HÔPITAUX UNIVERSITAIRES
PARIS NORD VAL DE SEINE
Bichat - Claude Bernard

Improving Risk Stratification in Asymptomatic Severe Aortic Stenosis

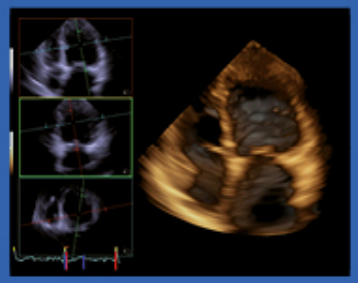
Valve Calcification by CT

université PARIS DIDEROT PARIS 7

Inserm
Chercheur en santé depuis 1964
Health research since 1964

50 ans

fire



EuroValve
March 27 - 28, 2015

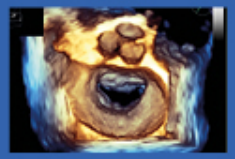
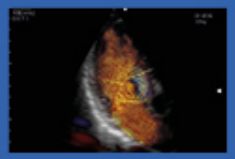
Faculty disclosure

David Messika-Zeitoun

I disclose the following financial relationships:

Consultant for Edwards, Abbott, Valtech
Receive grant / research support from Abbott
Advisory board of ACE Device Company
Paid speaker for Edwards, Abbott



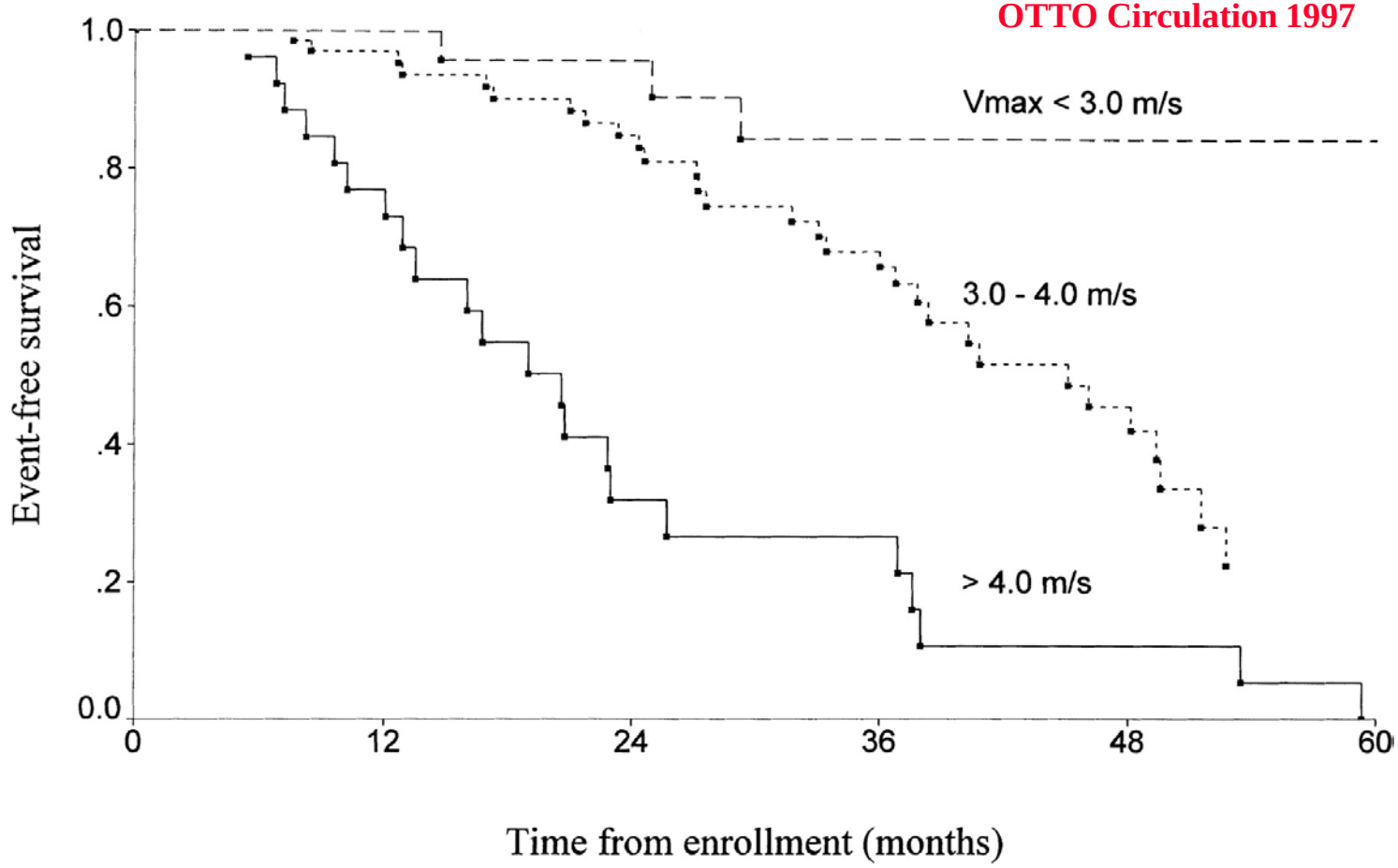
www.eurovalvecongress.com

Hemodynamic

- Mean gradient
- Peak transaortic velocity
- Aortic valve area

Outcome

OTTO Circulation 1997



Severe AS

	Sclerosis	Mild AS	Moderate AS	Severe AS
Peak velocity, m/sec	< 2.5	2.5 - 3	3 - 4	**> 4**
Mean gradient, mm Hg	Normal	< 25	25 – 40 (ou 50)	**40 (US) 50 (Europe)**
AVA, cm^2	Normal	≥ 1.5	1 – 1.5	**< 1 cm^2 < 0.6 cm^2/m^2**

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

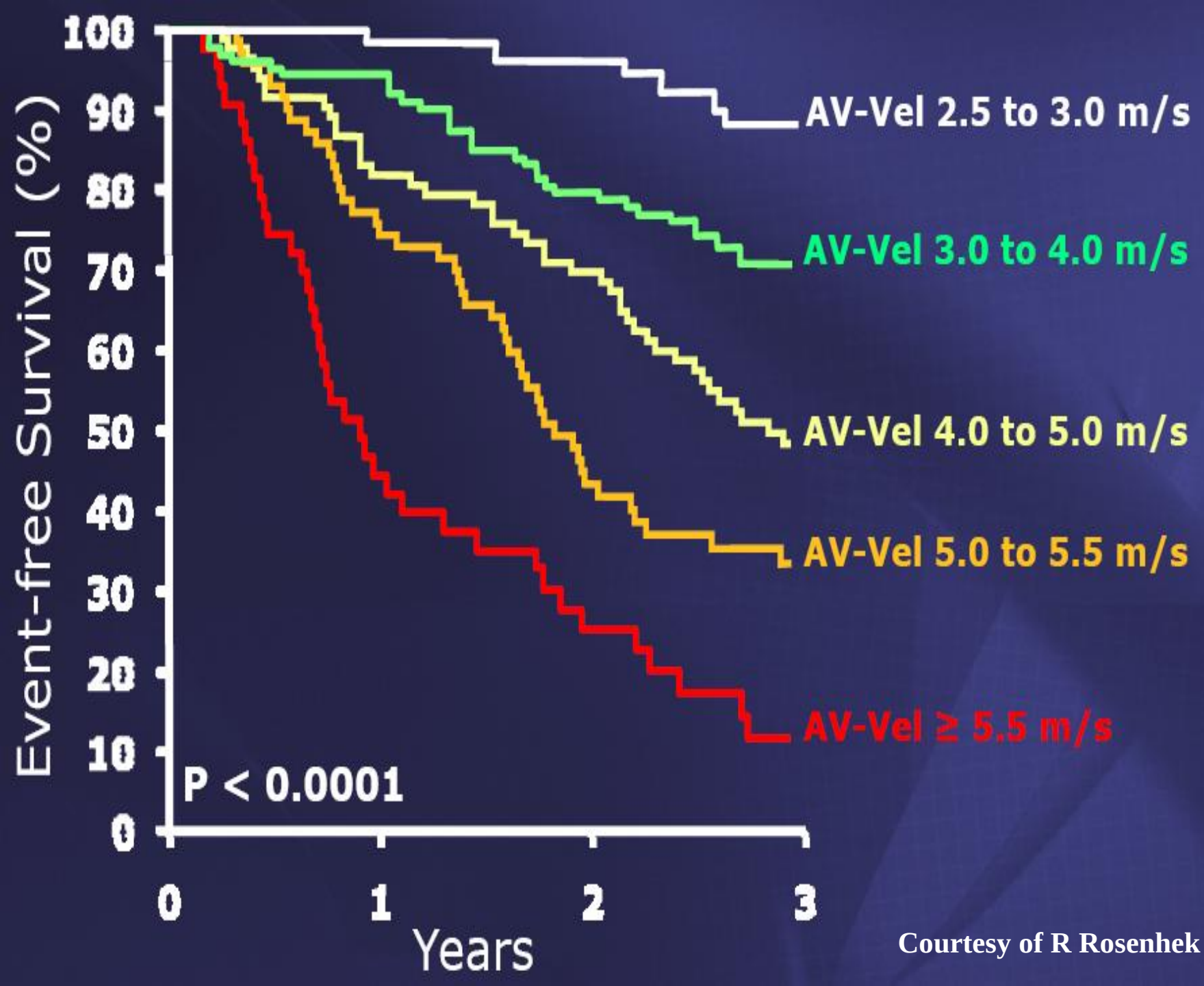
Natural History of Very Severe Aortic Stenosis

Raphael Rosenhek, MD; Robert Zilberszac; Michael Schemper, PhD; Martin Czerny, MD; Gerald Mundigler, MD; Senta Graf, MD; Jutta Bergler-Klein, MD; Michael Grimm, MD; Harald Gabriel, MD; Gerald Maurer, MD

Background—We sought to assess the outcome of asymptomatic patients with very severe aortic stenosis.

Methods and Results—We prospectively followed 116 consecutive asymptomatic patients (57 women; age, 67±16 years) with very severe isolated aortic stenosis defined by a peak aortic jet velocity (AV-Vel) ≥5.0 m/s (average AV-Vel, 5.37±0.35 m/s; valve area, 0.63±0.12 cm^2). During a median follow-up of 41 months (interquartile range, 26 to 63 months), 96 events occurred (indication for aortic valve replacement, 90; cardiac deaths, 6). Event-free survival was 64%, 36%, 25%, 12%, and 3% at 1, 2, 3, 4, and 6 years, respectively. AV-Vel but not aortic valve area was shown to independently affect event-free survival. Patients with an AV-Vel ≥5.5 m/s had an event-free survival of 44%, 25%, 11%, and 4% at 1, 2, 3, and 4 years, respectively, compared with 76%, 43%, 33%, and 17% for patients with an AV-Vel between 5.0 and 5.5 m/s ($P<0.0001$). Six cardiac deaths occurred in previously asymptomatic patients (sudden death, 1; congestive heart failure, 4; myocardial infarction, 1). Patients with an initial AV-Vel ≥5.5 m/s had a higher likelihood (52%) of severe symptom onset (New York Heart Association or Canadian Cardiovascular Society class >II) than those with an AV-Vel between 5.0 and 5.5 m/s (27%; $P=0.03$).

Conclusions—Despite being asymptomatic, patients with very severe aortic stenosis have a poor prognosis with a high event rate and a risk of rapid functional deterioration. Early elective valve replacement surgery should therefore be considered in these patients. (***Circulation*. 2010;121:151-156.**)

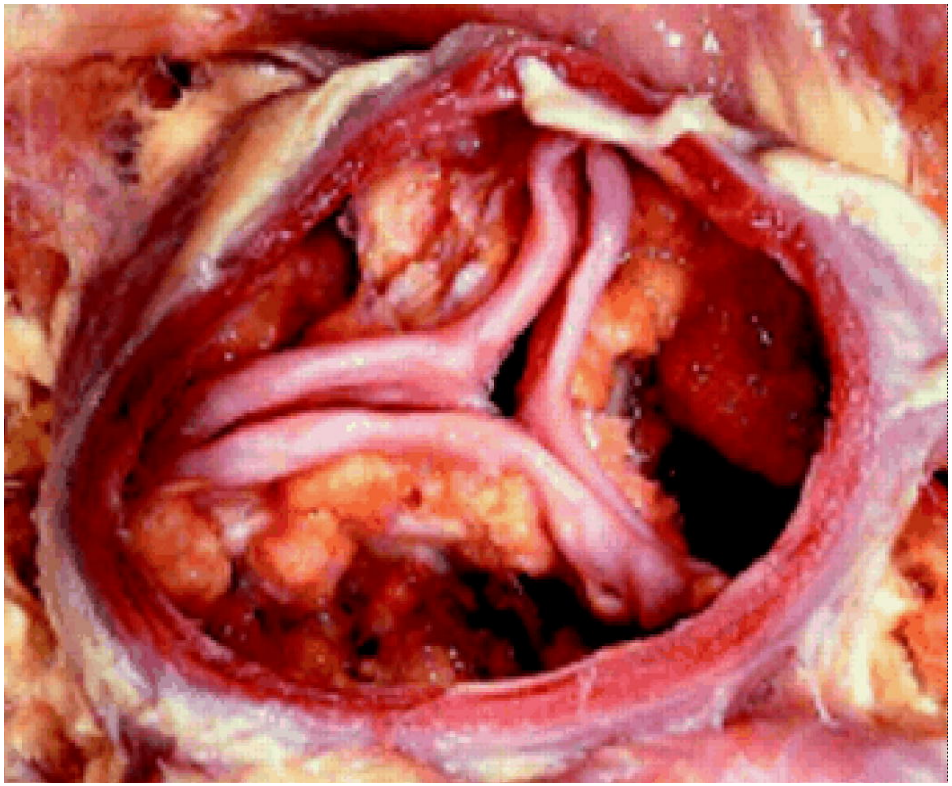


Courtesy of R Rosenhek

Severe AS

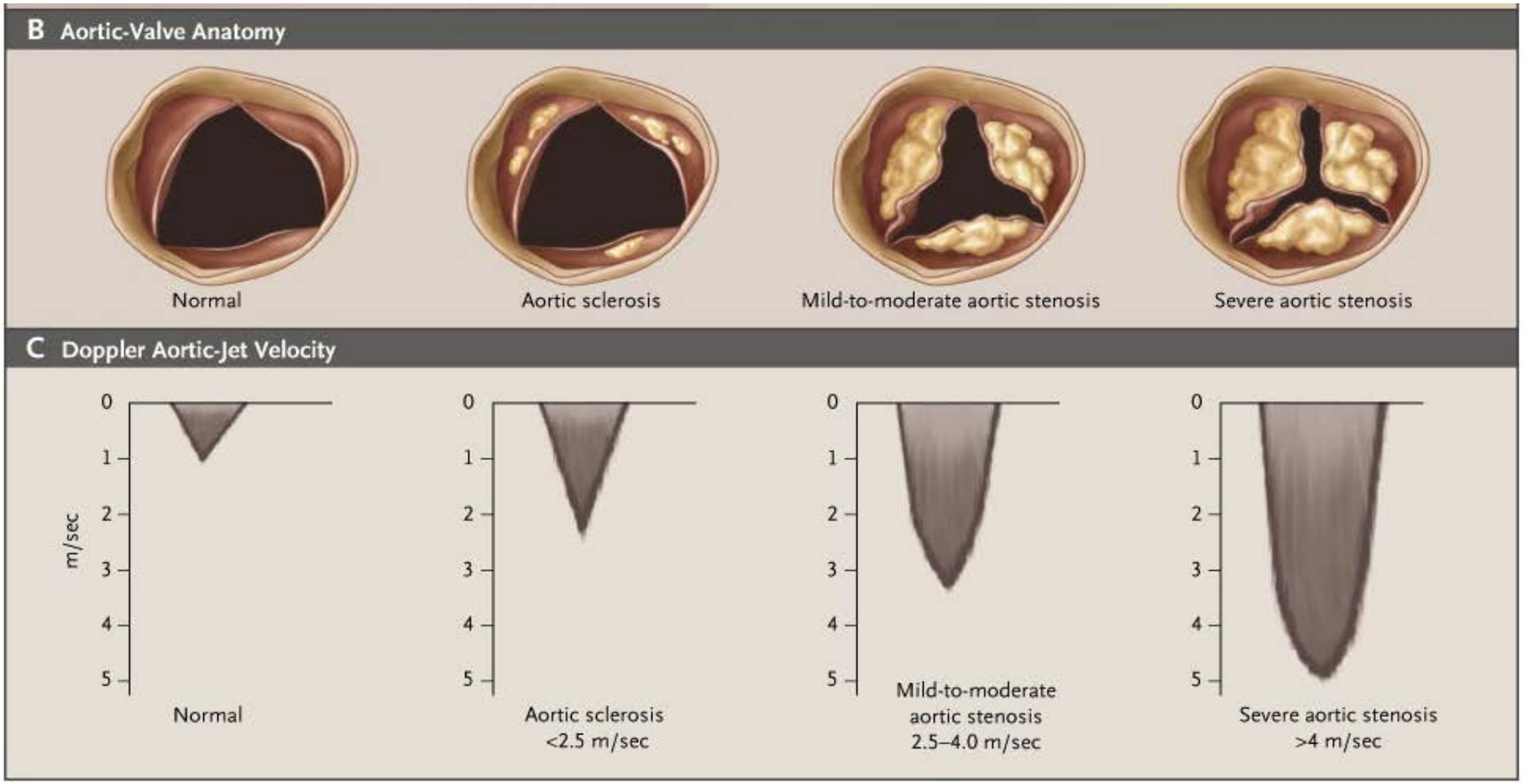
	Sclerosis	Mild AS	Moderate AS	Severe AS	Very Severe AS
Peak velocity, m/sec	< 2.5	2.5 - 3	3 - 4	**> 4**	**> 5.5**
Mean gradient, mm Hg	Normal	< 25	25 – 40 (ou 50)	**40 (US) 50 (Europe)**	
AVA, cm^2	Normal	≥ 1.5	1 – 1.5	**< 1 cm^2 < 0.6 cm^2/m^2**	

Aortic Valve Calcification



Leading process to Aortic Stenosis

Hemodynamic consequences



Otto CM. N Engl J Med 2008;359:1395-1398.


