

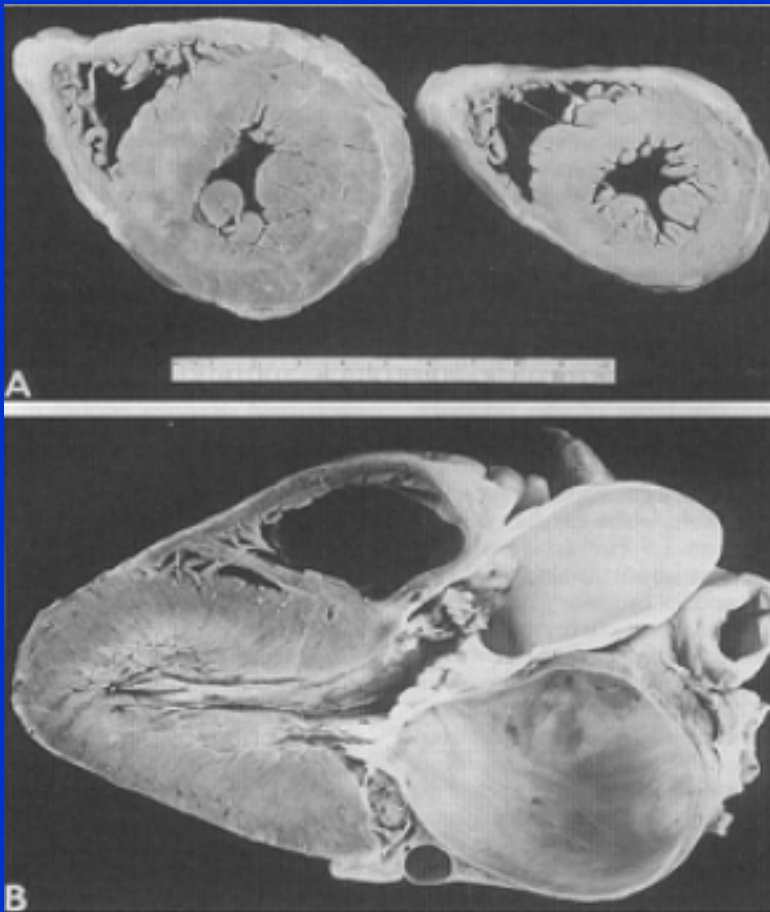


Come valutare la comparsa di ipertrofia e la disfunzione associate a stenosi aortica.

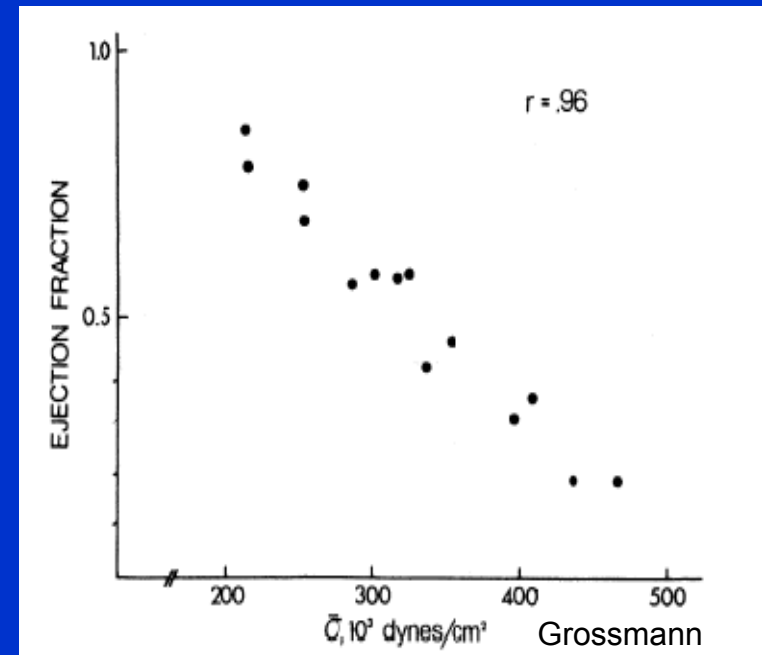
Un argomento fondamentale per migliorare la correttezza del timing chirurgico

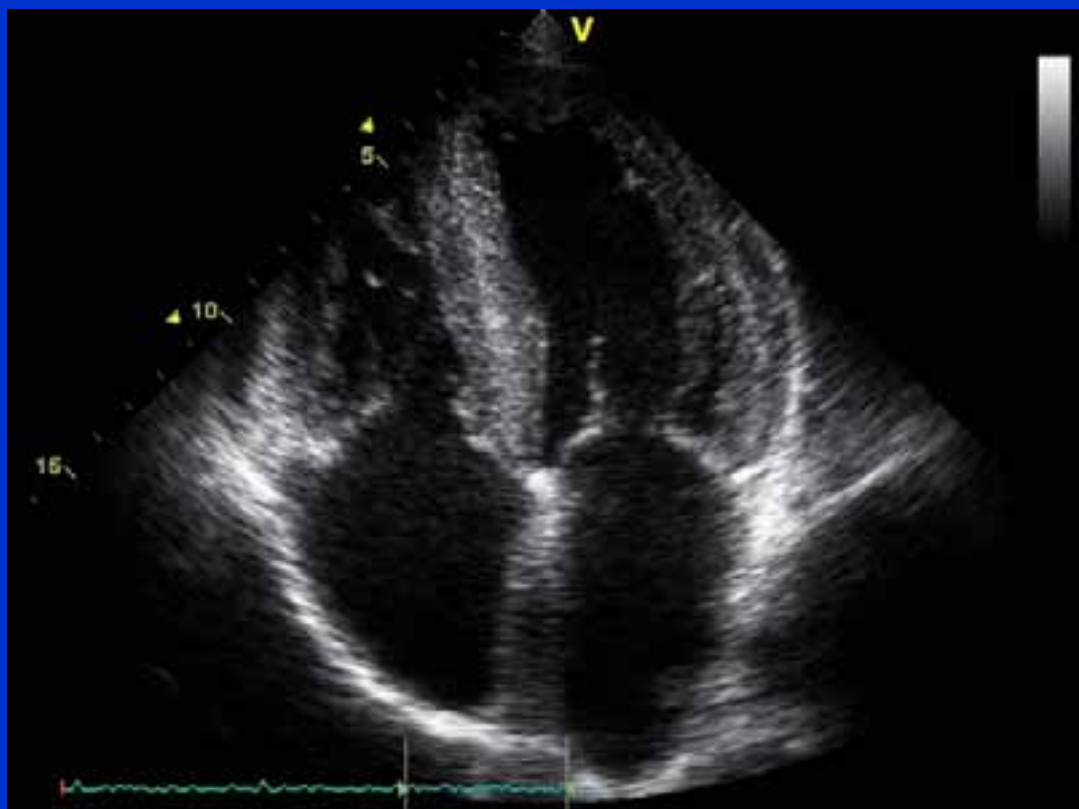
P. Faggiano - Brescia

L'ipertrofia concentrica rappresenta il meccanismo di adattamento e compenso al sovraccarico di pressione (afterload) imposto dal gradiente transvalvolare aortico, e consente di mantenere lo stress di parete entro i limiti di norma.



Nei soggetti in cui l'afterload è eccessivo e/o la reazione ipertrofica inadeguata (**afterload mismatch**) ne deriva una dilatazione e depressione della funzione contrattile del VS.





Formula di Devereux

$$\text{Massa VS} = 0,832 [(SIVd+Dd+PPd)^3 - Dd^3] \times 0,8 + 0,6$$

(convenzione Am Soc Echo)

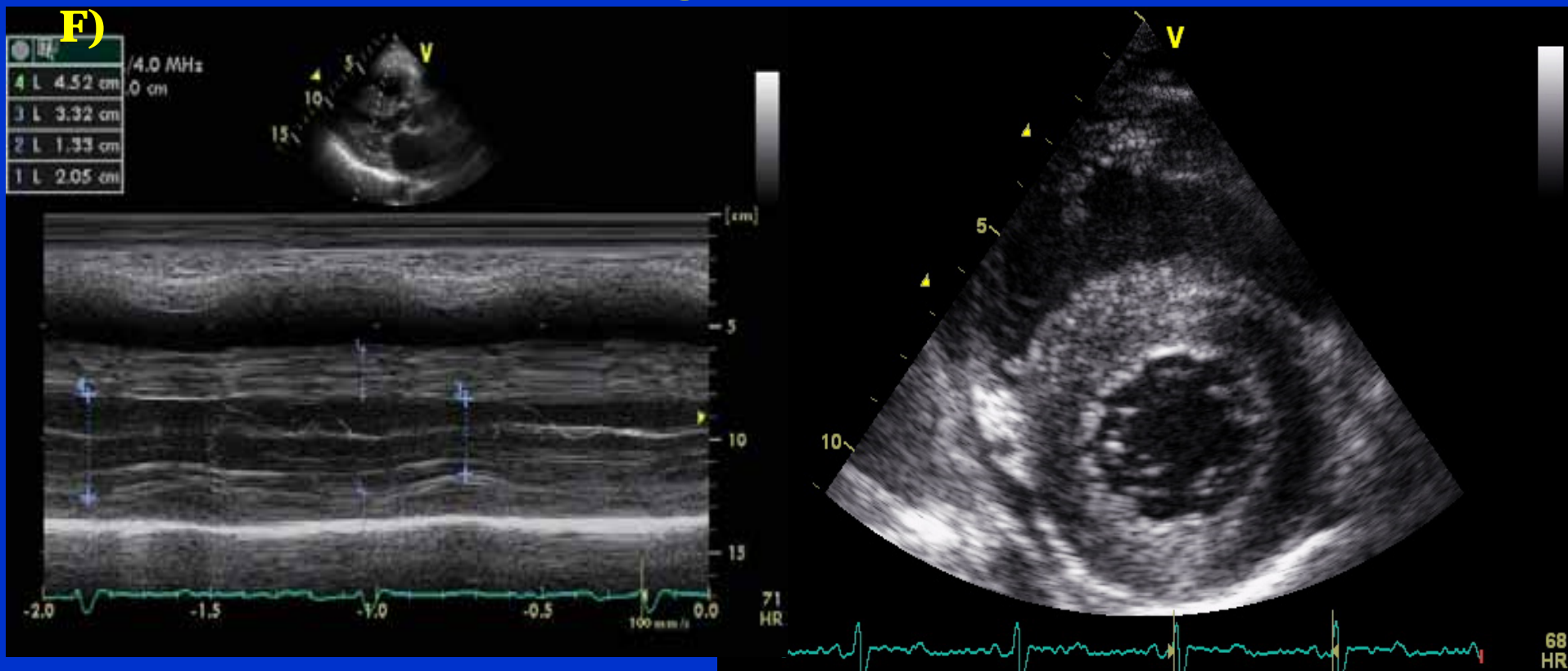
Ipertrofia VS :

Massa VS (g)/SC (m²) >125

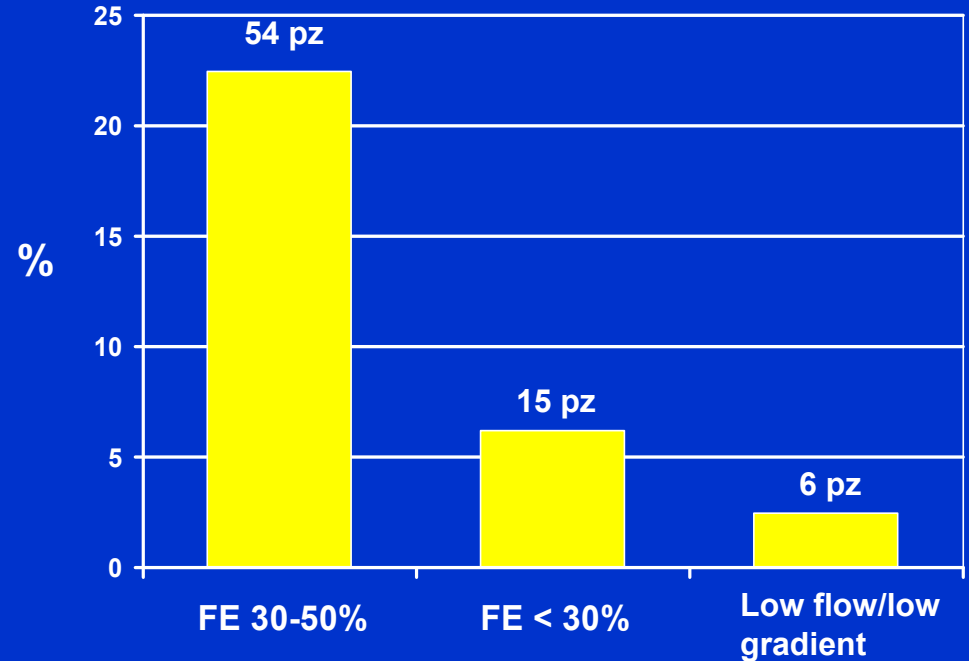
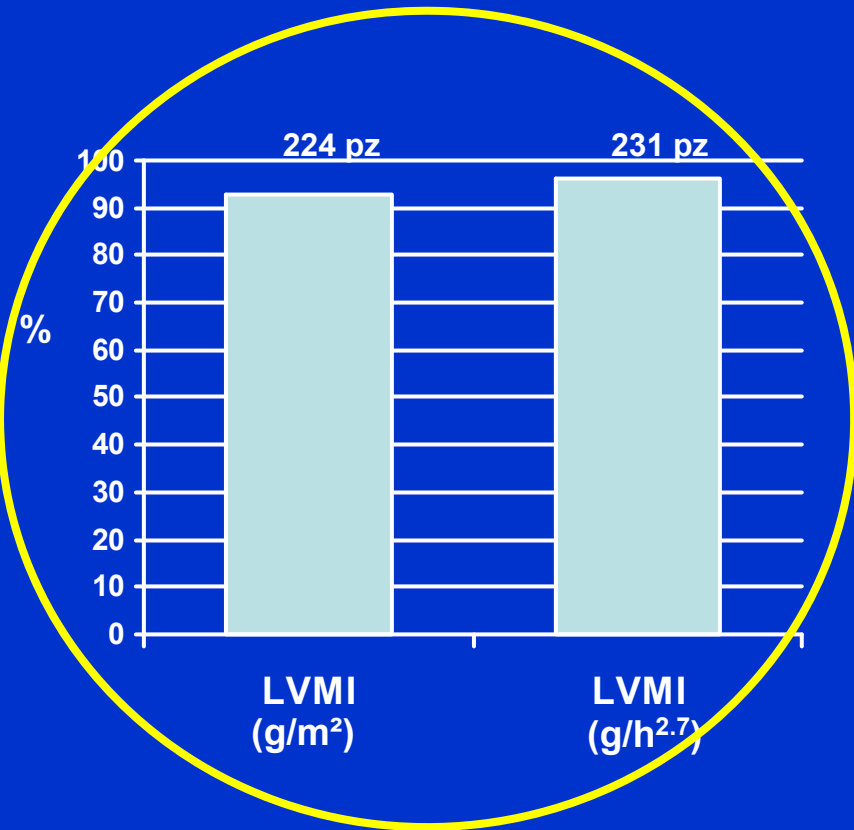
(M); >110 (F)

Massa VS (g)/altezza (m)^{2,7} > 51 (M e

F)



Ipertrofia e Disfunzione Sistolica VS: Prevalenza in 240 pazienti



Left ventricular mass index in aortic valve surgery: a new index for early valve replacement ?

Fuster et Al – Eur J Cardiothorac Surg 2003; 23: 696

- 614 pts underwent aortic valve replacement.
- Mean value of LV mass index : 178 ± 111 gr/m²
- Post-operative complications (low cardiac output , respiratory failure, arrhythmias, pneumoniae, hospital stay) and in-hospital mortality (11,4 % versus 3,2 %) were higher in patients with
- increased LV mass

On multivariate analysis: LV mass index, age, renal failure and cardio-pulmonary bypass time → independent predictors of early mortality.

“Outcome could be improved before a clinically significant increase in LV mass index”

Impact of Valve Prosthesis-Patient Mismatch on Left Ventricular Mass Regression Following Aortic Valve Replacement

Tasca G, Brunelli F, Cirillo M, DallaTomba M, Mhagna Z, Troise G, Quaini E.
Ann Thor Surg 2005; 79: 505

In Aortic Stenosis patients *prosthesis-patient mismatch* is associated with lesser regression of left ventricular hypertrophy after aortic valve replacement.

These findings may have important clinical implications given that *prosthesis-patient mismatch* is frequent in these patients.

