

ASPETTI CONTROVERSI DELLA STENOSI AORTICA Chairmen: A. Alberti (Milano), G. La Canna (Milano)

Stenosi aortica low flow-low gradient: esiste veramente?

Patrizia Celli - Paolo G. Pino

I U.O. Cardiologia - UTIC Azienda Ospedaliera San Camillo-Forlanini - Roma



Guidelines on the management of valvular heart disease (version 2012)

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

	Aortic stenosis	Mitral stenosis	Tricuspid stenosis
Valve area (cm²)	<1.0	<1.0	1
Indexed valve area (cm²/m² BSA)	<0.6	_	
Mean gradient (mmHg)	>40ª	>10b	≥5
Maximum jet velocity (m/s)	>4.0a	_	_
Velocity ratio	<0.25	_	_

AVA < 1.0 cm² or AVA index < 0.6 cm²/m²

normal flow; SVI >35 ml/m², Cl >3.0 l/min/m²



NF HG AS PGmean ≥40 mmHg LVEF ≥ or <50% normal flow high gradient normal or reduced LVEF – majority of patients



NF LG AS PGmean <40 mmHg AVA mostly 0.8-1.0 cm² LVEF ≥50% normal flow low gradient preserved EF

AVA - PG discordance may be due to:

- underestimation of LVOT area and flow
- small BSA

low flow

inconsistency of cut-offs for AVA and PG
 → mostly NON-severe AS

low flow; SVI ≤35 ml/m2, CI <3.0 l/min/m2



classical LF LG AS PGmean <40 mmHg LVEF <40% low flow
low gradient
reduced EF
enlarged LV
impaired myocardial contractility
worst prognosis



"paradoxical"
LF LG AS
PGmean <40 mmHg
LVEF >50%

low gradient
preserved EF
Exclude reasons for AVA - PG discordance
(see above)
small LV cavity, LVH
reduced LV longitudinal function
myocardial fibrosis
art. hypertension, older age, female
worse prognosis (compared to NF HG AS)

AVA < 1.0 cm² or AVA index < 0.6 cm²/m²

low flow; SVI \leq 35 ml/m², Cl \leq 3.0 l/min/m²



classical LF LG AS PGmean <40 mmHg LVEF <40% low flow
low gradient
reduced EF
enlarged LV
impaired myocardial contractility
worst prognosis



"paradoxical" LF LG AS PGmean <40 mmHg LVEF ≥50% low gradient
preserved EF
Exclude reasons for AVA - PG discordance
(see above)
small LV cavity, LVH
reduced LV longitudinal function
myocardial fibrosis
art. hypertension, older age, female
worse prognosis (compared to NF HG AS)

low flow

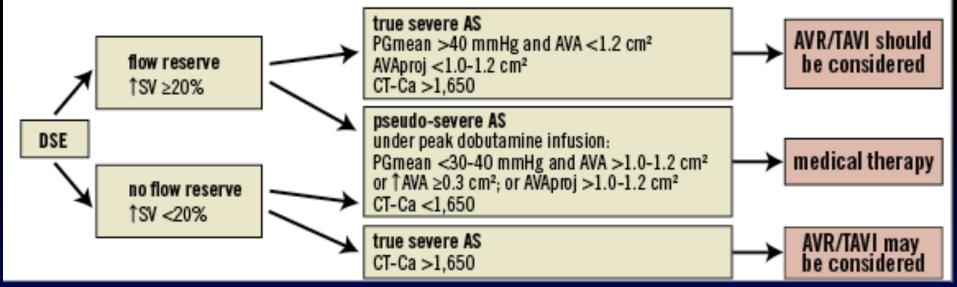
AVA $< 1.0 \text{ cm}^2 \text{ or AVA index } < 0.6 \text{ cm}^2/\text{m}^2$

low flow; SVI \leq 35 mVm², CI \leq 3.0 Vmin/m²

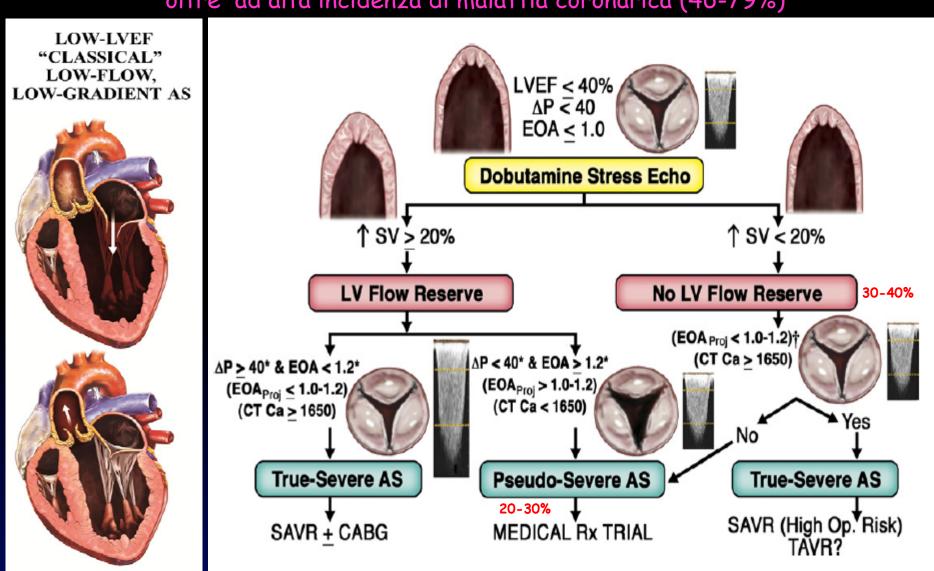
5 - 10%



classical LF LG AS PGmean <40 mmHg LVEF <40% low flow
low gradient
reduced EF
enlarged LV
impaired myocardial contractility
worst prognosis