You know what?
Echo is tough …
www.texavery.com

Echocardiographic Evaluation of Aortic Valve Calcification

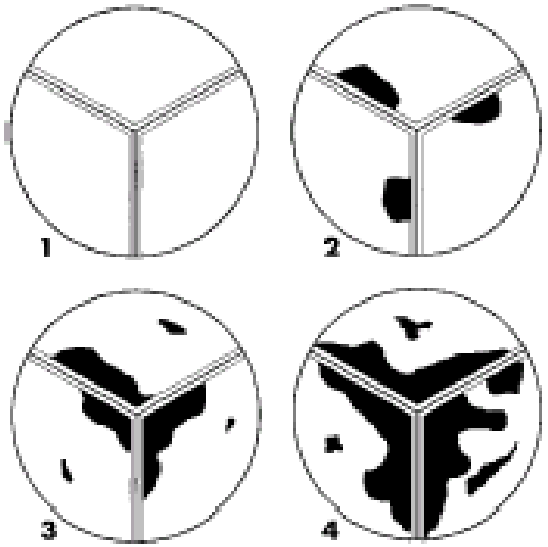
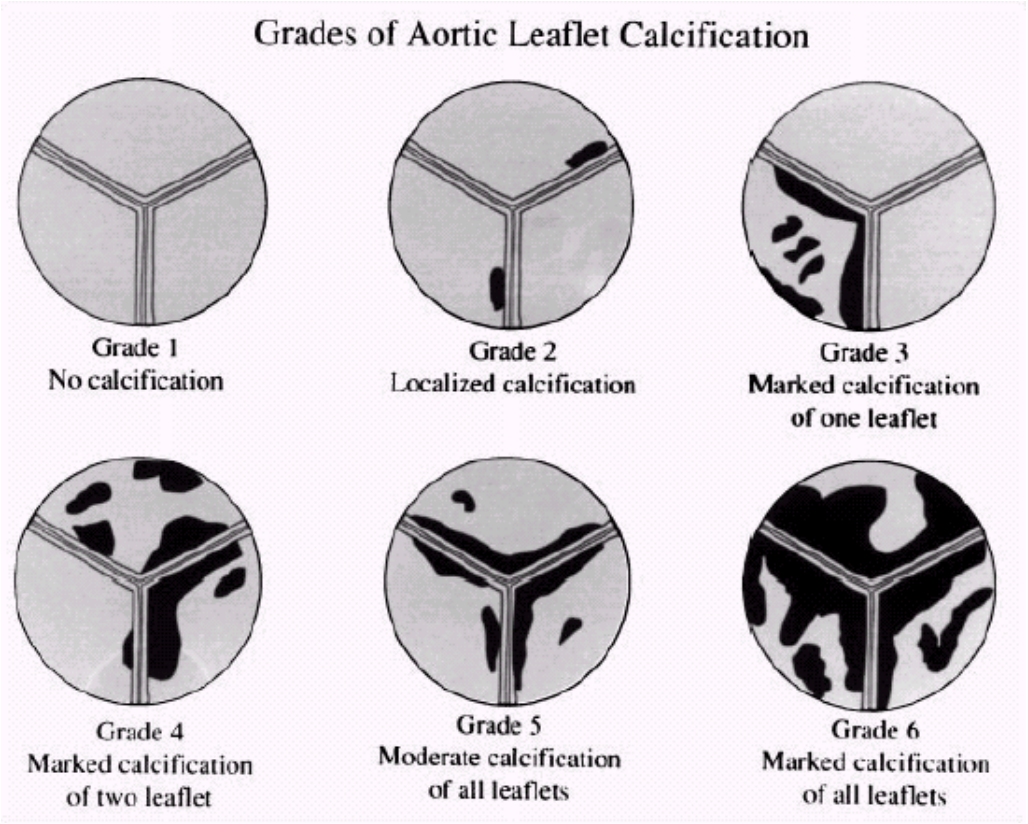
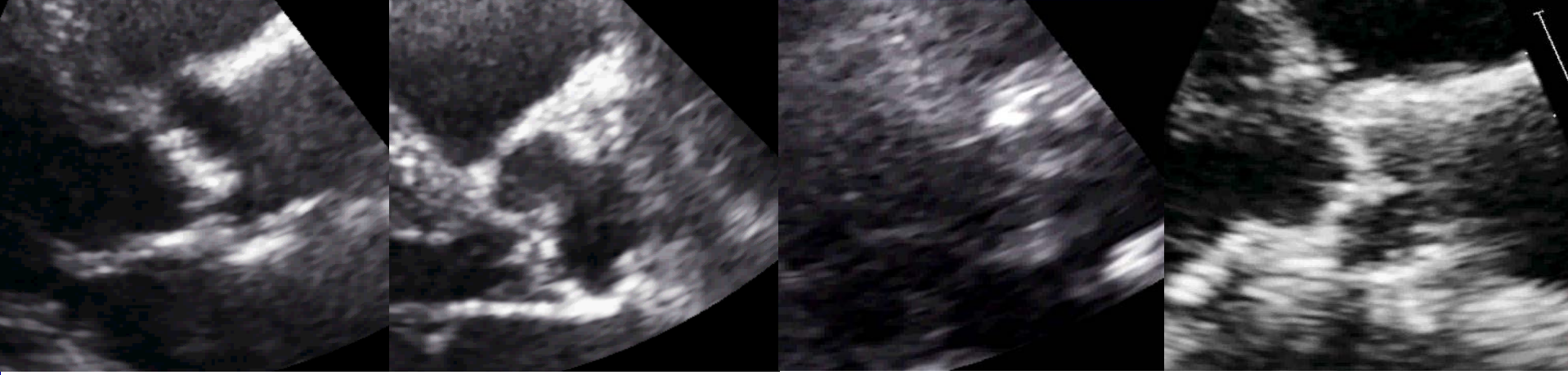
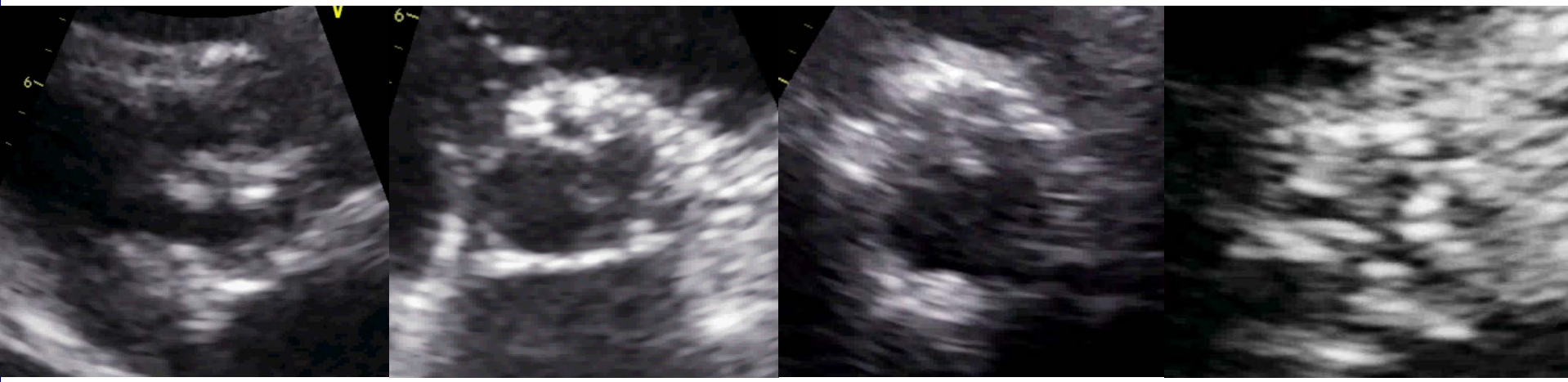


Figure 1. Diagrams of different grades of aortic valve calcification. Grade 1 *(1)*, no calcification; grade 2 *(2)*, mild calcification (small isolated spots of calcification); grade 3 *(3)*, moderate calcification (multiple larger spots of calcification); and grade 4 *(4)*, heavy calcification (extensive calcification of all aortic valve leaflets).

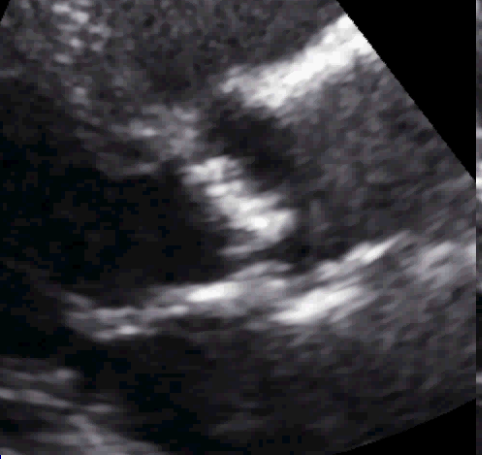
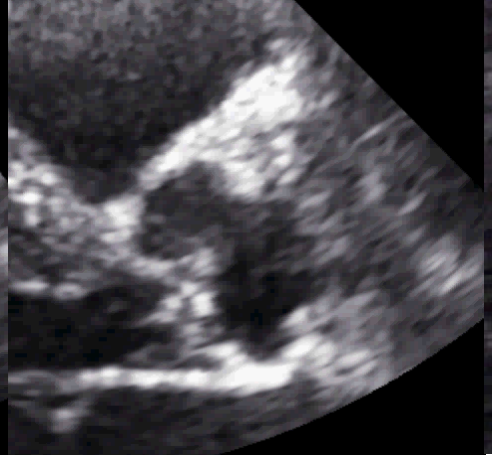
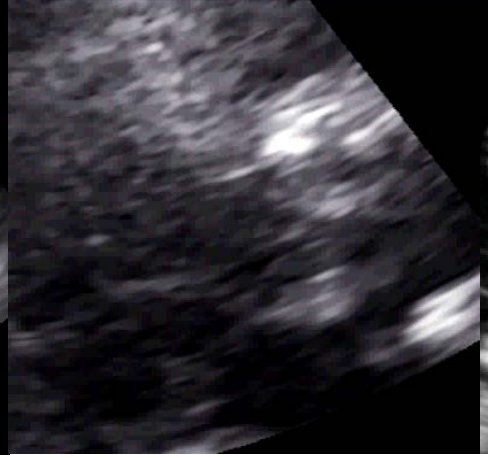
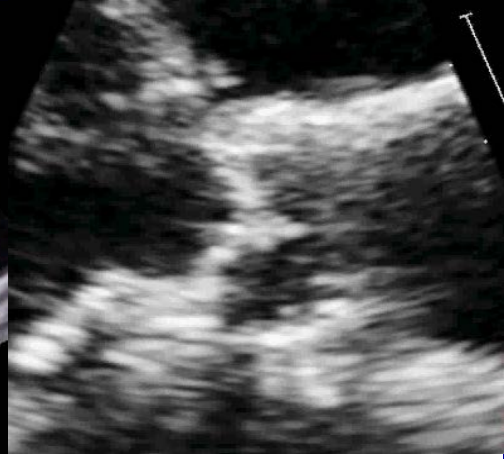
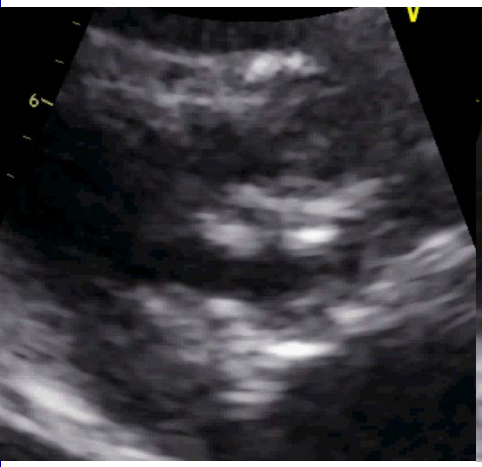
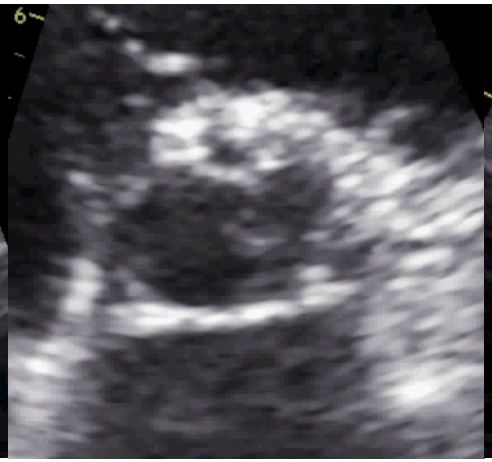


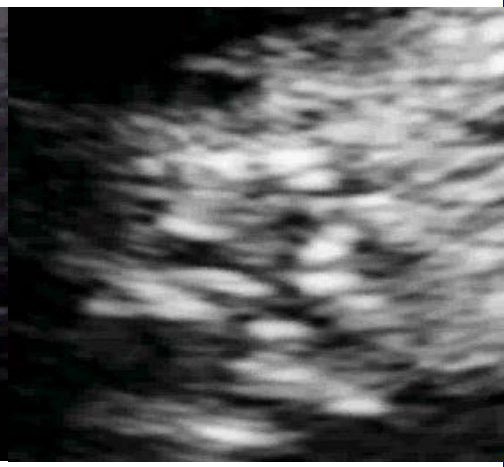
The severity of aortic valve calcification is usually graded from the parasternal short-axis view





What is the degree of aortic valve calcification for each of the 4 patients?

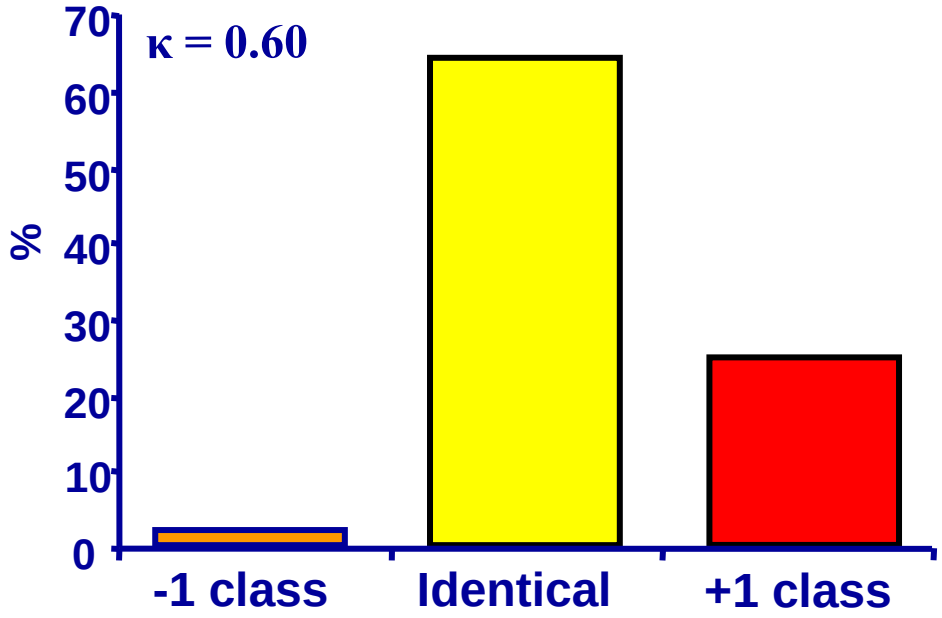









MG 22 mm Hg **MG 22 mm Hg** **MG 50 mm Hg** **MG 35 mm Hg**

Echocardiographic Evaluation of Aortic Valve Calcification

- None
- Mild: isolated spots
- Moderate: Multiples spots
- Severe : Large and diffuse calcifications



Echocardiographic Evaluation of Aortic Valve Calcification

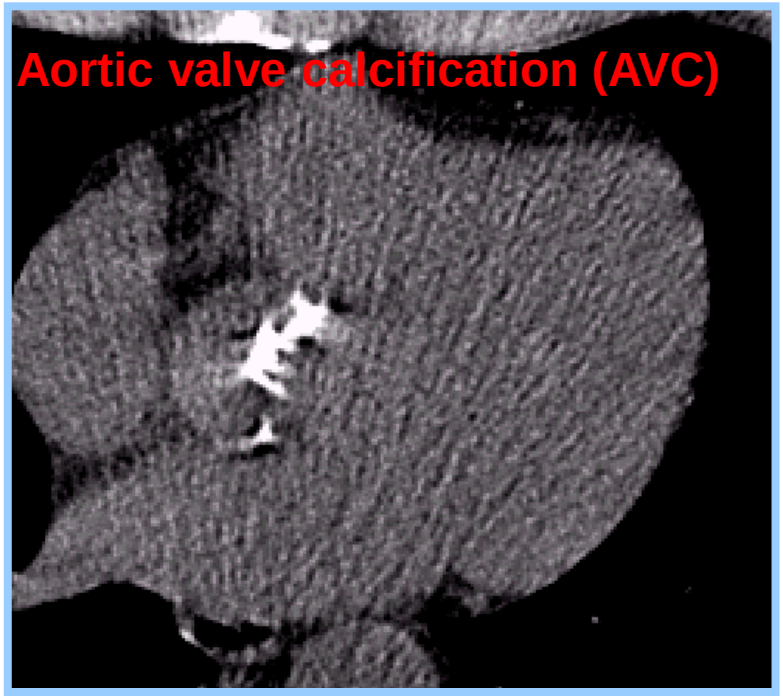
1. Subjective
2. Qualitative
3. Ga
4. Q mages

Inaccurate


solution

Aortic Valve Calcification (AVC)

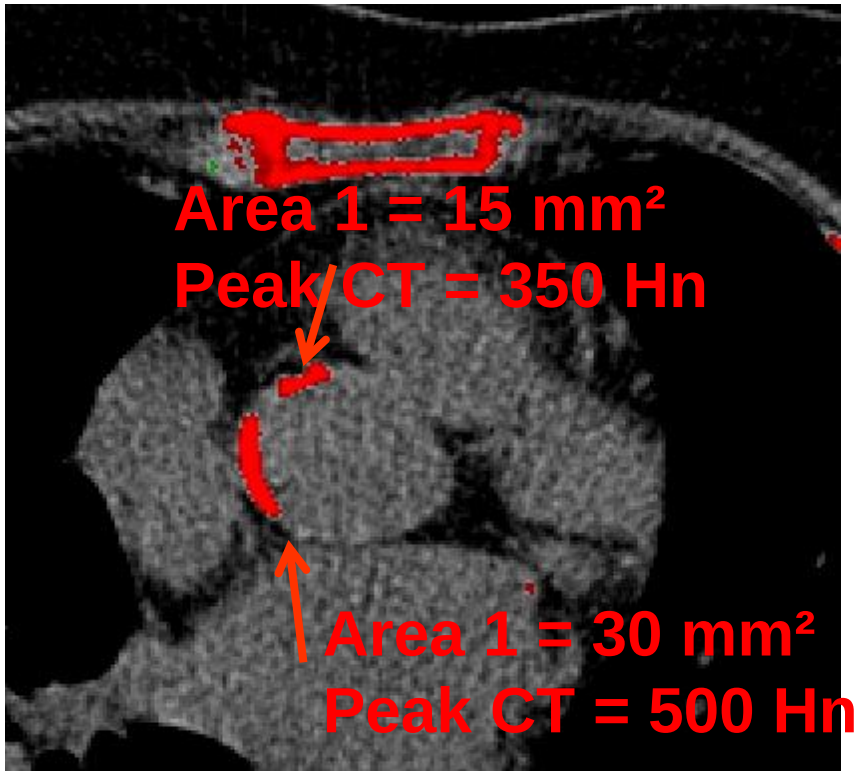
CT is ideally suited to objectively and quantitatively assessed calcifications



CT Scanner – Measurements of Calcifications

- Automated operator-independent image-processing software
- Calcification are defined as 4 adjacent pixels with density 130 Hounsfield units
- Radiologist affect the selected area to the coronary arteries, the aortic valve….

The Agatston Score



Peak density score

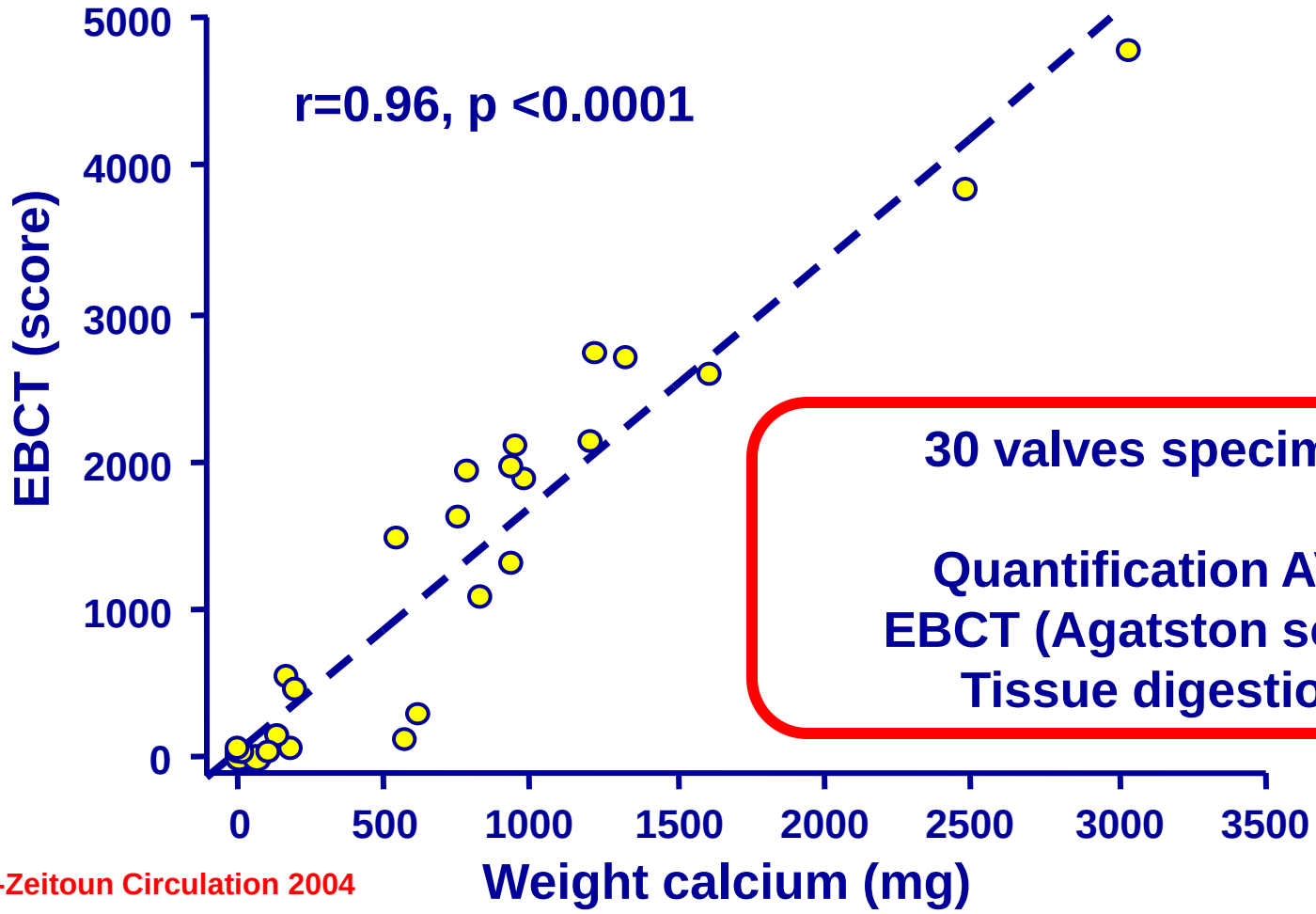
Hn	X Factor
130-199	1
200-299	2
300-399	3
> 400	4

Region 1. Score = 15 * 3 = 45

Region 2. Score = 30 * 4 = 120

- For each region of interest, score = density score * area
- Total score: sum of score of each region of interest in all slices

Anatomic validation for AVC

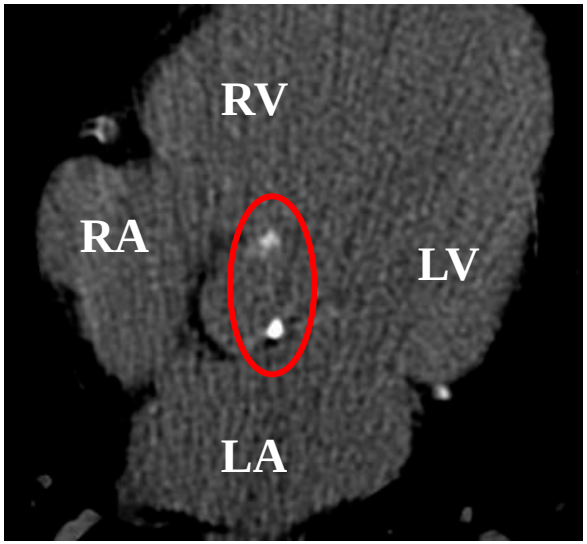


30 valves specimen

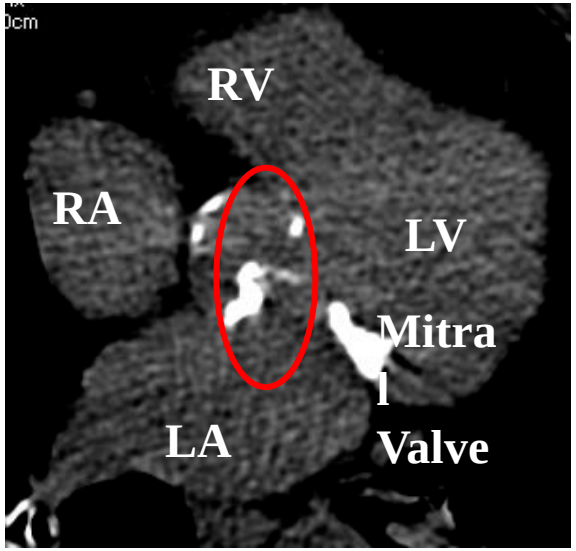
Quantification AVC
EBCT (Agatston score)
Tissue digestion

Messika-Zeitoun Circulation 2004

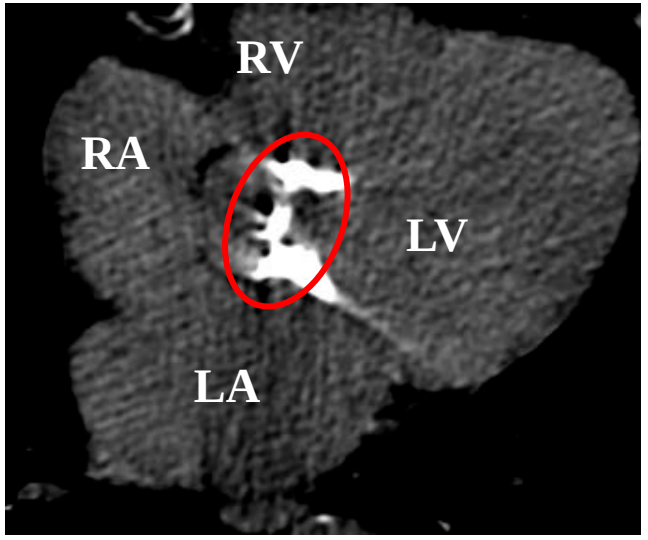
Examples of degree of AVC



Mild AVC. Score = 200 AU



Moderate AVC. score = 800



Severe AVC. Score = 2000

Why do I need another imaging modality?

