Great Ormond Street Hospital for Children NHS Foundation Trust

UCL

Right Ventricle in CHD: from High Afterload to High Preload and back

Jan Marek

Great Ormond Street Hospital
&
Institute of Cardiovascular Sciences, University College London

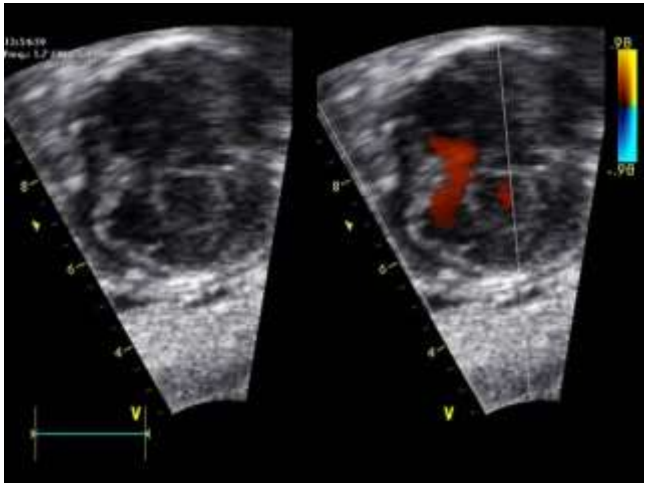
No disclosures

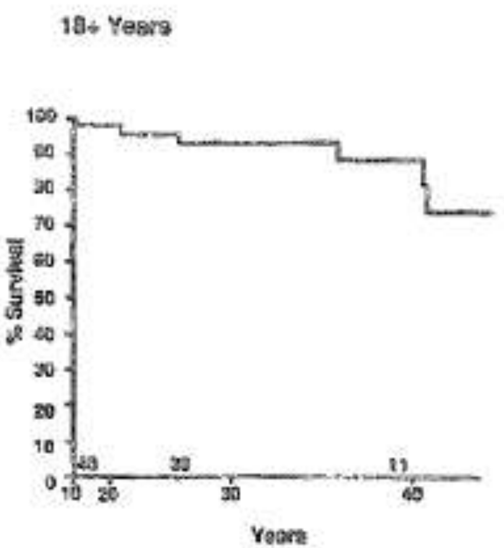
Natural history: Ebstein`s anomaly

Mortality rate 45% in utero

- Cardiomegaly
- TR
- Fetal hydrops
- Arrhythmia
- RV/LV dysfunction
- Cardiac failure

