DYSSYNCHRONY IN AORTIC STENOSIS AND NO FLOW RESERVE – A REALITY?

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Disclosure Statement of Financial Interest

I, Raluca Dulgheru, DO NOT HAVE a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation

Class I Indications for AVR/TAVR in AS

- ✓ **SEVERE AS**

  Echo Key exam in AS

- ✓ **SYMPTOMATIC PATIENT**
  - ✓ **EXERCISE INDUCED DYSPNEA/HEART FAILURE**
  - ✓ **EXERCISE INDUCED ANGINA**
  - ✓ **EXERCISE INDUCED SYNCOPE**

Echocardiographic criteria for the definition of severe valve stenosis: *an integrative approach*

	Aortic stenosis
Valve area (cm^2)	< 1.0
Indexed valve area (cm^2/m^2 BSA)	< 0.6
Mean gradient (mmHg)*	> 40
Maximum jet velocity (m/s) *	> 4.0
Velocity ratio	< 0.25

Advantages	Limitations
Measures EOA, less flow dependent	More prone to measurement errors
Very useful in small or very tall patients	More prone to measurement errors
Averaged from velocity curve; Units comparable to invasive measurements	Flow dependent; need for correct allignement
Direct measurement of velocity, strongest predictor of clinical outcome	Flow dependent; need for correct allignement
Less variablility compared to AVA, no need for LVOT	Limited longitudinal data

**** In the presence of normal flow***

Adapted from Baumgartner, EAE/ASE recommendations. *Eur J Echocardiogr.* 2010;10:1-25

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

EACTS

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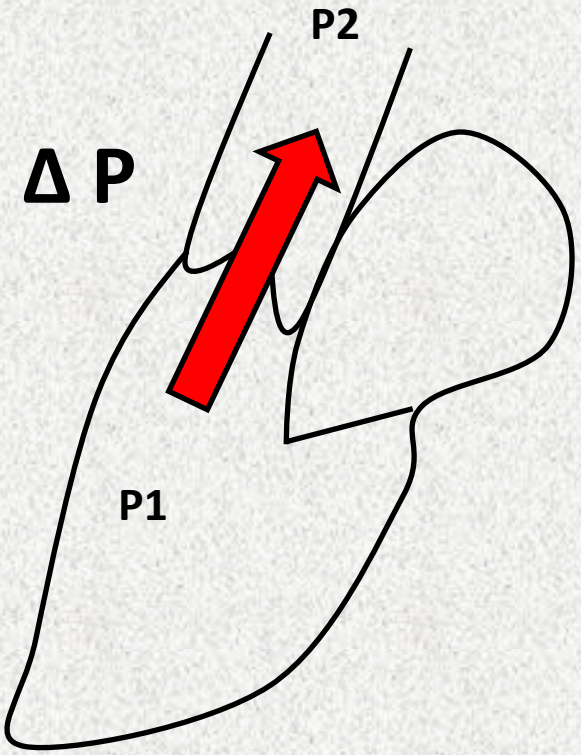
Gradient dependence on flow