1. Diagnosis of AS severity

2. Prognosis of AS

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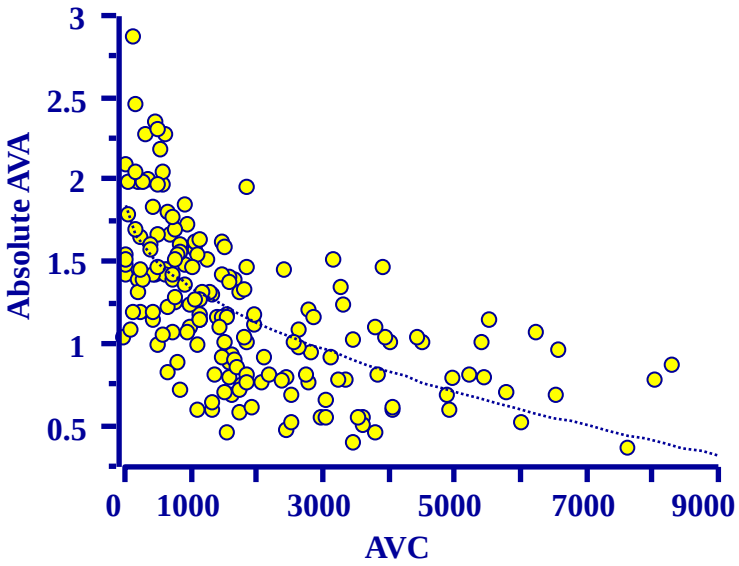
1. Diagnosis of AS severity

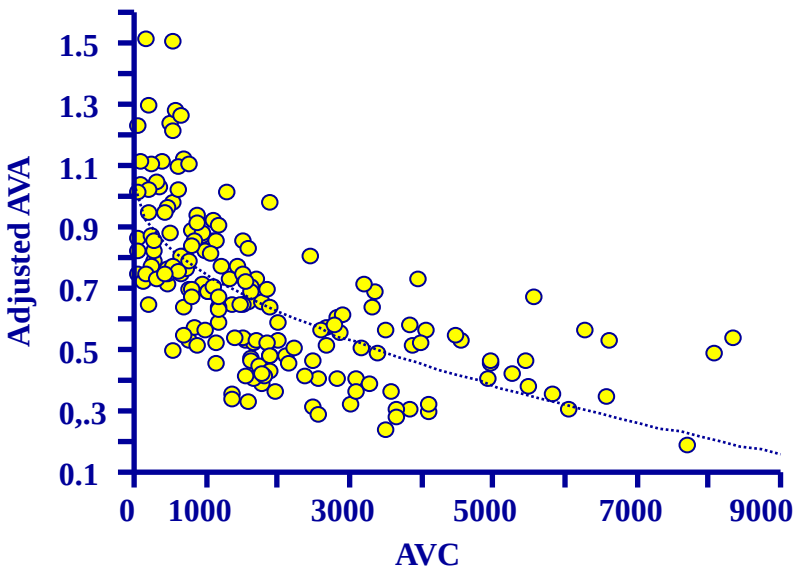
2. Prognosis of AS

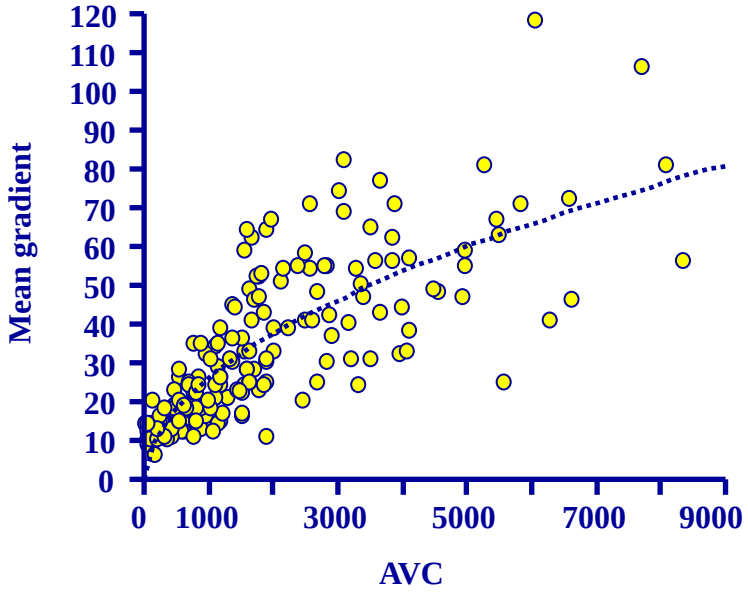
When do I need another imaging modality?

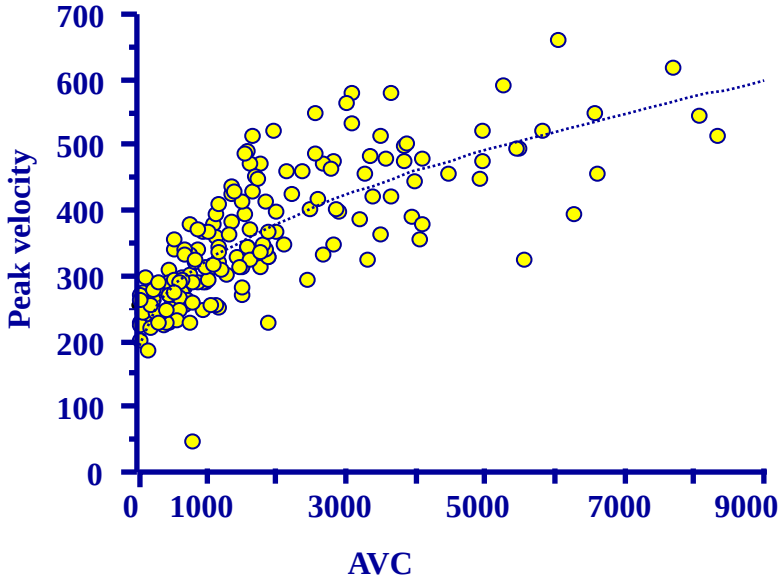
- Poor echocardiographic windows
- Discrepancies between symptoms and echocardiographic measurements
- Discordant grading AVA / MPG
  - Low EF
  - Normal EF

Relationship between AVC and Hemodynamic Severity

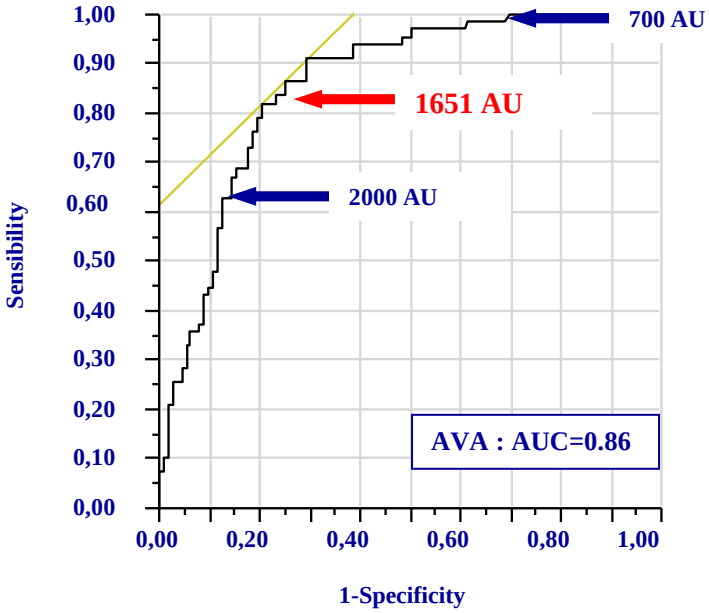


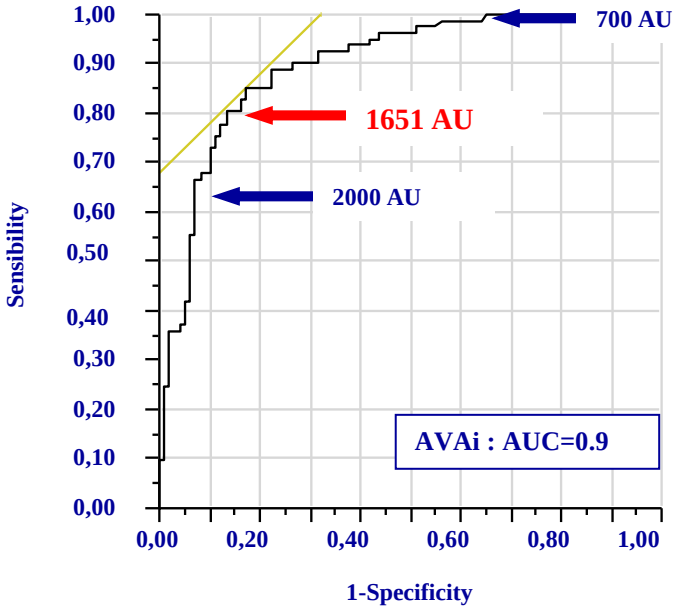


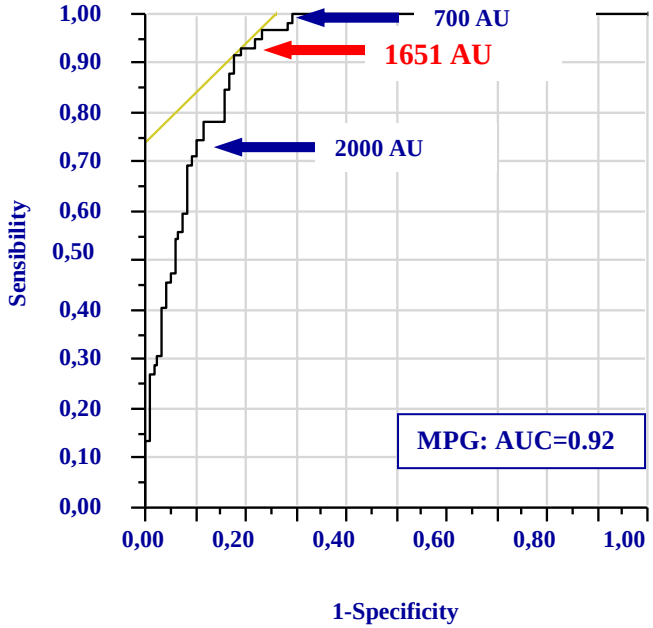


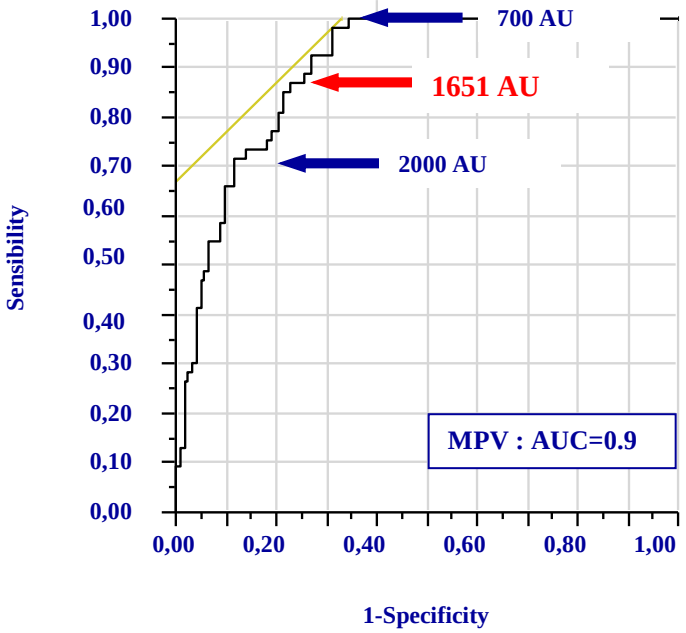


Cueff Heart 2011


Sensibility
1,00
0,90
0,80
0,70
0,60
0,50
0,40
0,30
0,20
0,10
0,00
0,00
0,20
0,40
0,60
0,80
1,00
1-Specificity
700 AU
1651 AU
2000 AU
AVA : AUC=0.86


Sensibility
1,00
0,90
0,80
0,70
0,60
0,50
0,40
0,30
0,20
0,10
0,00
0,00
0,20
0,40
0,60
0,80
1,00
1-Specificity
700 AU
1651 AU
2000 AU
AVAi : AUC=0.9


Sensibility
1,00
0,90
0,80
0,70
0,60
0,50
0,40
0,30
0,20
0,10
0,00
0,00
0,20
0,40
0,60
0,80
1,00
1-Specificity
700 AU
1651 AU
2000 AU
MPG: AUC=0.92


Sensibility
1,00
0,90
0,80
0,70
0,60
0,50
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0,30
0,20
0,10
0,00
0,00
0,20
0,40
0,60
0,80
1,00
1-Specificity
700 AU
1651 AU
2000 AU
MPV : AUC=0.9

Thresholds

Calcium Score	Sensitivity, %	Specificity, %	PPV, %	NPV, %
500	100	31	46	100
700	98	49	49	98
1000	94	65	55	94
1200	91	65	59	92
1651	**82**	**80**	**70**	**88**
2000	62	86	72	79
3000	57	91	74	72

Severe AS

	Sclerosis	Mild AS	Moderate AS	Severe AS	Very Severe AS
Peak velocity, m/sec	< 2.5	2.5 - 3	3 - 4	> 4	> 5.5
Mean gradient, mm Hg	Normal	< 25	25 – 40 (ou 50)	40 (US) 50 (Europe)	
AVA, cm²	Normal	≥ 1.5	1 – 1.5	< 1 cm² < 0.6 cm²/m²	
Calcium score, AU				**1650**	

Sex Differences in Aortic Valve Calcification Measured by Multidetector Computed Tomography in Aortic Stenosis

Shivani R. Aggarwal, MBBS*; Marie-Annick Clavel, DVM, PhD*; David Messika-Zeitoun, MD, PhD; Caroline Cueff, MD; Joseph Malouf, MD; Philip A. Araoz, MD; Rekha Mankad, MD; Hector Michelena, MD; Alec Vahanian, MD; Maurice Enriquez-Sarano, MD

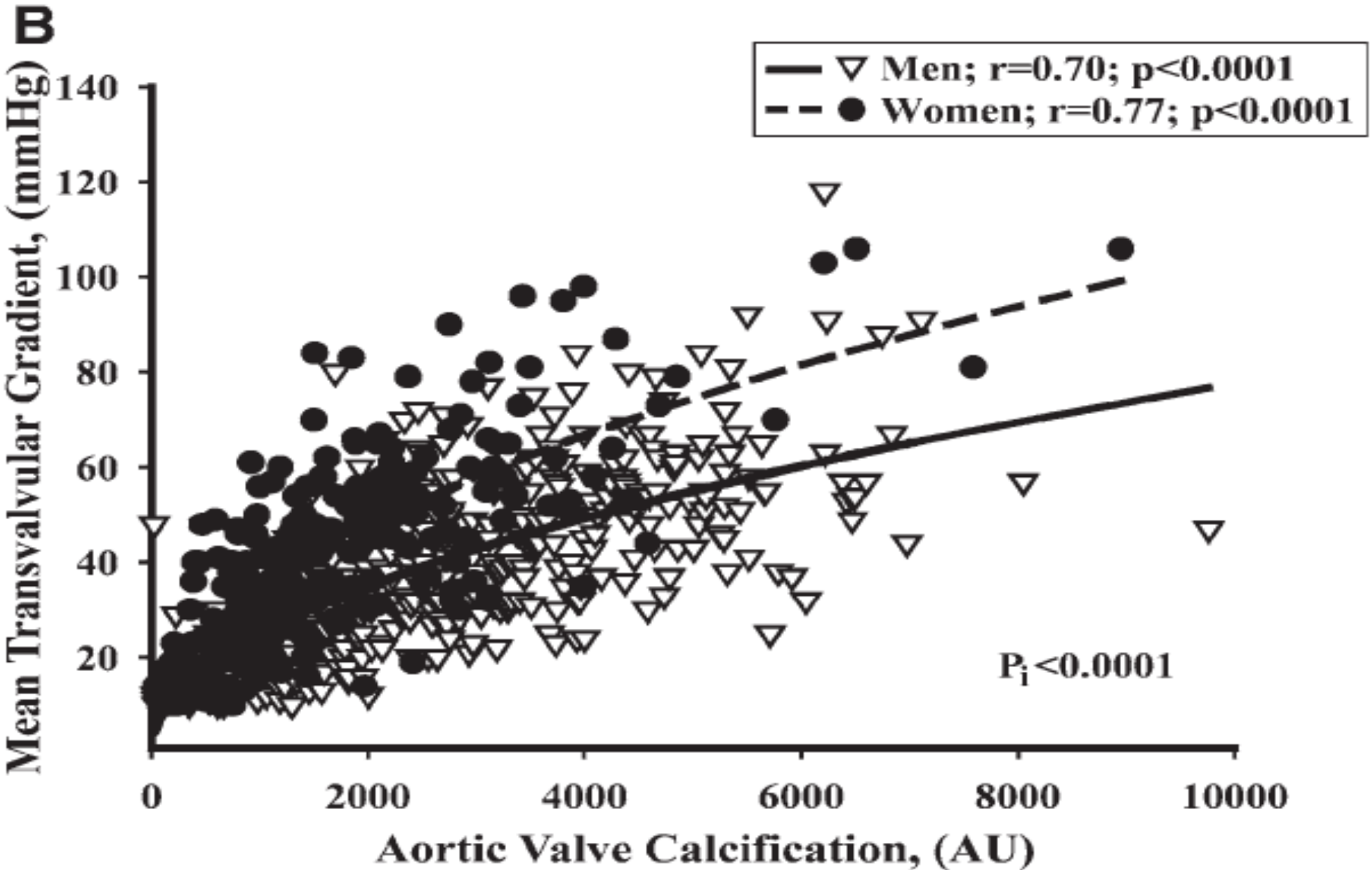
Background—Aortic valve calcification (AVC) is the intrinsic mechanism of valvular obstruction leading to aortic stenosis (AS) and is measurable by multidetector computed tomography. The link between sex and AS is controversial and that with AVC is unknown.

Methods and Results—We prospectively performed multidetector computed tomography in 665 patients with AS (aortic valve area, 1.05±0.35 cm^2; mean gradient, 39±19 mm Hg) to measure AVC and to assess the impact of sex on the AVC–AS severity link in men and women. AS severity was comparable between women and men (peak aortic jet velocity: 4.05±0.99 versus 3.93±0.91 m/s, P=0.11; aortic valve area index: 0.55±0.20 versus 0.56±0.18 cm^2/m^2; P=0.46). Conversely, AVC load was lower in women versus men (1703±1321 versus 2694±1628 arbitrary units; P<0.0001) even after adjustment for their smaller body surface area or aortic annular area (both P<0.0001). Thus, odds of high-AVC load were much greater in men than in women (odds ratio, 5.07; P<0.0001). Although AVC showed good associations with hemodynamic AS severity in men and women (all r>|0.67|; P<0.0001), for any level of AS severity measured by peak aortic jet velocity or aortic valve area index, AVC load, absolute or indexed, was higher in men versus women (all $P \leq 0.01$).

Conclusions—In this large AS population, women incurred similar AS severity than men for lower AVC loads, even after indexing for their smaller body size. Hence, the relationship between valvular calcification process and AS severity differs in women and men, warranting further pathophysiological inquiry. For AS severity diagnostic purposes, interpretation of AVC load should be different in men and in women. (***Circ Cardiovasc Imaging*. 2013;6:40-47.**)

Key Words: aortic valve calcification ■ aortic valve stenosis ■ Doppler echocardiography ■ multidetector computed tomography ■ sex differences

Sex Differences in Aortic Valve Calcification Measured by Multidetector Computed Tomography in Aortic Stenosis



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Mean gradient, mm Hg	Normal	< 25	25 – 40 (ou 50)	40 (US) 50 (Europe)	
AVA, cm^2	Normal	≥ 1.5	1 – 1.5	< 1 cm^2 < 0.6 cm^2/m^2	
Calcium score, AU				**Male 2000 Female 1250**	

When do I need another imaging modality?