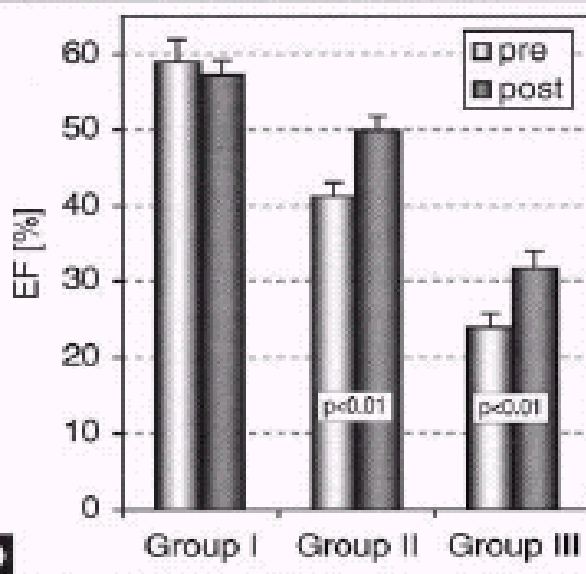
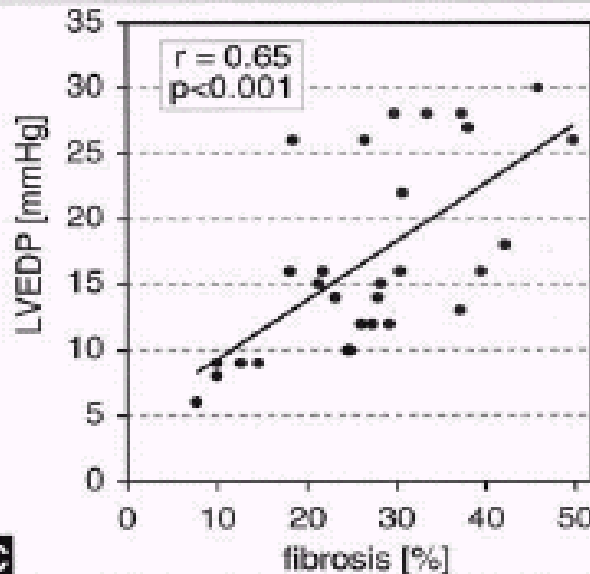
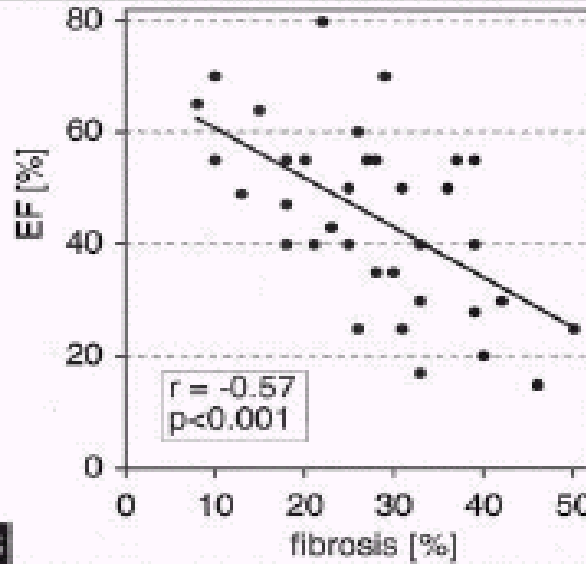
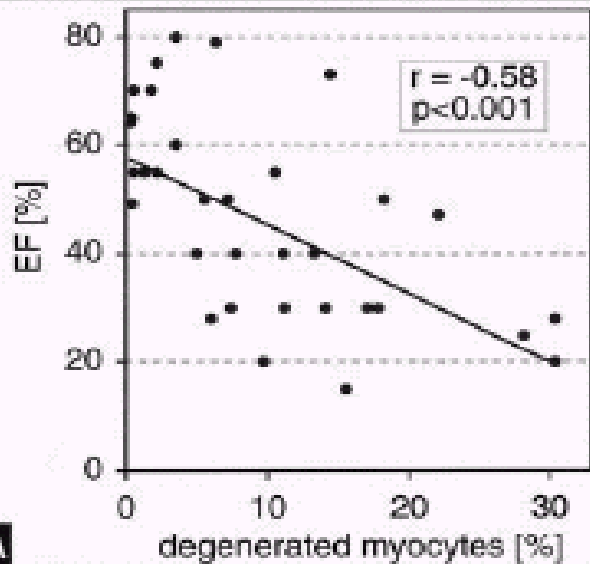
Progression from compensated hypertrophy to failure in the pressure-overloaded human heart

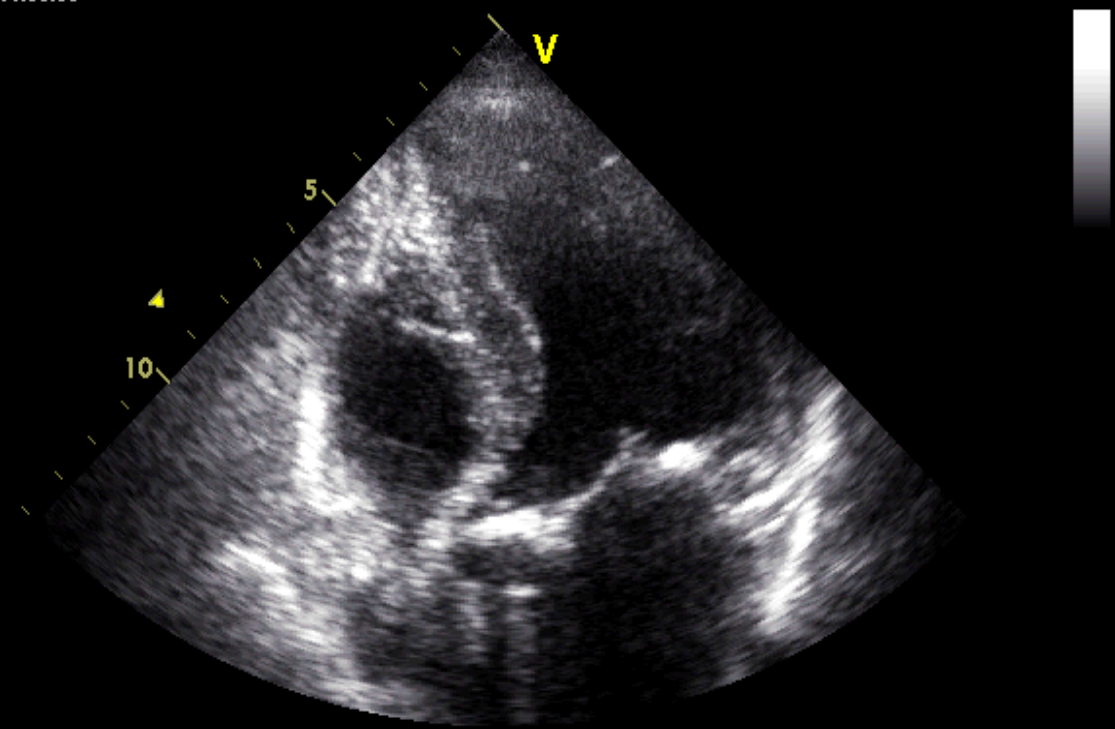
Hein et Al.
Circulation 2003;
107:984

“ a close correlation exists between cardiac function and myocardial morphology in AS patients.
...transition to heart failure occurs by fibrosis and myocyte degeneration, partially compensated by hypertrophy.
...postoperative recovery incomplete in patients with more abnormal structure-function relation.

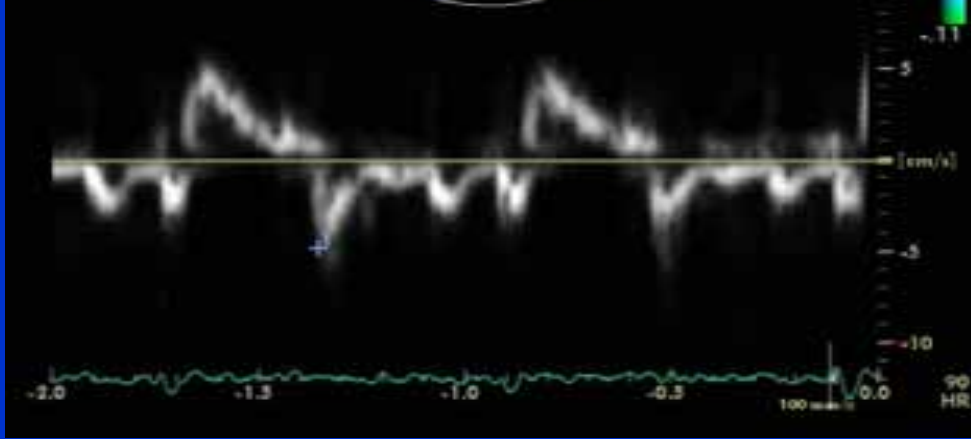
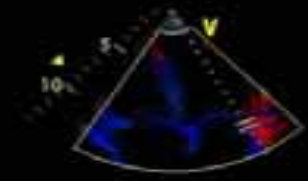
Arguments for earlier valve replacement

Lund



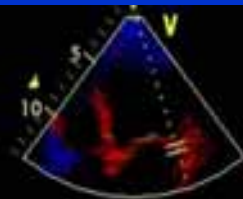


1 v 0.05 m/s
p 0.01 mmHg

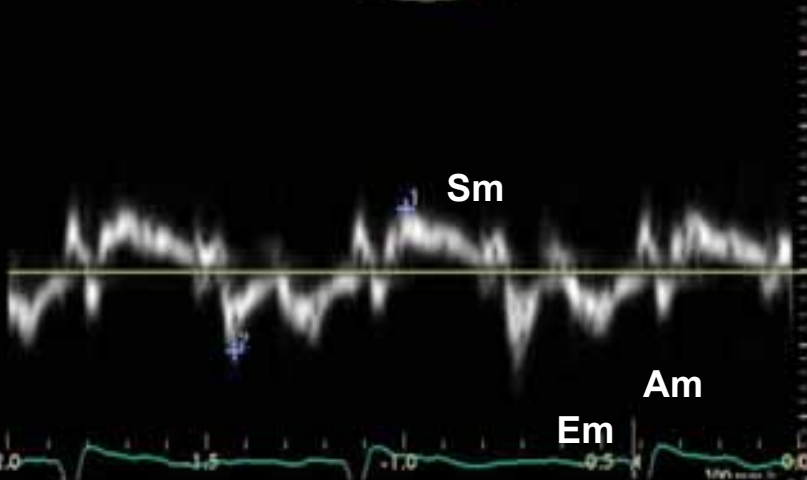


2 v	0.06 m/s
p	0.01 mmHg
1 v	0.04 m/s
p	0.01 mmHg

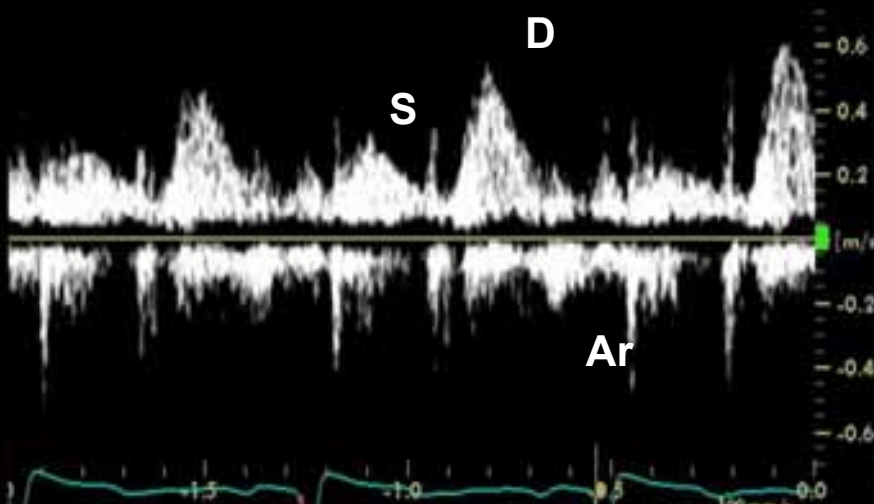
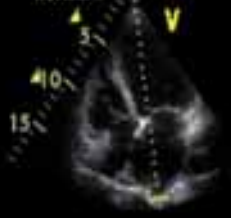
0 MHz



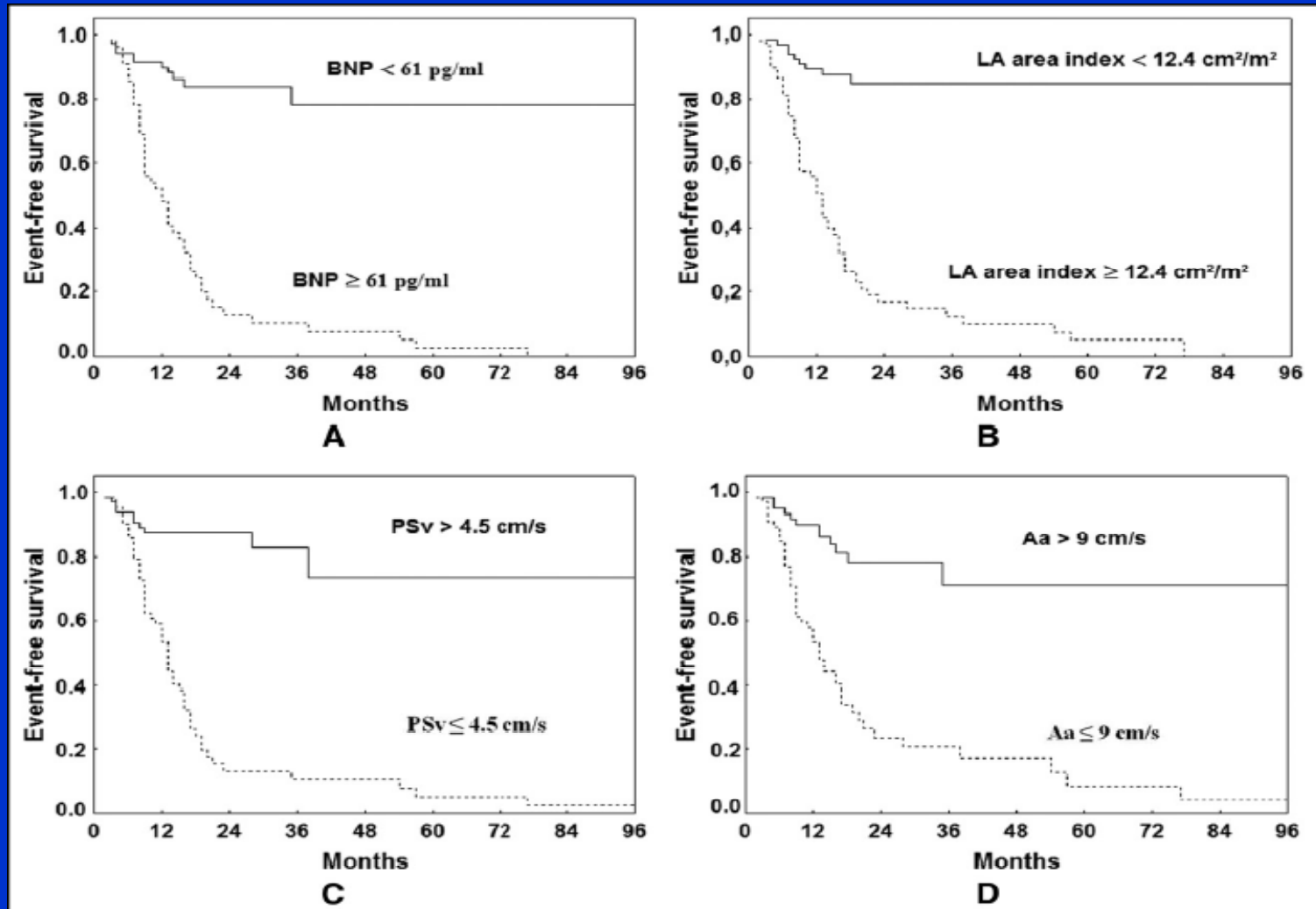
AV E Vel	1.30 m/s
AV DecT	103.51 ms
AV Dec Slope	12.51 m/s ²
AV A Vel	0.50 m/s
AV E/A Ratio	2.57



:59
1.9 MHz/4.0 MHz
ndita: 19.0 cm



Prognostic Effect of Long-Axis Left Ventricular Dysfunction and B-Type Natriuretic Peptide Levels in Asymptomatic Aortic Stenosis



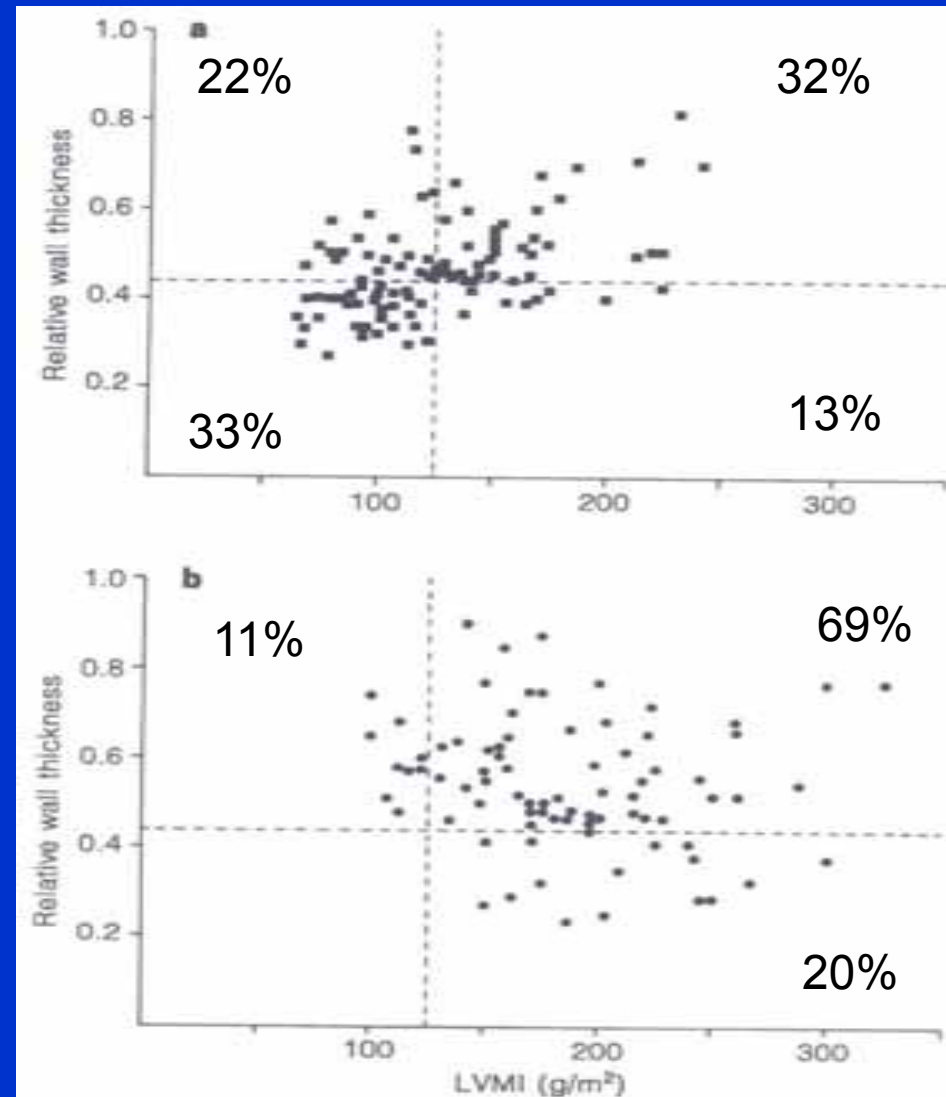
Left Ventricular geometric adaptation to chronic pressure overload: differences between systemic hypertension and valvular aortic stenosis.

An echocardiographic study.

