

Low Flow Low Gradient Aortic Stenosis with preserved LVEF

An elusive concept



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Madrid 8th November 2013



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Low Flow Low Gradient Aortic Stenosis with preserved LVEF

Does it exist?

Does AVR help?

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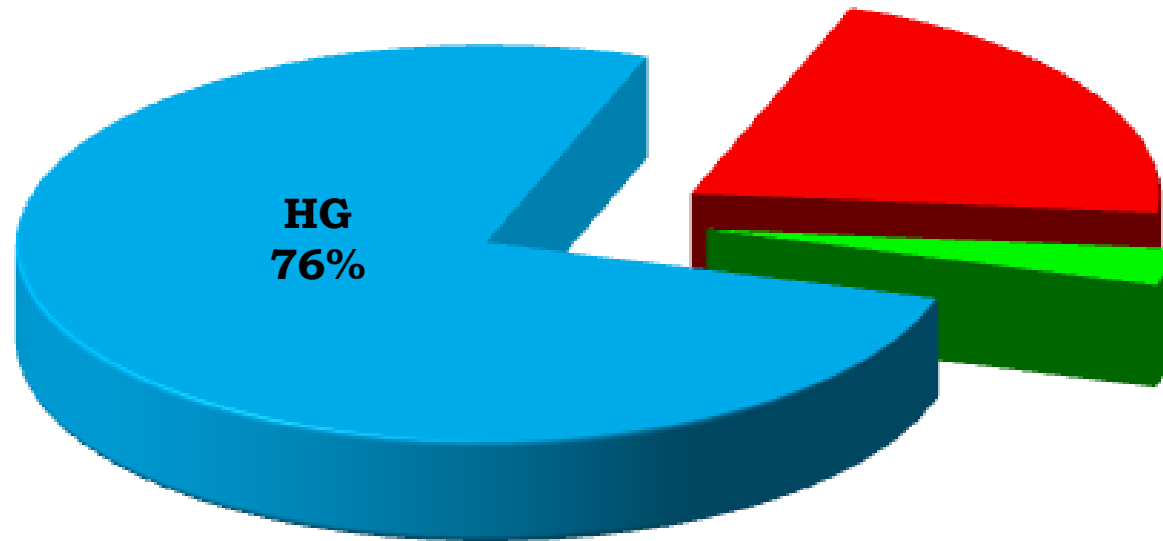


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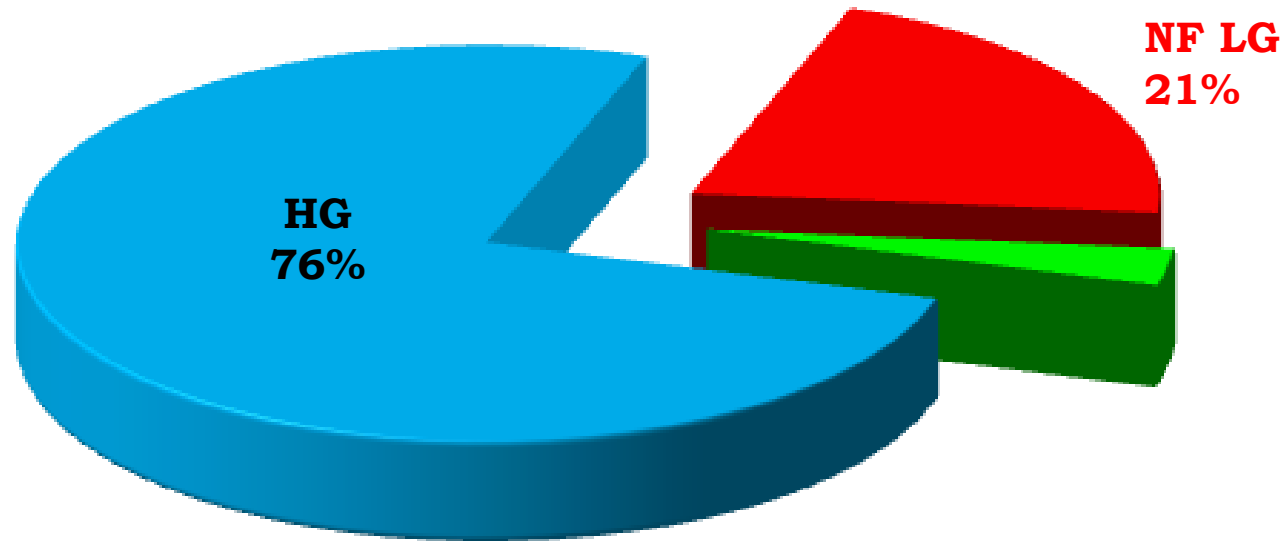
1704 severe AS with normal LVEF

Eleid MF- Circulation. 2013;128:1781-1789



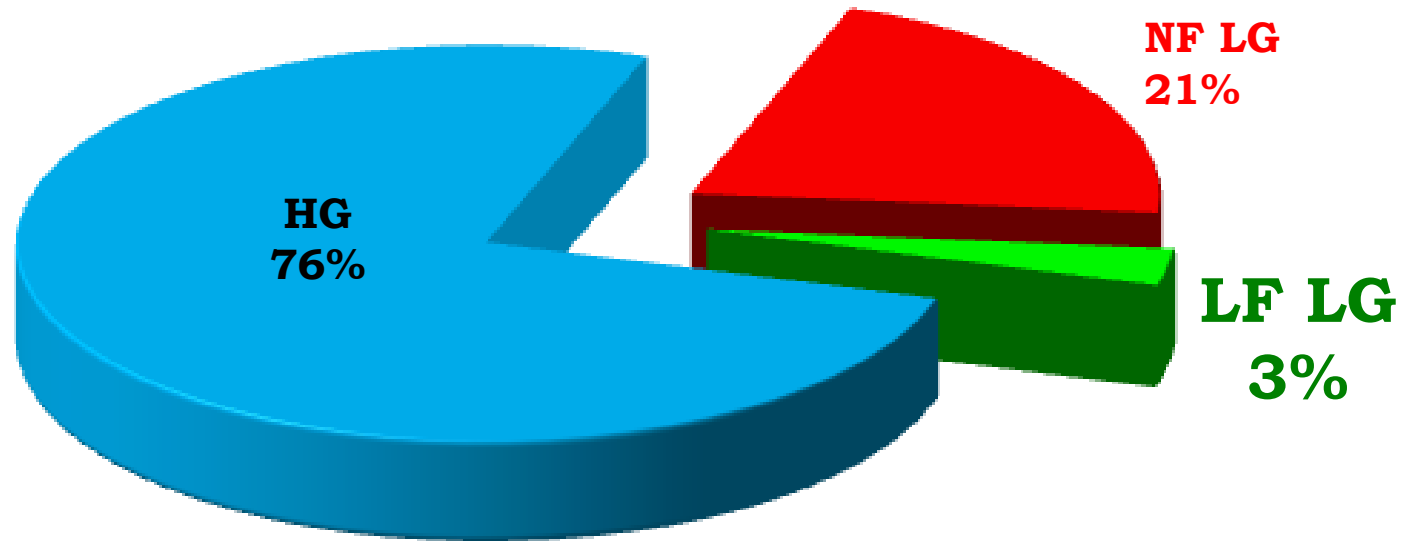
1704 severe AS with normal LVEF

Eleid MF- Circulation. 2013;128:1781-1789



1704 severe AS with normal LVEF

Eleid MF- Circulation. 2013;128:1781-1789



Paradoxical Low-Flow, Low-Gradient Severe Aortic Stenosis Despite Preserved Ejection Fraction Is Associated With Higher Afterload and Reduced Survival

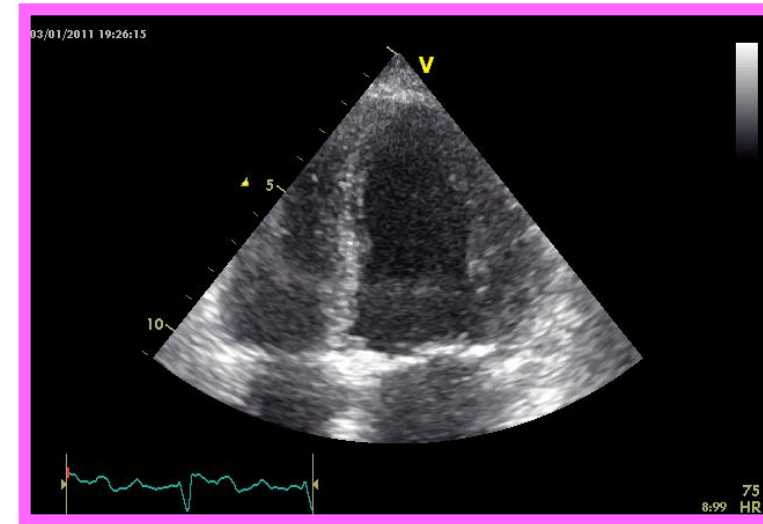
Hachicha Z , Pibarot P- *Circulation* 2007 ; 115 : 2856-64



Background—Recent studies and current clinical observations suggest that some patients with severe aortic stenosis on the basis of aortic valve area may paradoxically have a relatively low gradient despite the presence of a preserved left ventricular (LV) ejection fraction. The objective of the present study was to document the prevalence, potential mechanisms, and clinical relevance of this phenomenon.

Methods and Results—We retrospectively studied the clinical and Doppler echocardiographic data of 512 consecutive patients with severe aortic stenosis (indexed aortic valve area $\leq 0.6 \text{ cm}^2 \cdot \text{m}^{-2}$) and preserved LV ejection fraction ($\geq 50\%$). Of these patients, 331 (65%) had normal LV flow output defined as a stroke volume index $>35 \text{ mL} \cdot \text{m}^{-2}$, and 181 (35%) had paradoxically low-flow output defined as stroke volume index $\leq 35 \text{ mL} \cdot \text{m}^{-2}$. When compared with normal flow patients, low-flow patients had a higher prevalence of female gender ($P < 0.05$), a lower transvalvular gradient (32 ± 17 versus $40 \pm 15 \text{ mm Hg}$; $P < 0.001$), a lower LV diastolic volume index (52 ± 12 versus $59 \pm 13 \text{ mL} \cdot \text{m}^{-2}$; $P < 0.001$), lower LV ejection fraction ($62 \pm 8\%$ versus $68 \pm 7\%$; $P < 0.001$), a higher level of LV global afterload reflected by a higher valvulo-arterial impedance (5.3 ± 1.3 versus $4.1 \pm 0.7 \text{ mm Hg} \cdot \text{mL}^{-1} \cdot \text{m}^{-2}$; $P < 0.001$) and a lower overall 3-year survival (76% versus 86% ; $P = 0.006$). Only age (hazard ratio, 1.04; 95% CI, 1.01 to 1.08; $P = 0.025$), valvulo-arterial impedance $> 5.5 \text{ mm Hg} \cdot \text{mL}^{-1} \cdot \text{m}^{-2}$ (hazard ratio, 2.6; 95% CI, 1.2 to 5.7; $P = 0.017$), and medical treatment (hazard ratio, 3.3; 95% CI, 1.8 to 6.7; $P = 0.0003$) were independently associated with increased mortality.

Conclusion—Patients with severe aortic stenosis may have low transvalvular flow and low gradients despite normal LV ejection fraction. A comprehensive evaluation shows that this pattern is in fact consistent with a more advanced stage of the disease and has a poorer prognosis. Such findings are clinically relevant because this condition may often be misdiagnosed, which leads to a neglect and/or an underestimation of symptoms and an inappropriate delay of aortic valve replacement surgery. (*Circulation*. 2007;115:2856-2864.)



Low Flow Low Gradient AS

Does it exist ?



Low Flow Low Gradient AS

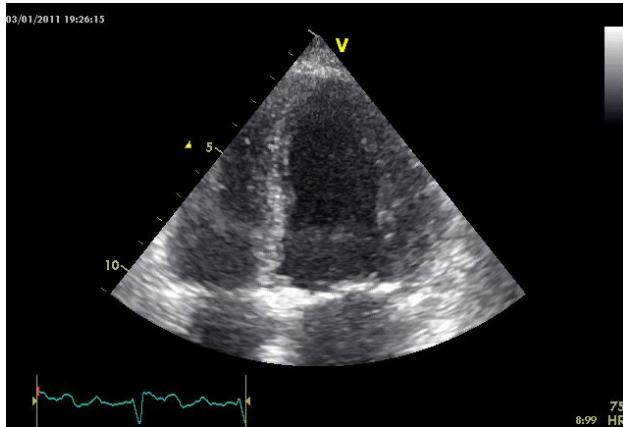
Does it exist ?