- Poor echocardiographic windows
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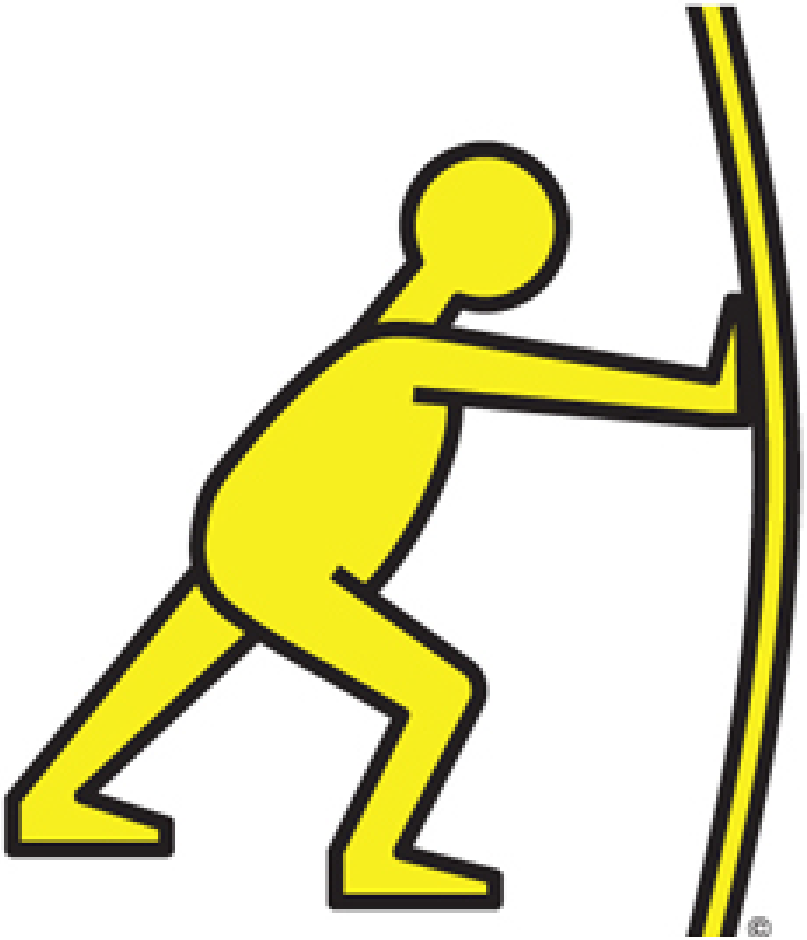
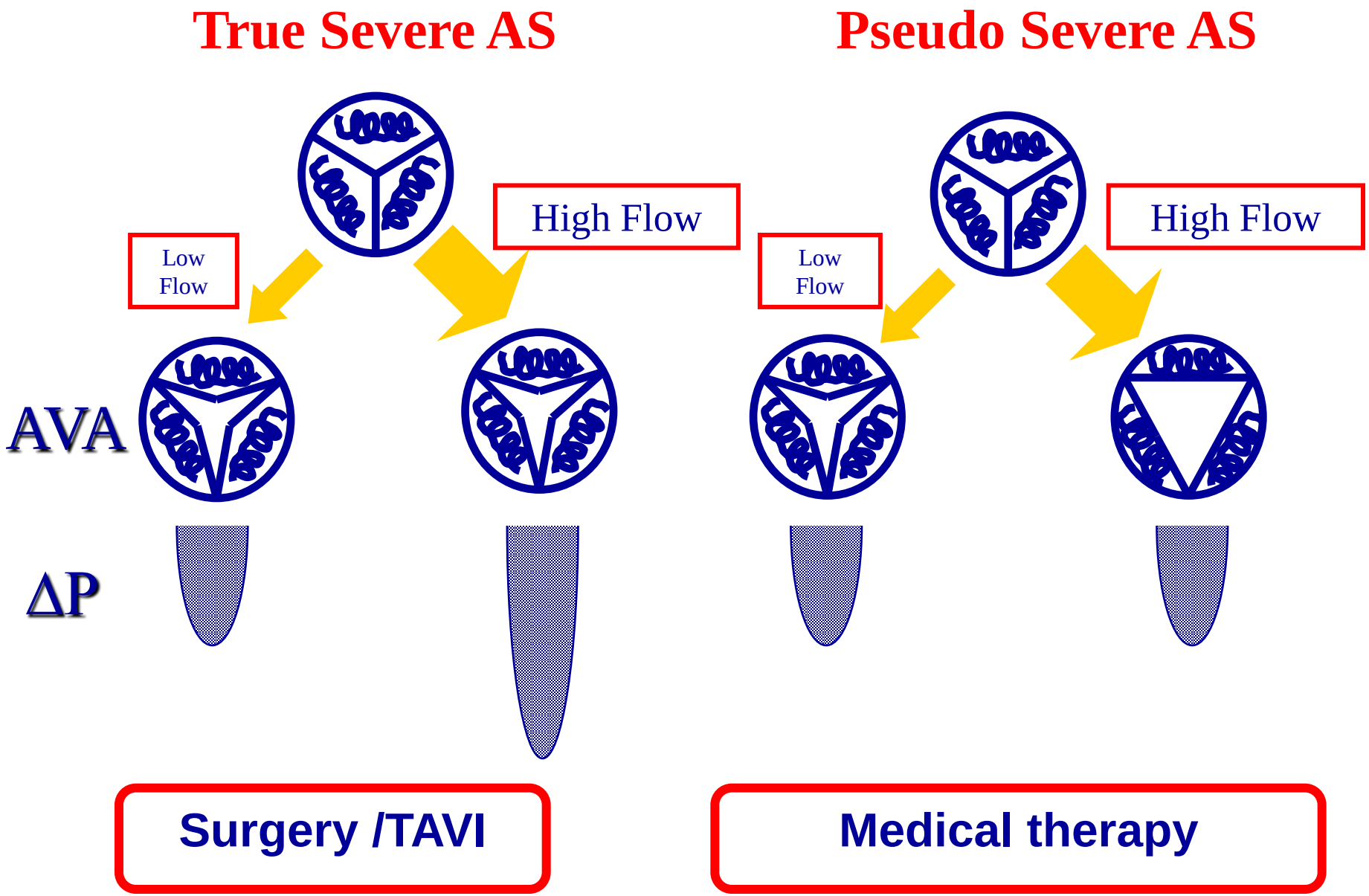
  - Low EF
  - Normal EF

Low gradient / Low EF



PUSH

Dobutamine Echocardiography



Low Gradient – Low Output
Low EF

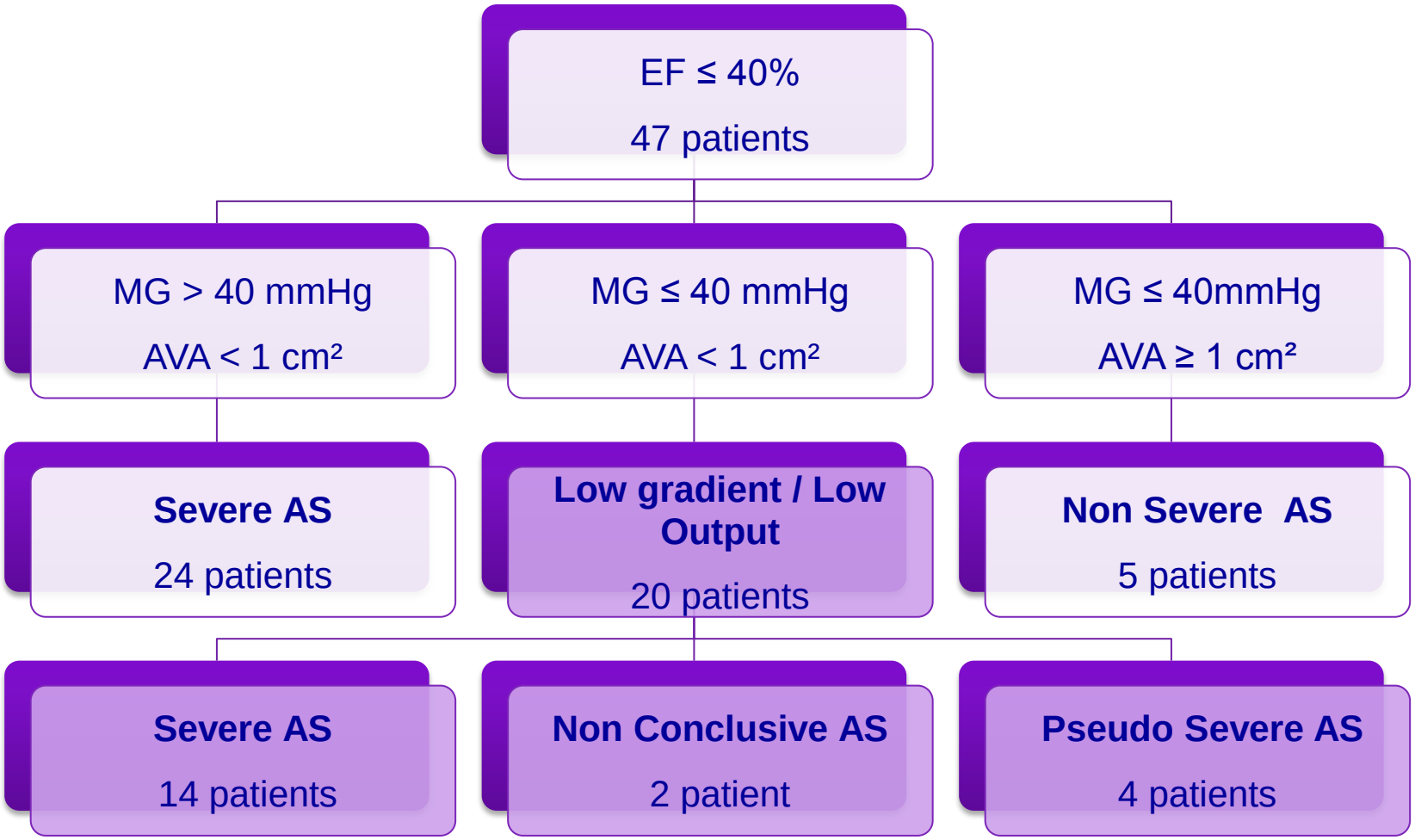
Dobutamine
up to 20 µg/kg/min

Not always easy

Non conclusive

Monin Circulation 2003; 108: 319-324

47 patients with Low EF



Cueff Heart 2011

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- Discordant grading AVA / MPG
  - Low EF
  - Normal EF

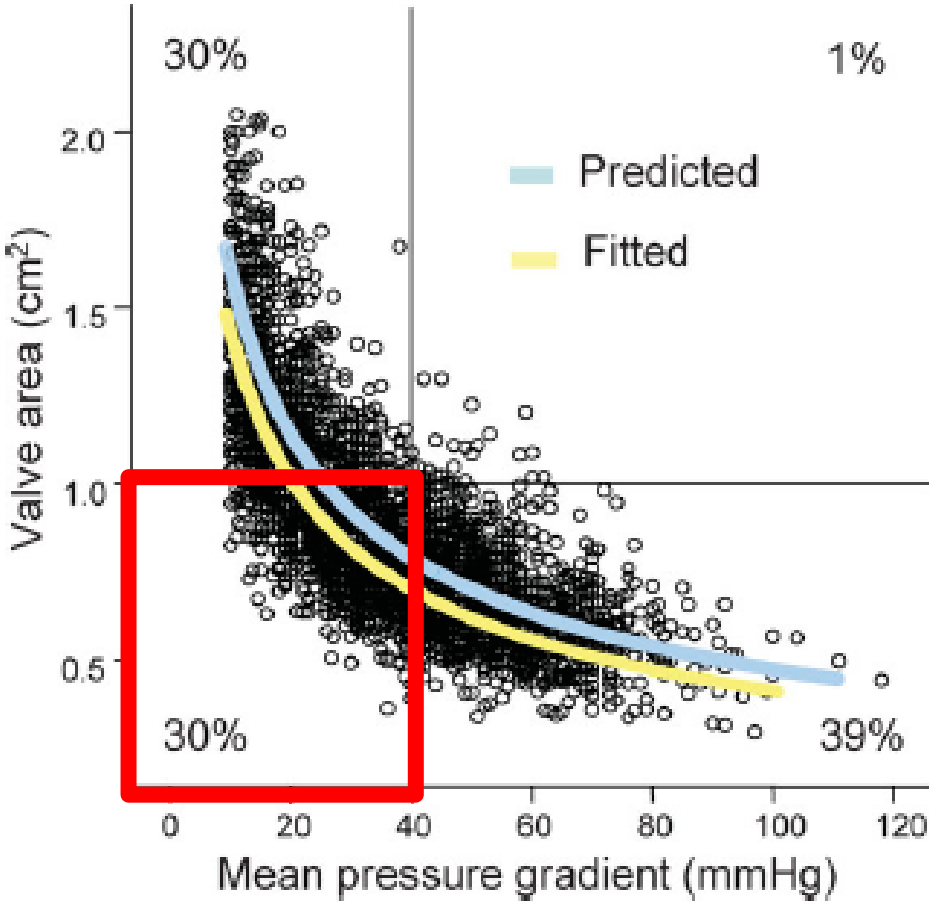
Discordant grading – Normal EF

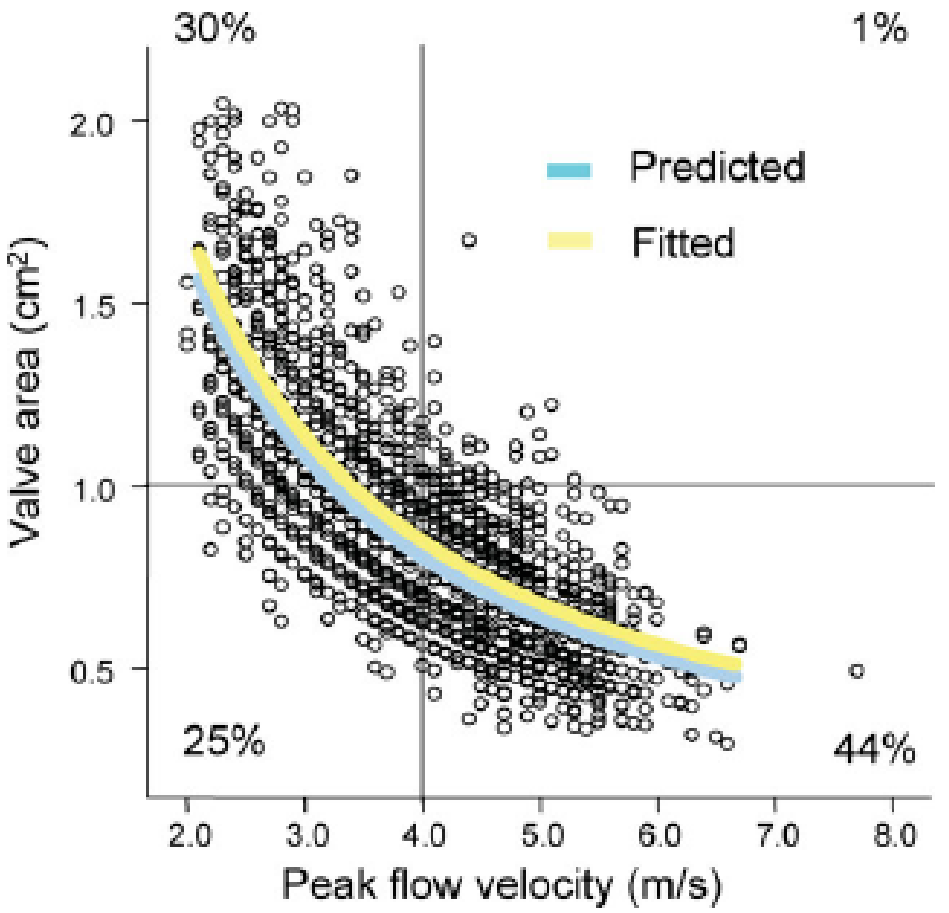
	Sclerosis	Mild AS	Moderate AS	Severe AS
Peak velocity, m/sec	< 2.5	2.5 - 3	**< 4**	> 4
Mean gradient, mm Hg	Normal	< 25	**< 40**	40 (US) 50 (Europe)
AVA, cm²	Normal	≥ 1.5	1 – 1.5	**< 1**

European Heart Journal (2008) 29, 1043–1048
doi:10.1093/eurheartj/ehm543

Inconsistencies of echocardiographic criteria for the grading of aortic valve stenosis

Jan Minners*, Martin Allgeier, Christa Gohlke-Baerwolf, Rolf-Peter Kienzle, Franz-Josef Neumann, and Nikolaus Jander

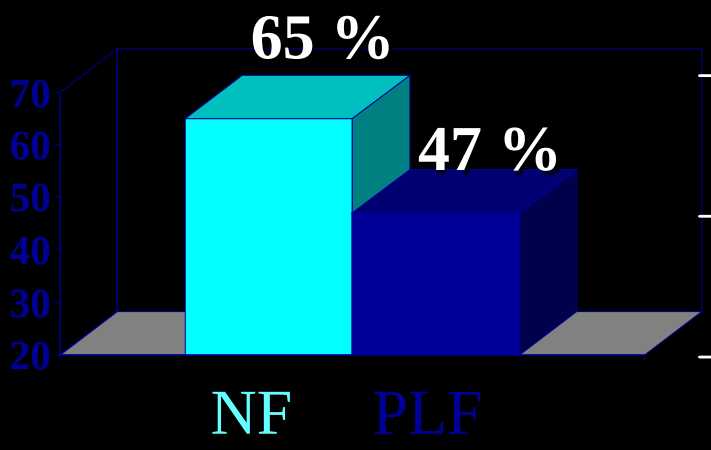


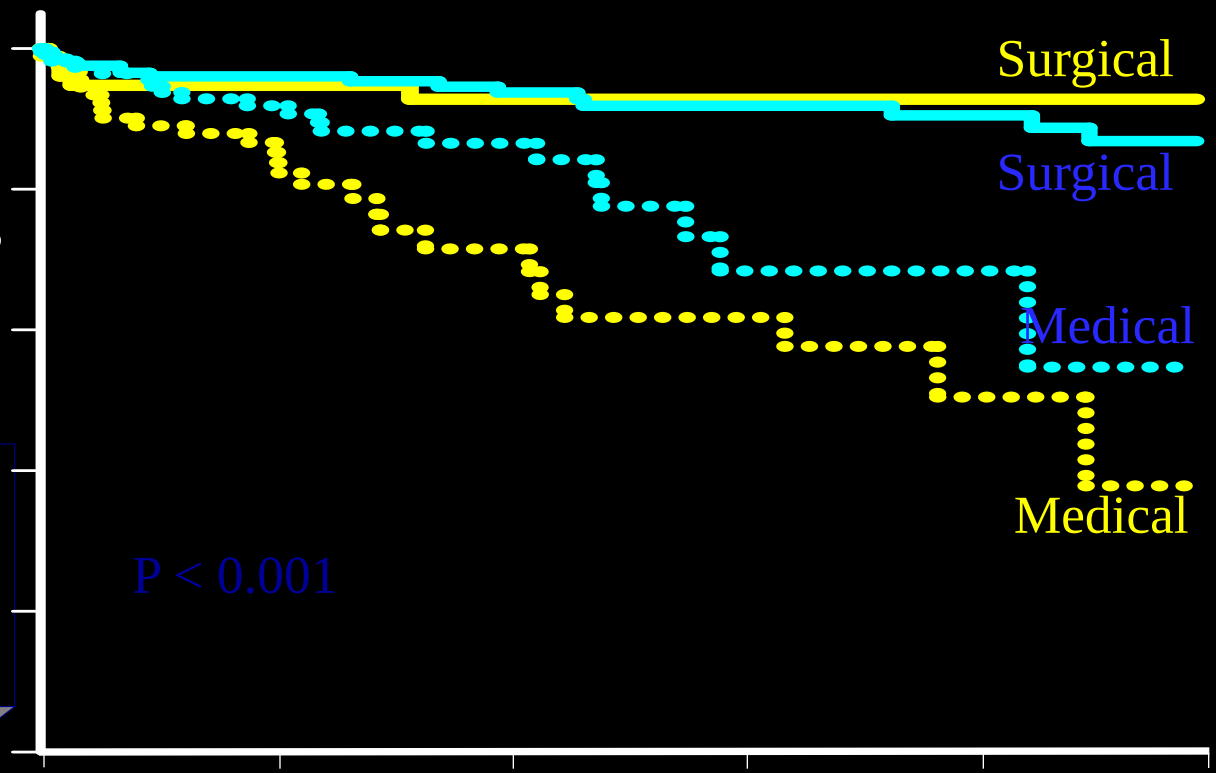


Outcome of Patients with PLF

512 Patients with LVEF ≥ 50%

Percentage of Patients Treated Surgically



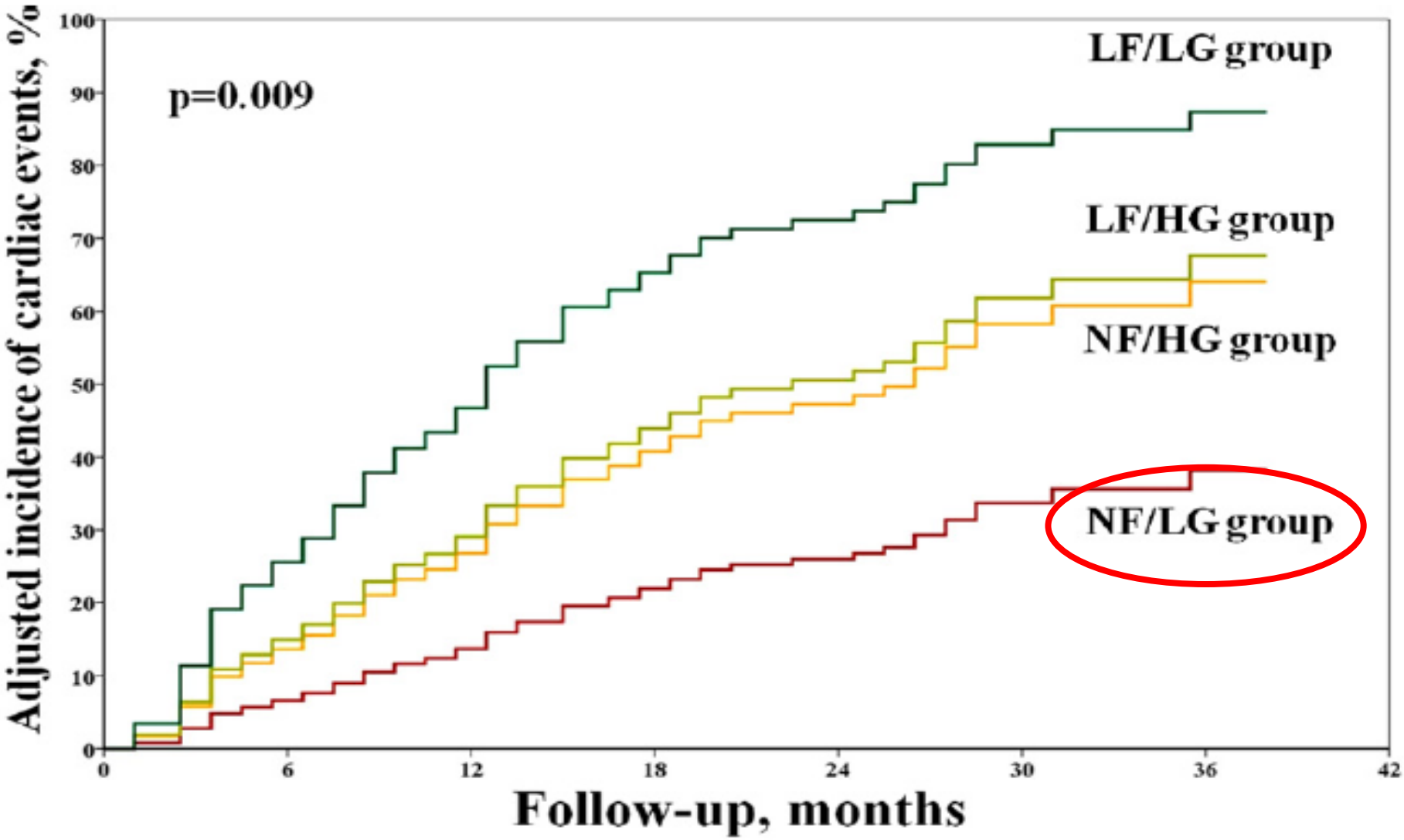


NF: Normal Flow: SVI>35 (65%)