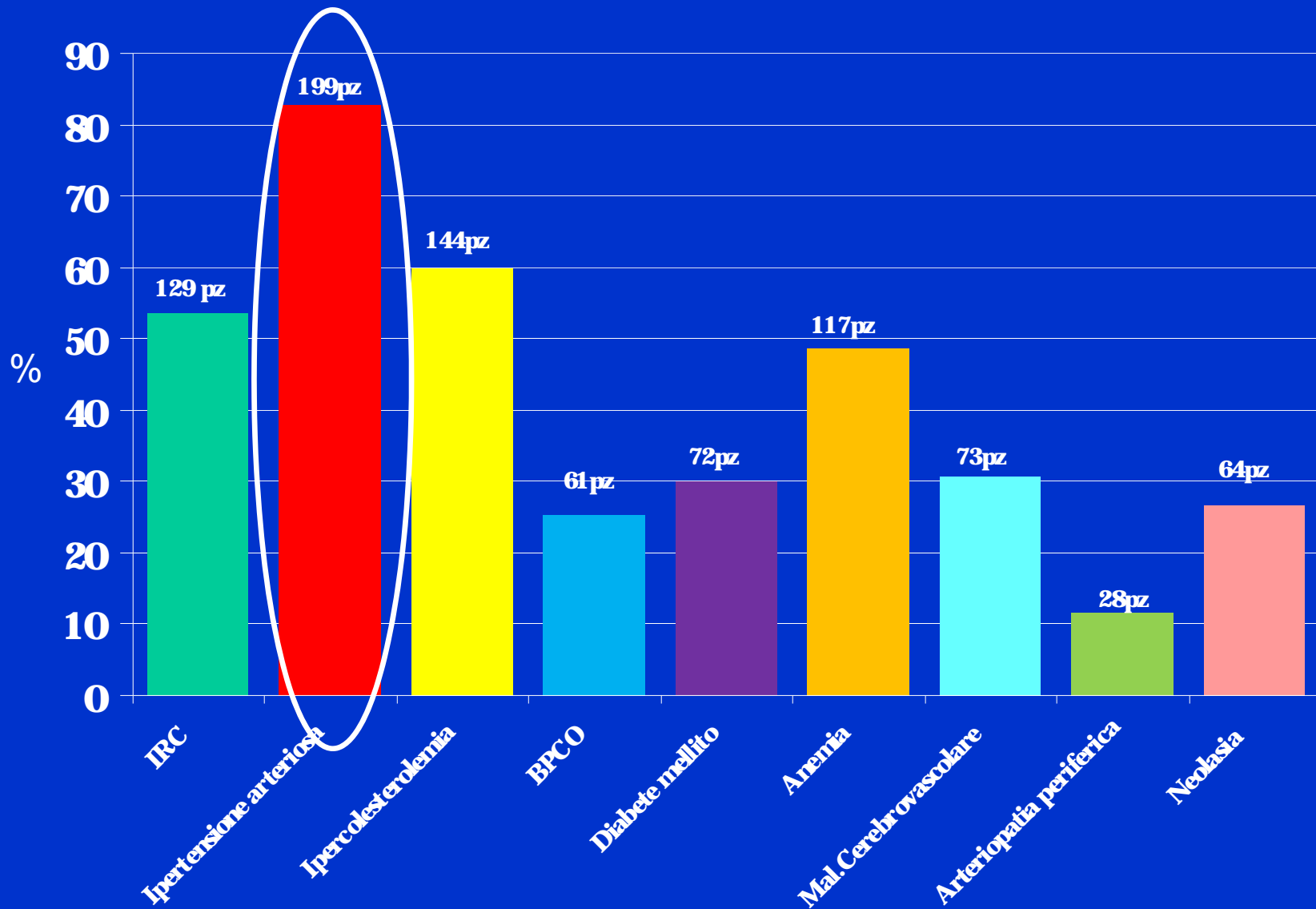
Faggiano et Al. Am J NonInvasive Card 1994; 8: 346

100 Pazienti ipertesi
Massa VS 128 ± 42 gr/m²

80 Pazienti con stenosi aortica
Storia ipertensione 40%
Massa VS 187 ± 50 gr/m²



Comorbidità in 240 pazienti



Survival after aortic valve replacement for aortic stenosis: does left ventricular mass regression have a clinical correlate?

Gaudino et al. Eur Heart J 2005; 26: 51

Table 4 Echocardiographic data

	LVMI (g/m ²)	LVEDDI (mm/m ²)	LVESDI (mm/m ²)	EF	IVST (mm)	PWT (mm)
Pre-operative (n = 260)	190 ± 43	29 ± 3	19 ± 4	0.55 ± 0.21	16 ± 2	13 ± 1
Six month follow-up (n = 248)	162 ± 69*	27 ± 2*	18 ± 3*	0.54 ± 0.18	14 ± 2*	10 ± 2*
Late follow-up (n = 205)	158 ± 70*	26 ± 2* ^{††}	17 ± 2* ^{††}	0.57 ± 0.16	14 ± 1*	10 ± 1*

LVMI regression in hypertensive vs. non-hypertensive patients

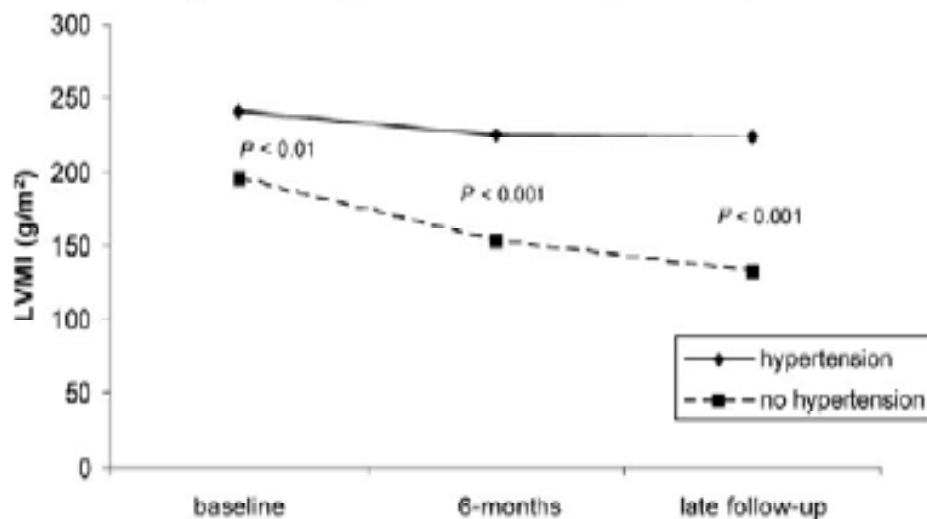
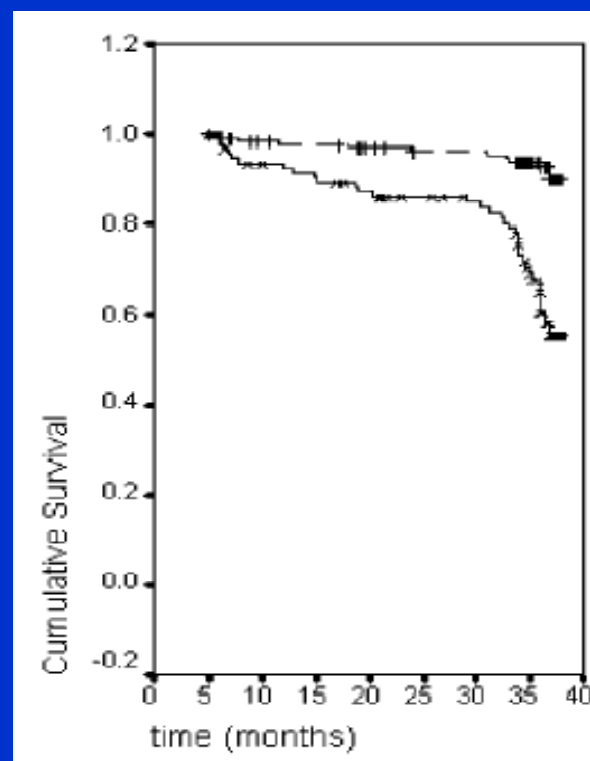


Figure 3 Wilcoxon signed-rank test was employed for evaluation of significance.

These observations underscore the important role of strict post-operative medical control of blood pressure to improve survival in patients submitted to AVR.



Inappropriate LV mass

“maladaptative response” to increased LV load is emerging as an *independent predictor of adverse prognosis*

Predicted values of LV mass in reference population

93 normotensive adults, normal weight, 18-85yrs o

1

Equation for
computation of
theoretical values of
LVM

$$\text{LVM} = 0.64 * \text{SW (g-metri)} - 18.1 * \text{female} + 6.63 * \text{height (m}^{2.7}) + 55.13$$

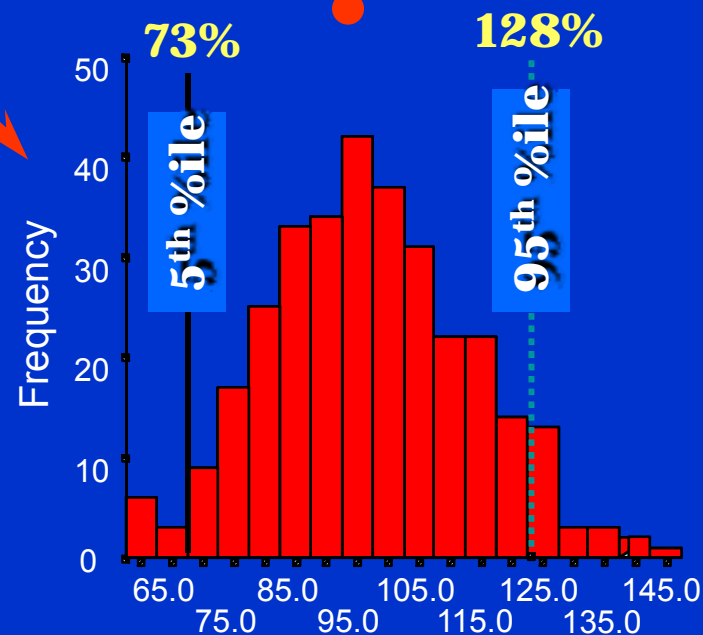
(Hypertension 1998. 31: 1077)

2

$$\frac{\text{Observed LVM}}{\text{Predicted LVM}} * 100$$

3

Normal distribution of
observed/predicted LVM
ratio:
inappropriate LVM >128%
of predicted



Prognostic value of inappropriate left ventricular mass in severe aortic stenosis

Cioffi et Al.

submitted

200 patients (75±11 years, 54% hypertensive) with severe AS

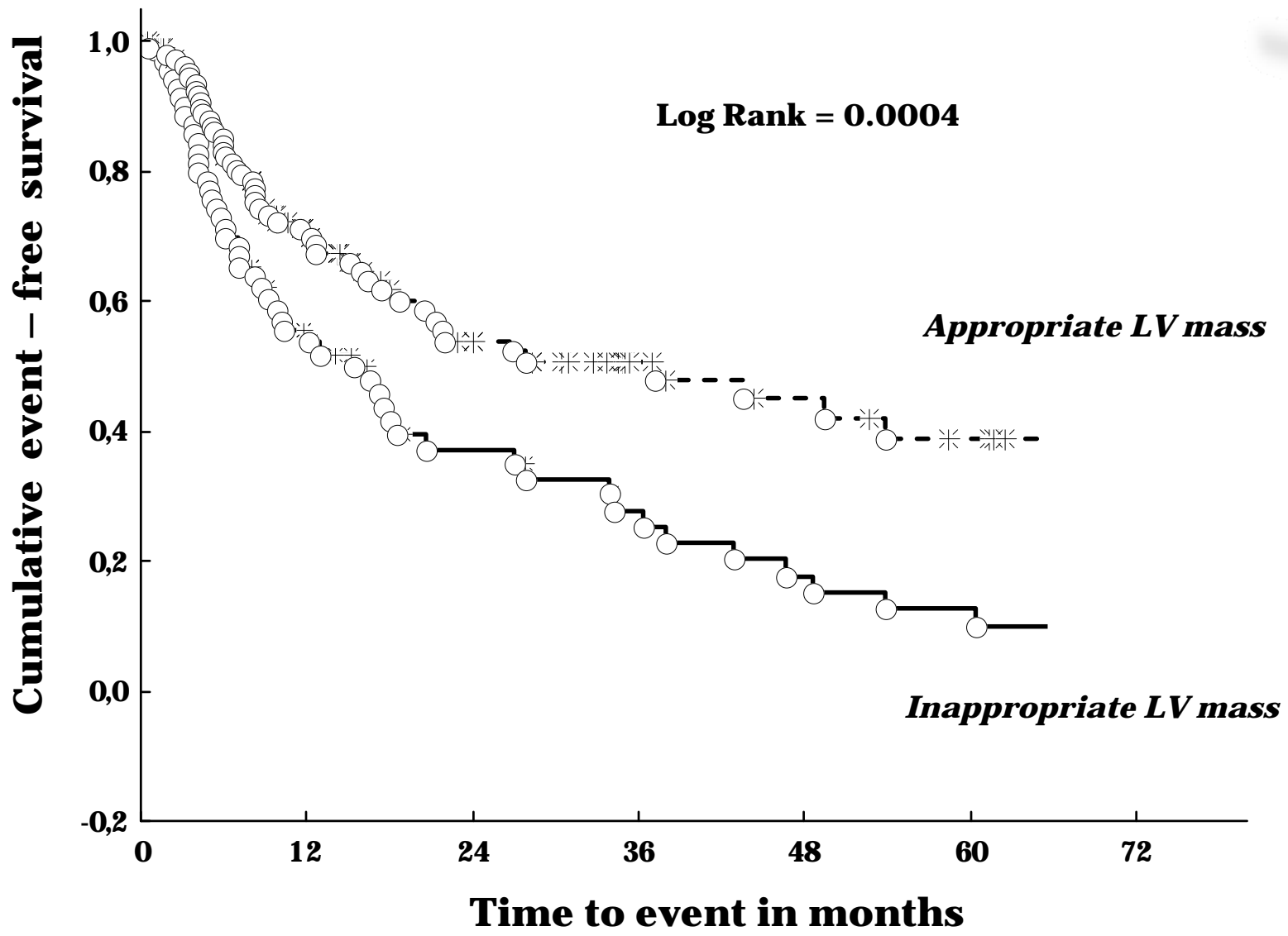
Inappropriate LV mass in 40.5%

- iLVM strong predictor of adverse outcome
- iLVM had a risk of adverse events 3.2-fold higher than counterparts with appropriate LV mass.

Conclusions: *iLVM is common in patients with severe AS and negatively influences outcome, independent of severity of valve disease, diabetes and functional status.*

In patients with traditional LV hypertrophy, iLVM provides additional prognostic information.

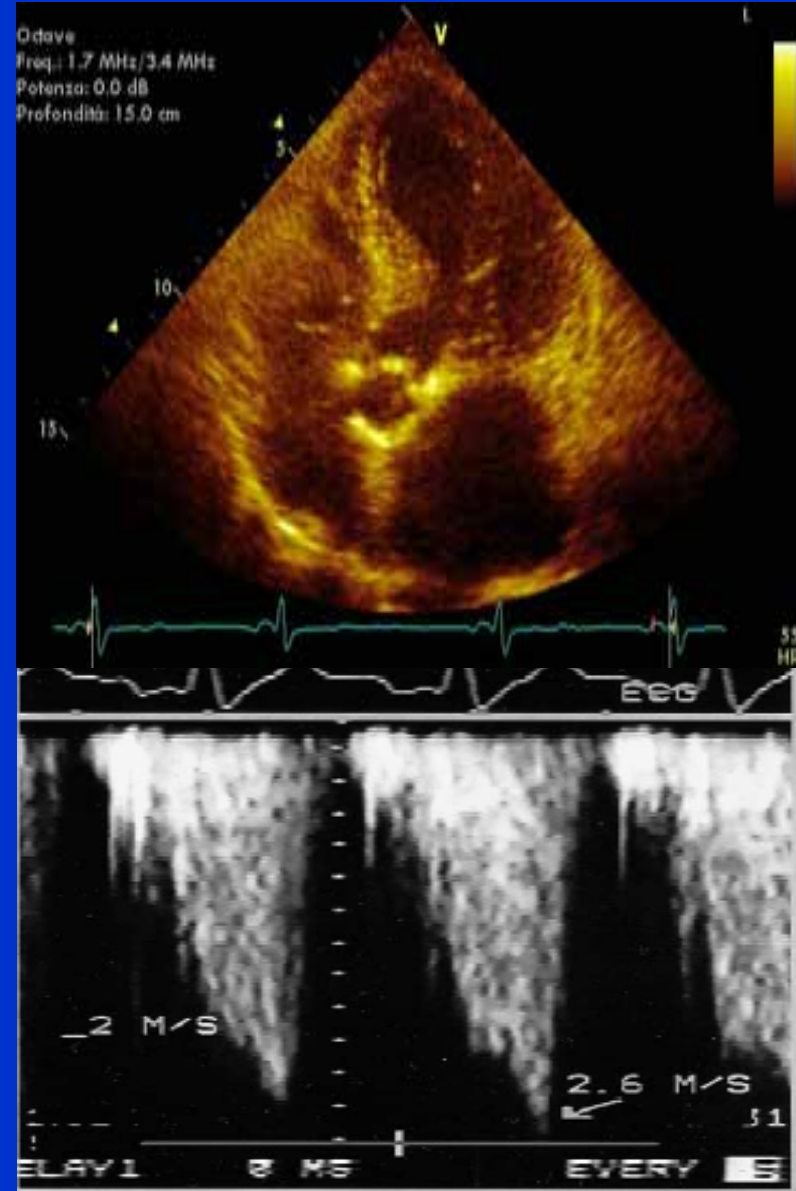
Fig. 2



Abnormal Left Ventricular Intracavitary Flow Acceleration in Patients Undergoing Aortic Valve Replacement for Aortic Stenosis A Marker for High Postoperative Morbidity and Mortality

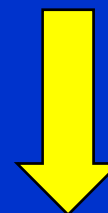
Aurigemma et Al. Circulation 1992;86:926-936

- Ostruzione dinamica intraventricolare con gradiente tardivo si verifica dopo sostituzione valvolare aortica per stenosi, **soprattutto nel sesso femminile**
- provocata o favorita da ridotto precarico e stimolo inotropo
- Betabloccante efficace
- Un pattern tipico (VS piccolo, ipercinetico, con pareti ipertrofiche) è predittivo del quadro post-op e dovrebbe essere identificato pre-op
- Elevata morbilità postoperatoria