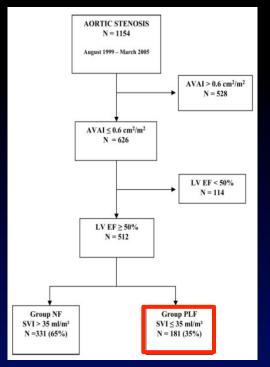
Sao LF-LG: sopravvivenza a 3aa <50% in terapia medica, ma rischio operatorio alto: 5 - 8% se presente riserva contrattile, dal 22 al 33% se assente riserva contrattile, oltre ad alta incidenza di malattia coronarica (46-79%)

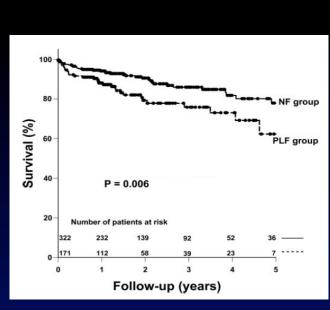


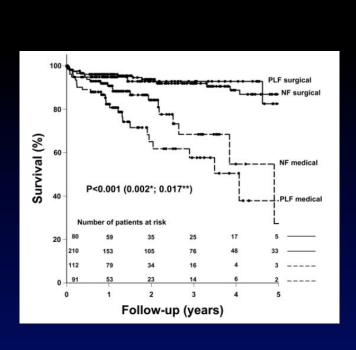
Paradoxical Low-Flow, Low-Gradient Severe Aortic Stenosis Despite Preserved Ejection Fraction Is Associated With Higher Afterload and Reduced Survival

Zeineb Hachicha, MD; Jean G. Dumesnil, MD; Peter Bogaty, MD; Philippe Pibarot, DVM, PhD

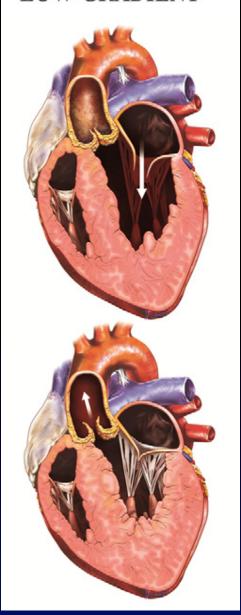
Conclusion—Patients with severe aortic stenosis may have low transvalvular flow and low gradients despite normal LV ejection fraction. A comprehensive evaluation shows that this pattern is in fact consistent with a more advanced stage of the disease and has a poorer prognosis. Such findings are clinically 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.)







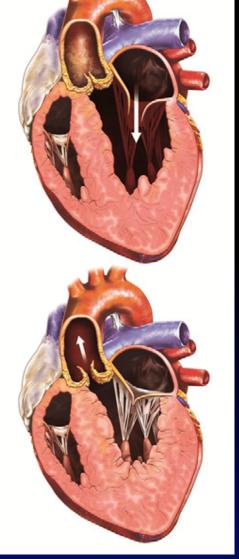
NORMAL-LVEF "PARADOXICAL" LOW-FLOW, LOW-GRADIENT



SAo PARADOSSA LOW FLOW- LOW GRADIENT: aspetti clinici

- pazienti anziani
- in genere di sesso femminile
- con storia di ipertensione inveterata
- sindrome metabolica
- insulino resistenza

NORMAL-LVEF "PARADOXICAL" LOW-FLOW, LOW-GRADIENT



Sao PARADOSSA LOW FLOW-LOW GRADIENT: aspetti fisiopatologici

- ventricoli piccoli e ipertrofici, con marcato rimodellamento concentrico e fibrosi miocardica
- riempimento ventricolare di tipo restrittivo
- disfunzione miocardica intrinseca, relata a fibrosi subendocardica e meglio valutata come accorciamento medio-parietale o longitudinale
- ridotta compliance arteriosa sistemica con normali valori di PA nonostante il basso flusso (pseudonormalizzazione)
- impedenza valvulo-arteriosa (Z_{va}) (espresione del carico emodinamico globale del Vsn) aumentata (vn ≤ 4,5mmHg/mL/m²)

SAO LOW FLOW- LOW GRADIENT: PITFALLS

sottostima dell'area del tratto di efflusso Vsn

(forma ovale e non rotonda !!)

E campionamento del PW in efflusso sinistro troppo

BASSO:

RIDOTTO STROKE VOLUME



SAO LOW FLOW- LOW GRADIENT: DIAGNOSI

VALVOLA AORTICA:

- Area < 1cmq, AreaI < 0,6cm²/m², DVI < 0,25
- Valvola calcifica o marcatamente ispessita
- ∆ medio < 40mmHg
- $Z_{va} > 4.5 \text{mmHg/ml/m}^2$

VENTRICOLO SINISTRO:

- DTD < 47mm, VTDi < 55ml/m²
- Spessore relativo di parete > 0,50
- Alterato riempimento Vsn (restrittivo)
- FE > 50%
- Strain globale longitudinale < 15%
- SVi < 35ml/m²

Left Ventricular Restrictive Filling Pattern and the Presence of Contractile Reserve in Patients with Low-Flow/Low-Gradient Severe Aortic Stenosis

(Echocardiography 2015;32:65-70)

Ragab A. Mahfouz, M.D., Ahmed El Zayat, M.D., and Ahmed Yousry, M.D.

