



La terapia per stabilizzare il cardiopatico congenito adulto o con esiti di correzione chirurgica

Marco Bonvicini

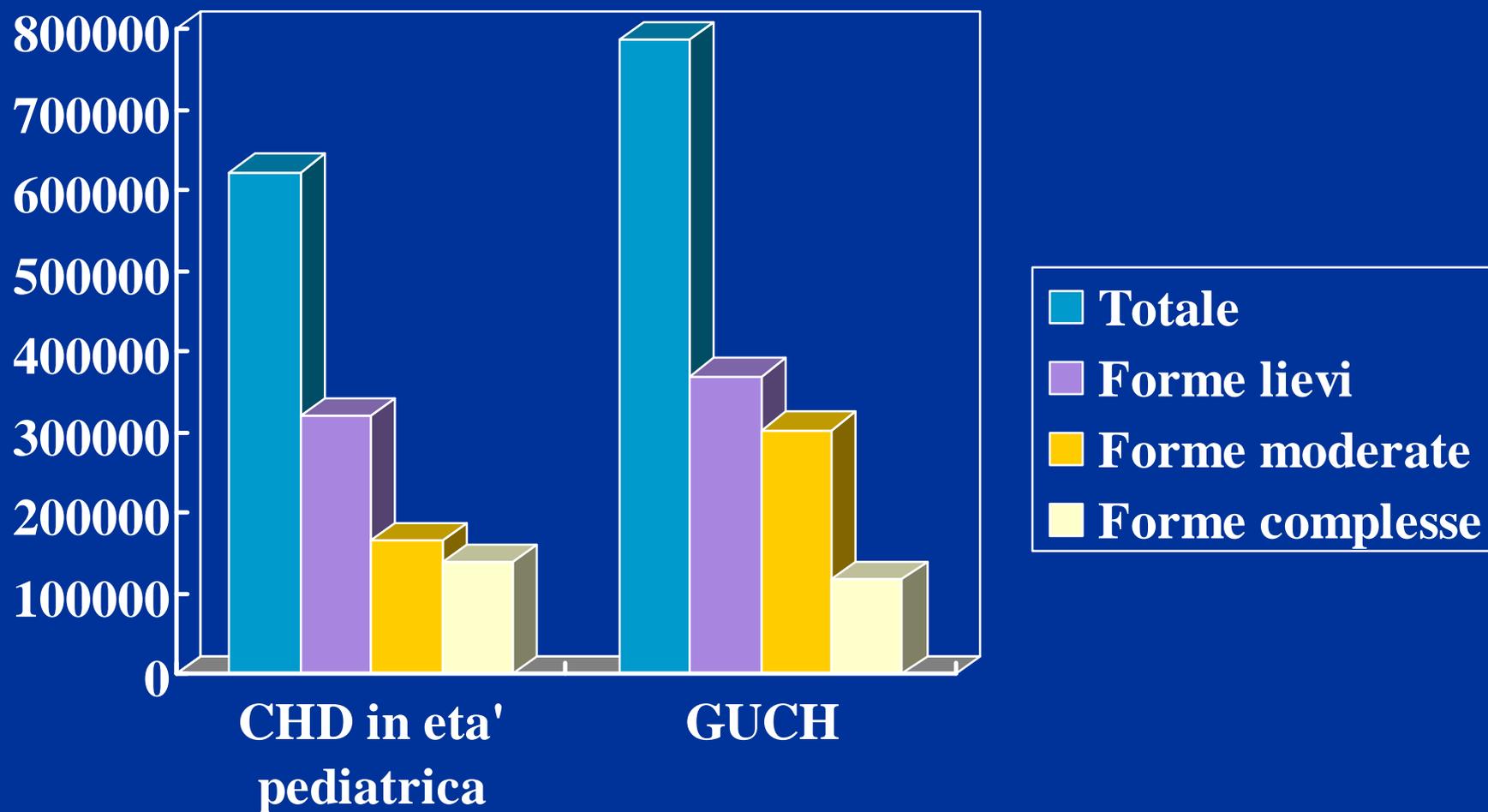
Cardiologia e cardiochirurgia
pediatrica e dell'età evolutiva

POLICLINICO S. ORSOLA

MALPIGHI BOLOGNA

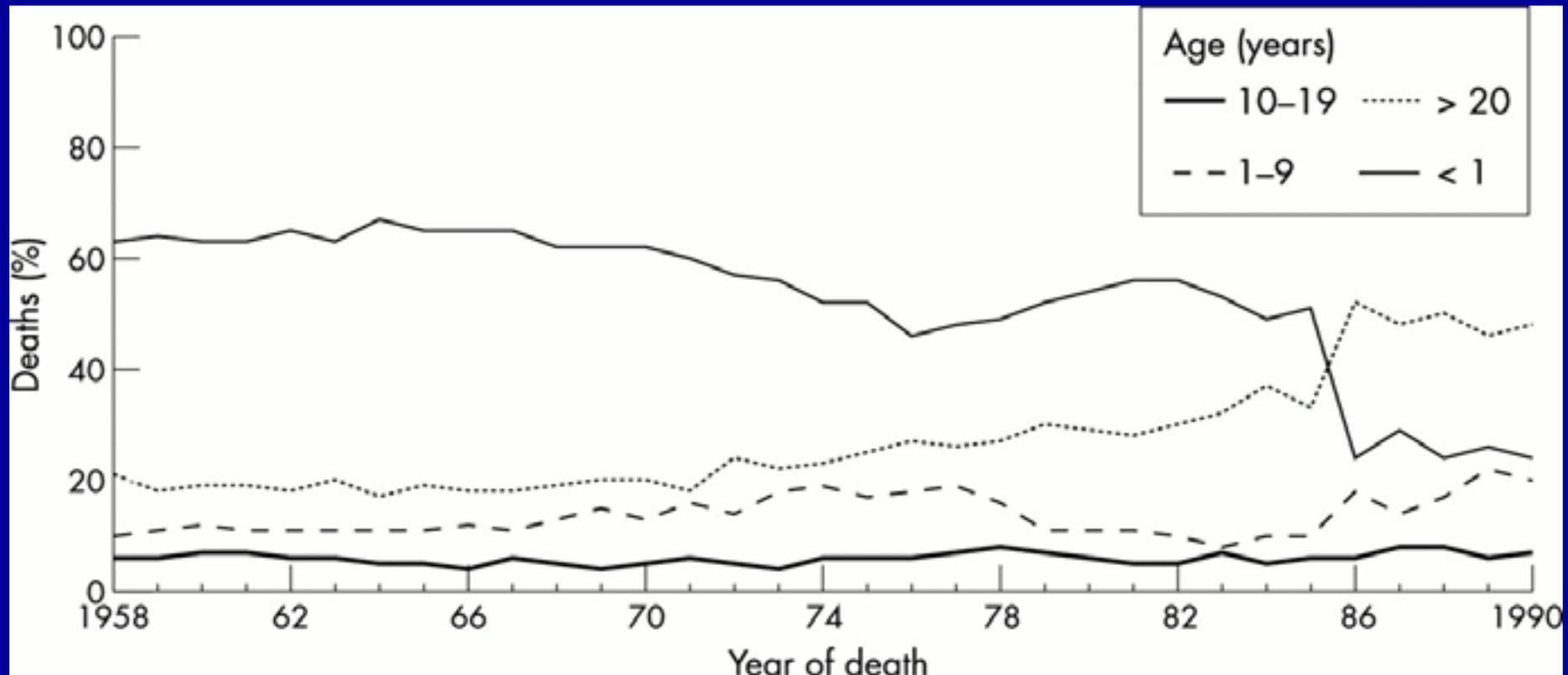
MILANO 2010

Stime sulla popolazione di adulti con cardiopatia congenita negli USA nel 2000

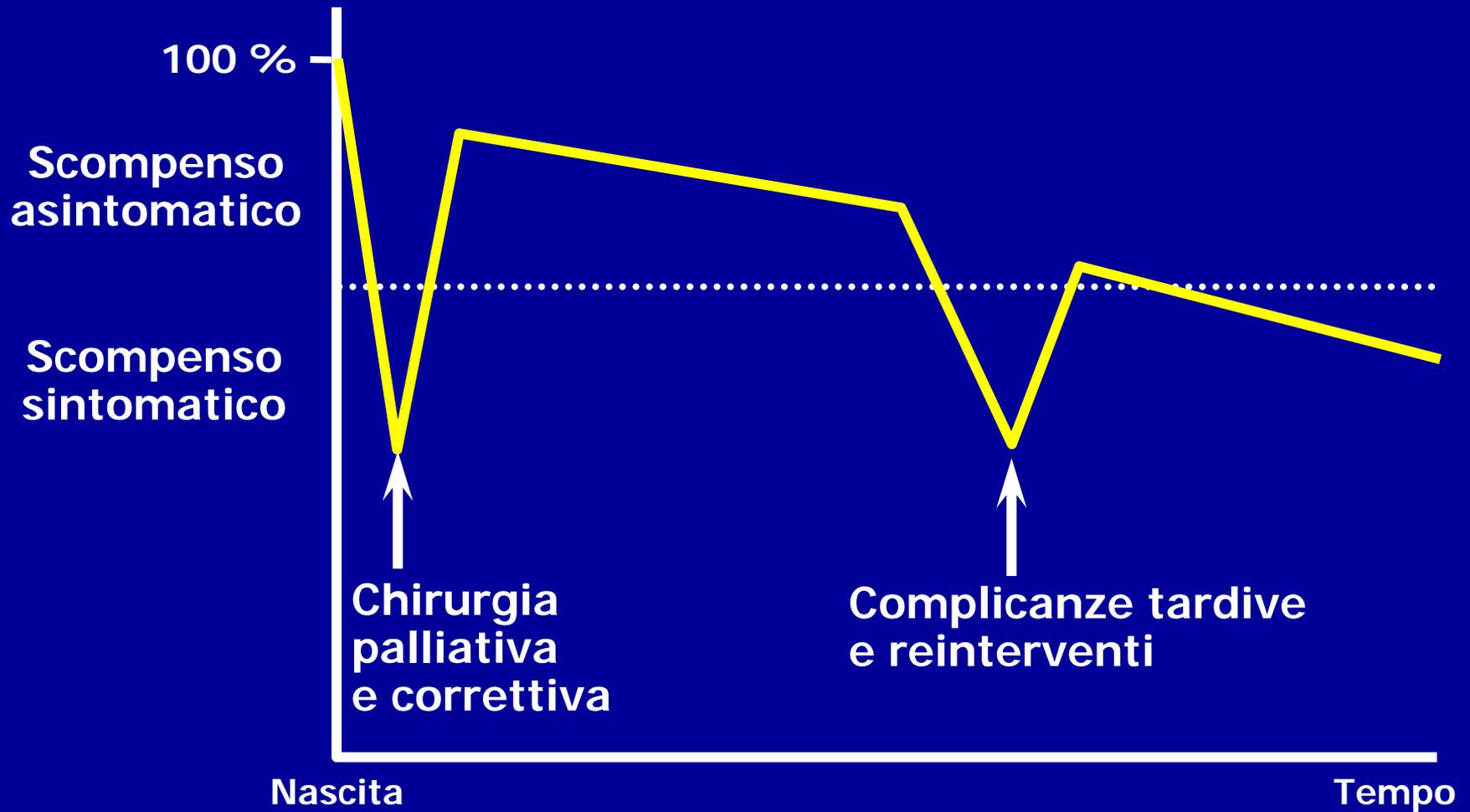


Data compiled from the statistics of the Office of Population Consensus and Surveys for England and Wales showing reported deaths from congenital heart disease in the various age groups.

Nel 1958 la mortalita' era piu' alta nella fascia di eta' pediatrica mentre a partire dal 1986 la mortalita' piu' alta si riscontra nella fascia di eta' sopra i 20 anni



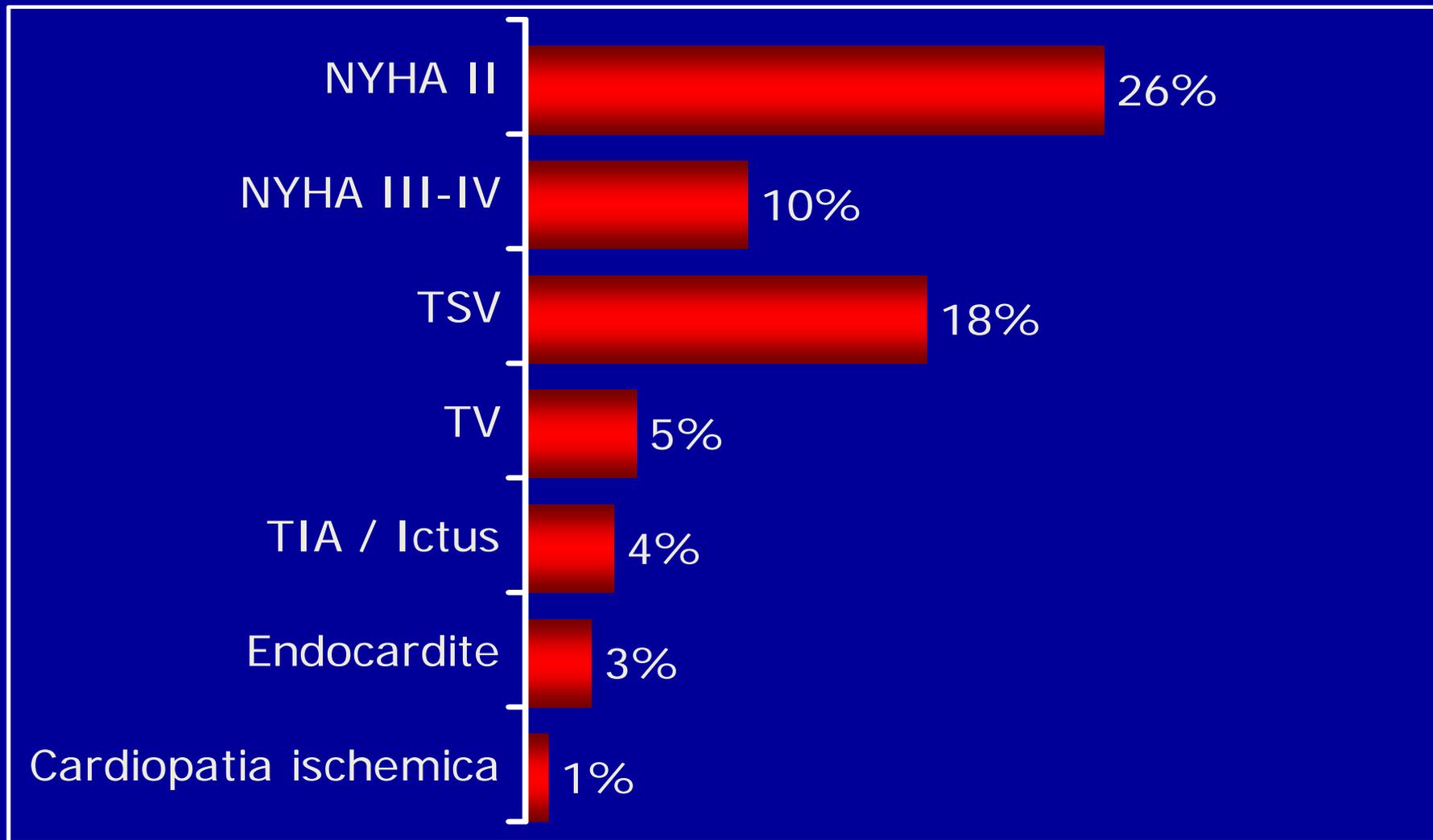
Cardiopatie congenite



Il follow-up del cardiopatico congenito adulto perche' il GUCH e' un paziente diverso

- Problematica relativamente nuova
- Conoscenza delle CC + degli interventi
- Problematiche mediche e chirurgiche peculiari
- Problematiche psicologiche
- Particolare valutazione funzionale ed imaging

MORBILITA'