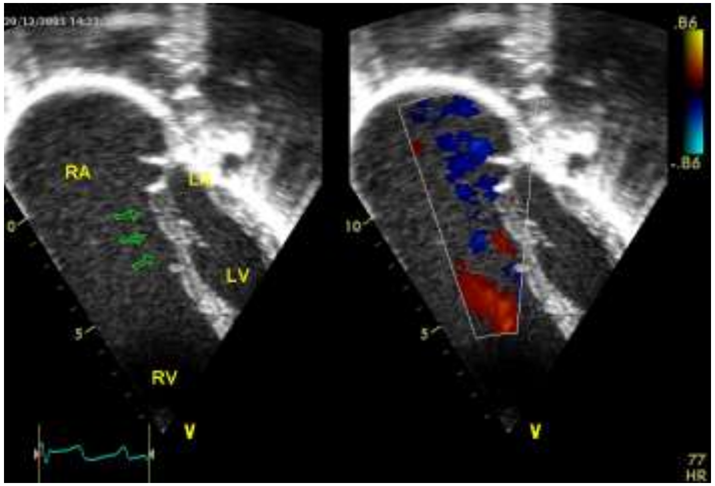
Fetus 28.wog



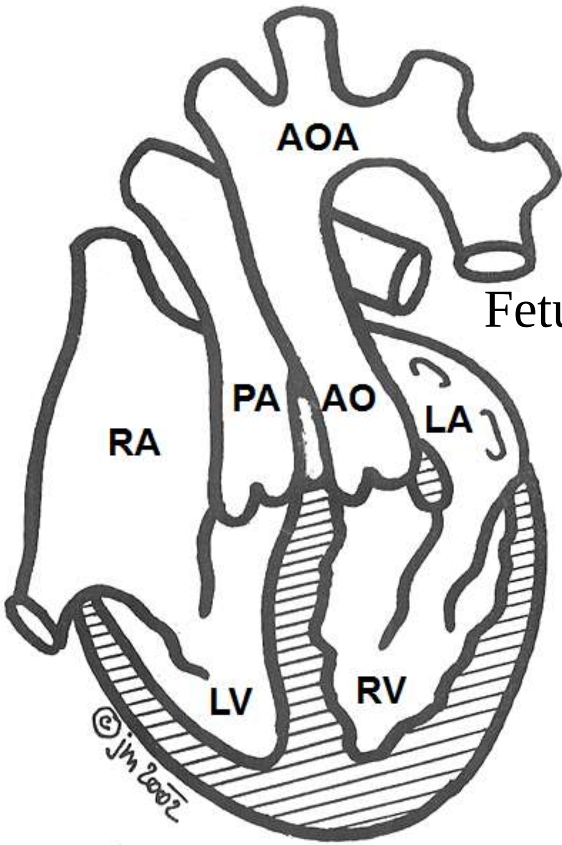


Celemajer D JACC 1992

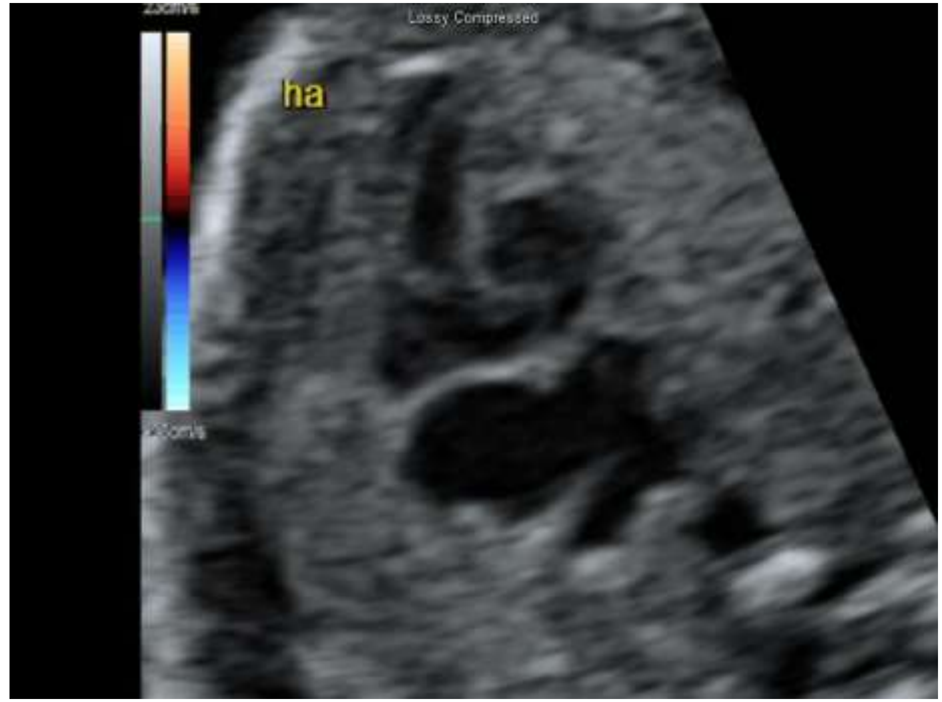
Child 18 yrs



Natural history: CcTGA

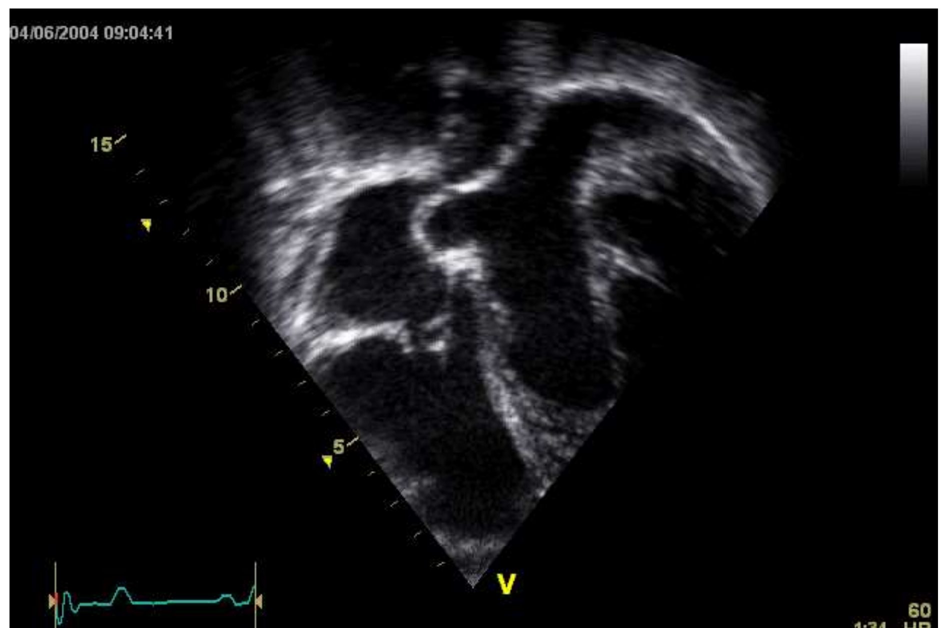


Fetus 32.wog



1 cm

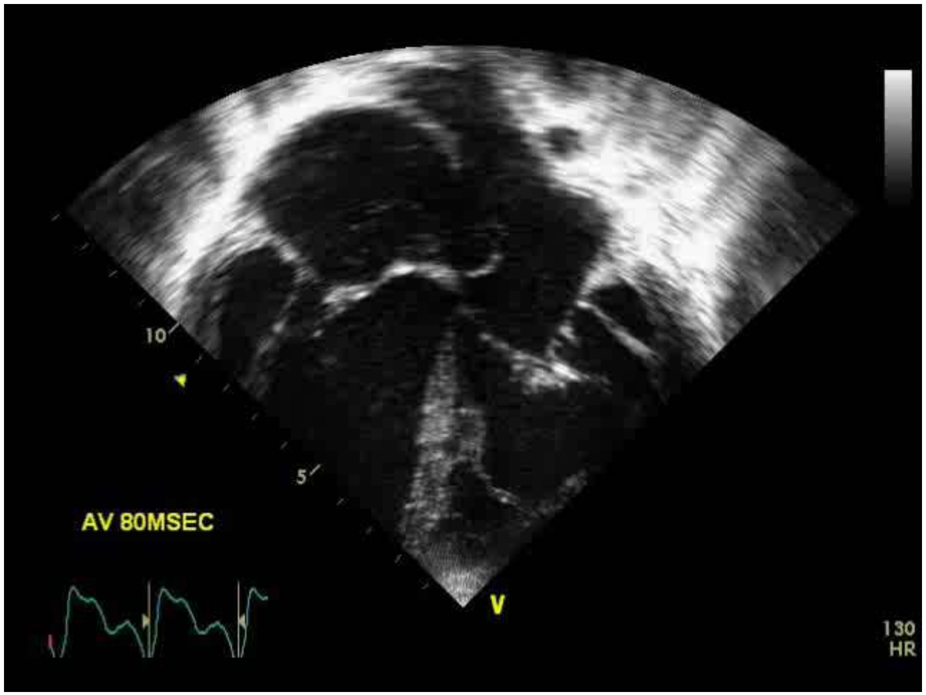
Adult 32.yrs

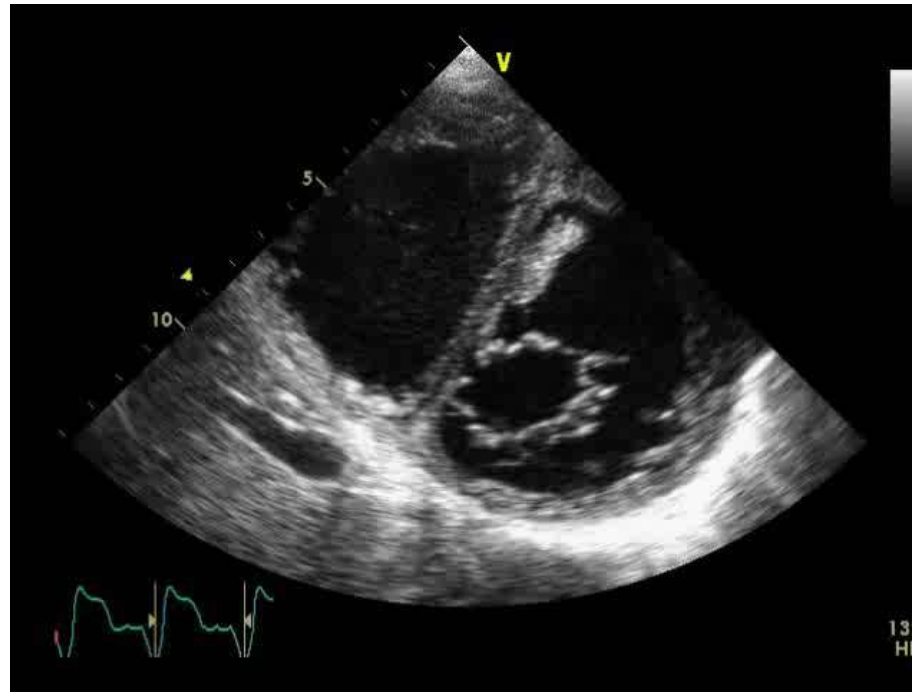


10 cm

Natural history: CcTGA

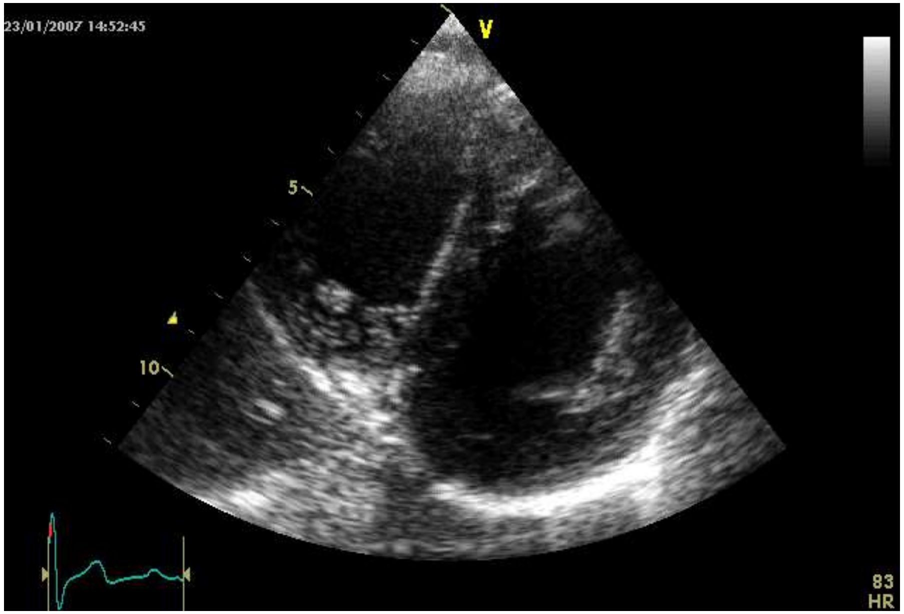
Child 12.yrs

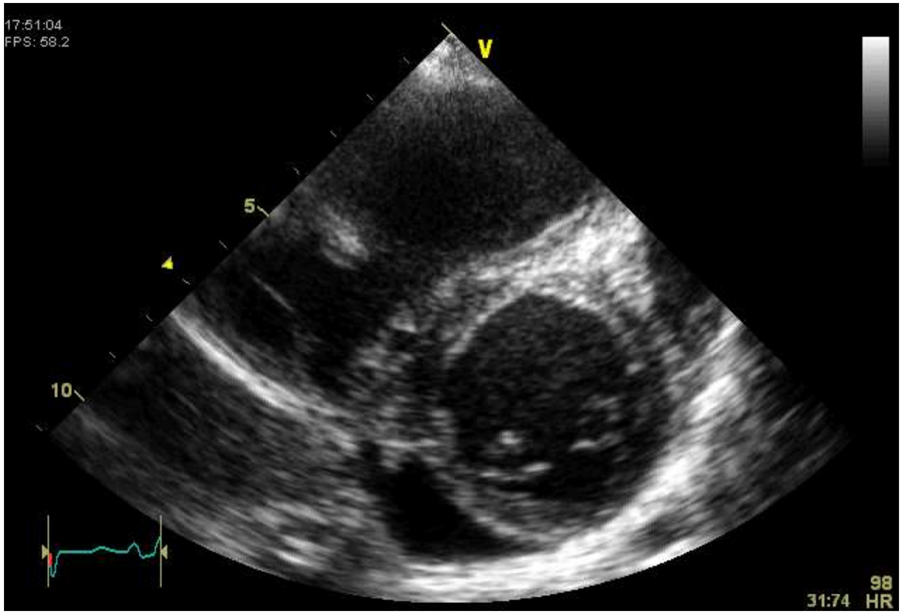




No response to CRT
(RV pacing, LV pacing or BiV pacing)

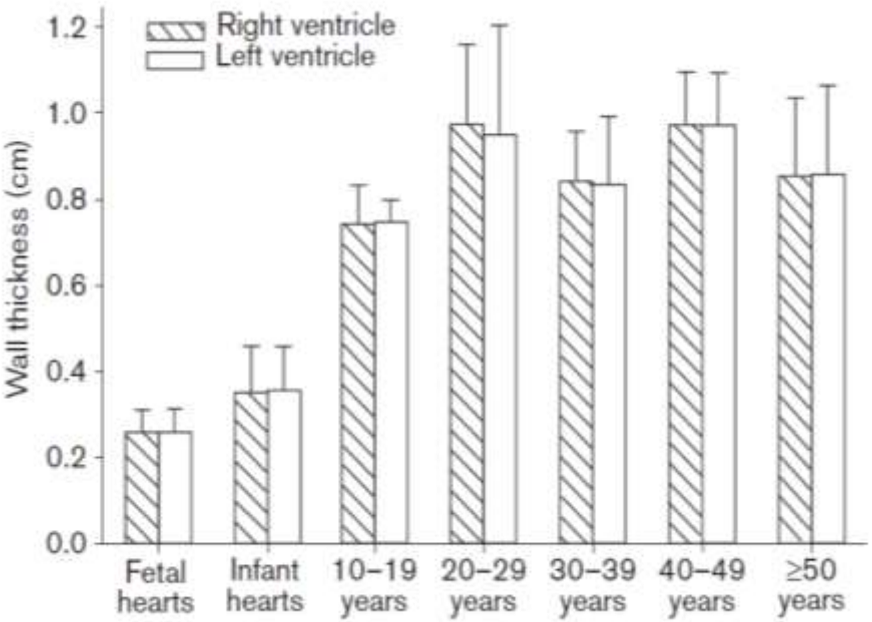
Systemic RV Eisenmenger sy	Pulmonay arterial hypertension