Yes, but unfrequent

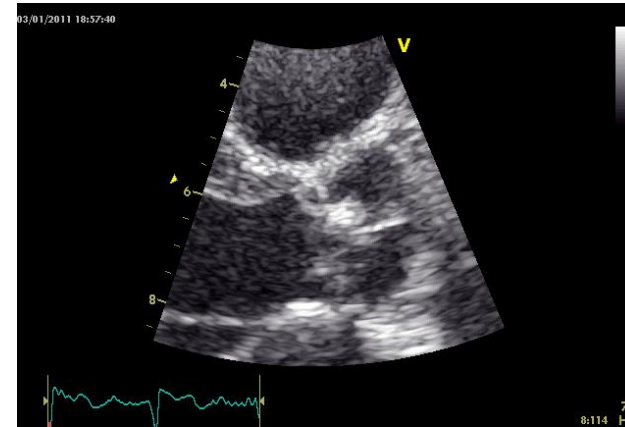


Patient 1: recent pulmonary edema

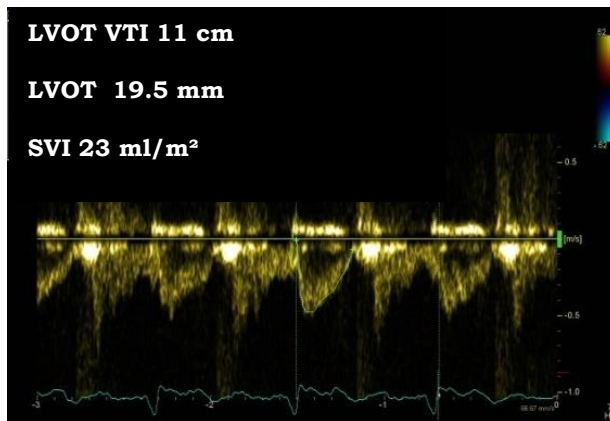
79 year-old woman, BSA 1.45 m², no CAD



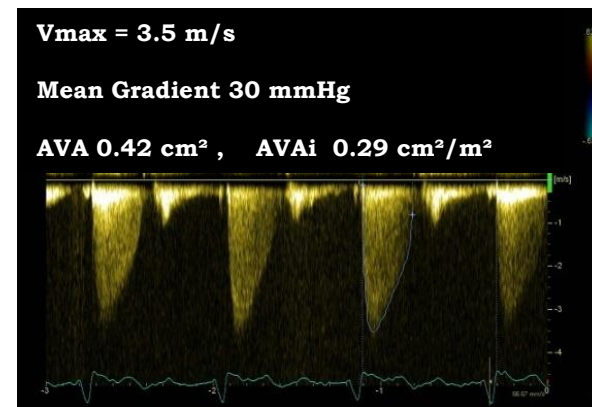
LVEF = 68%, LVH



Calcified aortic valve

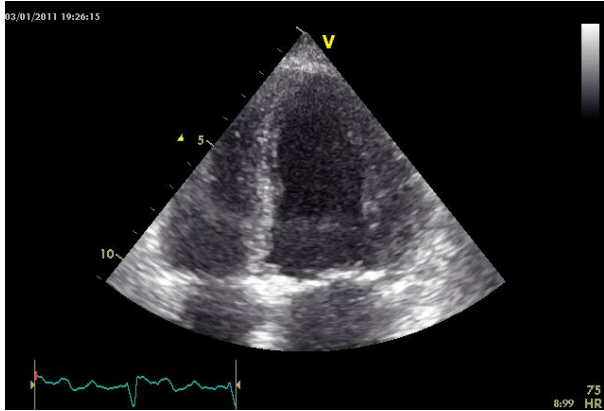


Low cardiac output



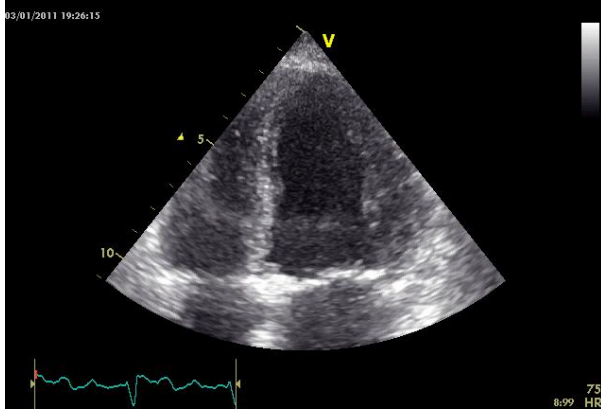
Severe AS, Low Gradient

Patient 1: recent pulmonary edema

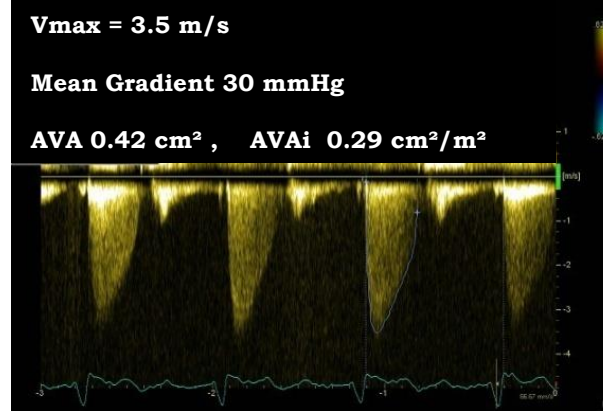


Normal LVEF

Patient 1: recent pulmonary edema

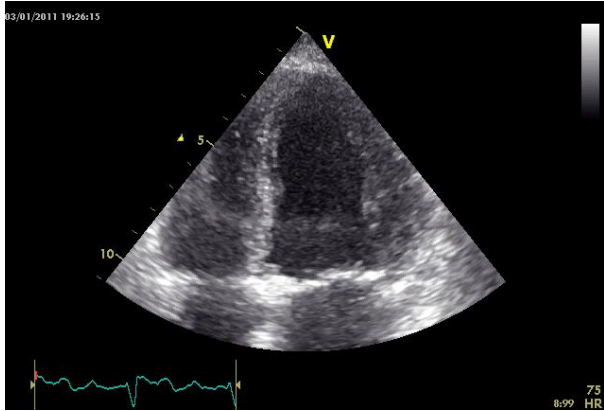


Normal LVEF

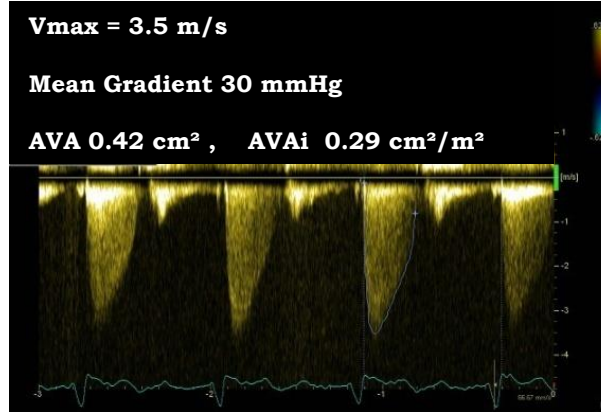


Low gradient

Patient 1: recent pulmonary edema

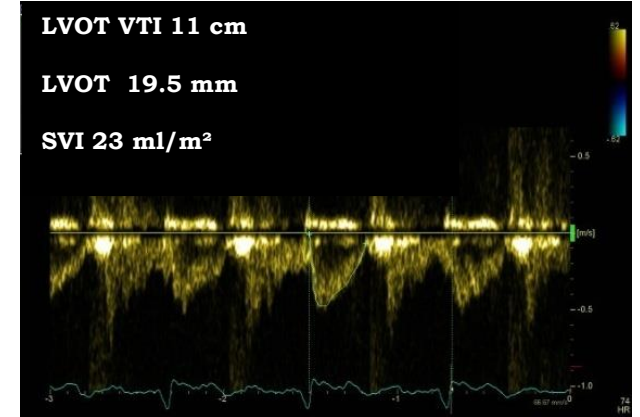


Normal LVEF



Vmax = 3.5 m/s
Mean Gradient 30 mmHg
AVA 0.42 cm², AVAi 0.29 cm²/m²

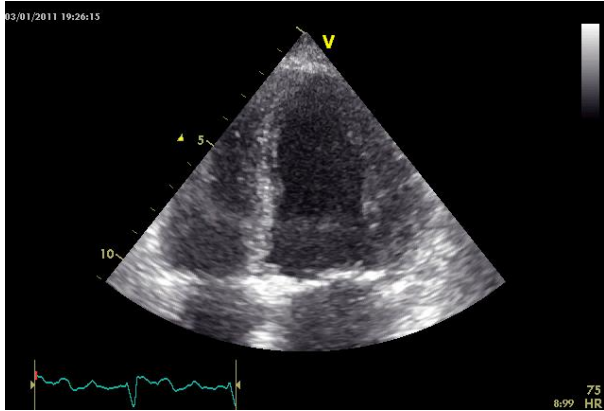
Low gradient



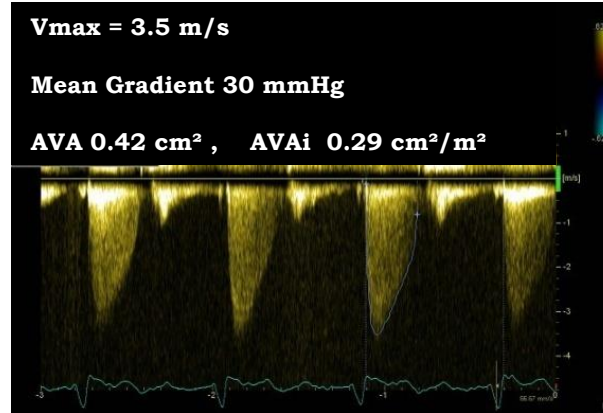
LVOT VTI 11 cm
LVOT 19.5 mm
SVI 23 ml/m²