The Euro Heart Survey on adult congenital heart disease, Eur Heart J 2005

SCOMPENSO CARDIACO

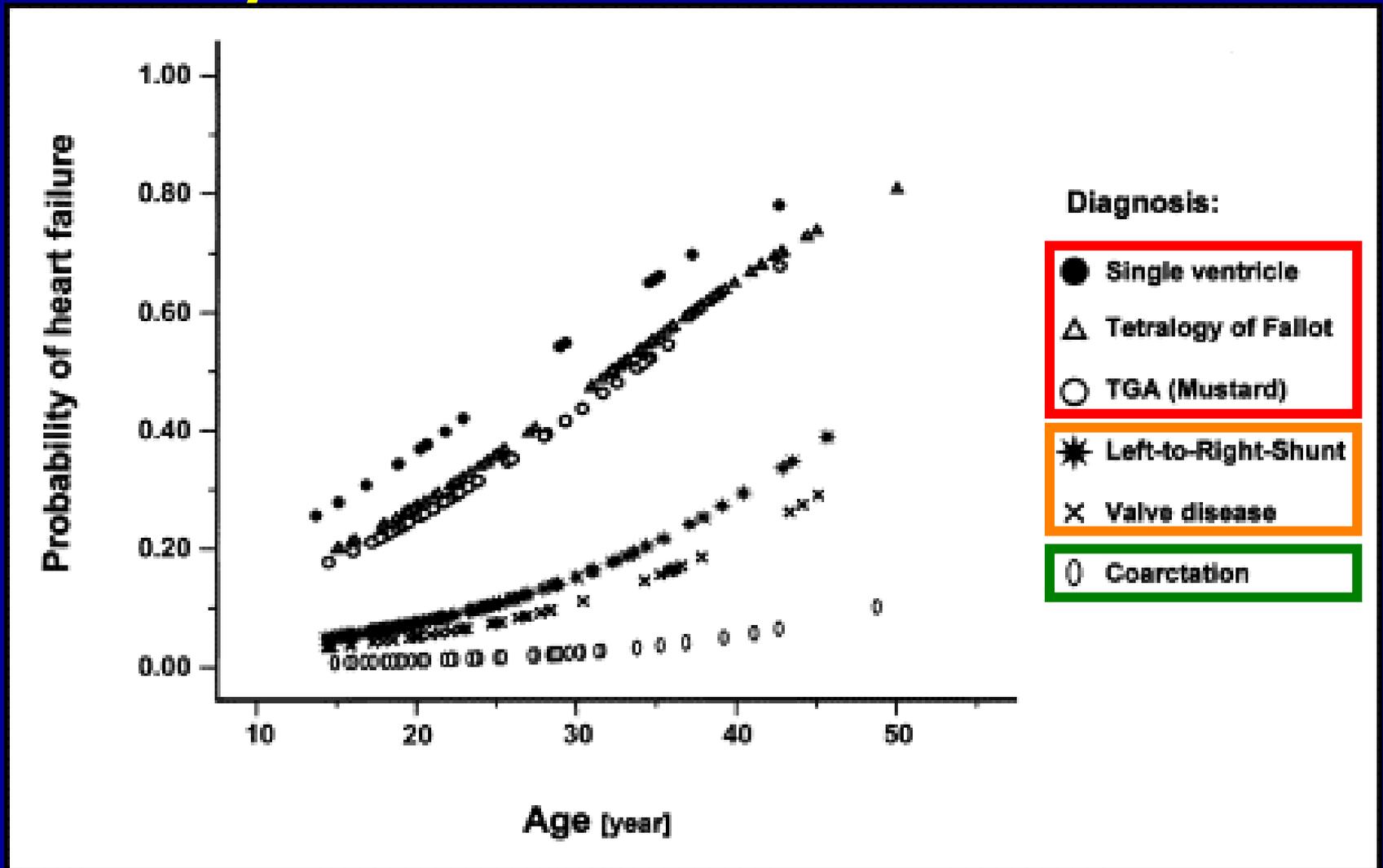
Cardiopatie acquisite

- ❖ *VSN dilatato-ipocinetico*
- ❖ *Disfunzione diastolica vsn*

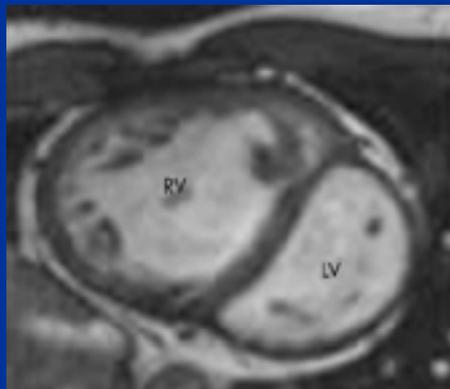
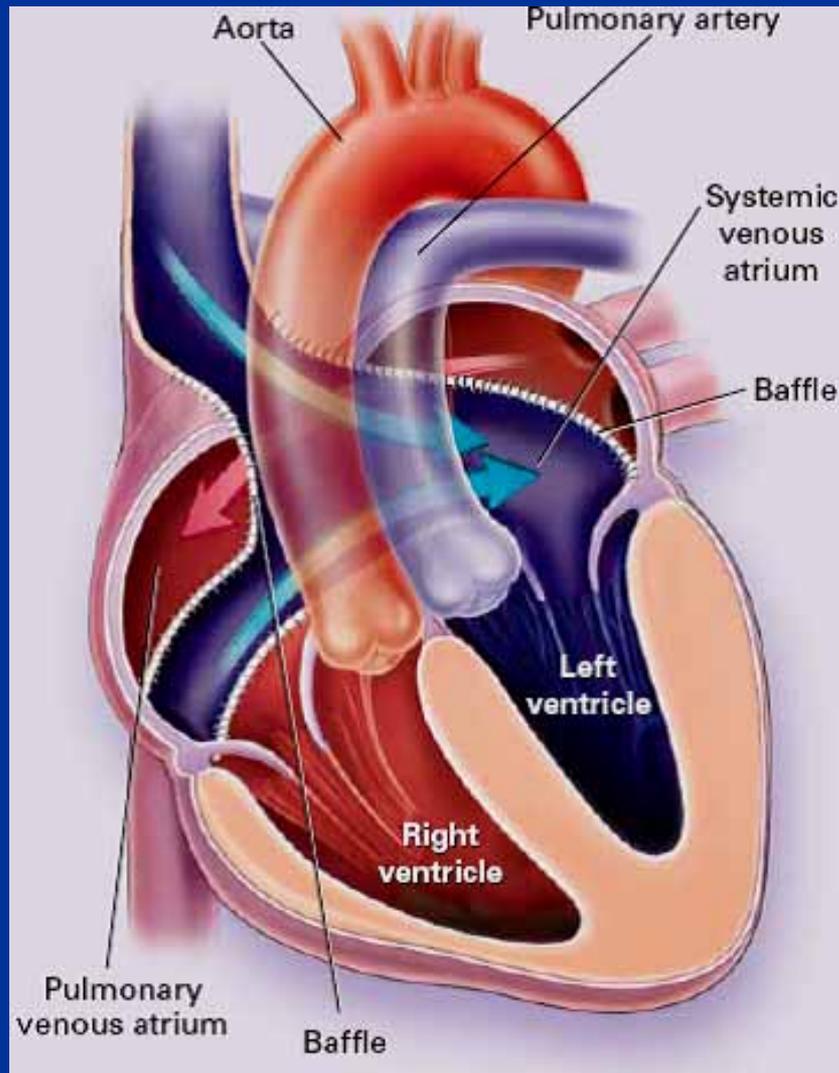
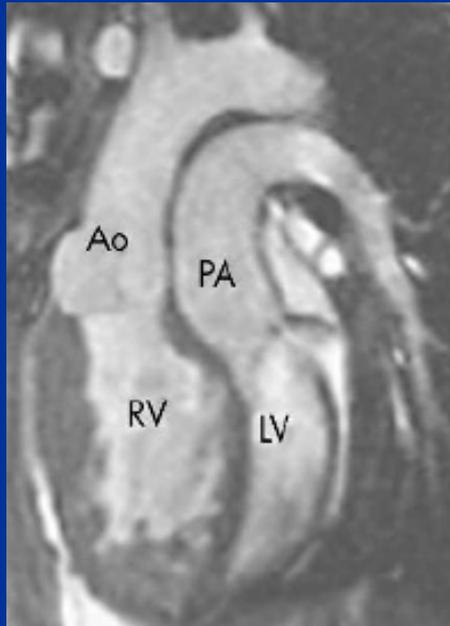
GUCH

- ❖ *VDX iperteso*
- ❖ *VDX dilatato*
- ❖ *Ventricolo unico*

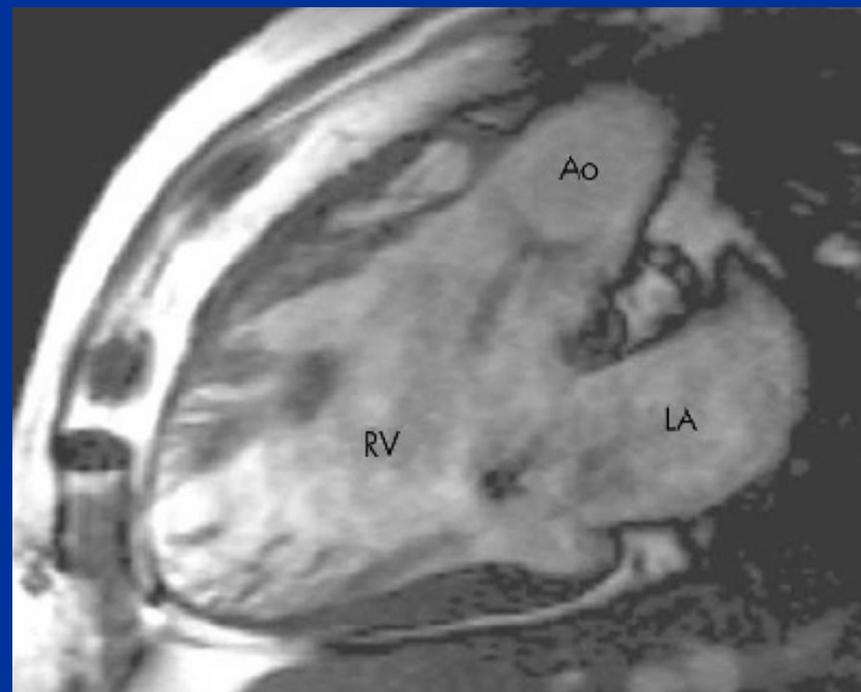
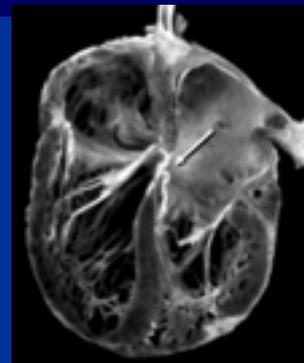
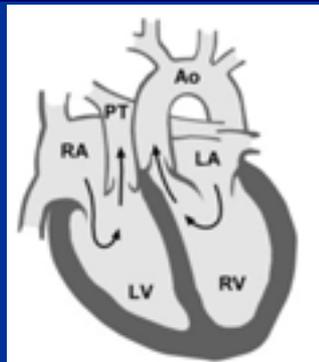
Scompenso cardiaco nel GUCH



Ventricolo destro sistemico: TGA S/P Mustard-Senning



Ventricolo destro sistemico: TCCGA



Ventricolo dx sistemico

Circolo sistemico = sovraccarico di pressione



Insufficienza
valvola AV sistemica

I pertrofia vdx sistemico



Ridotta riserva coronarica (ridotta densità
capillari)



I schemia e fibrosi miocardica



ORIGINAL ARTICLE

Volume 316:1429-1435 June 4, 1987 Number 23

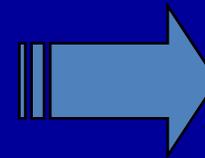
[List ►](#)

Effects of enalapril on mortality in severe congestive heart failure. Results of the Cooperative North Scandinavian Enalapril Survival Study (CONSENSUS). The CONSENSUS Trial Study Group

Effect of enalapril on survival in patients with reduced left ventricular ejection fractions and congestive heart failure. The SOLVD Investigators

Effect of captopril on mortality and morbidity in patients with left ventricular dysfunction after myocardial infarction. Results of the survival and ventricular enlargement trial. The SAVE Investigators

MA Pfeffer, E Braunwald, LA Moye, L Basta, EJ Brown, TE Cuddy, BR Davis, EM Geltman, S Goldman, GC Flaker, and et al.



GUCH

??

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Journal of Medicine

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Volume 334

MAY 23, 1996

Number 21

THE EFFECT OF CARVEDILOL ON MORBIDITY AND MORTALITY IN PATIENTS WITH CHRONIC HEART FAILURE

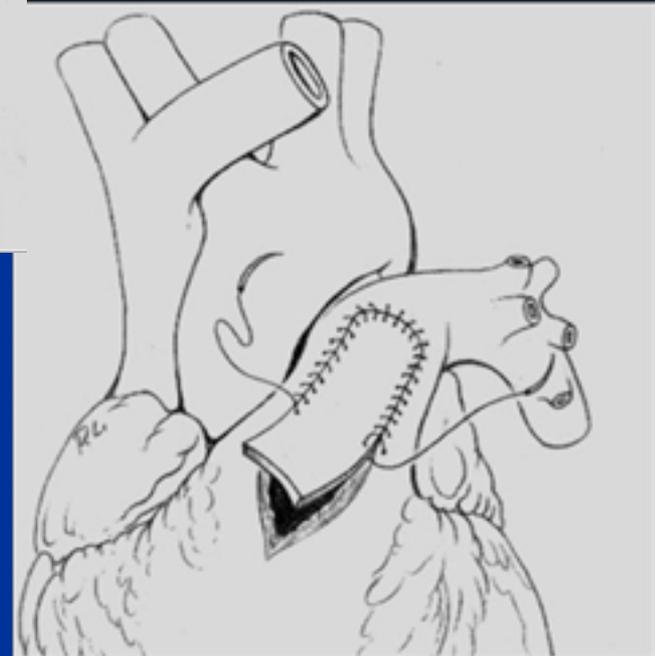
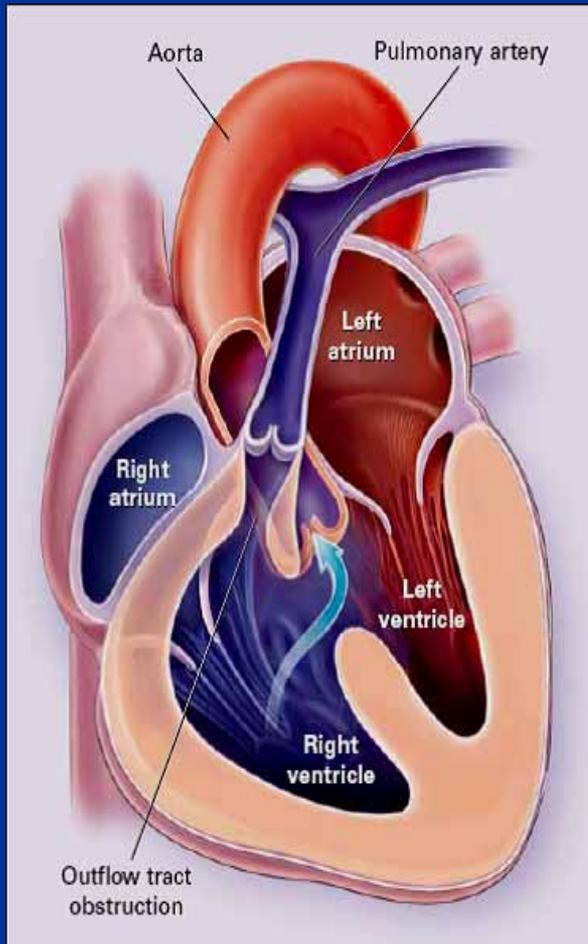
MILTON PACKER, M.D., MICHAEL R. BRISTOW, M.D., PH.D., JAY N. COHEN, M.D., WILSON S. COLUCCI, M.D., MICHAEL B. FOWLER, M.B., B.S., EDWARD M. GILBERT, M.D., AND NEIL H. SHUSTERMAN, M.D., FOR THE U.S. CARVEDILOL HEART FAILURE STUDY GROUP*

Ventricolo dx sistemico

	Agent	TGA/ccTGA	No	Follow-up (months)	MRI*	VO ₂ max	NYHA	Pro/retro	
β-blocker									
	Linderfeld et al ¹⁷	Carvedilol	ccTGA	1	7	↑	ND	ND	pro
	Giardini et al ¹⁸	Carvedilol	both	8	12	↑	=	↑	pro
	Josephson et al ¹⁴	Various	TGA	8	36	ND	ND†	↑	retro
	Doughan et al ¹⁵	Various	TGA	31	4	ND	ND	↑	retro
ACE inhibitor									
	Hechter et al ⁴¹	Various	TGA	14	24	=	=	ND	retro
	Robinson et al ⁴²	Enalapril	TGA	9	12	ND	=	ND	pro
	Therrien et al ⁴³	Ramipril	TGA	17	12	=	=	ND	pro
ATII antagonist									
	Dore et al ⁴⁴	Losartan	both	29	3.5	ND	=	ND	pro
	Lester et al ²⁴	Losartan	TGA	7	2	↑‡	ND	ND	pro

*Right ventricular ejection fraction as determined by MRI; †determined in minority of patients; ‡right ventricular ejection fraction as determined by echocardiography. ACE, angiotensin-converting enzyme; ATII, angiotensin II; ccTGA, congenitally corrected transposition of the great arteries; MRI, magnetic resonance imaging; ND, not determined; NYHA, New York Heart Association class; pro, prospective study design; retro, retrospective study designs; ↑, significant improvement; =, no significant change.