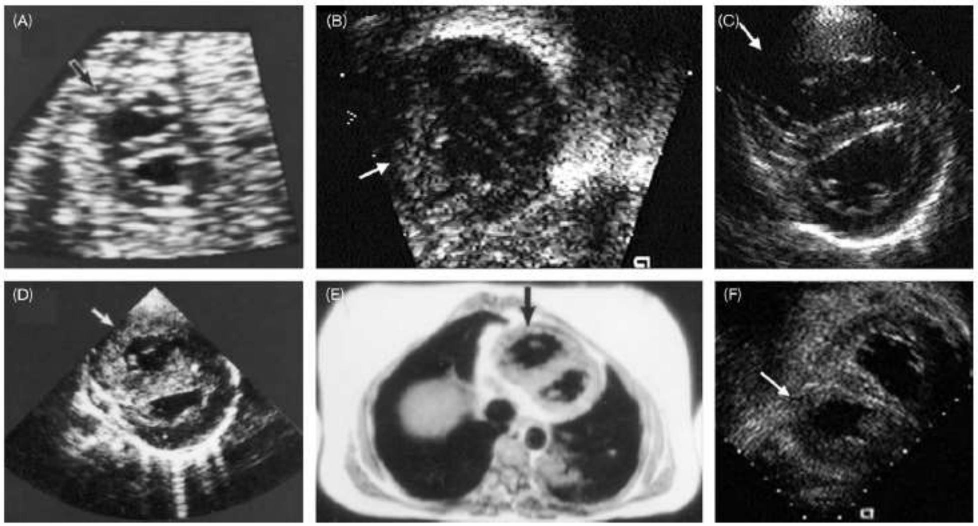




Same age patients, same PAp/PVR

Eisenmenger syndrome





In patients with Eisenmenger syndrome, **regression of right ventricular wall thickness never occurs** and **contractile function is preserved** for life in the majority of patients

Hopkins WE, Coron Art Dis 2005

Right ventricular function: questions to be answered

- Why fetal RV myocardium exposed to high afterload does not tolerate high afterload postnatally? **(PH)**

- Why conversely RV myocardium tolerates high afterload for decades? **(ccTGA)**

> Diagnosis of isolated CcTGA in 92-year old… *Karl T, EJCTS 2016*

- Why RV myocardium tolerates high preload postnatally decades **(PR in TOF, ASD)** but prenatally tends to fail within the days **(SVT, TTTS)**

- Why **Eisenmenger patients** are doing clinically better than **Pulmonary Hypertension patients**?

Postnatal RV adaptation

- **Differences between fetal and postnatal myocardium** in energy metabolism, myosin heavy chain characteristics and intra- extracellular components

- With the **fall of PVR postnatally**, RV remodels to a low pressure, high compliance chamber and becomes **sensitive to pressure load**

- **Chronic pressure loaded RV** (Eisenmenger s.) adapts a transition to a so-called ***"fetal gene program"*** with a shift from alpha to beta myosin heavy chain expression, an increase in adrenergic receptors, calcineurin activation and increased phosphodiesterase type 5 expression

Right Ventricle: Morphological and Functional Considerations

RV function

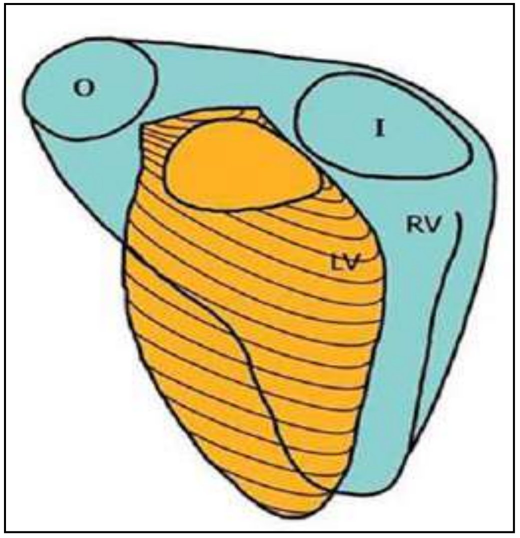
Peristaltic wave contraction from the inflow to the outflow regions, propelling the blood in the direction of the outflow tract

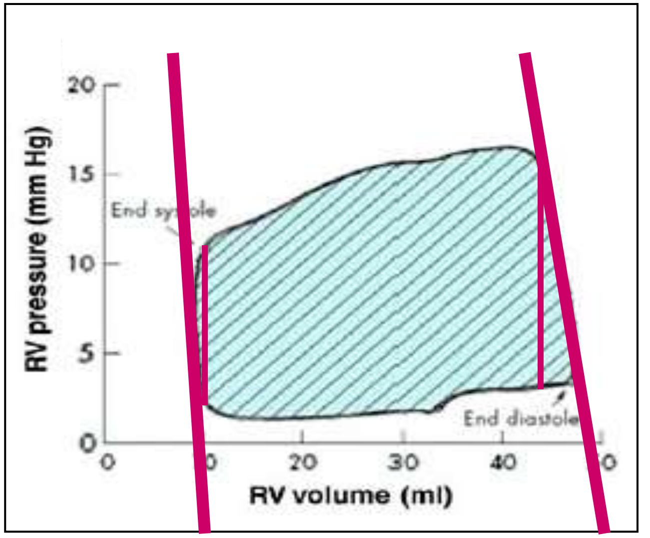
Mechanism of RV contraction:

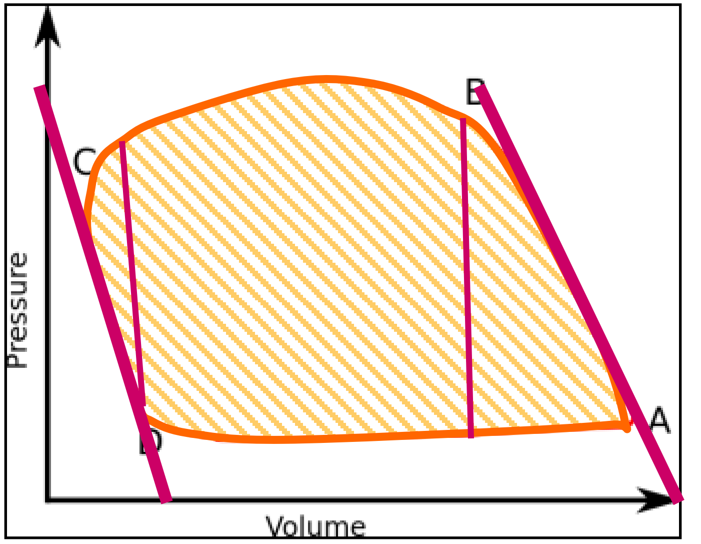
- **Inward movement** of the free wall (bellows effect)
- **Contraction of longitudinal fibers (deep layer)**
  Contraction of circumferential fibers (superficial layer)
- **Traction on the free wall** at points of attachment secondary to LV contraction

Asynchronous (peristaltic) contraction pattern

Interdependence with LV – **Septal function !**





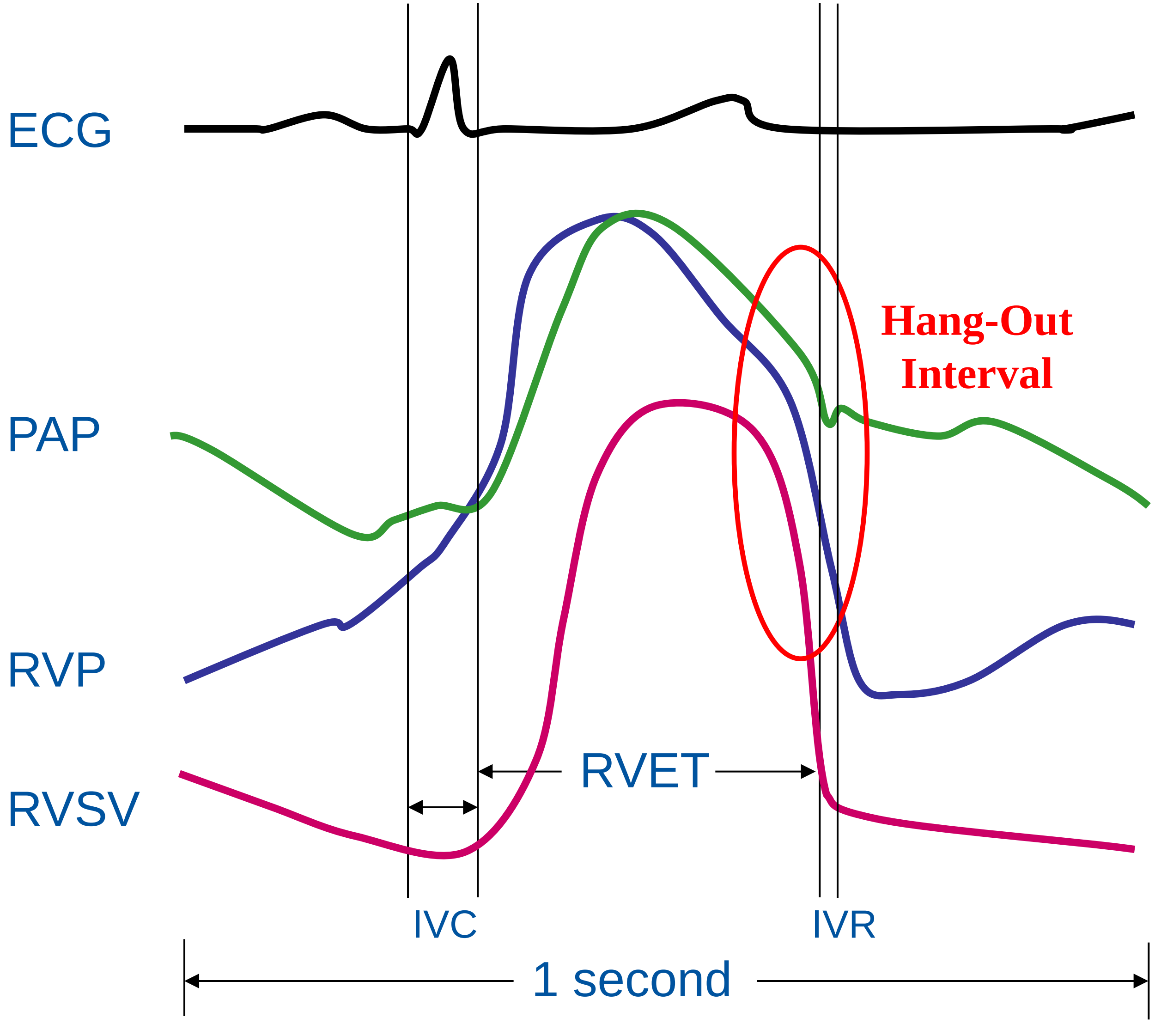


- RV stroke volume same as in LV but **RV stroke work less by 25%** (less energy cost)
- Trapeziodal shape of RV pressure–volume curve with **ill-defined isovolumic contraction and particularly isovolumic relaxation**
- Since RV systolic pressure exceeds rapidly the low pulmonary artery diastolic pressure, **RV isovolumic contraction time is extremely short**