Low flow

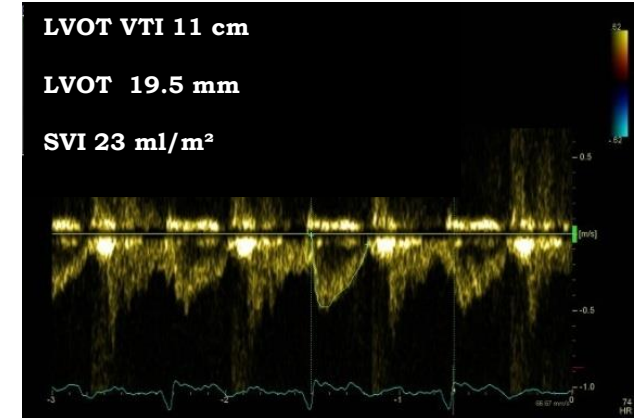
Patient 1: recent pulmonary edema



Normal LVEF



Low gradient

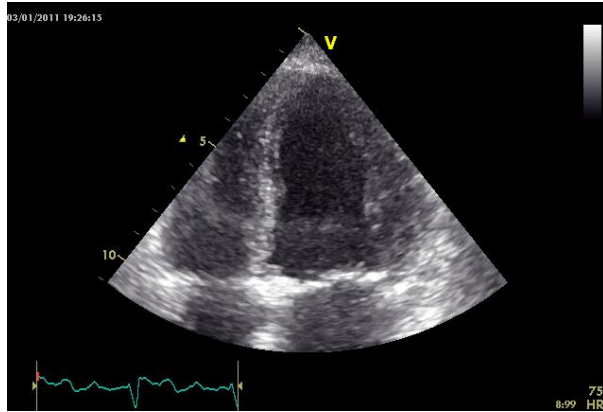


Low flow

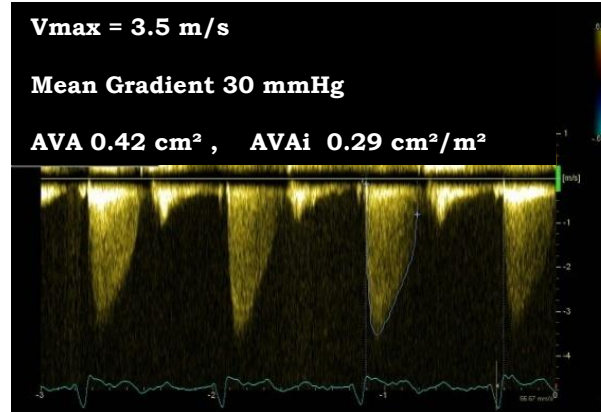
Severe aortic stenosis

Paradoxical low flow

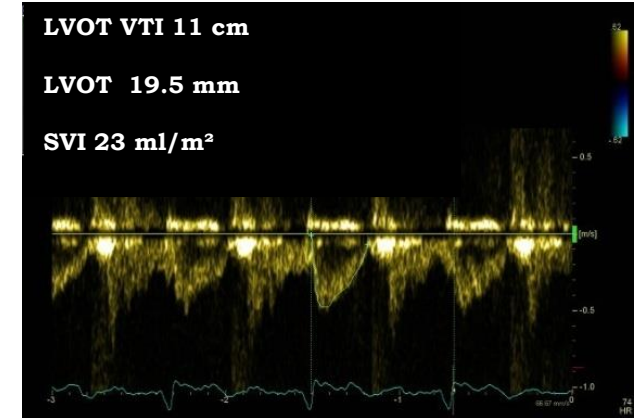
Patient 1: recent pulmonary edema



Normal LVEF



Low gradient

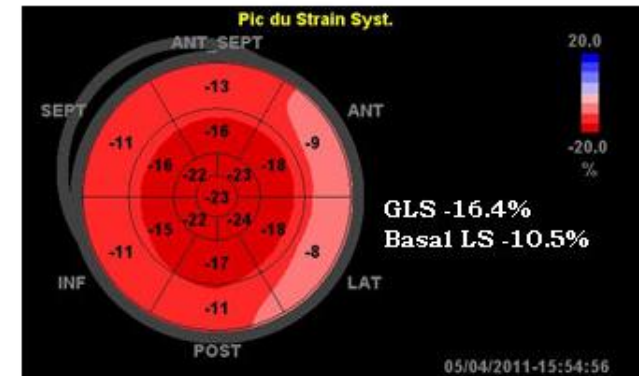


Low flow

Severe aortic stenosis

Paradoxical low flow

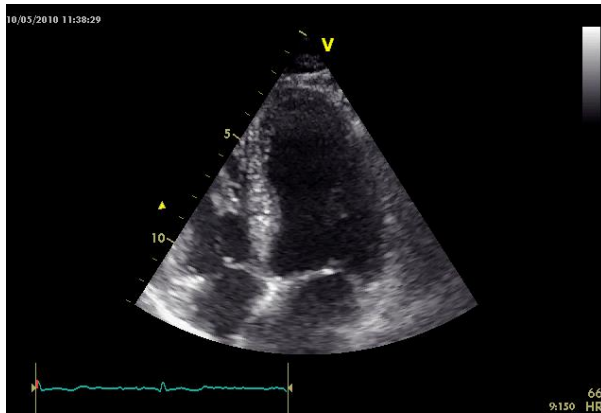
LV longitudinal dysfunction



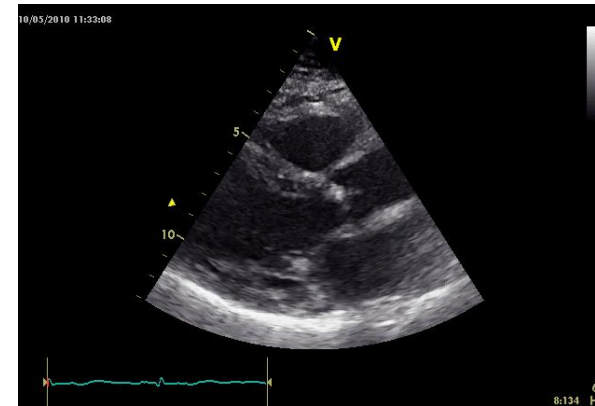
Adda J , Habib G – Circulation CV Imaging 2012

Patient 2: dyspnea on exertion

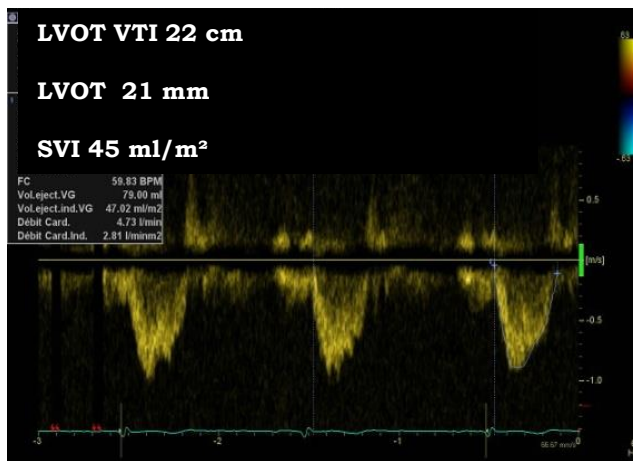
61 year-old woman, BSA 1.64 m², no CAD



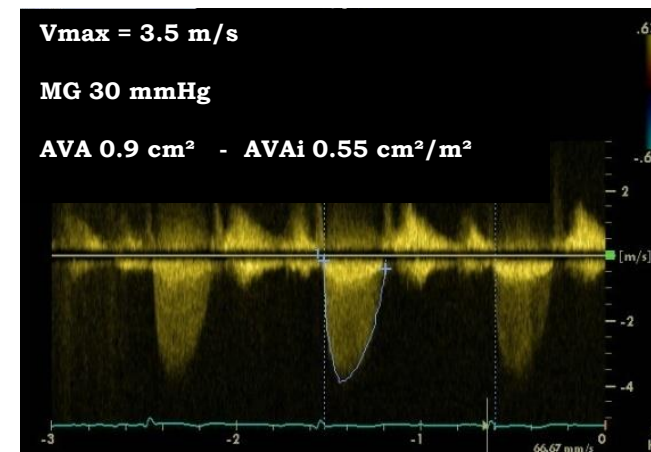
LVEF = 63% , moderate LVH



Calcified aortic valve

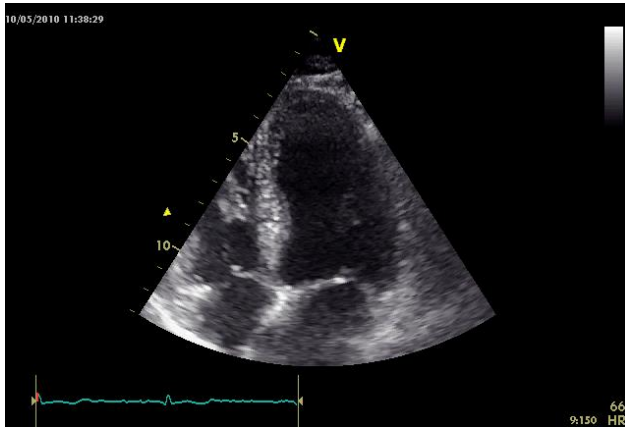


Normal cardiac output



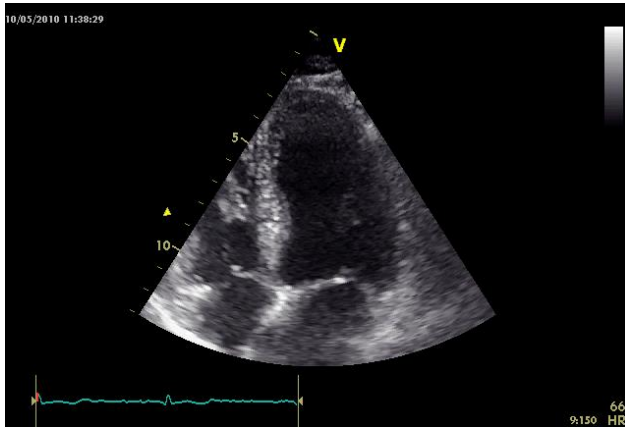
Severe AS, Low Gradient

Patient 2: dyspnea on exertion

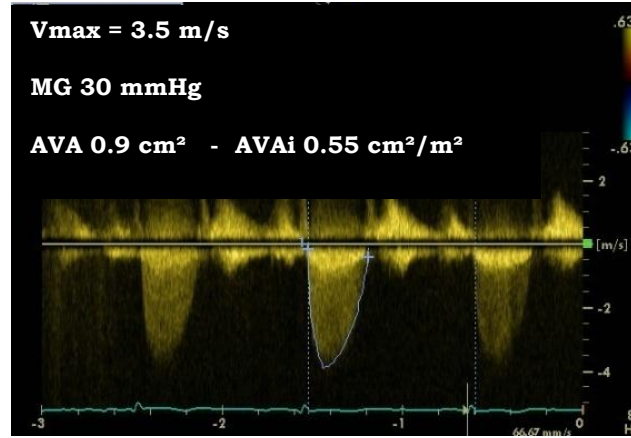


Normal LVEF

Patient 2: dyspnea on exertion

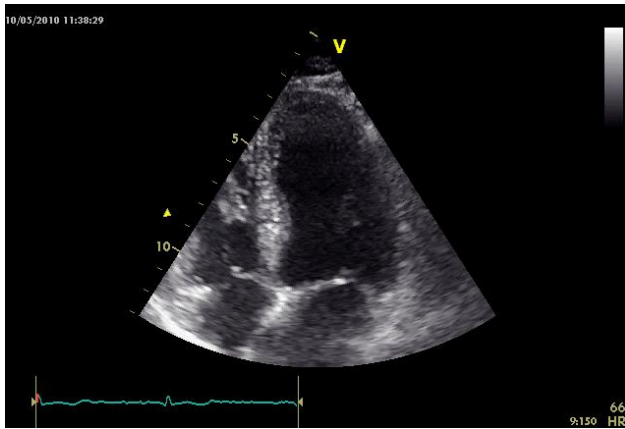


Normal LVEF

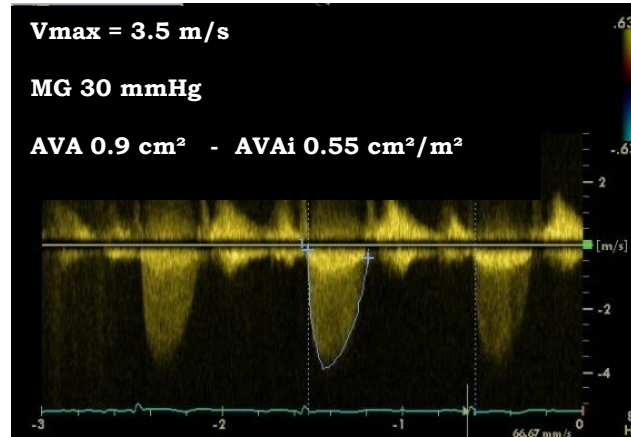


Low gradient

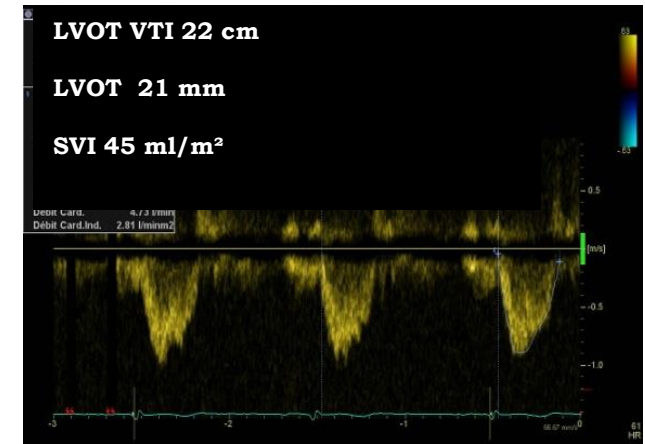
Patient 2: dyspnea on exertion



Normal LVEF

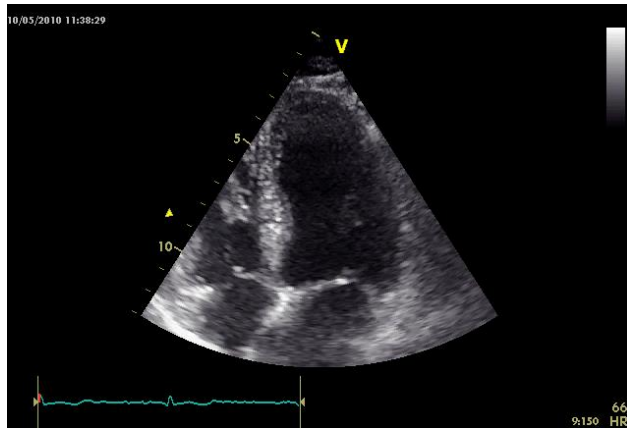


Low gradient

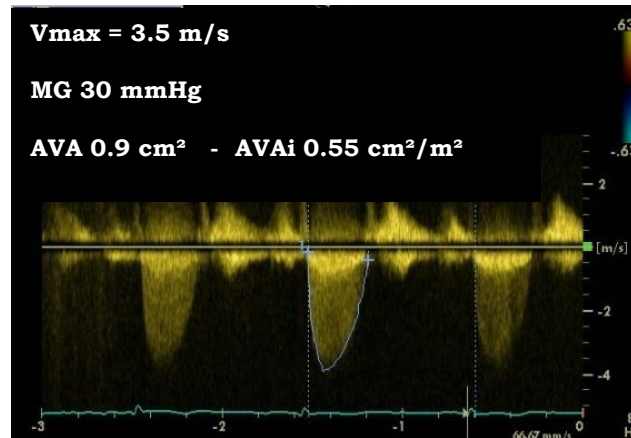


Normal Flow

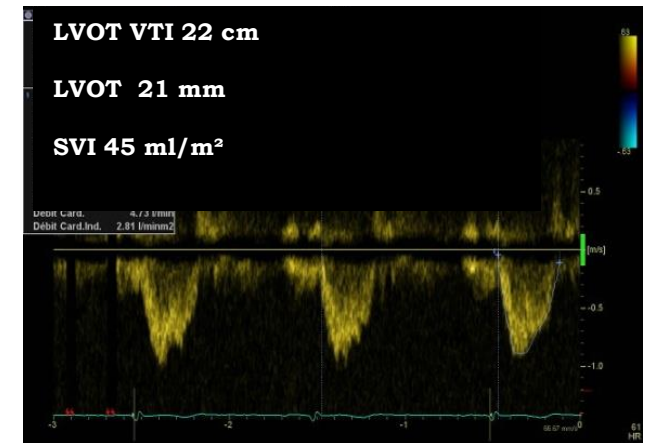
Patient 2: dyspnea on exertion



Normal LVEF



Low gradient



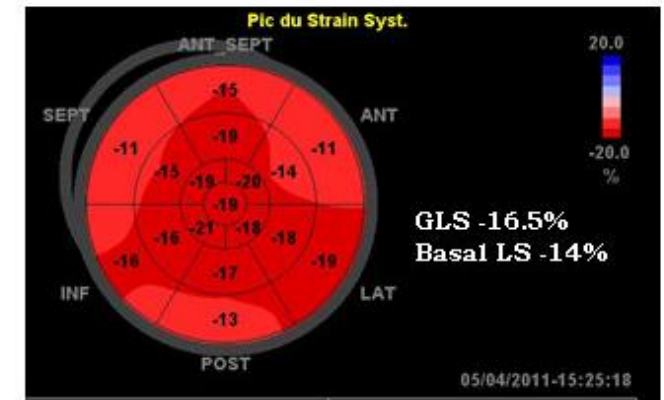
Normal Flow



Less severe aortic stenosis



Less severe LV longitudinal dysfunction



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2 questions for Philippe

- 1. Are you sure that both have severe AS?**
- 2. Will you send both patients to surgeon?**