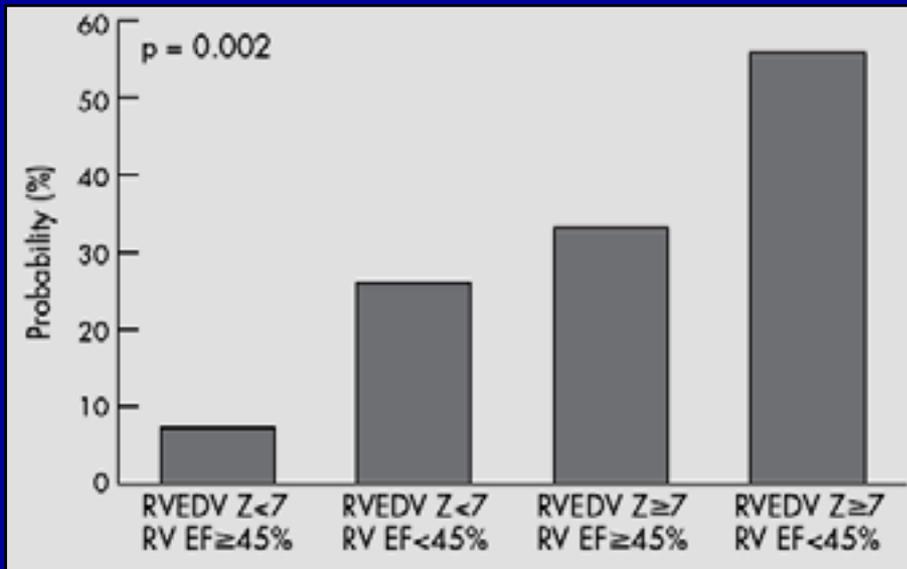
Ventricolo destro dilatato: Insufficienza polmonare nel Fallot



RM cardiaca

Ventricular size and function assessed by cardiac MRI predict major adverse clinical outcomes late after tetralogy of Fallot repair

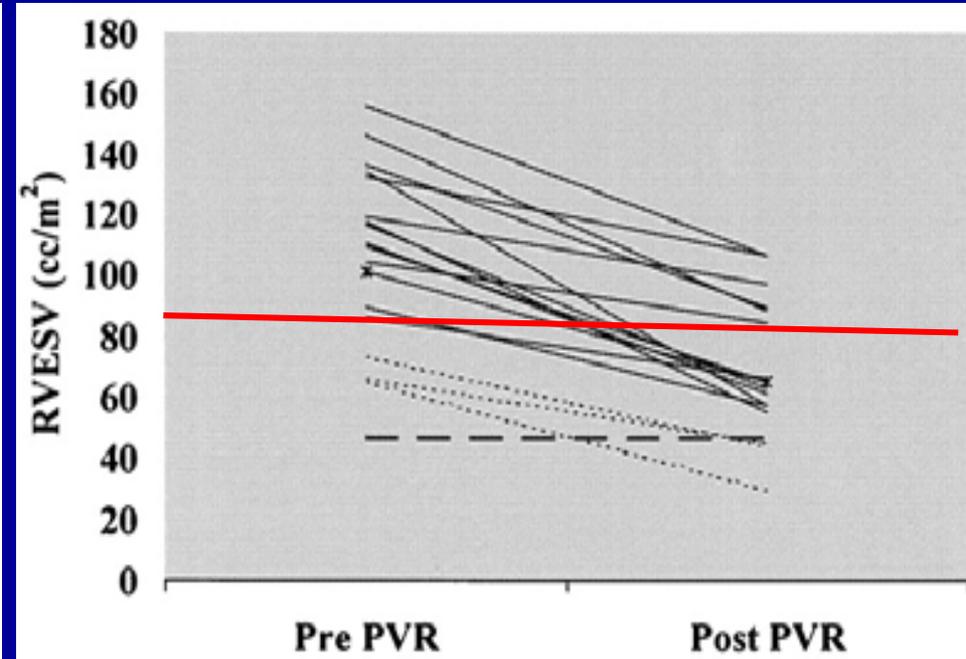
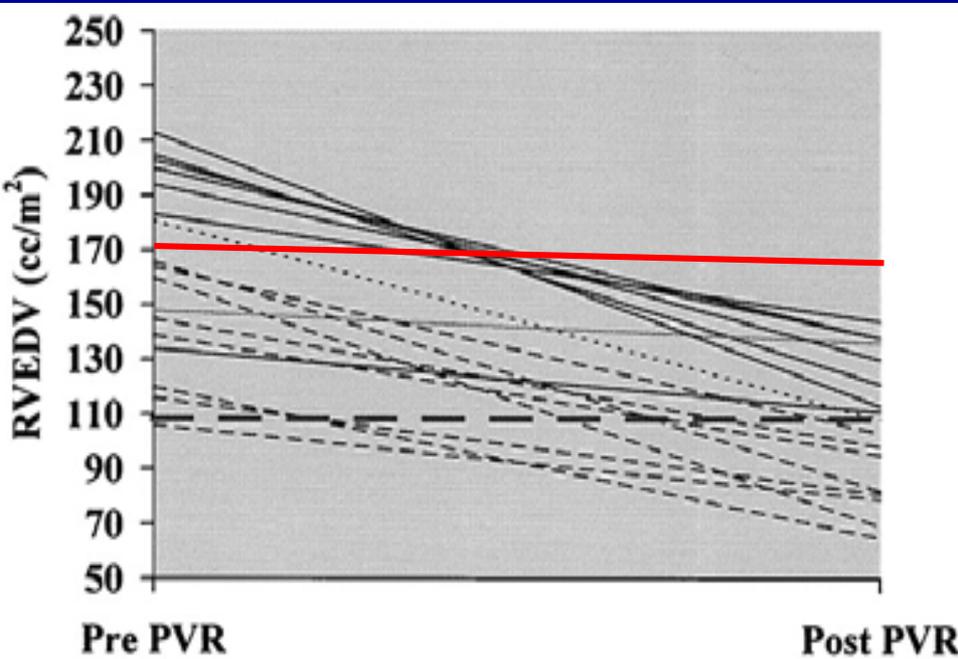
A L Knauth,^{1,2} K Gauvreau,¹ A J Powell,¹ M J Landzberg,^{1,2} E P Walsh,¹ J E Lock,¹ P J del Nido,³ T Geva¹



Optimal Timing for Pulmonary Valve Replacement in Adults After Tetralogy of Fallot Repair

Judith Therrien, MD, Yves Provost, MD, Naeem Merchant, MD, William Williams, MD, Jack Colman, MD, and Gary Webb, MD

Am J Cardiol 2005;95:779-82

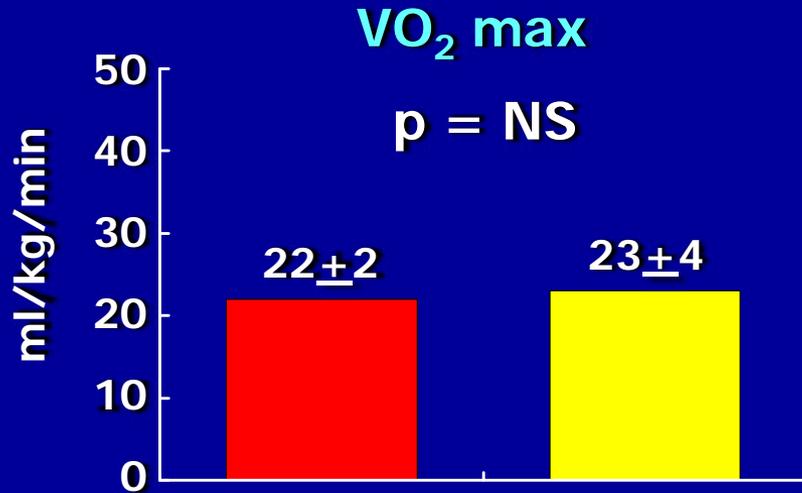


Criteria di timing per preservare la funzione del VDX ?

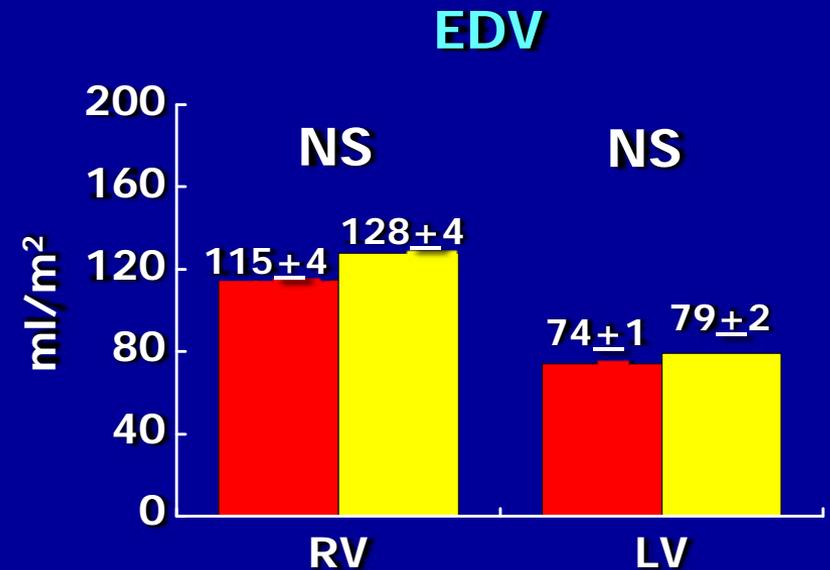
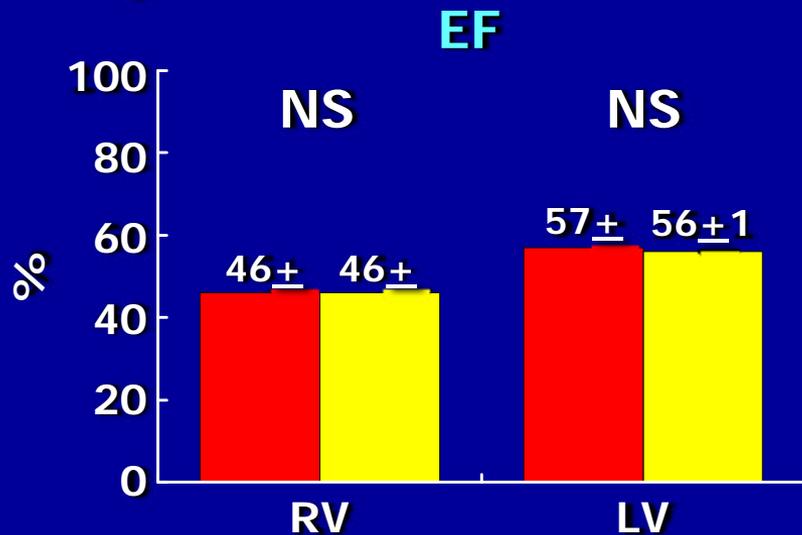
A prospective, randomized, double-blind, placebo controlled trial of beta-blockade in patients who have undergone surgical correction of tetralogy of Fallot

K. Norozi et al., *Cardiol Young* 2007; 17: 372-379

33 pz. - Età 31_±9 anni - NYHA I 36% NYHA II 64%



	Beta-blockade		p
	Start	End	
Brain natriuretic peptide (pg/ml)	206 ± 95	341 ± 250	< 0.05
Atrial natriuretic peptide (fmol/ml)	4117 ± 1837	5340 ± 2102	0.0005



VALVOLA POLMONARE PERCUTANEA

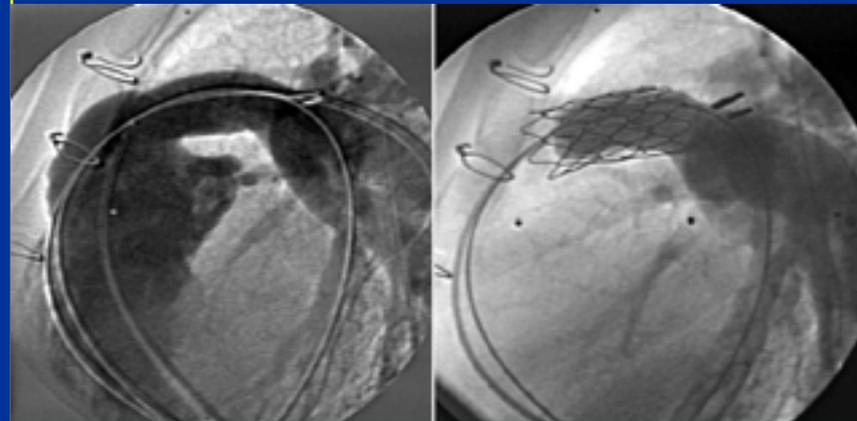
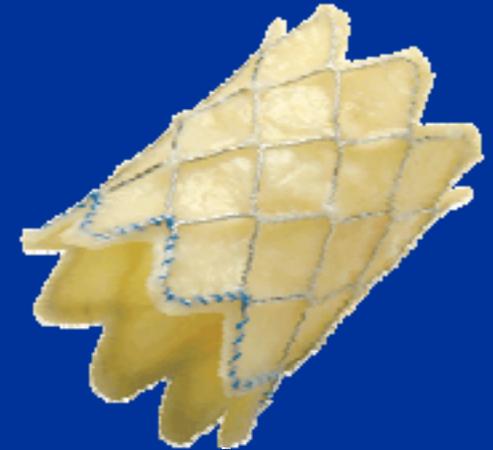
■ Indicazioni:

Disfunzione condotto VDX-AP

Stenosi, insufficienza, entrambe

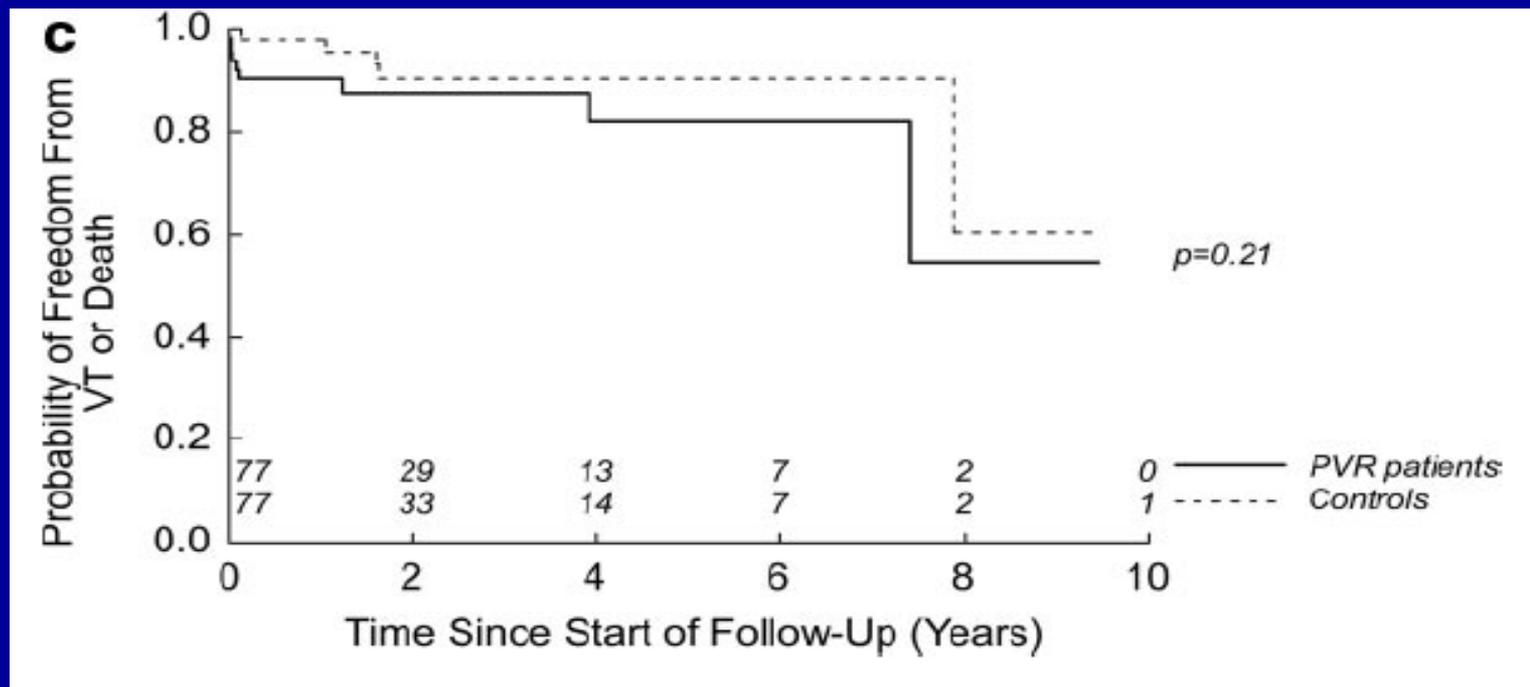
■ Obiettivi

- Risolvere la stenosi senza provocare rigurgito
- Risolvere l'insufficienza
- Preservare la funzione vdx
- Prolungare la durata del condotto, ritardare l'intervento chirurgico