- Physic Basics -

Force propelling the blood



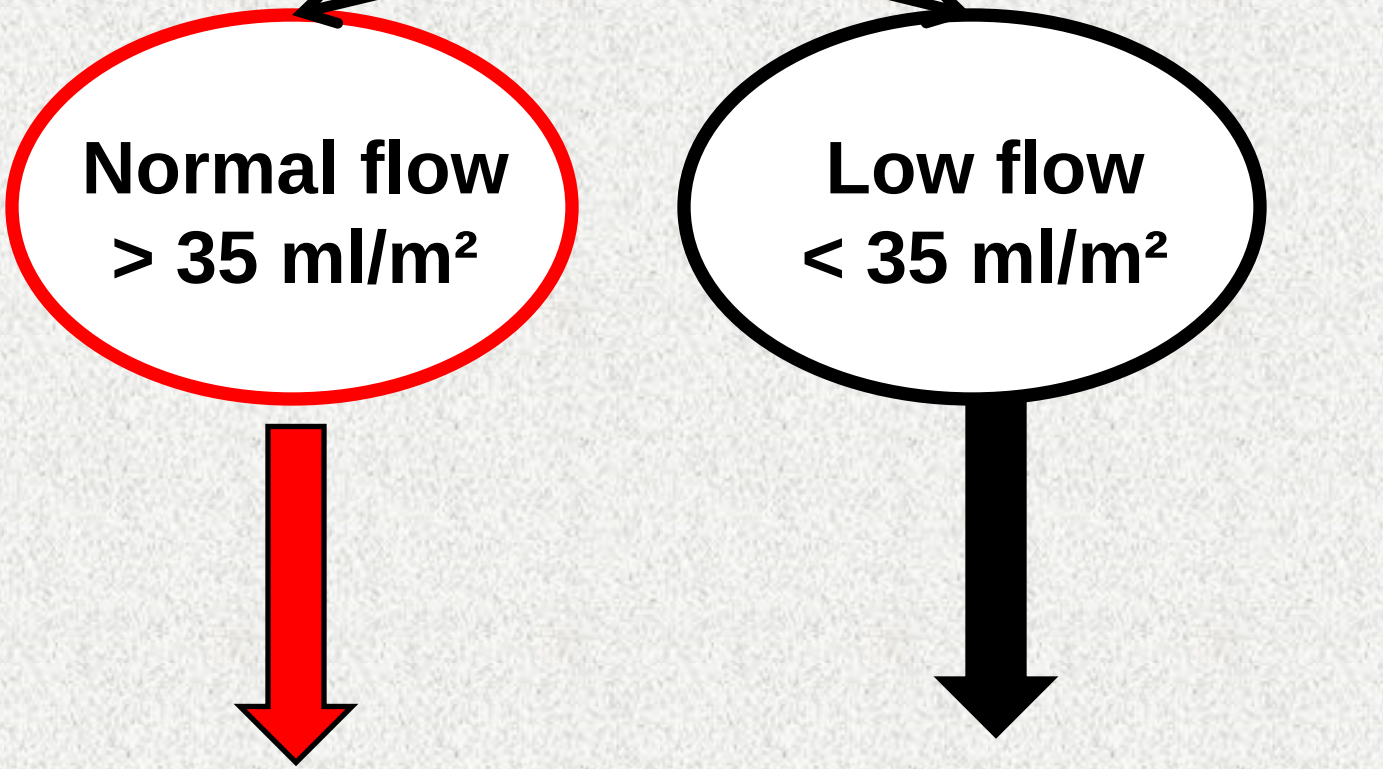
$$\text{Gradient} = Q^2 / k^* AVA^2$$

Fixed stenosis : any drecrease in flow will lead to a significant decrease in ΔP

AS PATIENTS

AVA less flow dependent

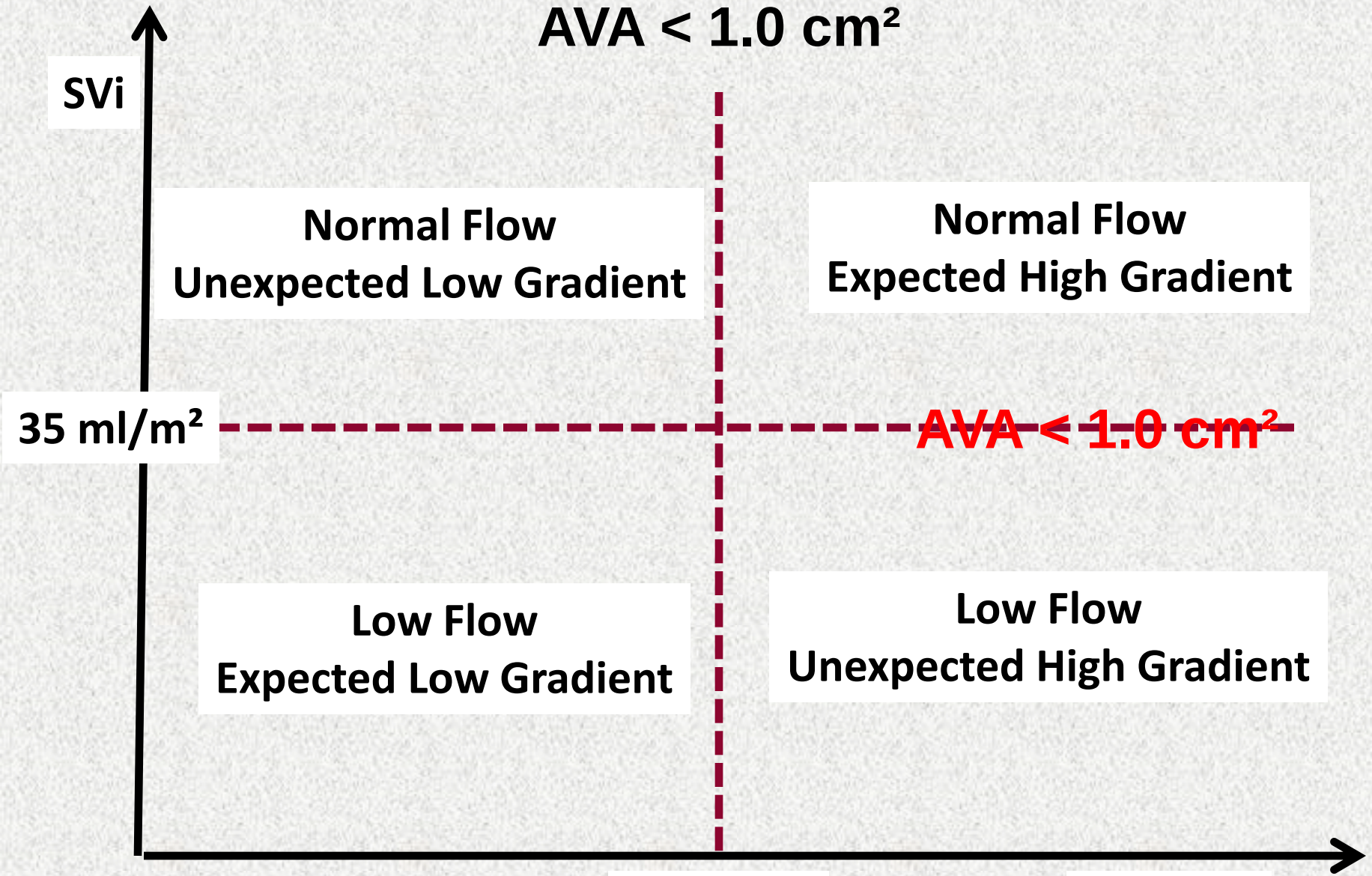
AVA < 1.0 cm²



Expected high MG
>40 mmHg

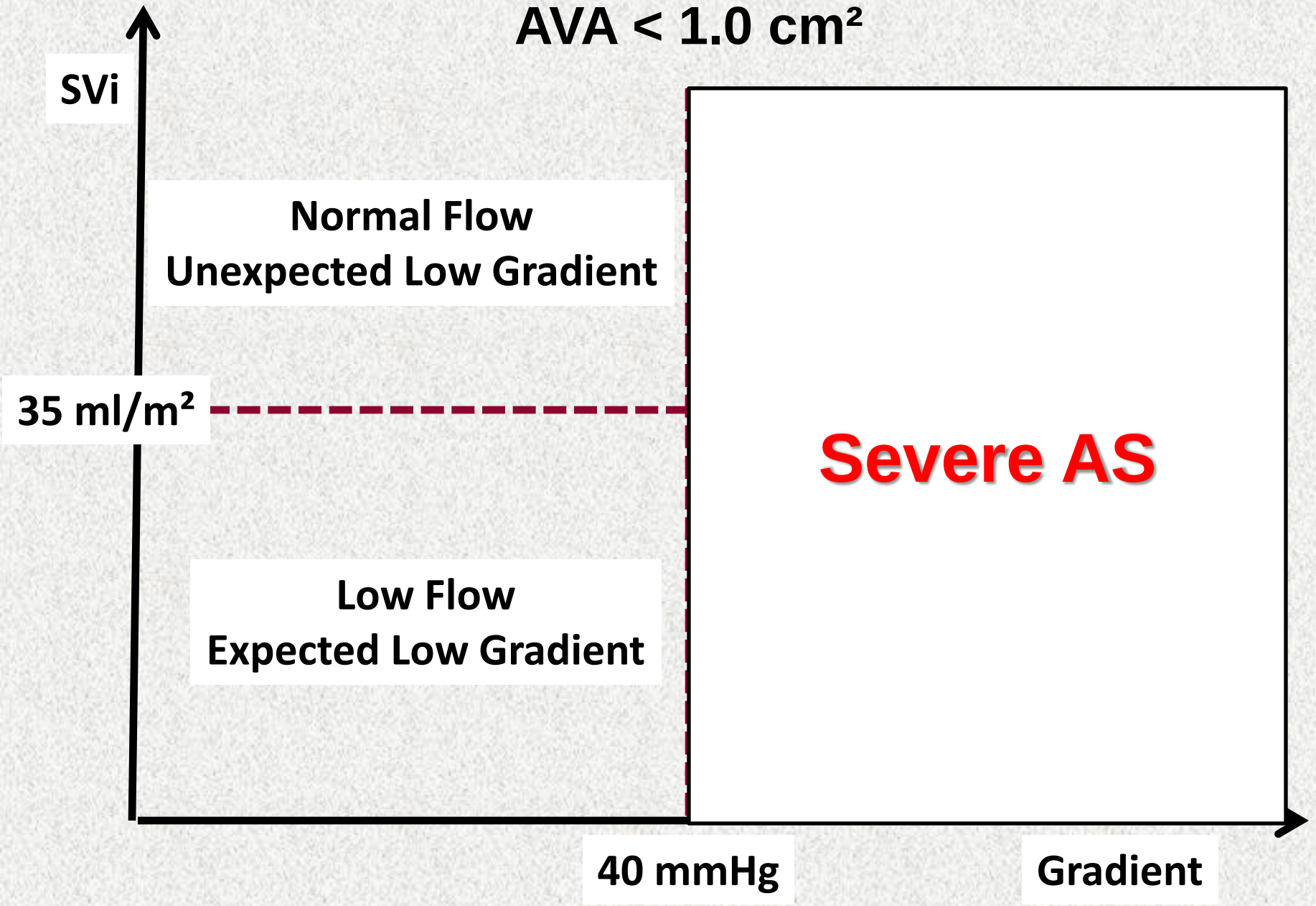
Expected low MG
<40 mmHg

AS PATIENTS: Reality

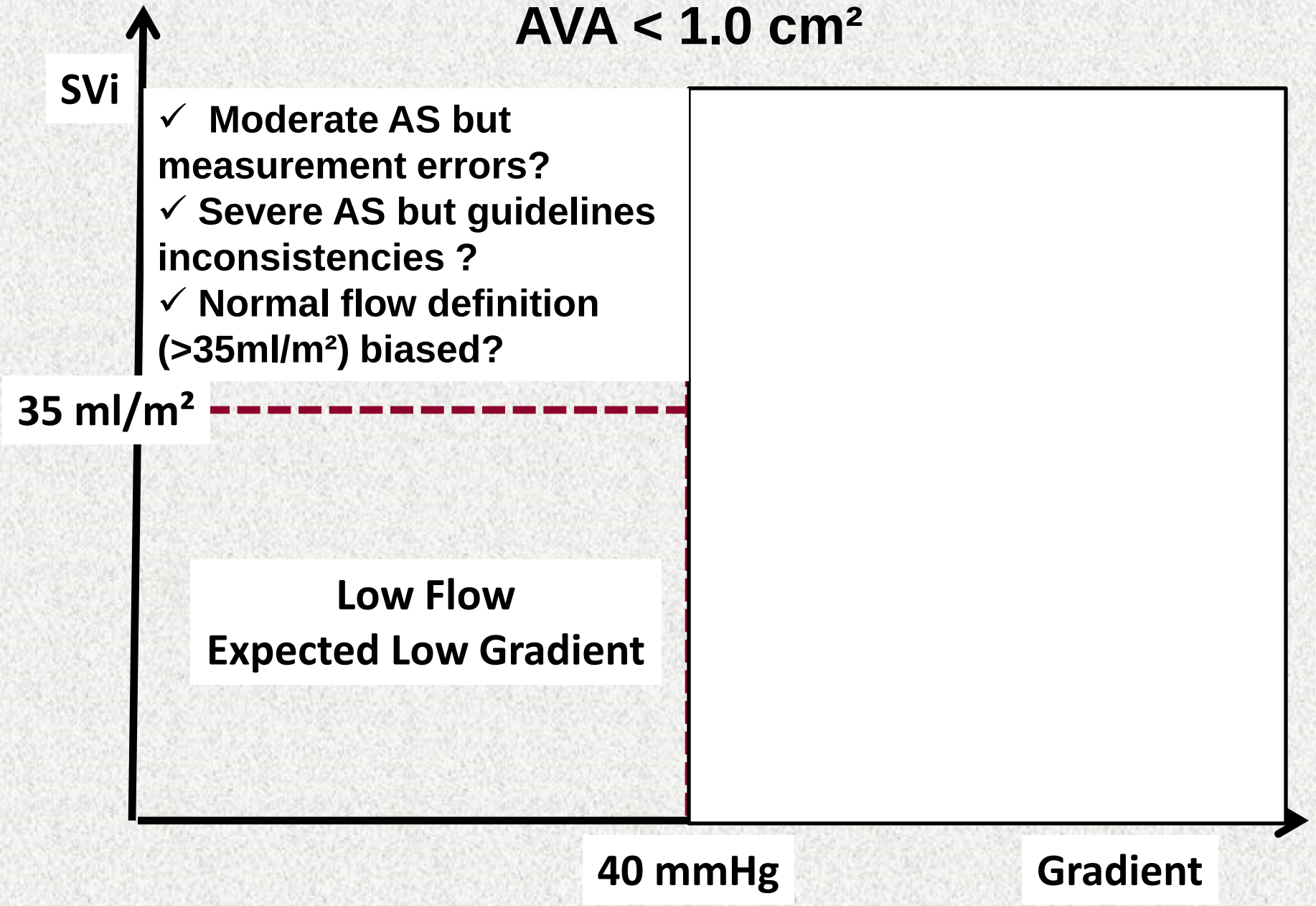


Dumesnil, Pibarot, EHJ 2010
Lancellotti, Magne, JACC 2012

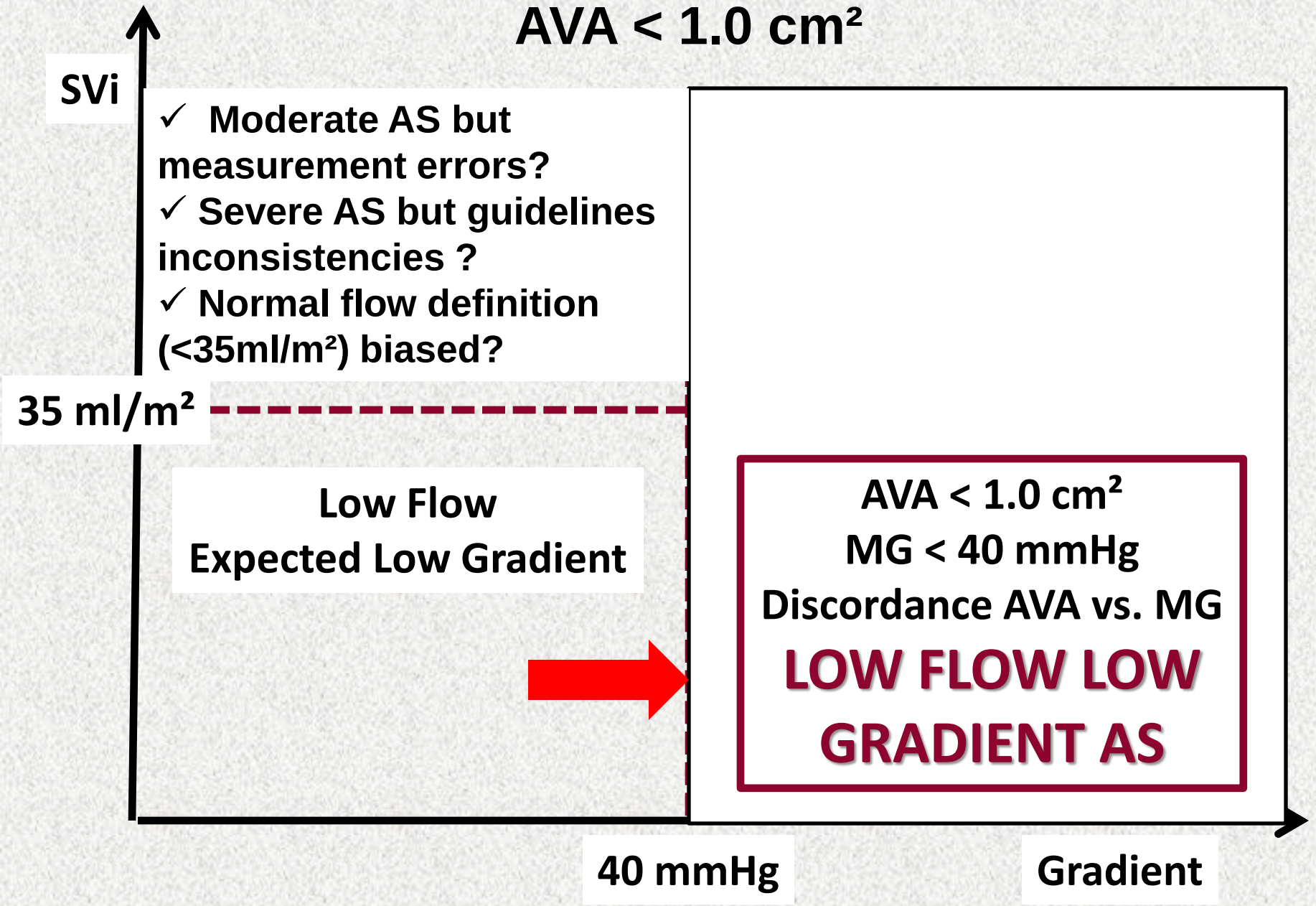
AS PATIENTS: Reality



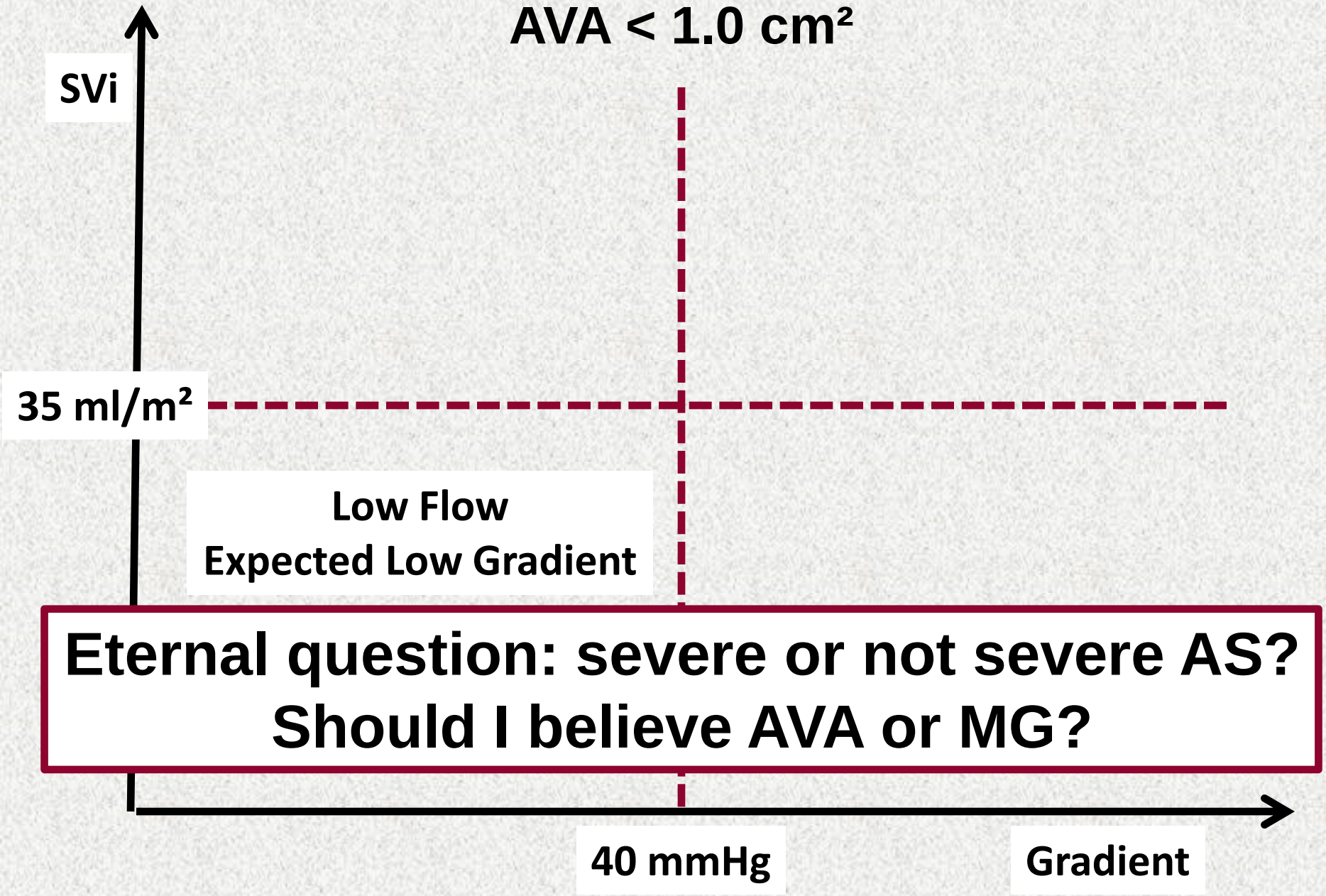
AS PATIENTS: Reality



AS PATIENTS: Reality

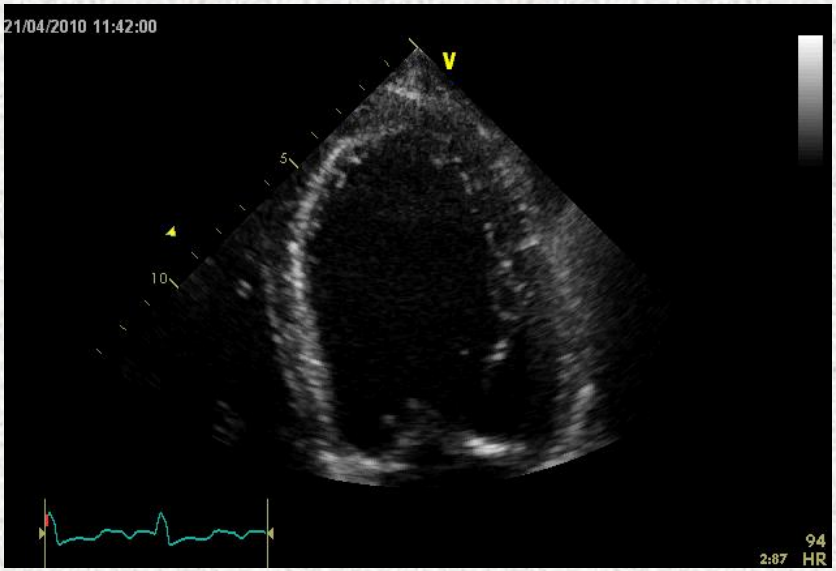


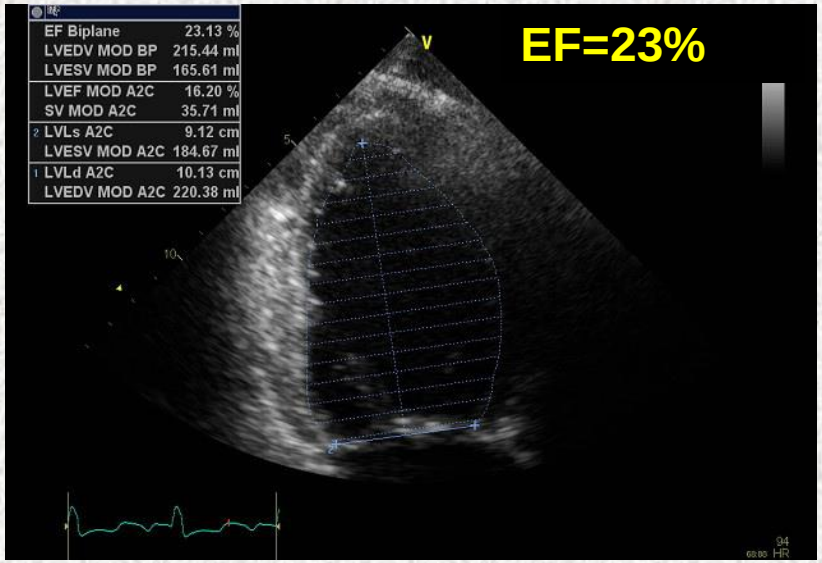
AS PATIENTS: Reality

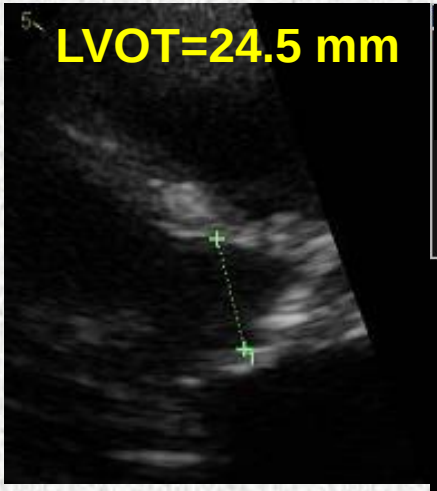


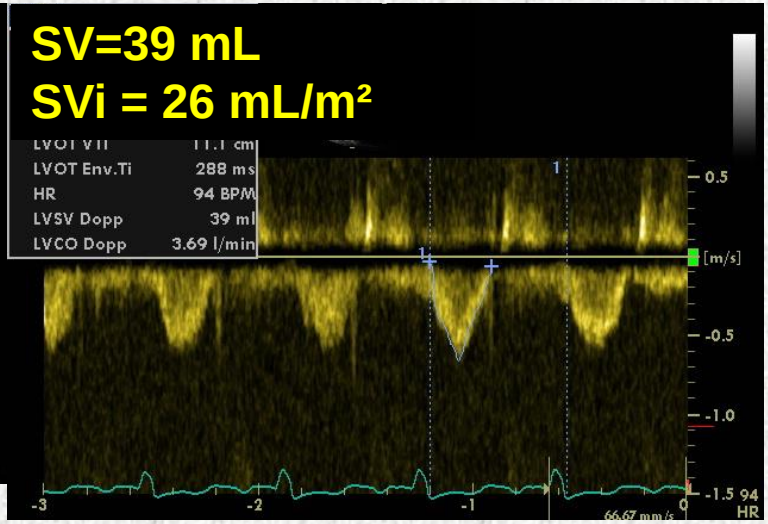
Before deciding…Normalize flow !!!

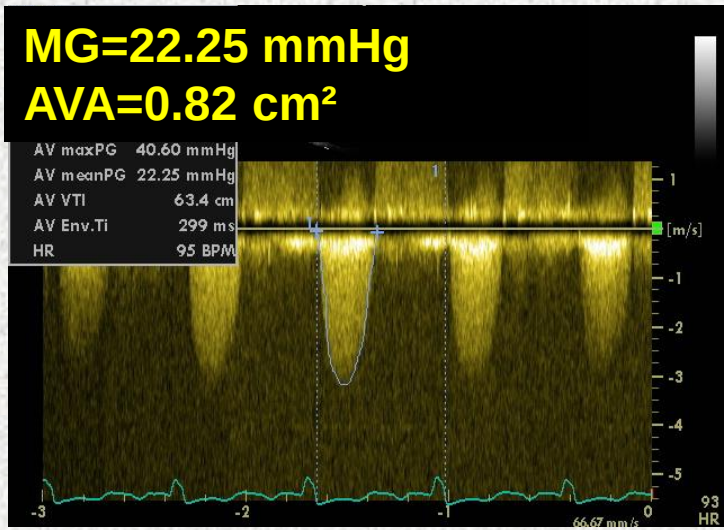
Low Flow Low Gradient AS with reduced LVEF











Usefulness of Dobutamine Stress Echo (DSE) in LF/LG AS

Low Flow, Low Gradient Severe AS

AVA <1.0 cm^2, ΔP_{mean} < 40 mmHg, LV EF < 50%

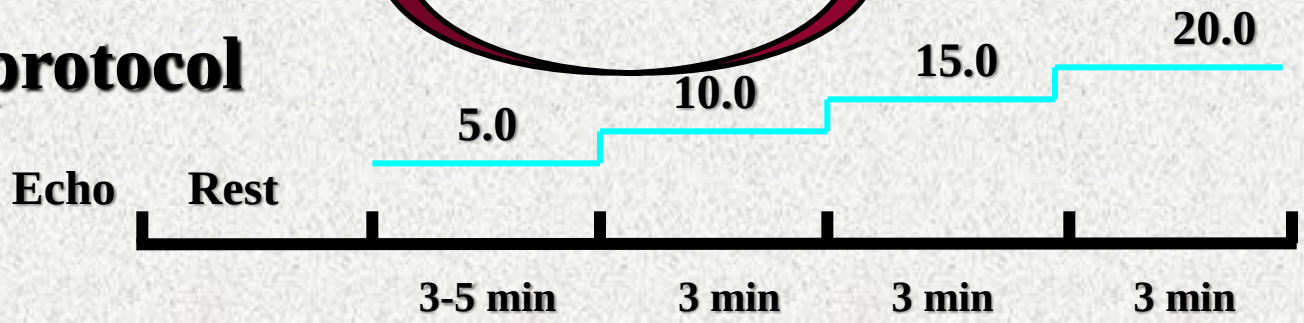
Dobutamine Stress Echocardiography

Normalize flow

Increase LV contractility

Stenosis Severity (True vs. Pseudo Severe AS)

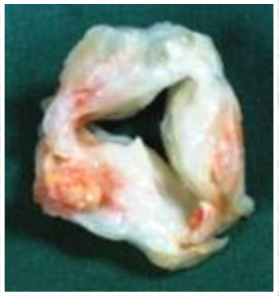
Infusion protocol



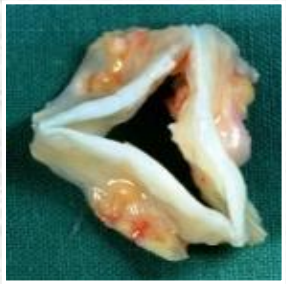
Monitoring: ECG, blood pressure

DeFillipi, AJC 1995

AVA is also flow dependent!



True-Severe AS



Pseudo-Severe AS

Normal flow

Low flow

