Università degli Studi di Padova

Hot Topics in Cardiologia 2024

Imaging in CRT and Heart Failure

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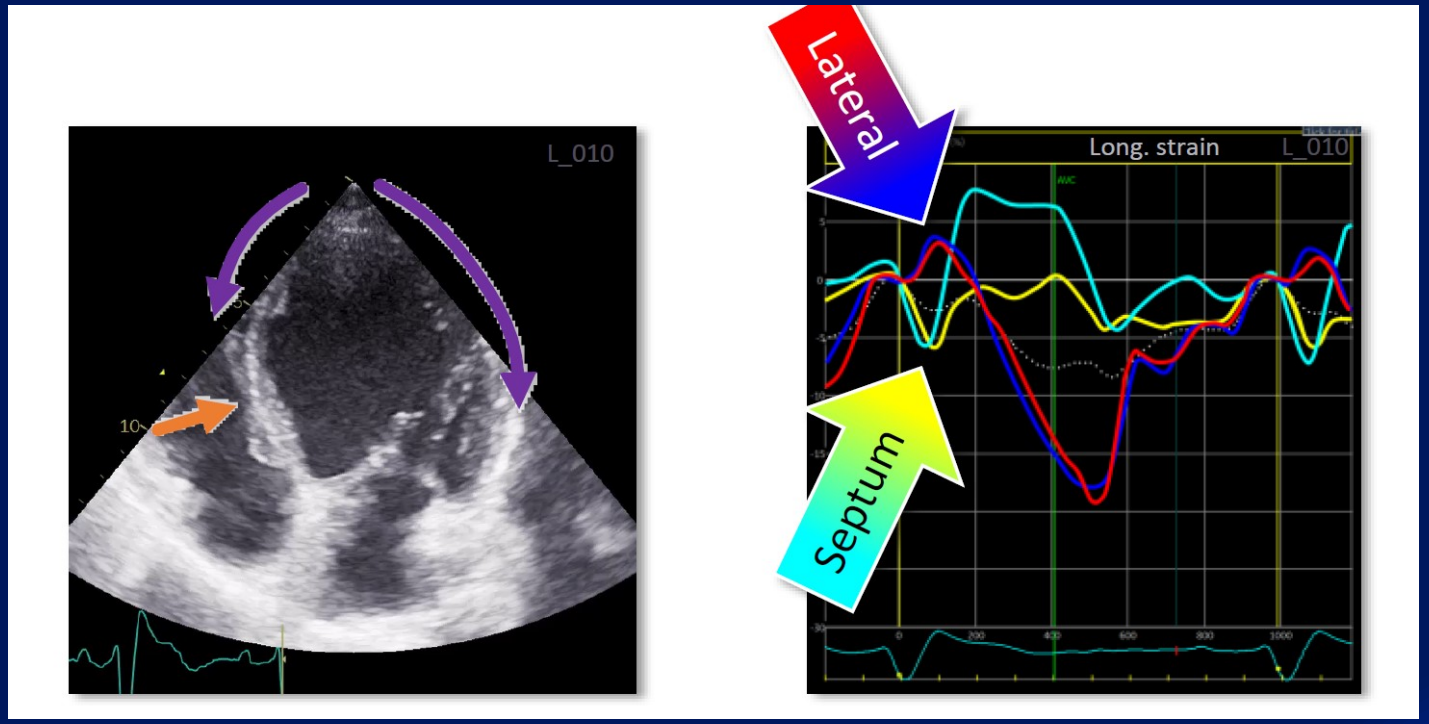
Chair Experimental Cardiology IRP

- CRT has been shown to improve LV function and improve HF related morbidity and mortality.
- However, despite significant research efforts, “non-responders”(depending on definition) range between 20% and 40% of patients



Fornwalt BK, et al. Agreement is poor among current criteria used to define response to cardiac resynchronization therapy. Circulation 2010;121:1985–91.

IJC Heart & Vasculature 39 (2022) 100979

Contents lists available at ScienceDirect

IJC Heart & Vasculature

journal homepage: www.sciencedirect.com/journal/ijc-heart-and-vasculature

Predictors of echocardiographic response to cardiac resynchronization therapy: A systematic review with Meta-Analysis

Rodrigo Martins [a], Natália António [a,b,*], Helena Donato [a,c], Bárbara Oliveiros [a]

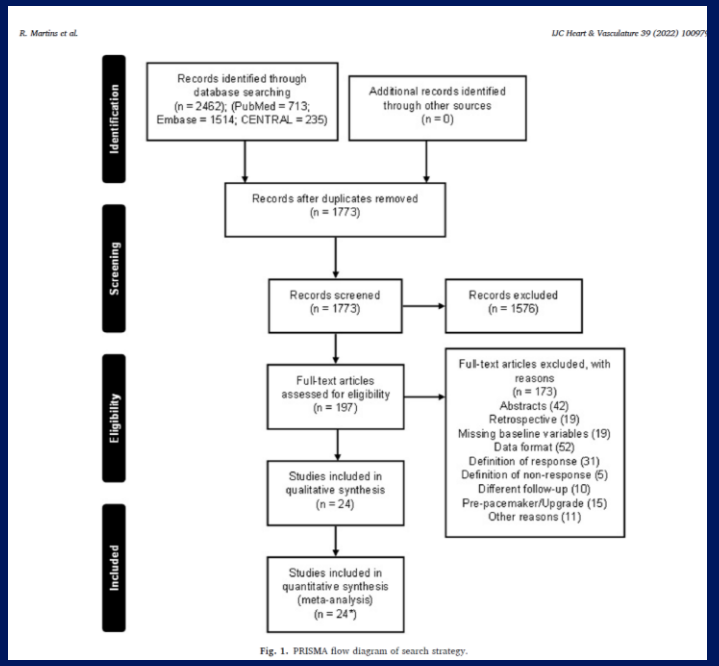
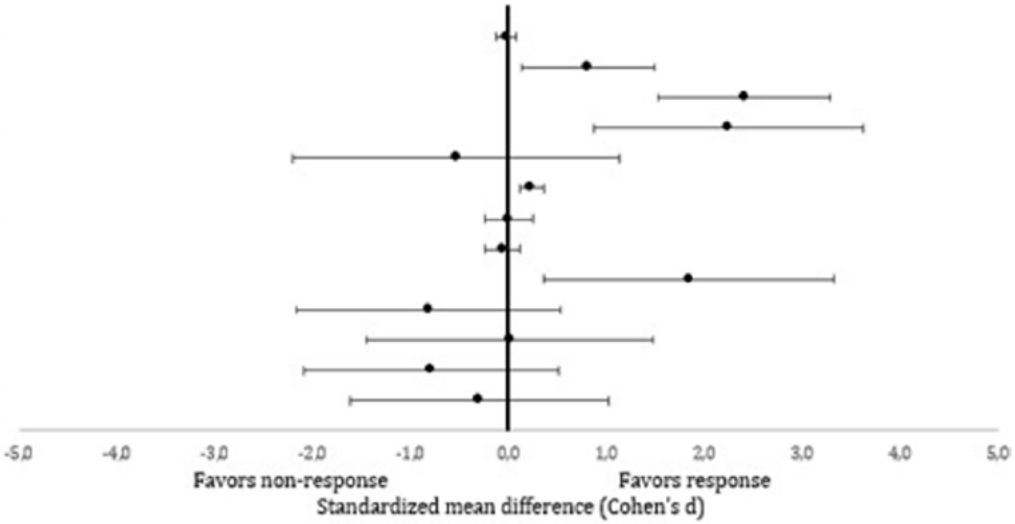


Fig. 1. PRISMA flow diagram of search strategy.

	I^2 (num. studies)	Num. subjects	Std Effect	95% CI	p	adj p
Age	36,83% (24)	2044	-0.020	-0.13 to 0.08	0.665	0,169
Female (%)	98,81% (24)	2044	0.820	**0,14 to 1,5**	**0,018**	0,077
Non-ischemic Etiology (%)	99,21% (24)	2044	2.410	**1,53 to 3,29**	**< 0.001**	**0,023**
Left bundle branch block (%)	98,85% (8)	773	2.250	**0,88 to 3,63**	**0,001**	**0,046**
Atrial fibrillation (%)	99,49% (5)	358	-0.530	-2,2 to 1,13	0,530	0,123
QRS duration (ms)	0,01% (24)	2044	0.240	**0,12 to 0,36**	**< 0.001**	**0,023**
Ejection faction(%)	0% (21)	1884	0.000	-0.24 to 0.25	0.976	0,192
LVESV (ml)	97,25% (20)	1618	-0.060	-0.24 to 0.12	0.537	0,138
% NYHA II	95,21% (7)	591	1.850	**0,37 to 3,33**	**0,014**	0,062
% NYHA III	98,96% (14)	1317	-0.810	-2,16 to 0,53	0,235	0,100
% NYHA IV	98,75% (8)	765	0.020	-1,44 to 1,48	0,976	0,192
% Diabetes	99,16% (10)	797	-0.790	-2,09 to 0,51	0,235	0,100
% HT	98,06% (8)	447	-0.300	-1,62 to 1,02	0,652	0,154

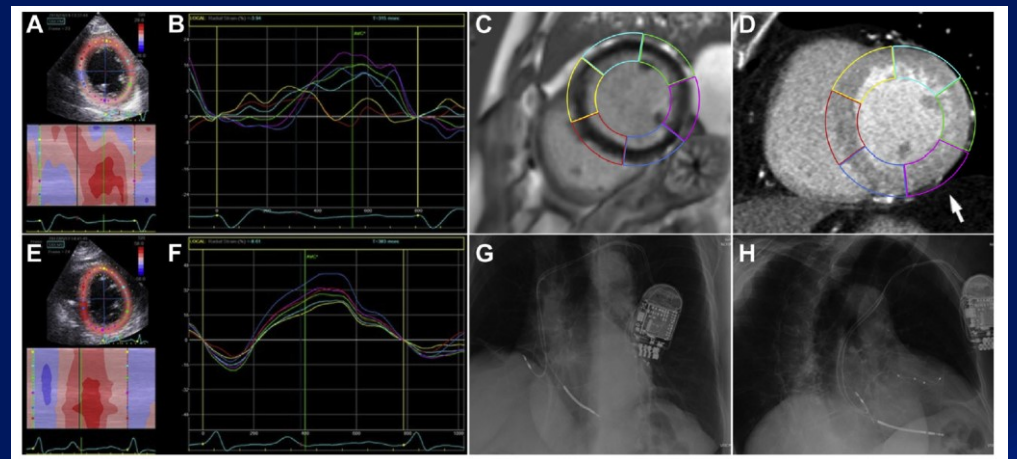


MMI for CRT

- Echocardiography has provided a means of evaluating segmental LV mechanical. Latest or adjacent to the latest activated segments.