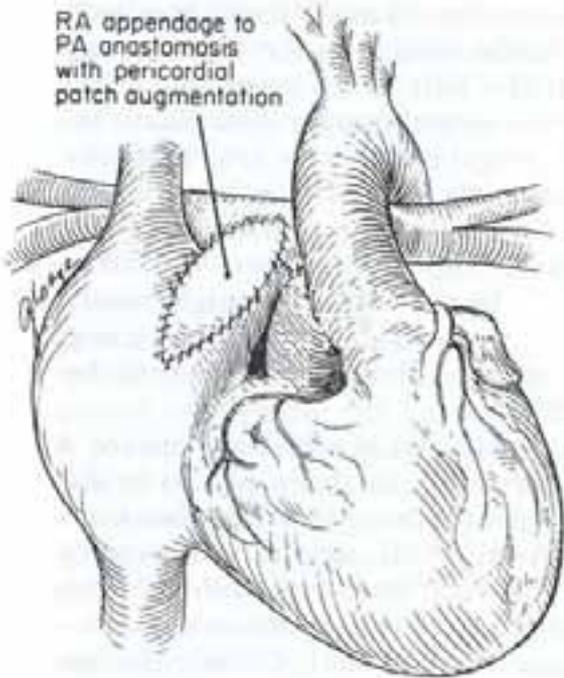


Pulmonary Valve Replacement in Tetralogy of Fallot Impact on Survival and Ventricular Tachycardia

David M. Harrild, MD, PhD; Charles I. Berul, MD; Frank Cecchin, MD; Tal Geva, MD;
Kimberlee Gauvreau, ScD; Frank Pigula, MD; Edward P. Walsh, MD

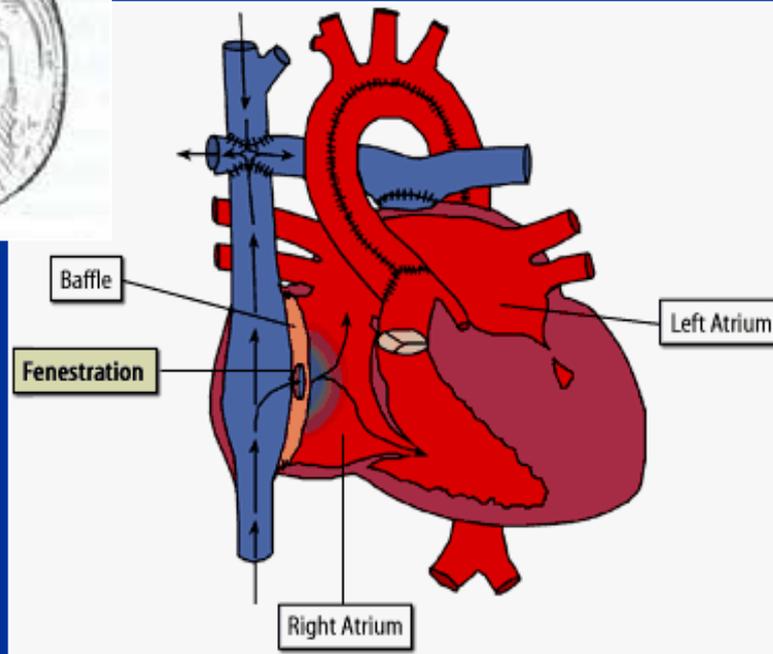


L'evoluzione della Fontan

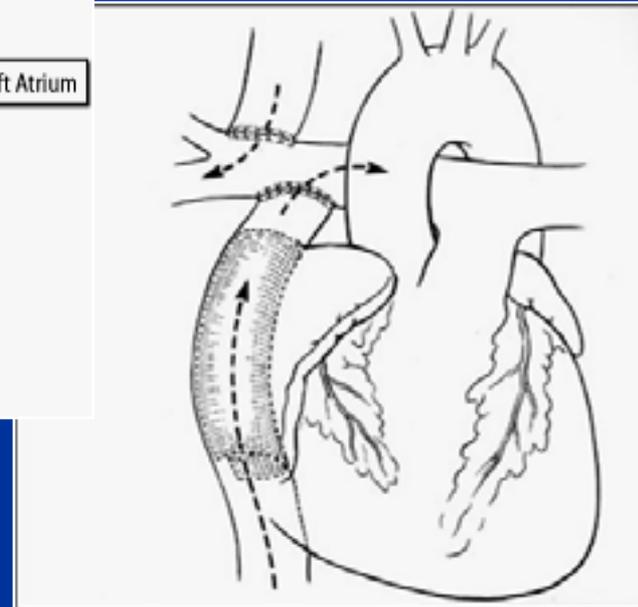


LATERAL TUNNEL
TCPC
1980

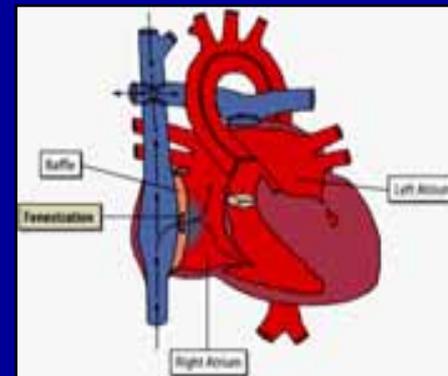
ATRIO-PULMONARY
CONNECTION
1971



EXTRACARDIAC
CONDUIT
1990 - 95



Il ventricolo unico - La Fontan



Stenosi circuito

Stenosi A. polmonari

Compressione VPo



RAP

Disfunzione ventricolare

Insuff. valvole AV

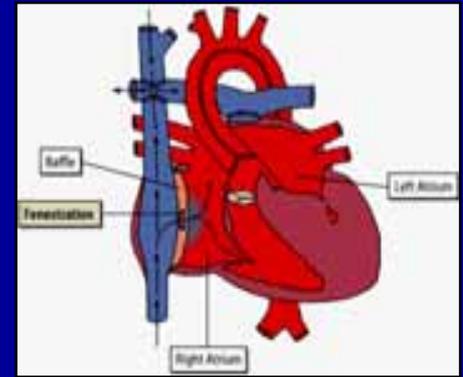
Aritmie

Enteropatia

Proteino-disperdente

**Scompenso
cardiaco**

Ventricolo unico - Fontan
Terapia dello scompenso cardiaco



*Angioplastica
± stent*

*Embolizzazione
Collaterali sist-Po*

Fenestrazione circuito

*Conversione a
Cavopolmonare totale*

Trapianto cardiaco

**Terapia medica
convenzionale ??**

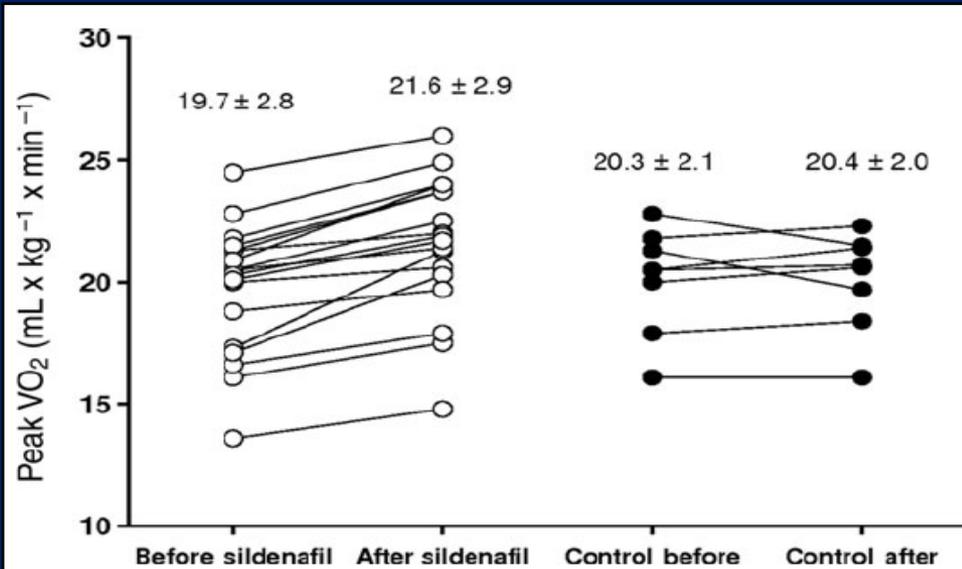
Ventricolo unico - Fontan

- ENALAPRIL per 10 settimane
- 18 pazienti
- Prospettico, randomizzato, cross-over
- Non modifica la capacità funzionale
- Non modifica la funzione diastolica
- Non modifica RVS nè IC a riposo

Effect of sildenafil on haemodynamic response to exercise and exercise capacity in Fontan patients

Alessandro Giardini*, Anna Balducci, Salvatore Specchia, Gaetano Gargiulo, Marco Bonvicini, and Fernando Maria Picchio

Pediatric Cardiology and Adult Congenital Unit, University of Bologna, Via Massarenti 9, 40138 Bologna, Italy



- ❖ 27 pazienti post Fontan
- ❖ Età : 22.8 ± 5 aa
- ❖ 70% classe NYHA II/III

Table 2 Change in cardiopulmonary and haemodynamic variables observed in exercise test nos 2 vs. 3 in the sildenafil treatment and in the control group at each exercise stage

Variable	Rest				Peak exercise			
	Sildenafil		Control		Sildenafil		Control	
	Before	After	Before	After	Before	After	Before	After
Cardiac index (L/min/m ²)	2.9 ± 0.8	3.7 ± 1.0	2.9 ± 0.9	2.9 ± 0.9	5.1 ± 0.9	5.6 ± 0.9	5.1 ± 0.9	5.2 ± 0.9
PBF index (L/min/m ²)	2.2 ± 0.6	2.8 ± 0.5	2.4 ± 0.5	2.4 ± 0.6	4.2 ± 0.5	4.7 ± 0.6	4.4 ± 0.6	4.4 ± 0.6

Conversion of atriopulmonary Fontan to extracardiac total cavopulmonary connection improves cardiopulmonary function

Alessandro Giardini^{a,*}, Carlo Pace Napoleone^b, Salvatore Specchia^a, Andrea Donti^a, Roberto Formigari^a, Guido Oppido^b, Gaetano Gargiulo^b, Fernando M. Picchio^a

^a *Pediatric Cardiology and Adult Congenital Unit, University of Bologna, Via Massarenti 9, 40138, Bologna, Italy*

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Received 15 September 2005; received in revised form 9 November 2005; accepted 15 November 2005

Available online 5 January 2006

Int J Cardiol 2006;113:341-544

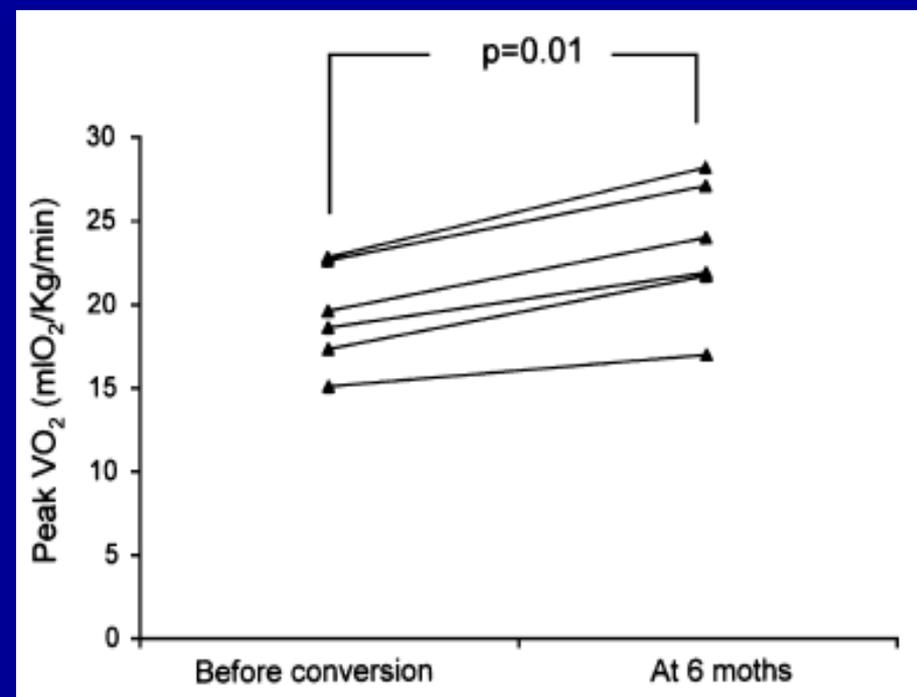


Table 2

Cardiopulmonary test results before vs. 6 months after conversion to extracardiac total cavopulmonary connection

	Before	After conversion	<i>p</i> value
Peak O ₂ pulse (ml O ₂ /kg/beat)	4.9 (2.5–10.5)	5.7 (3.5–11.5)	0.01
Peak HR (beats/min)	136 (117–160)	134 (121–159)	0.88
Peak VE (l/min)	55.4 (23.9–68.5)	56.5 (32.5–68.2)	0.63
VC (l/min)	3.5 (2.2–4.7)	3.4 (2.3–4.6)	0.66
FEV1 (l/s)	2.8 (1.9–3.9)	2.9 (1.9–3.9)	0.06
Arterial O ₂ saturation at peak exercise, %	91 (87–94)	92 (88–93)	0.7