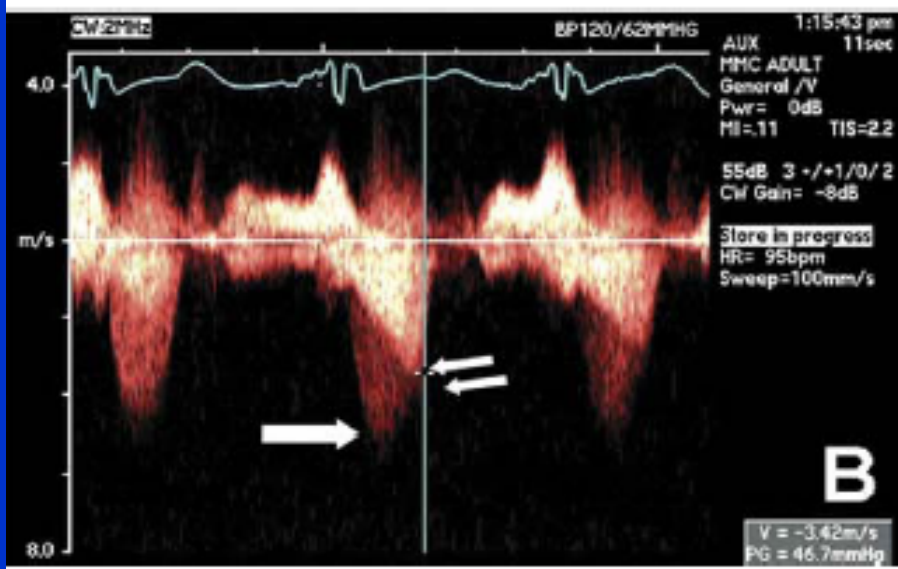
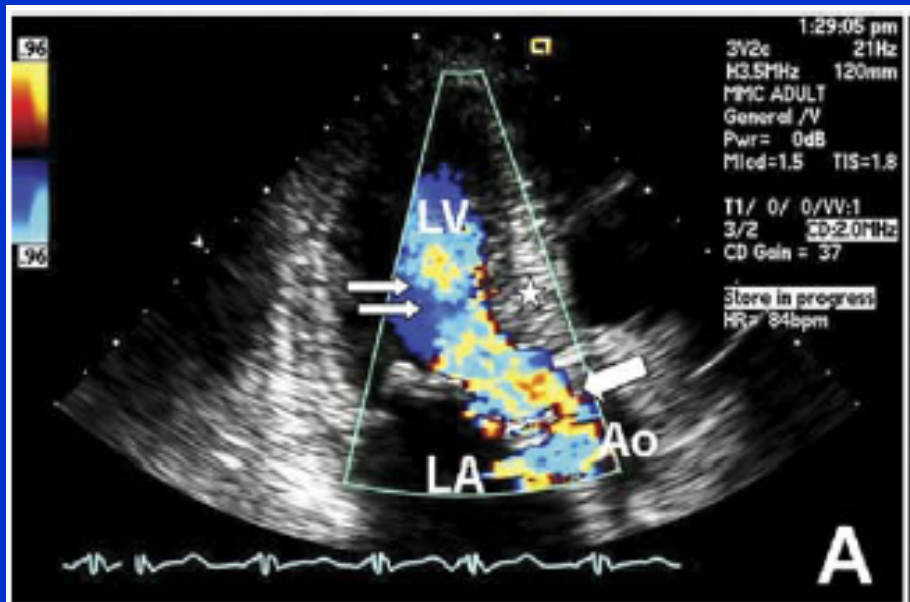


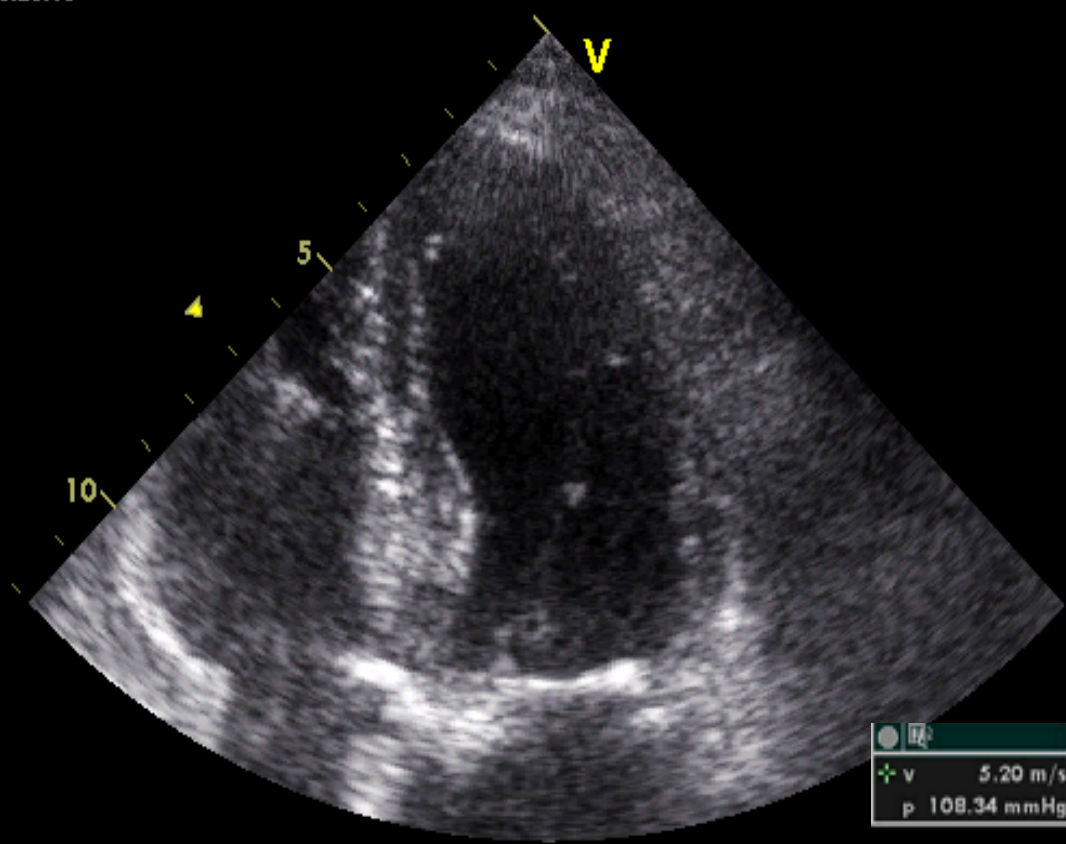
Ipertrofia VS (240 pazienti)

- $SIV \geq 1.5$ cm: 107 pz (44.5%)
- $SIV/PP \geq 1.3$ cm: 14 pz (5.8%)

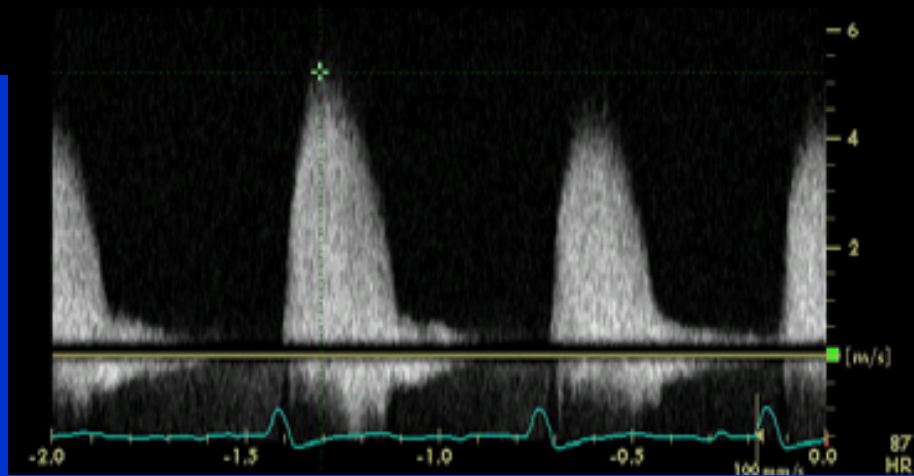


Miectomia settale associata a
Sostituzione valvolare aortica?

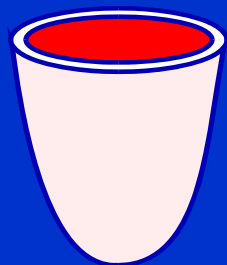




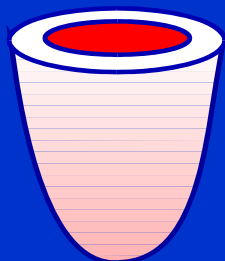
5.20 m/s
108.34 mmHg



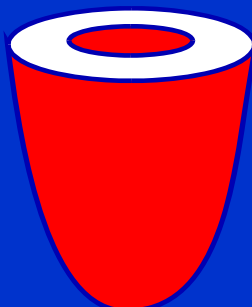
Ventricolo normale



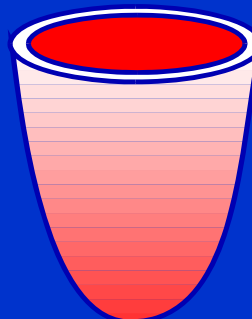
Rimodellamento
concentrico



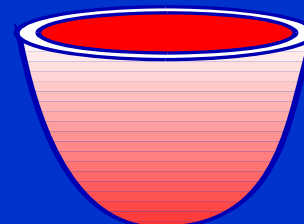
Ipertrofia
concentrica



Ipertrofia
eccentrica



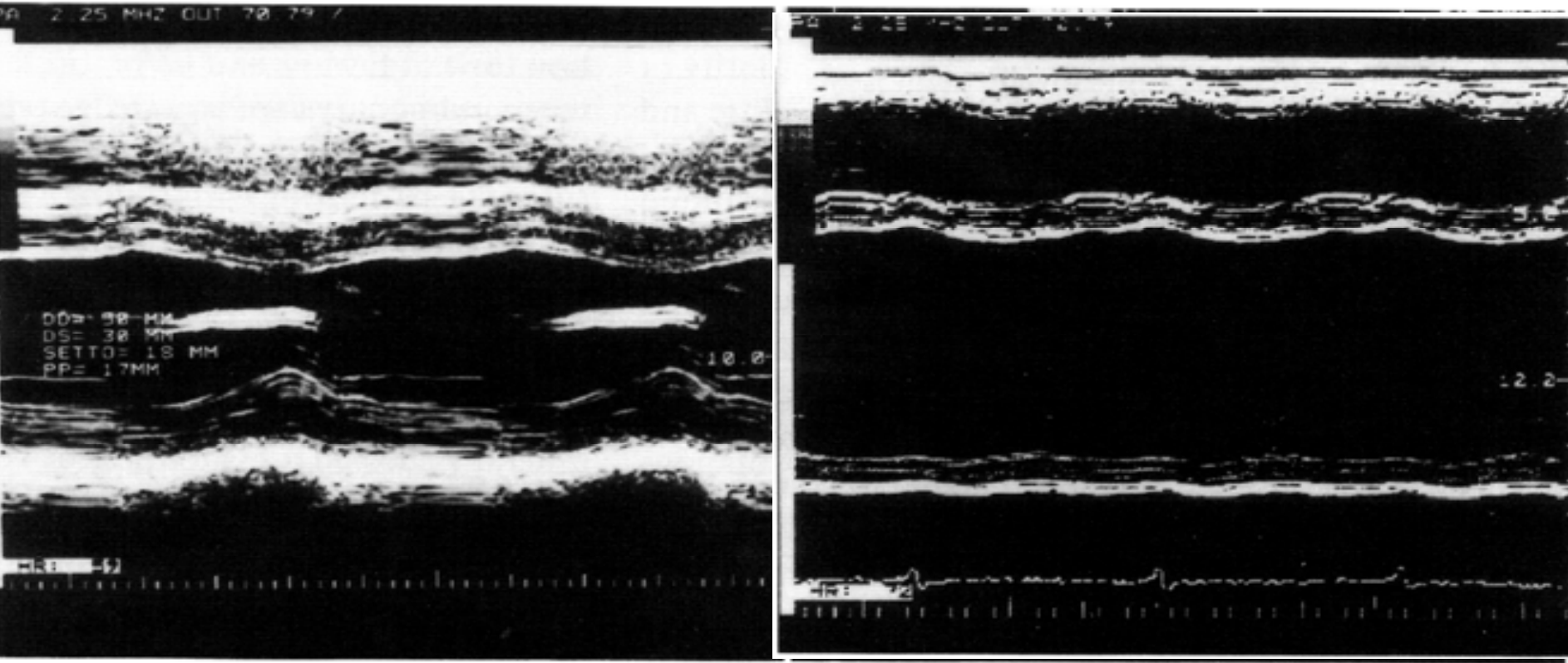
Disfunzione sistol. VS
Scompenso cardiaco



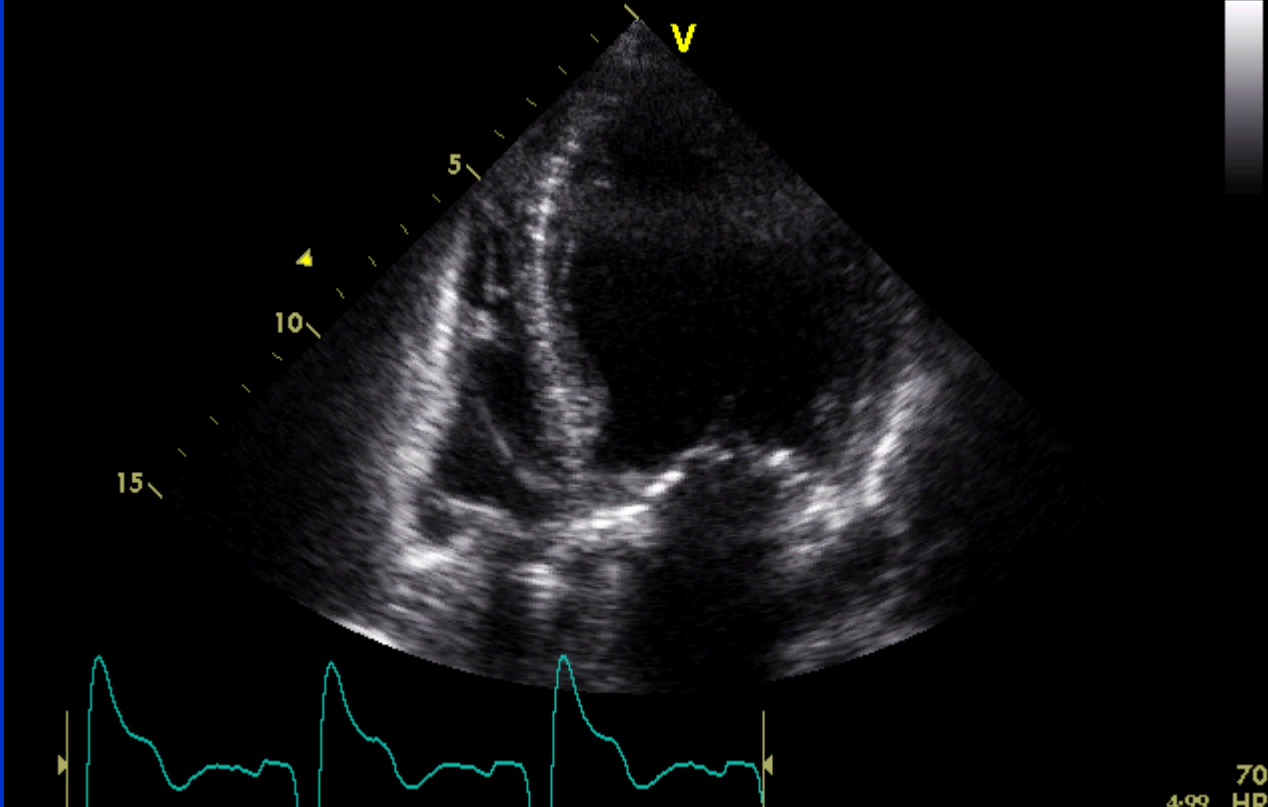
Ipertrofia

Dilatazione

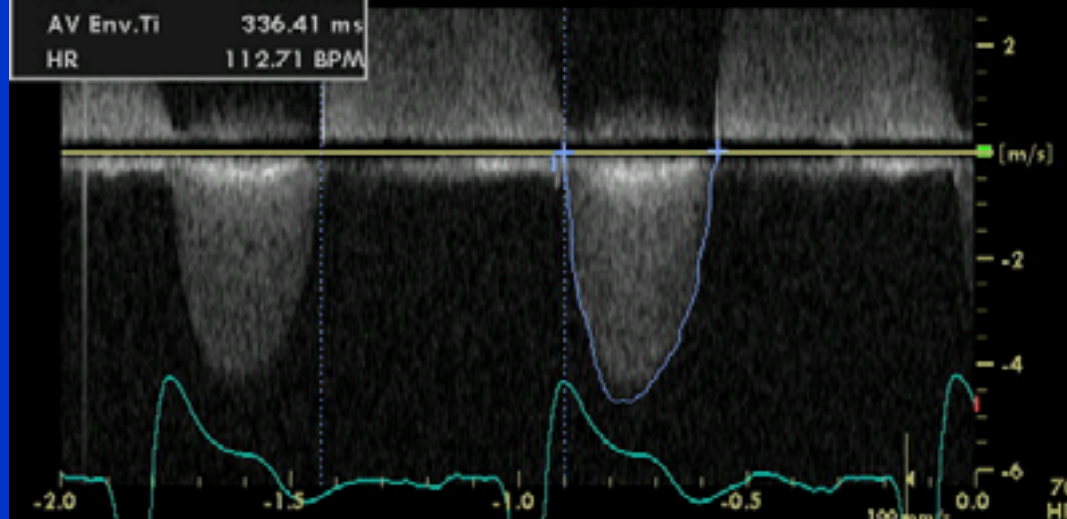
Progression from compensated hypertrophy to failure in the pressure-overloaded human heart



Faggiano et Al. Left ventricular remodeling in valvular aortic stenosis. Echocardiographic and clinical changes during follow-up. **Chest**, 1994; 105:1273



AV VTI	114.40 cm
AV Env.Ti	336.41 ms
HR	112.71 BPM



Numerosi studi successivi hanno confermato che la disfunzione sistolica VS anche severa associata ad un **elevato gradiente transvalvolare aortico**:

(1) condiziona in misura solo modesta il rischio operatorio,

(2) generalmente regredisce in misura più o meno completa dopo intervento di sostituzione valvolare

(3) consente una prognosi favorevole a lungo termine.