PLF: Paradoxical Low Flow: SVI≤35

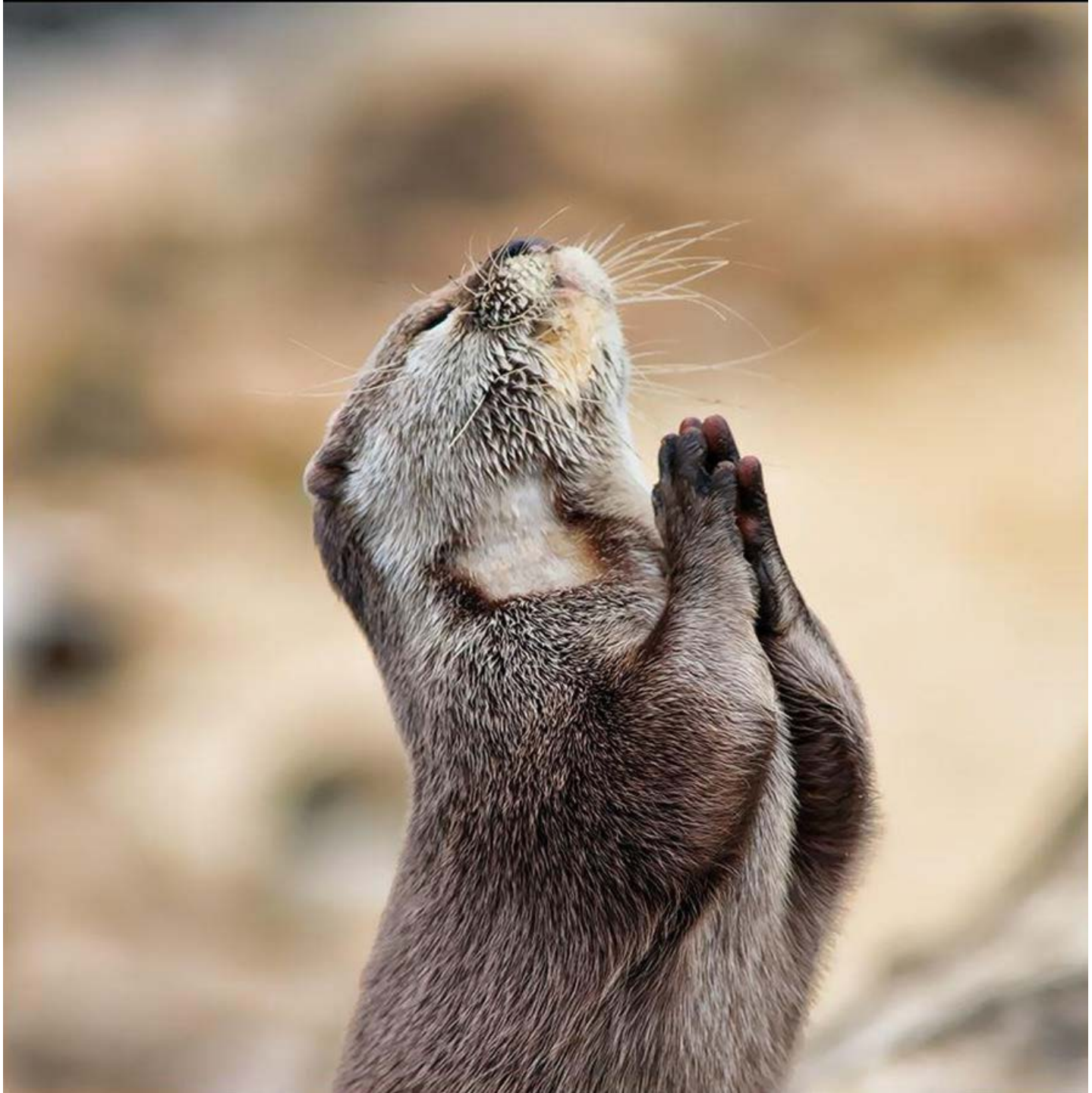
Clinical Outcome in Asymptomatic Severe Aortic Stenosis

Insights From the New Proposed Aortic Stenosis Grading Classification



Severe AS ?

High flow High gradient **G > 40 mm Hg** **Flow ≥ 35 ml/m²** 	**High flow low gradient** **G < 40 mm Hg** **Flow ≥ 35 ml/m²** 
Low flow High gradient **G > 40 mm Hg** **Flow < 35 ml/m²** 	**Low flow low gradient** **G < 40 mm Hg** **Flow < 35 ml/m²** 



The Complex Nature of Discordant Severe Calcified Aortic Valve Disease Grading

New Insights From Combined Doppler Echocardiographic and Computed Tomographic Study

Marie-Annick Clavel, DVM, PHD,* David Messika-Zeitoun, MD, PHD,†‡ Philippe Pibarot, DVM, PHD,§ Shivani R. Aggarwal, MBBS,* Joseph Malouf, MD,* Phillip A. Araoz, MD,* Hector I. Michelena, MD,* Caroline Cueff, MD,† Eric Larose, MD, MSC,§ Romain Capoulade, MSC,§ Alec Vahanian, MD,†‡ Maurice Enriquez-Sarano, MD*

Rochester, Minnesota; Paris, France; and Quebec City, Québec, Canada

Objectives With concomitant Doppler echocardiography and multidetector computed tomography (MDCT) measuring aortic valve calcification (AVC) load, this study aimed at defining: 1) independent physiologic/structural determinants of aortic valve area (AVA)/mean gradient (MG) relationship; 2) AVC thresholds best associated with severe aortic stenosis (AS); and 3) whether, in AS with discordant MG, severe calcified aortic valve disease is generally detected.

Background Aortic stenosis with discordant markers of severity, AVA in severe range but low MG, is a conundrum, unresolved by outcome studies.

Methods Patients ($n = 646$) with normal left ventricular ejection fraction AS underwent Doppler echocardiography and AVC measurement by MDCT. On the basis of AVA-indexed-to-body surface area (AVAi) and MG, patients were categorized as concordant severity grading (CG) with moderate AS (AVAi >0.6 cm^2/m^2, MG <40 mm Hg), severe AS (AVAi ≤ 0.6 cm^2/m^2, MG ≥ 40 mm Hg), discordant-severity-grading (DG) with low-MG (AVAi ≤ 0.6 cm^2/m^2, MG <40 mm Hg), or high-MG (AVAi >0.6 cm^2/m^2, MG ≥ 40 mm Hg).

Results The MG (discordant in 29%) was strongly determined by AVA and flow but also independently and strongly influenced by AVC-load ($p < 0.0001$) and systemic arterial compliance ($p < 0.0001$). The AVC-load (median [interquartile range]) was similar within patients with DG (low-MG: 1,619 [965 to 2,528] arbitrary units [AU]; high-MG: 1,736 [1,209 to 2,894] AU; $p = 0.49$), higher than CG-moderate-AS (861 [427 to 1,519] AU; $p < 0.0001$) but lower than CG-severe-AS (2,931 [1,924 to 4,292] AU; $p < 0.0001$). The AVC-load thresholds separating severe/moderate AS were defined in CG-AS with normal flow (stroke-volume-index >35 ml/m^2). The AVC-load, absolute or indexed, identified severe AS accurately (area under the curve ≥ 0.89, sensitivity $\geq 86\%$, specificity $\geq 79\%$) in men and women. Upon application of these criteria to DG-low MG, at least one-half of the patients were identified as severe calcified aortic valve disease, irrespective of flow.

Conclusions Among patients with AS, MG is often discordant from AVA and is determined by multiple factors, valvular (AVC) and non-valvular (arterial compliance) independently of flow. The AVC-load by MDCT, strongly associated with AS severity, allows diagnosis of severe calcified aortic valve disease. At least one-half of the patients with discordant low gradient present with heavy AVC-load reflective of severe calcified aortic valve disease, emphasizing the clinical yield of AVC quantification by MDCT to diagnose and manage these complex patients. (J Am Coll Cardiol 2013;62:2329–38)

The Complex Nature of Discordant Severe Calcified Aortic Valve Disease Grading

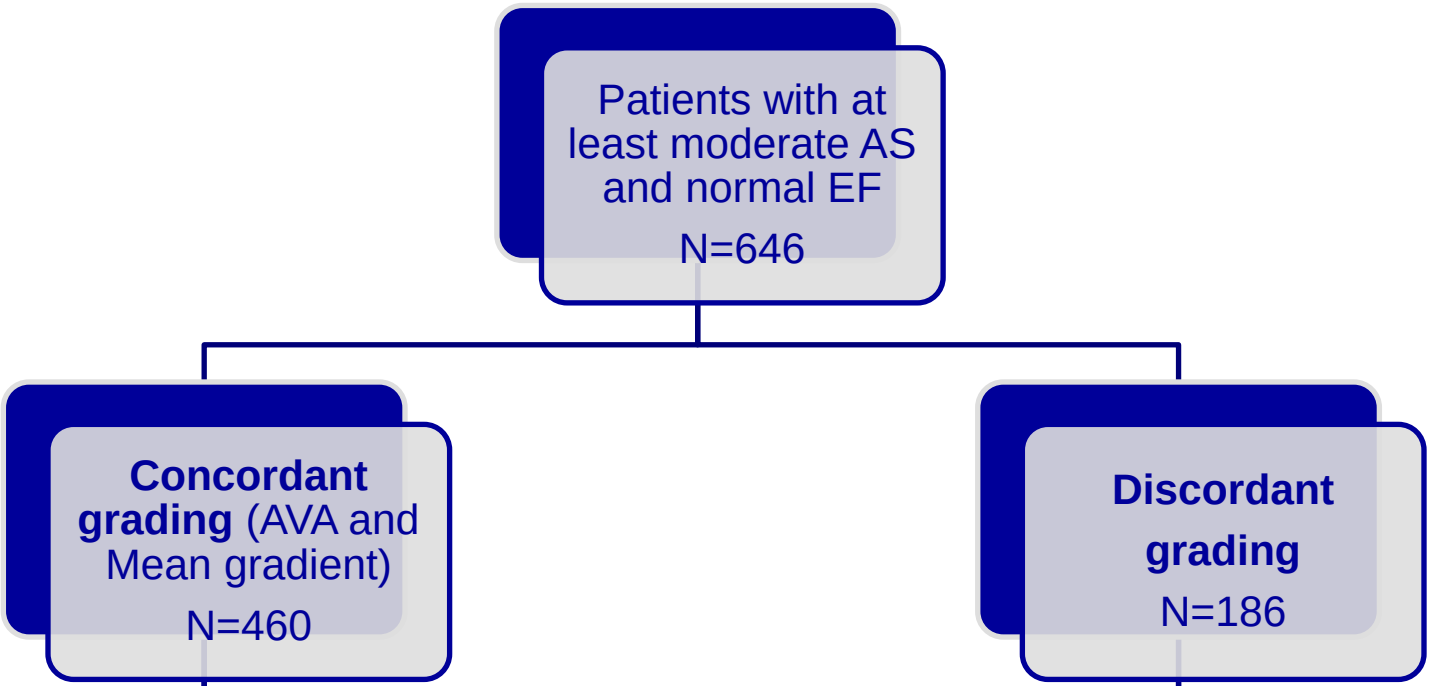
New Insights From Combined Doppler Echocardiographic and Computed Tomographic Study

Patients with at least moderate AS and normal EF

N=646

The Complex Nature of Discordant Severe Calcified Aortic Valve Disease Grading

New Insights From Combined Doppler Echocardiographic and Computed Tomographic Study



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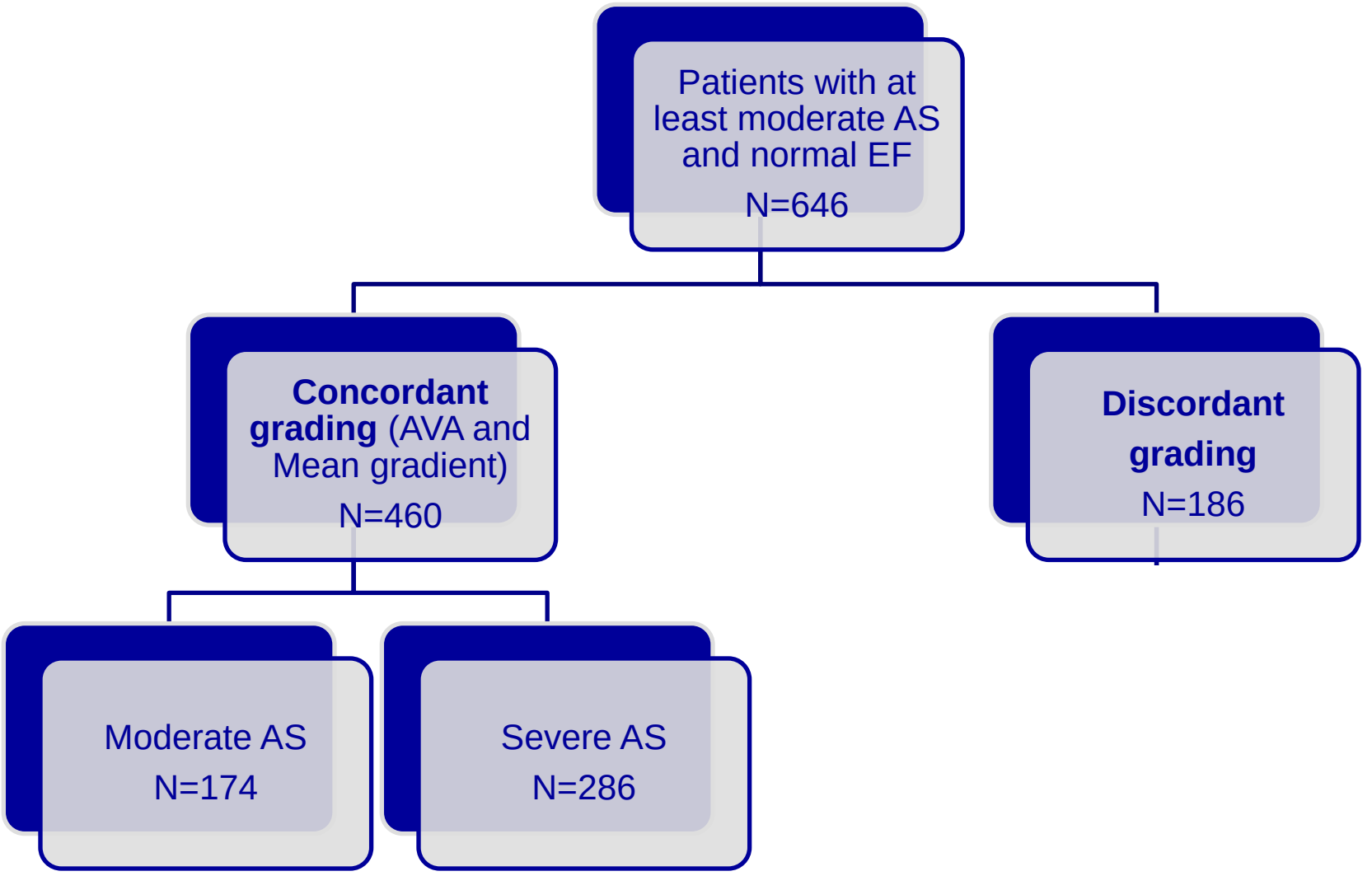
New Insights From Combined Doppler Echocardiographic and Computed Tomographic Study



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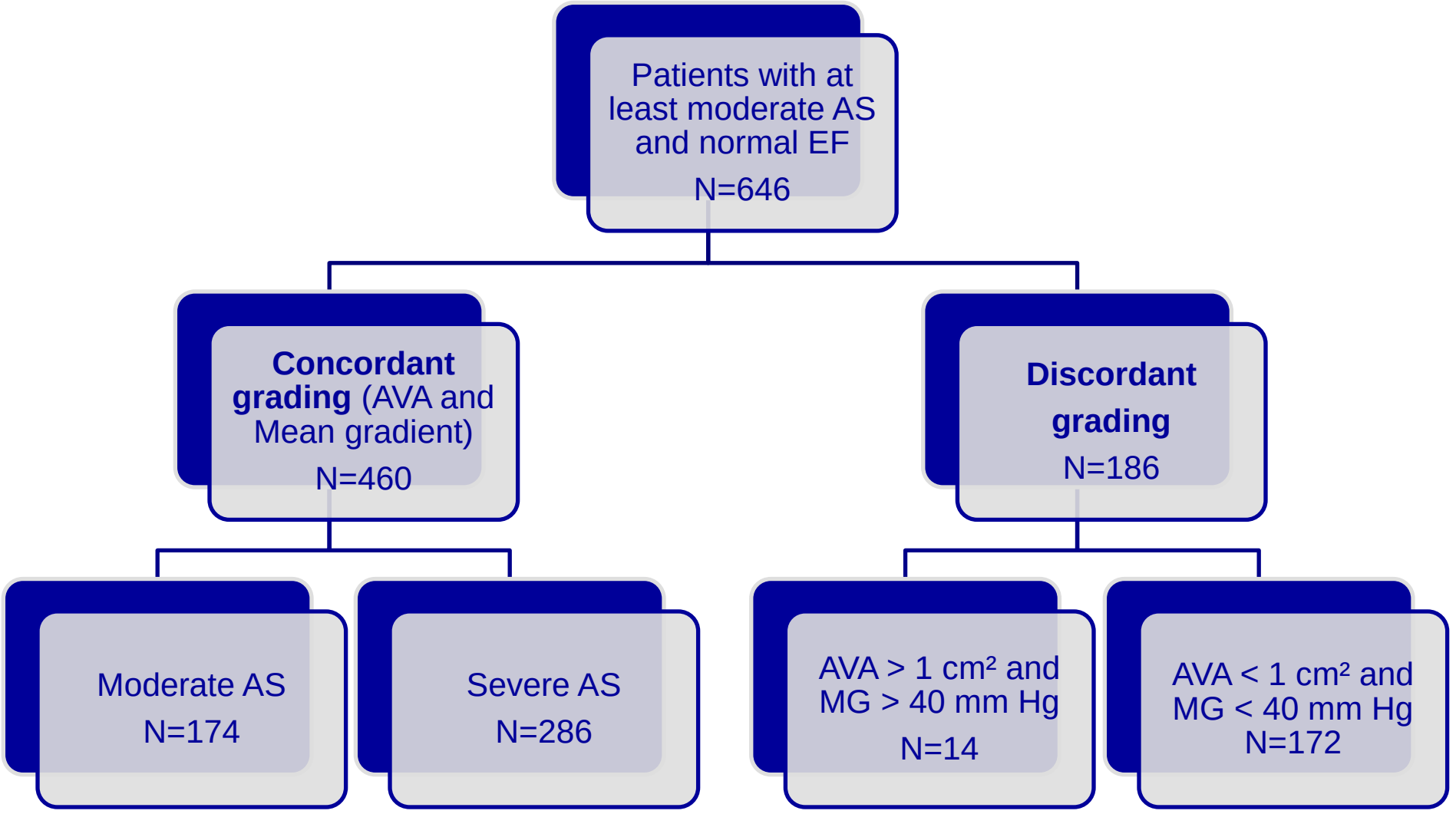
New Insights From Combined Doppler Echocardiographic and Computed Tomographic Study