LF LG AS: 3 important questions

1. Was LVOT correctly measured ?
2. Does the patient have both low gradient and low flow ?
3. Are the proposed cut-off values consistent ?



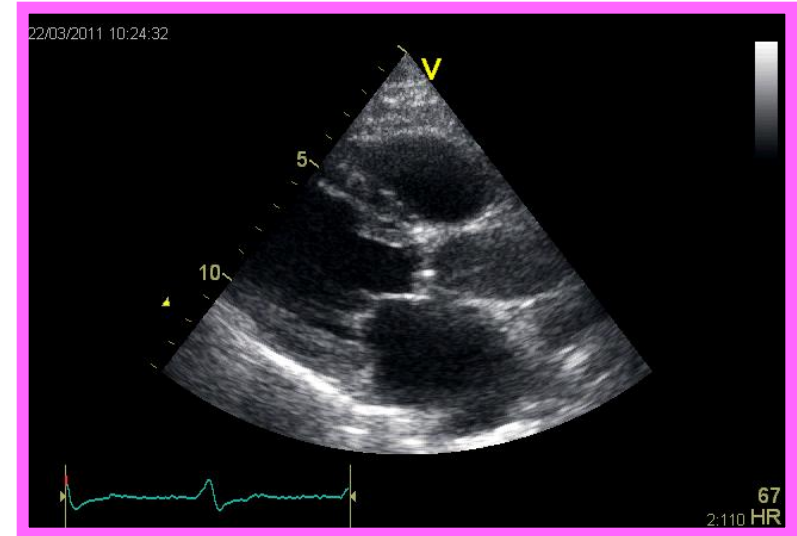
Critical issue: LVOT measurement

- underestimation of LVOT diameter leads to underestimation of AVA
- underestimation of stroke volume leads to false diagnosis of LFLG AS



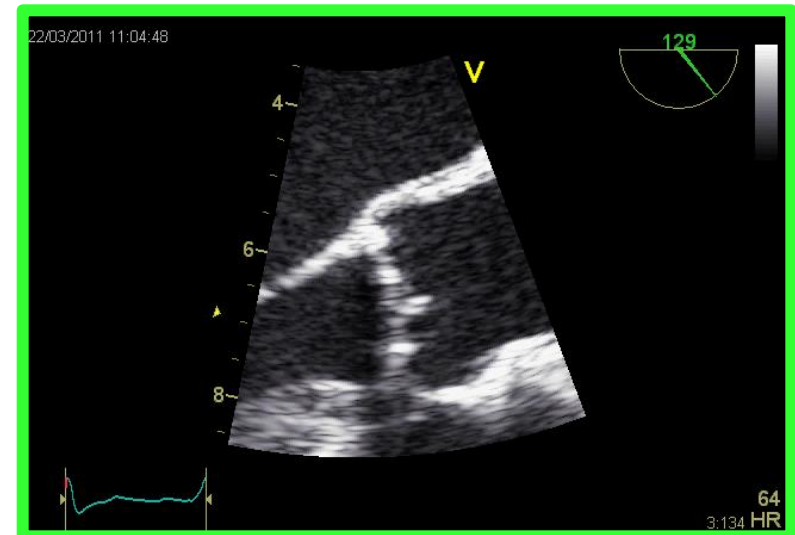
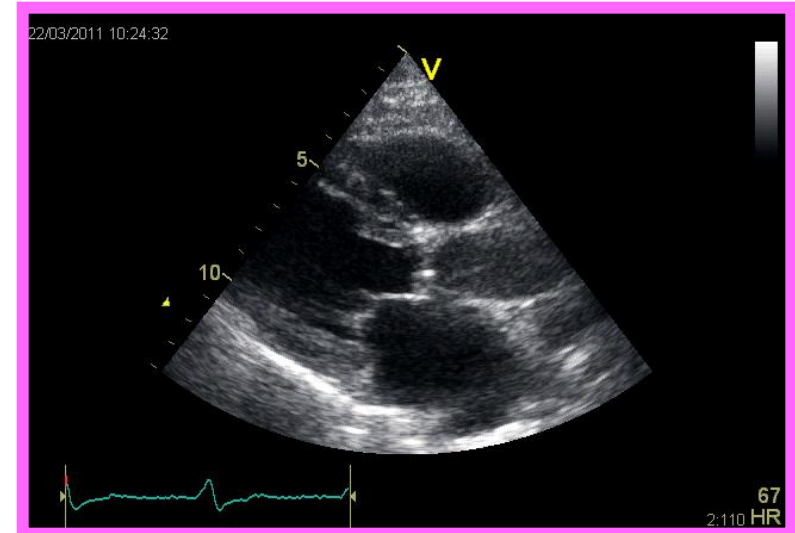
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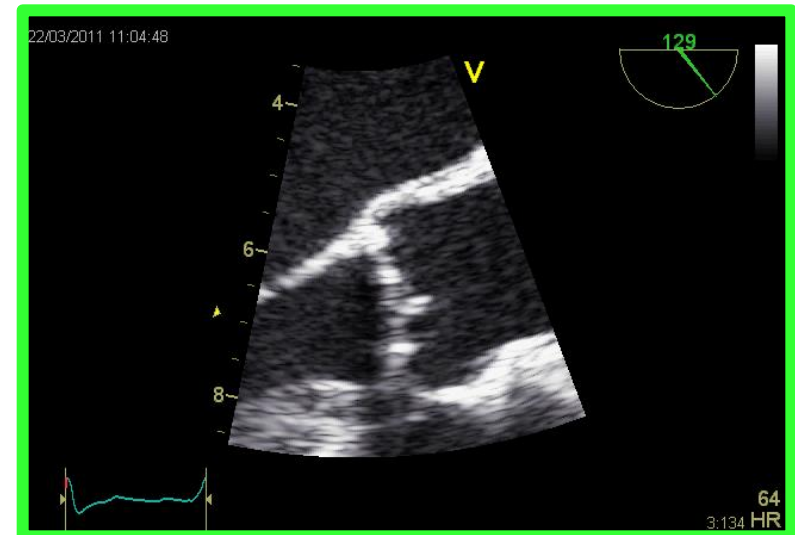
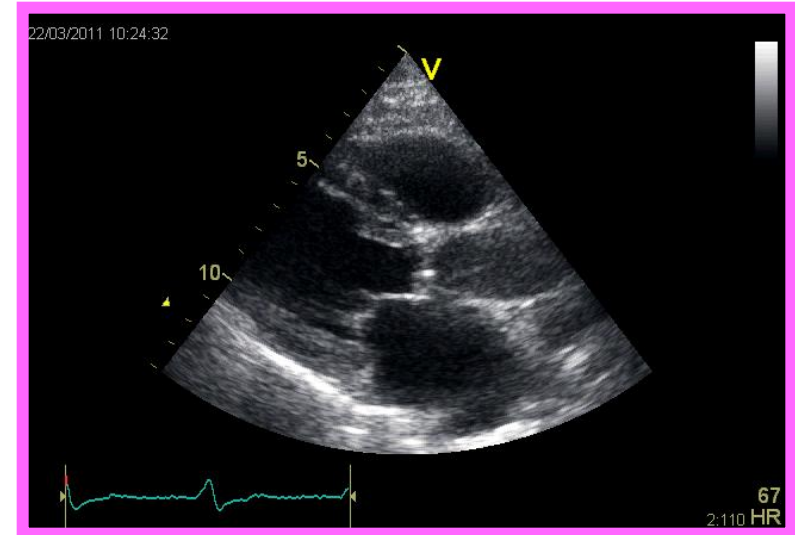
Critical issue: LVOT measurement

- underestimation of LVOT diameter leads to underestimation of AVA
- underestimation of stroke volume leads to false diagnosis of LFLG AS



Critical issue: LVOT measurement

- underestimation of LVOT diameter leads to underestimation of AVA
- underestimation of stroke volume leads to false diagnosis of LFLG AS
- ✦ re-check LVOT measurement
- ✦ perform TEE (and look at the valve !!)
- ✦ use alternative techniques to assess AS severity (CT scan, catheterization)



LF LG AS: 3 important questions

1. Was LVOT correctly measured ?
2. Does the patient have both low gradient and low flow ?
3. Are the proposed cut-off values consistent ?



Low gradient aortic stenosis

Adda J , Habib G – Circulation CV Imaging 2012

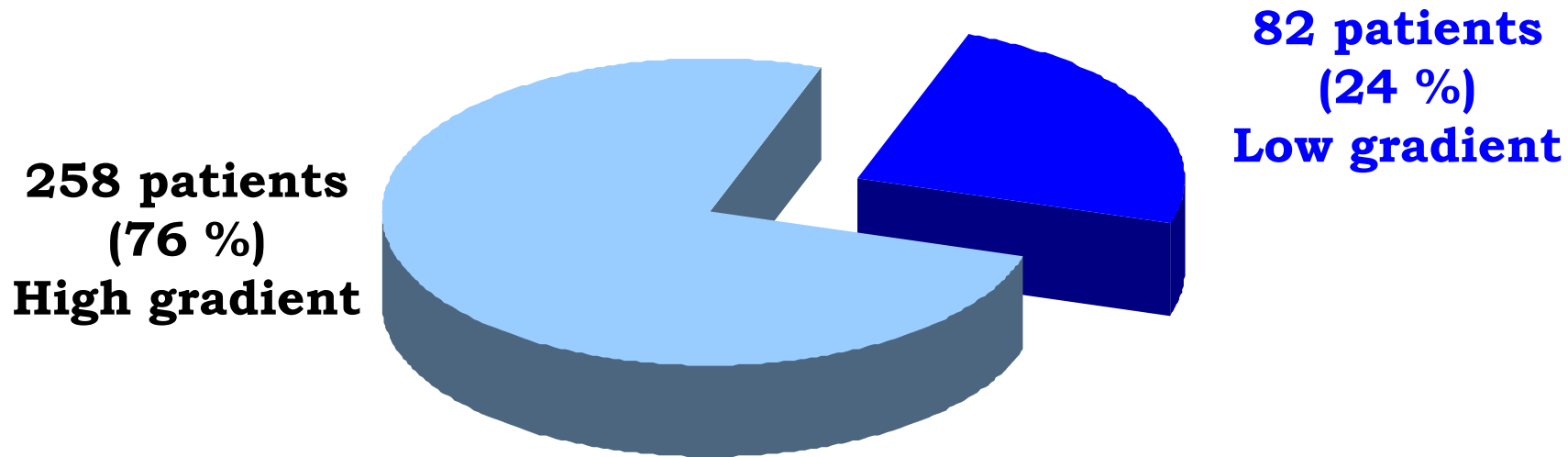
- **340 patients** severe AS - $AVA_i \leq 0.6 \text{ cm}^2/\text{m}^2$, LVEF > 50%
- **5 centers: Marseille, Liège, Rennes, Bordeaux, Montpellier**



Low gradient aortic stenosis

Adda J , Habib G – Circulation CV Imaging 2012

- **340 patients** severe AS - $AVA_i \leq 0.6 \text{ cm}^2/\text{m}^2$, LVEF > 50%