STENOSI AORTICA SEVERA BASSO GRADIENTE / BASSA PORTATA

- Elevata mortalità perioperatoria (Carabello, 1980; Brogan, 1993)
- Elevata mortalità tardiva (Lund, 1990; Blitz, 1998)
- Persistenza scompenso cardiaco grave (Carabello, 1980; Brogan, 1993)
- Persistenza disfunzione sistolica ventricolare sinistra (Connolly, 1997)
- Marker prognostico, soprattutto se associato a coronaropatia (Connolly, 1997; Blitz, 1998)

Stenosi Aortica “low flow/flow gradient”

Criteria diagnostici

The specific criteria for low-flow, low-gradient aortic stenosis vary widely in the literature, but have generally included a *composite of at least two* of the following measurements:

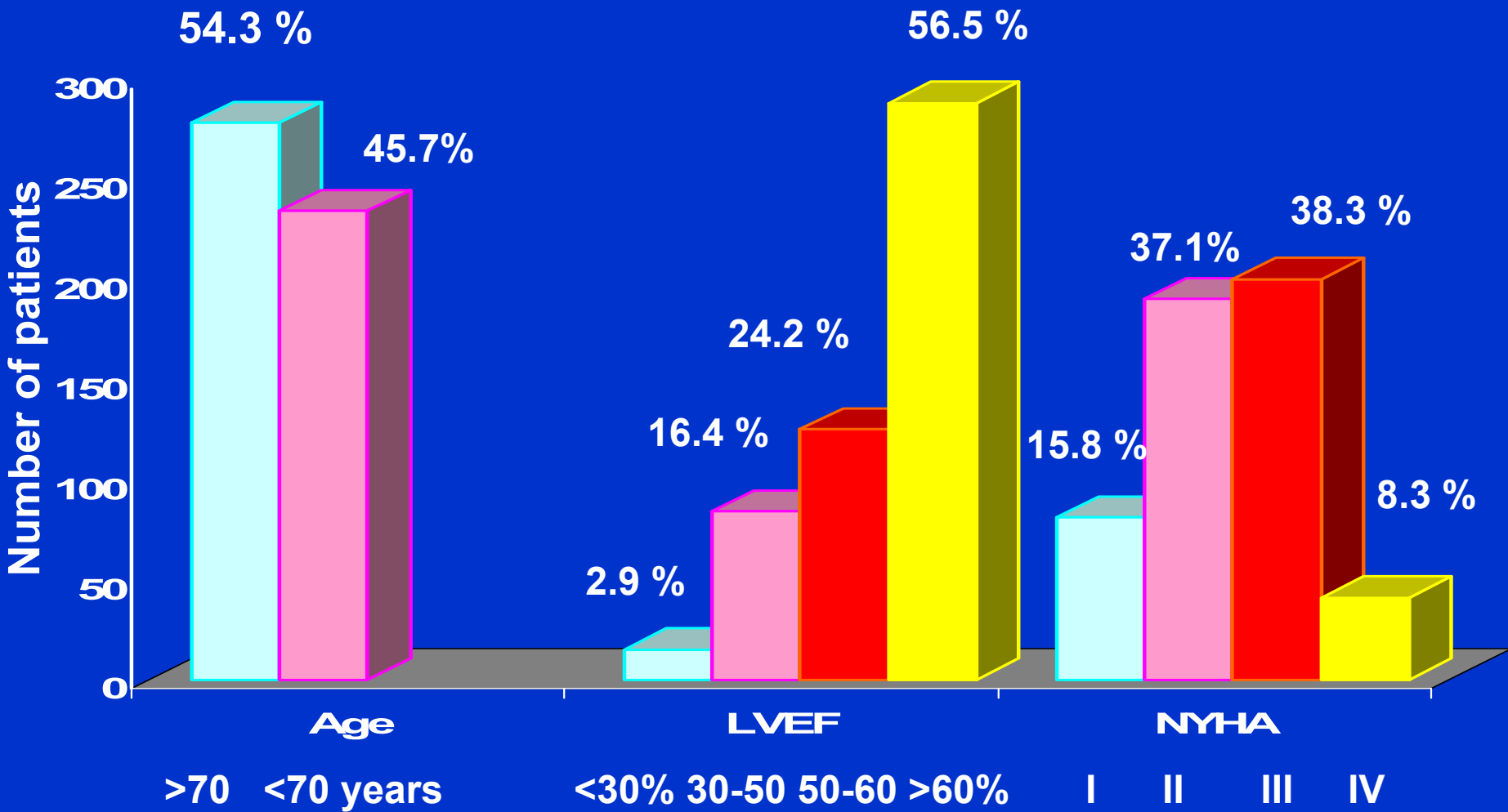
1. **aortic valve area 0.7–1.2cm²**
2. **mean transvalvular pressure gradient <30–40 mmHg**
3. **Left ventricular ejection fraction <30–45%**

The **greatest dilemma** regarding management, however, resides in those patients with **a left ventricular ejection fraction <35%, aortic valve area <1.0 cm² and a mean pressure gradient <30mmHg** .

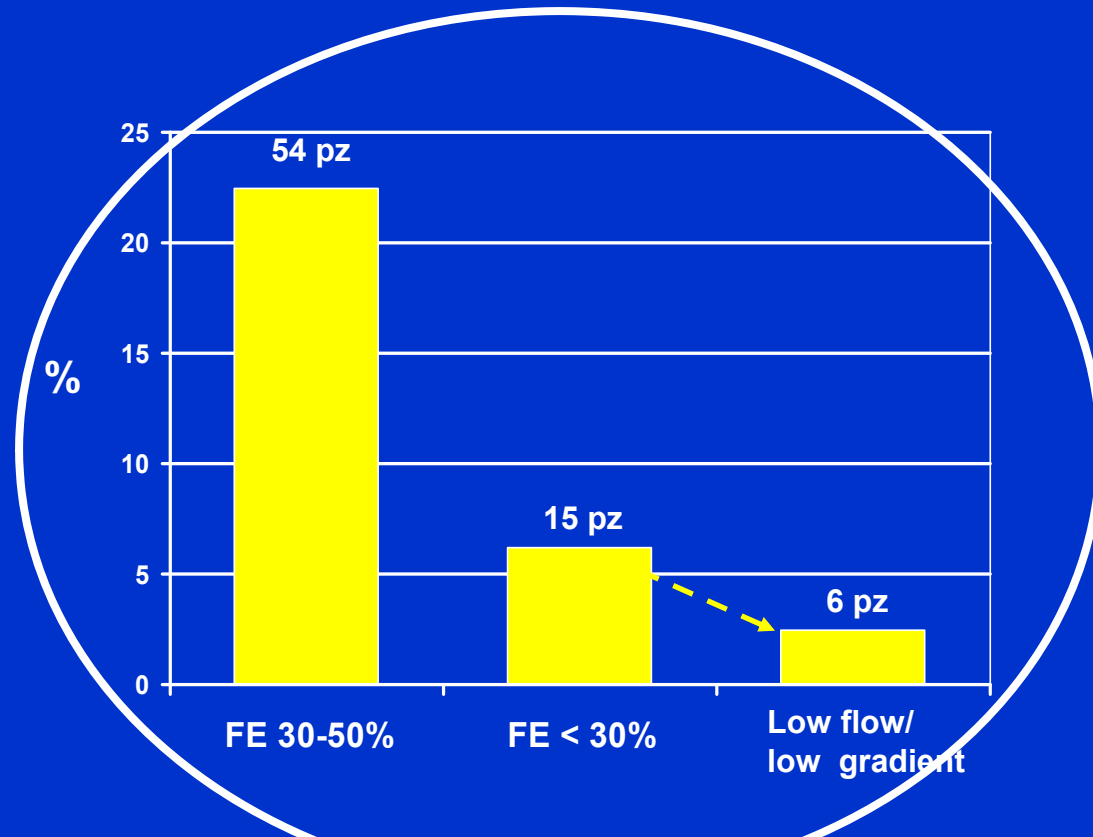
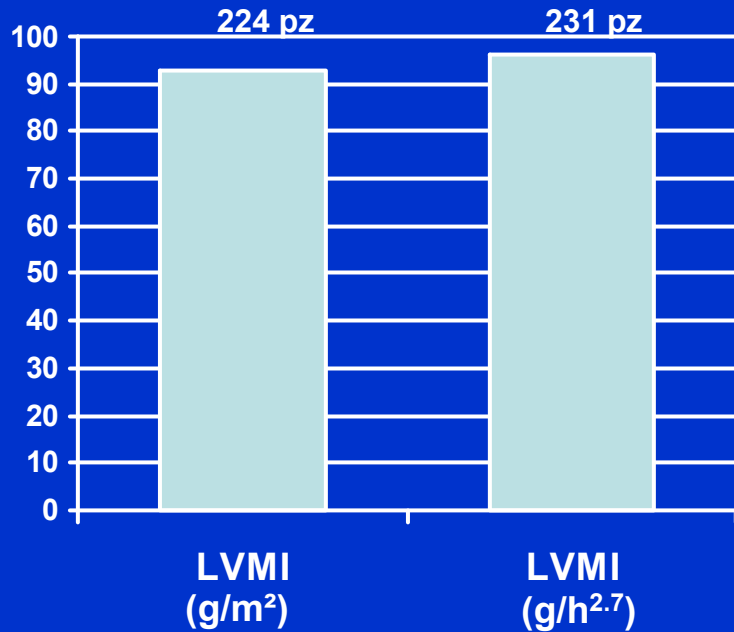
In these patients, the ‘true’ hemodynamic severity of the valve stenosis may be difficult to determine, AVR is associated with a high operative risk, and the potential benefits of AVR to alleviate symptoms and improve prognosis may be limited.

Euro Heart Survey on valvular heart disease

N= 512 AS patients who underwent valve intervention



Ipertrofia e Disfunzione Sistolica VS: Prevalenza in 240 pazienti



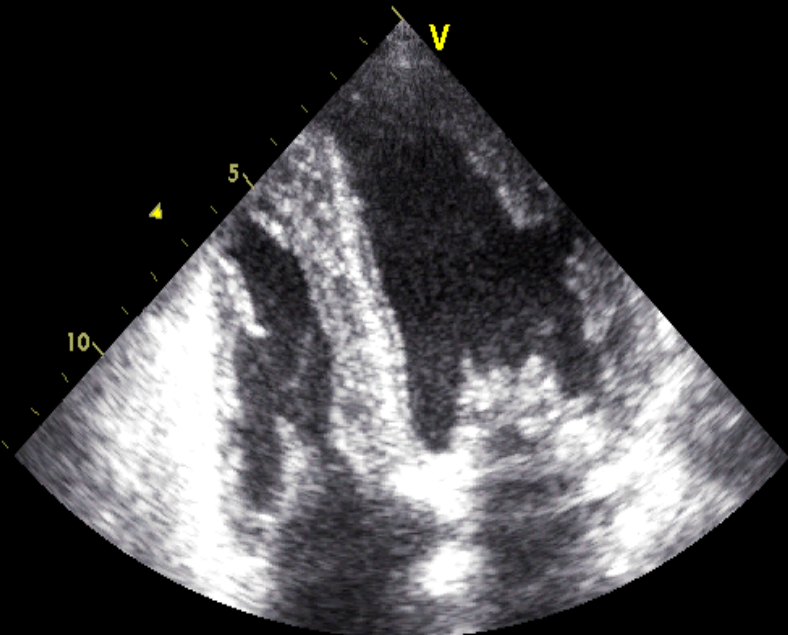
FR 65Hz
10cm

2D
70%
C 50
P Off
Gen



Temp. PAZ: 37.0C
Temp. TEE: 38.6C

489



68
2.192 HR

Il dilemma della stenosi aortica low flow/low gradient

Si tratta di una **stenosi aortica VERAMENTE SEVERA**, con afterload mismatch e depressione contrattile conseguente ?
Oppure si tratta di una **stenosi aortica PSEUDO-SEVERA (o Relativa)**, per cui la valvola, solo modestamente stenotica appare invece *criticamente* stenotica solo per una incapacità del ventricolo sinistro (disfunzionante per cause indipendenti dalla stenosi) a generare forza sufficiente a determinare una ottimale apertura sistolica delle cuspidi?

La diagnosi differenziale tra le 2 condizioni può essere clinicamente rilevante:

Nel 1° caso la sostituzione valvolare è indicata ed efficace (sintomi, FE, prognosi).

Nel 2° caso la sostituzione valvolare potrebbe non apportare alcuno beneficio.

Come distinguere la Stenosi Veramente severa dalla Pseudo-Stenosi ?

L'aumento della portata cardiaca, e quindi del flusso transvalvolare, indotta da un potente inotropo, come la dobutamina, o da un vasodilatatore, come il nitroprussiato, dovrebbe modificare poco la severità di una vera stenosi (orifizio fisso: area valvolare invariata, aumento gradiente), mentre dovrebbe determinare un rilevante aumento dell'area valvolare di una pseudo-stenosi (a livelli non più critici), con eventuale riduzione o stabilità del gradiente transvalvolare.

“ Diagnosis of Occult Critical Aortic Stenosis with Intravenous Infusion of Dobutamine”

Pearlman et al., Am J Noninvas Cardiol 1987; 1: 134-139

	Base 10y/Kg/min	Dobutamina
Portata	3.4	5.0
Gradiente	25	46
Area	0.67	0.73

STENOSI AORTICA SEVERA
GRADIENTE MEDIO < 30mmHg
FE < 45%

Riserva contrattile alla dobutamina
(aumento stroke volume > 20%)

SI

(12 pz) - Gruppo I

NO

(6 pz) - Gruppo II

Gradiente ↑

Area =

Gruppo I A

(7 pz)

Gradiente =

Area ↑

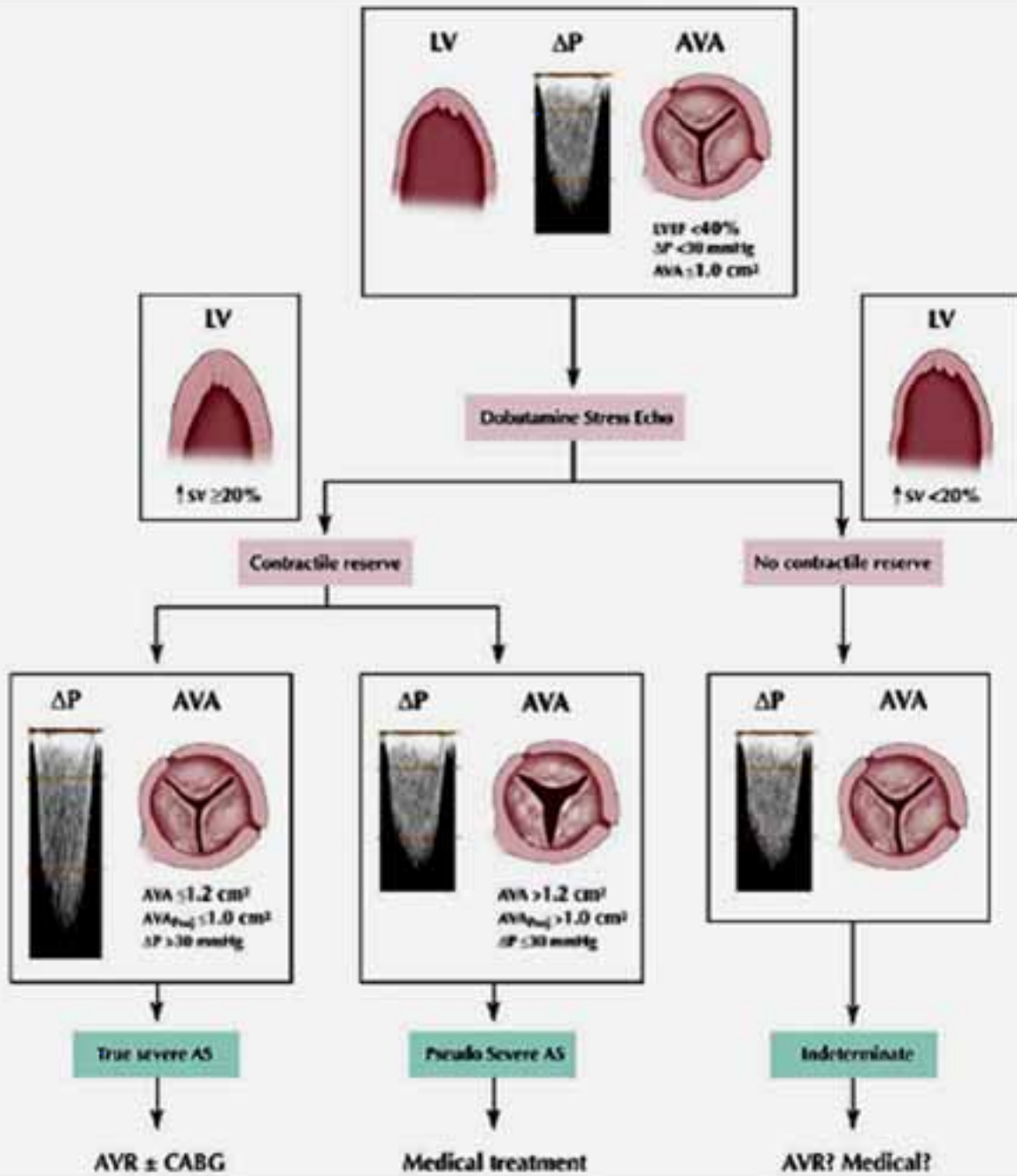
Gruppo I B

(5 pz)

STENOSI
INDETERMINATA

STENOSI
FISSA

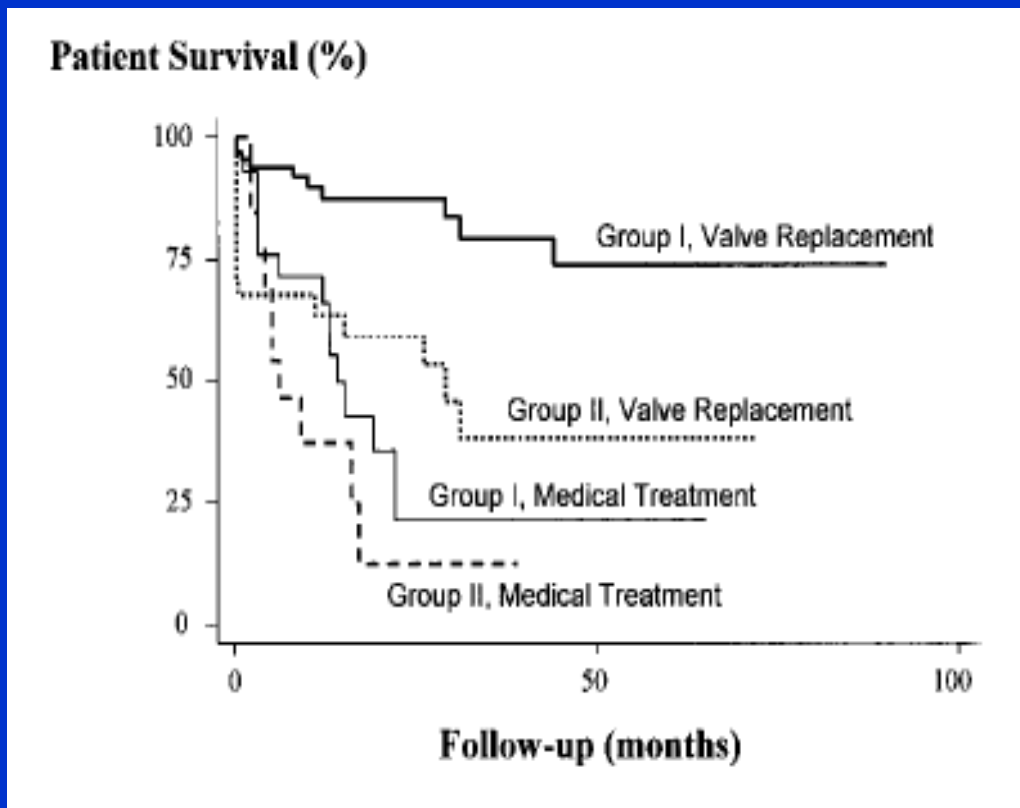
STENOSI
RELATIVA



La riserva contrattile

Durante test alla dobutamina, oltre al comportamento dell'area valvolare e del gradiente transvalvolare, assume particolare rilevanza, soprattutto prognostica, la valutazione della riserva contrattile.

L'assenza di riserva contrattile, cioè **stroke volume invariato o aumentato < 20%**, è il più forte predittore di mortalità operatoria (32% versus 5%) e a distanza.