AVA<1cm²

MG<40mmHg

AVA<1cm²

MG>40mmHg

AVA>1cm²

MG<40mmHg ⟷ MG<40mmHg

Low flow

AVA<1cm²

Adapted from P Pibarot, with permission

Low-dose Dobutamine Echocardiography in LF LG AS with LV dysfunction

Low-flow / Low-gradient AS (n=136)

LV Contractile Reserve = ↑ Stroke Volume > 20%

Contractile Reserve n= 92 (68%)	No Contractile Reserve n=44 (32%)
• AVR : 64 patients (70%) • Deaths (D30) n= 3 (5%) • Associated CABG (n= 19): Deaths (D 30) n= 2 (11%)	• AVR : 31 patients (70%) • Deaths (D 30) n= 10 (32%)* • Associated CABG (n= 8): Deaths (D 30) n= 5 (68%)*

*** p< 0.005 vs Group I**

Monin et al. Circulation. 2003;108: 319

Low Flow Low Gradient – LV dysfunction AS

Low-dose DSE

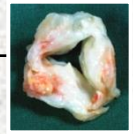
↑ SV ≥ 20%

↑ SV < 20%

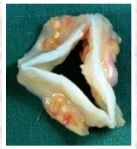
Flow Reserve

No Flow Reserve

ΔP_{mean} increases
AVA ≤ 1.0



ΔP_{mean} ≈ ct
AVA > 1.0



True Severe AS

Pseudo Severe

Indeterminate AS

MDCT: Ca++

AVR/TAVR±CABG

Medical treatment

Medical ? AVR/TAVR ?

LF LG AS with depressed LVEF

AVA < 1 cm^2 (<0.6 cm^2/m^2)

<u>with</u> LV Dysfunction (EF ≤ 40%, <50%)

<u>And</u> Mean Gr ≤ 40 mm Hg

Approximatively 5-10% of AS population

High risk pts : 3y survival rate < 50 %

If operated (AVR): operative mortality : 6-33%

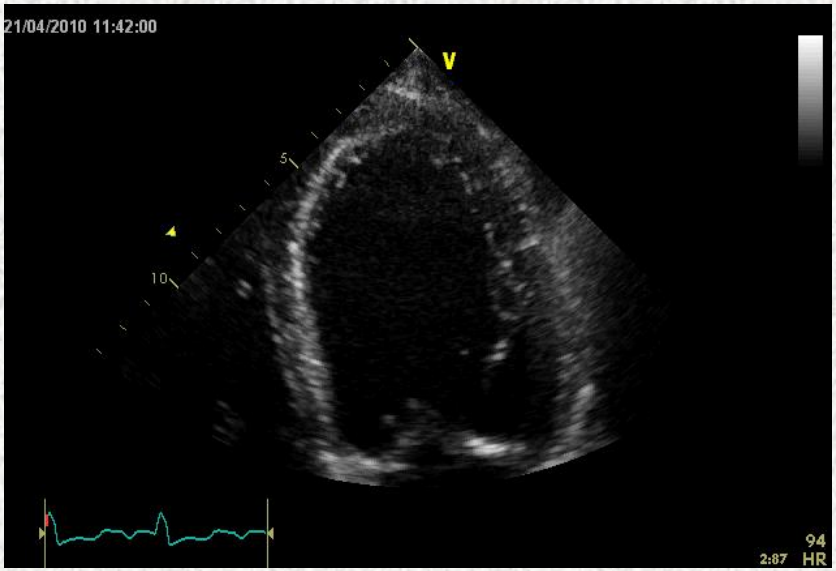
P Pibarot, JACC 2012

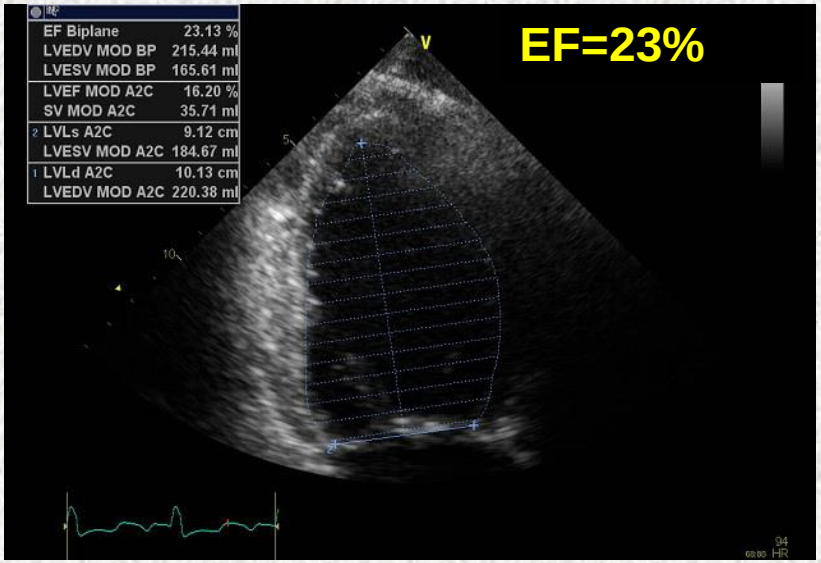
Approx. 30% do not have flow reserve

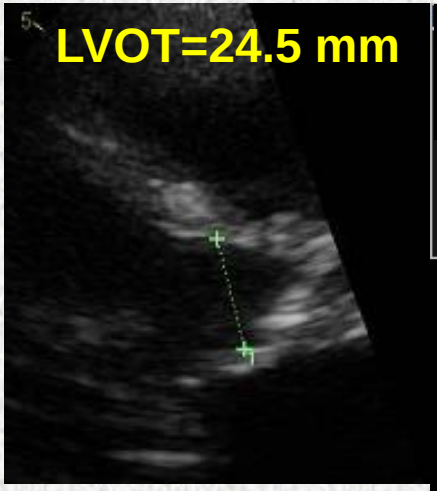
Monin, JACC 2001
Schwammenthal, Chest 2001
DeFillipi, AJC 1995
Monin, Circulation 2003