Conclusion:

In patients with low-flow/low-gradient severe aortic stenosis, presence of restrictive pattern of diastolic dysfunction on baseline echo Doppler study may predict lack of contractile reserve in such patients.

Strain analysis in patients with severe aortic stenosis and preserved left ventricular ejection fraction undergoing surgical valve replacement

Victoria Delgado, Laurens F. Tops, Rutger J. van Bommel, Frank van der Kley, Nina Ajmone Marsan, Robert J. Klautz, Michel I.M. Versteegh, Eduard R. Holman, Martin J. Schalij, and Jeroen J. Bax*

Aims

To evaluate myocardial multidirectional strain and strain rate (S-and-SR) in severe aortic stenosis (AS) patients with preserved left ventricular (LV) ejection fraction (EF), using two-dimensional speckle-tracking strain imaging (2D-STI). The long-term effect of aortic valve replacement (AVR) on S-and-SR was also evaluated.

Conclusion

In severe AS patients, impaired LV S-and-SR existed although LVEF was preserved. After AVR, a significant S-and-SR improvement in all the three directions was observed. These subtle changes in LV contractility can be detected by 2D-STI.

Strain analysis in

(A) radial,

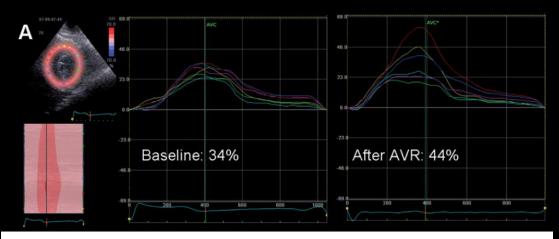
(B) circumferential and

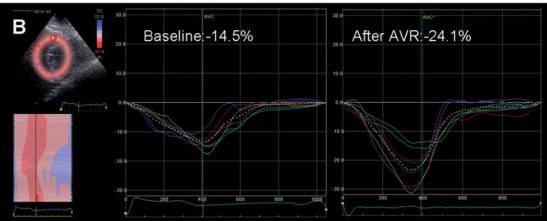
(C) longitudinal

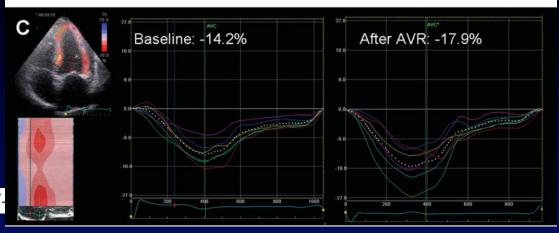
directions before and

after aortic valve

replacement







Two-Dimensional Strain for the Assessment of Left Ventricular Function in Low Flow-Low Gradient Aortic Stenosis, Relationship to Hemodynamics, and Outcome A Substudy of the Multicenter TOPAS Study

Philipp Emanuel Bartko, MD; Georg Heinze, PhD; Senta Graf, MD; Marie-Annick Clavel, DVM, PhD; Aliasghar Khorsand, PhD; Jutta Bergler-Klein, MD; Ian Gordon Burwash, MD; Jean Gaston Dumesnil, MD; Mario Sénéchal, MD; Helmut Baumgartner, MD; Raphael Rosenhek, MD; Philippe Pibarot, DVM, PhD; Gerald Mundigler, MD

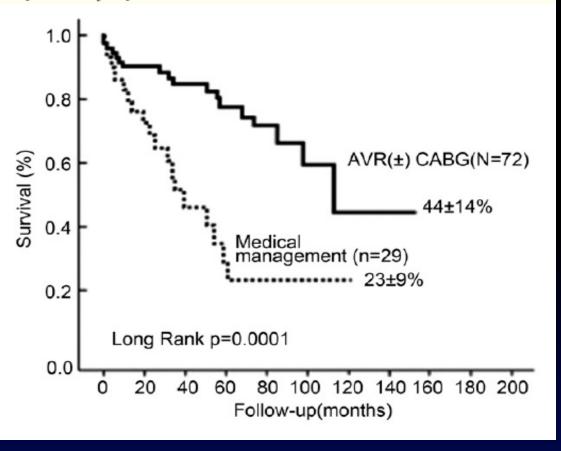
Circ Cardiovasc Imaging March 2013

Univariate Cox Regression Analyses of Mortality

Variable	Univariate HR (95% CI)	<i>P</i> Value	Variable	Univariate HR (95% CI)	<i>P</i> Value
Age (per decade)	1.40 (0.87-2.24)	0.1620	Mean transvalvular flow at rest	0.63 (0.37-1.07)	0.0875
Body surface area (per m²)	1.77 (0.22-14.3)	0.5903	(per 50 mL/s)	, == ===,	-
Society of Thoracic Surgeons score	1.04 (1.00-1.07)	0.045	Peak stress LVEF	0.89 (0.83-0.96)	0.0026
CAD (present vs absent)	2.40 (0.68-8.43)	0.1722	Peak stress EOA	0.30 (0.05-1.87)	0.1960
Type of treatment (valvular intervention	0.53 (0.18-1.62)	0.2680	Peak stress SVi	0.96 (0.91-1.00)	0.0496
vs medical)			Peak stress mean transvalvular flow	0.43 (0.22-0.84)	0.0135
NT-proBNP (per doubling)	2.21 (1.48-3.29)	0.0001	(per 100 mL/s)		
LVEF at rest (per 10%)	0.70 (0.31-1.56)	0.3770	Peak stress PLS	1.35 (1.15–1.58)	0.0002
EOA at rest (per 0.1 cm ²)	0.89 (0.70-1.14)	0.3526	Peak stress PLSR (per 0.1%)	1.56 (1.27-1.93)	<0.0001
SV at rest (per 10 mL/s)	0.86 (0.65-1.13)	0.2804	EOA projected (per 0.2 cm²)	0.74 (0.35-1.55)	0.417
SVi at rest (per 10 mL/m²)	0.67 (0.38–1.17)	0.1540	Contractile reserve (yes vs no)	0.64 (0.24-1.70)	0.3669