Vitarelli A, Heart Fail Rev 2010

Normal RV

2nd part systole: RV pressure lower than PA pressure



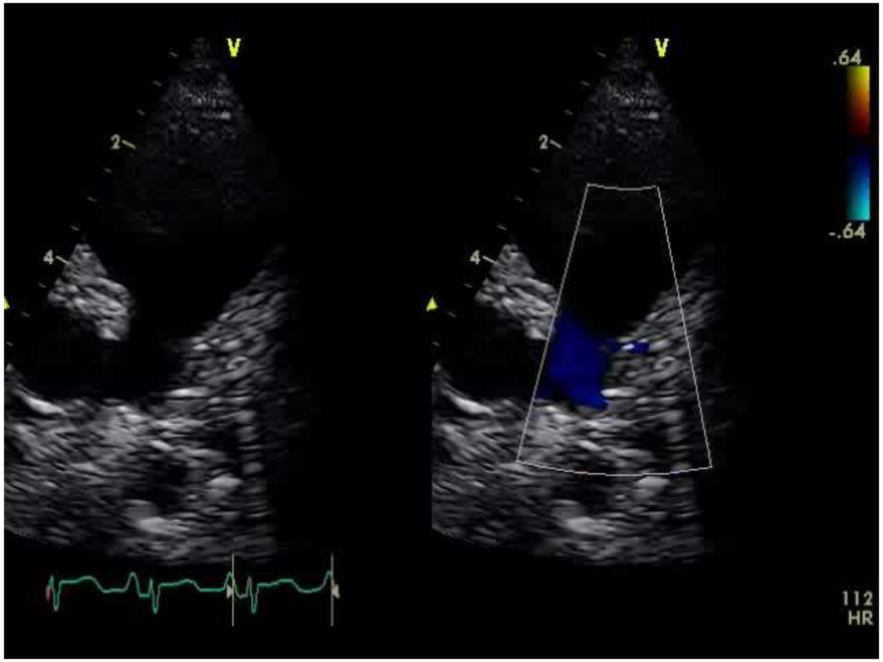
RV efficient for moving large volumes

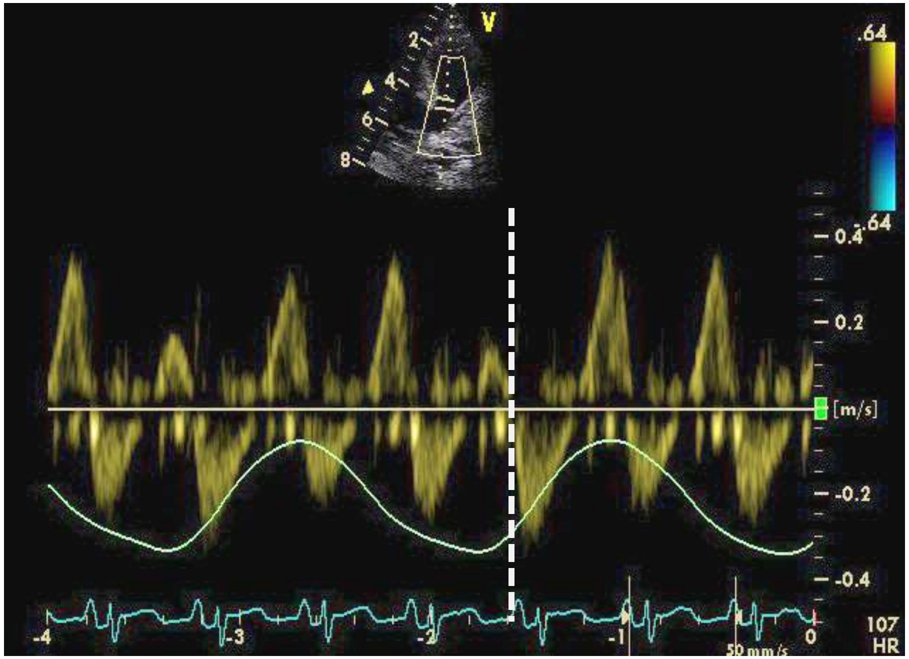
not for high pressures

Hamer & Pieper

“An Incompetent Infundibulum”

Role of the infundibulum in maintaining pulmonary valve competence





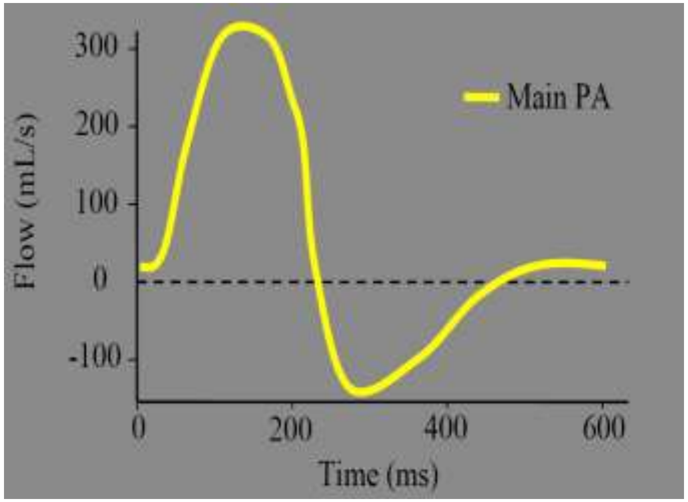
Expansion of an “atonic” infundibulum during atrial contraction with increased preload (Ebstein, Uhl)

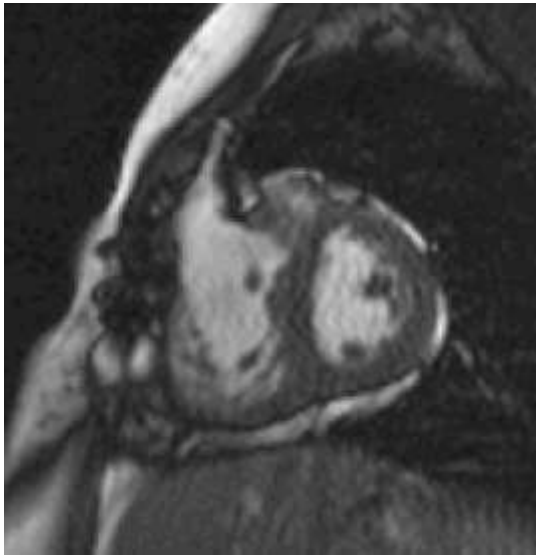
Charakida M, JACC 2010

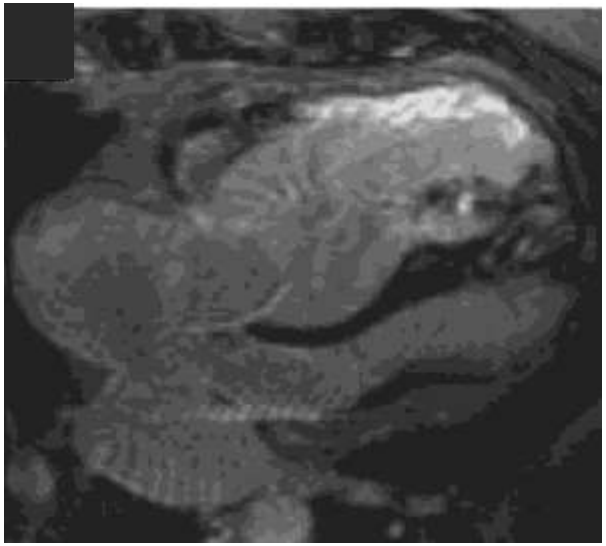
Right Ventricle: Functional assessment – any gold standard?