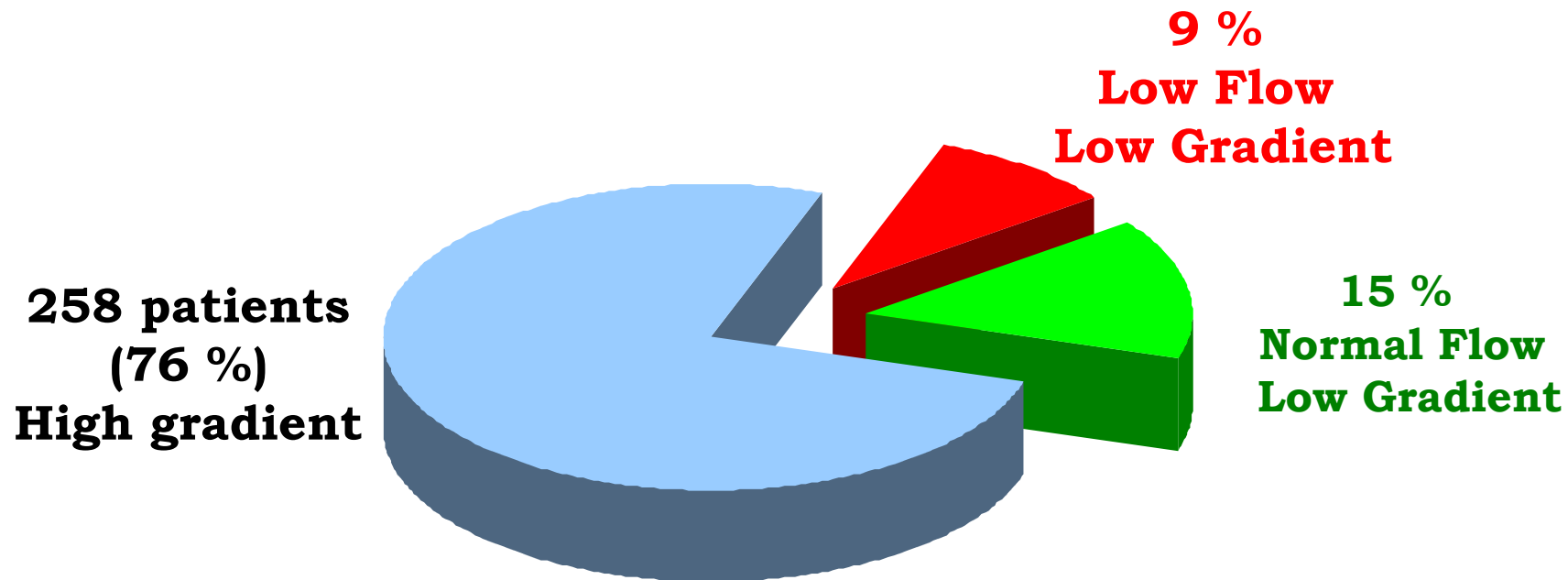
**258 patients
(76 %)
High gradient**

**82 patients
(24 %)
Low gradient**

Low gradient aortic stenosis

Adda J , Habib G – Circulation CV Imaging 2012

- **340 patients** severe AS - $AVA_i \leq 0.6 \text{ cm}^2/\text{m}^2$, LVEF > 50%



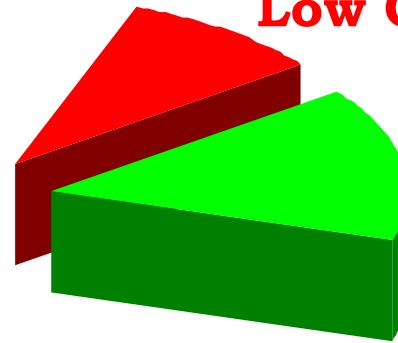
Low gradient aortic stenosis

Adda J , Habib G – Circulation CV Imaging 2012

- **340 patients** severe AS - $AVA_i \leq 0.6 \text{ cm}^2/\text{m}^2$, LVEF > 50%

1. **9% of severe AS**
2. **Very severe AS**
3. **High global afterload**
4. **Reduced longitudinal LV systolic function**

9 %
Low Flow
Low Gradient

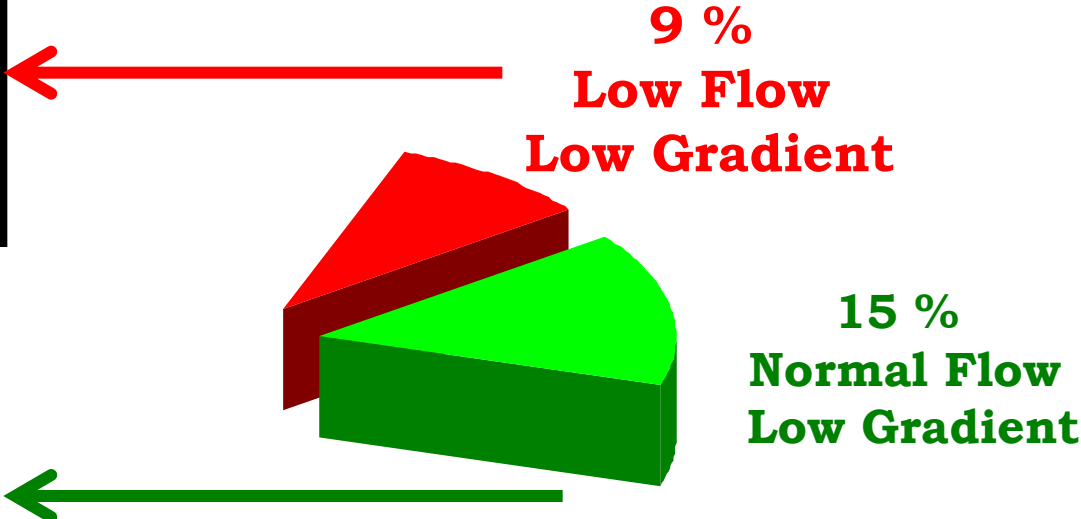


15 %
Normal Flow
Low Gradient

Low gradient aortic stenosis

Adda J , Habib G – Circulation CV Imaging 2012

- **340 patients** severe AS - $AVA_i \leq 0.6 \text{ cm}^2/\text{m}^2$, LVEF > 50%

- 
1. **9% of severe AS**
 2. **Very severe AS**
 3. **High global afterload**
 4. **Reduced longitudinal LV systolic function**

9 %
Low Flow
Low Gradient

1. **15% of severe AS**
2. **Less severe AS**
3. **Normal global afterload**
4. **Less severe LV longitudinal dysfunction**

15 %
Normal Flow
Low Gradient

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Clinical Outcome in Asymptomatic Severe Aortic Stenosis

Insights From the New Proposed
Aortic Stenosis Grading Classification

Patrizio Lancellotti, MD, PhD,* Julien Magne, PhD,* Erwan Donal, MD, PhD,† Laurent Davin, MD,*
Kim O'Connor, MD,*‡ Monica Rosca, MD,* Catherine Szymanski, MD,* Bernard Cosyns, MD, PhD,§
Luc A. Piérard, MD, PhD*

Liège, and Brussels, Belgium; Rennes, France; and Quebec, Canada



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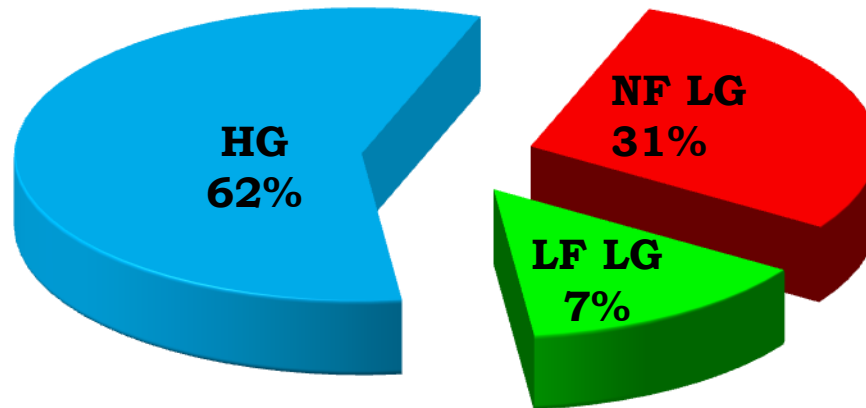
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LFLG AS: results

Magne J, Lancellotti P, Donal E – Euroecho 2011 – JACC 2012

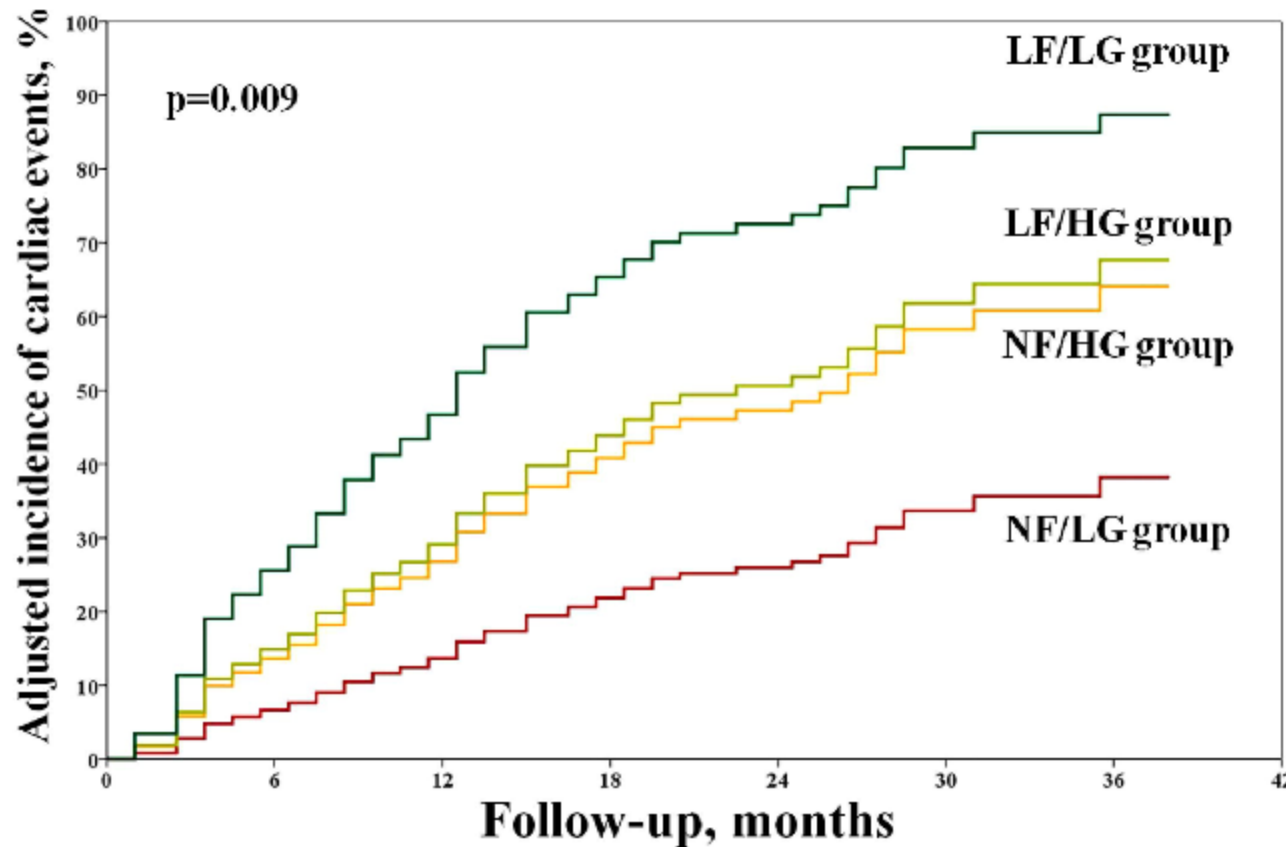
● 150 consecutive patients with asymptomatic severe AS and normal exercise test.



New classification of AS

Lancellotti P, JACC 2012

• 150 consecutive patients with asymptomatic severe AS and normal exercise test.



LF LG AS: 3 important questions

1. Was LVOT correctly measured ?
2. Does the patient have both low gradient and low flow ?
3. *Are the proposed cut-off values consistent ?*



Low-Gradient “Severe” Aortic Stenosis With Normal Systolic Function

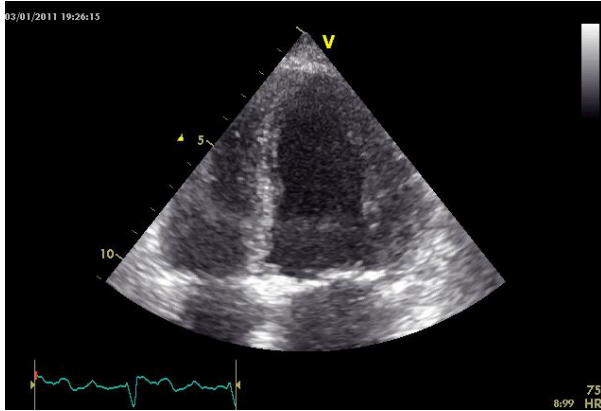
Time to Refine the Guidelines?