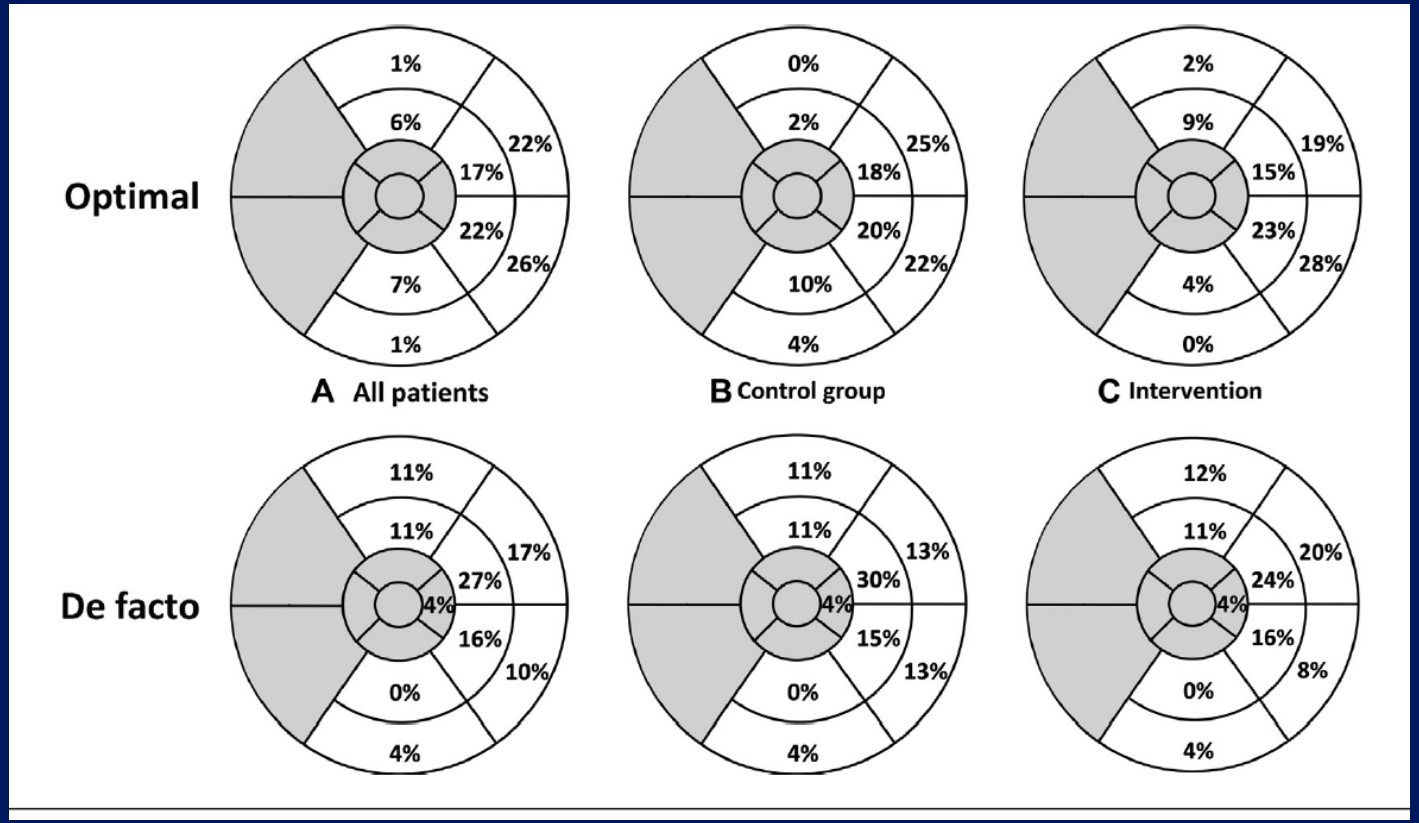
- Cardiac venous anatomy is variable, and cardiac CT before implantation can provide the implanter with pre-operative information on which segments are covered by suitable cardiac veins for lead placement.

- For assessment of myocardial scar, CMR with gadolinium-based contrast remains the gold standard



Borgquist, R. et al. J Am Coll Cardiol EP. 2020;6(10):1300-9.

The Importance of targeting the latest mechanically activated segment



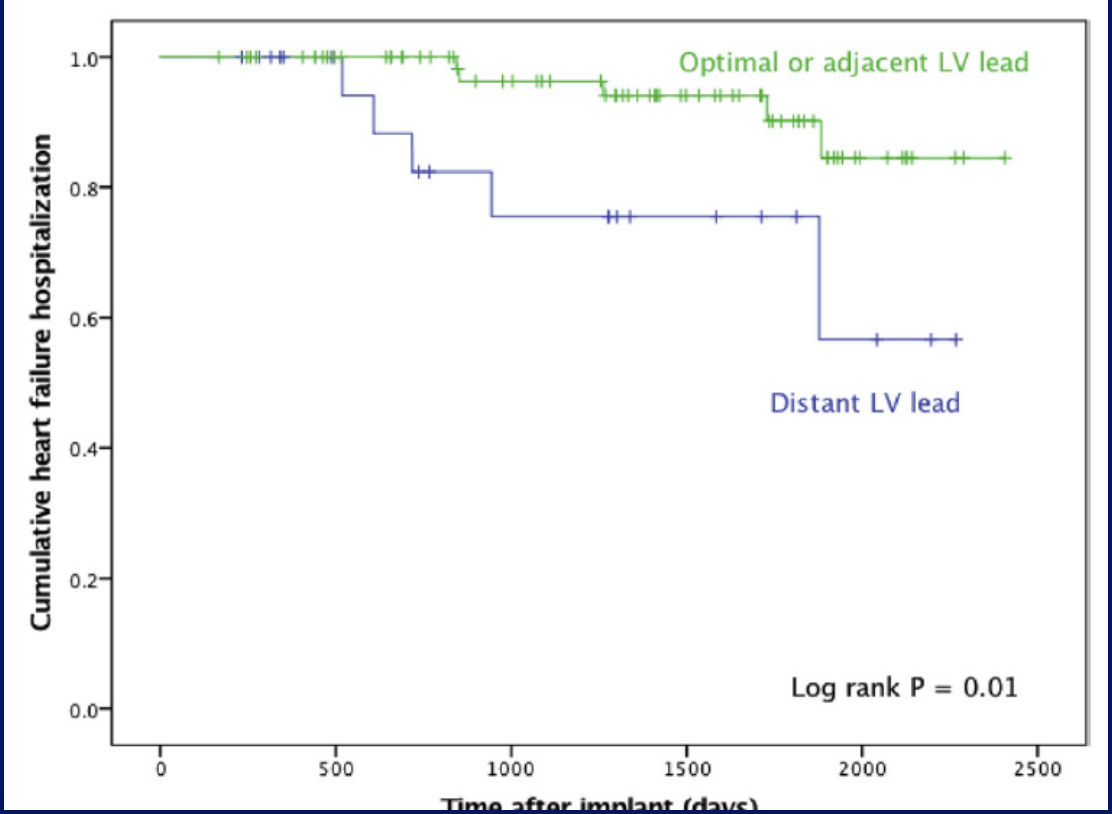
CRT HF and Scar

- In this prospective randomized study of >100 patients, there was no difference in outcome by targeting a late mechanically activated scar-free segment using multimodality imaging compared with standard of care.

- The intervention was not associated with a higher remodeling response rate nor with better clinical outcome.

Borgquist et al. JA C C : EP , 2 0 2 O

The Importance of targeting the latest mechanically activated segment

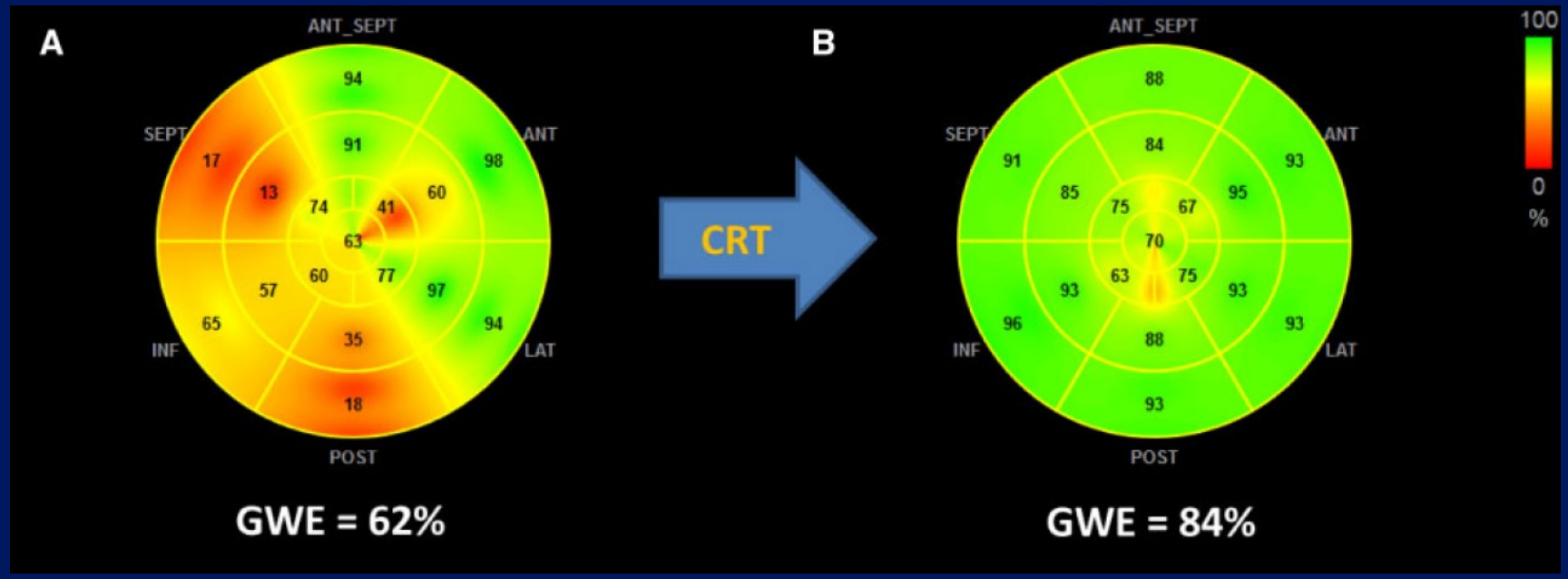


- In the on-treatment analysis, patients with concordant (optimal or adjacent) lead position did have a better clinical outcome compared with patients with distant LV lead placement.
- This difference was primarily driven by a reduced risk of hospitalization for HF, reduced mortality, but total mortality was low in both groups.
- **The on-treatment result could imply that when the implanter succeeded in targeting the latest mechanically activated segment, there was a beneficial clinical effect with regard to long-term outcome.**

Borgquist et al. JA C C : EP , 2 0 2 O

Prognostic implications of global, left ventricular myocardial work efficiency before cardiac resynchronization therapy

Pieter van der Bijl[1], Ngoc Mai Vo[1], Marina V. Kostyukevich[1,2], Bart Mertens[3], Nina Ajmone Marsan[1], Victoria Delgado[1], and Jeroen J. Bax[1]*