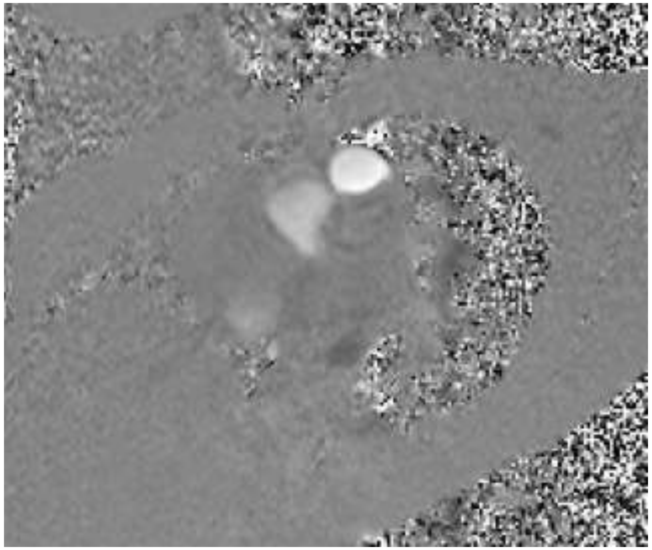
Magnetic Resonance Imaging

- RVOT morphology
- RV function (RVEDV, RVEF)
- RVOT function, % of pulmonary RF
- RV late Gadolinium enhancement



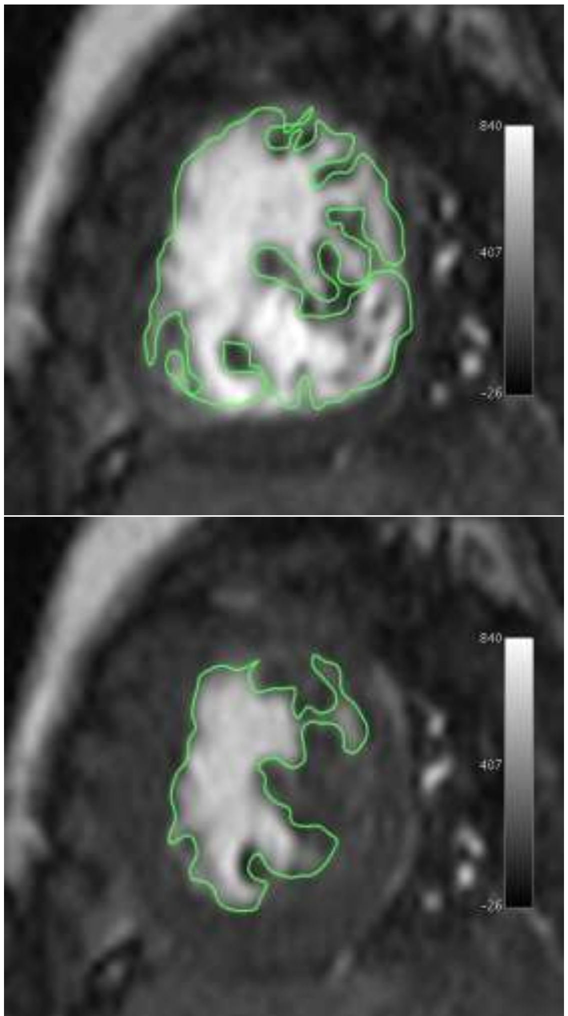




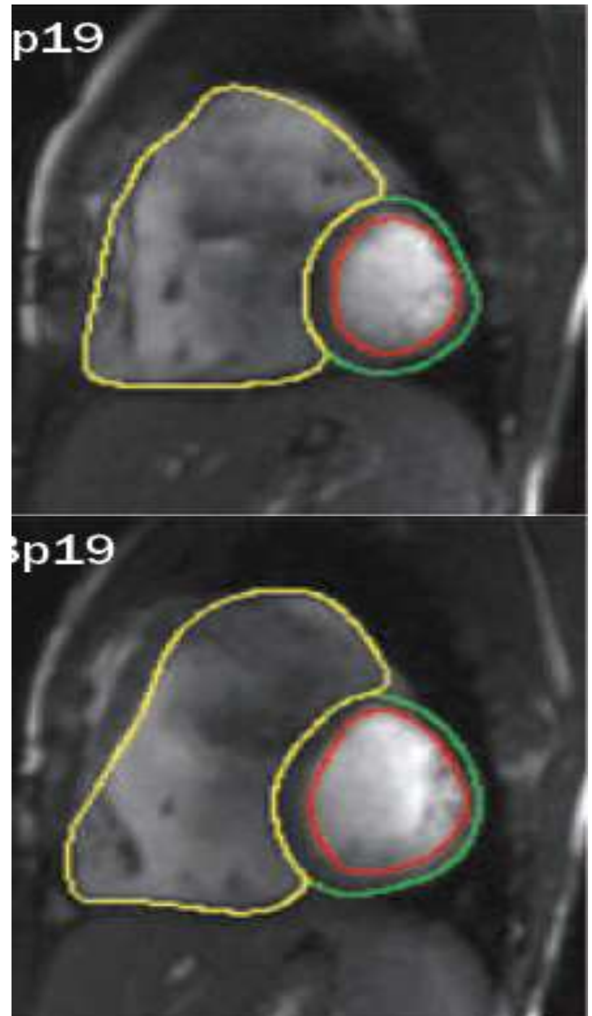


Cardiac MRI: Gold standard???

GOSH (London)

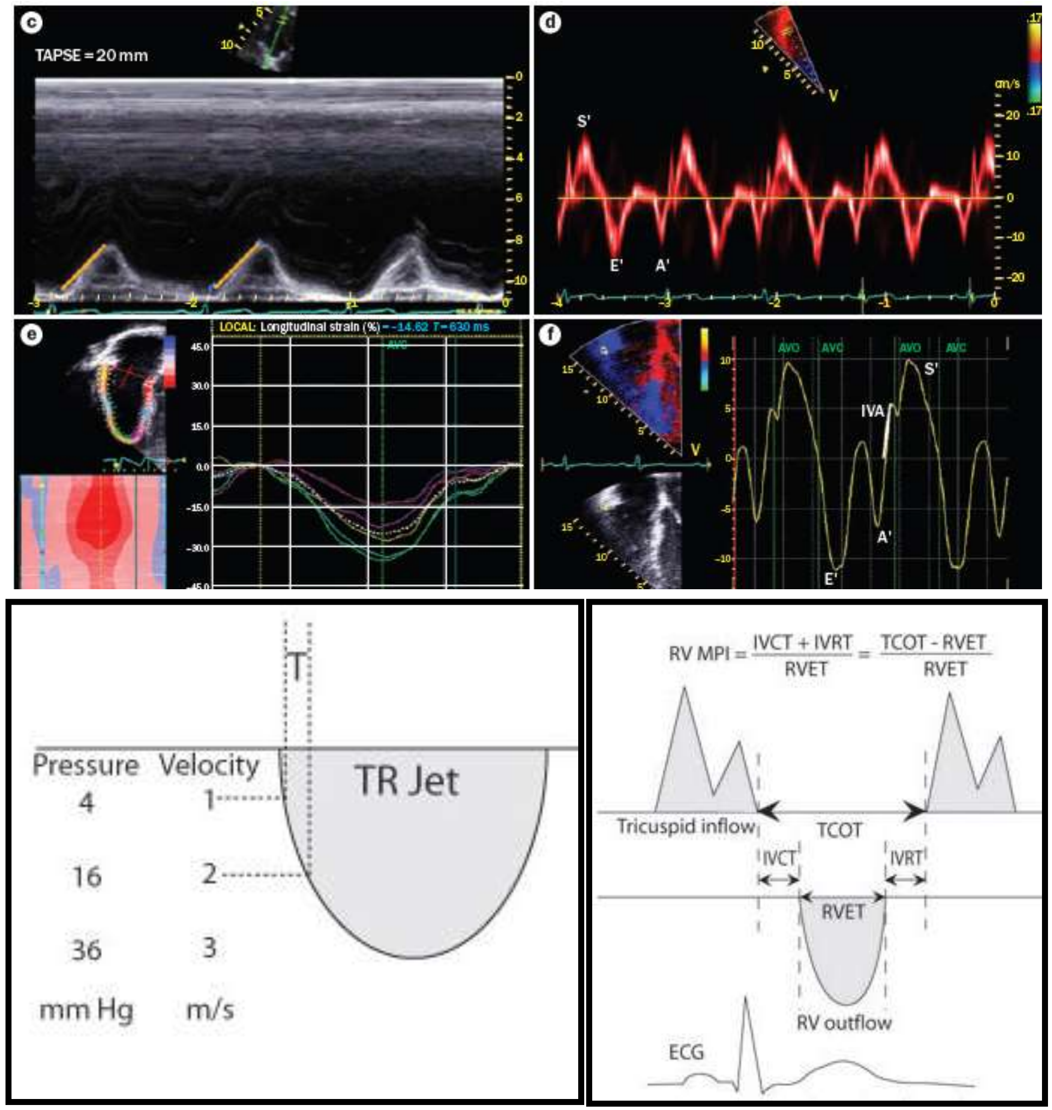


SickKids (Toronto)



RV function: Echocardiographic Challenges

- Eye balling
- FAC (%)
- TAPSE (mm)
- M-mode (AMM)
- S/D ratio
- +dP/dt (systemic RV)
- Tei index
- TDI (Strain, -SR)
- RT-3DE



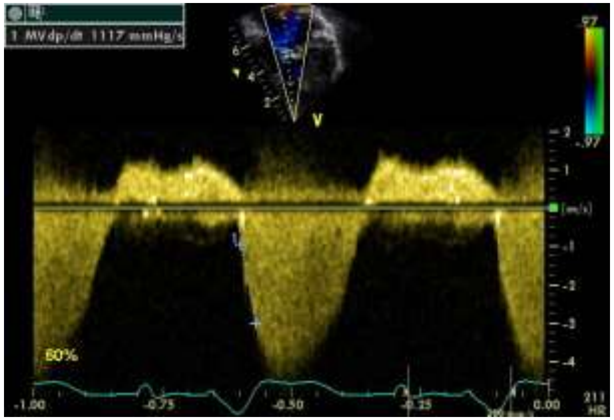
J Am Soc Echocardiogr 2010

EHJ-Cardiovascular Imaging 2015

+dP/dt: role of loading conditions

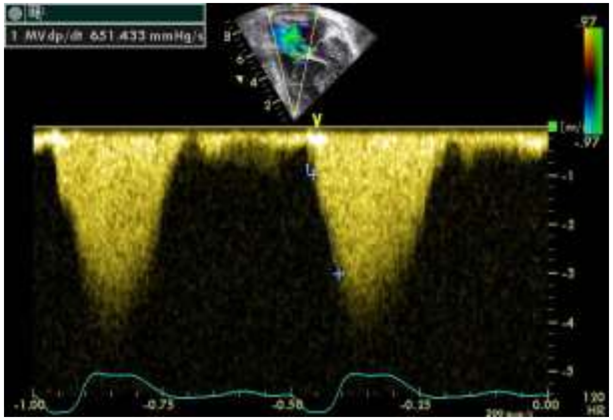
Fontan pt. on V-A ECMO
(bridge to recovery)