CRT e GUCH

Permanent CRT Studies

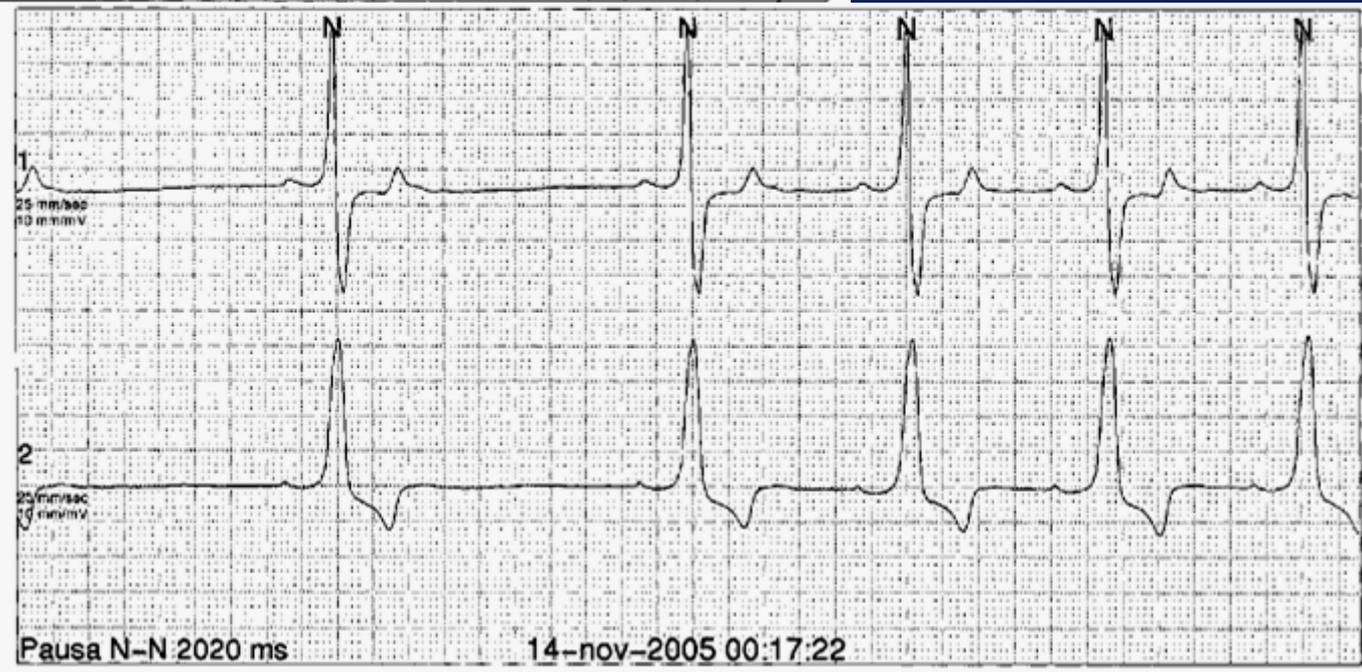
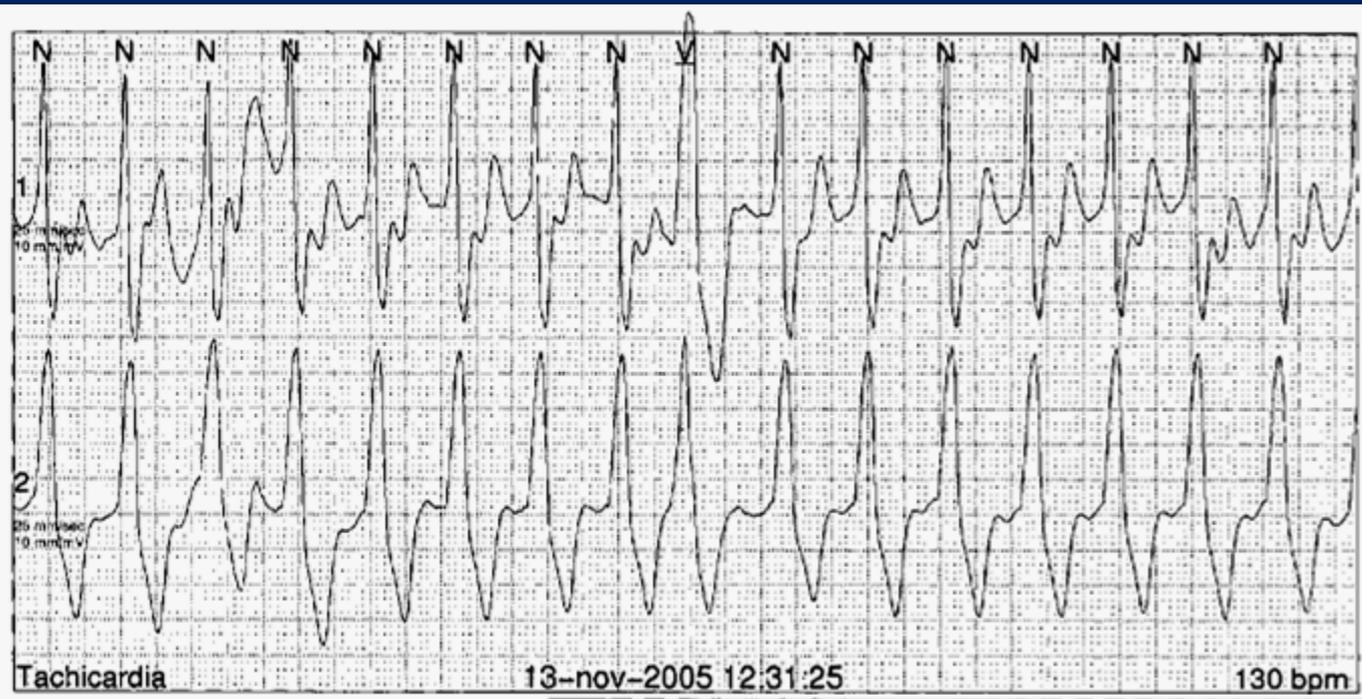
Study	N Total	N Systemic RV	N Single Ventricle	Conv. Pacing Prior to CRT	NYHA Class	Age at CRT [Years] Median	FUP [Months] Median (Range)	Nonresponders	Removed from Transplant List
Strieper et al., 2004 ⁹	7	1?	0	5	NA	7.3	16	2	5/7
Janousek et al., 2004 ¹⁰	8	8	0	6	median ₂	12.5	17.4	0	0/0
Dubin et al., 2005 ¹¹	103	17	7	46	1 = 15 2 = 49 3/4 = 39	12.8	4.0	11	3/18
Khairy et al., 2006 ¹²	13	4	0	7	NA	6.5	15.6	0	NA
Beek et al., 2006 ¹³	3	0	0	3	NA	1.5	(2-12)	0	0/0
Moak et al., 2006 ¹⁴	6	0	0	6	NA	10.8	10	0	2/2
Janousek et al., 2006 ¹⁵	74	22	3	58	median ₂	16.9	8.1	9	3/8
Total	214	52 (24.3%)	10 (4.7%)	131 (61.2 %)				22 (10.3%)	13/35 (37.1%)

Explanations: Conv. = conventional; CRT = cardiac resynchronization therapy; FUP = follow-up; NA = not available; RV = right ventricle.

J. Janousek et al., PACE 2008; 31: S21-S23

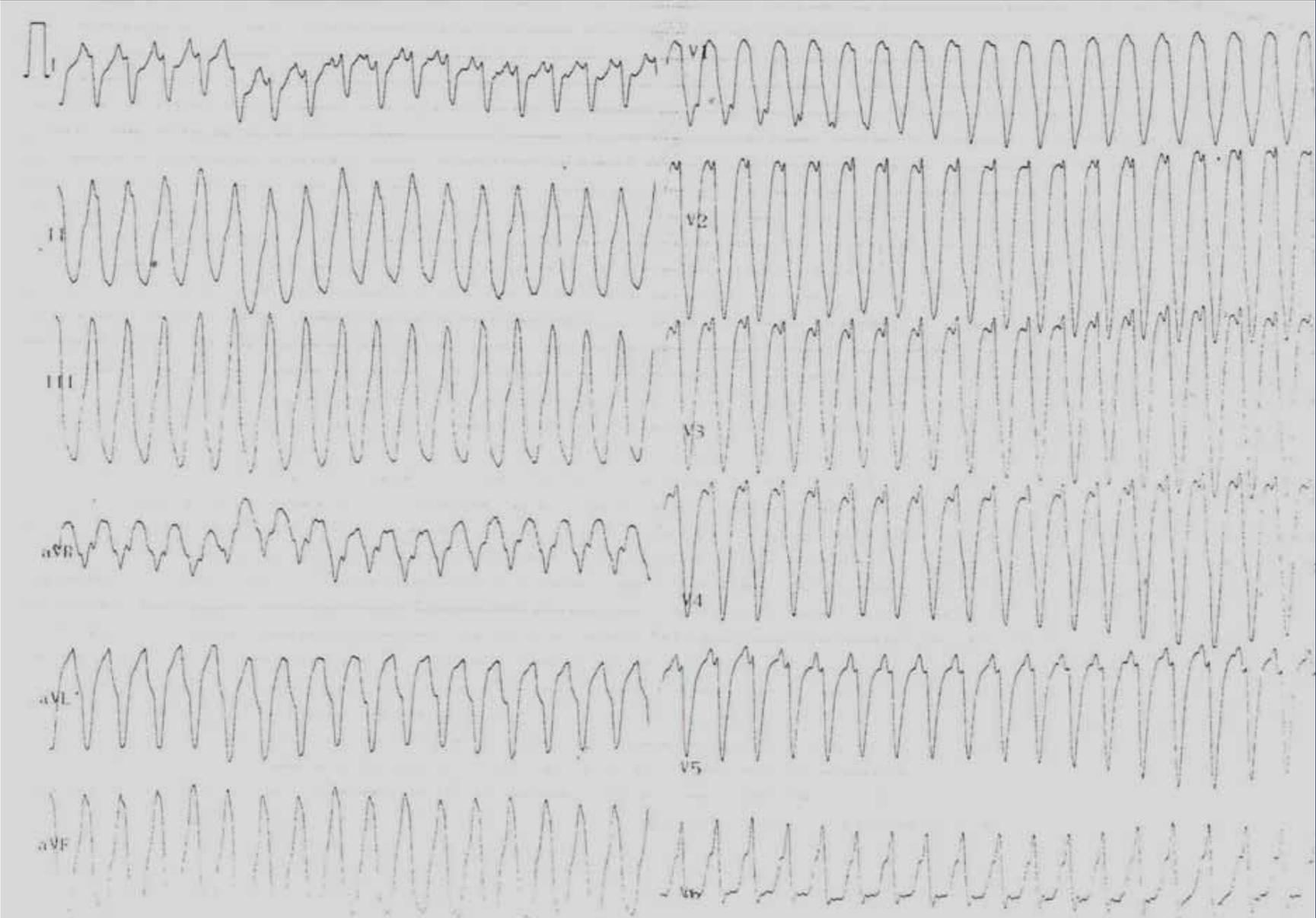
Aritmie nel GUCH

- ❖ Motivo principale di accesso in PS
- ❖ Frequente associazione di bradi-tachiaritmie (disfunzione nodo SA o AV)
- ❖ Causa di disfunzione ventricolare, trombosi, SCD
- ❖ Morbilità: farmaci, CVE, device, chirurgia



C.C. ♂ 22 anni
S/P Mustard

F.B. ♂ 50 anni, Fallot, S/P correzione con Hancock 30



Aritmie nel GUCH

Terapia farmacologica

❖ Meno efficace

❖ Meno tollerata

- Disfunzione nodo SA o AV
- Disfunzione ventricolare
- Ipotensione

❖ Effetto proaritmico !

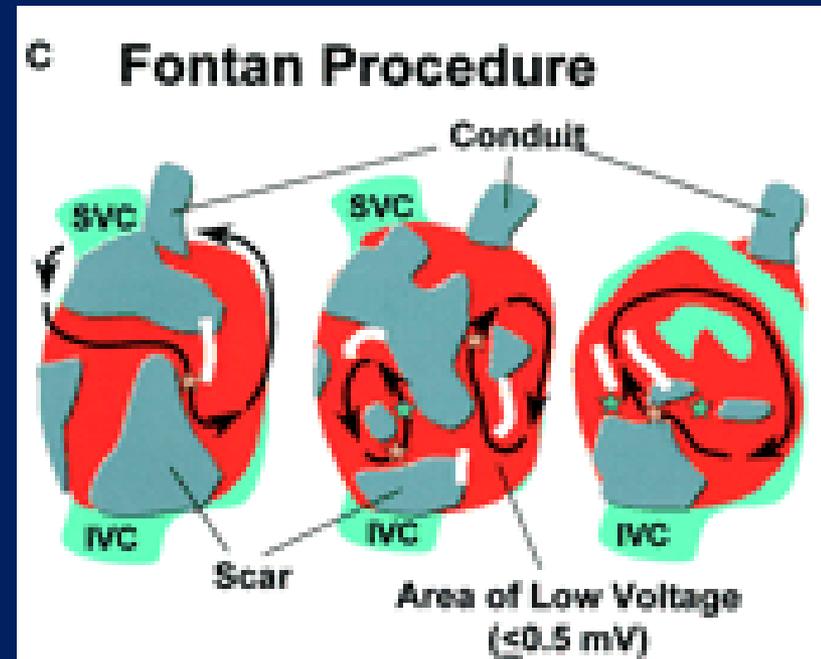


antiaritmici gruppo III (amiodarone)

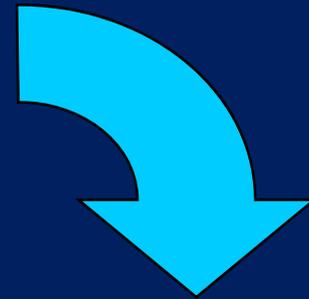
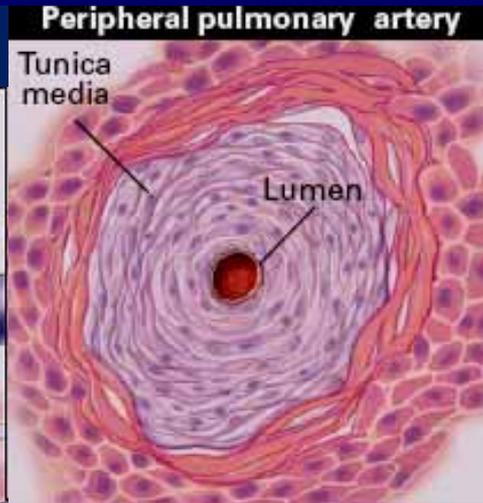
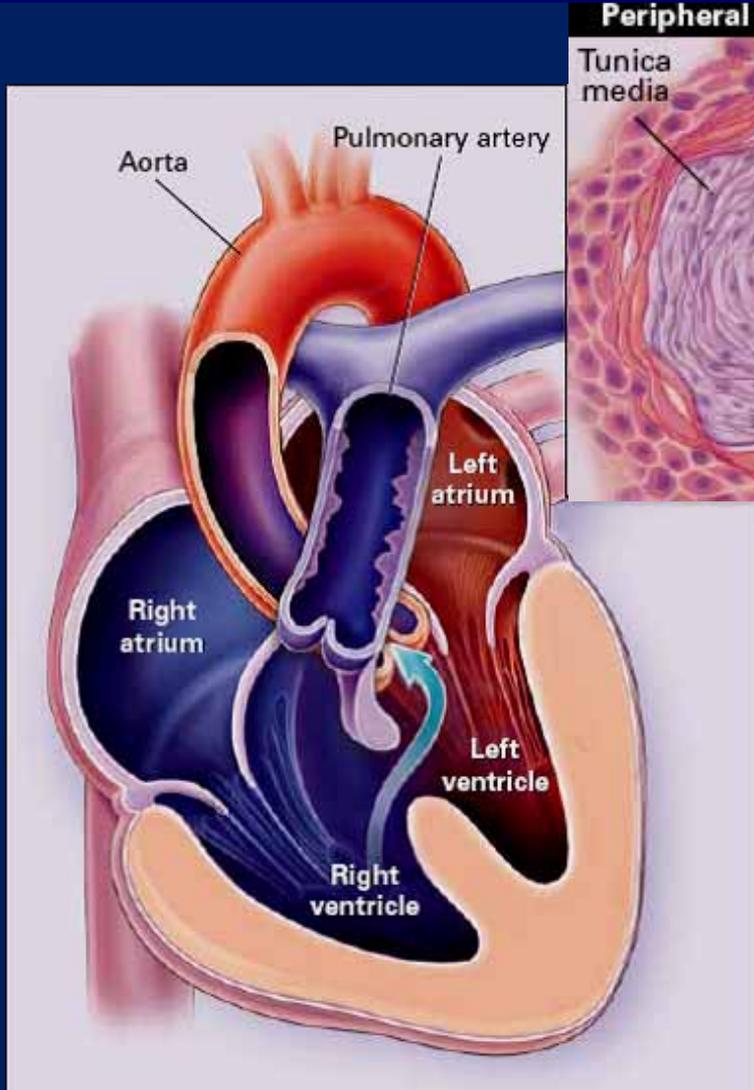
Aritmie nel GUCH

Ablazione transcatetere

- ❖ Anatomia complessa
- ❖ Circuiti di rientro ampi/multipli
- ❖ Accessi venosi limitati
- ❖ < successo immediato
- ❖ > recidive a distanza



Ventricolo destro sistemico: la sindrome di Eisenmenger



Vasodilatatore polmonare



>> shunt dx/sn ??

Bosentan

Bosentan Therapy in Patients With Eisenmenger Syndrome

A Multicenter, Double-Blind, Randomized, Placebo-Controlled Study

Nazzareno Galiè, MD; Maurice Beghetti, MD; Michael A. Gatzoulis, MD; John Granton, MD; Rolf M.F. Berger, MD; Andrea Lauer, PhD; Eleonora Chiossi, MSc; Michael Landzberg, MD; for the Bosentan Randomized Trial of Endothelin Antagonist Therapy-5 (BREATHE-5) Investigators

54 pazienti - classe WHO III - F.Up 16 sett.