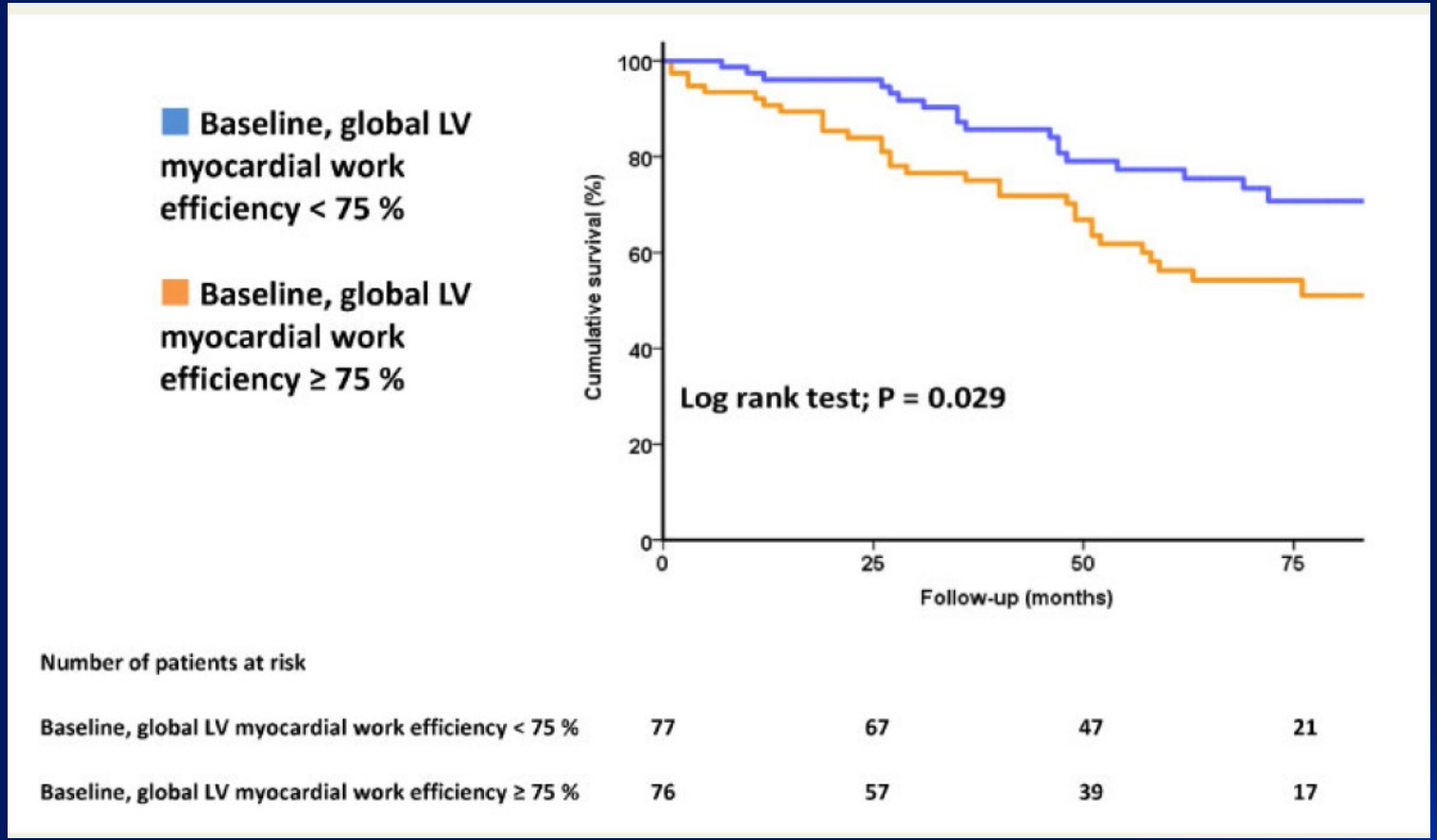


GWE= [constructive work/(constructive work - wasted work)]X100%]

Table I Baseline patient characteristics

	Overall population ($n = 153$)	GLVMWE <75% ($n = 77$)	GLVMWE ≥75% ($n = 76$)	*P*-value
Age (years)	65.5 ± 10.2	64.0 ± 9.9	66.9 ± 10.3	0.081
Gender male, *n* (%)	110 (71.9)	48 (62.3)	62 (81.6)	0.008
Ischaemic aetiology, *n* (%)	74 (48.4)	33 (42.9)	41 (53.9)	0.170
Heart rhythm at baseline, *n* (%)				
Sinus rhythm	139 (90.8)	72 (93.5)	67 (88.2)	0.400
Paced rhythm	14 (9.2)	5 (6.5)	9 (11.8)	0.251
NYHA functional class, *n* (%)				
II	48 (31.4)	22 (26.8)	26 (34.2)	0.489
III	90 (58.8)	47 (61.0)	43 (56.6)	0.575
IV	15 (9.8)	8 (10.4)	7 (9.2)	0.806
6 MWT (min)	344.7 ± 114.7	371.3 ± 111.3	316.7 ± 112.4	0.011
QoL score	30.2 ± 19.4	27.8 ± 17.8	33.0 ± 20.9	0.135
Diabetes, *n* (%)	24 (15.7)	8 (10.4)	16 (21.1)	0.070
eGFR <60 mL/min/1.73 m^2, *n* (%)	55 (35.9)	27 (38.0)	28 (40.0)	0.810
LVEF (%)	24.9 ± 6.9	22.4 ± 6.9	27.5 ± 5.8	<0.001
LVEDV (mL)	216.1 ± 78.5	232.3 ± 81.8	199.8 ± 71.8	0.010
LVESV (mL)	164.2 ± 67.2	182.2 ± 71.8	146.0 ± 57.1	<0.001
GLVMWE (%)	74.6 (IQR 66.2–81.4)	66.3 (IQR 61.1–70.6)	81.4 (IQR 77.5–85.3)	<0.001[a]

Cardiac work which is performed by an early-activated LV segment on an opposing, late-activated LV segment (elongating the late activated segment during contraction of the early-activated segment), does not contribute to the LV stroke volume, and leads to inefficient LV function



Number of patients at risk

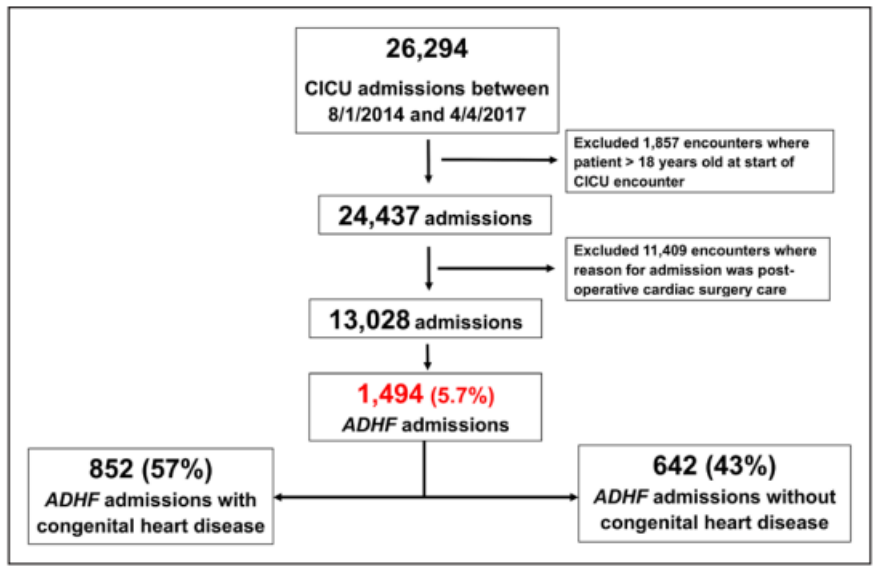
Baseline, global LV myocardial work efficiency < 75 %	77	67	47	21
Baseline, global LV myocardial work efficiency ≥ 75 %	76	57	39	17

Pediatric Heart Failure

- There are some 11,000-14,000 heart failure-related admissions in children annually in the United States.

St Luke healing the Dropsical Child, Giovanni Lanfranco 1620

PHF Morbidity and Mortality



Pediatric CICU admissions to define the epidemiology of critical ADHF and to determine risk factors for mortality in a multicenter North American clinical registry dedicated to this patient population (Pediatric Cardiac Critical Care Consortium [PC4]).

Lasaet al. Circ Heart Fail. 2020;13:e006101. DOI: 10.1161/CIRCHEARTFAILURE.119.006101

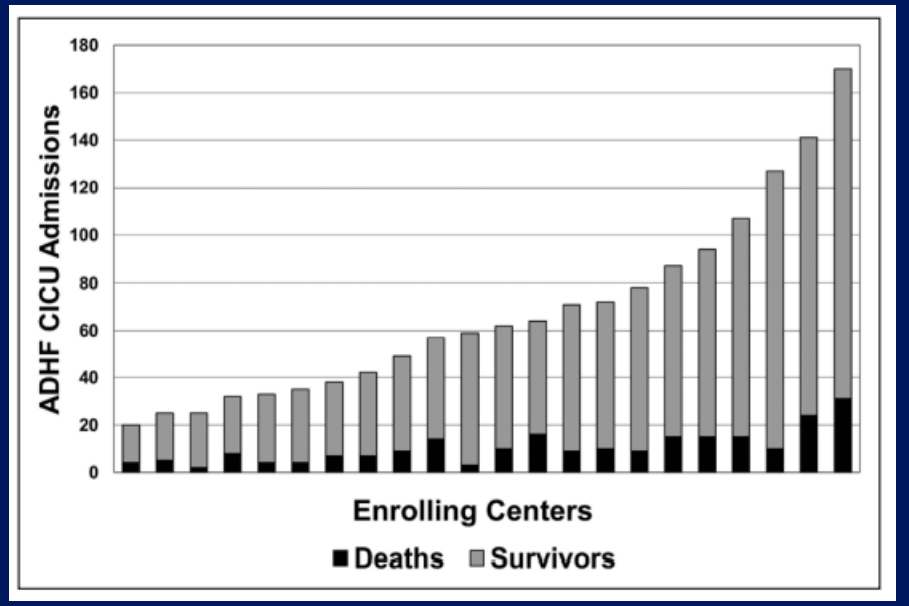
PHF vs AHF

- **Adults with ADHF** are more likely to present with features of **congestion and fluid overload**, requiring treatment with diuretics,
- **Children with ADHF** present rather than with features of a **low cardiac output** state or **respiratory failure** necessitating the addition of **vasoactive medications or mechanical ventilation**.

van Diepen S, et al. Int J Cardiol. 2014;177:840–846. doi: 10.1016/j. ijcard.2014.11.007

PHF Mortality

- Hospital-wide and CICU-specific mortality rates were **19% and 15%,** respectively, compared with reports of **4% to 9%** all-cause 30-day mortality in adults with acute HF syndromes admitted to higher acuity units.
- **Inotropic** medications are utilized in **14% to 53% of adults** hospitalized in an ICU for ADHF
- **Children in PC4** were treated with inotropes much more frequently (**up to 88**%).



Etiology in PHF

- Adult HF mainly relates to ischemia (60-70% of cases), PHF is consequence of CHDs or cardiomyopathies in most of the cases.

Table 1 Etiology of pediatric heart failure.