Low-Flow, Low-Gradient Aortic Stenosis With Normal and Depressed Left Ventricular Ejection Fraction

Philippe Pibarot, DVM, PHD, Jean G. Dumesnil, MD Québec City, Québec, Canada

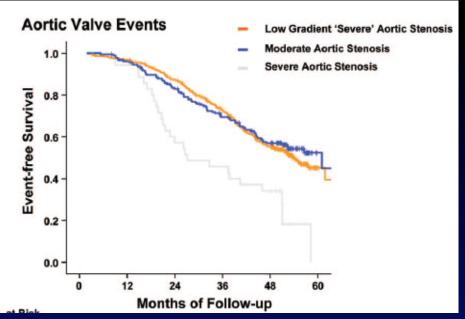


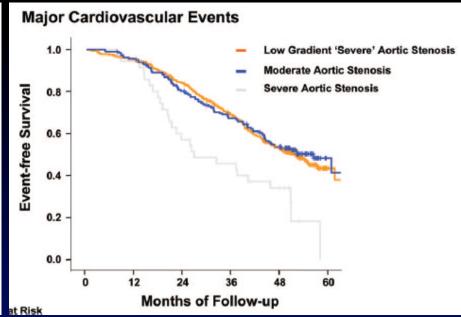
Impact of AVR on Survival in Patients With Paradoxical LF-LG AS

Outcome of Patients With Low-Gradient "Severe" Aortic Stenosis and Preserved Ejection Fraction

Nikolaus Jander, MD*; Jan Minners, MD, PhD*; Ingar Holme, PhD; Eva Gerdts, MD, PhD; Kurt Boman, MD, PhD; Philippe Brudi, MD; John B. Chambers, MD; Kenneth Egstrup, MD, PhD; Y. Antero Kesäniemi, MD, PhD; William Malbecq, PhD; Christoph A. Nienaber, MD; Simon Ray, MD; Anne Rossebø, MD; Terje R. Pedersen, MD, PhD; Terje Skjærpe, MD, PhD; Ronnie Willenheimer, MD, PhD; Kristian Wachtell, MD, PhD; Franz-Josef Neumann, MD; Christa Gohlke-Bärwolf, MD

Conclusions—Patients with low-gradient "severe" aortic stenosis and normal ejection fraction have an outcome similar to that in patients with moderate stenosis. (Circulation. 2011;123:887-895.)

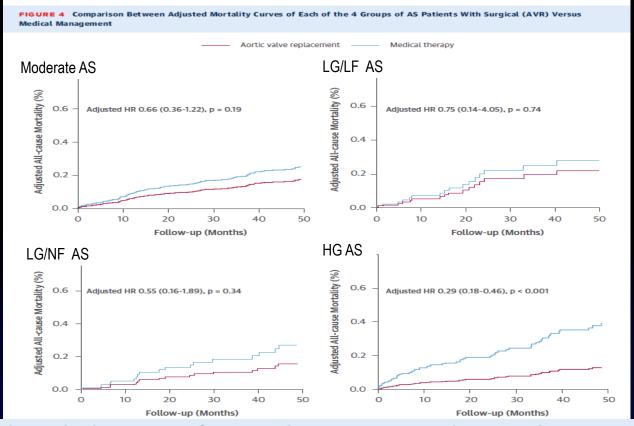




Low-Gradient, Low-Flow Severe Aortic Stenosis With Preserved Left Ventricular Ejection Fraction

Characteristics, Outcome, and Implications for Surgery

Christophe Tribouilloy, MD, PhD,*† Dan Rusinaru, MD, PhD,*‡ Sylvestre Maréchaux, MD, PhD,\$ Anne-Laure Castel, MD,* Nicolas Debry, MD,§ Julien Maizel, MD, PhD,† Romuald Mentaverri, PharmD, PhD,† Said Kamel, PharmD, PhD,† Michel Slama, MD, PhD,† Franck Lévy, MD*†

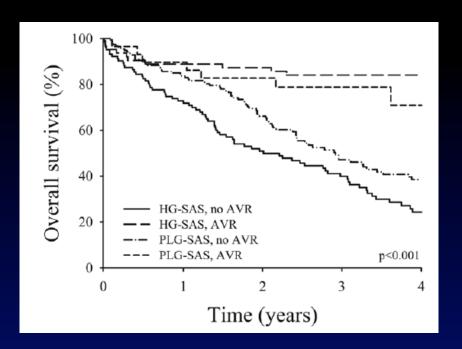


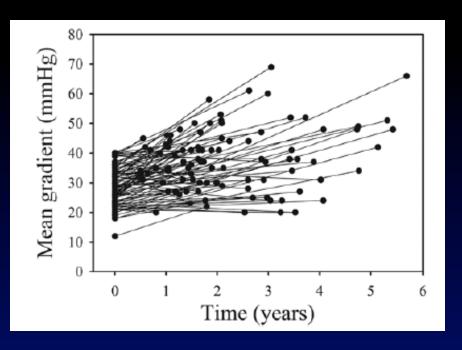
CONCLUSIONS In this study, the outcome of severe LG/LF aortic stenosis with preserved EF was similar to that of mild-to-moderate aortic stenosis and was not favorably influenced by aortic surgery. Further research is needed to better understand the natural history and the progression of LG/LF aortic stenosis. (J Am Coll Cardiol 2015;65:55–66)