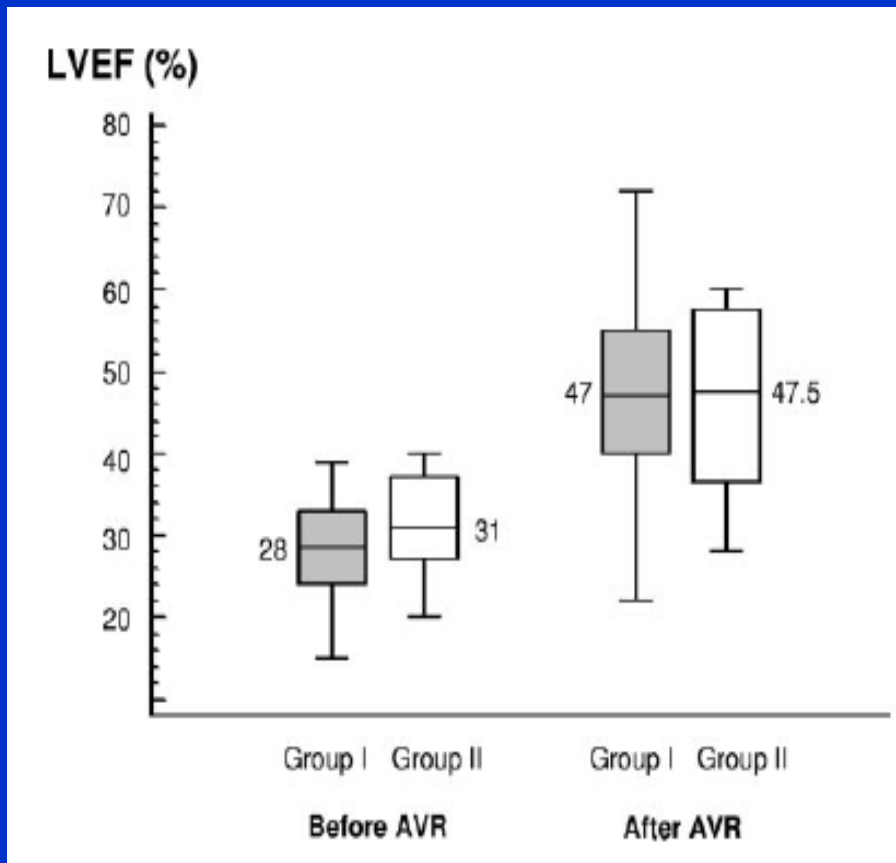
Gruppo 1: riserva contrattile presente

Gruppo 2: riserva contrattile assente

... ma il miglioramento della frazione di eiezione e dei sintomi dopo sostituzione valvolare è indipendente dalla presenza o assenza di riserva contrattile all'eco-dobutamina

Miglioramento ≥ 1 classe NYHA 96% in gruppo 1 e 90% in gruppo 2

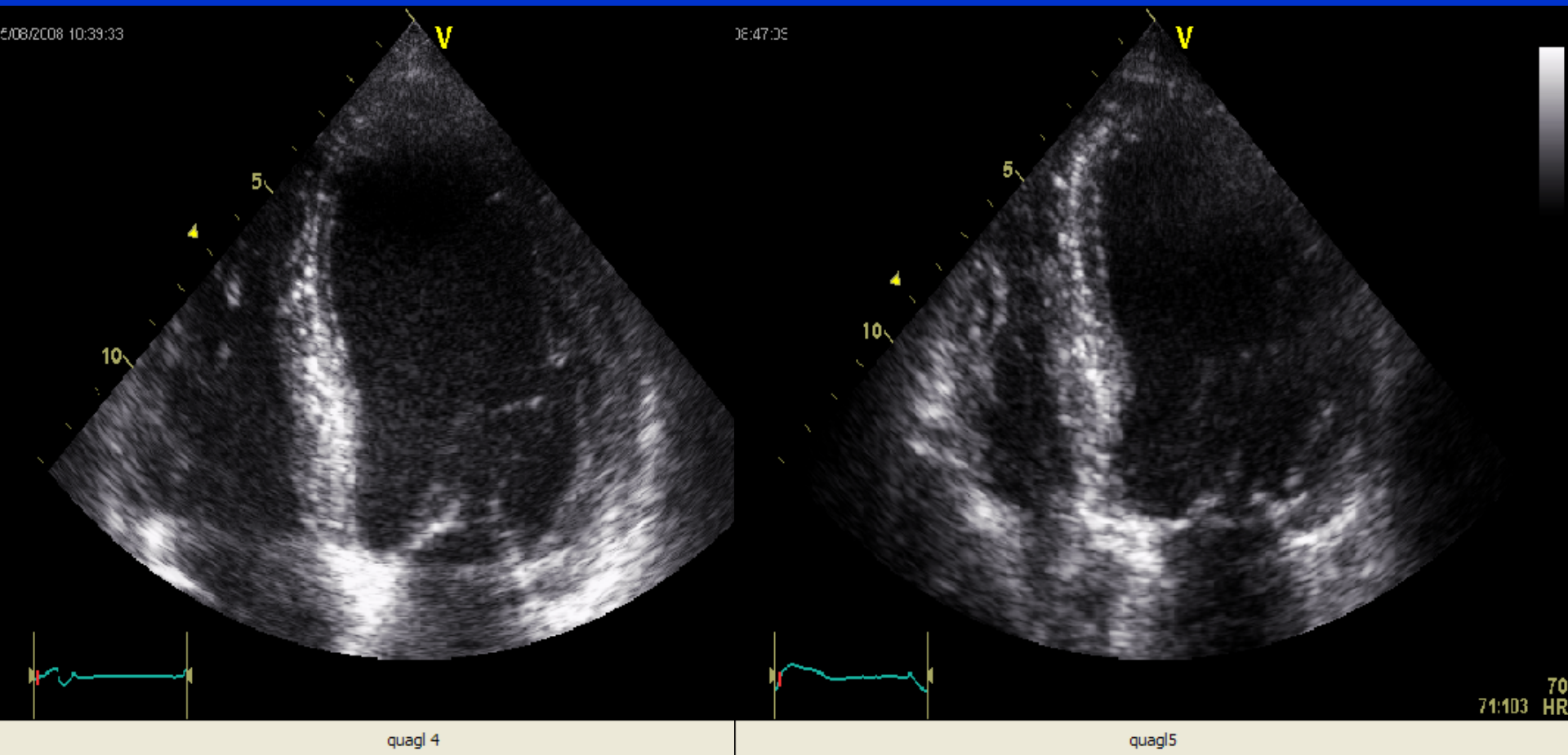
Miglioramento ≥ 2 classi NYHA 59% in gruppo 1 e 55% in gruppo 2



“These data support the concept that surgery should not be contraindicated on the basis of absence of contractile reserve alone.”

Circulation. 2006;113:1738-1744

Uomo di 85 anni, low-flow/low-gradient aortic stenosis sottoposto a sostituzione percutanea di valvola aortica - CoreValve



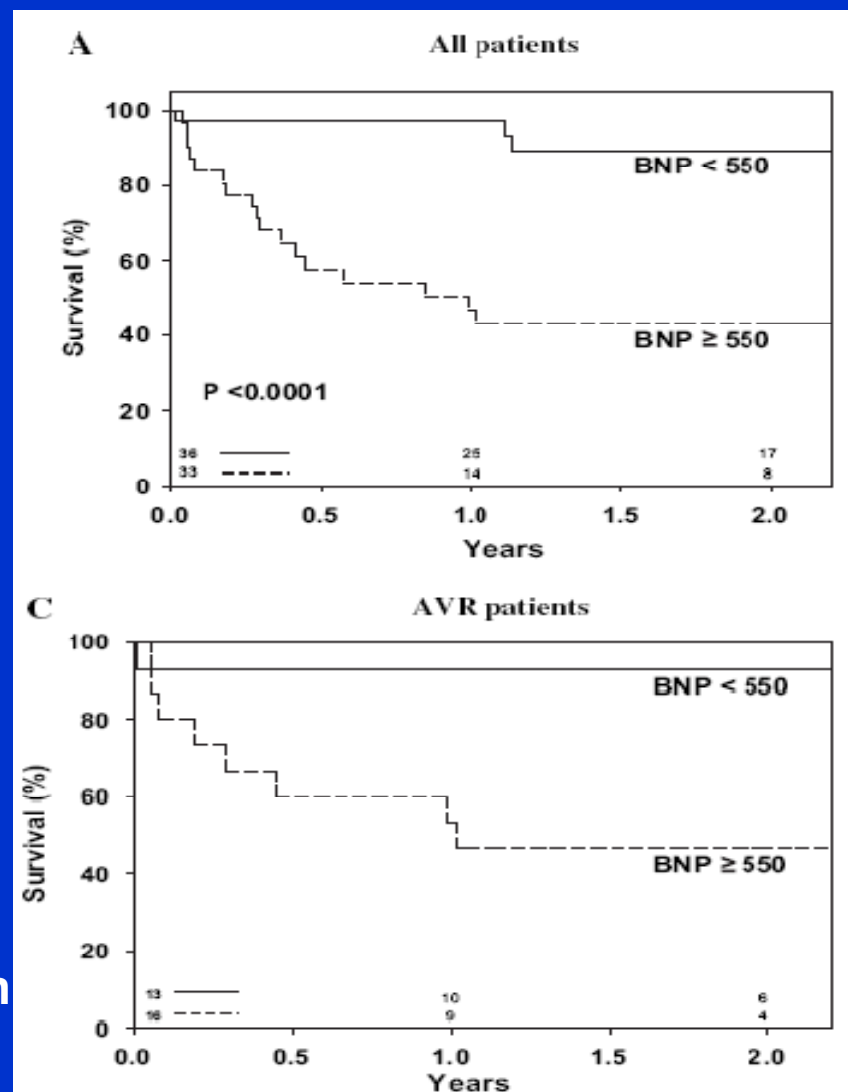
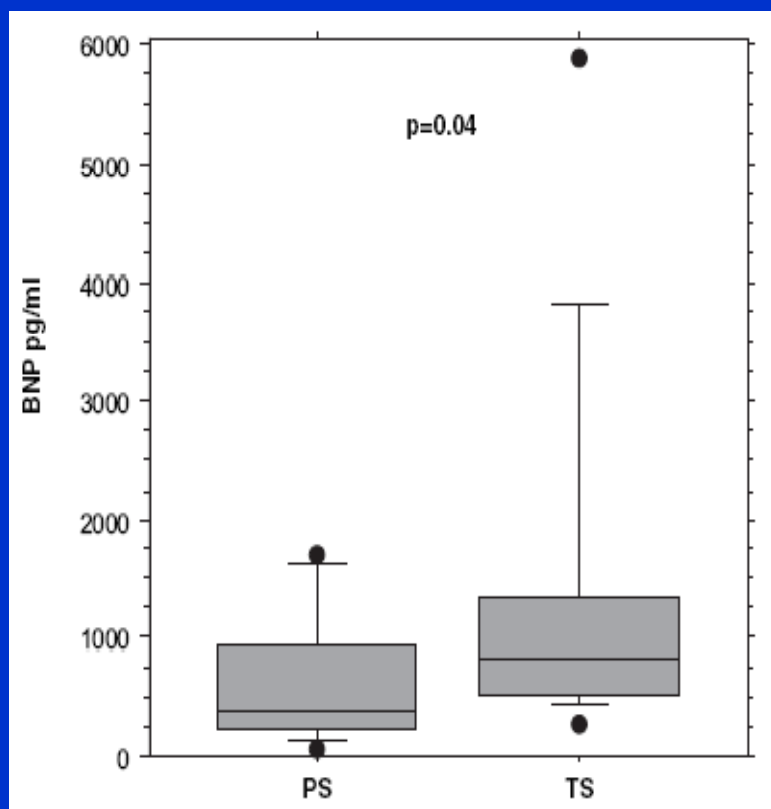
Prima : NYHA IV, FE 25%

2 settimane dopo : NYHA II, FE 40%

B-Type Natriuretic Peptide in Low-Flow, Low-Gradient Aortic Stenosis

Relationship to Hemodynamics and Clinical Outcome: Results From the Multicenter Truly or Pseudo-Severe Aortic Stenosis (TOPAS) Study

Circulation.
2007;115:2848



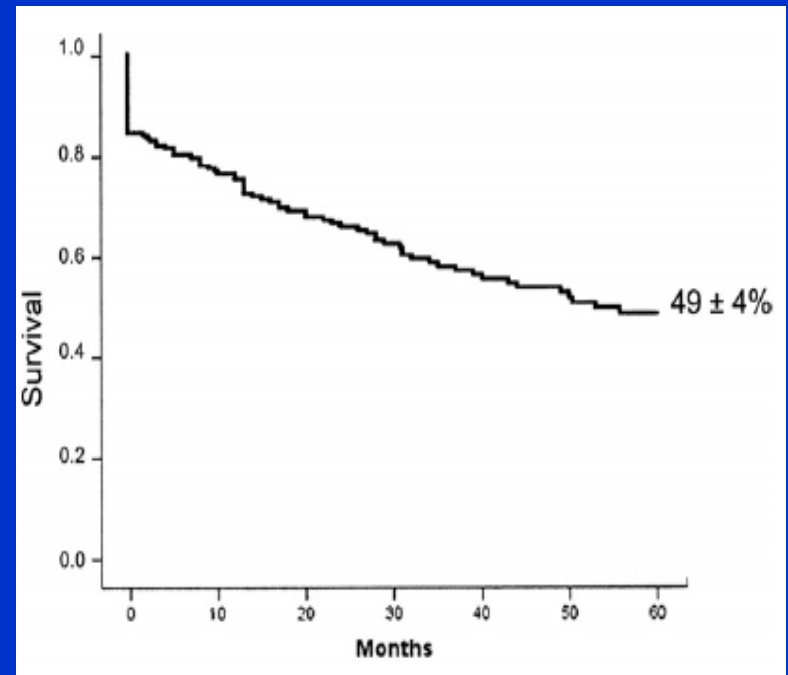
BNP is significantly higher in truly severe than pseudosevere low-gradient AS and predicts survival of the whole cohort and in patients undergoing valve replacement.

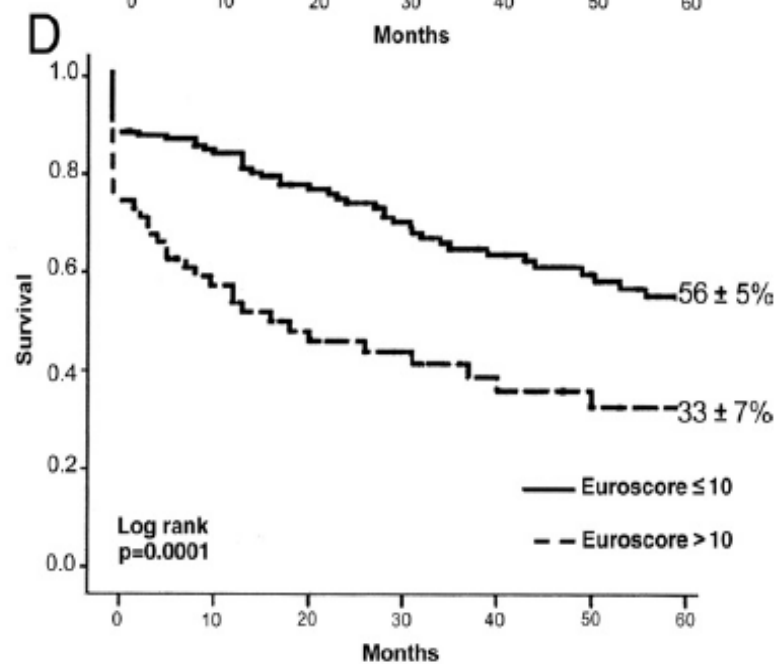
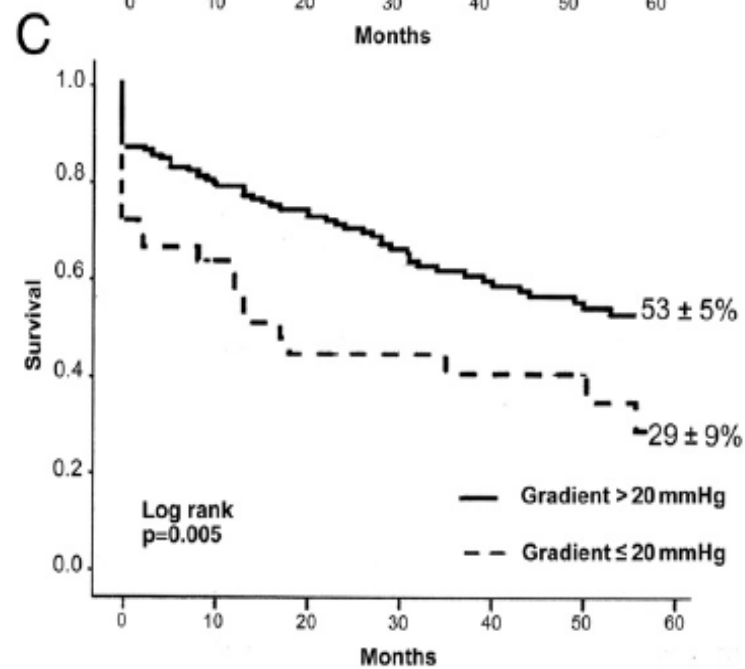
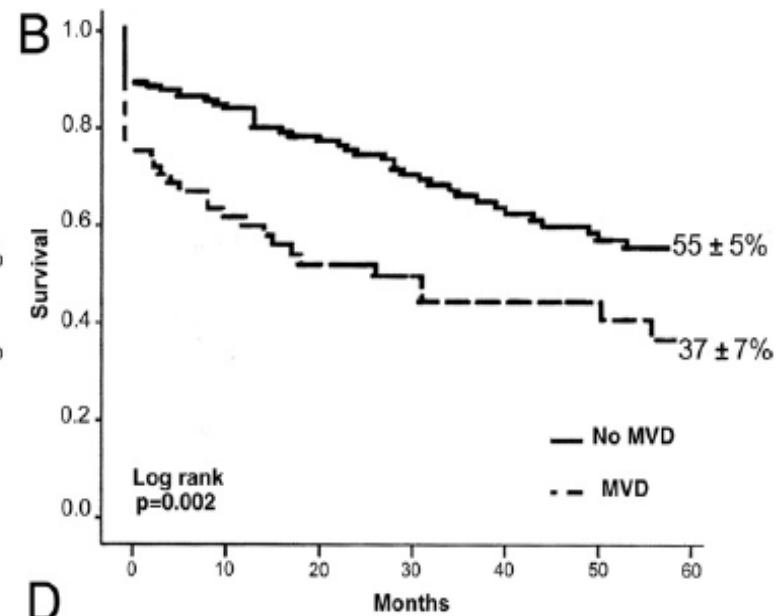
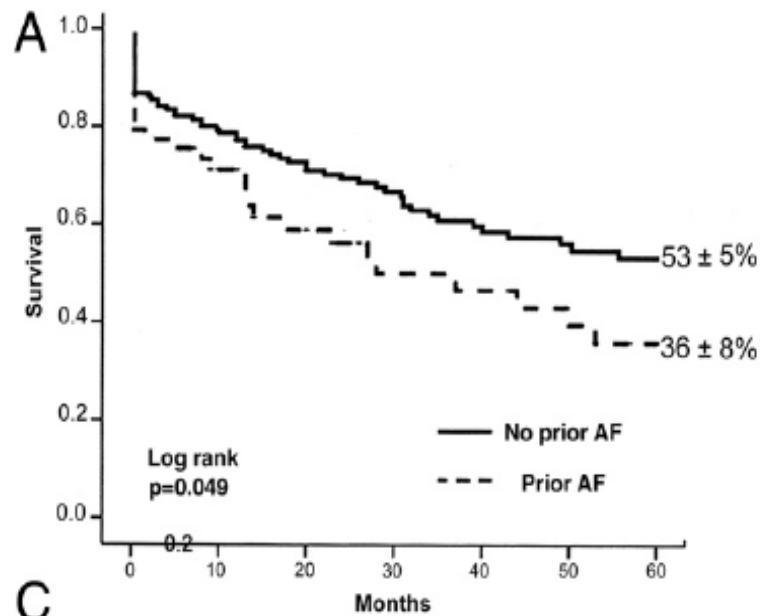
Aortic Valve Replacement for Low-Flow/Low-Gradient Aortic Stenosis

Operative Risk Stratification and
Long-Term Outcome: A European Multicenter Study

217 consecutive patients (168 men, 77%) with severe aortic stenosis (area ≤ 1 cm²), low ejection fraction (<35%), and low mean gradient (<30 mm Hg) who underwent aortic valve replacement (AVR) between 1990 and 2005.