Full flow ECMO



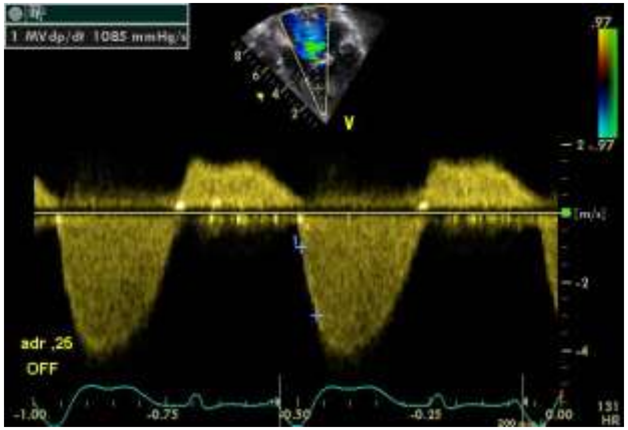
1,117 mmHg.s-1

30% flow ECMO



611 mmHg.s-1

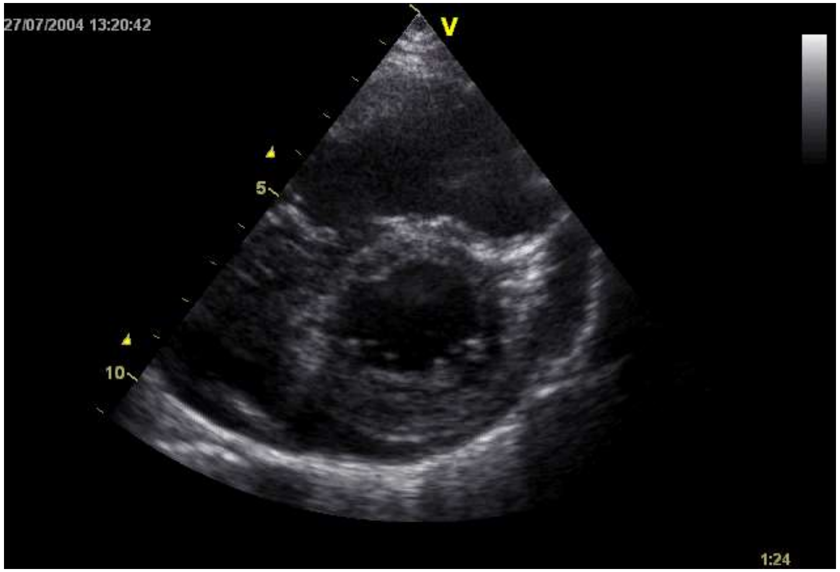
Off ECMO
+
Adr 0.01, Mil 0.5

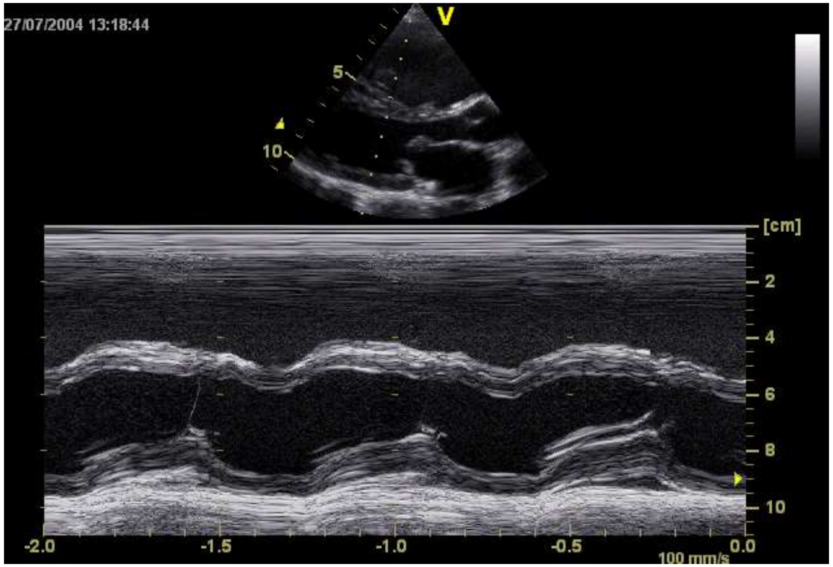


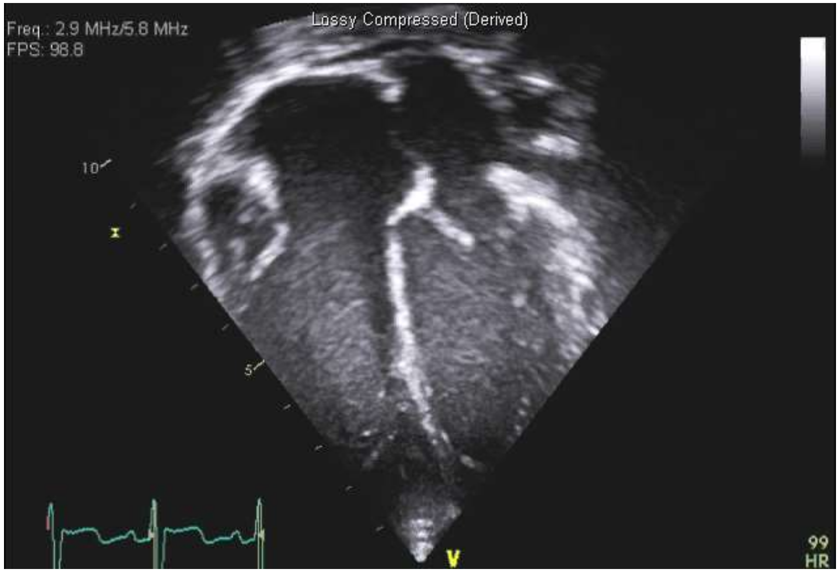
1,085 mmHg.s-1

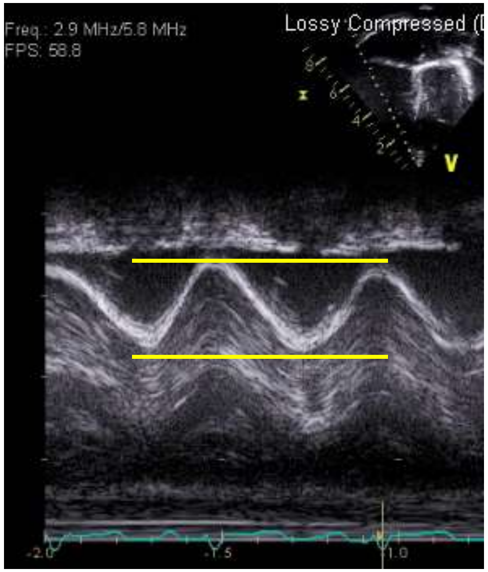
Right Ventricle Exposed to High Preload

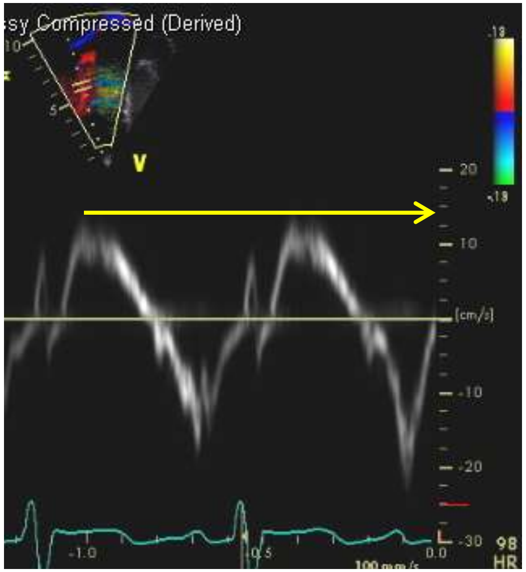
RV function in ASD



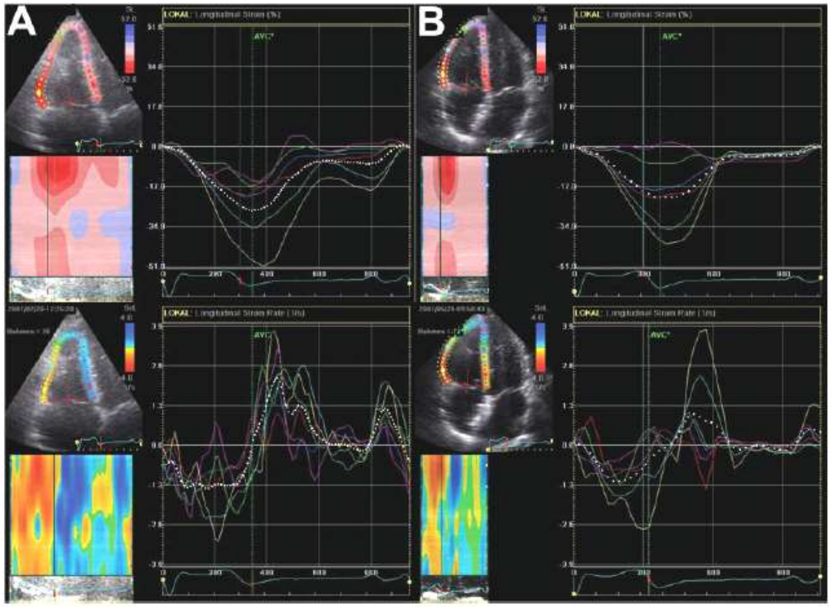


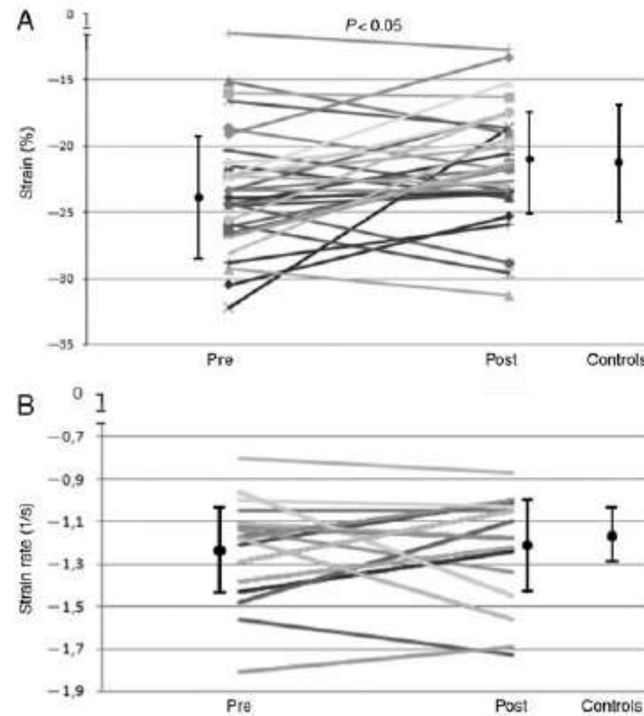






RV function in ASD
(pre- and after trans-catheter closure)