Type of diseases	Pathophisiology	Examples
Congenital heart diseases	Left to right shunt (volume overload)	Ventricular septal defects Complete atrioventricular canal defects Patent ductus arteriosus Aorto–pulmonary windows
	Valvular regurgitation (volume overload)	Mitral regurgitation Aortic regurgitation
	Outflow tract obstruction (pressure overload)	Aortic stenosis Tunnel type subaortic stenosis Supravalvular aortic stenosis Pulmonary stenosis Pulmonary vein stenosis
	Coronary insufficiency (decreased O_2 supply to cardiomyocyte)	Coronary artery anomalies
Cardiomyopathies (inherited or acquired)	Systolic dysfunction (low cardiac output) Diastolic dysfunction (elevated pulmonary capillary pressure)	Dilated cardiomyopathy - Myocarditis - Barth syndrome - Carnitine deficency - Familial dilated cardiomyopathy - Neuromuscular disorder (i.e., Becker dystrophy/ Duchenne dystrophy) Hypertrophic cardiomyopathy - Pompe diseases - Noonan syndrome - Maternal diabetes - Mitochondrial diseases - Familial hypertrophic cardiomyopathy Idiopathic restrictive cardiomyopathy
Arrhythmias	Systolic dysfunction (low cardiac output)	Tachycardia induced cardiomyopathy - Atrio–ventricular node reentry tachycardia - Atrio–ventricular reentry tachycardia - Ectopic atrial tachycardia Congenital third degree atrio–ventricular block
Infection	Systolic dysfunction	Sepsis induced myocardial dysfunction
High output state	Volume overload	Thyrotoxicosis Systemic arteriovenous fistula Severe anemia

PHF The CHD Impact

- Congenital heart disease was:
  - present in over half of those hospitalized with ADHF
  - was associated with greater resource utilization,
  - higher complication rates,
  - longer length of stay,
  - increased likelihood of readmission,
  - and poorer survival when compared with children without CHD.
  - Important additional risk factors associated with death include age <1 yrs

Medical therapy for PHF

Current pharmacological therapies for HF in children is extrapolated from adult cardiology practices rather than evidence from controlled clinical trials.

Main goals:
- decrease of pulmonary wedge pressure
- increase of cardiac output
- improvement of end organ perfusion
- delay of disease progression.

Table 4 Drugs used in pediatric heart failure.

Drugs	Routes of administration	Doses
Furosemide	Oral	1–2 mg/kg q6–12h
Furosemide	Intermittent bolus	0.5–2 mg/kg q6–12h
Furosemide	Continuous infusion	0.1–0.4 mg/kg/h
Captopril	Oral	0.3–2 mg/kg q8h
Enalapril	Oral	0.05–0.25 mg/kg q12h
Losartan	Oral	0.5–1.5 mg/kg/d
Carvedilol	Oral	0.05 mg/kg/d q12h
Metoprolol	Oral	0.25 mg/kg/d q12h
Spironolactone	Oral	0.5–1.5 mg/kg q12h
Nitroglycerin	Continuous infusion	0.5–10 μg/kg/min
Nitroprusside	Continuous infusion	0.5–4 μg/kg/min
Hydralazine	Intermittent bolus	0.1–0.2 mg/kg every 4–6 h
Hydralazine	Oral	0.3–1 mg/kg/d in q8–12h
Digoxin	Oral	5–10 μg/kg/d
Dobutamine	Continuous Infusion	2.5–10 μg/kg/min
Epinephrine	Continuous Infusion	0.01–0.1 μg/kg/min
Epinephrine	Intermittent bolus	0.01 μg/kg
Milrinone	Continuous Infusion	0.5–1 μg/kg/min
Levosimendan	Continuous Infusion	0.05–0.2 μg/kg/min

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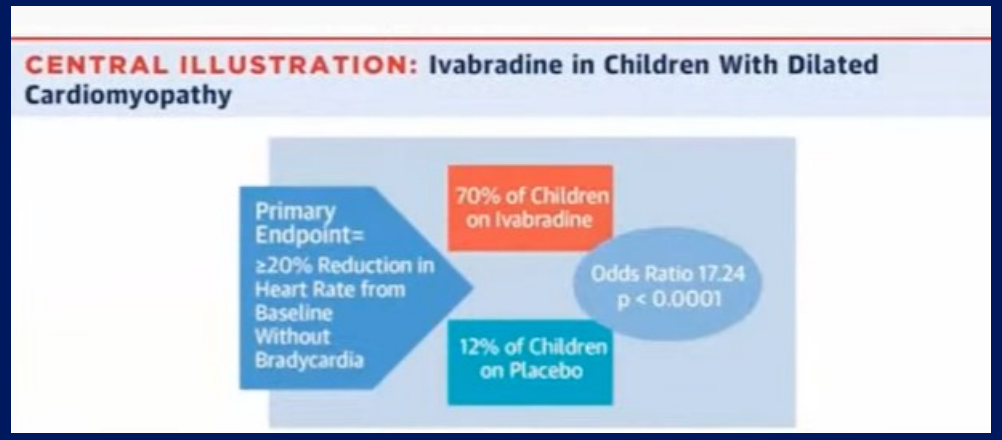
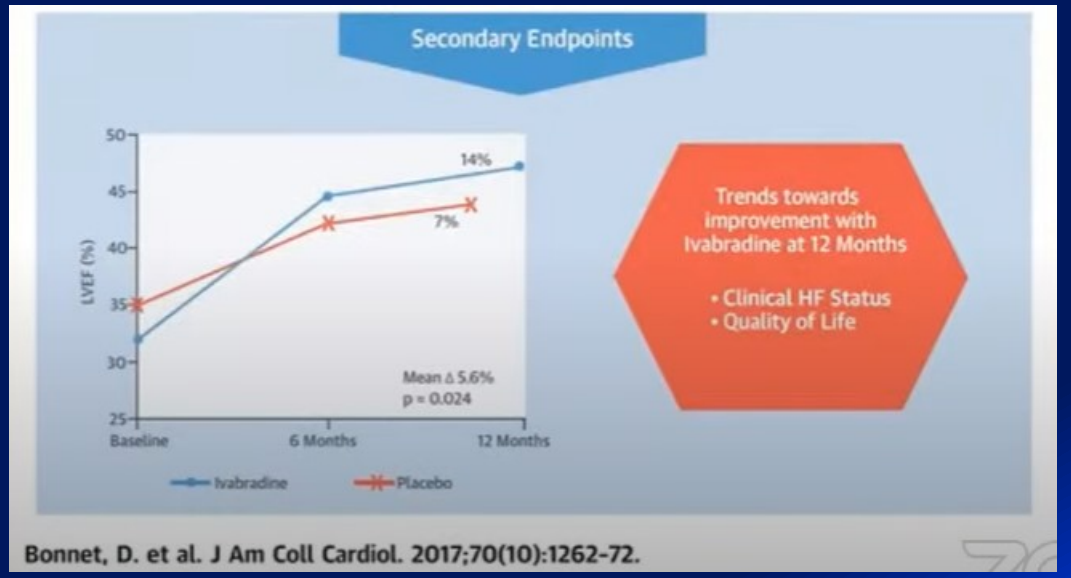
Clinical Trials in PHF

Title	Journal/Year (Reference)	Key Findings
Carvedilol for children and adolescents with HF. A randomized control trial	JAMA, 2007 [25]	N = 161; no significant difference between treatment vs. placebo group in the primary endpoint (clinical improvement) or secondary endpoint (ventricular function or serum BNP).
Safety of enalapril in infants with single ventricle (SV) physiology, multicenter randomized trial	Circulation, 2010 [26]	N − 230; no improvement in somatic growth, ventricular function, or heart failure severity. Routine use of enalapril not recommended in SV patients.
Ivabradine in children with DCM and symptomatic chronic HF trial: a randomized, double-blind, placebo-controlled trial with 12-months follow-up	JACC, 2017 [27]	N = 116; primary endpoint reached by 51 of 73 children taking Ivabradine (70%); Ivabradine safely reduced the resting heart rate of children with chronic HF and dilated cardiomyopathy; improvement in ejection fraction, functional class, and NT-pro BNP was noted.





Pulmonary Artery Band

- The regenerative strategy is the basis of reversible PAB in infants and young children with dilated cardiomyopathy.
- Application of a reversible PAB for months can increase the contractility of LV by ventricle–ventricle interaction as both RV and LV share a common septum.

FEATURED INNOVATION

Pulmonary artery banding in infants and young children with left ventricular dilated cardiomyopathy: A novel therapeutic strategy before heart transplantation

Dietmar Schranz, MD,[a] Stefan Rupp, MD,[a] Matthias Müller, MD,[a] Dorle Schmidt, MD,[a]

Table 1 Data of Patients With Dilated Cardiomyopathy at Admission and at Final Outcome (See Text)

Pt	Further diagnoses	Weight (kg)	Age (days)	Vent. at admission	Initial BNP (pg/ml)	RVEF (%)	LVEF initial (%)	LVEDD, mm (z-score)
1	MR III°, P 35 wks, hydrops fetalis	2.4	1	Yes	6,910	Almost N, echo	13, echo	41 (+8.6)
2	MR II-III°	10	561	No	1,219	55, MRI	22, MRI	52 (+6.2)
3	MR II°, LVNC, Noonan, CPR	3.7	51	Yes	4,324	Almost N, echo	15, echo	35 (+5.8)
4	MR II°, CPR, ECMO, ASD II	9.4	756	Yes	4,858	Almost N, echo	12, echo	45 (+4.9)
5	MR III°, LVNC	6.3	216	No	4,65	46, MRI	15, MRI	52 (+7.9)
6	LVNC, MR II°, MCP, CPR	4.8	69	Yes	5,970	54, MRI	10, MRI	50 (+8.5)
7	MR II°, MCP	8.1	451	No	3,651	29, MRI	12, MRI	48 (+6.2)
8	MR II°, CPR	5.2	185	Yes	2,998	31, MRI	4, MRI	50 (+8.2)
9	MR II°, LVNC	3.5	53	No	924	53, MRI	15, MRI	42 (+7.8)
10	MR I-II°, LVNC	4.1	67	No	1,012	65, MRI	24, MRI	37 (+6.0)
11	MR I-II°, CPR	6.2	188	No	7993	48, MRI	15, MRI	53 (+8.2)
12	MR I-II°	6.4	181	No	843	47, MRI	18, MRI	43 (+5.9)
Mean		5,8	232		3431	48	14.5	46 (+7.0)
SEM		0.68	67.9		735.5	3.8	1.5	1.8 (+0.4)
SD		2.37	235.4		2610.4	11.5	5.2	6.1 (+1.3)