Perioperative mortality was 16% and decreased dramatically from 20% in the 1990 to 1999 period to 10% in the 2000 to 2005 period.





CONCLUSIONI

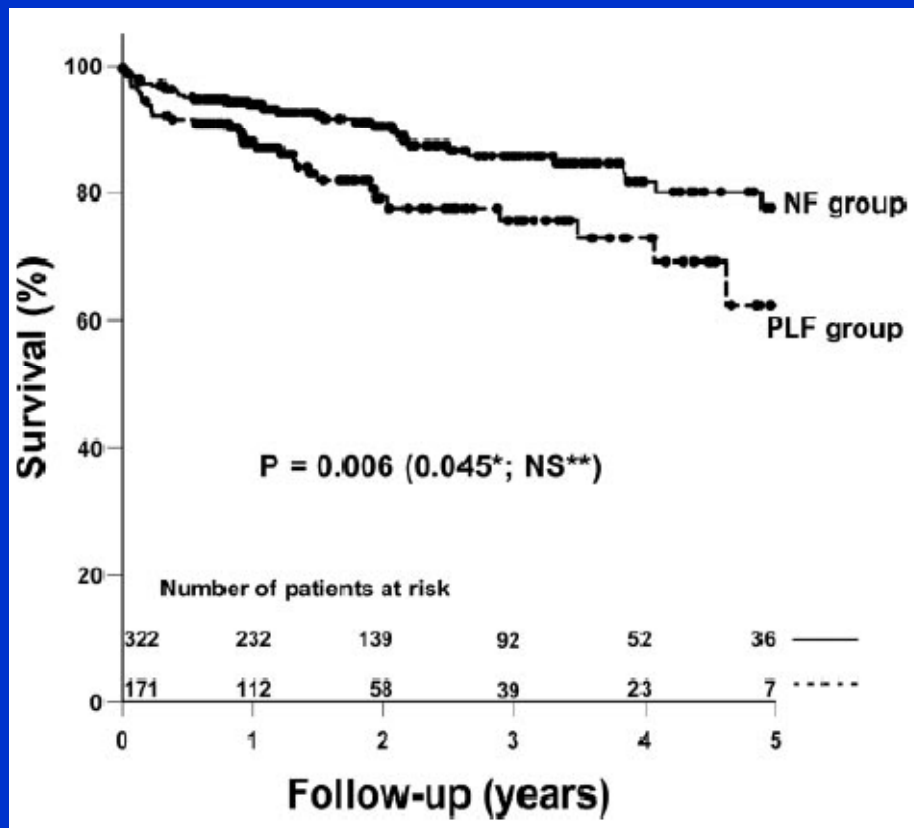
“In view of the very poor prognosis of unoperated patients, the current operative risk, and the long-term outcome after surgery, AVR is the treatment of choice in the majority of cases of LowFlow/LowGradient Aortic Stenosis.”

In questi pazienti una attenta valutazione clinico-strumentale volta a valutare da un lato la riserva di apertura valvolare e dall'altro la riserva contrattile del ventricolo sinistro dovrebbe permettere di identificare i pazienti che potrebbero trarre il maggior beneficio dalla sostituzione valvolare.

grazie per l'attenzione

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

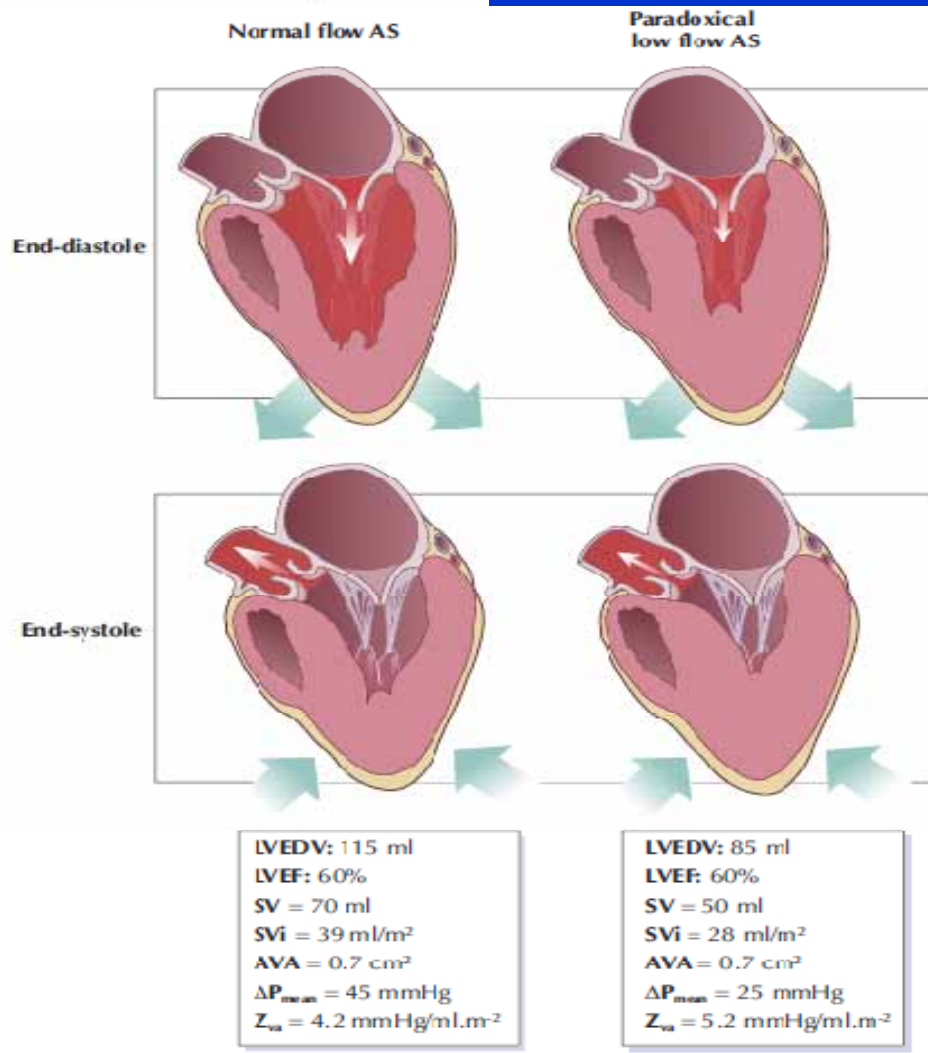


1) An important proportion of patients with severe AS have low transvalvular flow rates and low transvalvular gradients despite preserved LVEF;
2) this pattern is associated with higher global LV afterload, more pronounced concentric remodelling, evidence of intrinsic myocardial dysfunction, and lower survival,
3) this condition may often be misdiagnosed, which leads to underestimation or neglect of symptoms and inappropriate delay of AVR.

Circulation. 2007;115:2856-2864

Low-Flow Aortic Stenosis in Asymptomatic Patients

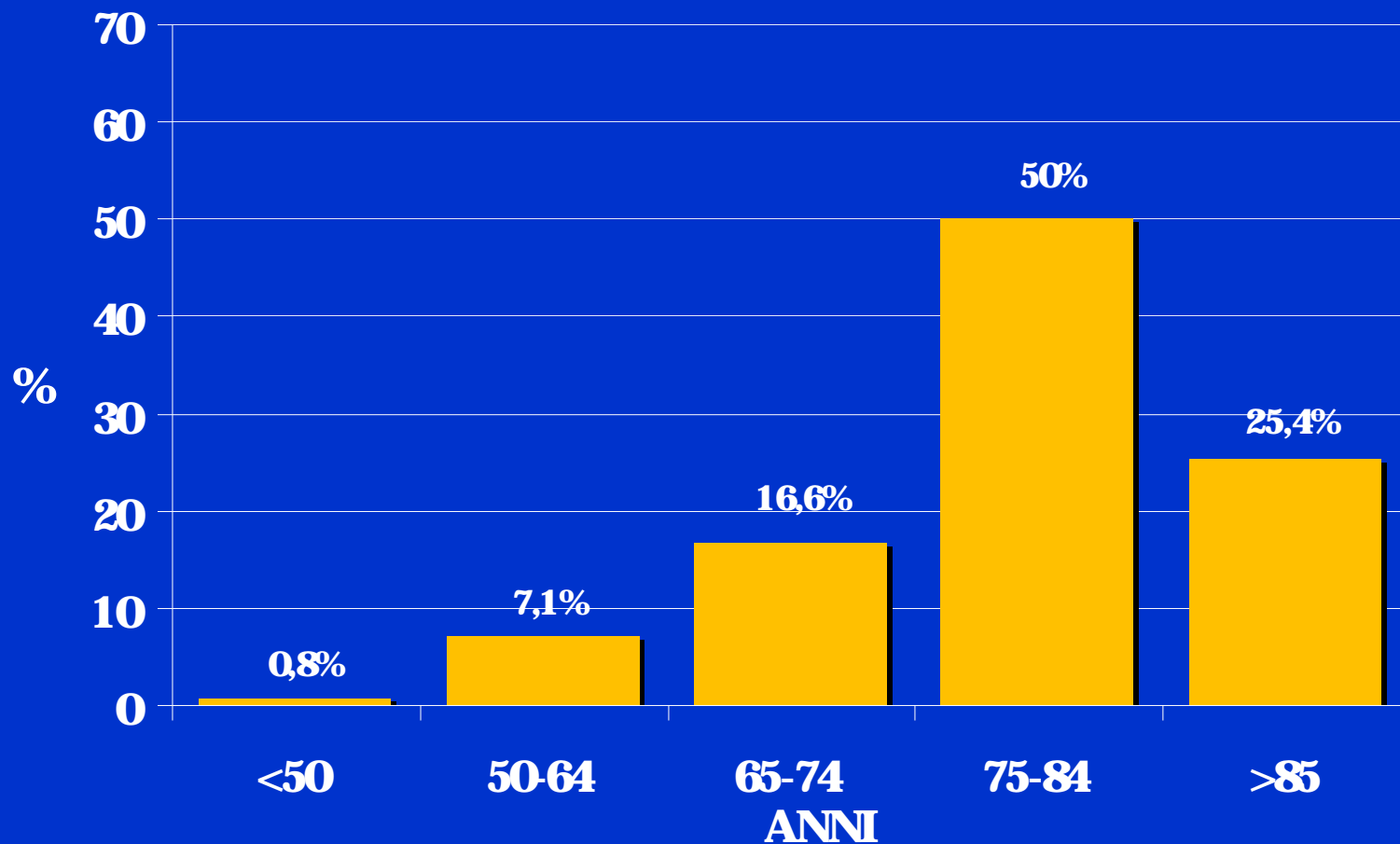
Valvular-Arterial Impedance and Systolic Function From the SEAS Substudy



La nostra casistica

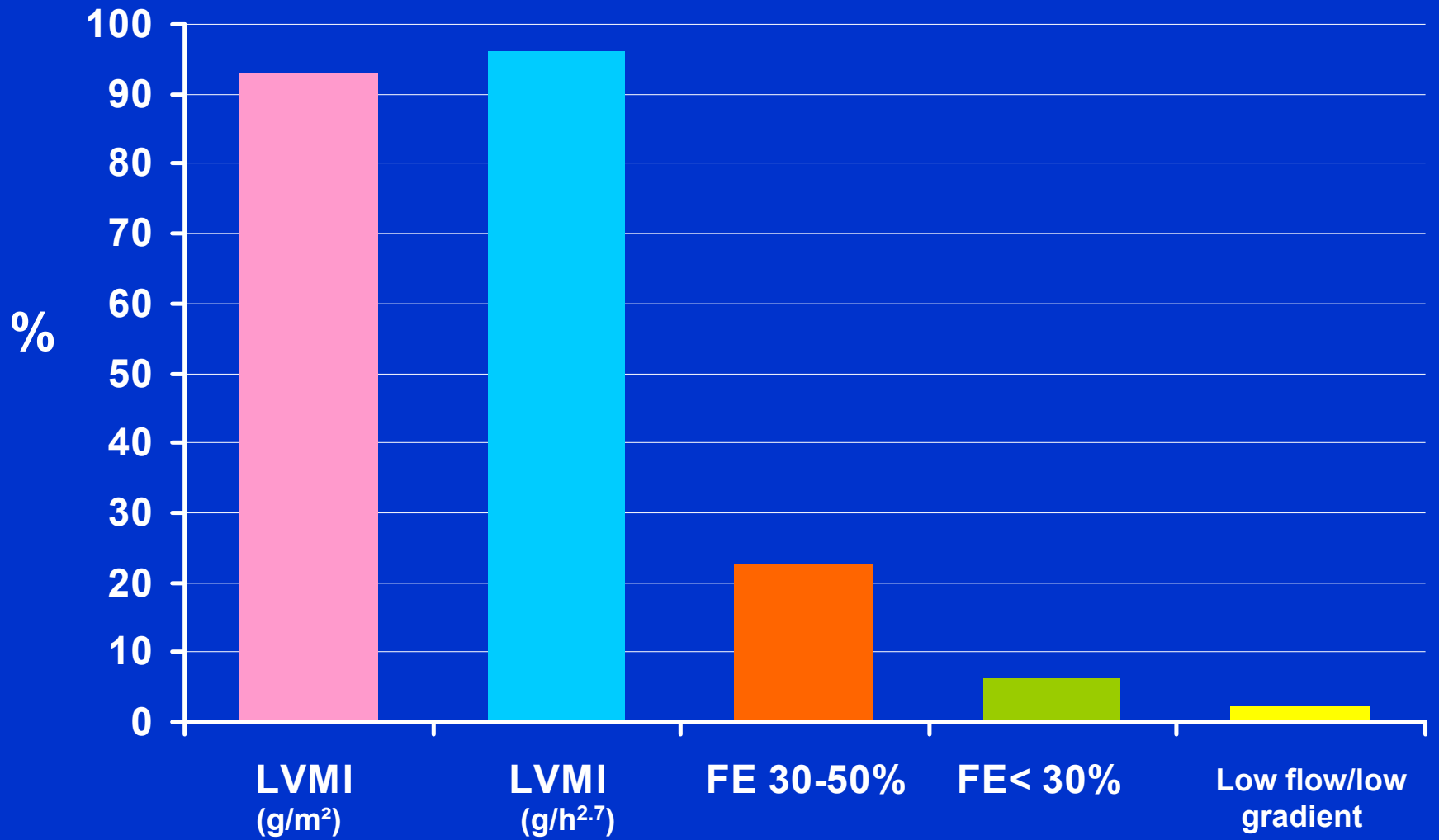
Popolazione totale	240 pazienti
Età (anni)	78,6 ± 8.93 (range 37-96)
Sesso (M/F)	96 / 144 (40%/60%)
BSA (m²)	1.79 ± 0.192 (range 1.34-2.61)
BMI	25.3 ± 3,9 (range 15- 46.6)
> 30 Kg/m²	24 (10%)

Distribuzione della popolazione in base all'età

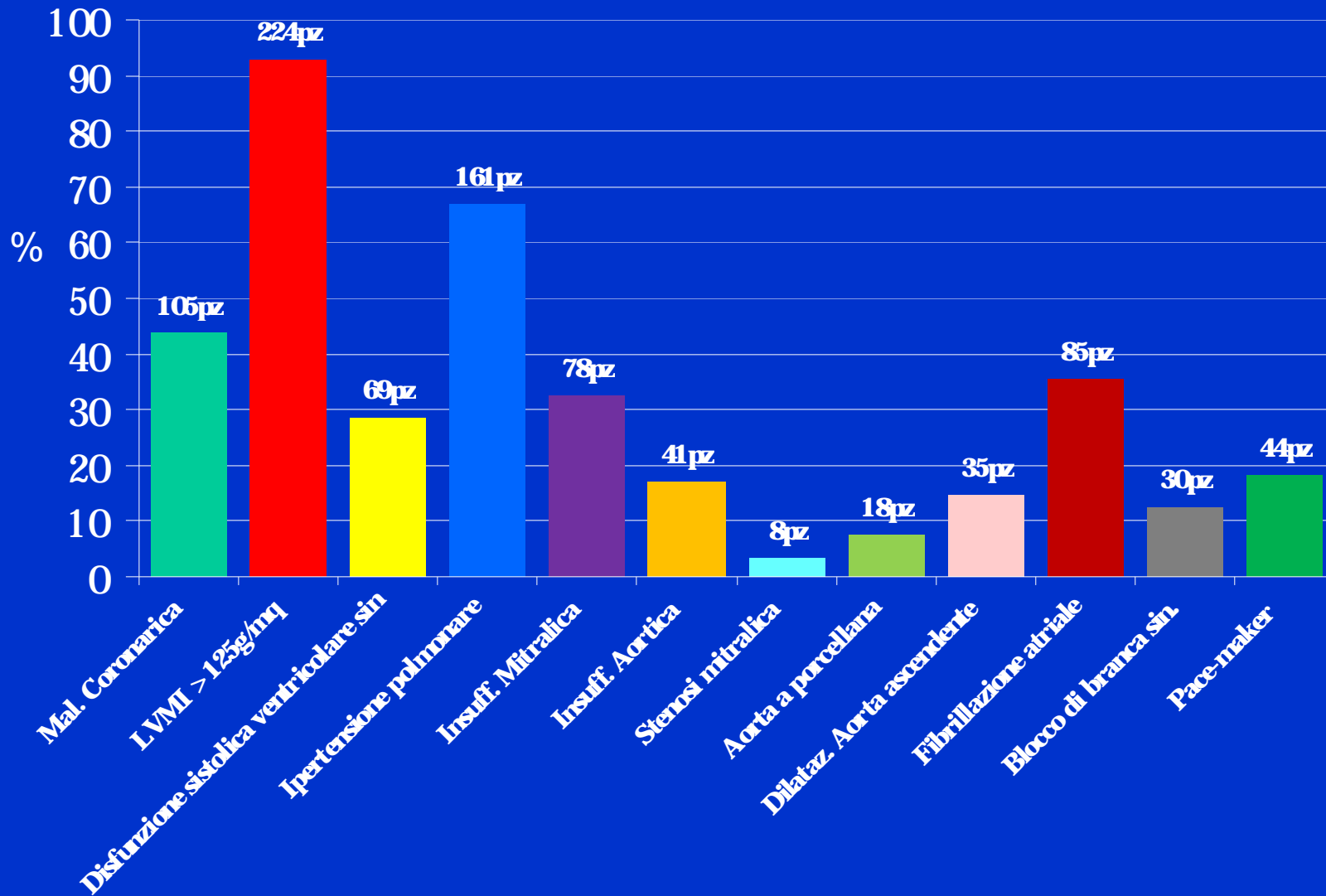


Caratteristiche ecocardiografiche

	Popolazione totale
Area valvolare aortica (cm²) Area < 1 cm²	0.7 ± 0.2 cm² 196 (81.6%)
Gradiente di picco (mmHg)	75.6 ± 27.4
Gradiente medio (mmHg)	50 ± 18.4
Frazione d'eiezione VS (FE %) FE < 50 %	51.2 ± 12.9 69 (28.7%)
Pressione sistolica in arteria polmonare (mmHg) PAPs > 35 mmHg	41.6 ± 12.9 161 (67%)