William A Zoghbi -Circulation. 2011;123:838-840

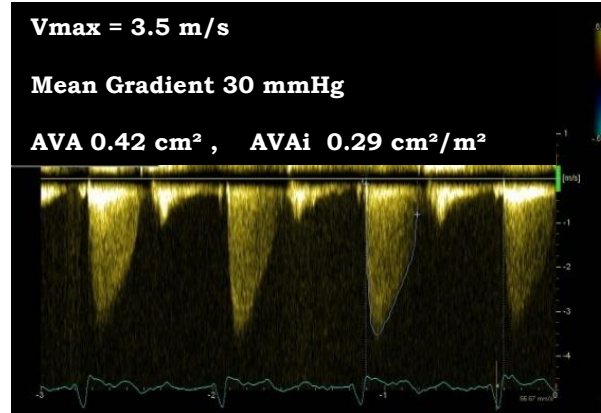
- 1. « When one combines the current prospective clinical data with earlier hemodynamic echo and invasive data that relate maximal velocity and gradients across the valve for severe AS, a good argument can be made for bringing the cut-off valve area for severe AS closer to 0.8 cm² (index 0.45 cm²/m²).**
- 2. A refinement of the guidelines in this respect would help harmonize the definition of severe AS....**
- 3. ...and would appropriately reclassify some patients with “severe” AS into moderate severity”**



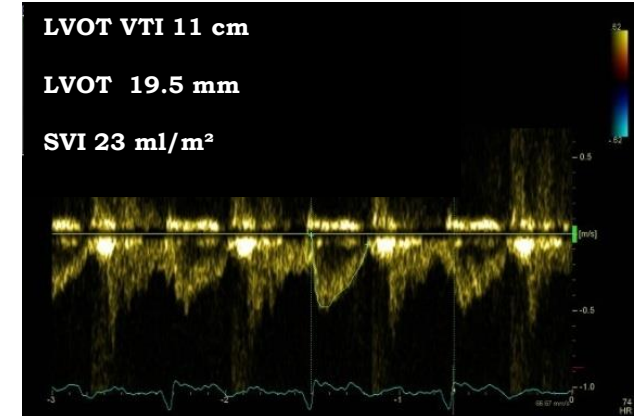
Patient 1: recent pulmonary edema



Normal LVEF



Low gradient

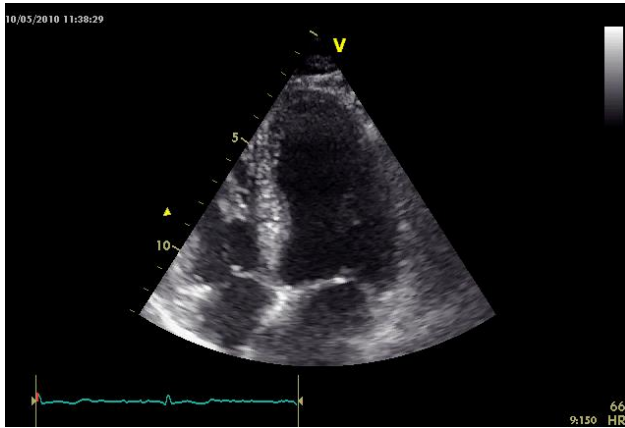


Low flow

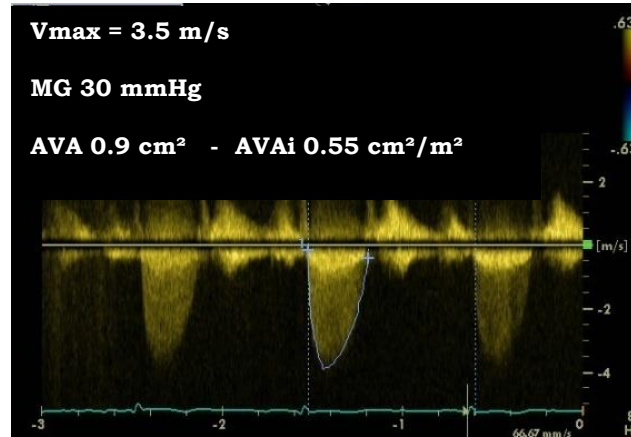
Severe aortic stenosis

Paradoxical low flow

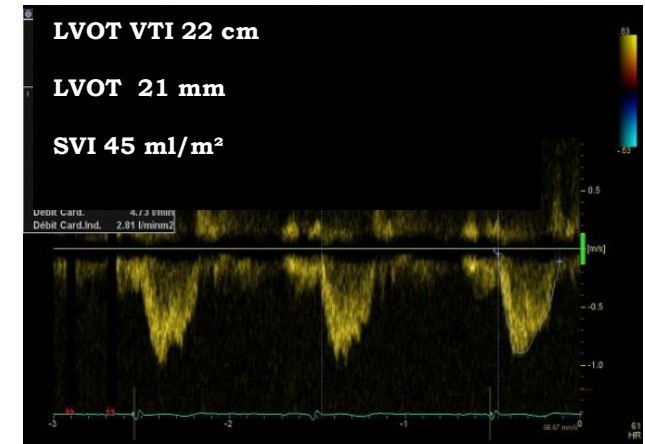
Patient 2: dyspnea on exertion



Normal LVEF



Low gradient



Normal Flow



Moderate aortic stenosis

LFLG aortic stenosis

1. Does it really exist ?
2. *Does AVR help ?*



Are patients with severe AS and low gradient improved by surgery ?

I don't know !!!



Studies on the role of surgery in LFLG AS

Author	LF / LG AS (n)	AVR (n)
1. Hachicha Z - Circulation 2007 ;	181 LF AS	(80 AVR)
2. Barasch E – J Heart Valve Dis 2008;	47 LG AS	(15 AVR)
3. Pai RG - Ann Thorac Surg 2008;	52 LGAS	(18 AVR)
4. Dumesnil JG - Eur Heart J 2009;	123 LFLG AS	(44 AVR)
5. Tarantini G - Ann Thorac Surg 2011;	102 LFLG AS	(73 AVR)
6. Jander N – Circulation 2011;	435 LG AS	(183 AVR)
7. Clavel AM – JACC 2012;	187 LFLG AS	(83 AVR)
8. Ozkan A – Circulation 2013;	260 LG AS	(123 AVR)



Limitations of previous studies

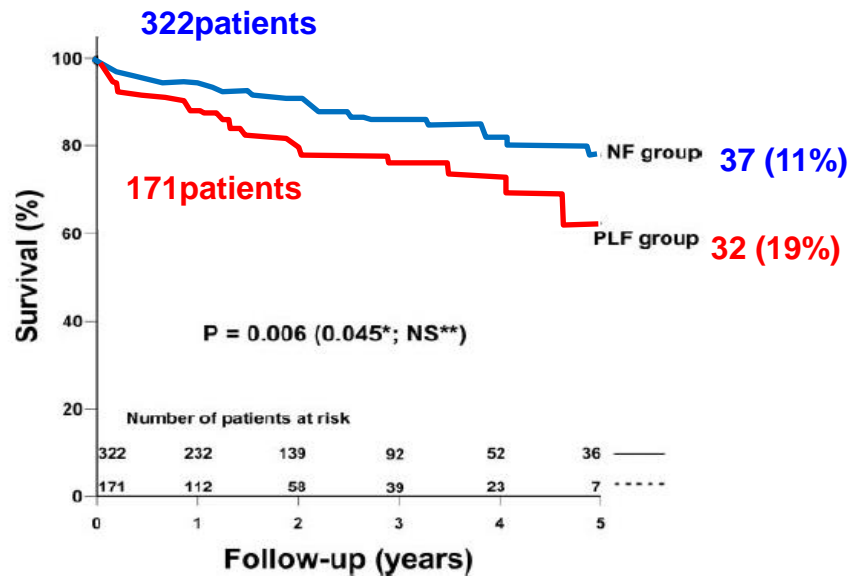
1. Retrospective, non randomized
2. Few studies, few patients, few events
3. Symptomatic status unknown in the majority
4. Various definitions of AS severity and of LF and/or LG AS
5. Reasons for surgery / no surgery unknown in the majority
6. Influence of associated CABG
7. Comorbidities not taken into account



Effect of surgery on LF AS

Hachicha Z - Circulation 2007 ; 115 : 2856-64

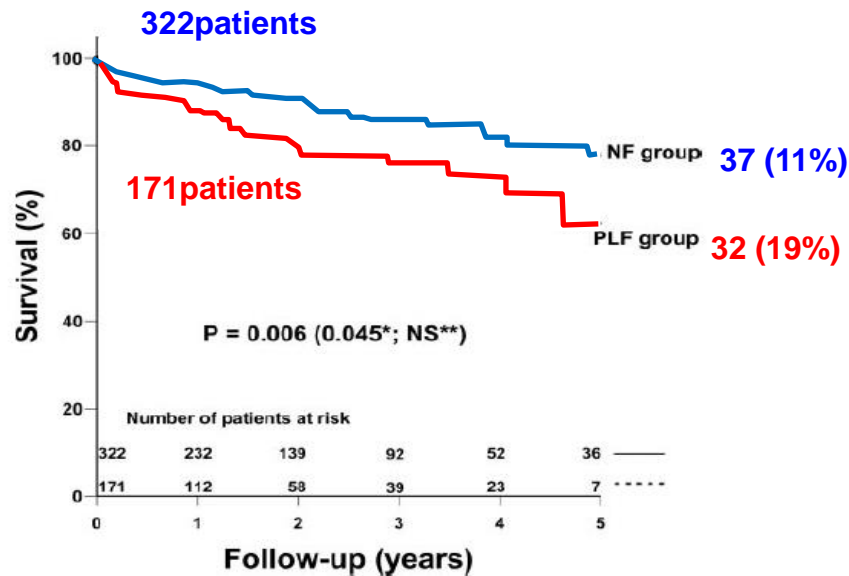
493 severe AS
and LVEF > 50%



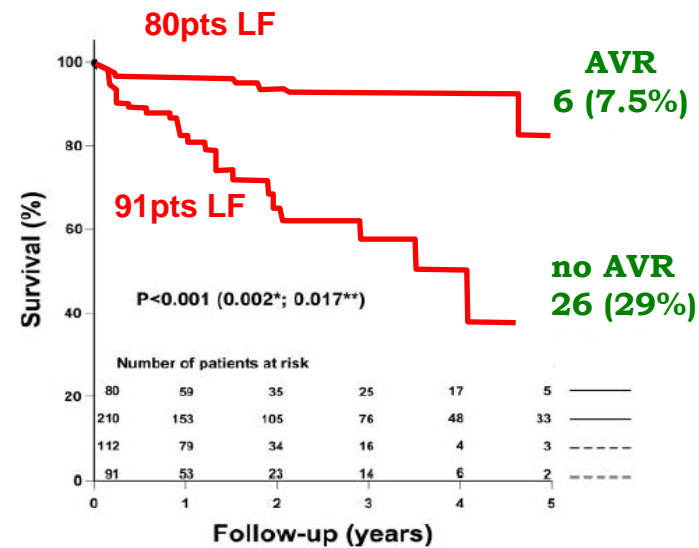
Effect of surgery on LF AS

Hachicha Z - Circulation 2007 ; 115 : 2856-64

493 severe AS
and LVEF > 50%



171 patients with
Low-Flow AS



Surgery does not improve outcome

Jander N – Circulation 2011; 123: 887-95

1. prospective study (SEAS study)
2. 1525 asymptomatic AS
3. 435 LG severe AS (MG < 40 mmHg, AVA < 1 cm²)
4. 184 moderate AS (MG 25-40 mmHg, AVA < 1.5-1 cm²)
5. 45 +/-14 months follow-up
6. Significant CAD excluded



LG AS is no more than a moderate AS

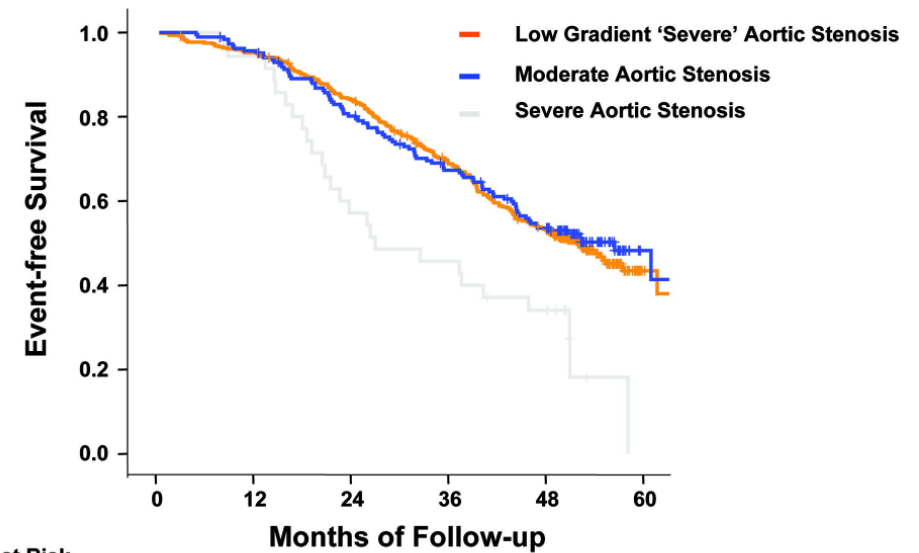
Jander N – Circulation 2011; 123: 887-95