Parameter	Change From Baseline		Treatment Effect	
	Placebo (n=17)*	Bosentan (n=37)*	(Bosentan-Placebo)	P
Heart rate, bpm	-0.8 (2.7)	-2.0 (1.9)	-1.2 (3.4)	0.7329
Mean pulmonary arterial pressure, mm Hg	0.5 (1.4)	-5.0 (1.6)	-5.5 (2.5)	0.0363
Mean left atrial pressure, † mm Hg	0.5 (1.2)	0.4 (0.6)	-0.2 (1.3)	0.8862
Pulmonary flow index, L · min ⁻¹ · m ⁻²	0.0 (0.1)	0.1 (0.1)	0.1 (0.1)	0.4675
Pulmonary vascular resistance index, dyne · s · cm ⁻⁵	155.1 (134.0)	-316.9 (138.3)	-472.0 (221.9)	0.0383
Mean systemic arterial pressure, mm Hg	2.5 (2.2)	-3.8 (1.6)	-6.3 (2.8)	0.0282
Mean right atrial pressure, mm Hg	0.4 (0.9)	0.3 (0.5)	-0.1 (1.0)	0.9448
Systemic flow index, L · min ⁻¹ · m ⁻²	-0.2 (0.1)	0.9 (0.8)	1.1 (1.1)	0.2981
Systemic vascular resistance index, dyne · s · cm ⁻⁵	378.9 (246.8)	-372.9 (244.6)	-751.8 (388.4)	0.0595

Bosentan Therapy in Patients With Eisenmenger Syndrome

A Multicenter, Double-Blind, Randomized, Placebo-Controlled Study

Nazzareno Galiè, MD; Maurice Beghetti, MD; Michael A. Gatzoulis, MD; John Granton, MD; Rolf M.F. Berger, MD; Andrea Lauer, PhD; Eleonora Chiossi, MSc; Michael Landzberg, MD; for the Bosentan Randomized Trial of Endothelin Antagonist Therapy-5 (BREATHE-5) Investigators

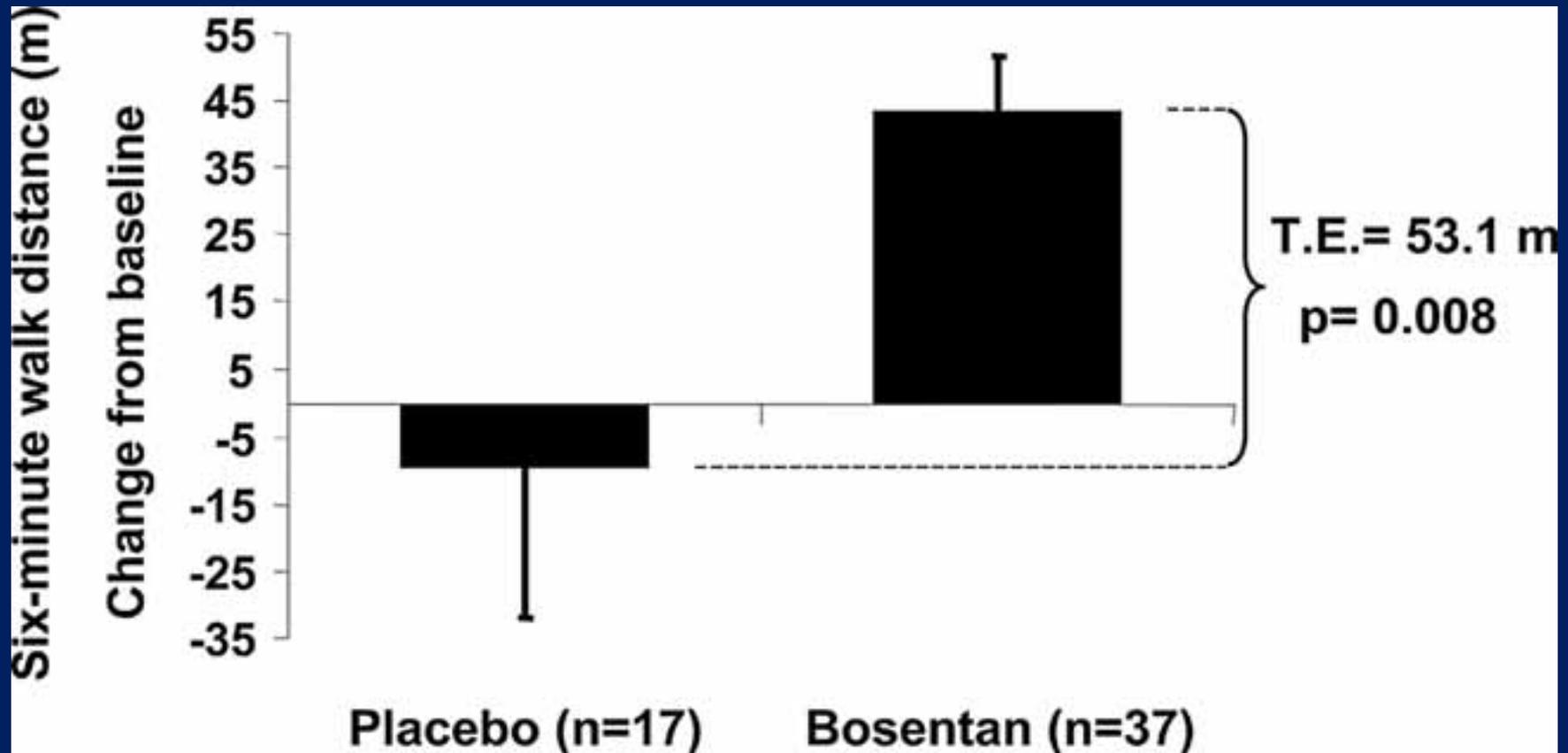


Table 3 Effect of placebo and sildenafil as add-on therapy to bosentan

	Placebo and bosentan (mean difference)	Sildenafil and bosentan (mean difference)	Mean difference (95% CI)	P-value
6 min walk distance (meter)	7.9	21.1	13.1 (−25.3 to 51.3)	0.48
Systolic blood pressure (mmHg)	2.4	−3.8	6.18 (−2.8 to 15.2)	0.17
Diastolic blood pressure (mmHg)	2.2	0.4	1.8 (−8.8 to 12.4)	0.73
Systemic oxygen saturation at rest (%)	−1.8	2.9	4.7 (1.9 to 7.5)	<0.01
Systemic oxygen saturation during exercise (%)	−2.9	3.9	6.8 (−0.5 to 14.2)	0.07
NT-proBNP (mmol/L)	−9.9	2.2	12.0 (−27.7 to 51.7)	0.53
NYHA class	−0.13	−0.26	−	0.29
Pulmonary blood flow (L/min) ^a	0.23	−0.38	−0.61 (−1.83 to 0.61)	0.31
Systemic blood flow (L/min) ^a	0.33	−0.19	−0.53 (−3.36 to 2.30)	0.70
Pulmonary/systemic blood flow ^a	0.09	−0.07	−0.16 (−0.37 to 0.05)	0.13
Pulmonary vascular resistance (wood)	−2.07	0.48	2.55 (−3.44 to 8.55)	0.38
Systemic vascular resistance (wood)	1.85	−0.90	−2.75 (−10.32 to 4.82)	
Pulmonary blood flow (L/min) ^b	−0.25	0.32	0.58 (−0.21 to 1.36)	0.14
Systemic blood flow (L/min) ^b	0.02	−0.03	0.2 (−1.33 to 1.22)	0.93
Pulmonary/systemic blood flow ^b	−0.04	0.06	0.10 (−0.10 to 0.30)	0.30

NT-proBNP, N-terminal pro brain natriuretic peptide; NYHA, New York Heart Association.

^aData from catheterization.

^bData from magnetic resonance imaging.



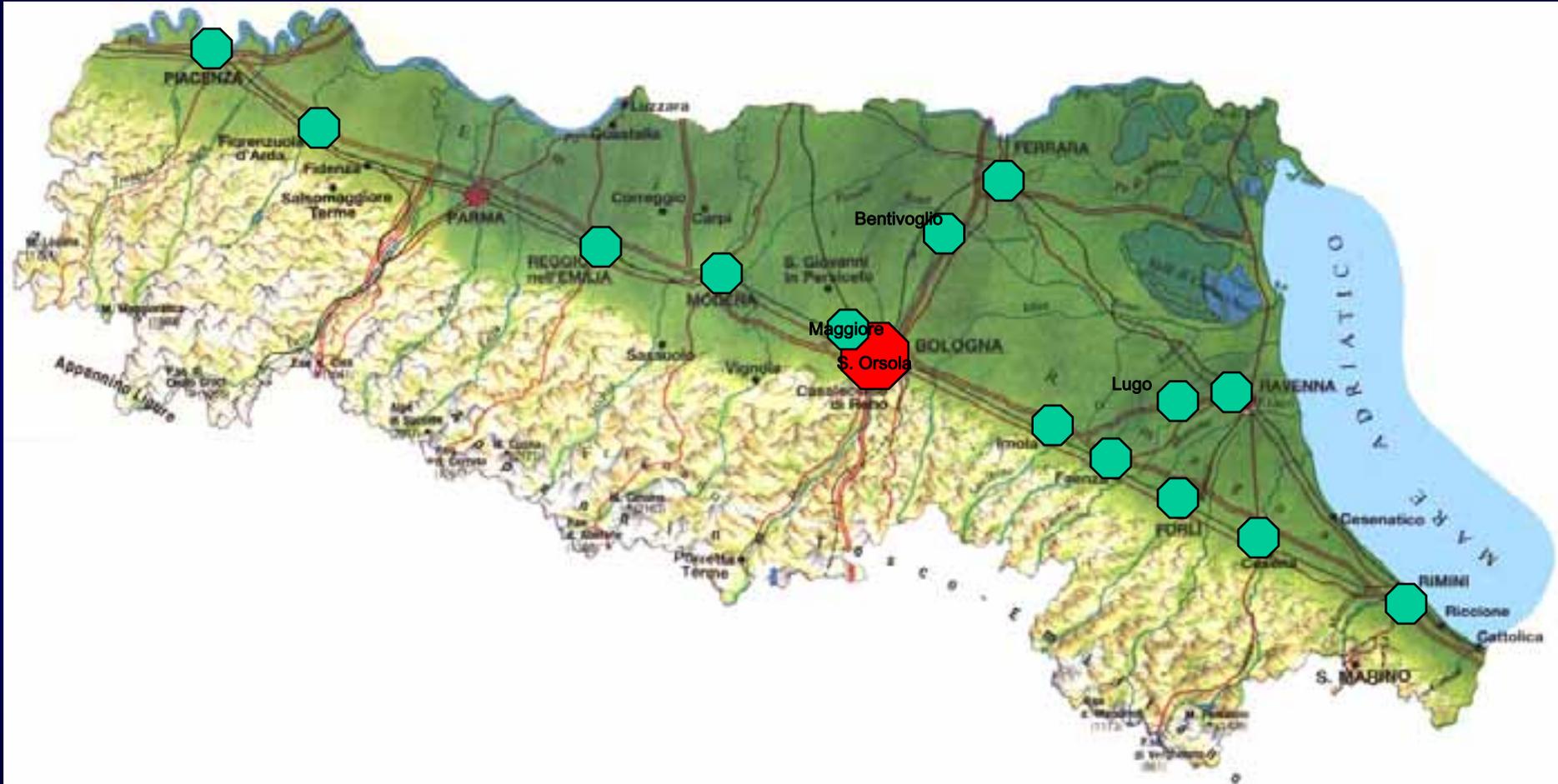
Il salasso nel paziente cianotico :

- Ht > 65% o Hb > 20g/dl + sintomi da iperviscosità.
- Ht > 60% in caso di intervento chirurgico

Componenti chiave dell'approccio alla cura del paziente GUCH

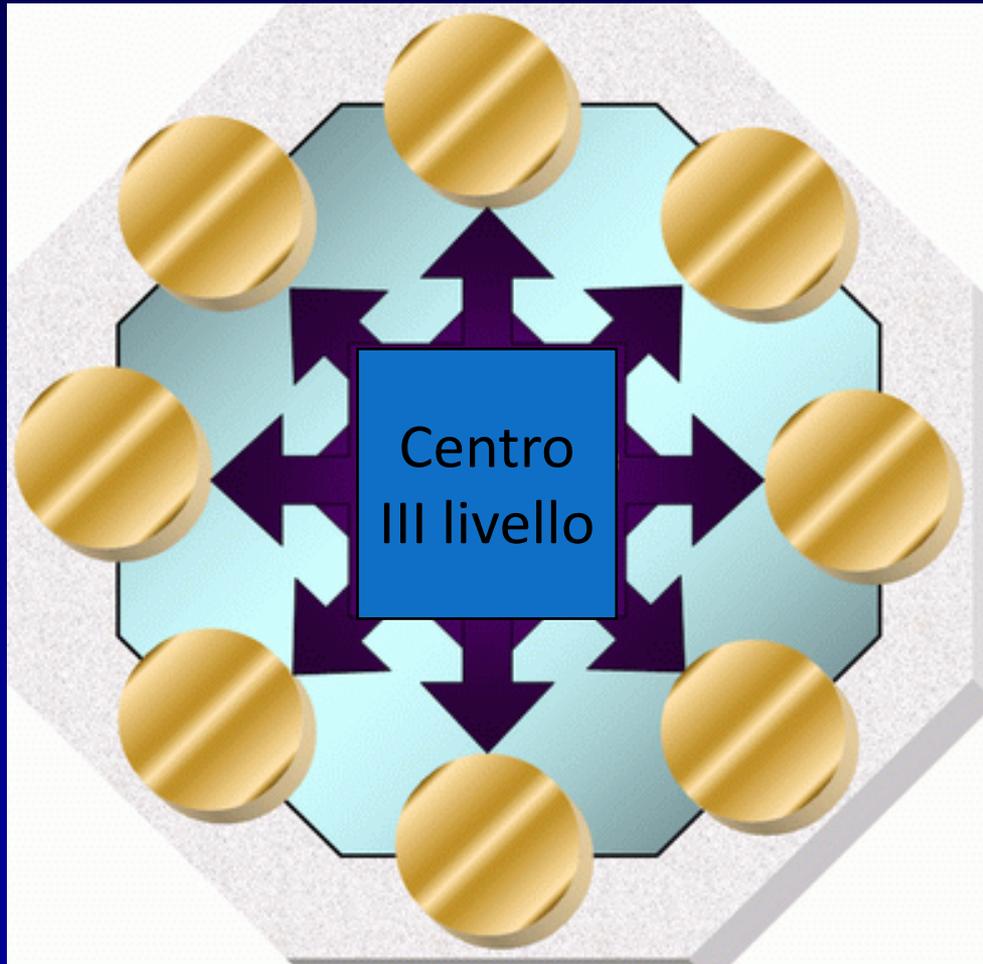
- Identificazione ed educazione del paziente
- Sviluppo di una rete tra centri specializzati e territorio
- Organizzazione della diagnosi e cura
- Identificazione dei fattori di rischio per la prognosi
- Espansione e formazione di specialisti dedicati

Una possibile soluzione organizzativa: l'Hub and Spoke



Education, education, education!!!

Come gestire il cardiopatico congenito adulto



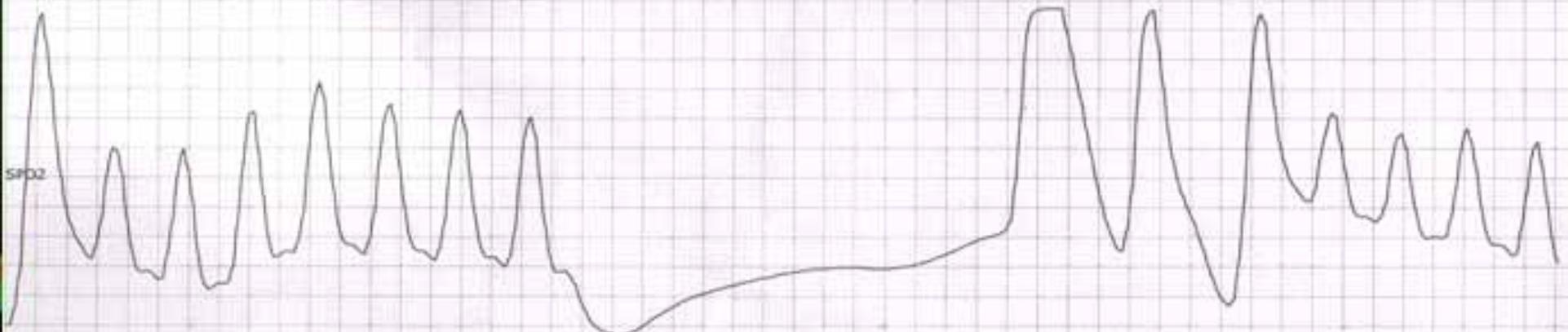
- ❖ Conoscenza
- ❖ Esperienza
- ❖ Collaborazione