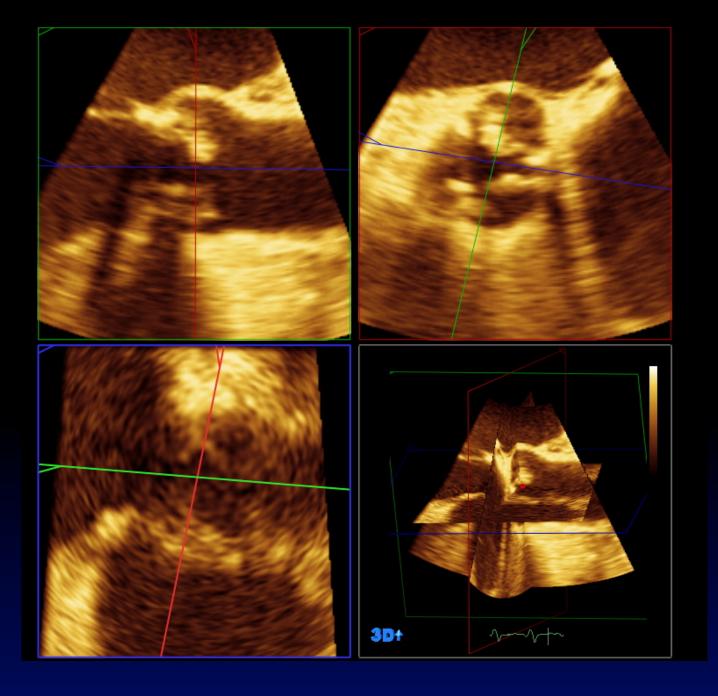
Natural History of Paradoxical Low-Gradient Severe Aortic Stenosis

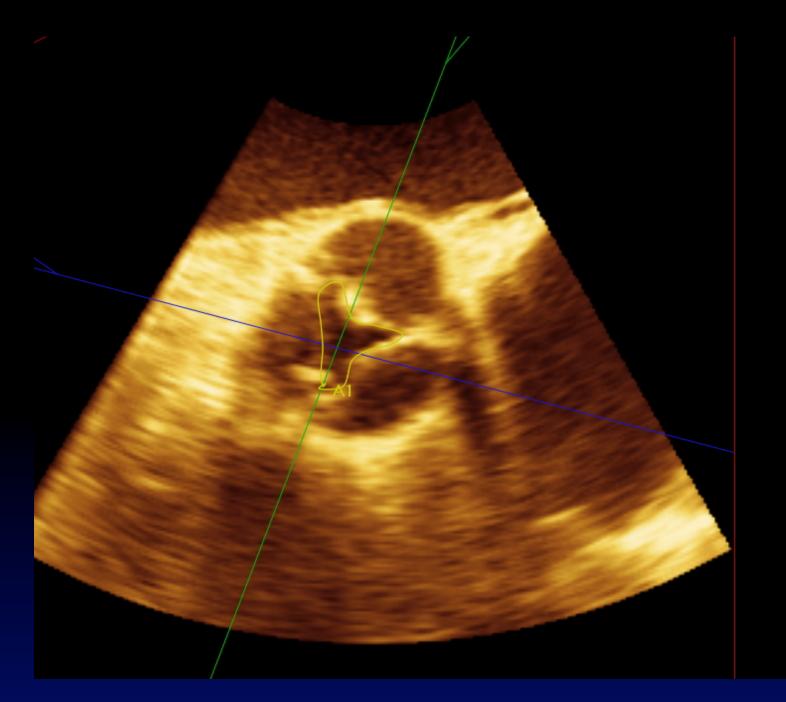
Frédéric Maes, MD*; Jamila Boulif, MS*; Sophie Piérard, MD; Christophe de Meester, MS; Julie Melchior, MD; Bernhard Gerber, MD, PhD; David Vancraeynest, MD, PhD; Anne-Catherine Pouleur, MD, PhD; Siham Lazam, MS; Agnès Pasquet, MD, PhD; Jean-Louis Vanoverschelde, MD, PhD

Conclusions—Our study indicates that PLG-SAS is a less malignant form of AS compared with HG-SAS, because their spontaneous outcome is better. We further demonstrated that patients with PLG-SAS are en route toward the more severe HG-SAS form, because the majority of them evolve into HG-SAS over time. (Circ Cardiovasc Imaging. 2014;7:714-722.)