Patologie cardiache associate



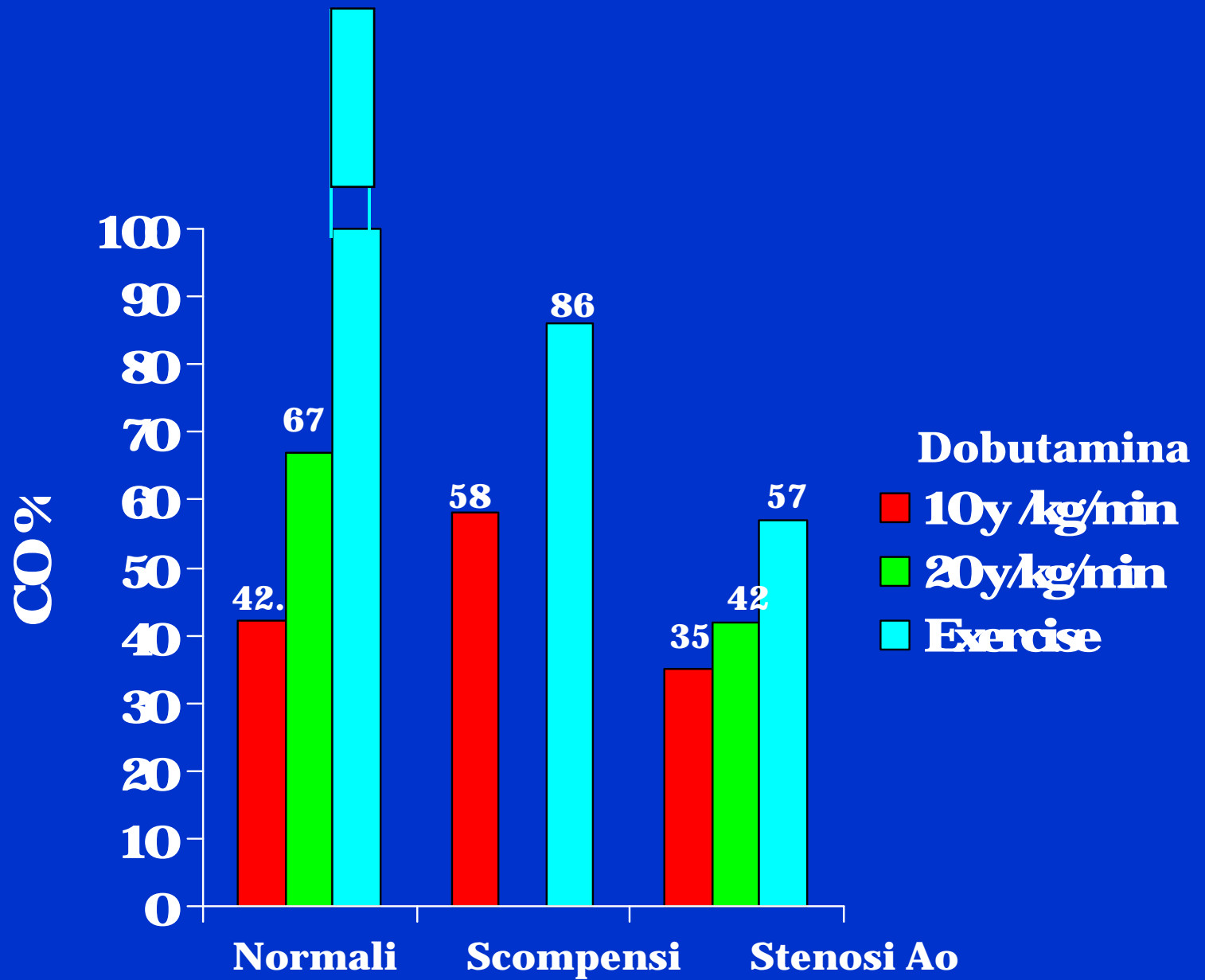
Sex Differences in Left Ventricular Geometry in Aortic Stenosis: Impact on Outcome

Donna L. Milavetz, Sharonne N. Hayes, Susan A. Weston, James B. Seward, Charles J. Mullany and Véronique L. Roger

Chest 2000;117:1094-1099

Table 2—Doppler Echocardiography Variables at Aortic Valve Replacement*

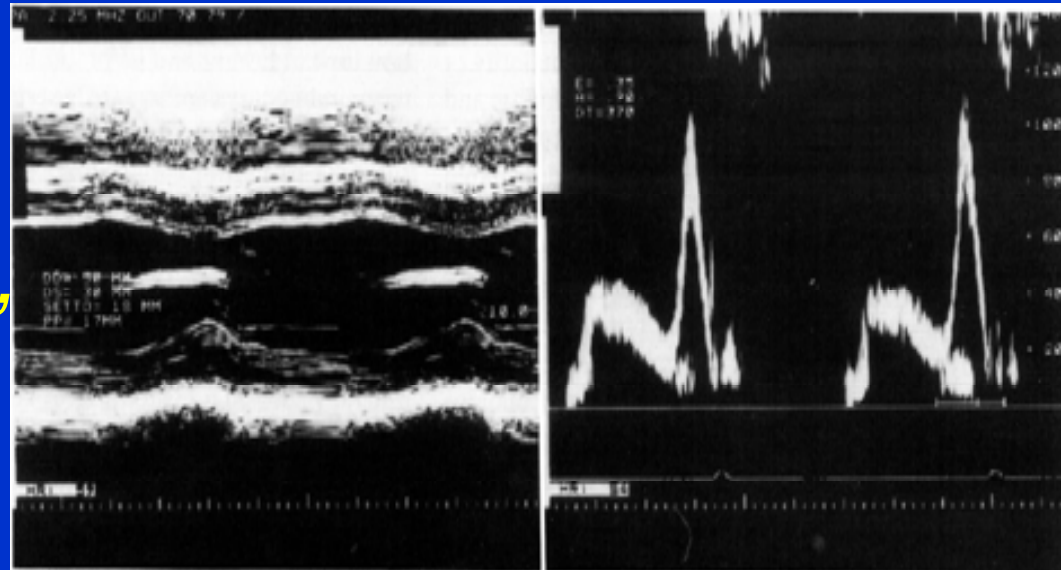
Variable	Women	n	Men	n	P Value
AVA, cm ²	0.63 ± 0.14	88	0.69 ± 0.15	76	0.0026
AVA index, cm ² /m ²	0.37 ± 0.08	88	0.36 ± 0.09	76	0.23
Mean gradient, mm Hg	58.5 ± 21.8	91	59.6 ± 14.4	81	0.14
LVEDD, mm	48.2 ± 7	64	53.6 ± 7.6	51	0.0001
LVEDD index, mm/m ²	28.6 ± 3.7	64	27.8 ± 7.7	51	0.0103
LVESD, mm	30.0 ± 8.8	62	35.2 ± 10.3	48	0.0008
LVESD index, mm/m ²	17.8 ± 4.8	62	18.5 ± 8.4	48	0.93
EF, %	59.2 ± 13.4	91	53.9 ± 15.8	82	0.02
Septal wall thickness, mm	13.3 ± 3	52	14.1 ± 2.7	42	0.17
Posterior wall thickness, mm	12.7 ± 2.5	52	13.2 ± 2.6	42	0.29
Relative wall thickness	0.54 ± 0.15	50	0.51 ± 0.14	40	0.47
LV mass, g	250.6 ± 85.8	50	300.4 ± 88	40	0.0055
LV mass index, g/m ²	148.2 ± 47.5	50	150.5 ± 37.3	40	0.62
LVH, %	51	92	49	82	0.76
Cardiac output, L/min	5.5 ± 1.3	65	5.8 ± 1.8	51	0.30
Cardiac index, L/min/m ²	3.2 ± 0.79	65	2.8 ± 0.78	51	0.0031



Numerosi studi hanno documentato che il sesso femminile presenta generalmente un differente adattamento del ventricolo sinistro al sovraccarico cronico di pressione rispetto al sesso maschile:

- **Massa minore**
- **Cavità ventricolare più piccola**
- **Pareti più spesse (*relativamente* alla cavità)**
- **Funzione sistolica supernormale**
- **Funzione diastolica più compromessa**

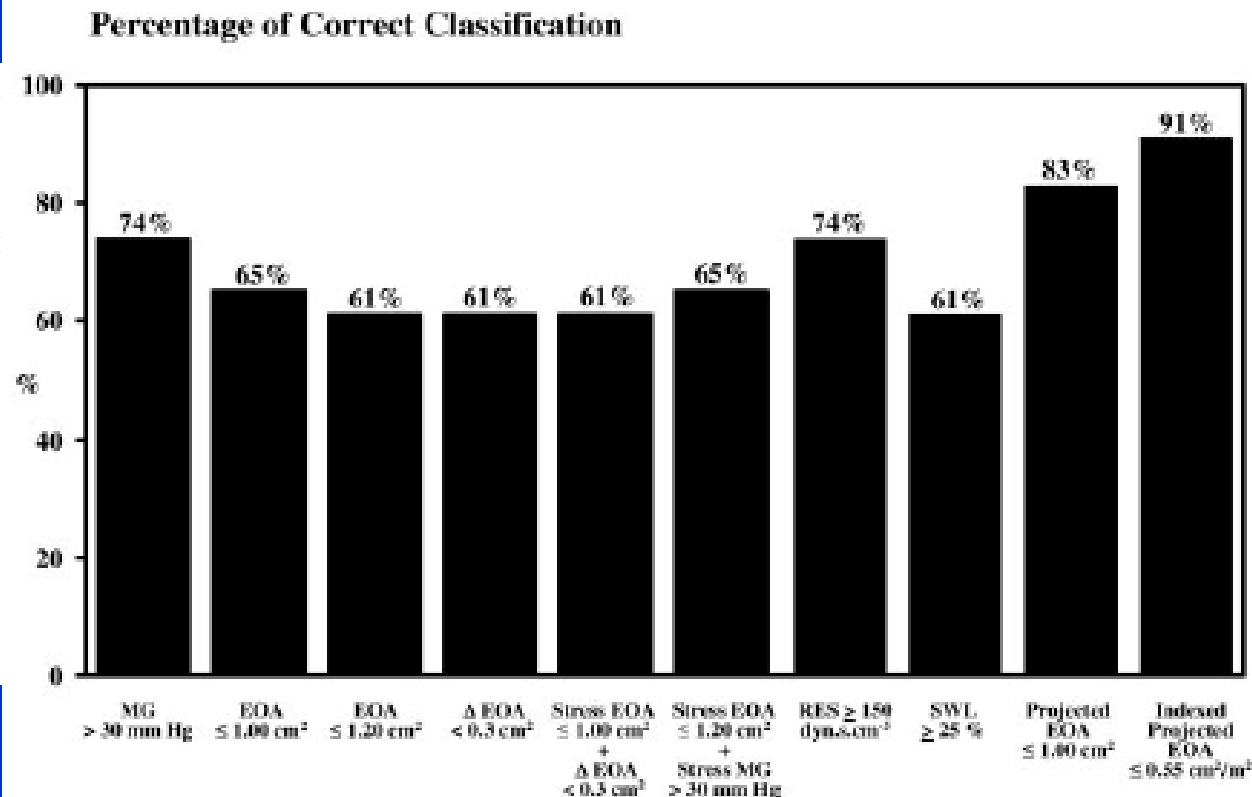
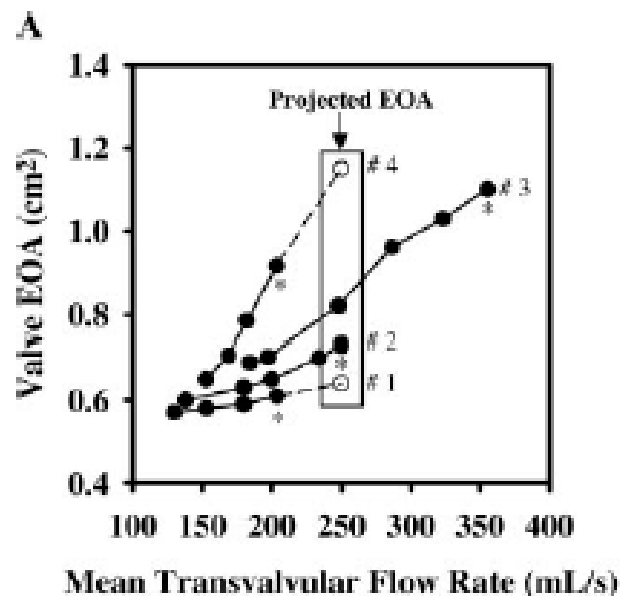
“ipertrofia concentrica”



Projected Valve Area at Normal Flow Rate Improves the Assessment of Stenosis Severity in Patients With Low-Flow, Low-Gradient Aortic Stenosis.

The Multicenter TOPAS (Truly or Pseudo-Severe Aortic Stenosis) Study

Blais et al. Circ 2006;113: 711-721

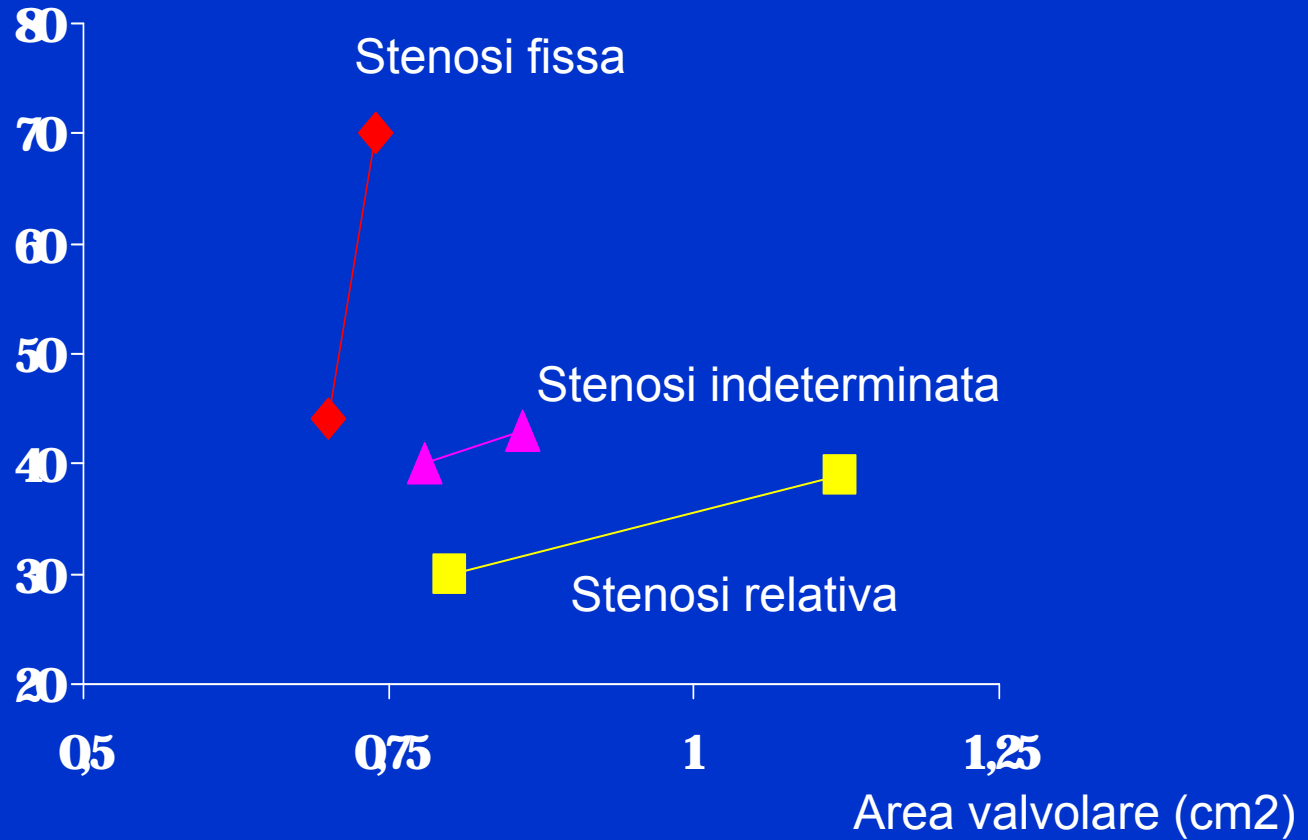


EOAproj provides a standardized evaluation of AS severity with DSE and improves the diagnostic accuracy for distinguishing TS and PS AS in patients with low-flow, low-gradient AS

La stragrande maggioranza dei pazienti con stenosi valvolare aortica, anche severa e sintomatica, presenta una normale funzione sistolica ventricolare sinistra.

Allora quale è il problema ?

Peak Grad (mmHg)



Gruppo IA

Gruppo IB

Gruppo II