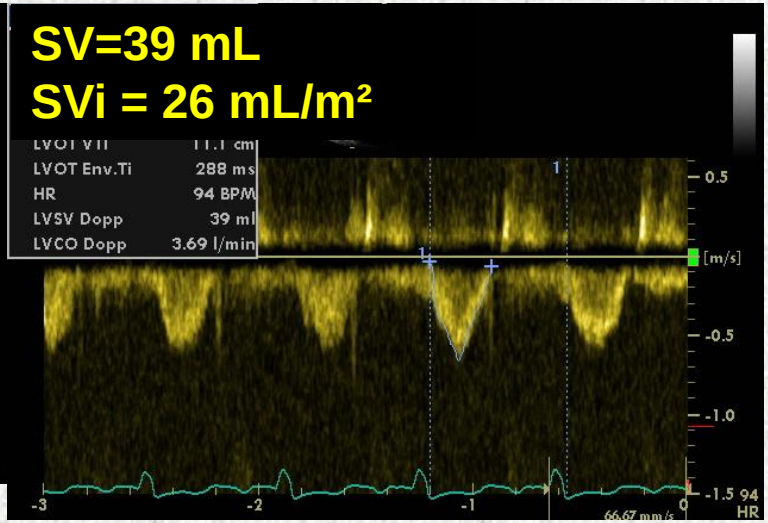
True Severe AS – Easy case

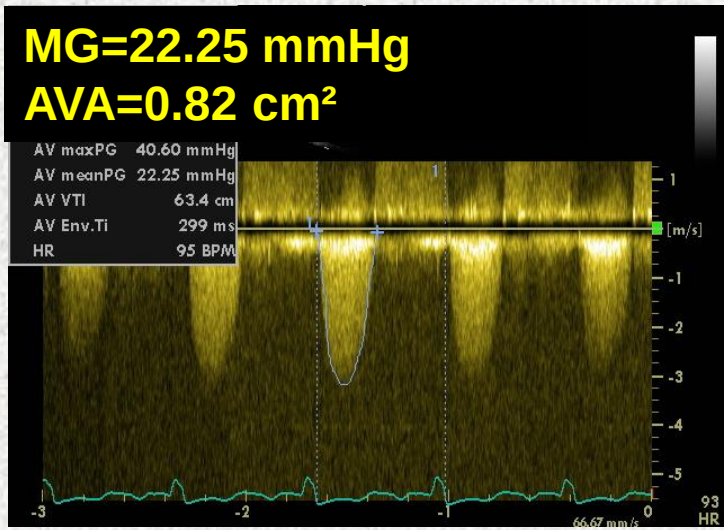
Baseline







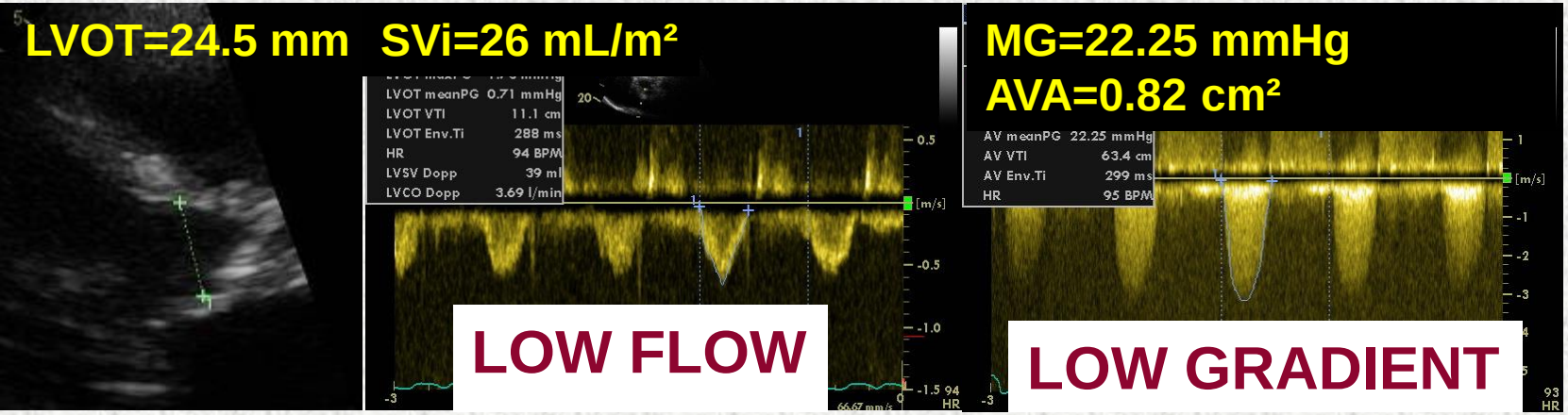




True Severe AS – Easy case

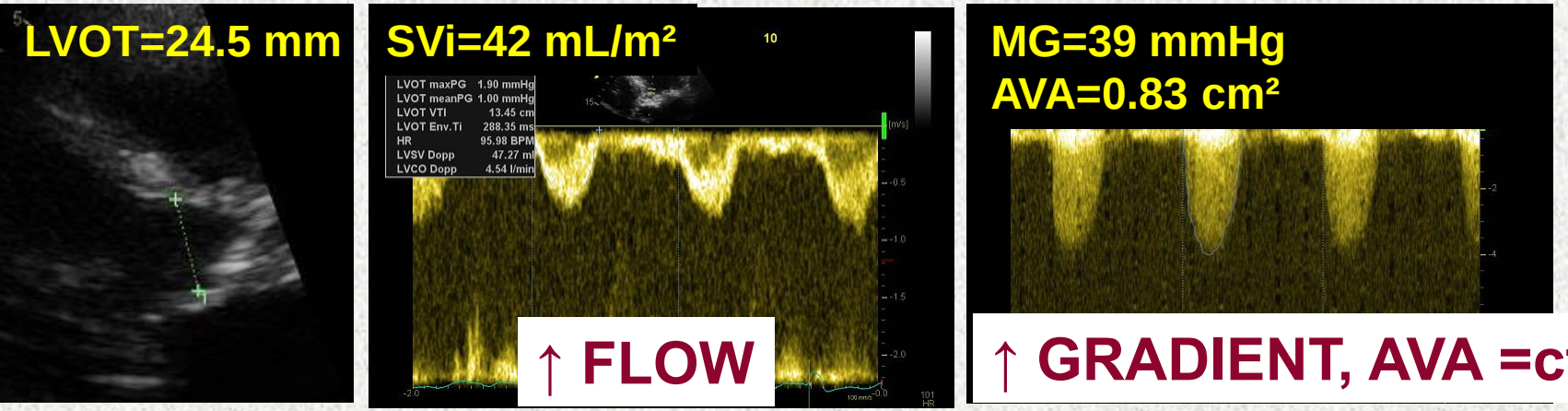
Dobutamine Stress Echocardiography

BASELINE



DOBUTAMINE (10γ/Kgc/min)

TRUE SEVERE AORTIC STENOSIS



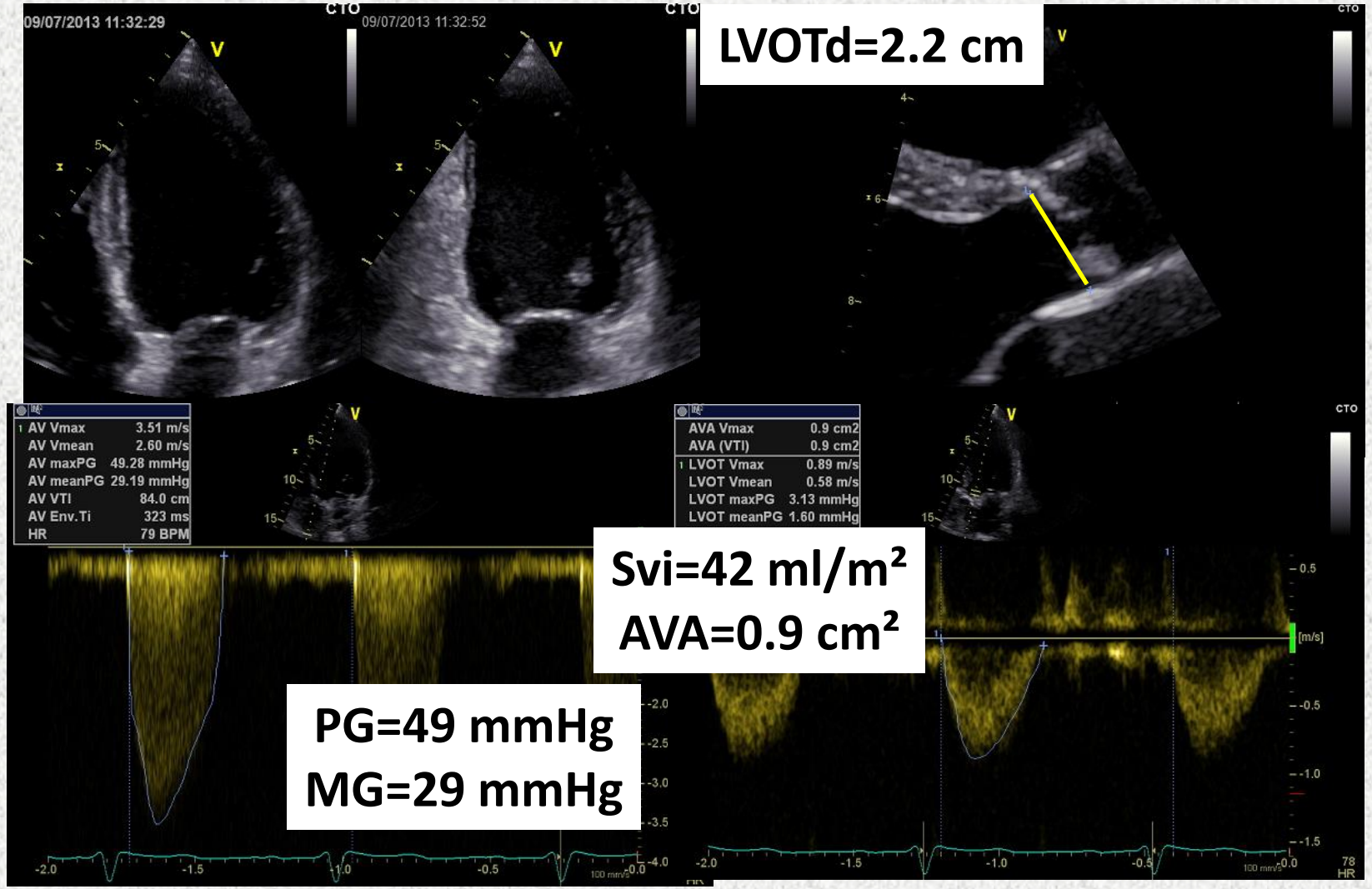
Indications for AVR in symptomatic AS

	Class	Level
AVR is indicated in patients with severe AS and any symptoms related to AS.	I	B
AVR is indicated in patients with severe AS undergoing CABG, surgery of the ascending aorta or another valve.	I	C
AVR should be considered in patients with moderate AS undergoing CABG, surgery of the ascending aorta or another valve.	IIa	C
AVR should be considered in high risk patients with severe symptomatic AS who are suitable for TAVI but in whom surgery is favoured by a “heart team” based on the individual risk profile and anatomic suitability.	IIa	B
AVR should be considered in symptomatic patients with low flow, low gradient (< 40 mmHg) AS with normal EF only after careful confirmation of severe AS.	IIa	C
AVR should be considered in symptomatic patients with severe AS, low flow, low gradient with reduced EF, and evidence of flow reserve.	IIa	C
AVR may be considered in symptomatic patients with severe AS low flow, low gradient, and LV dysfunction without flow reserve.	IIb	C