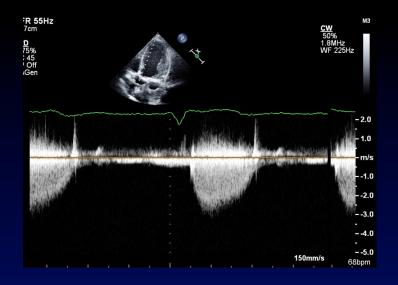


ECO STRESS BASE







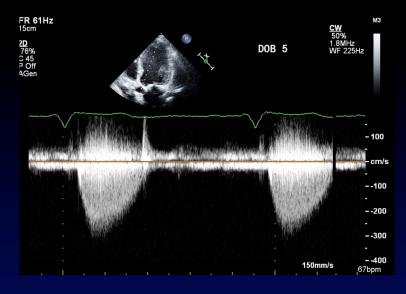


ECO STRESS Dobutamina 5γ/Kg/min









ECO STRESS Dobutamina 107/Kg/min



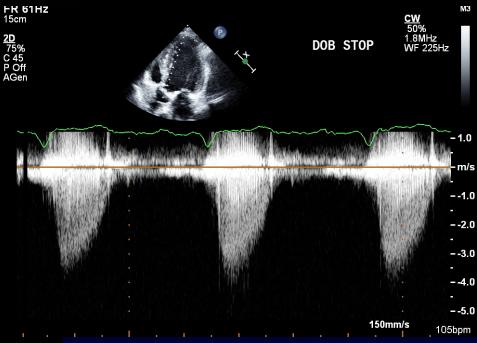






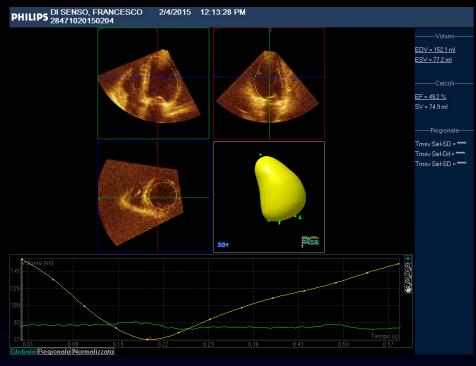
PHILIPS DI SENSO, FRANCESCO 28471020150204 FR 55Hz 17cm M3 PD DOB STOP AGen P JPEG 104 bpm

ECO STRESS ACME Dobutamina 20γ/Kg/min



Calcolo di FE e SV di base e dopo ECO Dob





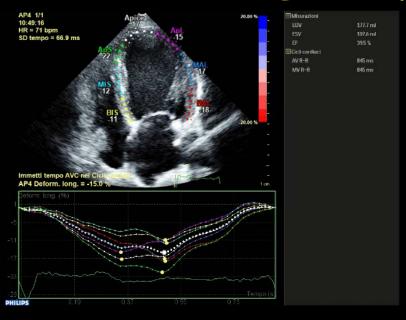
Calcoli

EF= 39,0% SV= 62,3 ml SVI= 34,6ml

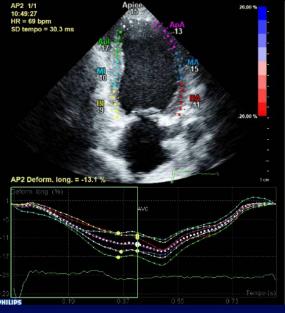
Calcoli

EF= 49,2% SV= 74,9 ml SVI= 41,6ml

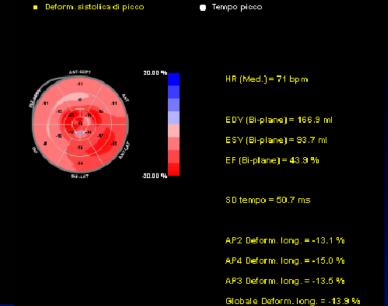
STRAIN BASE



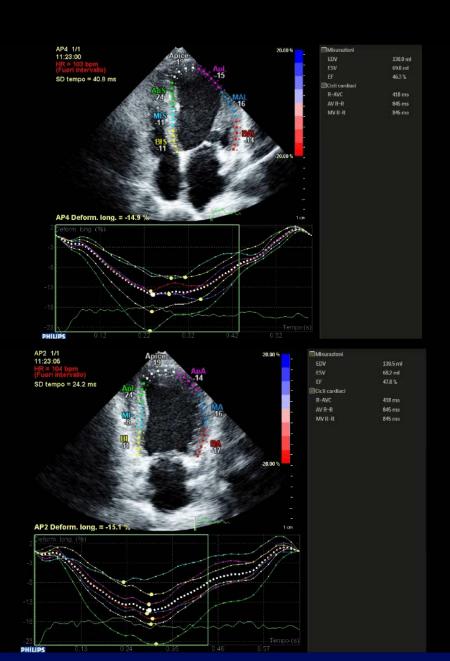


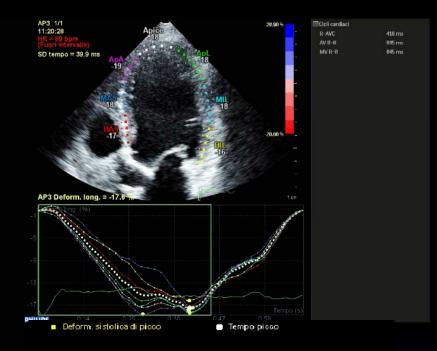


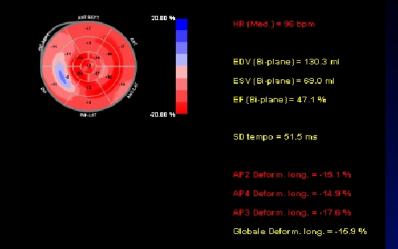




STRAIN DOBUTAMINA







CALCOLO FE

PRE

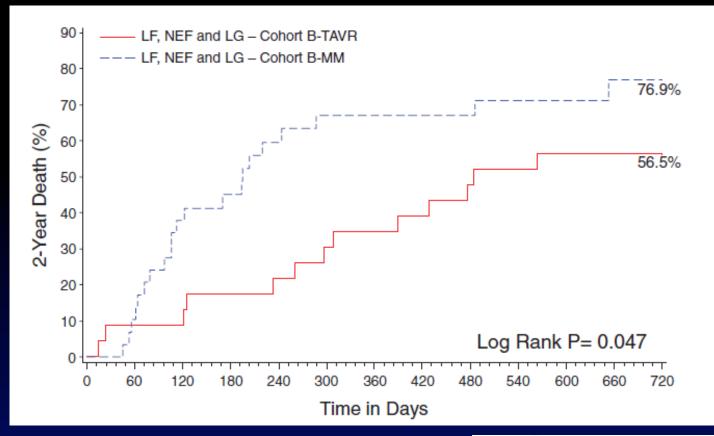
POST



Predictors of Mortality and Outcomes of Therapy in Low-Flow Severe Aortic Stenosis

