area, cm²	0.9 [0.8-1.1]	1.1 [1.0-1.3]	0.8 [0.7-1.0]	0.0001
Indexed area, cm²	0.5 [0.4-0.6]	0.6 [0.5-0.7]	0.5 [0.4-0.5]	0.0001
Baseline BNP, pg/ml	58 [30-111]	30 [14-64]	83 [43-165]	0.0001
BNP (2), pg/ml	66 [32-173]	36 [16-71]	161 [64-242]	0.0001

Monin et al. *Circulation.* 2009; 120: 69-75

Development cohort : Independent predictors of outcome

Variable at baseline	Odds ratio	95% confidence interval	p value
Baseline serum BNP	3.9	1.8 - 8.1	0.0001
Baseline Peak-jet velocity	6.2	2.1 - 17.9	0.001
Female gender	5.2	1.5 - 18.6	0.012

RISK SCORE calculation :

Score = [Peak velocity (m/s) x 2] + [natural Log of BNP x 1.5] + 1.5 (if female gender).

Monin et al. *Circulation*. 2009; 120: 69-75

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Patients outcome according to Score quartiles (Development cohort: Créteil, FR)
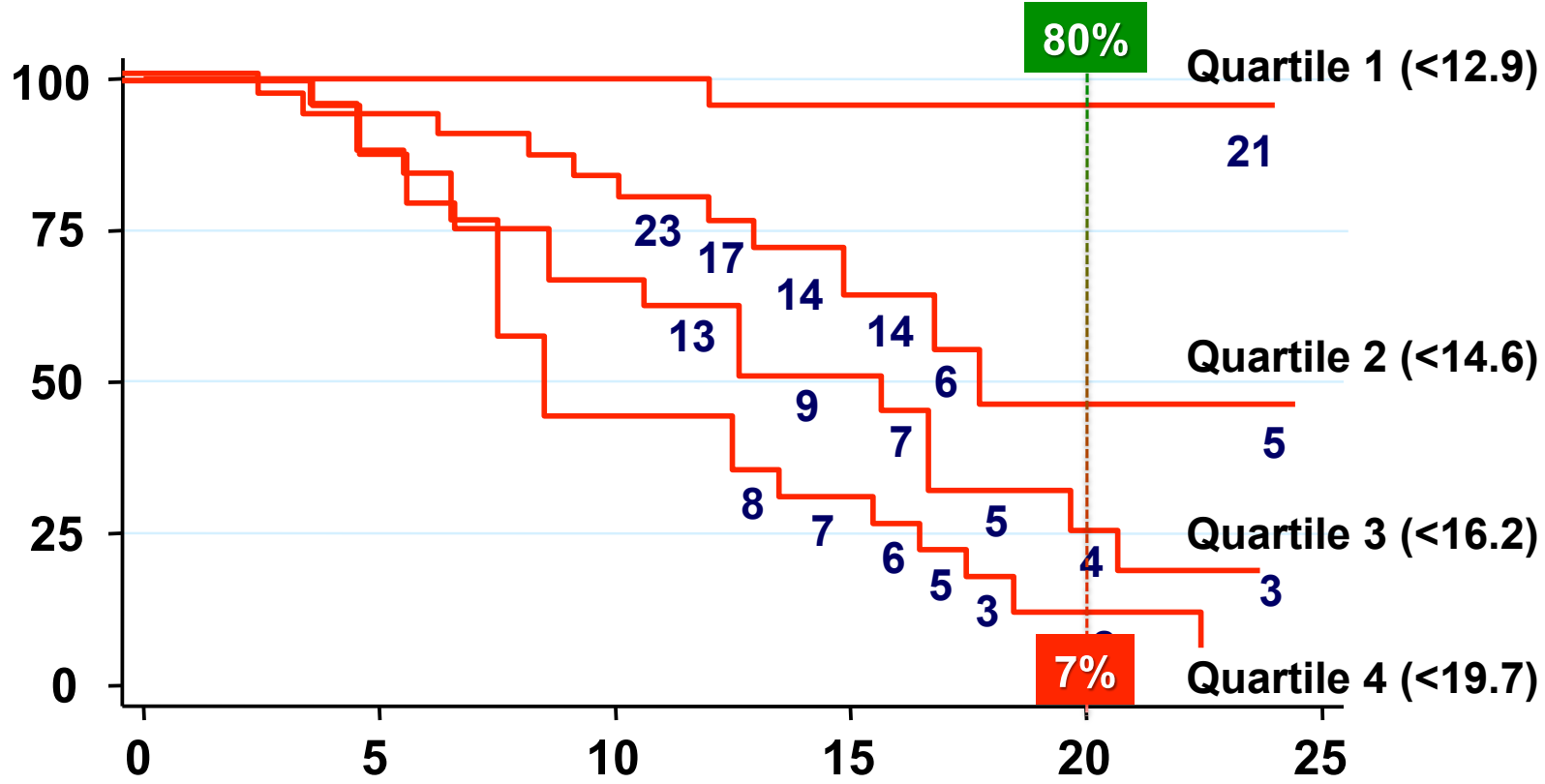
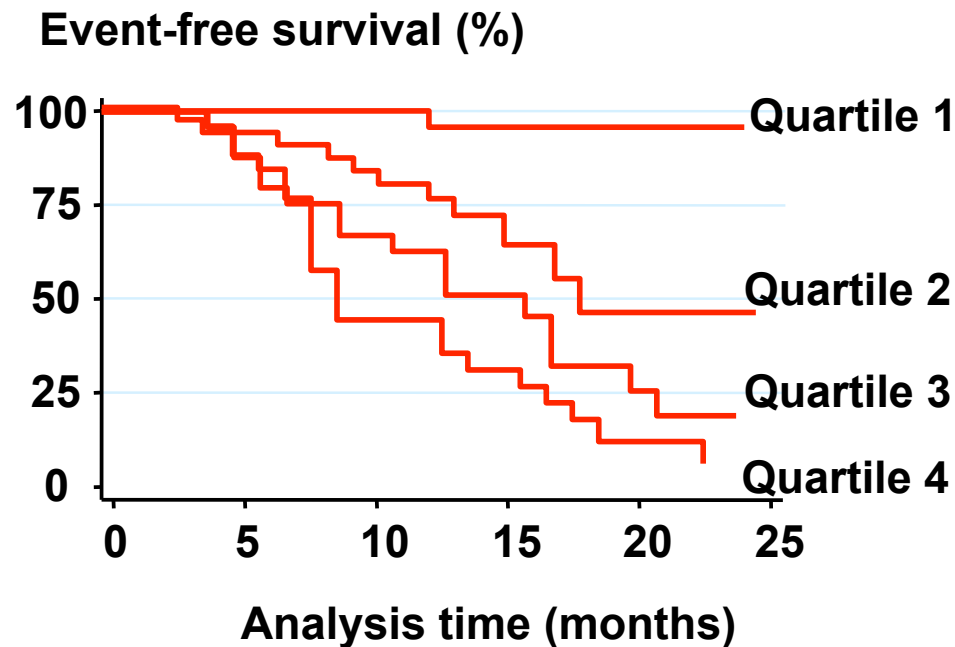Monin et al. *Circulation.* 2009; 120: 69-75

Validation cohort (Liège, Belgium)

- N= 107 asymptomatic patients (71 years [66-78]; 42 women);

- Peak aortic-jet velocity, 4.1 m/s [3.7-4.6]

- Aortic valve area, 0.8 cm² [0.7-0.9]

- Mean pressure gradient, 42 mm Hg [34-49]

- Serum BNP, 59 pg/ml [33-113]

- All patients were prospectively followed (January 2003 to December 2008

- Same protocol for echocardiographic and BNP measurements / same indications for valve replacement according to ESC guidelines