Strain

Strain Rate

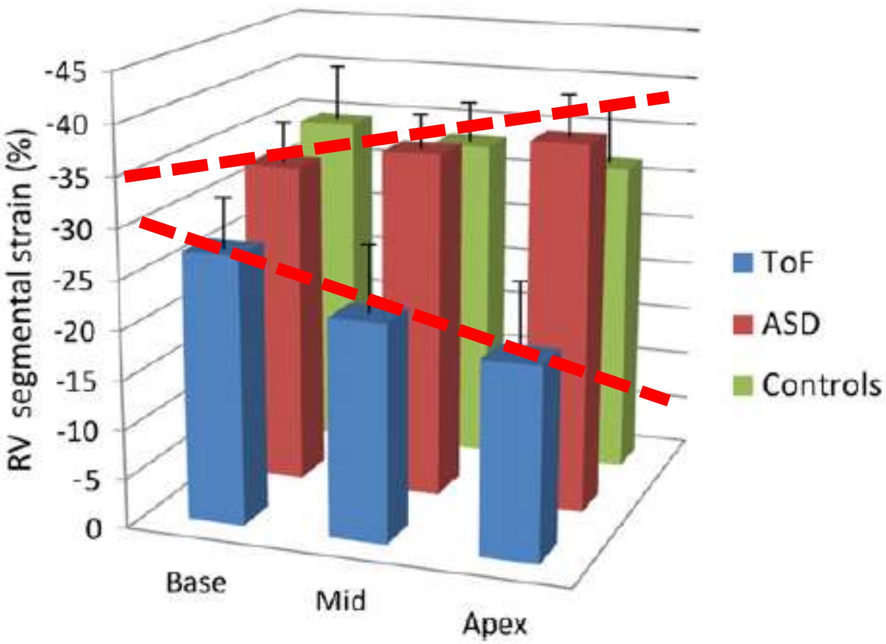
Table 2 Echocardiographic diameters and TAPSE (tricuspid annulus plane systolic excursion) in the control group and in atrial septal defect patients before and 3 months after closure

	Control group	ASD		*P*-value
		Pre	Post	
LA (mm)	38.5 ± 5.0	41.0 ± 6.9	42.1 ± 7.4	n.s.
RVEDD (mm)	25.6 ± 3.9	36.4 ± 8.9	29.3 ± 7	<0.05
LVEDD (mm)	52.6 ± 5.3	45.0 ± 6.6	49.8 ± 5.5	<0.05
TAPSE (mm)	18.6 ± 6.4	21.5 ± 9.0	18.7 ± 6.1	<0.05

- TAPSE and Strain more load dependent
- Strain rate did not show any difference in contraction

Jategaonkar SR, EHJ 2009

RV function in ASD vs TOF+PR

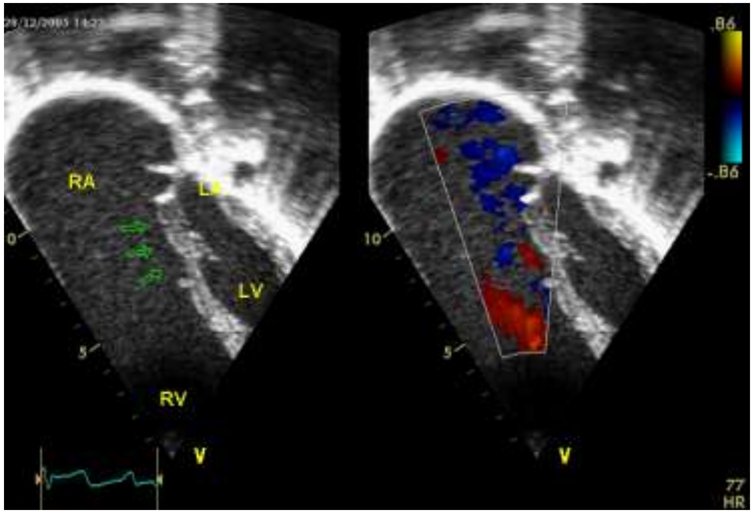


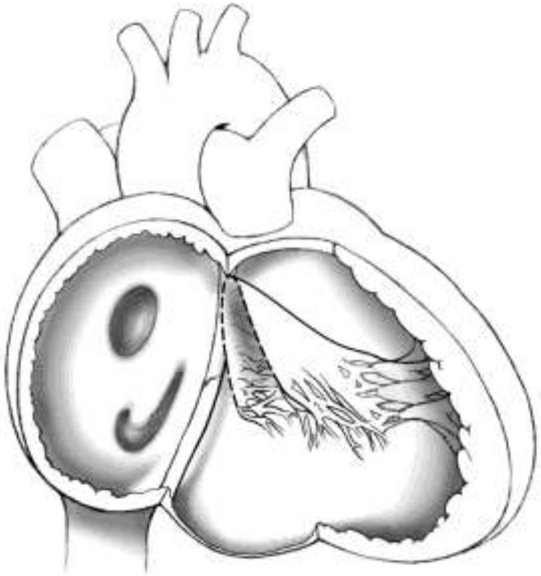
- Global and regional myocardial RV deformation is differently affected by chronic volume loading in ASD versus TOF patients
- This suggests a different adaptation mechanism in both diseases with mainly **apical segments affected in TOF**

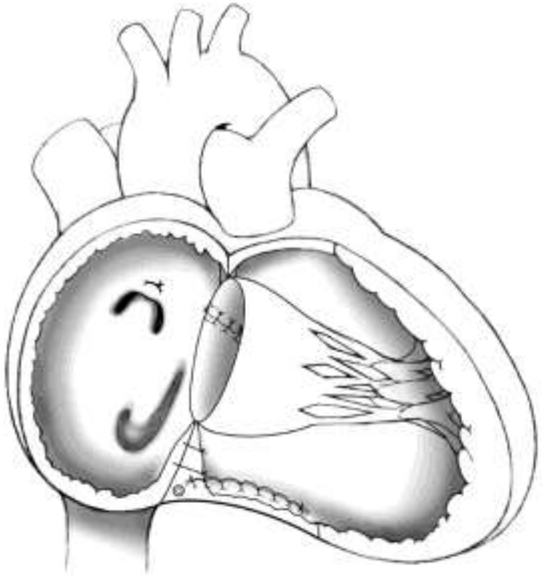
Dragulescu A, Int Am J 2012

Ebstein`s anomaly: Cone operation

- Antero-Superior and Inferior leaflets mobilised and detached from their position in RV and rotated clockwise and sutured to the septal margin of AS leaflet (=cone)
- Septal leaflet (if present) delaminated and incorporated in cone
- Annuloplasty
- Right atrium plicated and ASD closed (if present)





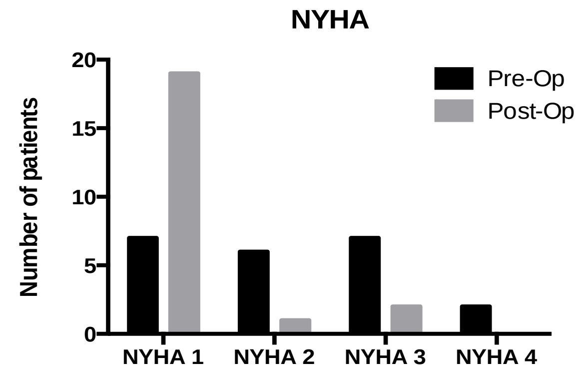


Da Silva JP, Arq Brasil Cardiol 2004, J Thor Cardiovasc Surg 2007

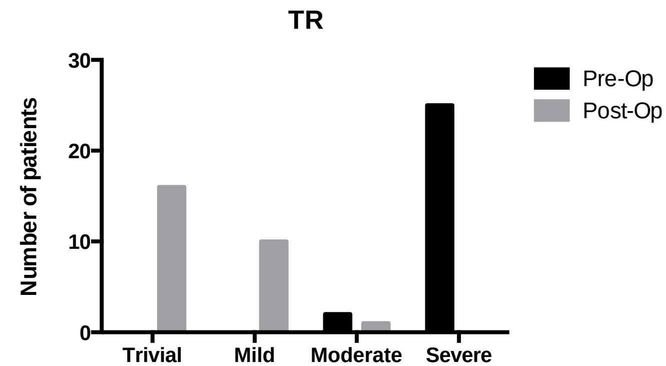
Cone reconstruction for Ebstein's anomaly: Patient outcomes, biventricular function, and cardiopulmonary exercise capacity