A Placement of Aortic Transcatheter Valves (PARTNER) Trial Analysis

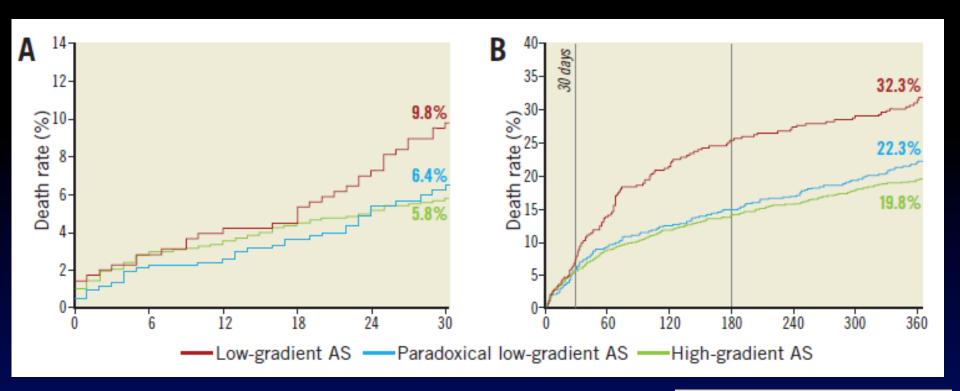
Howard C. Herrmann, MD; Philippe Pibarot, PhD; Irene Hueter, PhD; Zachary M. Gertz, MD; William J. Stewart, MD; Samir Kapadia, MD; E. Murat Tuzcu, MD; Vasilis Babaliaros, MD; Vinod Thourani, MD; Wilson Y. Szeto, MD; Joseph E. Bavaria, MD; Susheel Kodali, MD; Rebecca T. Hahn, MD; Mathew Williams, MD; D. Craig Miller, MD; Pamela S. Douglas, MD; Martin B. Leon, MD



Circulation. 2013;127:2316-2326.

TAVI for low-flow, low-gradient severe aortic stenosis with preserved or reduced ejection fraction: a subgroup analysis from the German Aortic Valve Registry (GARY)

Alexander Lauten^{1*}, MD; Hans R. Figulla², MD; Helge Möllmann², MD; David Holzhey³, MD; Joachim Kötting⁴, MSc; Andreas Beckmann⁵, MD; Christof Veit⁴, MD; Jochen Cremer⁶, MD; Karl-Heinz Kuck⁷, MD; Rüdiger Lange⁸, MD; Ralf Zahn⁹, MD; Stefan Sack¹⁰, MD; Gerhard Schuler³, MD; Thomas Walther¹¹, MD; Friedhelm Beyersdorf¹², MD; Michael Böhm¹³, MD; Gerd Heusch¹⁴, MD; Thomas Meinertz¹⁵, MD; Till Neumann¹⁶, MD; Armin Welz¹⁷, MD; Friedrich W. Mohr³, MD; Christian W. Hamm², MD; on behalf of the GARY Executive Board



Management of Paradoxical Low-Flow, Low-Gradient Aortic Stenosis

Need for an Integrated Approach, Including Assessment of Symptoms, Hypertension, and Stenosis Severity*

Philippe Pibarot, DVM, PhD, Marie-Annick Clavel, DVM, PhD

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY © 2015 BY THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION

..... first rule out measurement errors and confirm that this is bona fide paradoxical LF/LG AS and not moderate AS with an underestimated SVi and AVA or severe AS with an underestimated gradient

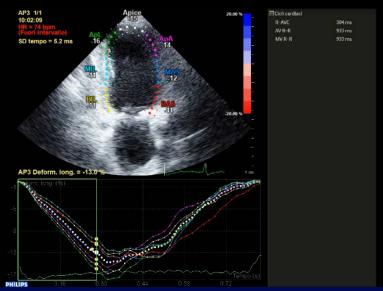
STEP 1: IS THE PATIENT SYMPTOMATIC? If asymptomatic (confirmed by exercise testing), the patient can likely be managed conservatively. If syntomatic:

STEP 2: IS THE PATIENT HYPERTENSIVE? If so, antihypertensive therapy should be initiated or optimized, and symptoms and echocardiographic parameters should be reassessed after normalization of blood pressure.

STEP 3: IS THE STENOSIS SEVERE? Pseudosevere AS, which may be present in 30% to 40% of LF/LG AS patients, must be ruled out. Low-dose dobutamine stress echocardiography may be used, but may not be applicable and/or conclusive in a significant proportion of patients with paradoxical LF/LG AS, particularly in those with restrictive LV physiology. Alternatively, true severe versus pseudosevere AS may be differentiated using quantification of aortic valve calcification by MDCT, by applying different cutpoints in women (>1,200 AU) versus men (>2,000 AU).