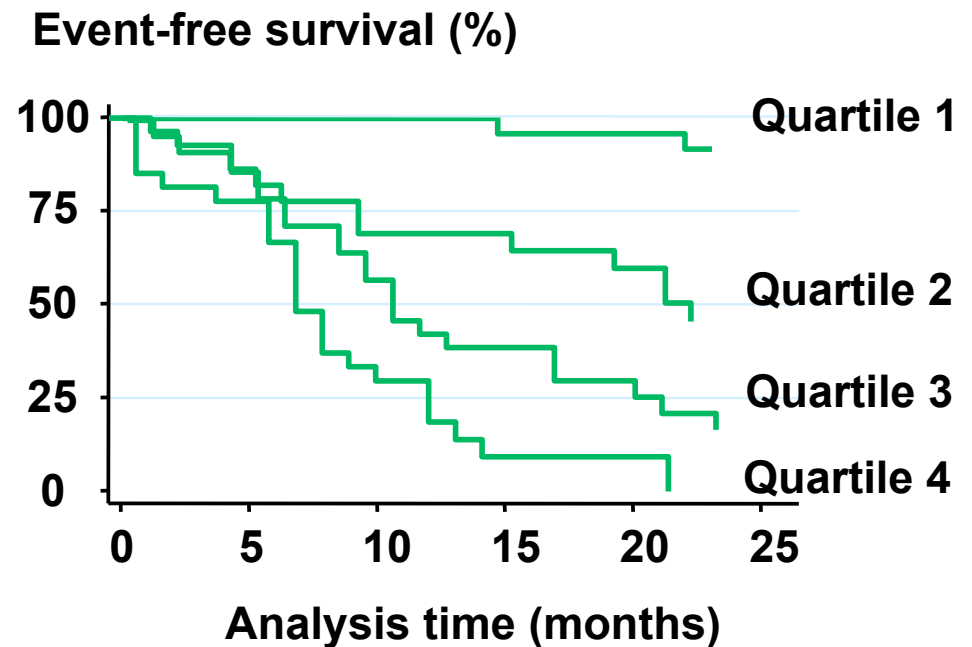Score = [Peak velocity (m/s) x 2] + [natural Log of BNP x 1.5] + 1.5 (if female gender).

Development Cohort (N= 104)

Validation Cohort (N= 107)

Event-free survival (%)

Event-free survival (%)

Monin et al. *Circulation.* 2009; 120: 69-75

Validation cohort: 5 preoperative deaths

Sex	Age, years	Peak Velocity, m/s	Serum BNP, pg/ml	Risk Score	FU Duration, Months	Cause of Death
Male	84	3.4	521	16.1 (Q3)	9	CHF
Male	77	4.0	123	15.2 (Q3)	6	Pulmonary Edema
Male	78	4.3	229	16.8 (Q4)	8	CHF
Female	68	5.6	71	19.1 (Q4)	13	Sudden death
Female	49	4.8	116	18.3 (Q4)	19	Sudden death

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CONCLUSIONS

- Risk Score based on the 3 independent predictors of outcome in asymptomatic patients with mostly severe AS.

- According to this Score, 80% of patients within the first quartile remained free from events after 20 months.

- In contrast, only 7% of patients within the fourth quartile remained free of events after 20 months.

- If further validation is achieved, this Score may be useful to predict outcome in individual patients with asymptomatic AS in order to select those who might benefit from early surgery.

When to Operate Asymptomatic AS

- What is severe aortic stenosis ? Who are the patients at risk ?

- The risk of sudden death :
    Are we racing into the wall ?

- Exercise Testing/ Stress Echo / BNP

- Usefulness of Zva or Risk Score ?

- **What about the Guidelines ?**

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European Guidelines :
Indications for Surgery in AS

Severe AS and any symptoms	**I**
Severe AS undergoing CABG or other cardiac surgery	**I**
Asymptomatic severe AS with LV dysfunction (LVEF <50%)	**I**
Asymptomatic patients with severe AS and Abnormal exercise test showing symptoms on Exercise	**I**

European Guidelines : Indications for Surgery in AS

Asymptomatic severe AS with exercise test showing <u>fall in blood pressure</u>	**IIa**
Moderate AS undergoing CABG or other cardiac surgery	**IIa**
Asymptomatic severe AS with moderate-to-severe valve calcification and a progression of peak velocity >0.3 m/s per year	**IIa**
Asymptomatic severe AS and abnormal exercise test showing complex ventricular arrhythmias	IIb
Asymptomatic patients with severe AS and excessive LV hypertrophy (>15 mm) unless due to hypertension	IIb

ESC Guidelines /Task Force Report. *Eur Heart J.* 2007;28:230-68.

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