TERAPIA SCOMPENSO NEI GUCH

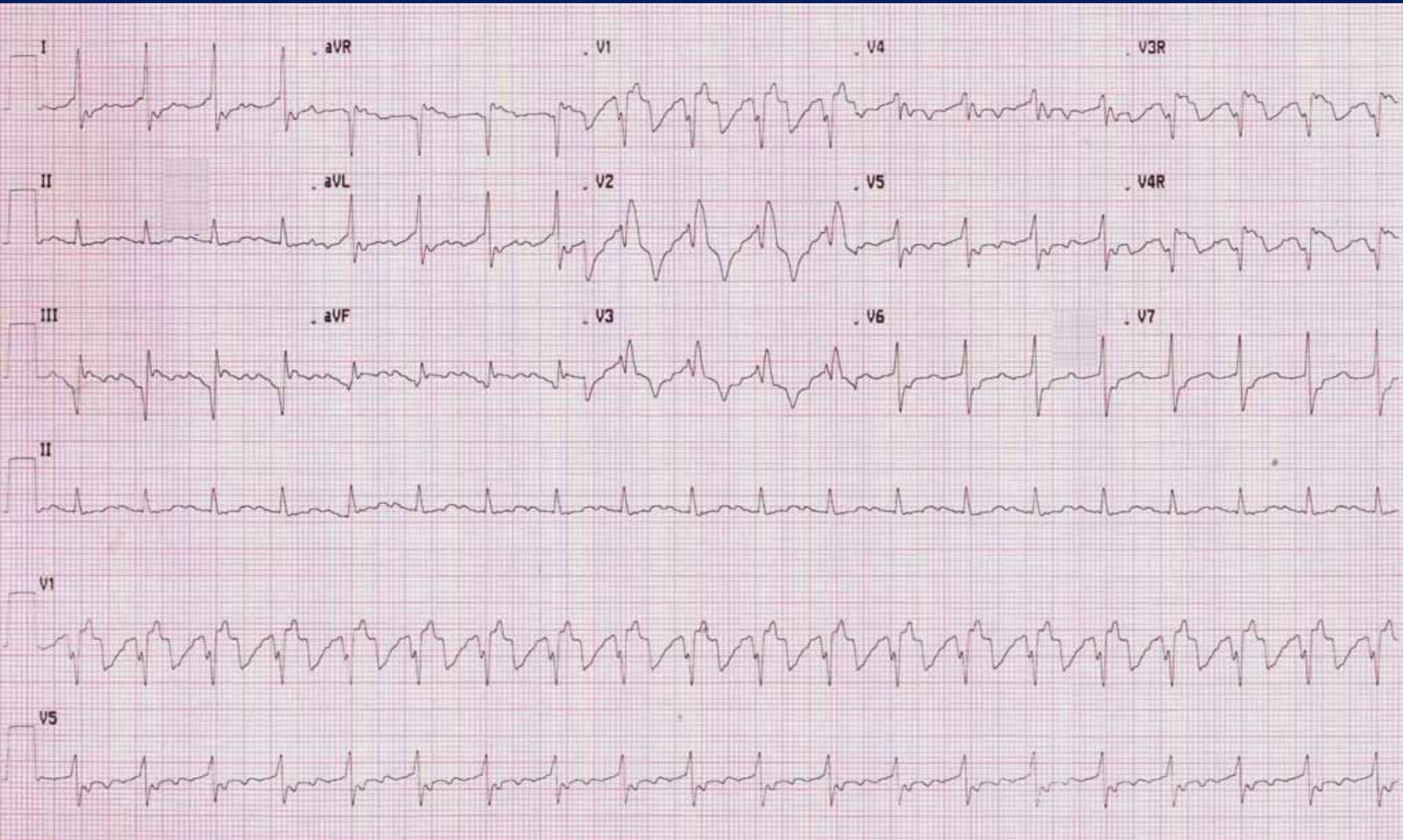
- Considerare la chirurgia o la procedura interventistica
- L'applicazione delle raccomandazioni per le cardiopatie acquisite non è supportata da sufficienti evidenze
- Necessari studi prospettici e multicentrici

44 anni, TGA S/P Mustard, IART-AF-SND

i.v. β -blocker → //

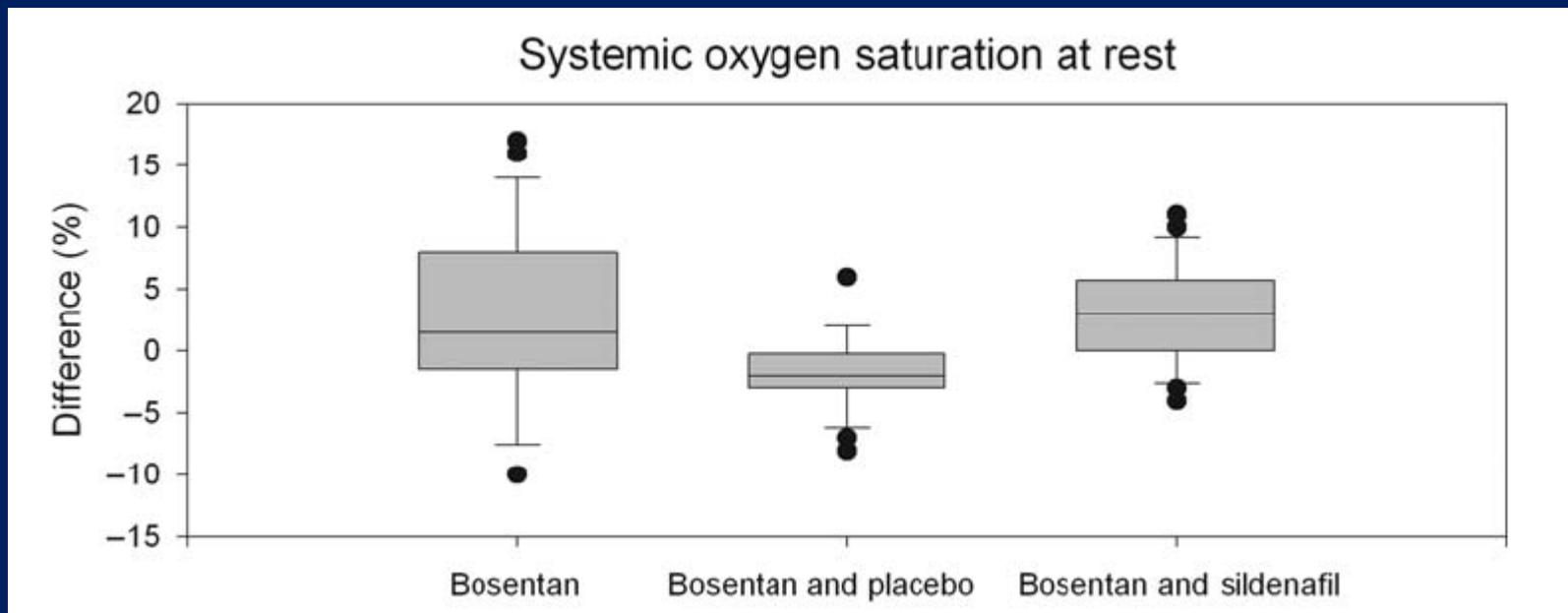


F.B. ♂ 50 anni, Fallot, S/P correzione con Hancock 30



Combination therapy with bosentan and sildenafil in Eisenmenger syndrome: a randomized, placebo-controlled, double-blinded trial[†]

Kasper Iversen¹, Annette S. Jensen¹, Tim V. Jensen², Niels G. Vejlstrup¹, and Lars Søndergaard^{1*}



Mean difference 4,7 ($p < 0,01$)

Aritmie dopo intervento di Fontan

- *Gruppo con aritmia*
- n = 39
- Scompenso 46 %
- Trombosi ADX 31 %
- Mortalità 10 %
- *Gruppo senza aritmia*
- n = 55
- Scompenso 13 % p<0.004
- Trombosi ADX 4 % p<0.006
- Mortalità 9 %
- *Ghai et al, JACC, 1997*

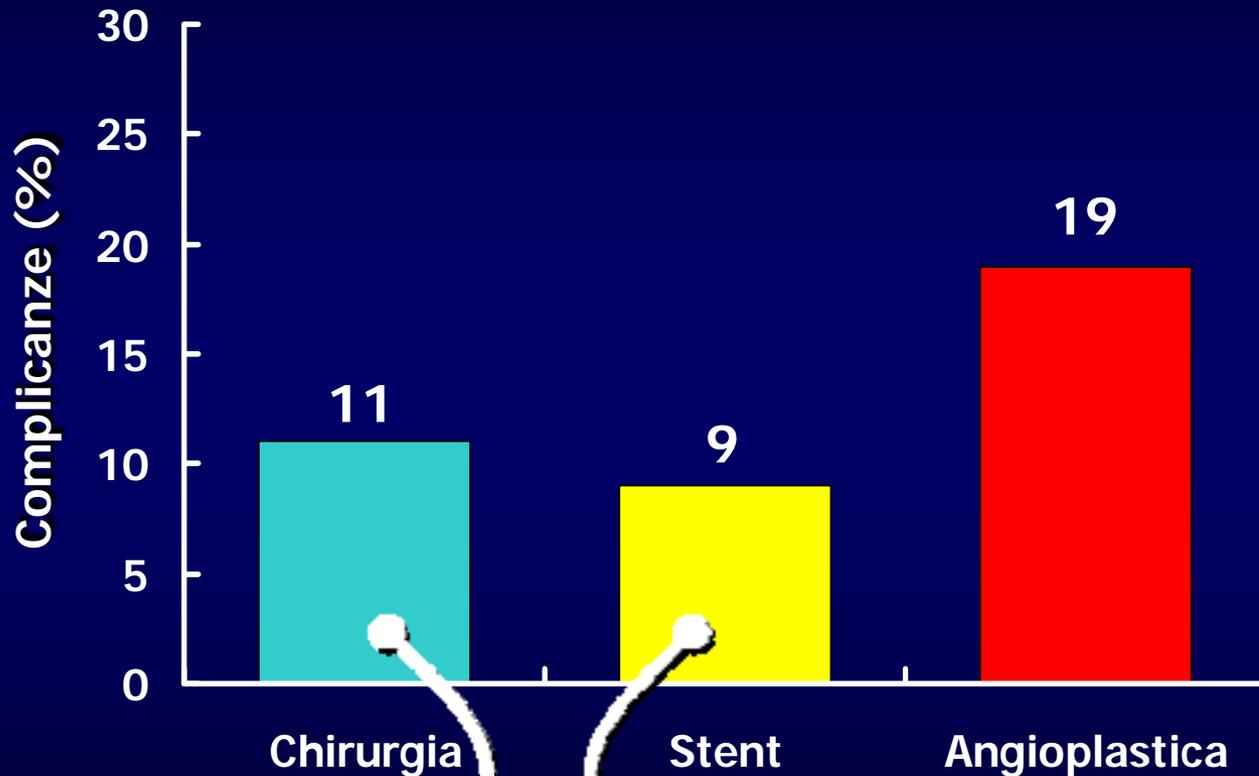


The Results of Catheter-Based Therapy Compared With Surgical Repair of Adult Aortic Coarctation

John Alfred Carr, MD

Chicago, Illinois

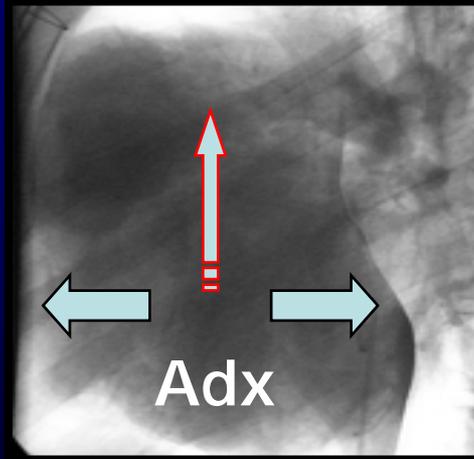
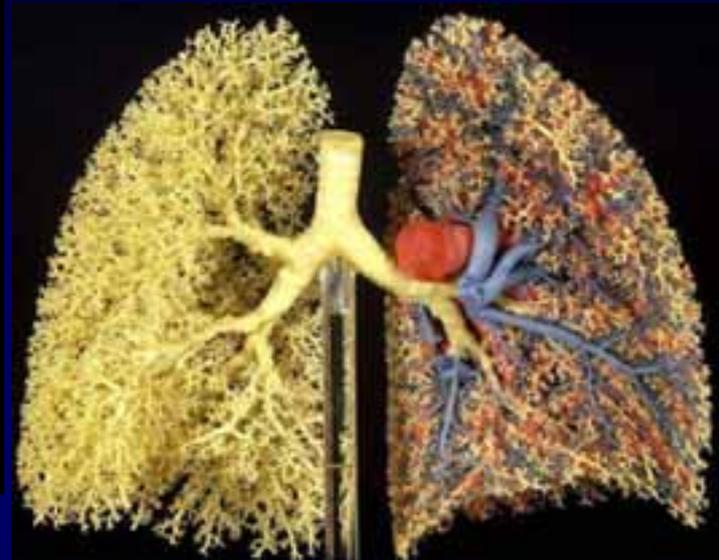
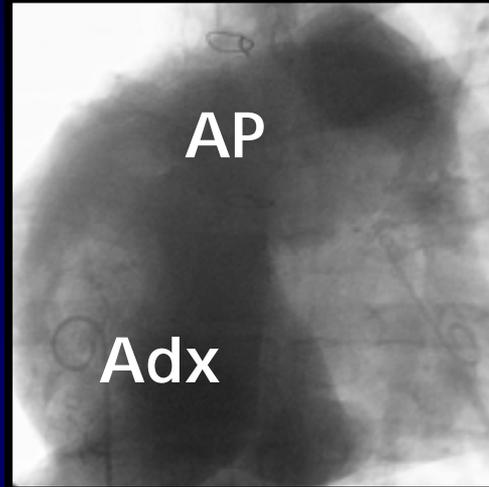
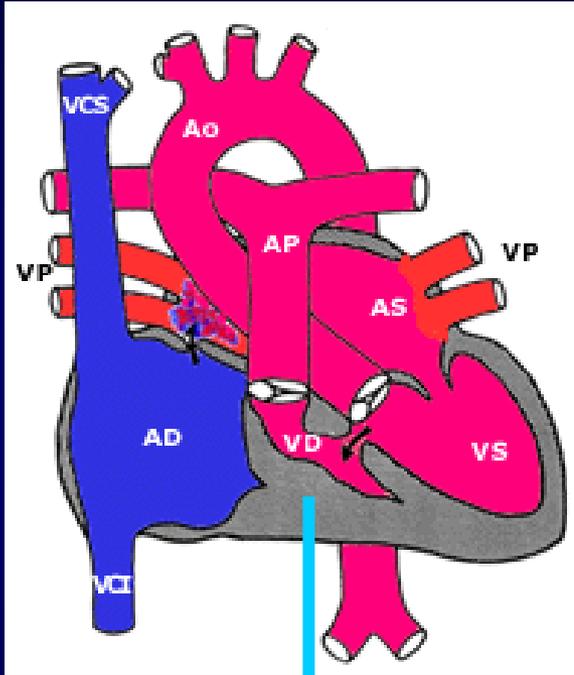
633 pz. Stent/PTCA vs 213 pz. Chirurgia (1995-2005)



- Sanguinamento
- Lesione n. laringeo

- Aneurisma Ao
- Dissezione Ao
- Migrazione stent
- AIT/Ictus

La circolazione tipo Fontan Il ventricolo "poco riempito"



↑ PCO2 Perdita
 flusso pulsatile
 (↓ NO)

Assenza del ventricolo sottopolmonare

Perdita energia cinetica anterograda

↑ RVP

Neurohormonal Activation and the Chronic Heart Failure Syndrome in Adults With Congenital Heart Disease

Aidan P. Bolger, BSc, MRCP; Rakesh Sharma, BSc, MRCP; Wei Li, MD, PhD; Marjolein Leenarts, MD; Paul R. Kalra, MA, MRCP; Michael Kemp, MPath; Andrew J.S. Coats, DM; Stefan D. Anker, MD, PhD; Michael A. Gatzoulis, MD, PhD

Circulation.2002;106:92-993

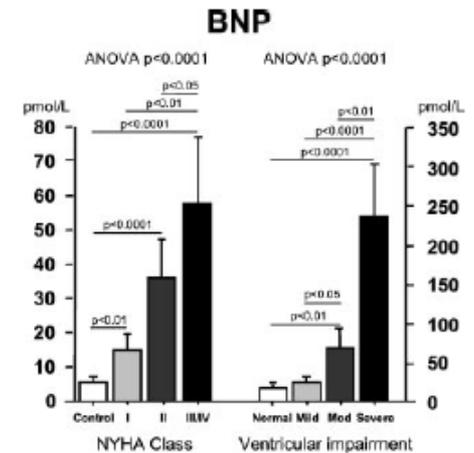
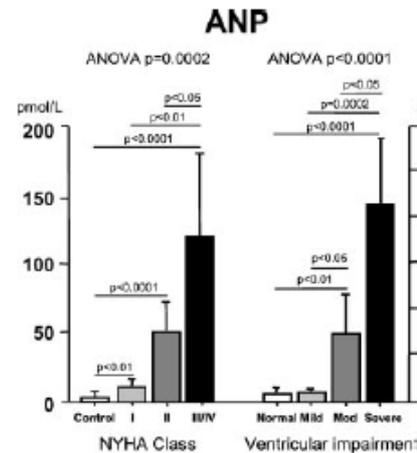
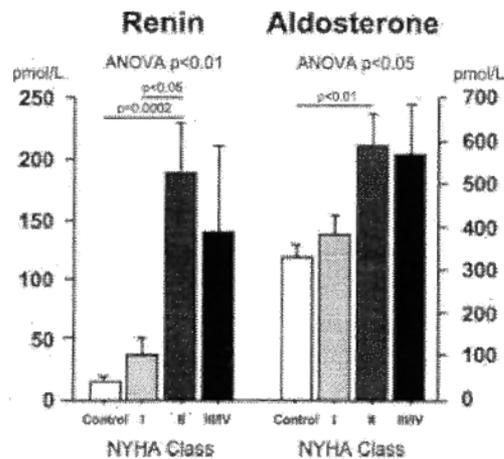
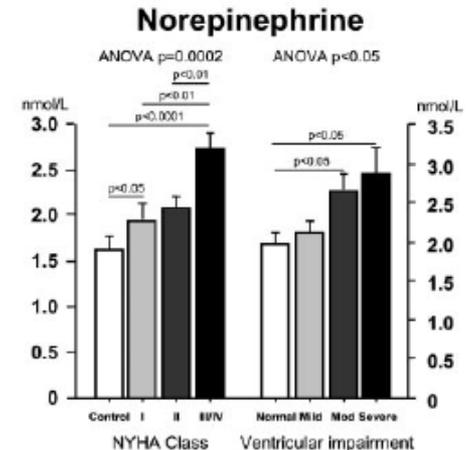
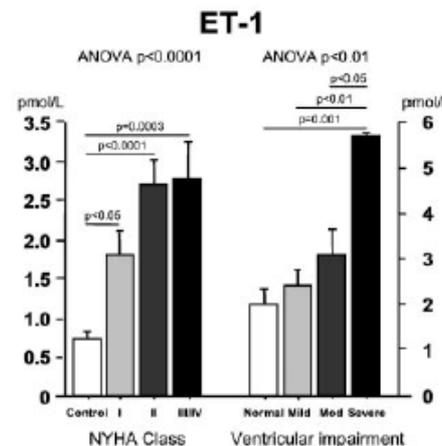