- 435 LG - SAS
- 35 HG – SAS
- 184 moderate AS

- No significant difference in major cardiovascular events or death

- No beneficial effect of surgery

B Major Cardiovascular Events

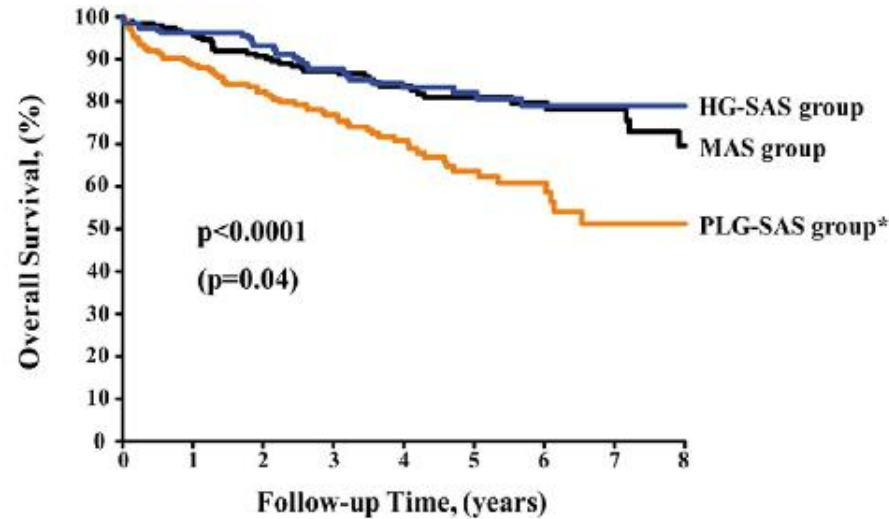


No. at Risk	0	12	24	36	48	60
LGSAS	435	413	364	296	225	17
Moderate AS	184	175	146	122	93	10
Severe AS	35	33	21	16	11	0

Surgery is beneficial ?

Clavel MA - J Am Coll Cardiol 2012

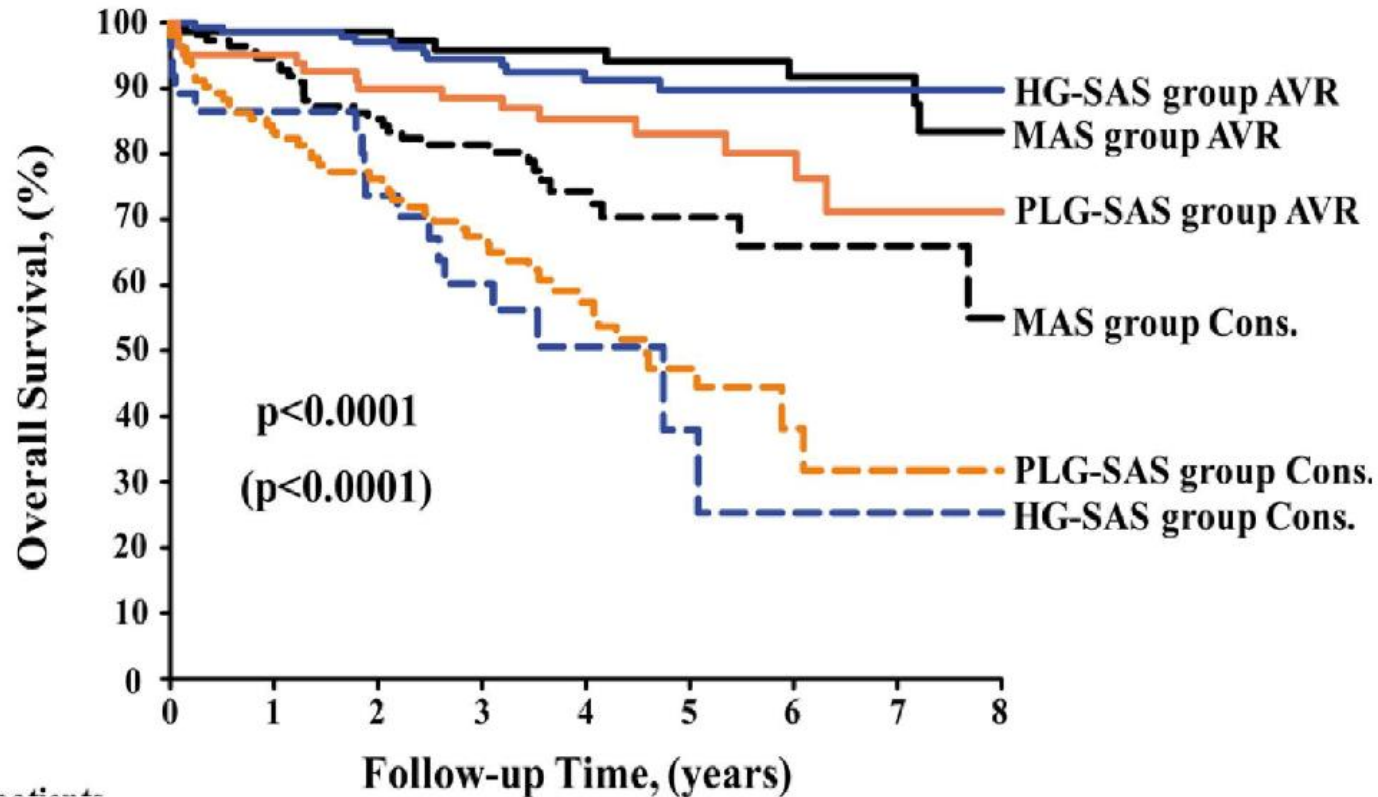
- 187 PLG - SAS
- 187 HG - SAS
- 187 moderate AS



N patients at risk:	187	178	163	141	101	75	56	35	22	—
	187	163	143	119	80	53	31	18	11	—
	187	175	149	115	86	63	46	36	18	—

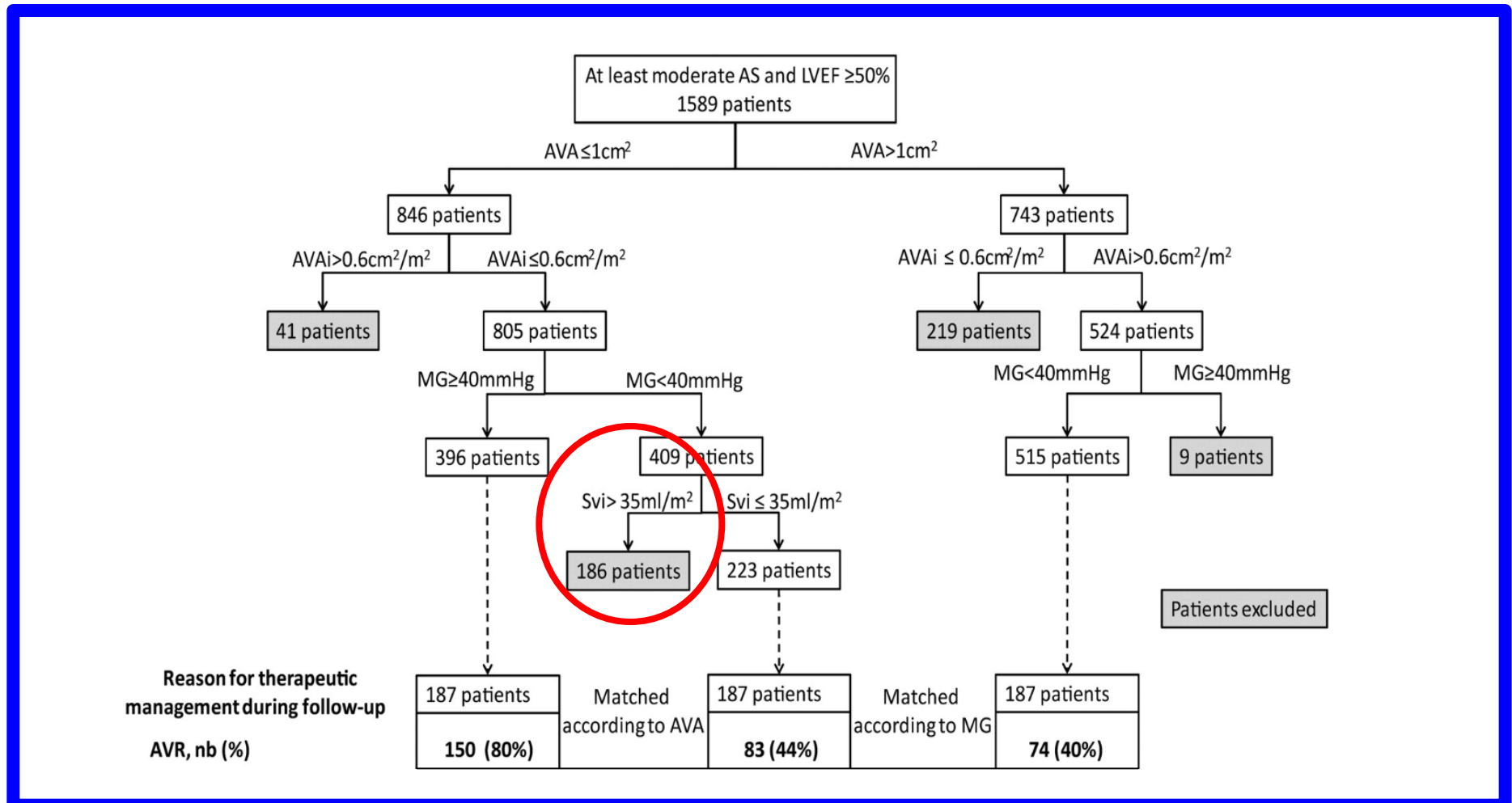
Surgery is beneficial?

Clavel MA - J Am Coll Cardiol 2012



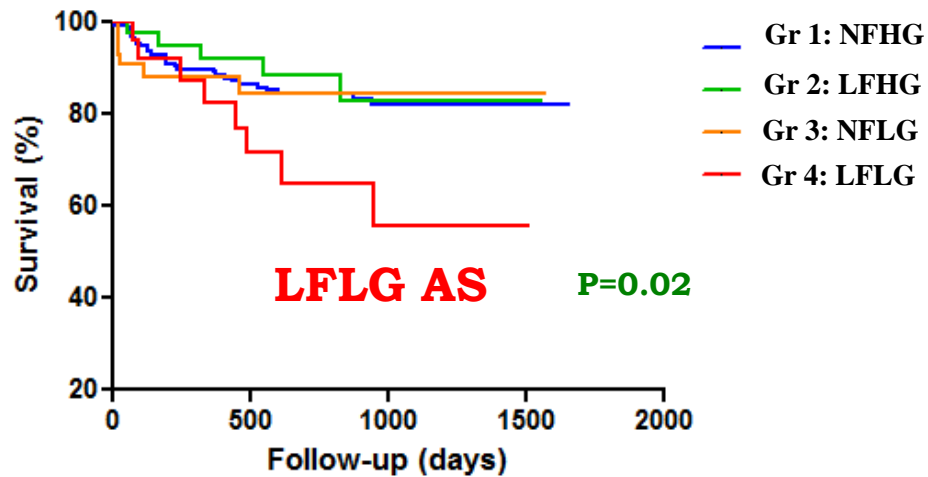
Surgery is beneficial ?