Table 2 Continued

LVEDD at last FU/age in years	BNP at follow-up, pg/ml	DP-PAB at latest or pre-PAB ballooning	Outcome[a]	PAB-ballooning yes/no
			(months after PAB)	(times)
mm (z-score)	(months after PAB)	(mm Hg)		
34 (−0.2)/6.6	15 (78)	90	Ross I (72 months)	Yes (2×)
35 (−0.2)/6.4	27 (58)	64	Ross I (54 months)	Yes (2×)
…	55 (11)	75	Ross I. de-PAB (8 months later)	Died after 1×
42 (+2.1)/5.4	115 (42)	55	Ross I (42 months)	Yes (2×)
46 (+3.1)/3.8	29 (18)	80	Ross I (38 months)	Yes (1×)
33 (+2.1)/1.7	155 (7)	75	Ross I De-PAB (9 months)	Died after (1×)
38 (+2.5)/2	74 (18)	61	Ross II (14 months)	No
25 (+1.1)/1.5	89 (10)	85	Ross II (16 months)	Yes (1×)
26 (+0.8)/1	103 (8)	80	Ross II (12 months)	No
25 (+0.3)/1	314 (11)	59	Ross I (12 months)	Yes (1×)
32 (+1.6)/0.9	3 (8)	53	Ross I (11 months)	No
…	249 (1)	43	Ross II (1 month)	No
34 (1.32)	102	68		
2.24 (0.36)	27.7	4.19		
7.1 (1.14)	96	14.5		

The Journal of Heart and Lung Transplantation, Vol 32, No 5, May 2013

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Methods

- Consecutive patients since September 2015

- Inclusion criteria:
  - age < 4 years
  - hospitalization for heart failure due to LV-DCM
  - preserved RV function
  - failure to wean from inotropes or more than two ICU admissions within the same hospitalization
  - listed for heart transplantation

- Exclusion criteria:
  - biventricular failure
  - TR ≥ moderate
  - idiopathic or reactive pulmonary hypertension (out of proportion with LV-DCM)
  - associated major CHD (ie ALCAPA, ARCAPA, …)

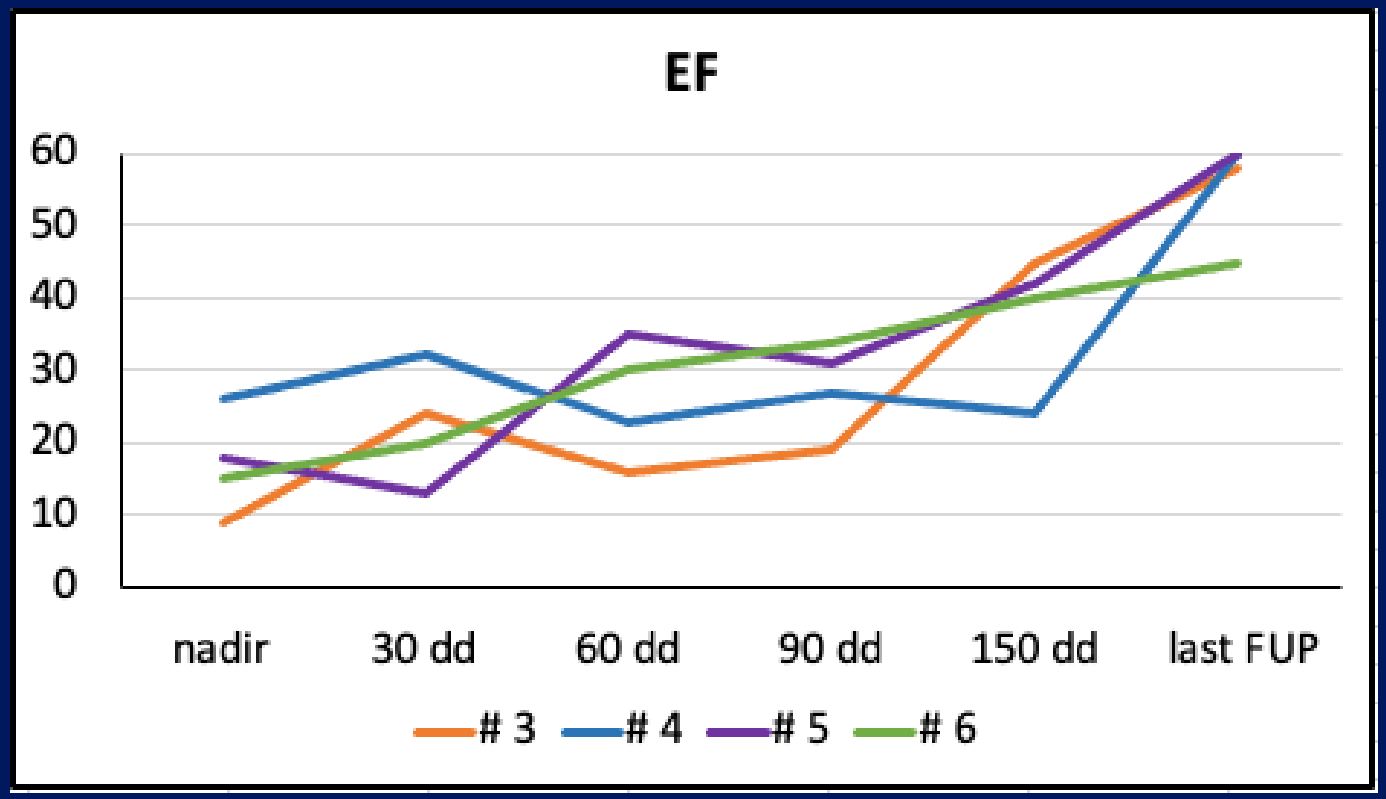
- Outcomes:
  - survival of study population
  - reduction of the need for MCS and OHT
  - improvement of LV shape and function

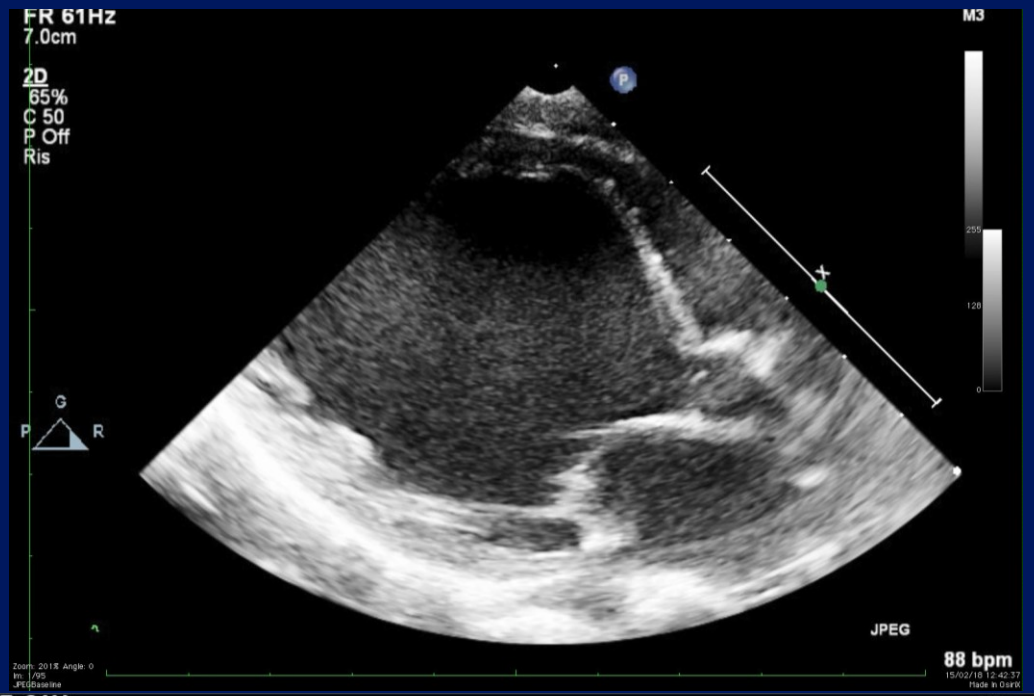
Di Candia A, et al. (2020) Pulmonary Artery Banding for Ventricular Rehabilitation in Infants With Dilated Cardiomyopathy: Early Results in a Single-Center Experience. Front. Pediatr. 8:347. doi: 10.3389/fped.2020.00347