The Complex Nature of Discordant Severe Calcified Aortic Valve Disease Grading

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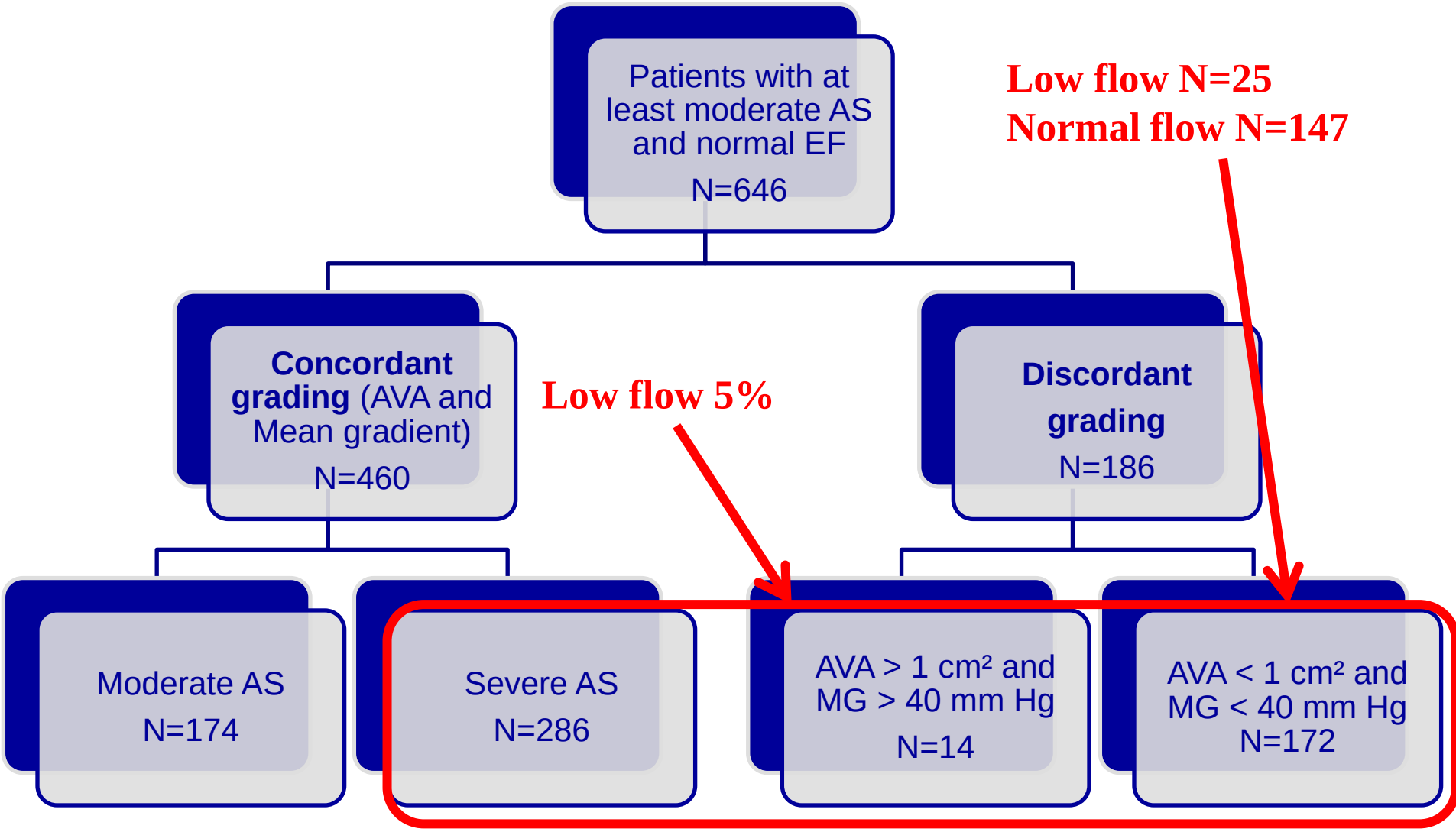


The Complex Nature of Discordant Severe Calcified Aortic Valve Disease Grading

New Insights From Combined Doppler Echocardiographic and Computed Tomographic Study

		Patients with Concordant Grading	
AVC showing severe AS, n (%):		Moderate AS (n=174)	Severe AS (n=286)
Absolute AVC	Best Cut-off	28 (16)	251 (88)
AVCd	Best Cut-off	33 (19)	260 (91)

The Complex Nature of Discordant Severe Calcified Aortic Valve Disease Grading

New Insights From Combined Doppler Echocardiographic and Computed Tomographic Study

Half of patients with paradoxical low gradient AS have severe AS based on measurement of Aortic valve calcification

		Patients with Discordant Grading	
		High MG (n=14)	Low MG (n=172)
Absolute AVC	Best Cut-off	10 (71)	77 (45)
AVCd	Best Cut-off	10 (71)	91 (53)

Irrespective of the flow +++

Look for

- Small body surface area
- Errors measurements
- Hypertension

Fraction

Reduced

Gradient < 40 mm Hg
Peak velocity < 4 m/sec
AVA < 1cm²

Normal SV

Low SV

Gradient < 40 mm Hg
Peak velocity < 4 m/sec
AVA > 1cm²

Moderate AS

Gradient > 40 mm Hg
Peak velocity > 4 m/sec
AVA < 1cm²

Gradient > 40 mm Hg
Peak velocity > 4 m/sec
AVA > 1cm²

Dobutamine
and Calcium scoring

Severe AS

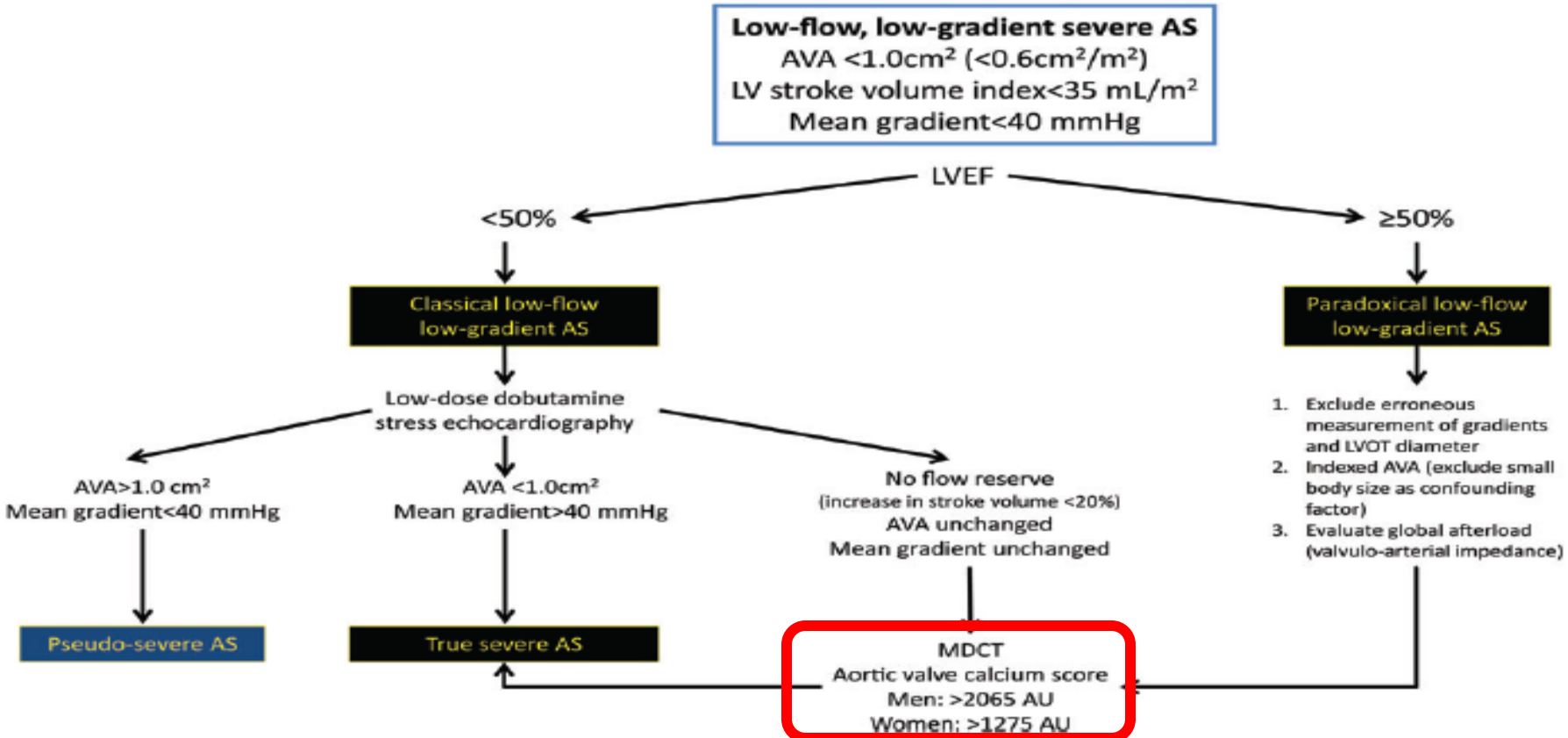
Pseudo-severe AS

Pseudo-severe AS

Severe AS

Open issues in transcatheter aortic valve implantation. Part 1: patient selection and treatment strategy for transcatheter aortic valve implantation

Jeroen J. Bax[1]*, Victoria Delgado[1], Vinayak Bapat[2], Helmut Baumgartner[3], Jean P. Collet[4], Raimund Erbel[5], Christian Hamm[6], Arie P. Kappetein[7], Jonathon Leipsic[8], Martin B. Leon[9], Philip MacCarthy[10], Nicolo Piazza[11,12], Philippe Pibarot[13], William C. Roberts[14], Josep Rodés-Cabau[15], Patrick W. Serruys[7], Martyn Thomas[2], Alec Vahanian[16], John Webb[8], Jose Luis Zamorano[17], and Stephan Windecker[18]



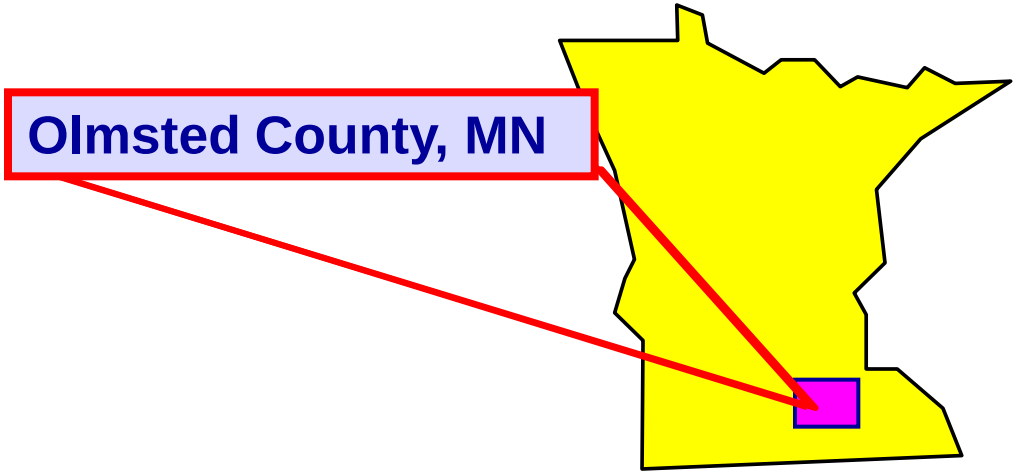
Why do I need another imaging modality?

1. Diagnosis of AS severity

2. Prognosis of AS

Determinants of the Progression of Aortic Valve Calcification

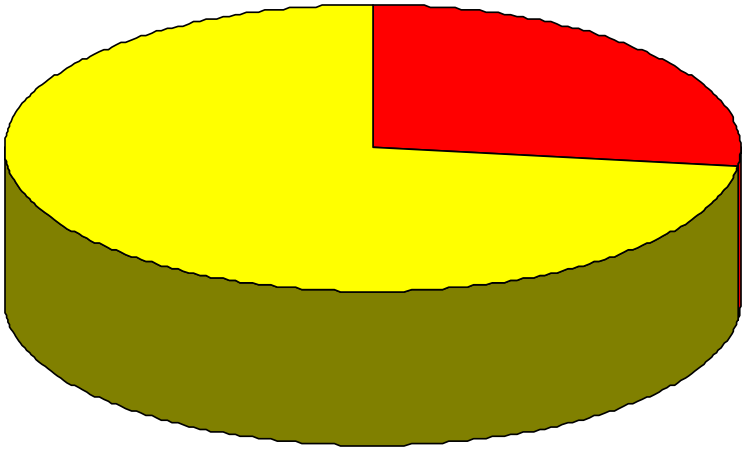
- Epidemiology of Coronary Artery Calcification Study
- Ongoing population-based study part of the Rochester Family Heart study.
- Baseline extensive evaluation of cardiovascular risk factors and EBCT.



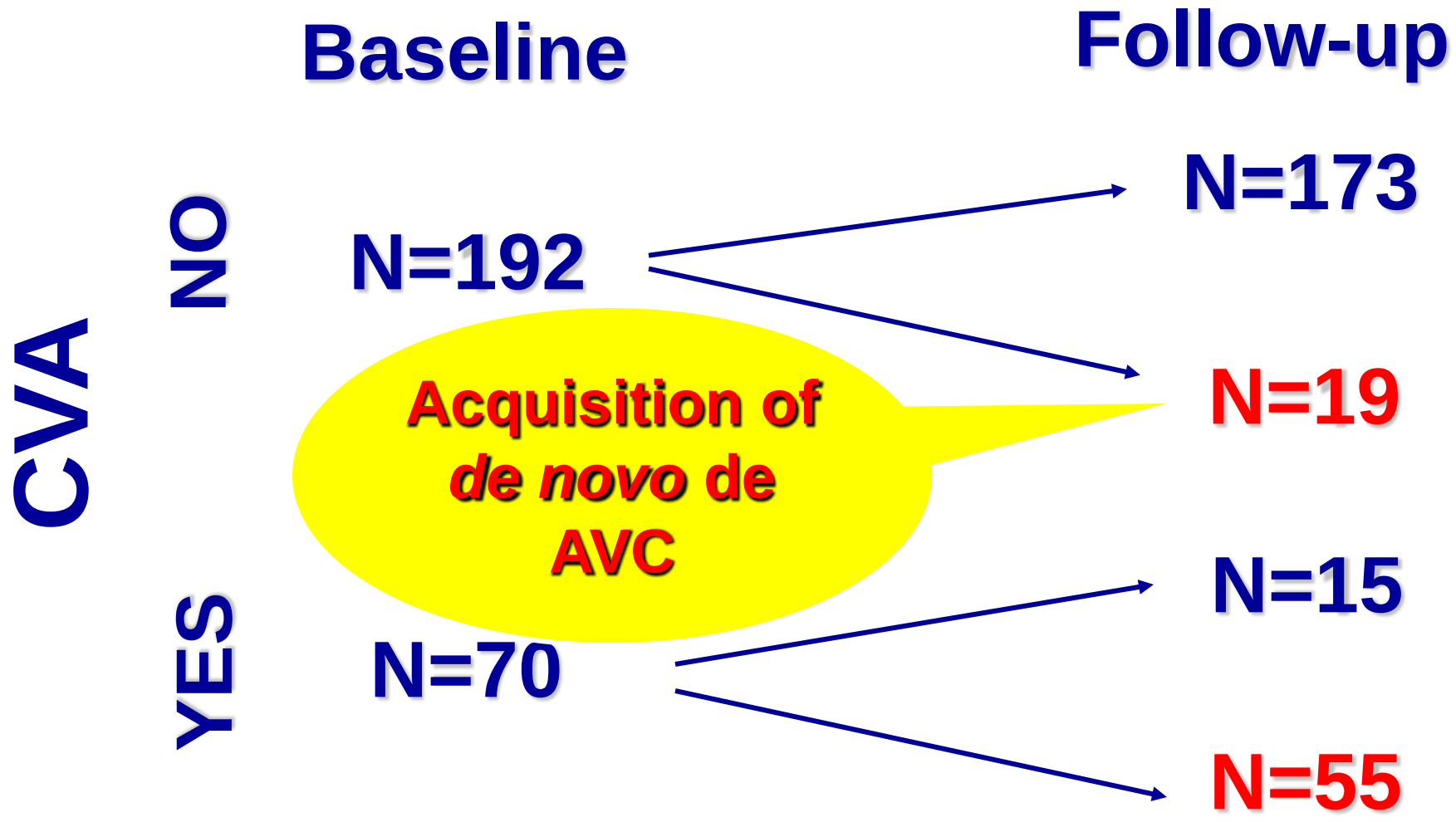
Prevalence of Aortic Valve Calcifications

- Score : 54±173 (0 to 1944)
- Baseline characteristics
  - 262 participants
  - 68±5 years
  - Male: 43%
  - Body mass index: 29±5 kg/m^2
  - History of smoking: 124 (47%)
  - Hypertension: 179 (68%)
  - Diabetes under medical therapy: 25 (10%)
  - History of CAD: 25 (10%)
  - Total cholesterol: 210±34 mg/dL
  - LDL-cholesterol: 122±29 mg/dL

27%

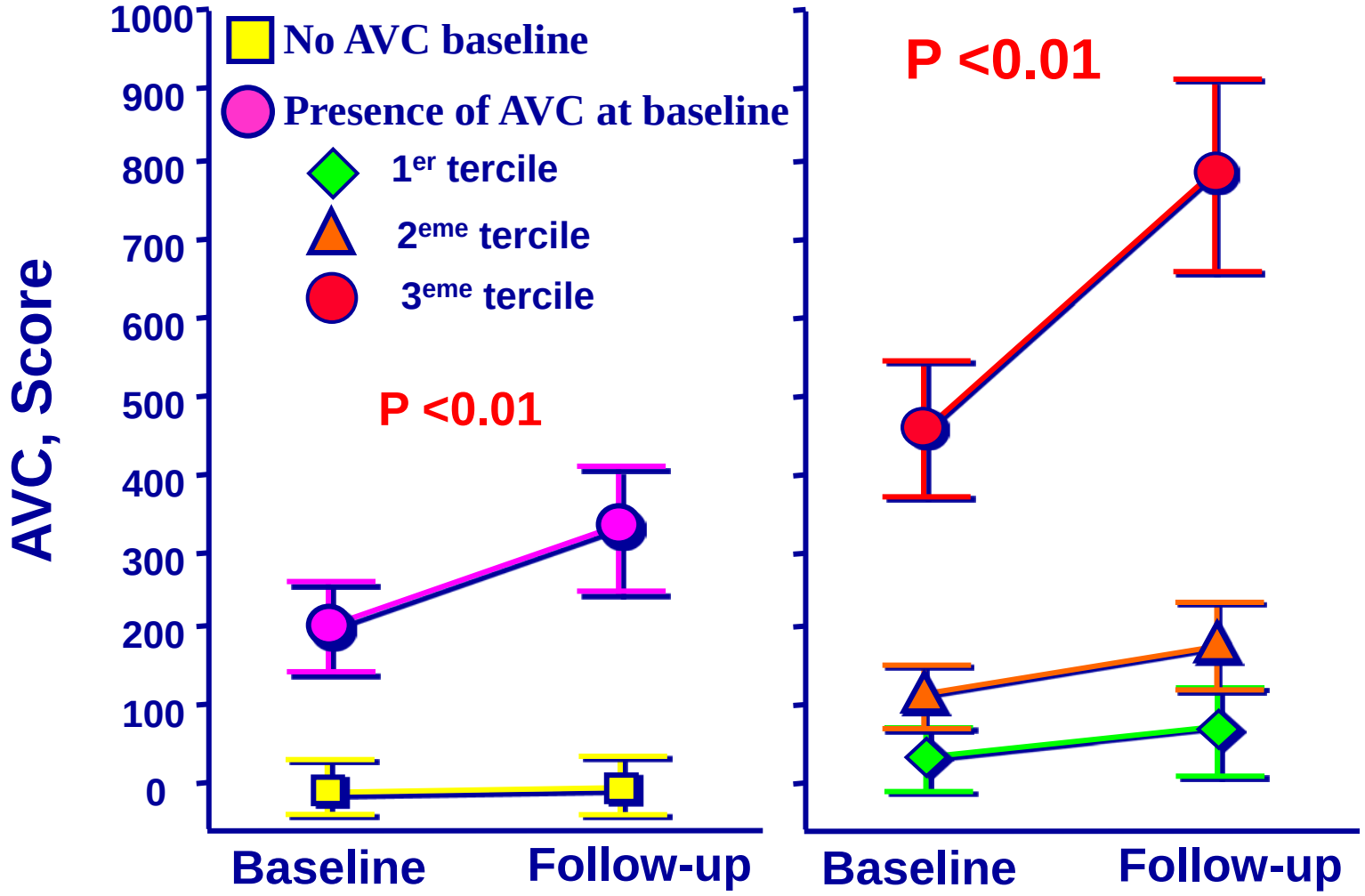


Progression of Aortic Valve Calcification



	No AVC at follow-up (n=173)	Acquisition of AVC (n=19)	Established AVC (n=70)
Age, years	67±5	67±4	70±5
Male gender, %	40	37	53
Body mass index, kg/m^2	28±5	28±5	30±6
Systolic blood pressure, mmHg	132±17	140±22	138±20
Pack year	12±19	13±17	18±28
History of hypertension, %	66	58	77
Diabetes under medical therapy, %	6	16	17
Glucose, mg/L	98±24	103±27	109±40
Total cholesterol, mg/dL	209±33	235±39	205±35
LDL-C, mg/dL	121±27	141±31	120±31
Fibrinogene, mg/dL	318±75	351±65	340±93
Baseline CAC score	223±503	668±940	331±481
Follow-up CAC score	328±637	966±1214	513±610
CAC annualized progression rate	29±47	78±87	53±58
AVC annualized progression rate	0±1	9±8	39±53

Progression faster with AVC Load



Predictors of aortic progression

LDL-cholesterol was the only independent determinant of acquisition of aortic calcification and aortic score of progression of aortic calcification in participants with established calcifications

Haemodynamic and anatomic progression of aortic stenosis

Virginia Nguyen,[1,2,3] Claire Cimadevilla,[1,2] Candice Estellat,[4] Isabelle Codogno,[1] Virginie Huart,[5] Joelle Benessiano,[5] Xavier Duval,[6] Philippe Pibarot,[7] Marie Annick Clavel,[8] Maurice Enriquez-Sarano,[8] Alec Vahanian,[1,2,3] David Messika-Zeitoun[1,2,3]

ABSTRACT

Background Aortic valve stenosis (AS) is a progressive disease, but the impact of baseline AS haemodynamic or anatomic severity on AS progression remains unclear.