STRAIN POST OPERATORIO

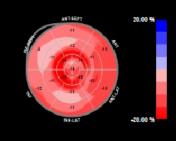






Deform, sistolica di picco

Tempo picco



IR (Med.) = 71 bpm

EDV (Bi-plane) = 131.0 ml

ESV (Bi-plane) = 77.6 ml EF (Bi-plane) = 40.8 %

SD tempo = 72.2 ms

AP2 Deform, long = -12.5 %

AP4 Deform. long. = -13.5 %

AP3 Deform, Jong = -13.0 %

Globale Deform. long. = -13.0 %

Guidelines on the management of valvular heart disease (version 2012)

Indications for aortic valve replacement in aortic stenosis

	Classa	Levelb
AVR is indicated in patients with severe AS and any symptoms related to AS.	I	В
AVR is indicated in patients with severe AS undergoing CABG, surgery of the ascending aorta or another valve.	1	С
AVR is indicated in asymptomatic patients with severe AS and systolic LV dysfunction (LVEF <50%) not due to another cause.	I	С
AVR is indicated in asymptomatic patients with severe AS and abnormal exercise test showing symptoms on exercise clearly related to AS.	1	С



Guidelines on the management of valvular heart disease (version 2012)

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.	lla	В
AVR should be considered in asymptomatic patients with severe AS and abnormal exercise test showing fall in blood pressure below baseline.	lla	С
AVR should be considered in patients with moderate ASd undergoing CABG, surgery of the ascending aorta or another valve.	lla	С
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. ^e	lla	С
AVR should be considered in symptomatic patients with severe AS, low flow, low gradient with reduced EF, and evidence of flow reserve.	lla	С
AVR should be considered in asymptomatic patients, with normal EF and none of the above mentioned exercise test abnormalities, if the surgical risk is low, and one or more of the following findings is present: • Very severe AS defined by a peak transvalvular velocity >5.5 m/s or, • Severe valve calcification and a rate of peak transvalvular velocity progression ≥0.3 m/s per year.	lla	С
AVR may be considered in symptomatic patients with severe AS low flow, low gradient, and LV dysfunction without flow reserve. ^f	IIb	С
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 and without other explanations • Increase of mean pressure gradient with exercise by >20 mmHg • Excessive LV hypertrophy in the absence of hypertension.	llb	C

2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: Executive Summary

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

Table 7.	Summary	of Recommendations	for AS:	Timing of Intervention
----------	---------	--------------------	---------	------------------------

Recommendations	COR	LOE	References
AVR is recommended for symptomatic patients with severe high-gradient AS who have symptoms by history or on exercise testing (stage D1)	T T	В	(10,57-59)
AVR is recommended for asymptomatic patients with severe AS (stage C2) and LVEF $<$ 50%	T .	В	(60,61)
AVR is indicated for patients with severe AS (stage C or D) when undergoing other cardiac surgery	1	В	(62,63)
AVR is reasonable for asymptomatic patients with very severe AS (stage C1, aortic velocity \geq 5.0 m/s) and low surgical risk	lla	В	(64,65)
AVR is reasonable in asymptomatic patients (stage C1) with severe AS and decreased exercise tolerance or an exercise fall in BP	lla	В	(27,38)
AVR is reasonable in symptomatic patients with low-flow/low-gradient severe AS with reduced LVEF (stage D2) with a low-dose dobutamine stress study that shows an aortic velocity \geq 4.0 m/s (or mean pressure gradient \geq 40 mm Hg) with a valve area \leq 10 cm ² at any dobutamine dose	lla	В	(66-68)
AVR is reasonable in symptomatic patients who have low-flow/low-gradient severe AS (stage D3) who are normotensive and have an LVEF ≥50% if clinical, hemodynamic, and anatomic data support valve obstruction as the most likely cause of symptoms	lla	С	N/A
AVR is reasonable for patients with moderate AS (stage B) (aortic velocity 3.0–3.9 m/s) who are undergoing other cardiac surgery	lla	С	N/A
AVR may be considered for asymptomatic patients with severe AS (stage C1) and rapid disease progression and low surgical risk	llb	С	N/A

AS indicates aortic stenosis; AVR, aortic valve replacement by either surgical or transcatheter approach; BP, blood pressure; COR, Class of Recommendation; LOE, Level of Evidence; LVEF, left ventricular ejection fraction; and N/A, not applicable.

PRACTICE GUIDELINE

2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: Executive Summary

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

Table 7. Summary of Recommendations for AS: Timing of Intervention

Recommendations	COR	LOE
AVR is recommended for symptomatic patients with severe high-gradient AS who have symptoms by history or on exercise testing (stage D1)	I	В
AVR is recommended for asymptomatic patients with severe AS (stage C2) and LVEF < 50%	1	В
AVR is indicated for patients with severe AS (stage C or D) when undergoing other cardiac surgery	1	В

PRACTICE GUIDELINE

2014 AHA/ACC Guideline for the Management of CrossMark Patients With Valvular Heart Disease: Executive Summary

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

AVR is reasonable in symptomatic patients with low-flow/low-gradient severe AS with reduced	lla	В	(66-68)
LVEF (stage D2) with a low-dose dobutamine stress study that shows an aortic			
velocity \geq 4.0 m/s (or mean pressure gradient \geq 40 mm Hg) with a valve area \leq 10 cm ² at			
any dobutamine dose			
AVR is reasonable in symptomatic patients who have low-flow/low-gradient severe AS (stage	lla	C	N/A
D3) who are normotensive and have an LVEF ≥50% if clinical, hemodynamic, and anatomic			
data support valve obstruction as the most likely cause of symptoms			