Results

Outpatient visits
n=4

3, 4, 5, 6 : Median follow up 34.9 (range 8.2 - 42.6) months

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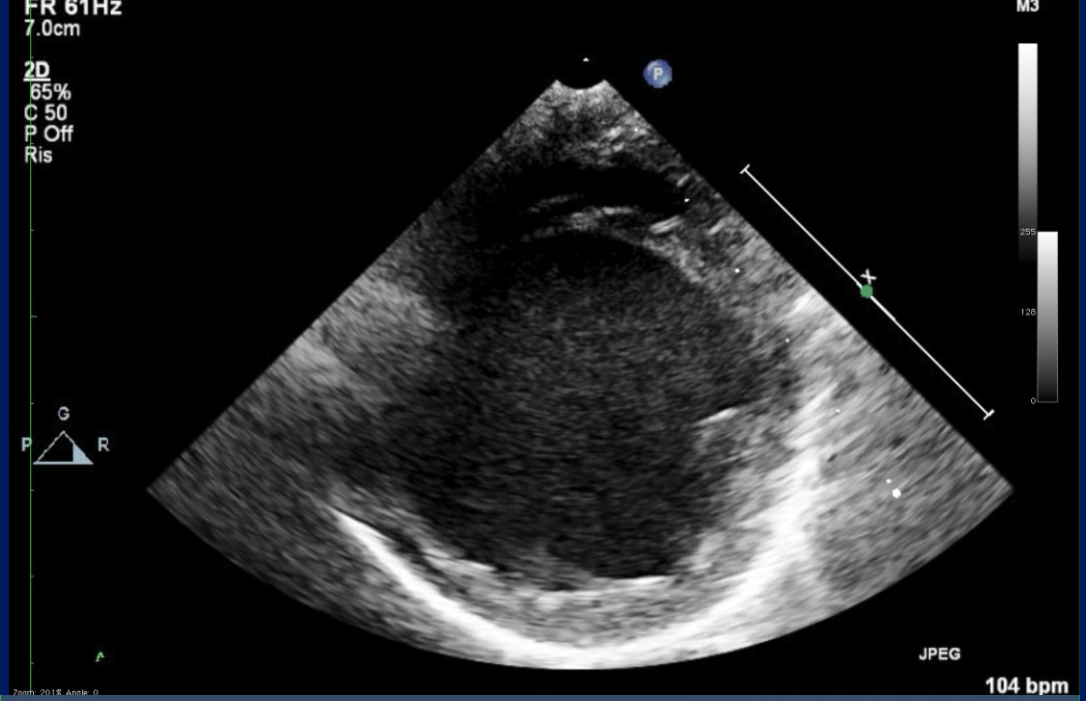
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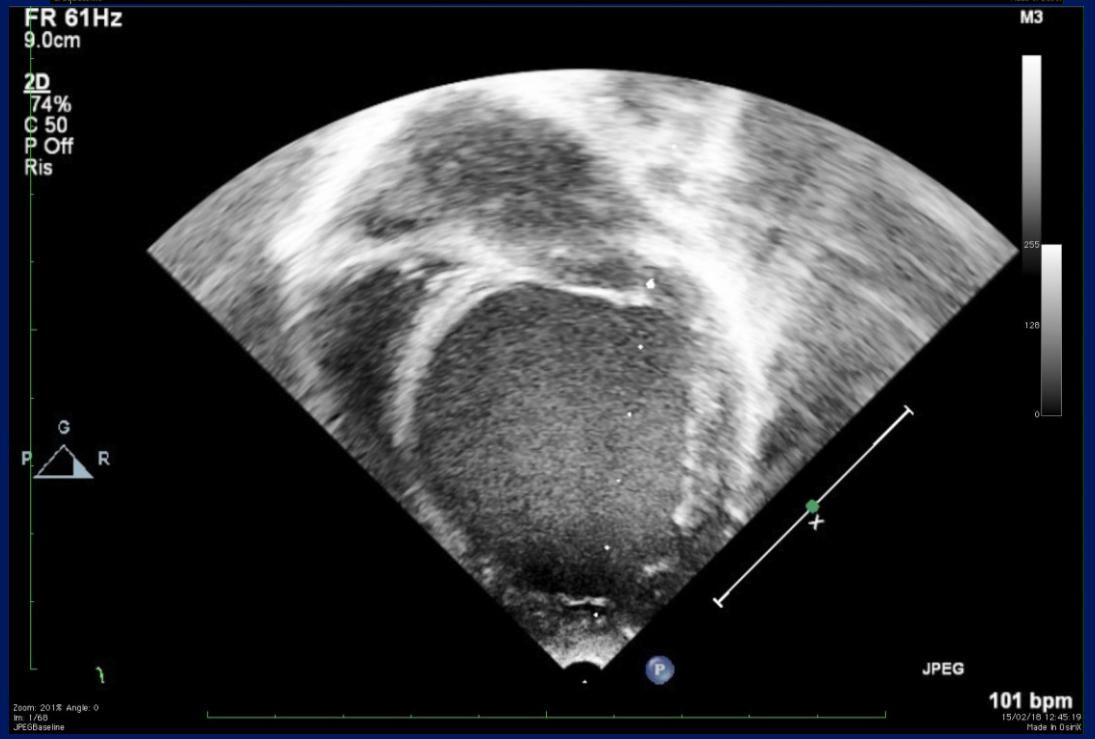
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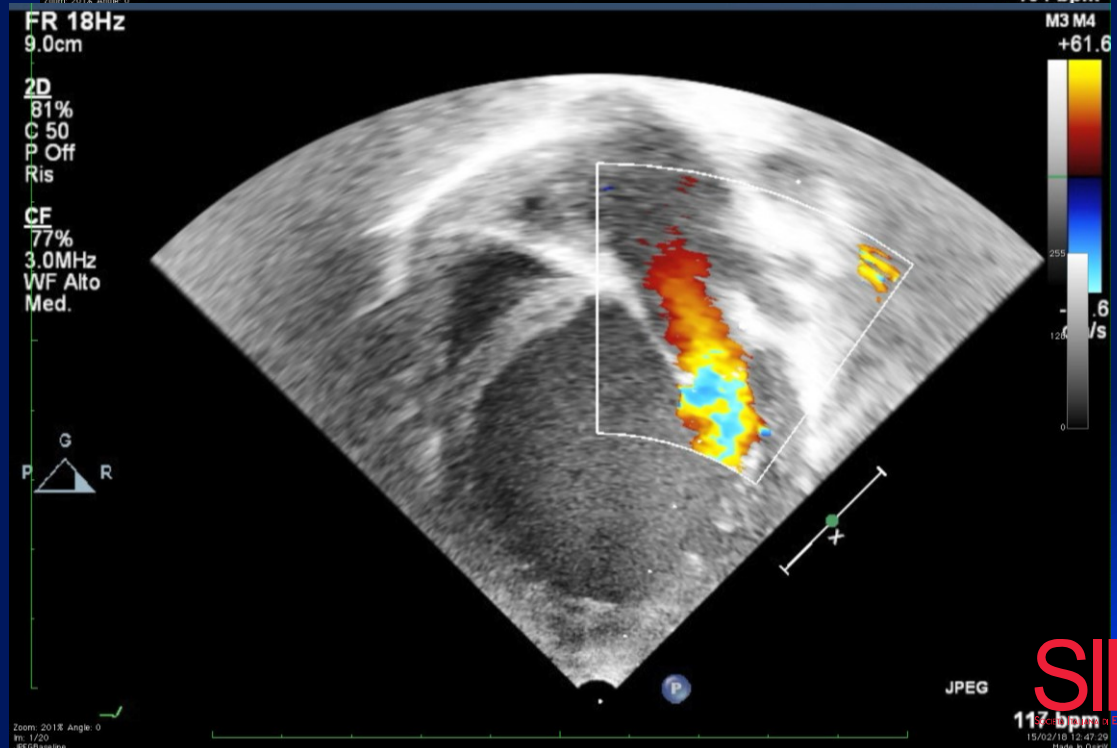
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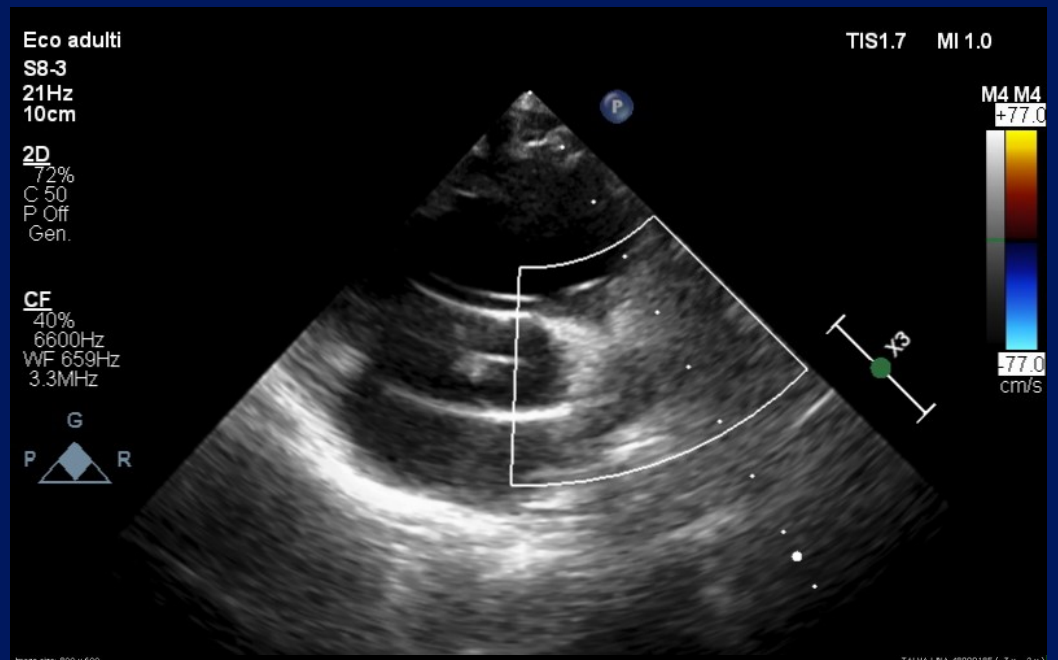
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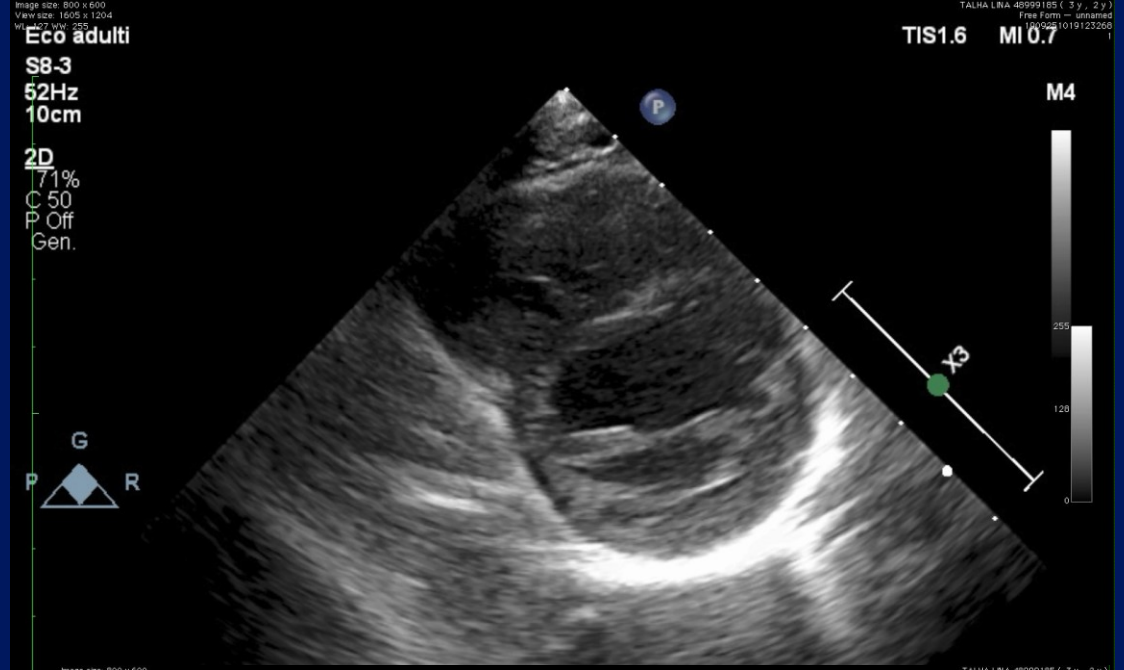
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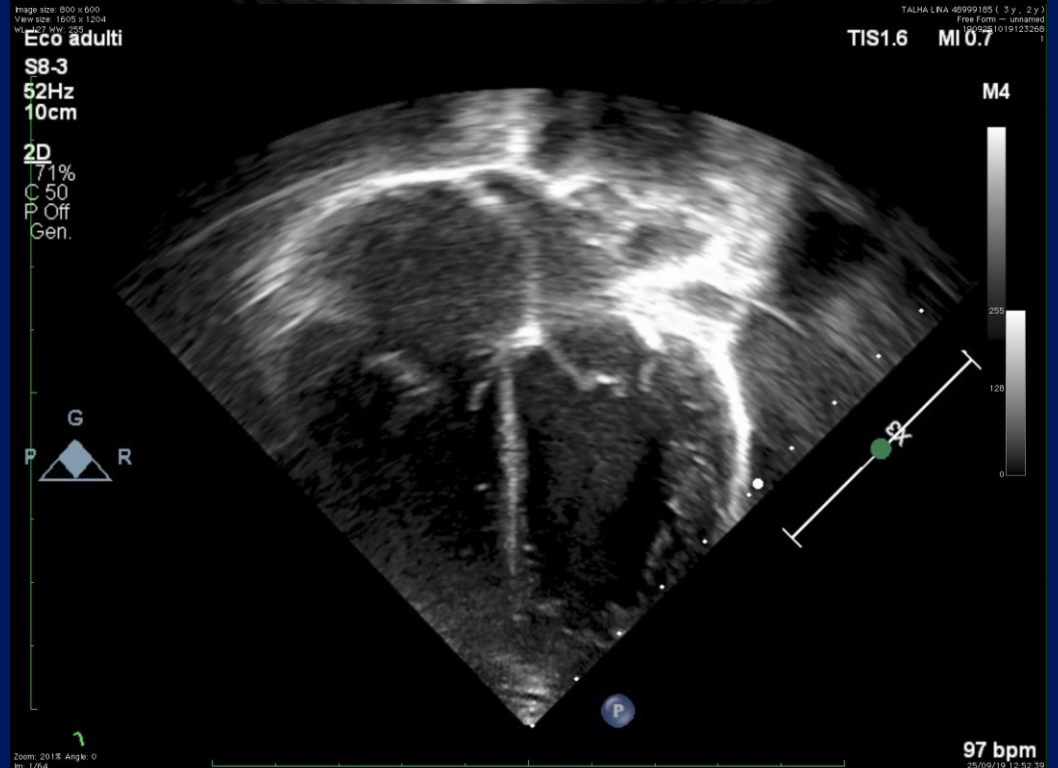
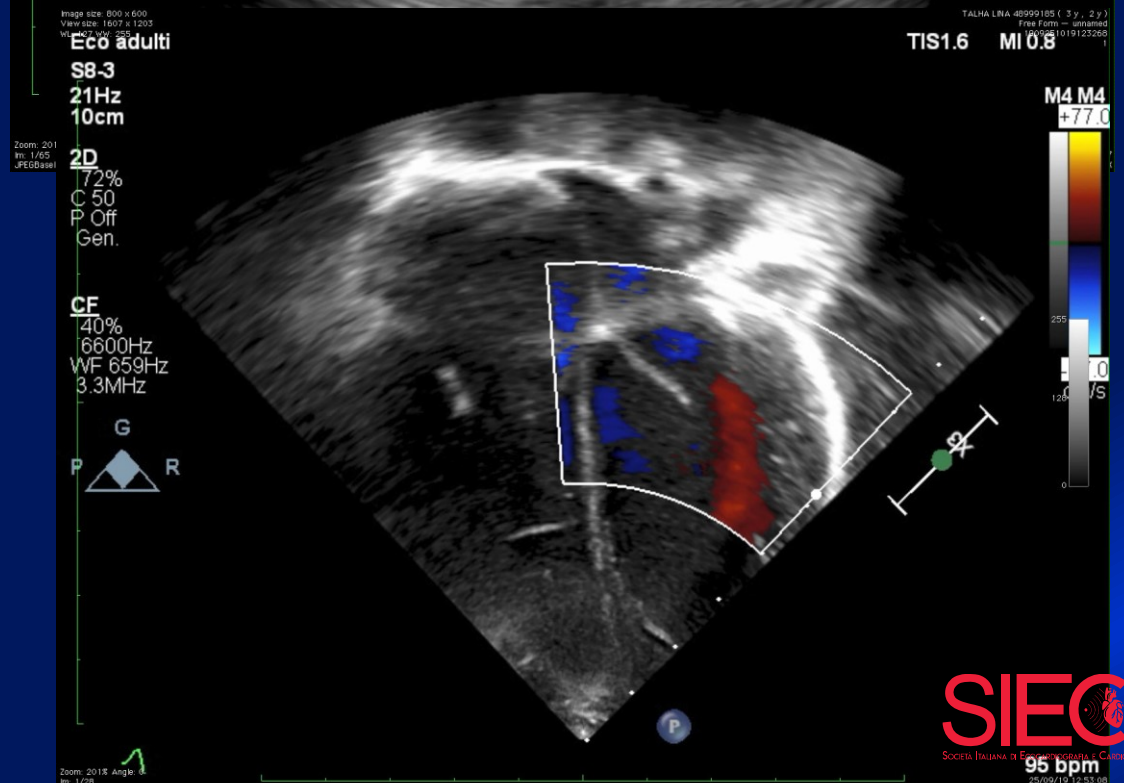
M4
X3
G
P
R