Methods In 149 patients (104 mild AS, 36 moderate AS and 9 severe AS) enrolled in 2 ongoing prospective cohorts (COFRASA/GENERAC), we evaluated AS haemodynamic severity at baseline and yearly, thereafter, using echocardiography (mean pressure gradient (MPG)) and AS anatomic severity using CT (degree of aortic valve calcification (AVC)).

Results After a mean follow-up of 2.9±1.0 years, mean MGP increased from 22±11 to 30±16 mm Hg (+3±3 mm Hg/year), and mean AVC from 1108±891 to 1640±1251 AU (arbitrary units) (+188±176 AU/year). Progression of AS was strongly related to baseline haemodynamic severity (+2±3 mm Hg/year in mild AS, +4±3 mm Hg/year in moderate AS and +5±5 mm Hg/year in severe AS (p=0.01)), and baseline haemodynamic severity was an independent predictor of haemodynamic progression (p=0.0003). Annualised haemodynamic and anatomic progression rates were significantly correlated (r=0.55, p<0.0001), but AVC progression rate was also significantly associated with baseline haemodynamic severity (+141±133 AU/year in mild AS, +279±189 AU/year in moderate AS and +361±293 AU/year in severe AS, p<0.0001), and both baseline MPG and baseline AVC were independent determinants of AVC progression (p<0.0001).

Conclusions AS progressed faster with increasing haemodynamic or anatomic severity. Our results suggest that a medical strategy aimed at preventing AVC progression may be useful in all subsets of patients with AS including those with severe AS and support the recommended closer follow-up of patients with AS as AS

(AVC) is the main process leading to AS, and can be accurately and quantitatively measured (calcium score) in vivo using multislice CT (MSCT).[5 6] The degree of AVC—AS anatomic severity—is closely related to AS haemodynamic severity as assessed using echocardiography and can be considered as a complementary method for the evaluation of severity of AS in difficult clinical situations.[7 8]

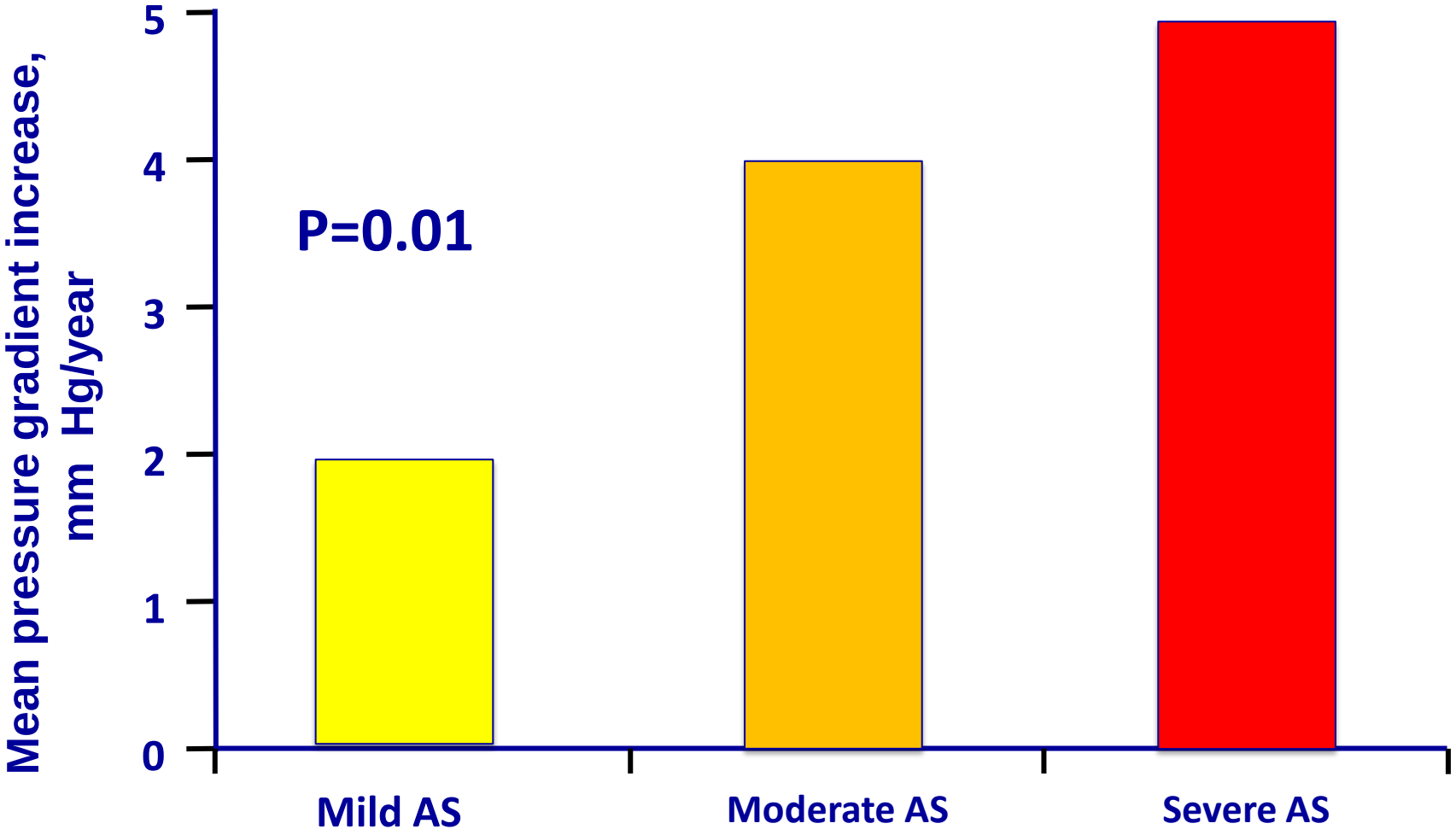
Calcific AS is a progressive disease,[9] and despite recent progress, determinants of AS progression remain unclear. AS progression is highly variable among individuals, and the impact of baseline—haemodynamic or anatomic—AS severity remains unknown. Thus, in 2 ongoing prospective cohorts, we aimed to evaluate the impact of baseline AS severity assessed, either by using echocardiography (haemodynamic assessment) or MSCT (anatomic assessment) on AS progression.

METHODS

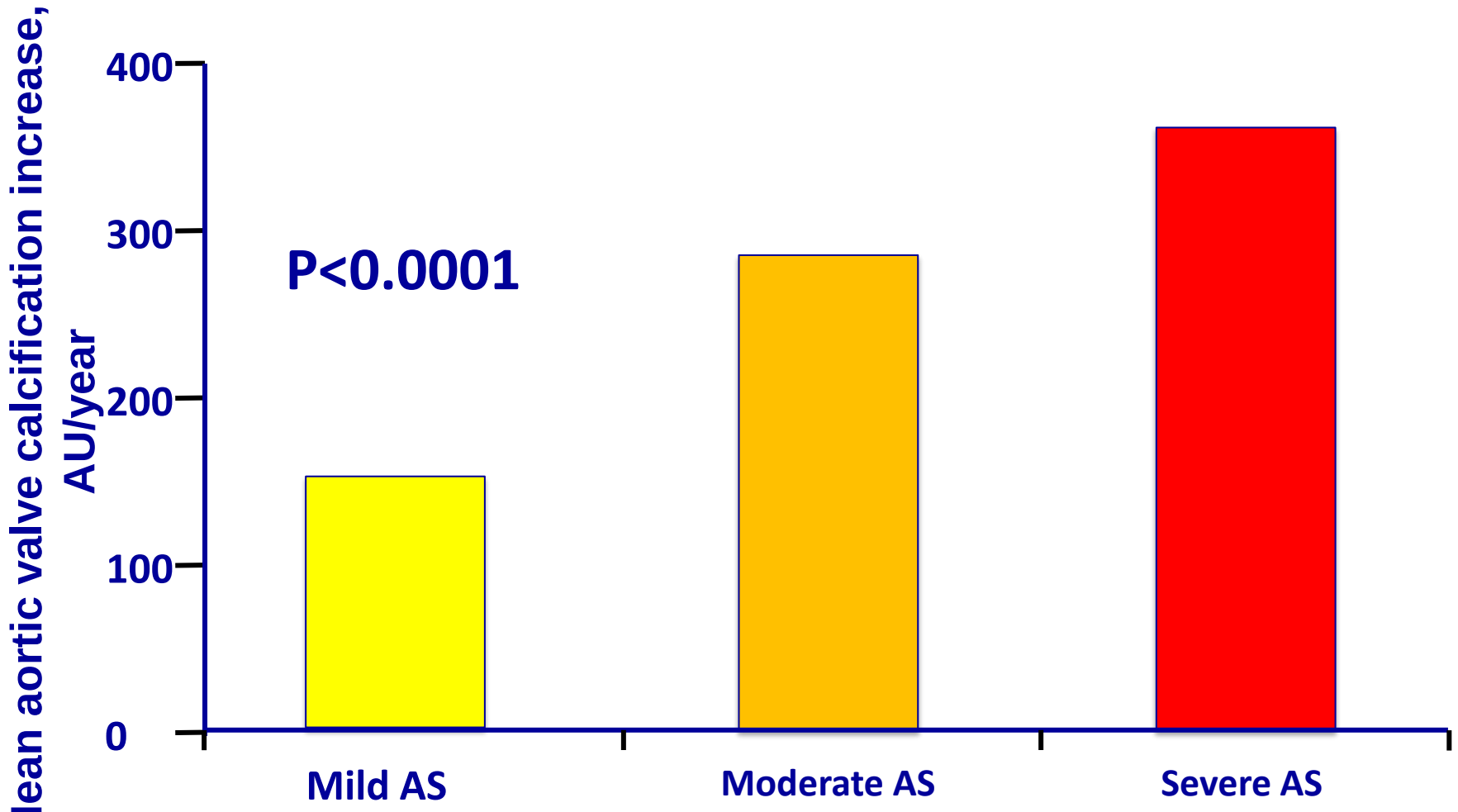
Study design

Patients with degenerative AS, enrolled between November 2006 and May 2013 in two ongoing prospective studies, COFRASA (clinicalTrial.gov number NCT 00338676) and GENERAC (clinicalTrial.gov number NCT00647088), with at least 2 years of follow-up were considered in the present study. COFRASA and GENERAC aim at evaluating the determinants of AS occurrence and progression, and all participants underwent a comprehensive clinical, transthoracic echocardiography (TTE) and MSCT evaluation at study entry and yearly thereafter. Inclusion criteria are pure, at least mild (defined by a mean pressure gradient (MPG) ≥10 mm Hg and aortic valve structural changes (thickening/calcification)) asymptomatic AS. Exclusion criteria were AS

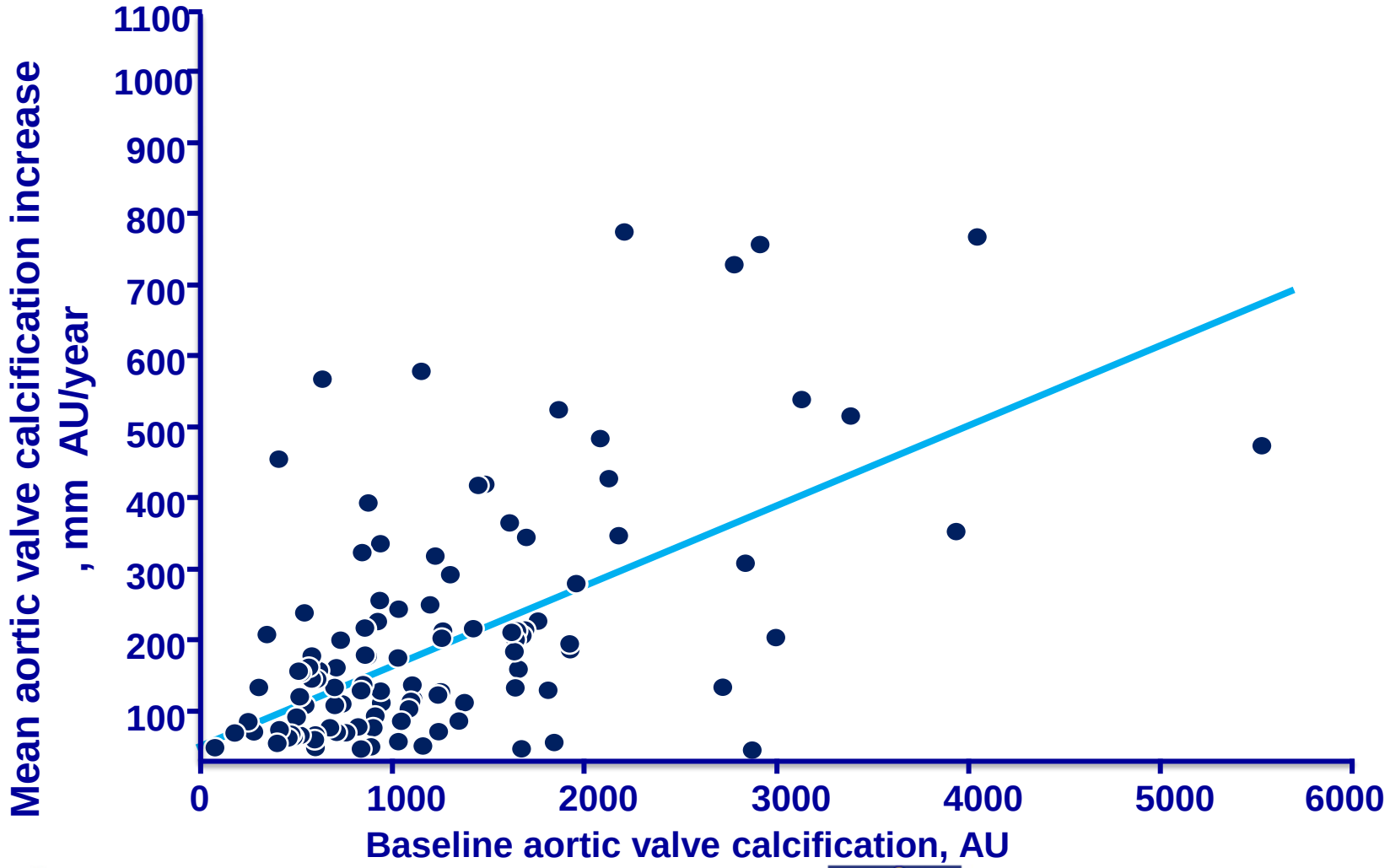
Progression of Aortic Valve Calcification in Aortic Stenosis - Impact of Severity. The COFRASA - GENERAC Study



Progression of Aortic Valve Calcification in Aortic Stenosis - Impact of Severity. The COFRASA - GENERAC Study

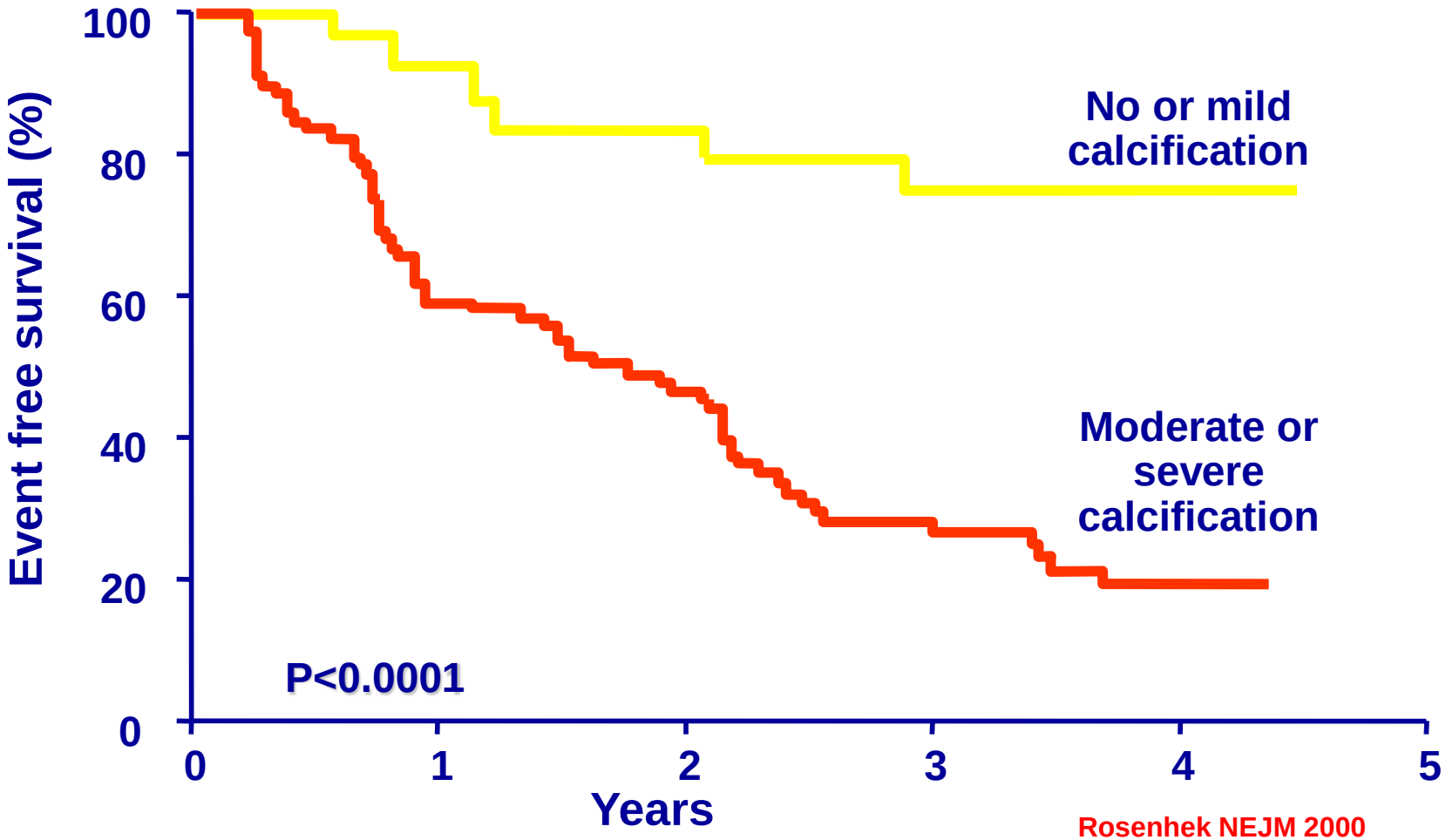


Progression of Aortic Valve Calcification in Aortic Stenosis - Impact of Severity. The COFRASA - GENERAC Study



Prognostic value of AVC

Echocardiographic assessment

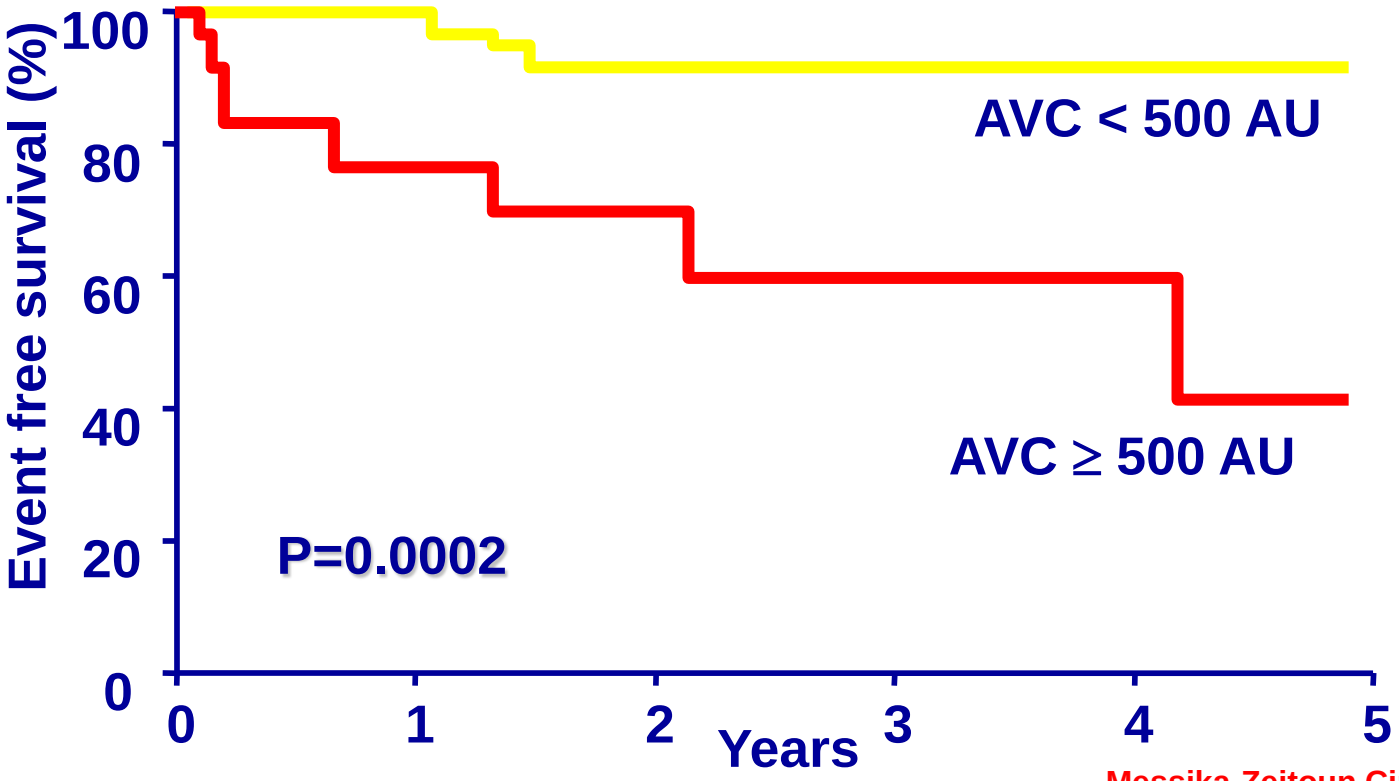


Rosenhek NEJM 2000

Prognostic value of AVC

CT assessment

AVC and hemodynamic severity provide complementary prognostic information



Messika-Zeitoun Circulation 2004

Impact of Aortic Valve Calcification, as Measured by MDCT, on Survival in Patients With Aortic Stenosis

Results of an International Registry Study

Marie-Annick Clavel, DVM, PhD,* Philippe Pibarot, DVM, PhD,† David Messika-Zeitoun, MD, PhD,‡§ Romain Capoulade, PhD,† Joseph Malouf, MD,* Shivani Aggarval, MBBS,* Phillip A. Araoz, MD,* Hector I. Michelena, MD,* Caroline Cueff, MD,‡ Eric Larose, MD, MSc,† Jordan D. Miller, PhD,* Alec Vahanian, MD,‡§ Maurice Enriquez-Sarano, MD*

ABSTRACT

BACKGROUND Aortic valve calcification (AVC) load measures lesion severity in aortic stenosis (AS) and is useful for diagnostic purposes. Whether AVC predicts survival after diagnosis, independent of clinical and Doppler echocardiographic AS characteristics, has not been studied.