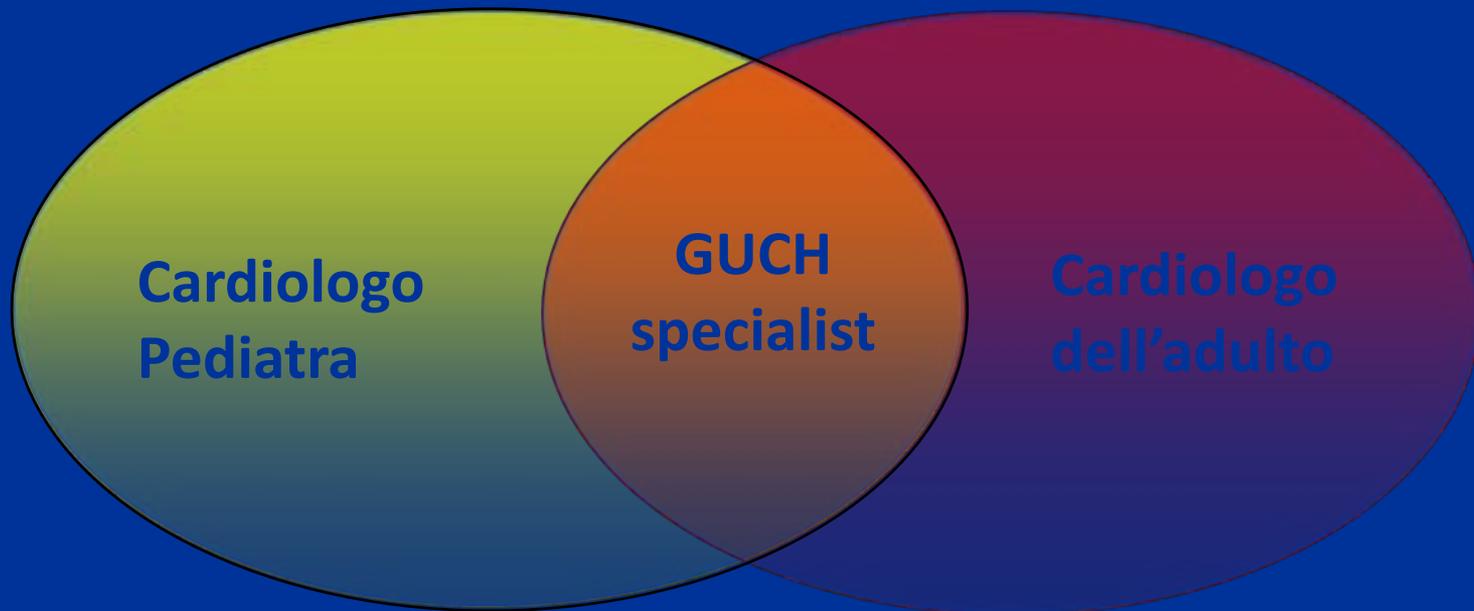
TABLE 4. Neurohormone Levels in Adults With Congenital Heart Disease and Healthy Controls

	Congenital Heart Disease Patients (n=53)	Control Subjects (n=15)	P
ANP, pmol/L	56.6 (17.5)	3.1 (0.6)	<0.0001
BNP, pmol/L	35.8 (7.7)	5.7 (0.9)	<0.0001
ET-1, pmol/L	2.52 (0.21)	0.72 (0.08)	<0.0001
Norepinephrine, nmol/L	2.19 (0.09)	1.63 (0.13)	0.003
Epinephrine, nmol/L	0.52 (0.03)	0.43 (0.05)	0.12
Renin, pmol/L	147.5 (28.1)	16.3 (1.9)	0.003
Aldosterone, pmol/L	546.3 (47.3)	337.4 (22.9)	0.024

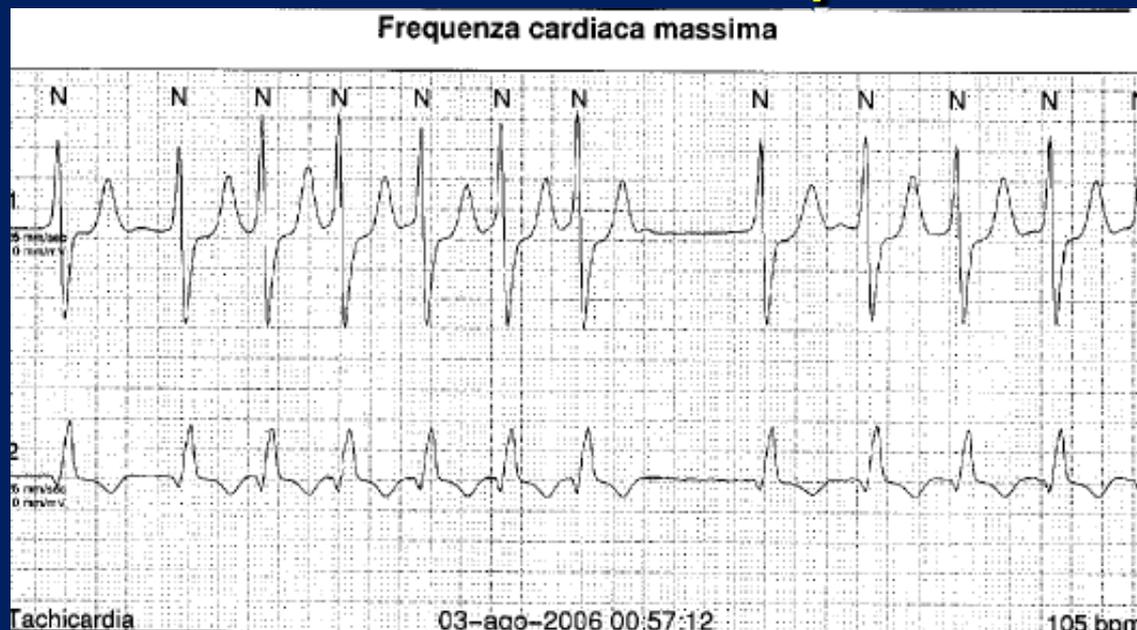


Il follow-up del cardiopatico congenito adulto

Problema della competenza



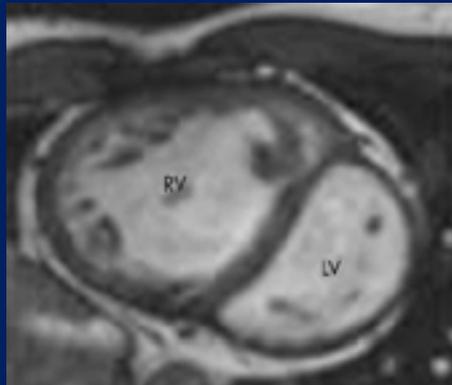
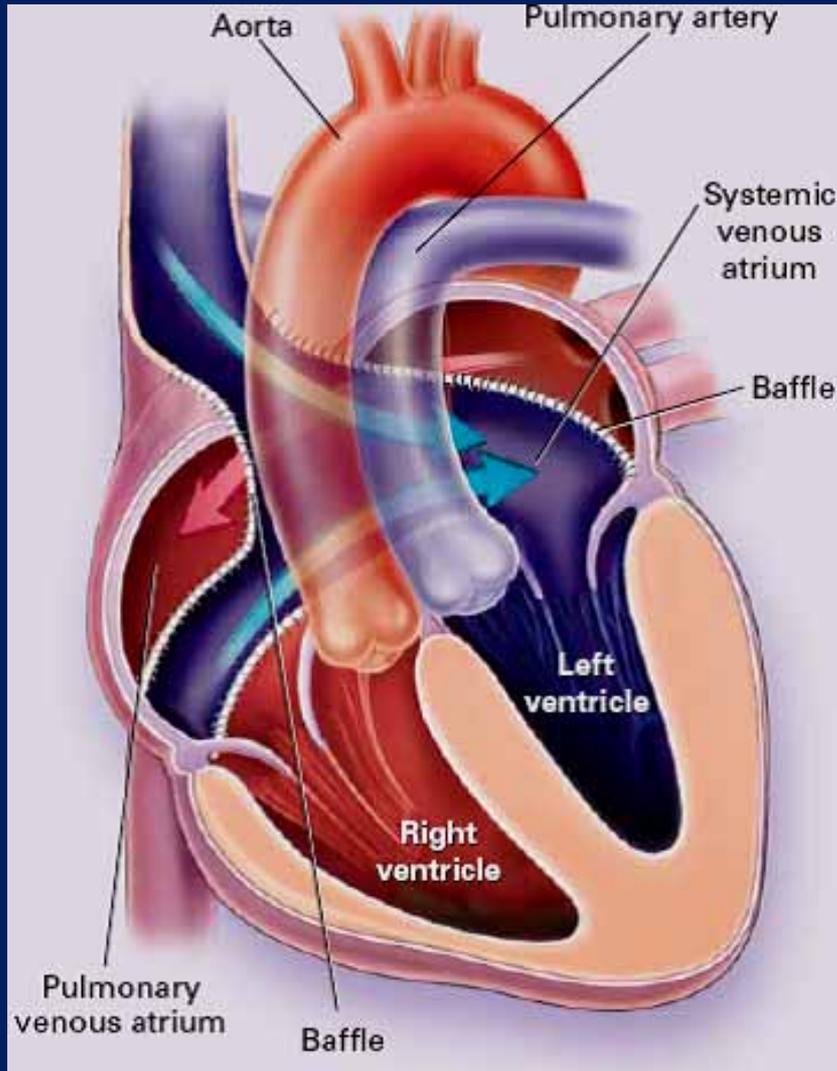
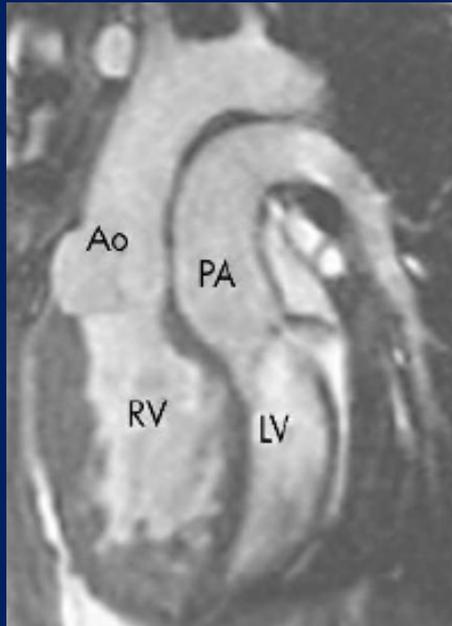
**B.A. ♂ 62 anni ,
Fallot S/P Waterstone e successivo patch infundibolare**



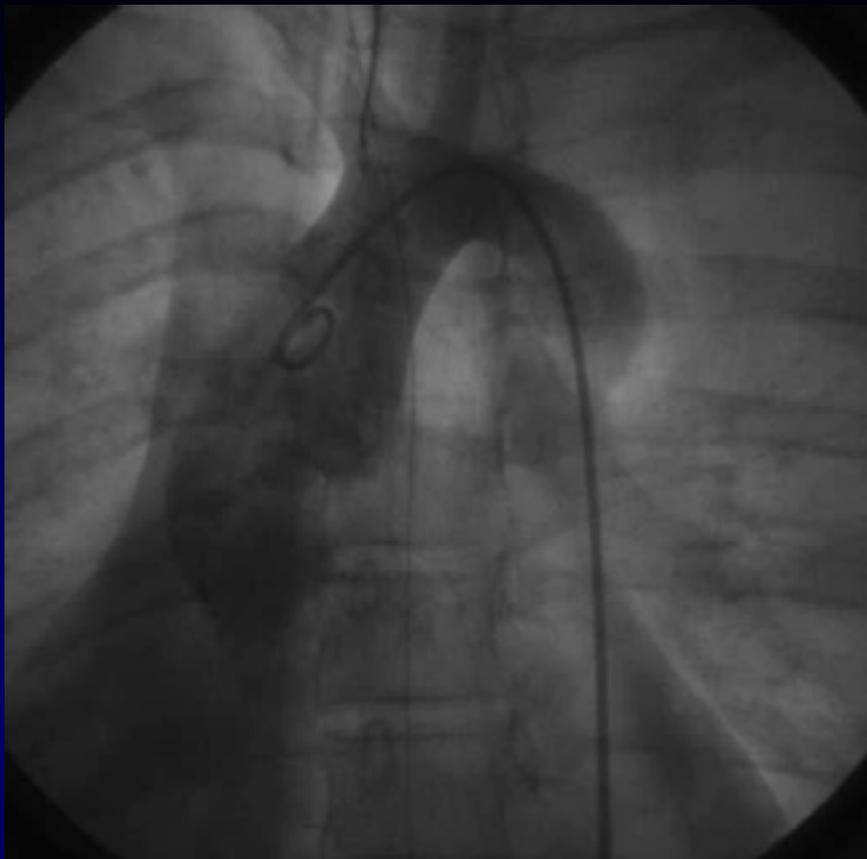
RR MAX



Ventricolo destro sistemico: TGA S/P Mustard-Senning



*Lo stent
nella coartazione aortica*



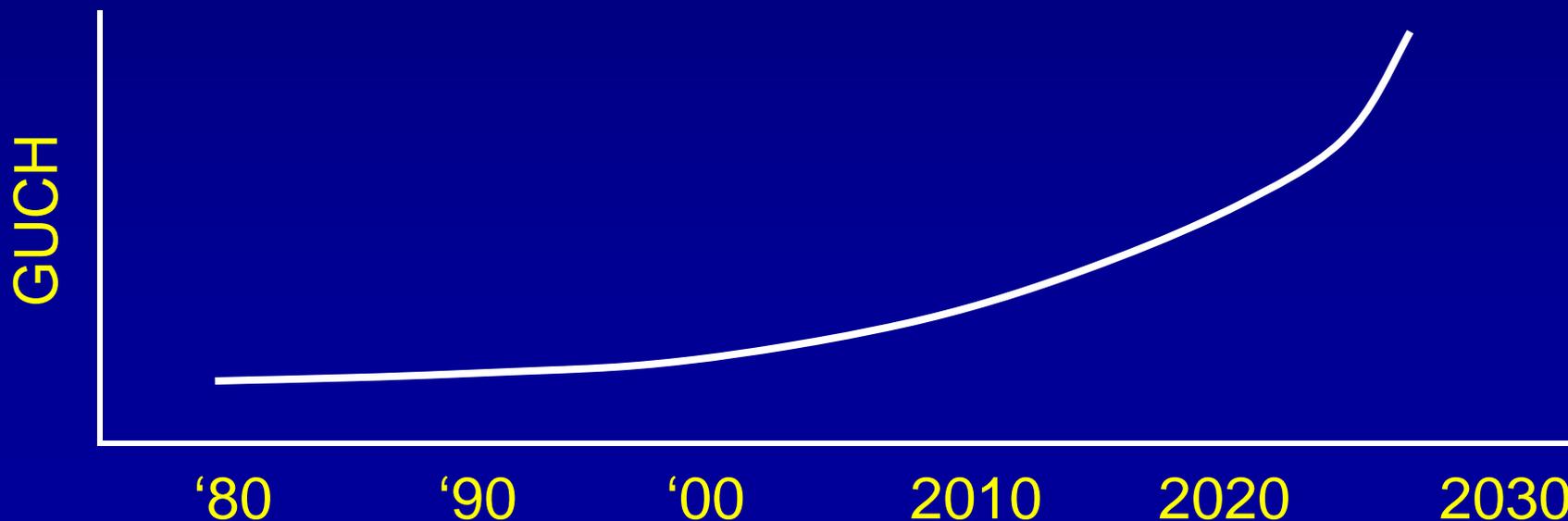
Il follow-up del cardiopatico congenito adulto

Dimensione del problema

Incidenza delle CC alla nascita stabile nei paesi occidentali

Miglioramento della gestione medica, chirurgica ed anestesiologicala → aumento sopravvivenza

Immigrazione



Congenital heart disease