Clavel MA - J Am Coll Cardiol 2012



Survival is worse in LFLG

Adda J, Habib G – Euroecho 2011

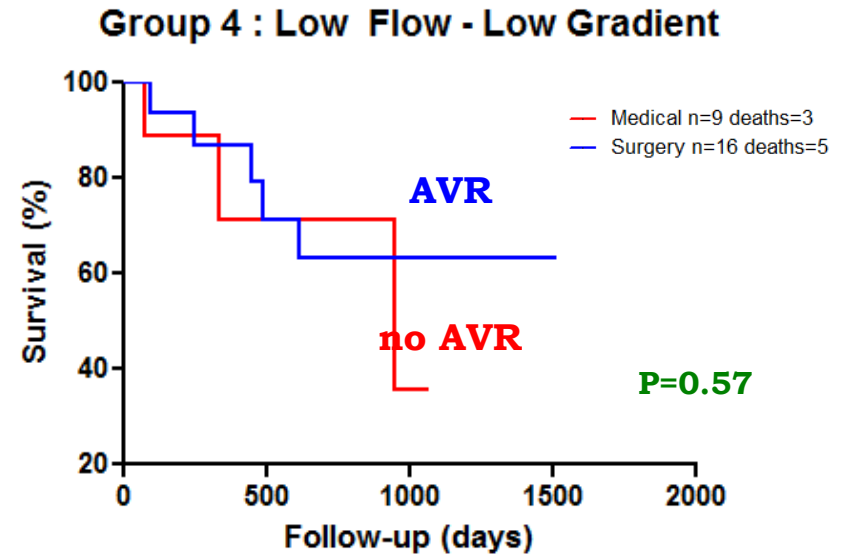
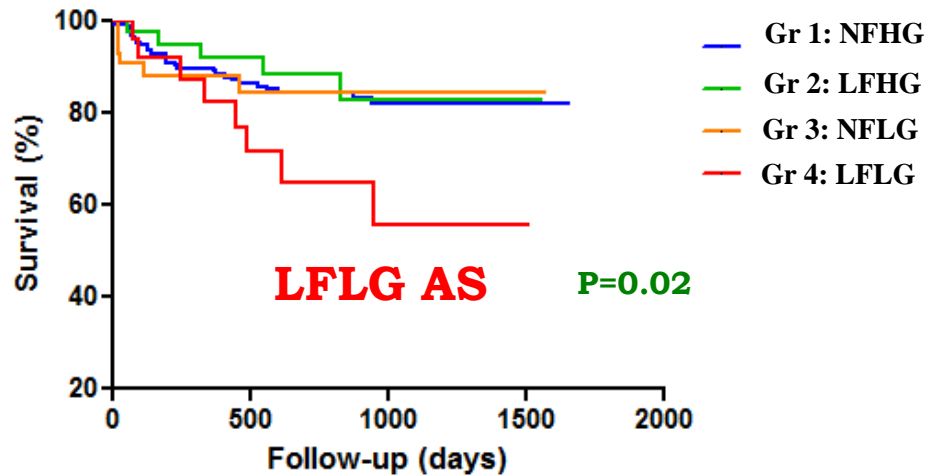


Survival in Low Flow Low Gradient vs other groups



Survival is worse in LFLG

Adda J, Habib G – Euroecho 2011



Survival in Low Flow Low Gradient vs other groups

Take-home messages

1. LF LG aortic stenosis is a real entity observed in 10% cases of severe AS with normal LVEF
2. These patients present with high global afterload and reduced longitudinal systolic function, as assessed by 2D strain
3. They are associated with worse prognosis
4. **They must be differentiated from patients with NFLG aortic stenosis**
5. Benefit of surgery is not proven in LG aortic stenosis but it is probably beneficial in selected symptomatic patients with both low flow and low gradient AS



Conclusion

Paradoxical Low-Flow, Low-Gradient Aortic Stenosis

Adding New Pieces to the Puzzle*

“Additional outcome studies are needed to determine the most appropriate modality and timing of treatment in patients with low-flow, low-gradient AS.....”



Conclusion

Paradoxical Low-Flow, Low-Gradient Aortic Stenosis

Adding New Pieces to the Puzzle*

Pibarot P, Dumesnil JG - JACC 2011; 58: 413-5

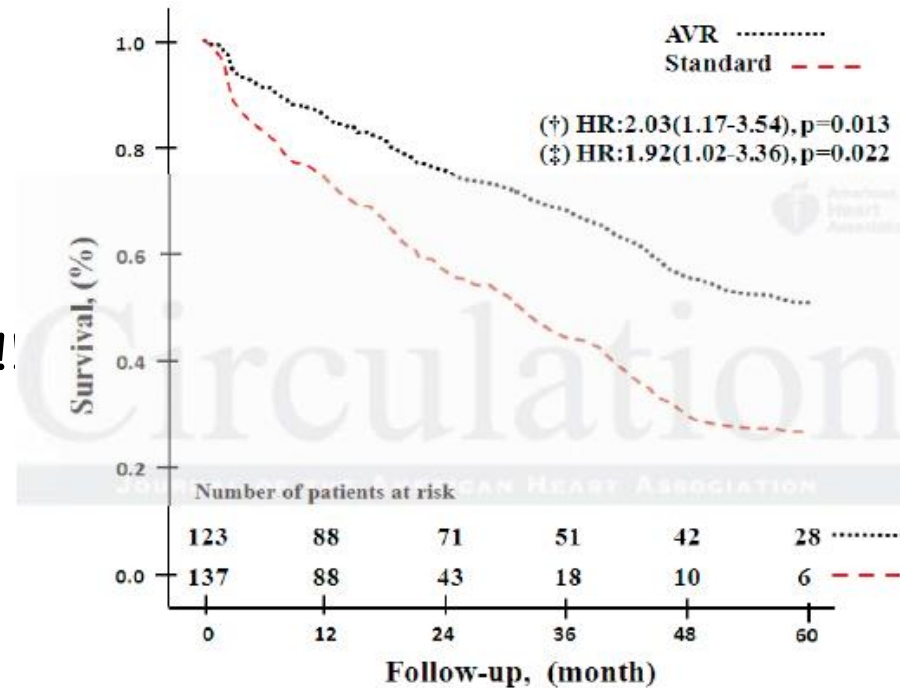
“Additional outcome studies are needed to determine the most appropriate modality and timing of treatment in patients with low-flow, low-gradient AS.....”



Is surgery beneficial ?

Ozkan A – Circulation 2013

- 260 PLG – SAS
- AVR in 123 (47%) patients
- 28 +/- 24 months FU
- 105 (40%) deaths during FU
- 73% deaths in medical group !

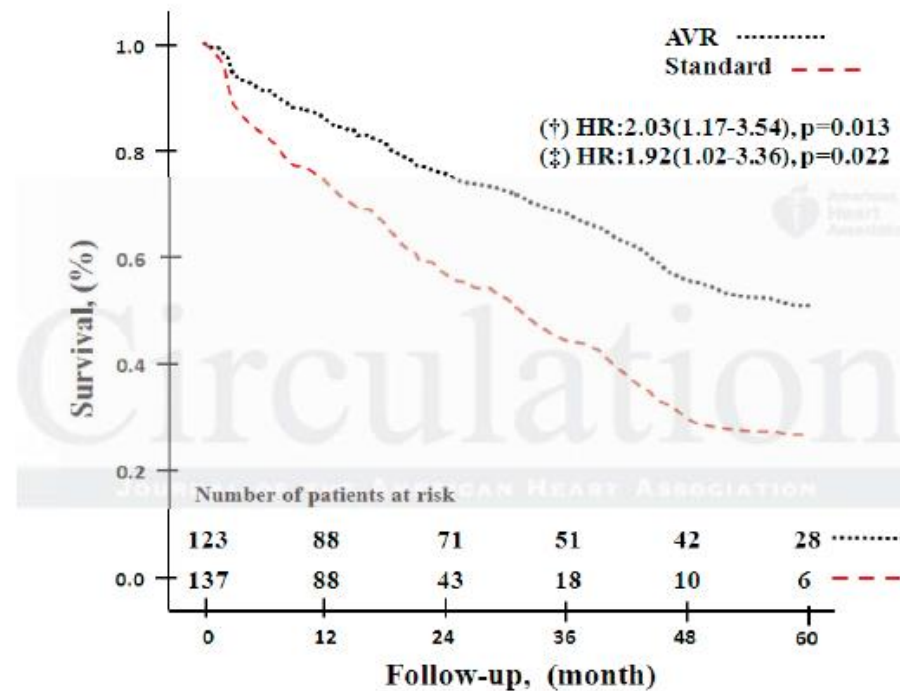


Medical therapy = 2-fold increase in mortality than AVR

Is surgery beneficial ?

Ozkan A – Circulation 2013

- Non randomized study
- Patients without AVR
 - Higher prevalence of diabetes
 - Lower SVI
 - Higher sPAP
 - Higher creatinin level



Medical therapy = 2-fold increase in mortality than AVR

**Since the healthier group of patients underwent surgery,
it is not surprising
that AVR was associated with lower mortality**

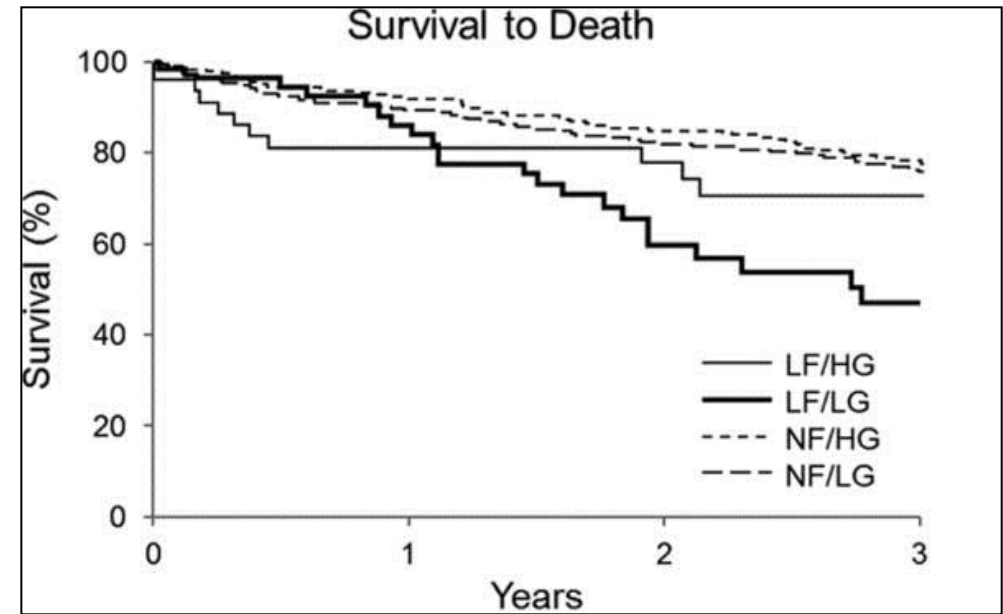
**So it must be cautioned that the finding that
AVR substantially reduces mortality
may be an overestimate of the true benefit**



Is surgery beneficial ?

Eleid MF- Circulation. 2013;128:1781-1789

- 1704 severe AS with normal LVEF
- 352 (21%) NFLG AS
- 53 (3%) LFLG AS



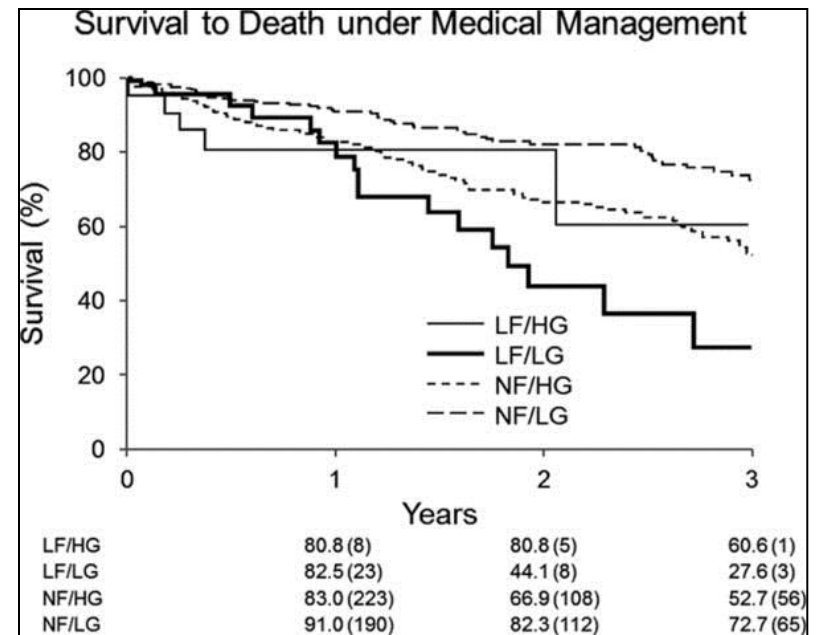
Good outcome under medical therapy in NFLG AS

Reduced survival in LFLG AS

Is surgery beneficial ?

Eleid MF- Circulation. 2013;128:1781-1789

- 1704 severe AS with normal LVEF
- 352 (21%) NFLG AS
- 53 (3%) LFLG AS



Better outcome after surgery in LFLG AS

No survival benefit after surgery in NFLG AS

Take-home messages

1. Verify that AS is really severe
2. Verify that the symptoms of the patients are related to AS
3. Verify that the patient has both LF and LG AS
4. Consider comorbidity and operative risk
5. Propose surgery in selected symptomatic patients with both low flow and low gradient AS and acceptable operative risk



Conclusion

**Don't send to surgery
patients with moderate AS !!**





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