OBJECTIVES This study evaluated the impact of AVC load, absolute and relative to aortic annulus size ($AVC_{density}$), on overall mortality in patients with AS under conservative treatment and without regard to treatment.

METHODS In 3 academic centers, we enrolled 794 patients (mean age, 73 ± 12 years; 274 women) diagnosed with AS by Doppler echocardiography who underwent multidetector computed tomography (MDCT) within the same episode of care. Absolute AVC load and $AVC_{density}$ (ratio of absolute AVC to cross-sectional area of aortic annulus) were measured, and severe AVC was separately defined in men and women.

RESULTS During follow-up, there were 440 aortic valve implantations (AVIs) and 194 deaths (115 under medical treatment). Univariate analysis showed strong association of absolute AVC and $AVC_{density}$ with survival (both, $p < 0.0001$) with a spline curve analysis pattern of threshold and plateau of risk. After adjustment for age, sex, coronary artery disease, diabetes, symptoms, AS severity on hemodynamic assessment, and LV ejection fraction, severe absolute AVC (adjusted hazard ratio [HR]: 1.75; 95% confidence interval [CI]: 1.04 to 2.92; $p = 0.03$) or severe $AVC_{density}$ (adjusted HR: 2.44; 95% CI: 1.37 to 4.37; $p = 0.002$) independently predicted mortality under medical treatment, with additive model predictive value (all, $p \leq 0.04$) and a net reclassification index of 12.5% ($p = 0.04$). Severe absolute AVC (adjusted HR: 1.71; 95% CI: 1.12 to 2.62; $p = 0.01$) and severe $AVC_{density}$ (adjusted HR: 2.22; 95% CI: 1.40 to 3.52; $p = 0.001$) also independently predicted overall mortality, even with adjustment for time-dependent AVI.

CONCLUSIONS This large-scale, multicenter outcomes study of quantitative Doppler echocardiographic and MDCT assessment of AS shows that measuring AVC load provides incremental prognostic value for survival beyond clinical and Doppler echocardiographic assessment. Severe AVC independently predicts excess mortality after AS diagnosis, which is greatly alleviated by AVI. Thus, measurement of AVC by MDCT should be considered for not only diagnostic but also risk-stratification purposes in patients with AS. (J Am Coll Cardiol 2014;64:1202–13) © 2014 by the American College of Cardiology Foundation.

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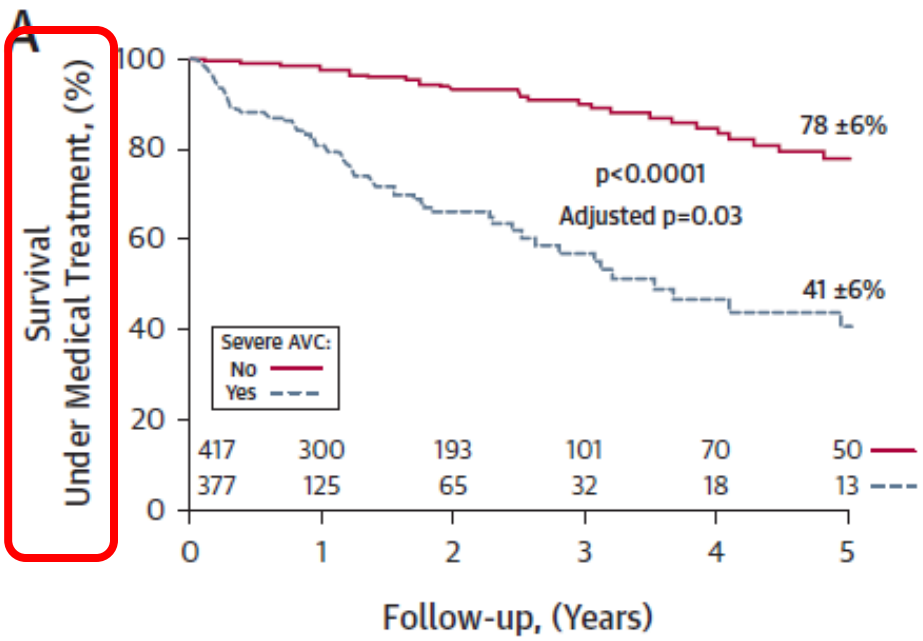

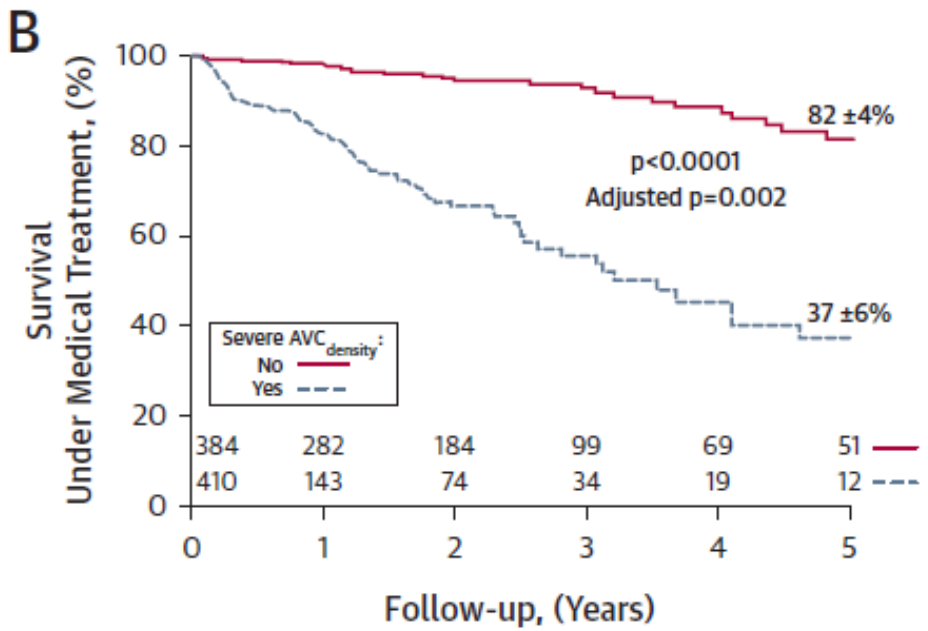

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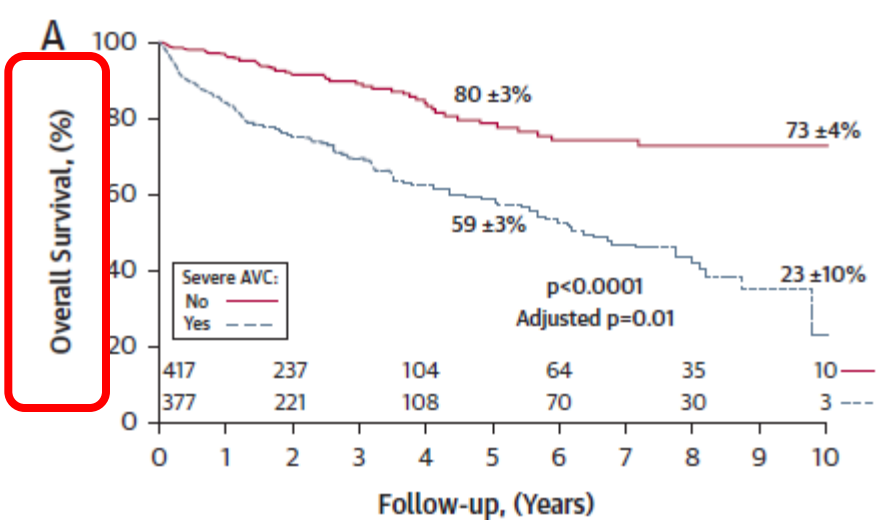

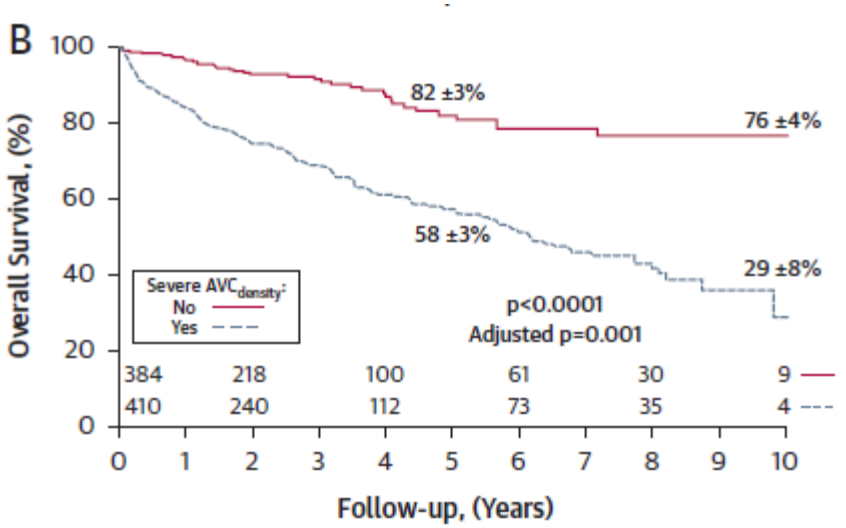

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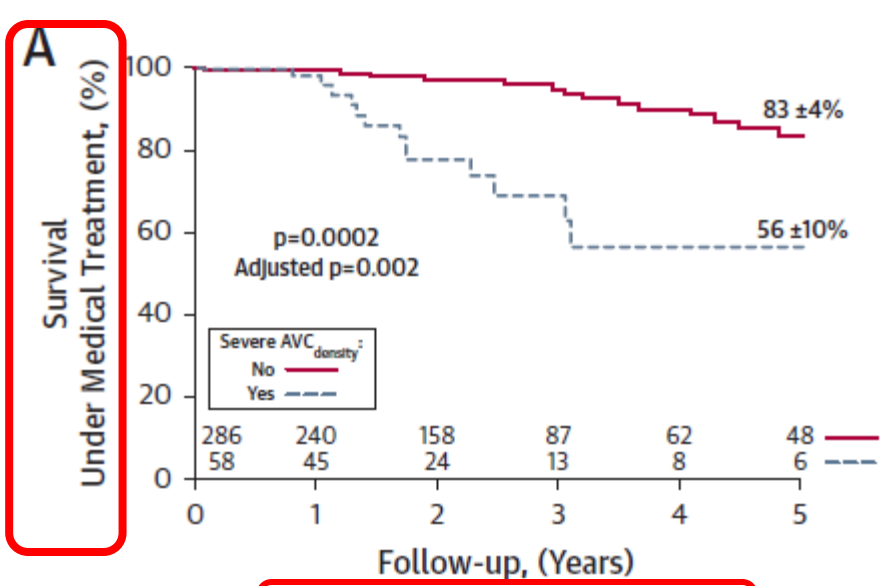
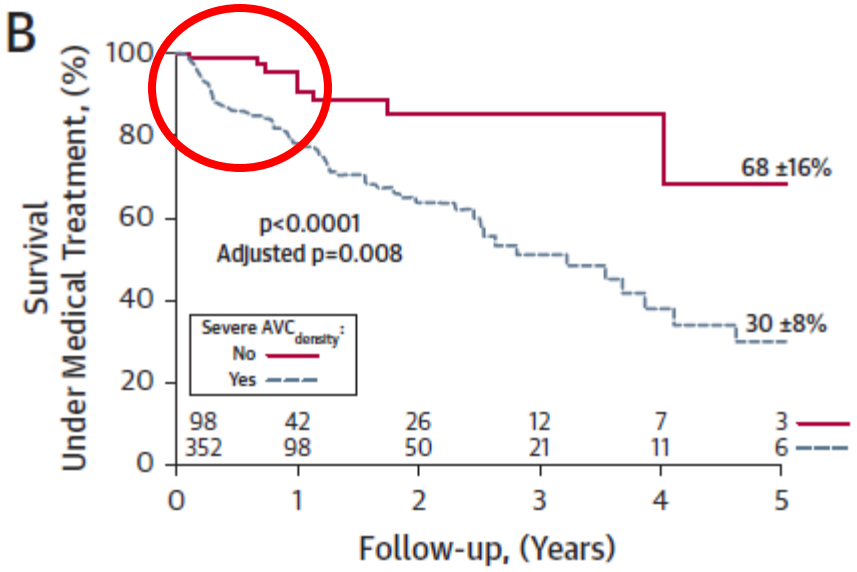
Marie-Annick Clavel, DVM, PhD,* Philippe Pibarot, DVM, PhD,† David Messika-Zeitoun, MD, PhD,‡§
Romain Capoulade, PhD,† Joseph Malouf, MD,* Shivani Aggarval, MBBS,* Phillip A. Araoz, MD,*
Hector I. Michelena, MD,* Caroline Cueff, MD,‡ Eric Larose, MD, MSc,† Jordan D. Miller, PhD,* Alec Vahanian, MD,‡§
Maurice Enriquez-Sarano, MD*





Non severe AS

Severe AS

HÔPITAUX UNIVERSITAIRES PARIS NORD VAL DE SEINE
Bichat - Claude Bernard

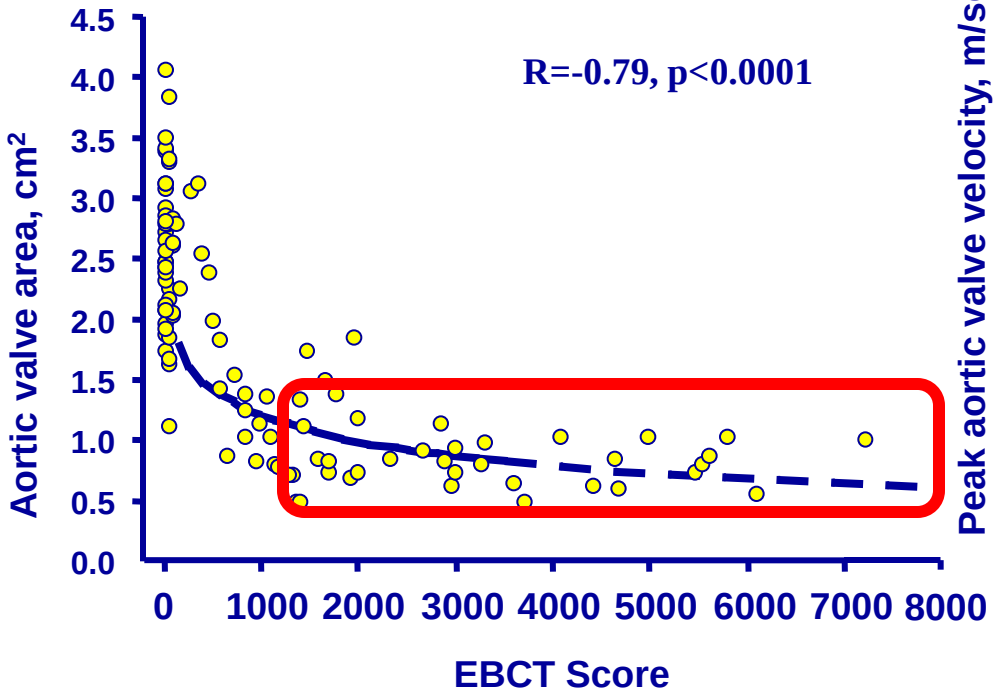
Inserm
Chercheur en santé depuis 1964
Health research since 1964

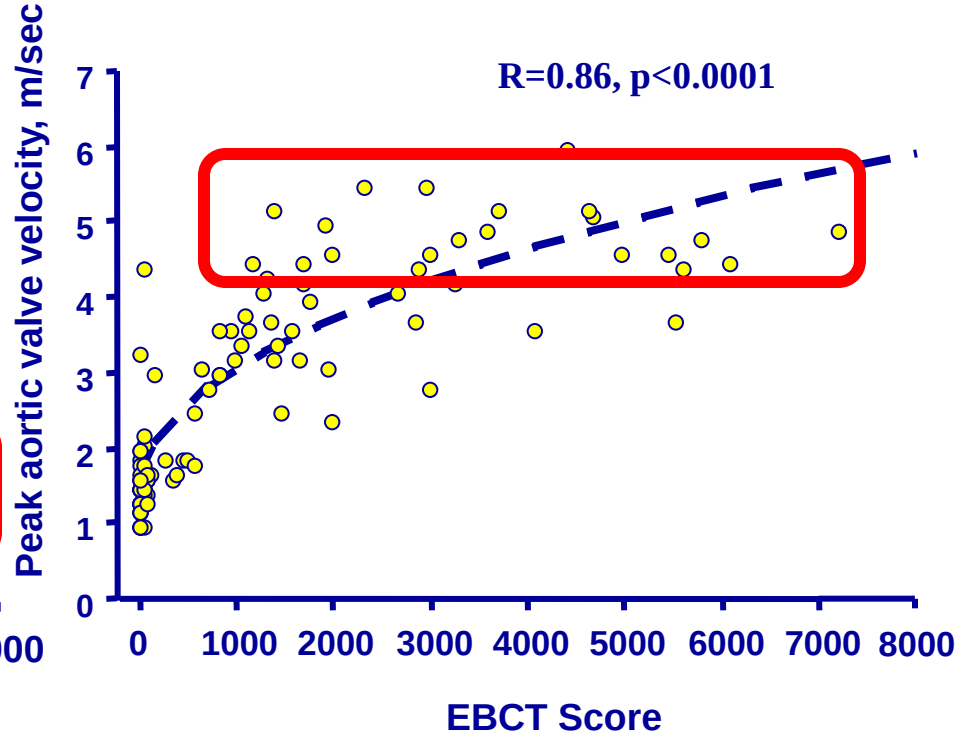
50 ans

fire

université PARIS DIDEROT PARIS 7

AVC and Hemodynamic Severity are Not Equivalent





Messika-Zeitoun Circulation 2004

Indications for aortic valve replacement in asymptomatic aortic stenosis

	Class	Level
AVR is indicated in asymptomatic patients with severe AS and systolic LV dysfunction (LVEF < 50%) not due to another cause.	I	C
AVR is indicated in asymptomatic patients with severe AS and abnormal exercise test showing symptoms on exercise clearly related to AS.	I	C
AVR should be considered in asymptomatic patients with severe AS and abnormal excercise test showing fall in blood pressure below baseline	IIa	C
AVR should be considered in asy… none of the above mentioned ex… …sk is low, and one or more of the follo… • ***very severe AS defined by a pe… transvalvular velocity > 5.5 m/s,*** • ***severe valve calcification and a rate of peak of transvalvular velocity progression ≥ 0.3 m/s per year.***	IIa	C
AVR may be considered in asymptomatic patients with severe AS, normal EF and none of the above mentioned exercise test abnormalities, if surgical risk is low, and one or more of the following findings is present : • ***markedly elevated natriuretic peptide levels confirmed by repeated measurements without other explanations,*** • ***increase of mean pressure gradient with exercise by > 20 mmHg,*** • ***excessive LV hypertrophy in the absence of hypertension.***	IIb	C

Threshold?

European Heart Journal 2012 - doi:10.1093/eurheartj/ehs109 & European Journal of Cardio-Thoracic Surgery 2012 - doi:10.1093/ejcts/ezs455).

www.escardio.org/guidelines

EACTS

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Take Home Messages

1. **Aortic valve calcification can be objectively and quantitatively assessed using CT**

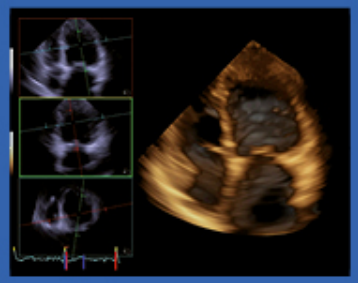
Conclusion

2. **Degree of aortic valve calcification is highly correlated to AS hemodynamic severity and calcium scoring can be considered as an additional method to assess AS severity in difficult subset of patients**
   - **Poor echogenicity**
   - **Discordance between echo and symptoms**
   - **Low gradient – low ejection fraction**
   - **Discording grading and normal EF**

Conclusion

3. **Aortic valve calcification progressively increased**
   - **Progression is independent of CV risk-factors**
   - **Aortic valve calcification (and AS hemodynamic severity) increase faster with baseline AS severity and baseline calcium load**

4. **Aortic valve calcification provide important prognostic information but thresholds need to be further defined**

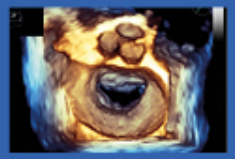
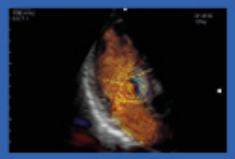


EuroValve

March 27 - 28, 2015

Thank you



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