Vahanian et al. Eur Heart J 2012

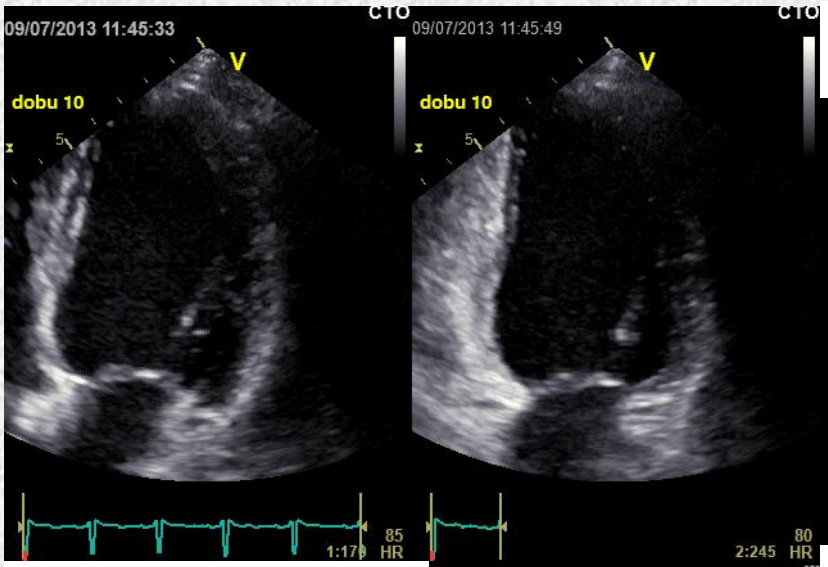
Pseudo Severe AS – Easy case as well

Baseline

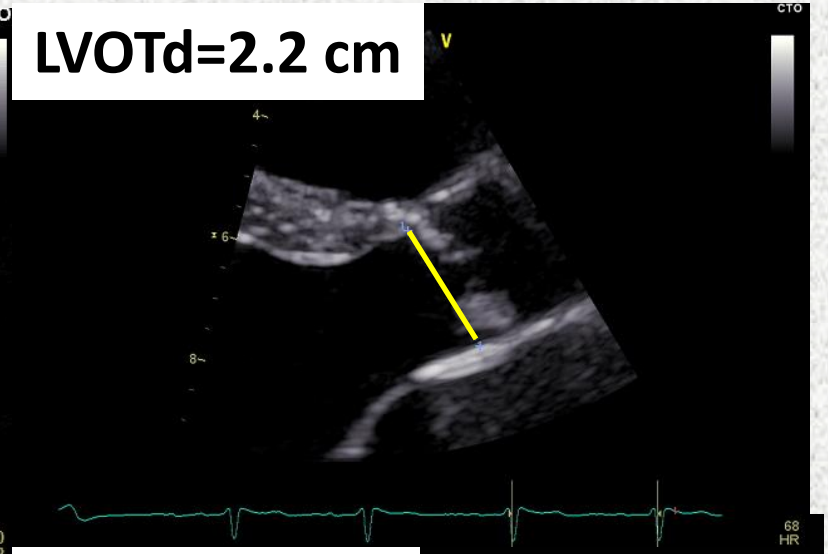


Pseudo Severe AS – Easy case as well

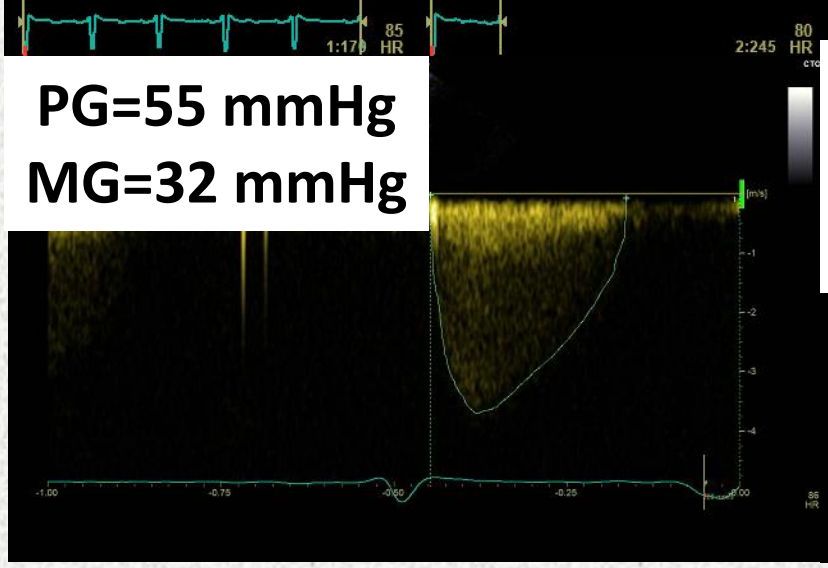
Dobutamine Stress Echocardiography



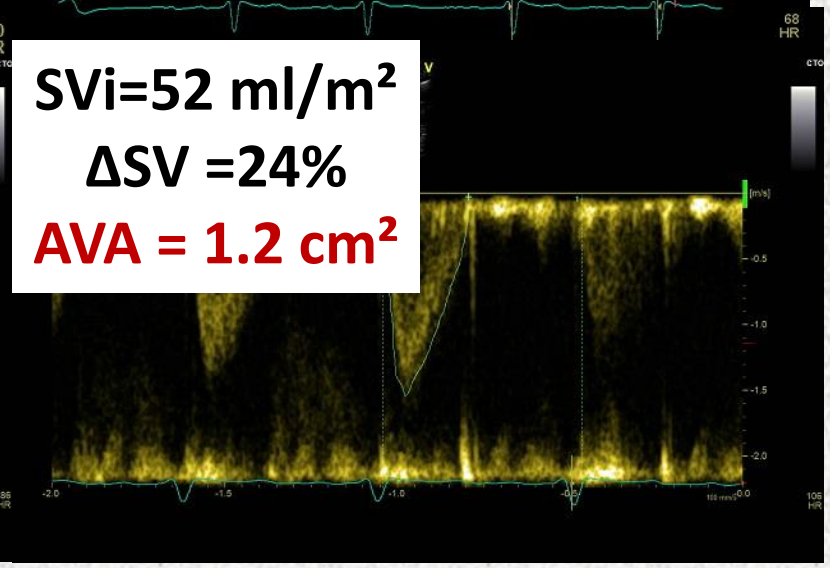
LVOTd=2.2 cm



PG=55 mmHg
MG=32 mmHg



SVi=52 ml/m²
ΔSV =24%
AVA = 1.2 cm²



Outcomes of Pseudo-Severe AS under Conservative Treatment

- 107 patients with LF/LGAS (Age: 76±13 years, 78% males) followed under conservative treatment > 6 months

According to DSE results :

- Group IA: 43 patients with True-severe AS

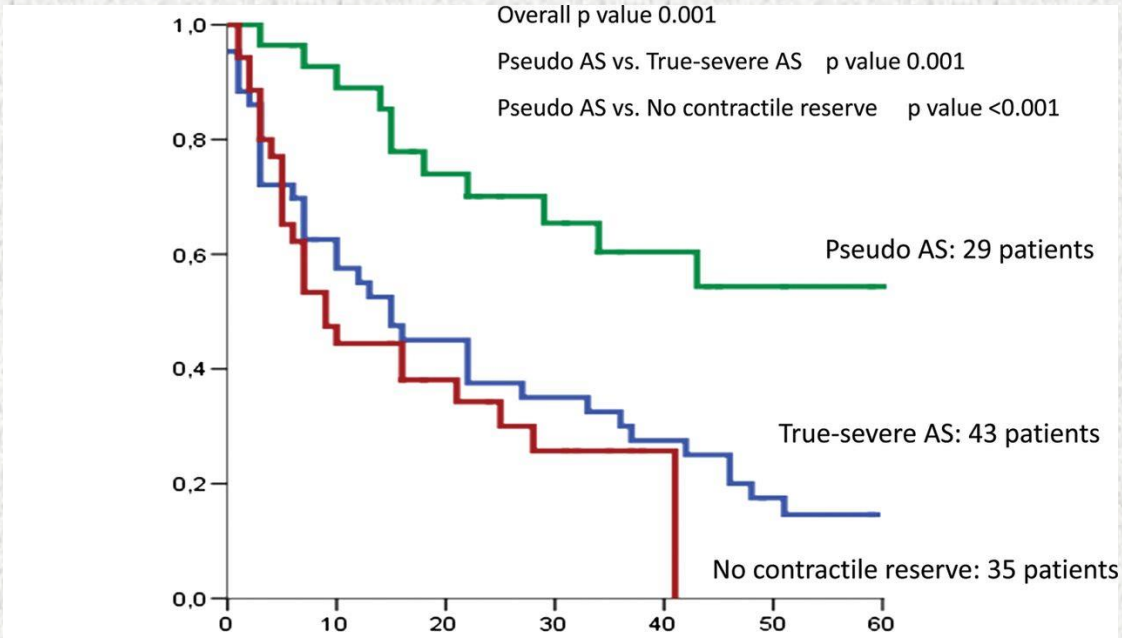
- Group IB: 29 patients with Pseudo-severe AS, defined by a Dobutamine AVA ≥1.2 cm^2 /peak MPG <40 mm Hg

- Group II: 35 patients without LV contractile reserve

Fougères et al. *Eur Heart J 2012*

Outcomes of Pseudo-Severe AS under Conservative Treatment

Rate of deaths within 24 months in group IB (28%), lower than group IA (60%, p=0.008) and group II (63%, p=0.04).



Patients at risk

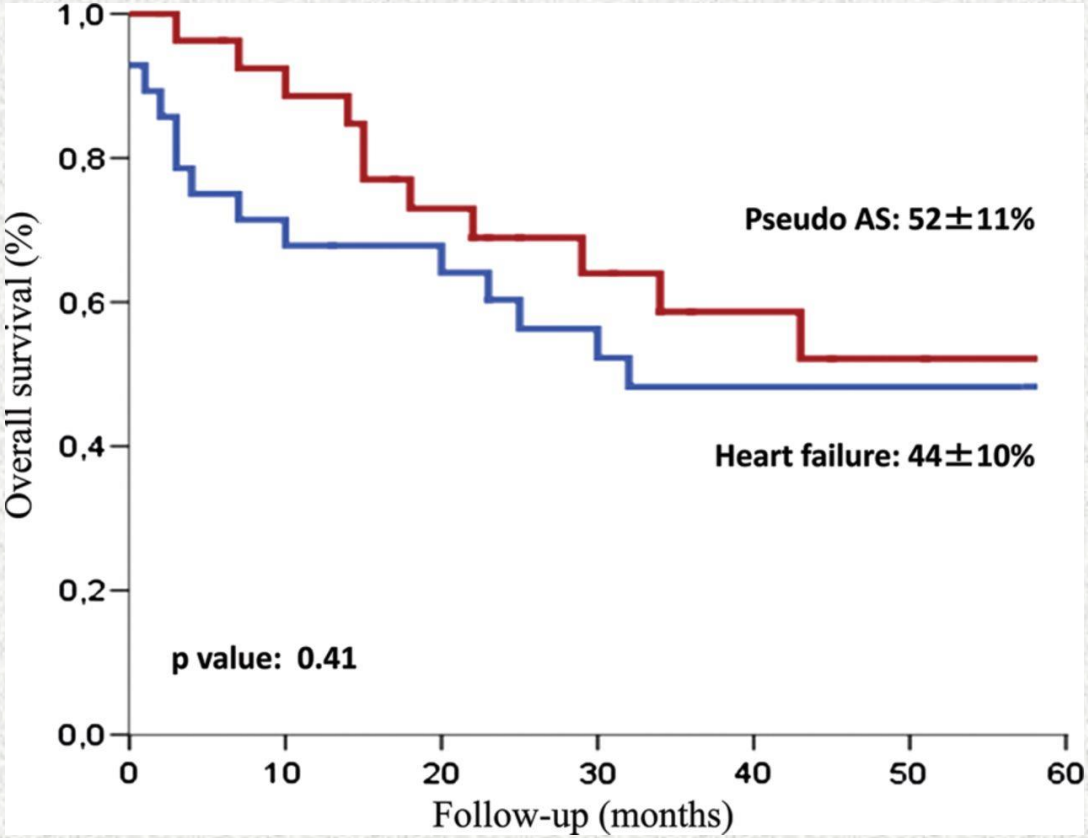
True-severe AS	43	24	18	14	11	6	4
Pseudo AS	29	25	19	14	10	7	5
No contractile reserve	35	15	10	6	1	0	0

This remained significant after adjustment for currently established risk factors.

Fougères et al. *Eur Heart J 2012*

Outcomes of Pseudo-Severe AS under Conservative Treatment

5-year survival of pseudo-severe AS patients is comparable to that of propensity-matched patients with CHF and no valve disease (57±11% vs. 54±9%, p=0.56)

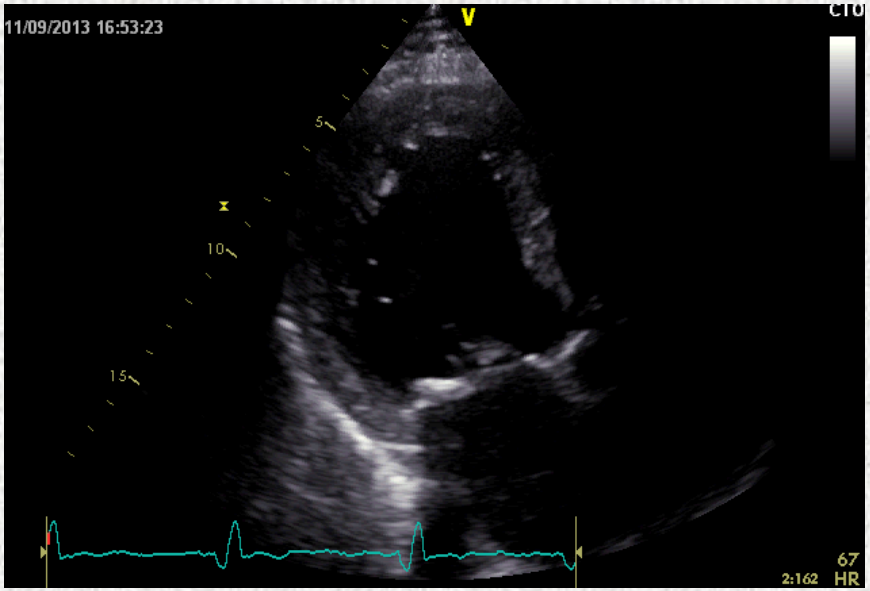


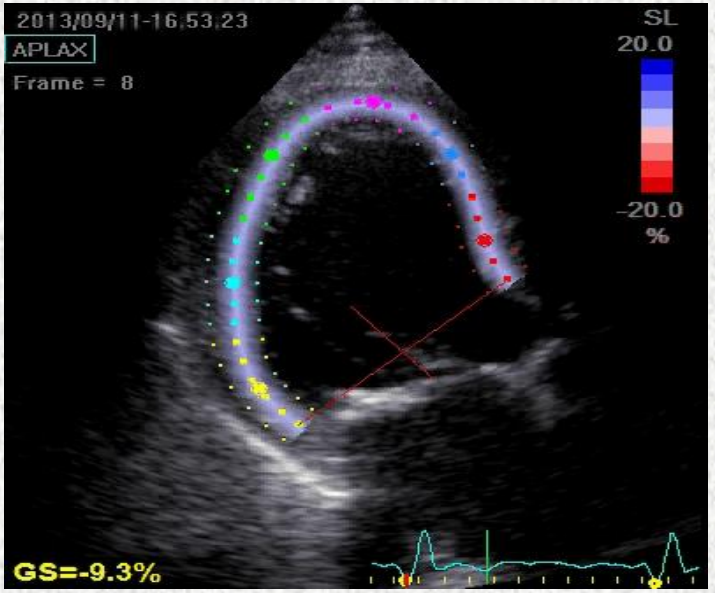
Patients with pseudo-severe AS may benefit from initial optimization of medical therapy and further evaluation at mid-term