Eco adulti
S8-3
52Hz
10cm
2D
71%
C 50
P Off
Gen.
TIS1.6 MI 0.7
M4
X2
G
P
R
97 bpm


Eco adulti
S8-3
21Hz
10cm
2D
72%
C 50
P Off
Gen.
CF
40%
6600Hz
WF 659Hz
3.3MHz
TIS1.6 MI 0.8
M4 M4
+77.0
X2
G
P
R
95 bpm

Received: 13 April 2021 | Revised: 7 June 2021 | Accepted: 20 August 2021

DOI: 10.1111/aor.14057

MAIN TEXT

Artificial Organs WILEY

Surgical strategies for the management of end-stage heart failure in infants and children: A 15-year experience with a patient-tailored approach

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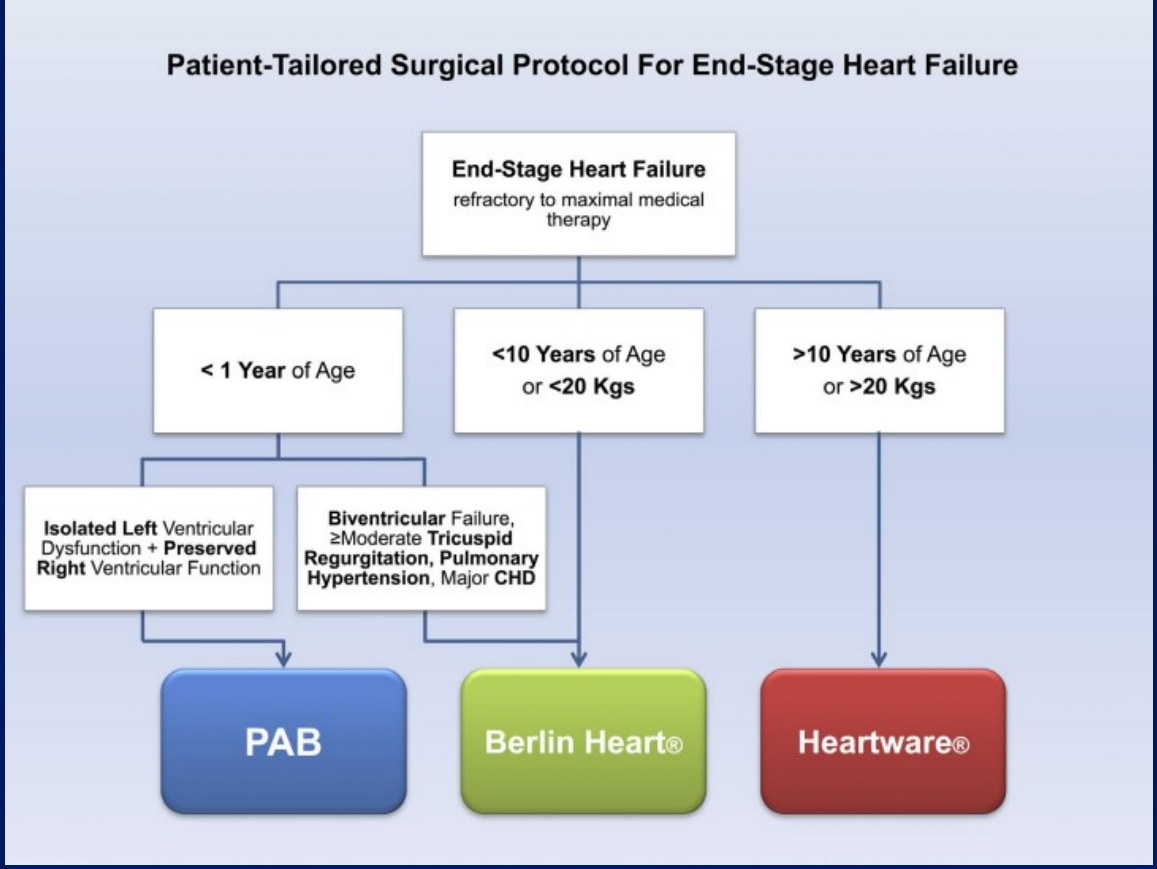
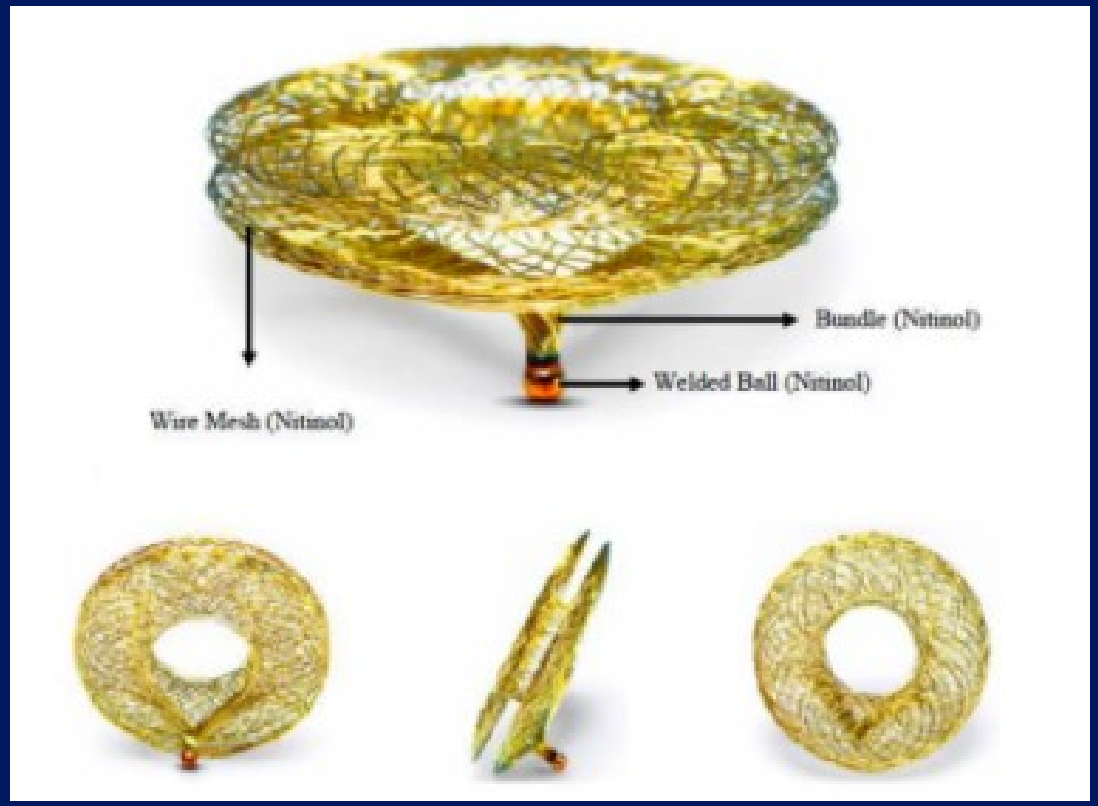


THERAPEUTIC ALTERNATIVES: Atrial Flow Regulator



- Self-expandable percutaneous-delivered fenestrated device
- The device is implanted into the interatrial septum
- Maintain a permanent interatrial communication
- Predetermined diameter

ATRIAL FLOW REGULATOR

Indications
- Heart failure
- Pulmonary hypertension
- Fontan fenestration
- Venting in ECMO