Fougères et al. *Eur Heart J 2012*

Undetermined AS – Hard case

Low Flow Low Gradient AS with reduced LVEF

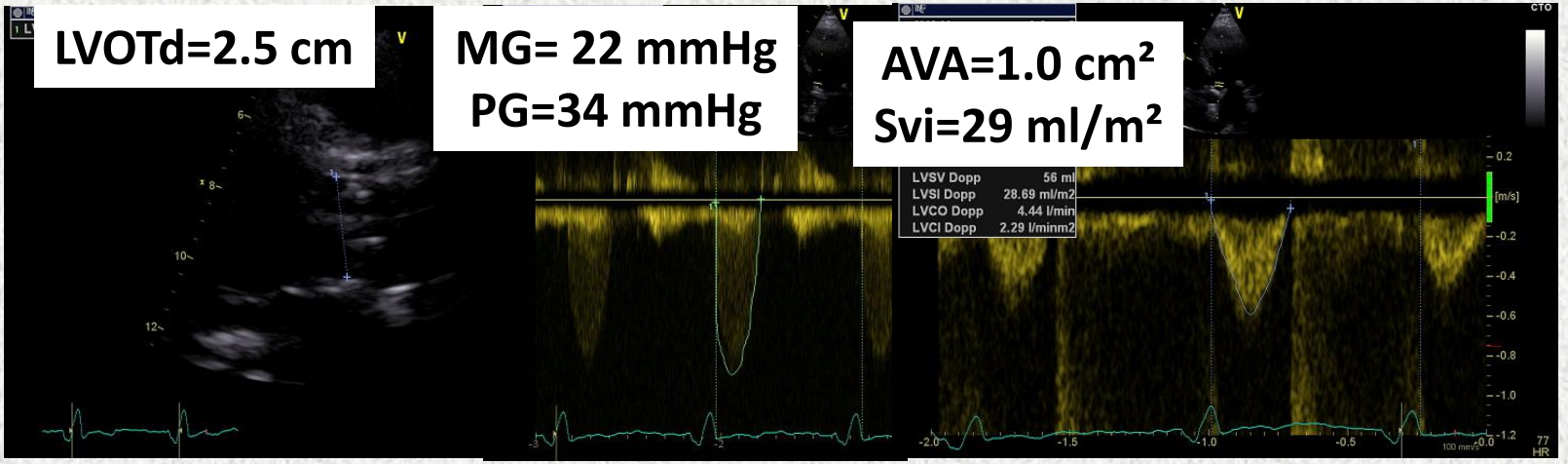




LVOTd=2.5 cm

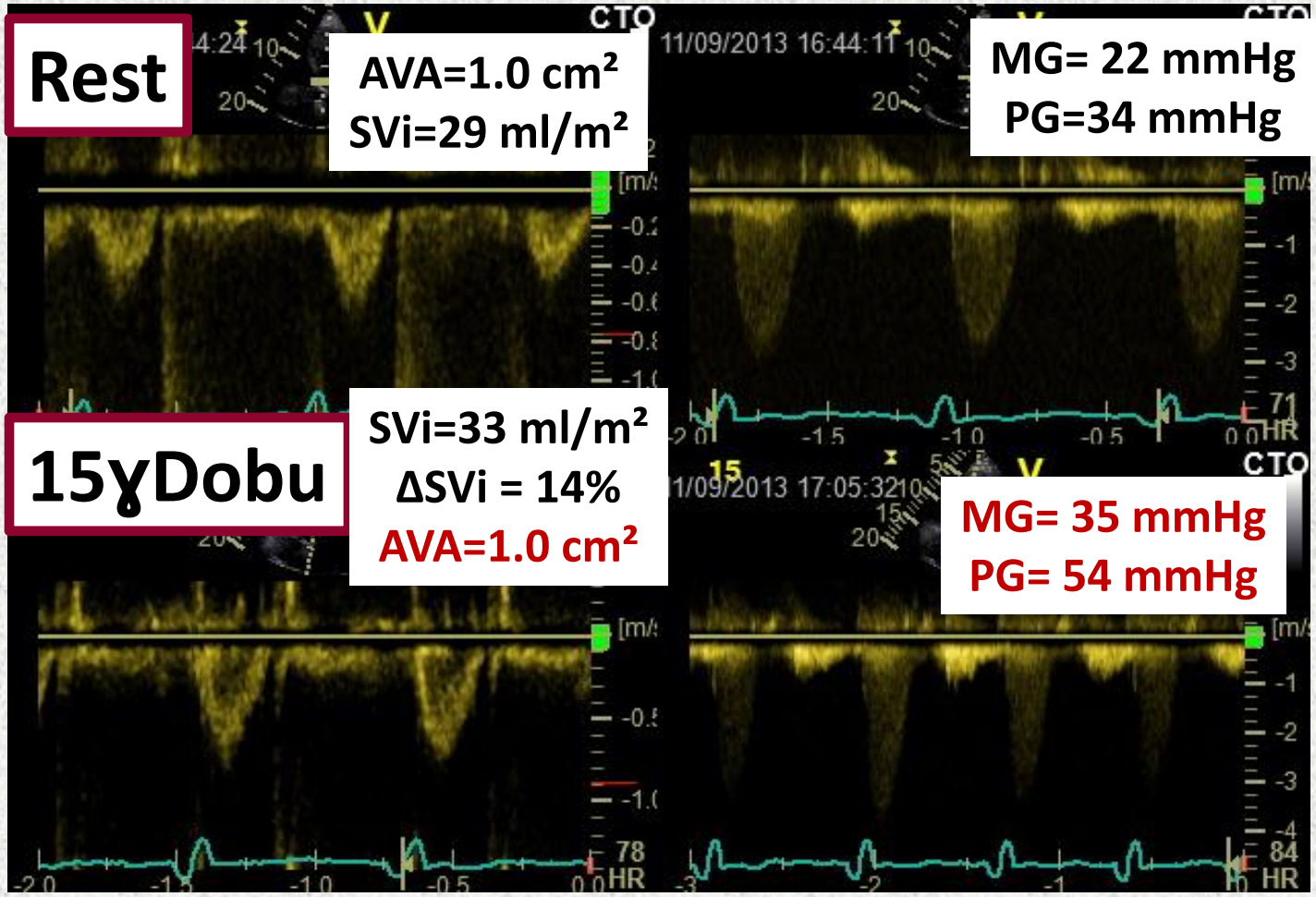
MG= 22 mmHg
PG=34 mmHg

AVA=1.0 cm²
Svi=29 ml/m²



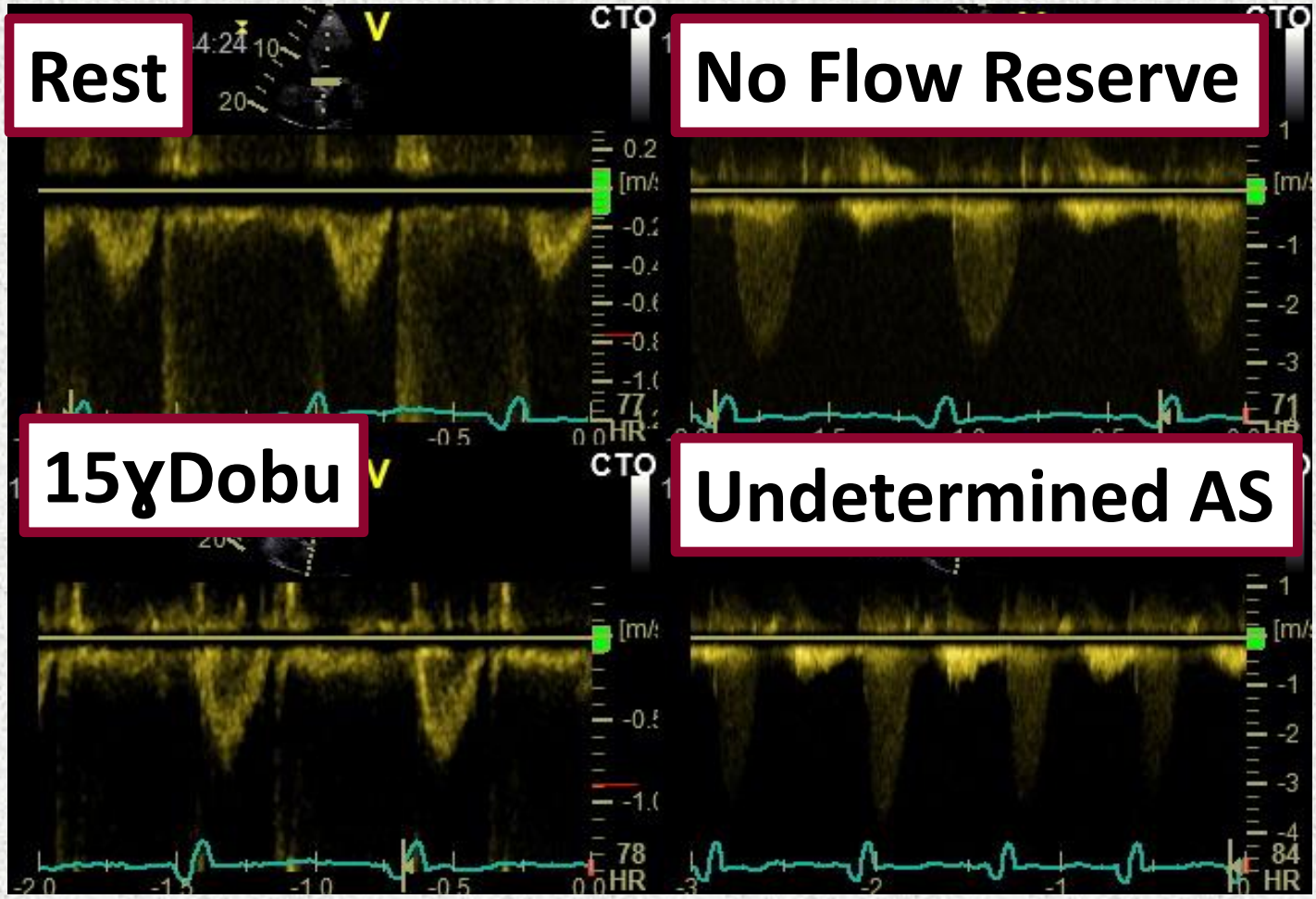
Undetermined AS

DSE Results



Undetermined AS

Low Flow Low Gradient AS with reduced LVEF



What if he has severe AS?

Wouldn’t he benefit fromTAVR?

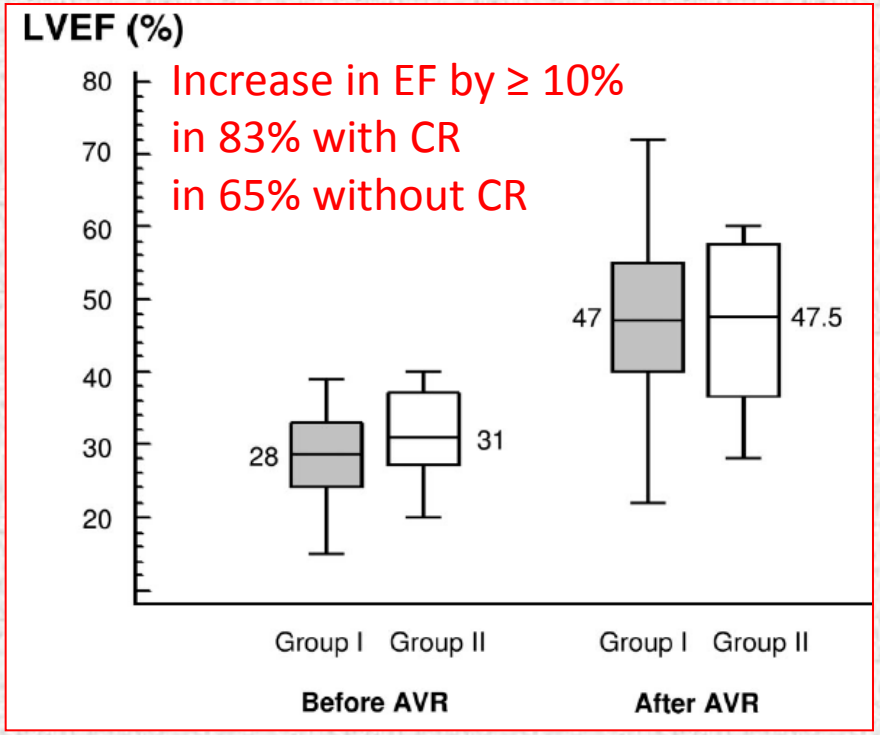
Wouldn’t you look back at your exam to see what went wrong?

Absence of flow reserve does not predict absence of recovery of LV function after AVR in LFLG with LV dysfunction

In LFLG AS with reduced EF you would like to predict which patient will increase LV systolic function after alleviation of the valve obstruction

1. **SV looks at LV ejection**
2. **Change in SV during DSE looks at change in LV ejection/emptying**
3. **Change in LV ejection does not equal change in myocardial contractility**

Postoperative LVEF is NOT related to LV Flow Reserve

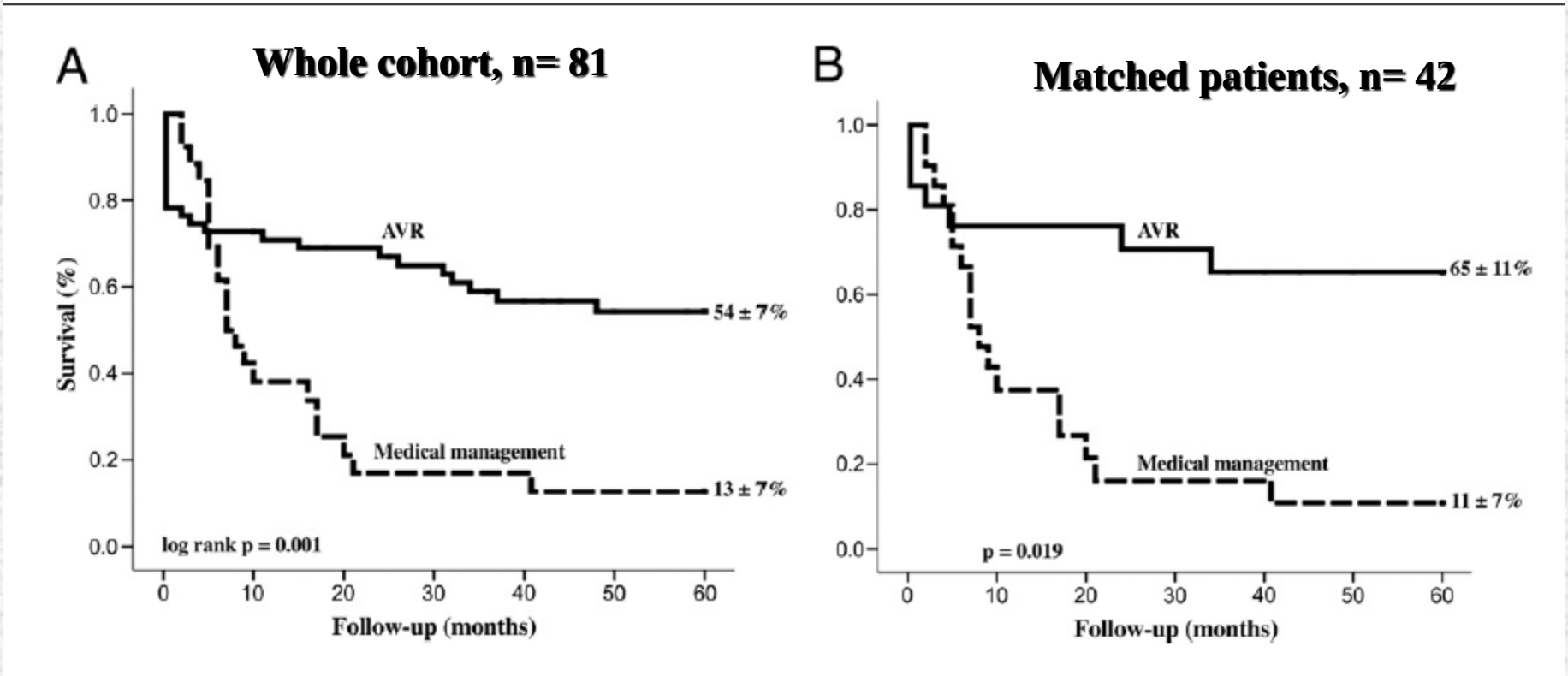


Quere et al. Circulation. 2006;113:1738-44

Substantial benefit of AVR in Patients without flow reserve

81 consecutive patients with LGAS

But no flow reserve, Operative mortality = 22%

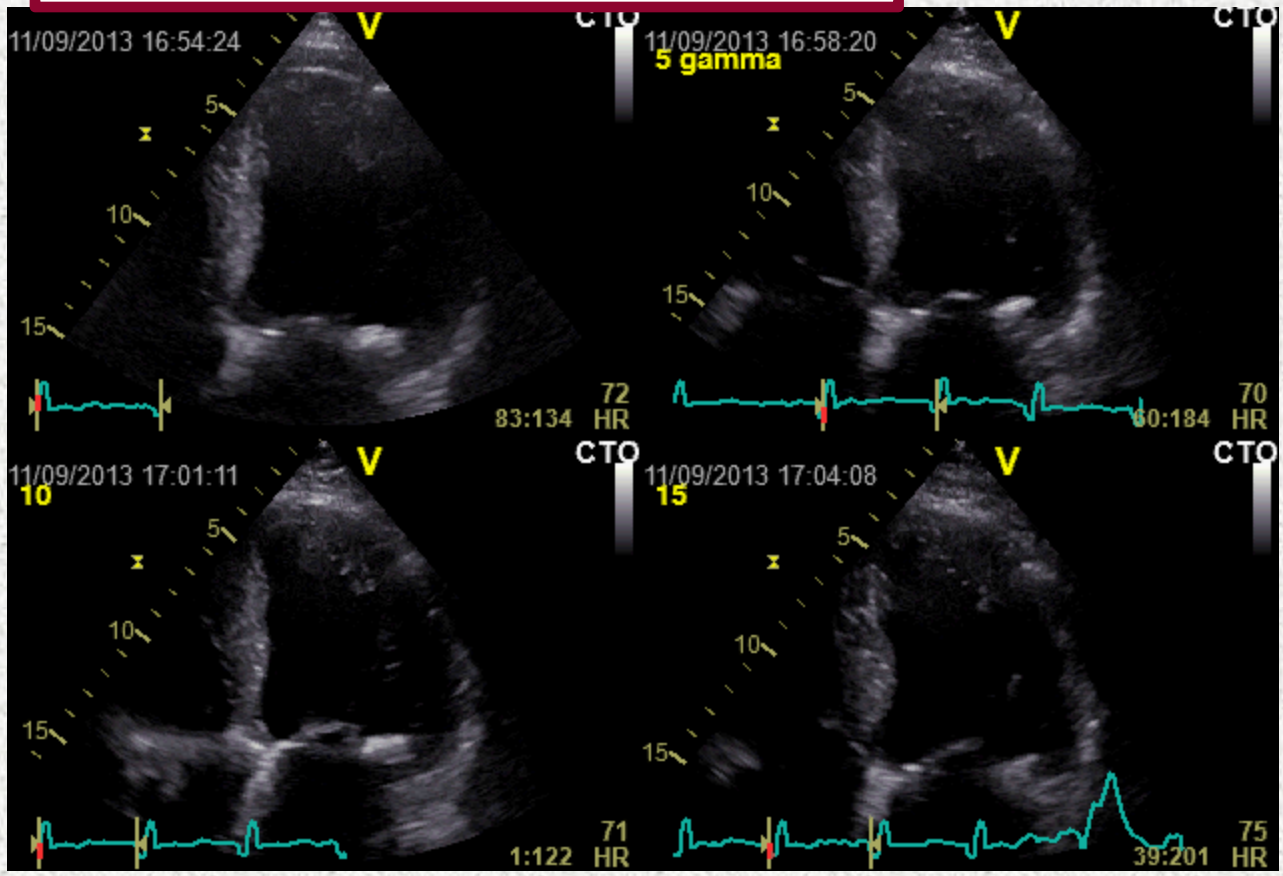


Tribouilloy et al. JACC : 1865-73

Undetermined AS

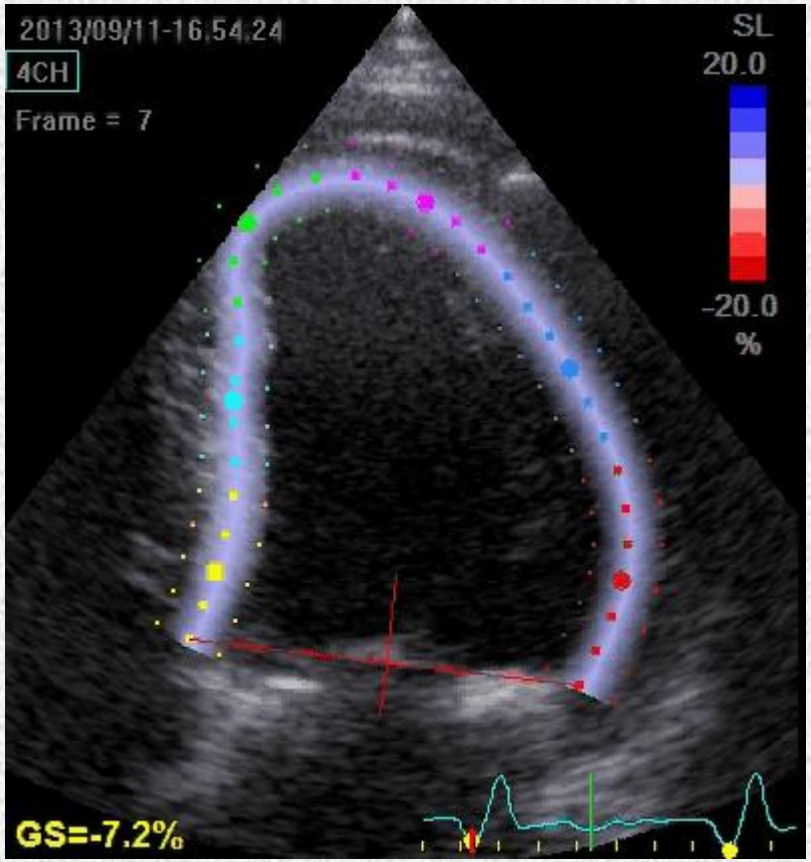
No flow reserve, Not a good candidate for AVR