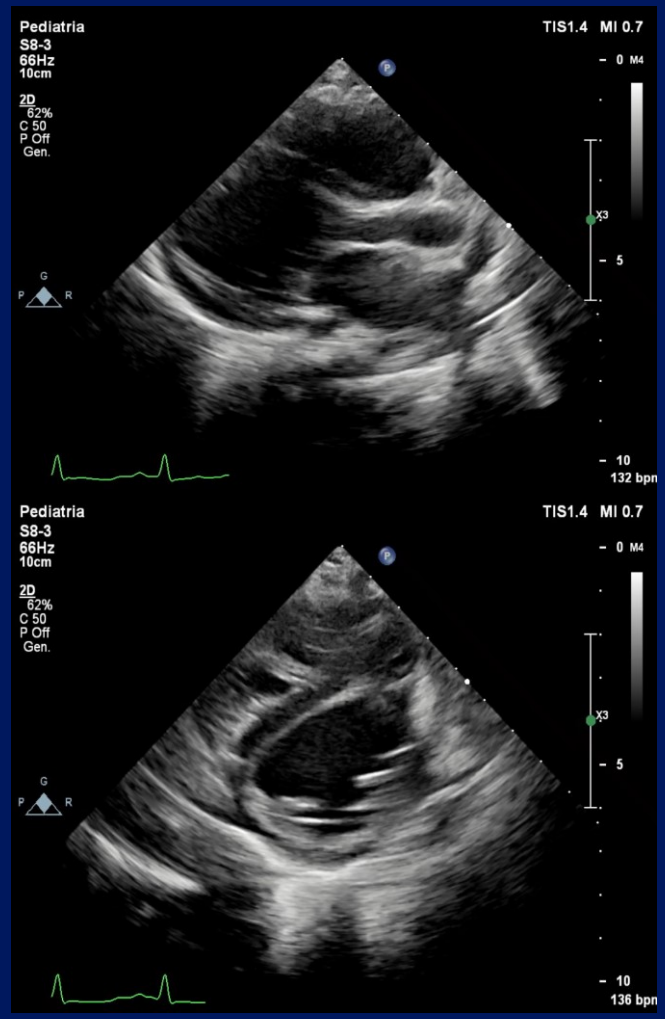
Goals
- Create a small, controlled left-to-right interatrial shunt
- Reduced elevated LA pressure

ATRIAL FLOW REGULATOR: Our experience

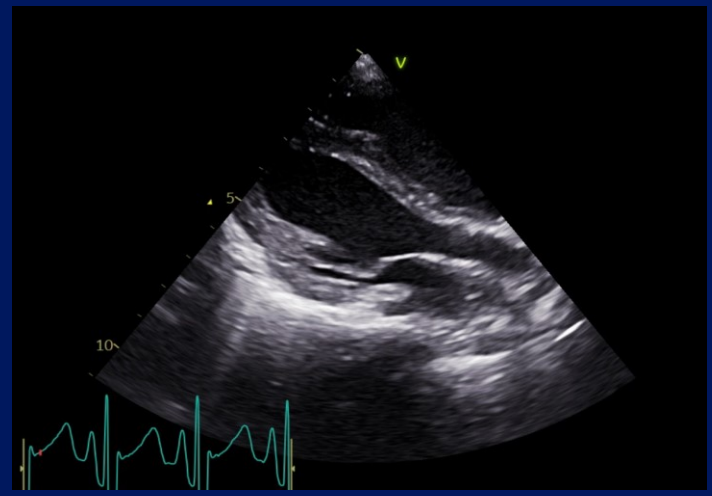
7 months old baby girl, BW 6.2 kg
New diagnosis of CMD

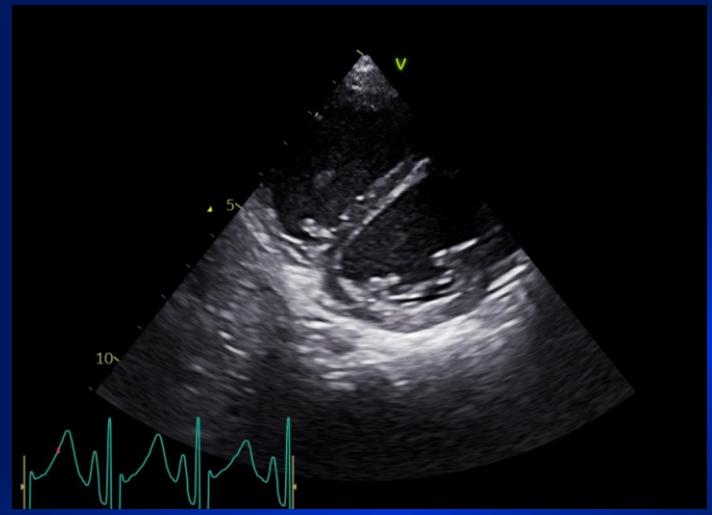
Clinical examination:
- Tachycardia
- Metabolic acidosis
- Oliguria
- Feeding intolerance

ECHO
- EF 5-10%
- severe mitral insufficiency



After AFR





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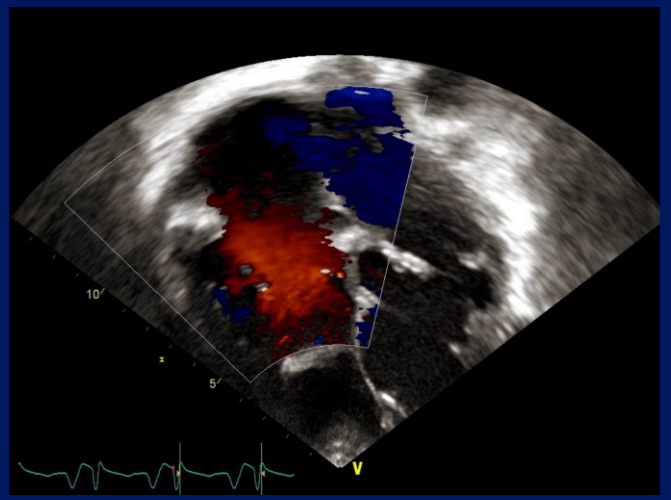
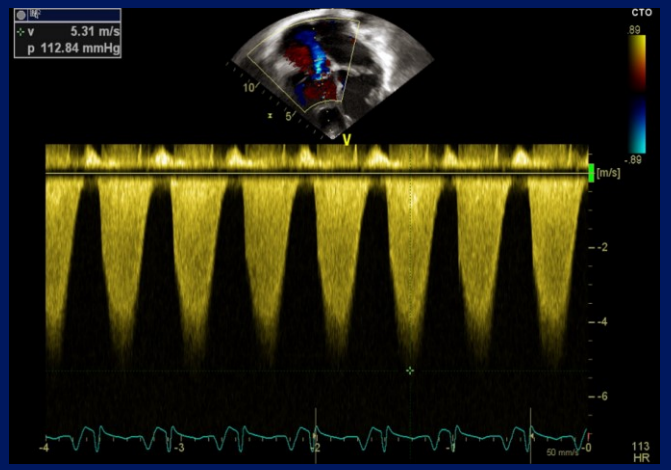
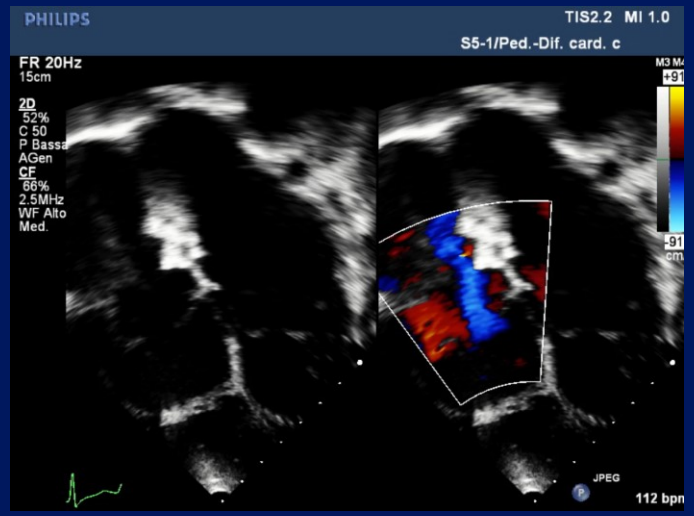
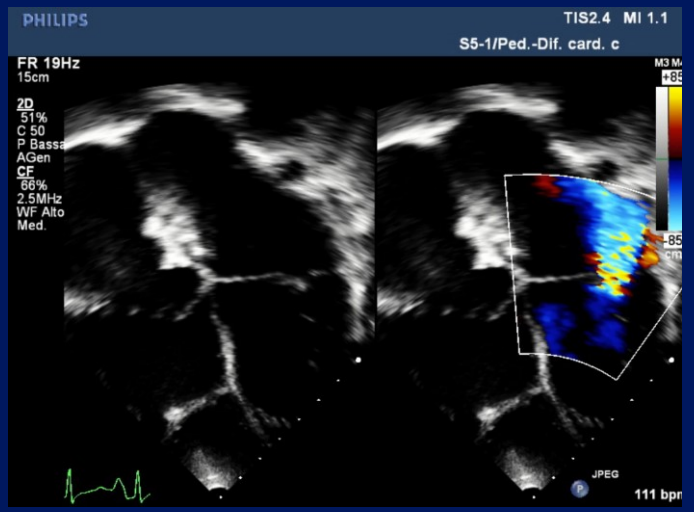
ATRIAL FLOW REGULATOR:
Our Experience

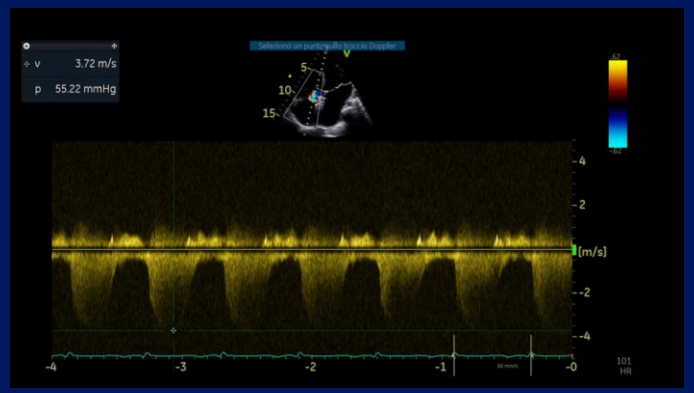
After AFR

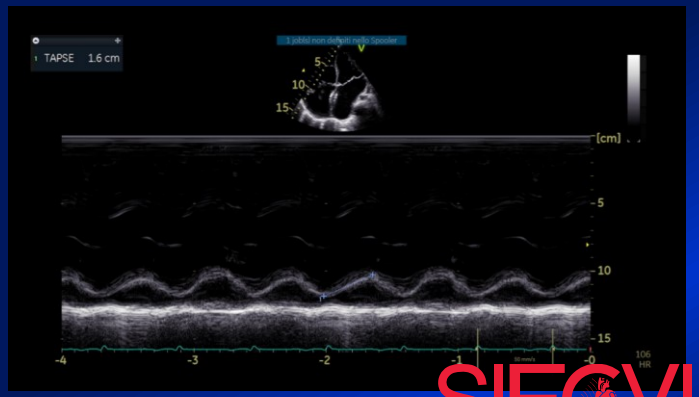












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Conclusions