DSE main message : high surgical risk

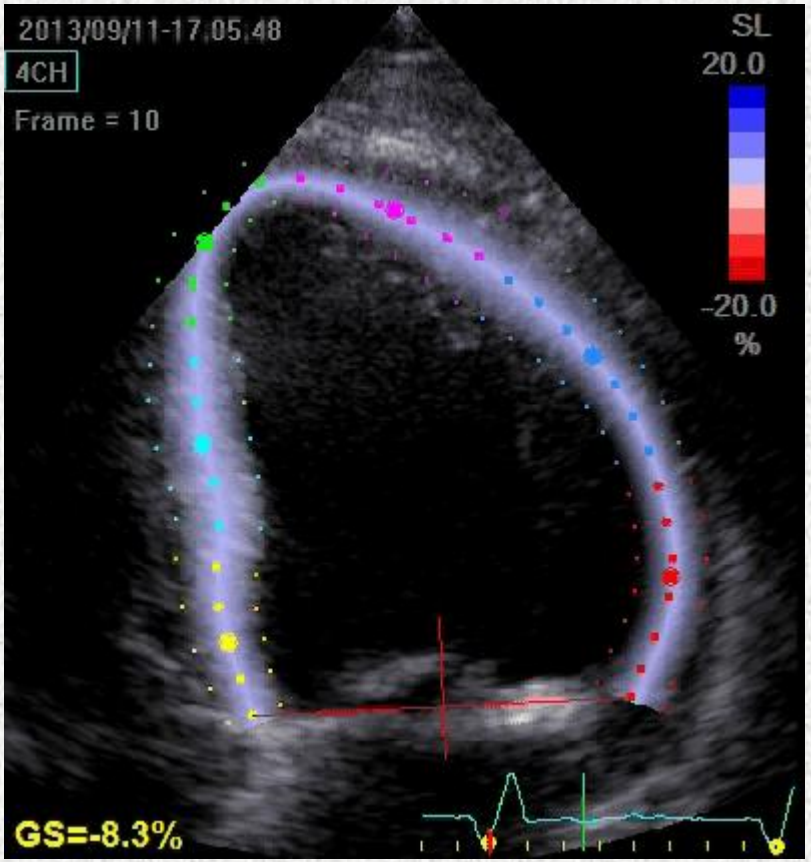


Undetermined AS

Baseline

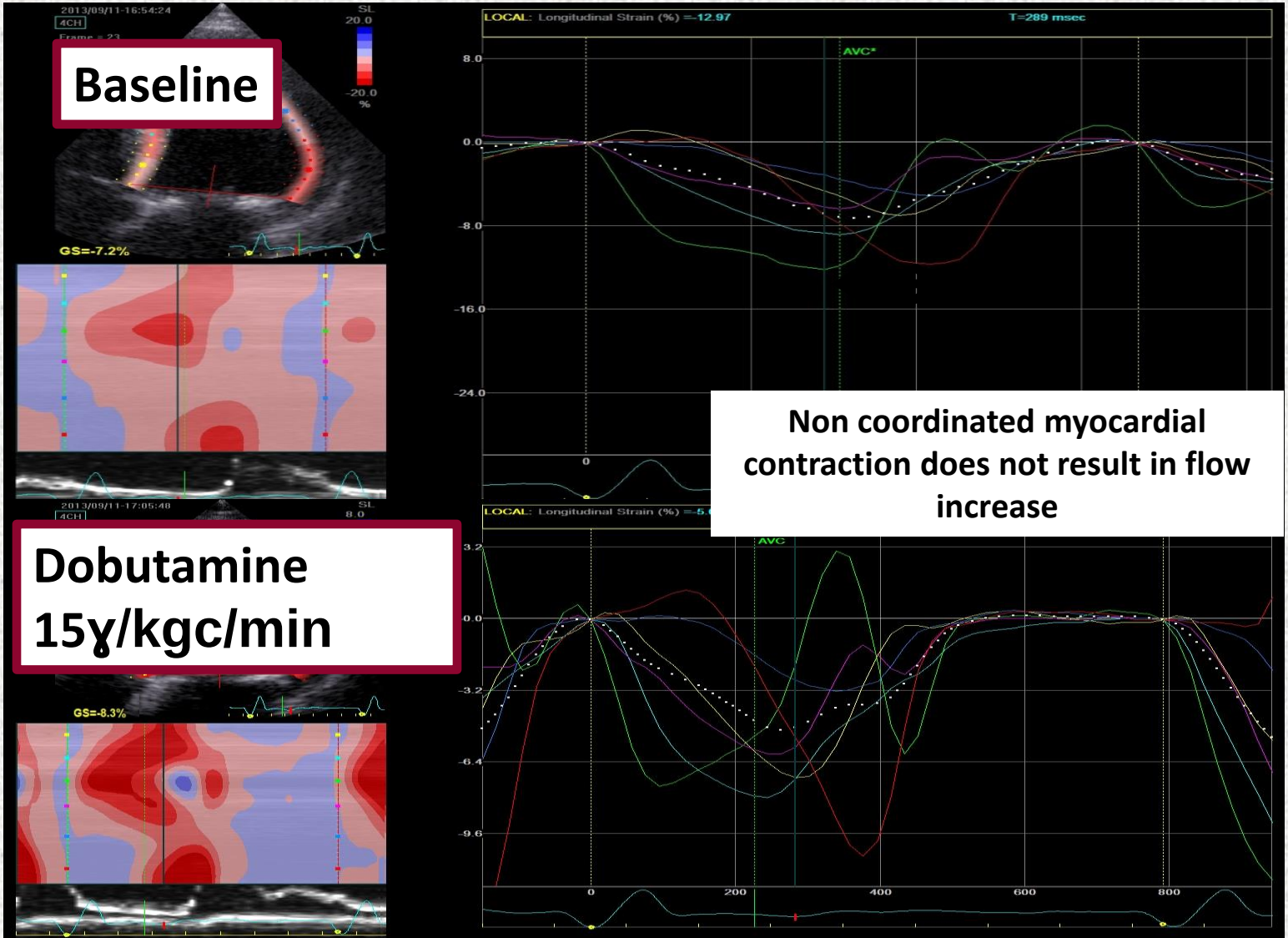


Dobutamine 15γ/kgc/min



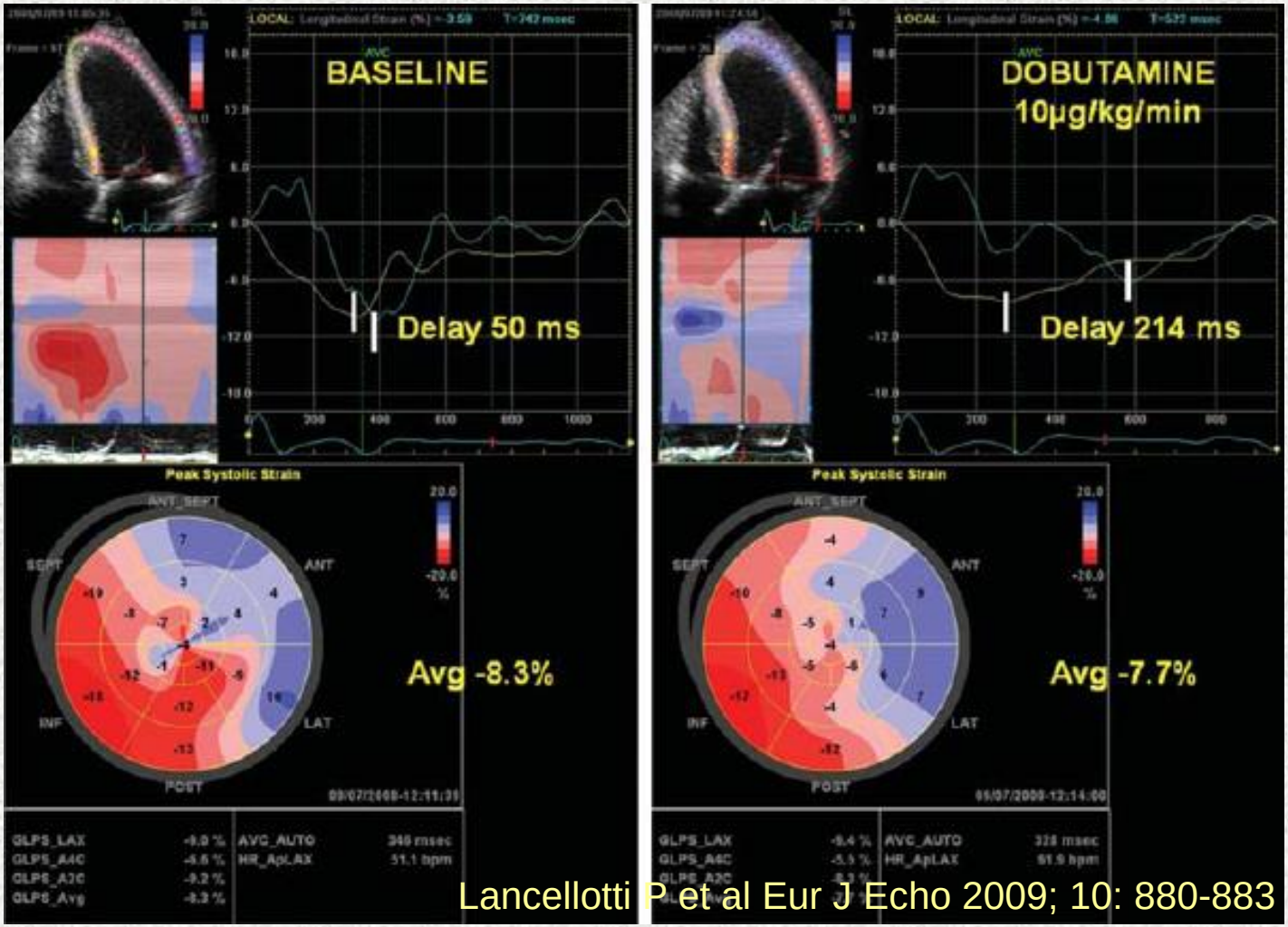
Undetermined AS

Low Flow Low Gradient AS with reduced LVEF



Can you guess why flow did non increase during DSE?

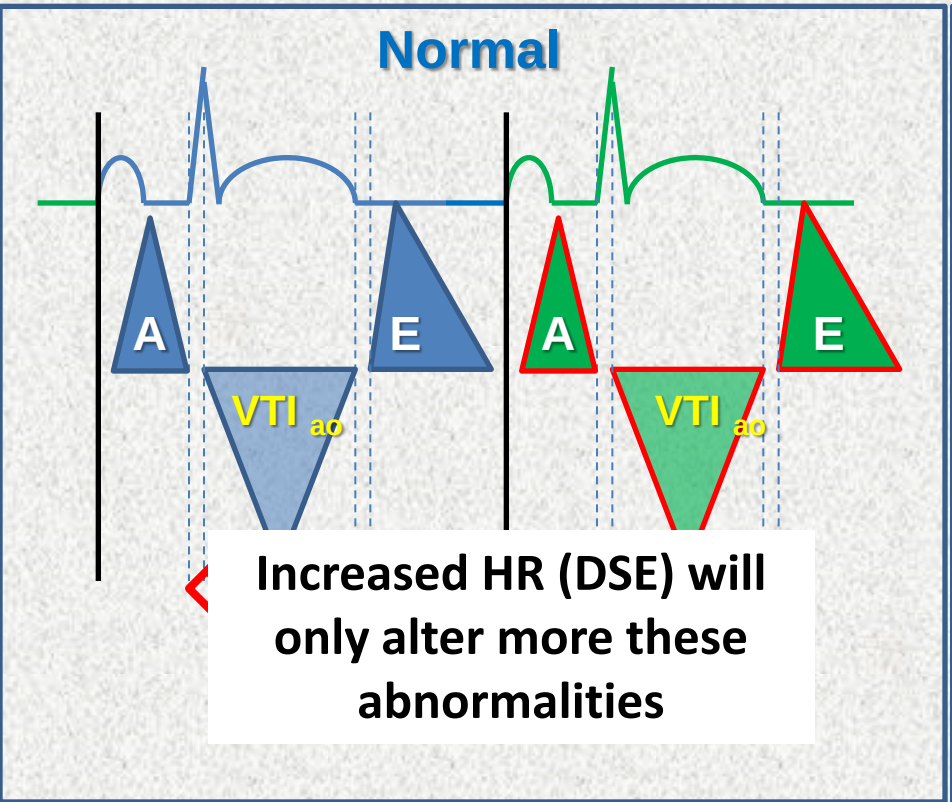
Dynamic left ventricular dyssynchrony: a potential cause of no flow reserve in pts with LG AS

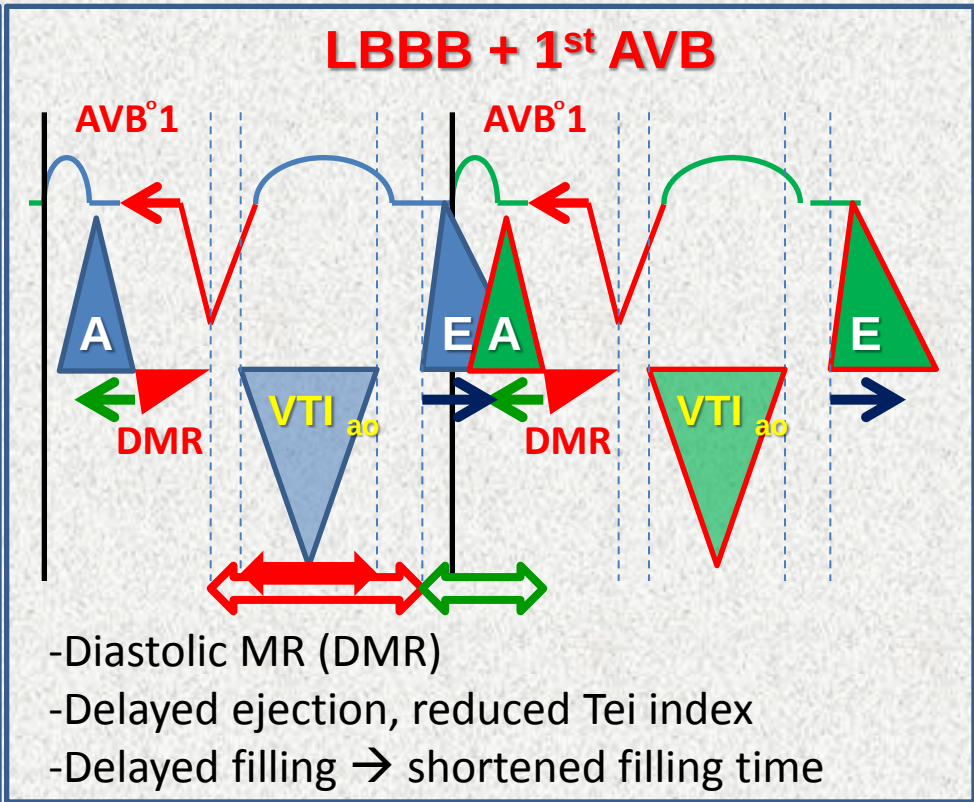


Lancellotti P et al Eur J Echo 2009; 10: 880-883

The reasoning behind dynamic dyssynchrony and lack of flow reserve in AS

1. Mechanical dyssynchrony comes from disturbed timings and alters LV ejection (the SV that we measure in echo): post-systolic contraction + prolongation of IVC and IVR
2. The key components: L/RBBB and sometimes 1st degree AV block (often have LV dysfunction, thus prone to have low flow AS)
3. *Ejection (SV) is a reflection of LV function, but not a direct measure of contractility, thus DSE because it looks at ejection (change in SV) will probably leave uninfluenced SV in patients with asynchrony. Thus in these patients "contractile reserve" should be assessed by deformation imaging not by looking at flow*





Potential causes of absence of flow reserve during DSE in AS

- LV myocardial disease:
  - ischemic
  - non ischemic, but extensive fibrosis

- LV afterload mismatch = final pathway in long standing severe AS patients (LV exhausted)

- **LV dyssynchrony (induction/aggravation of LV dyssynchrony with DSE)**

- Mix of the above situations

LF LG with LV dysfunction and no flow reserve

- 30% of LF LG AS with LV dysfunction

- Assessing severity is challenging because of absence of flow reserve

- Absence of flow reserve indicates a high surgical risk, but should not preclude surgery (at the cost of high mortality) or TAVR

- LV dyssynchrony (induction/aggravation of LV dyssynchrony with DSE) should be suspected in such patients, especially if LBBB at rest/ developing during DSE

- Studies regarding outcomes and treatment strategies are needed in this subset