Michael Ibrahim, MD, PhD,[a,b] Victor T. Tsang, MD, FRCS,[a,b,c] Maryanne Caruana, MD,[d]
Marina L. Hughes, DPhil, FRACP,[d,e] Synetta Jenkyns, BD,[e] Elodie Perdreau, MD,[e]
Alessandro Giardini, MD,[c,e] and Jan Marek, MD, PhD[c,e]

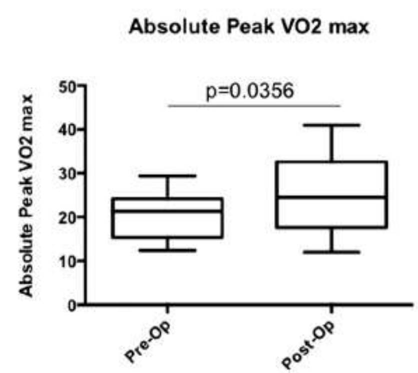
Improves functional status

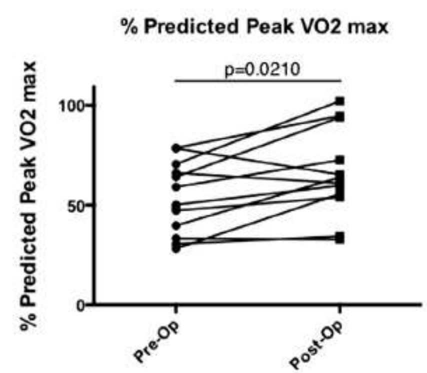


Reduces TR



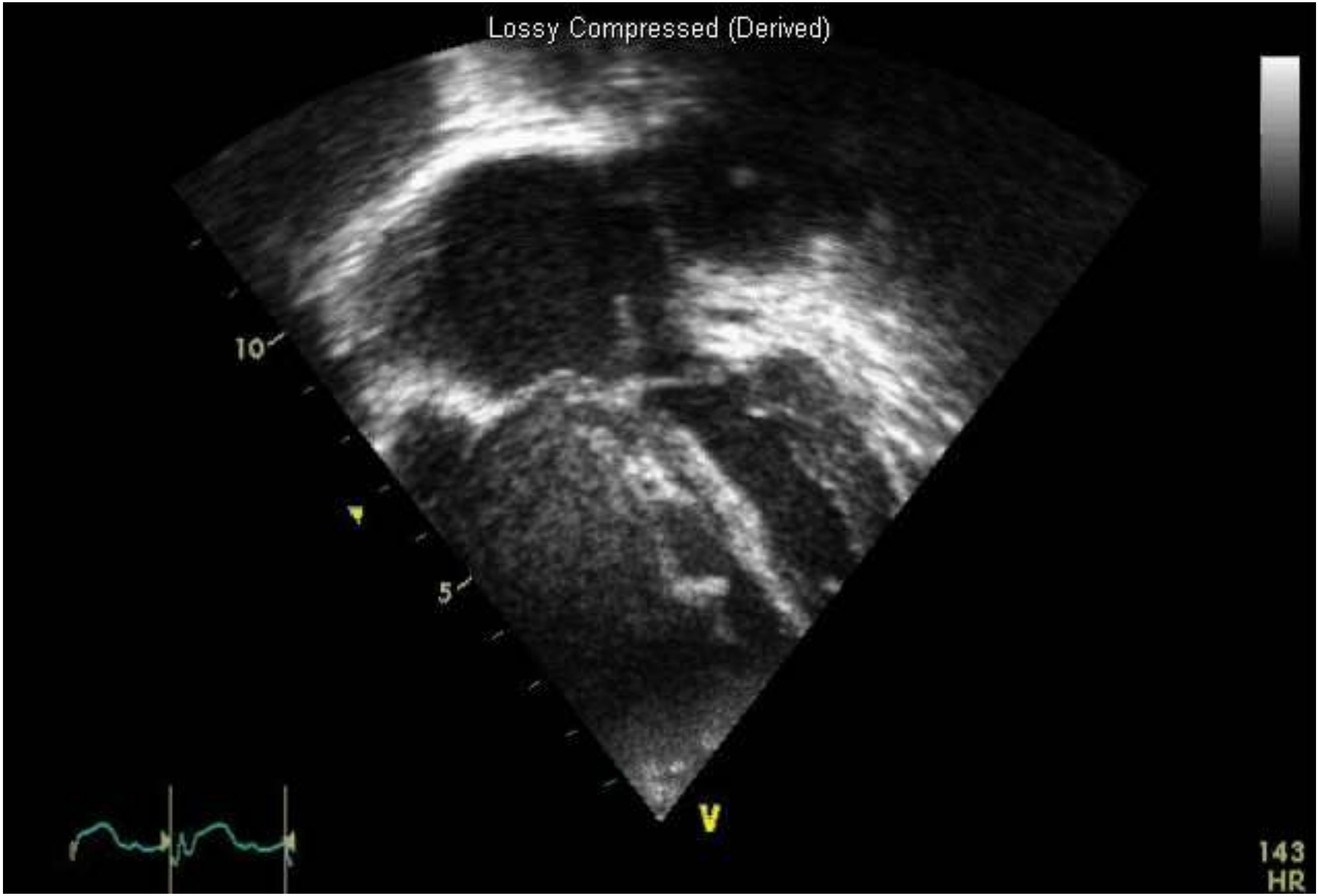
Improve exercise tolerance





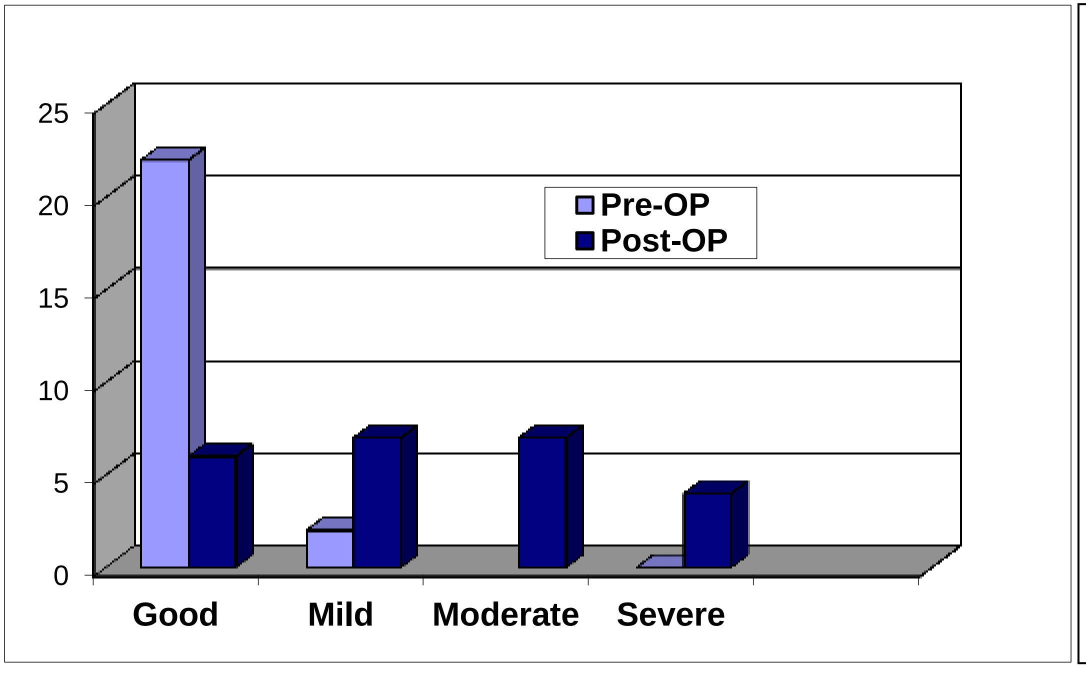
JTCS 2015

....but

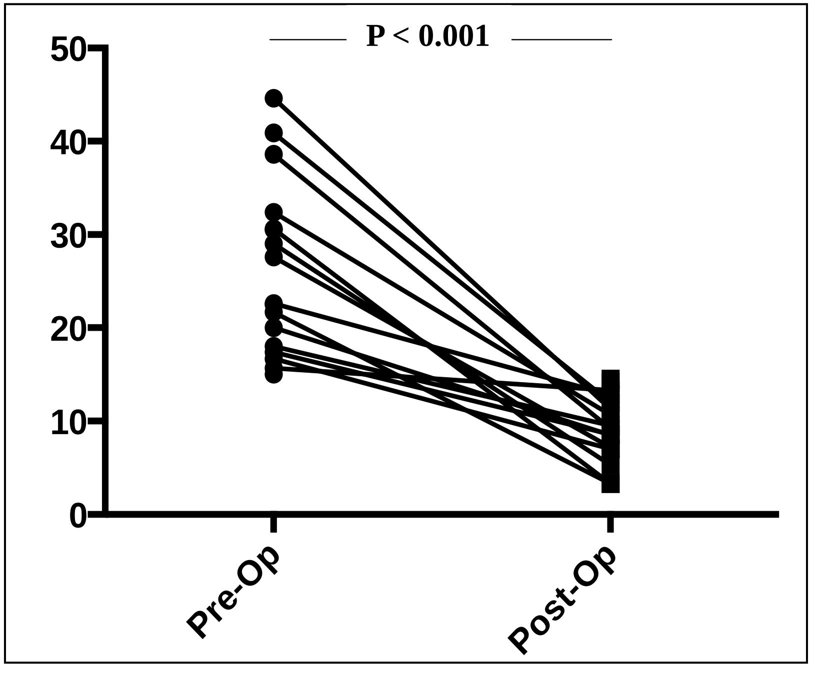


….but, despite clinical improvement, markedly reduces RV function …!?

ECHO: eyeballing



ECHO: TAPSE

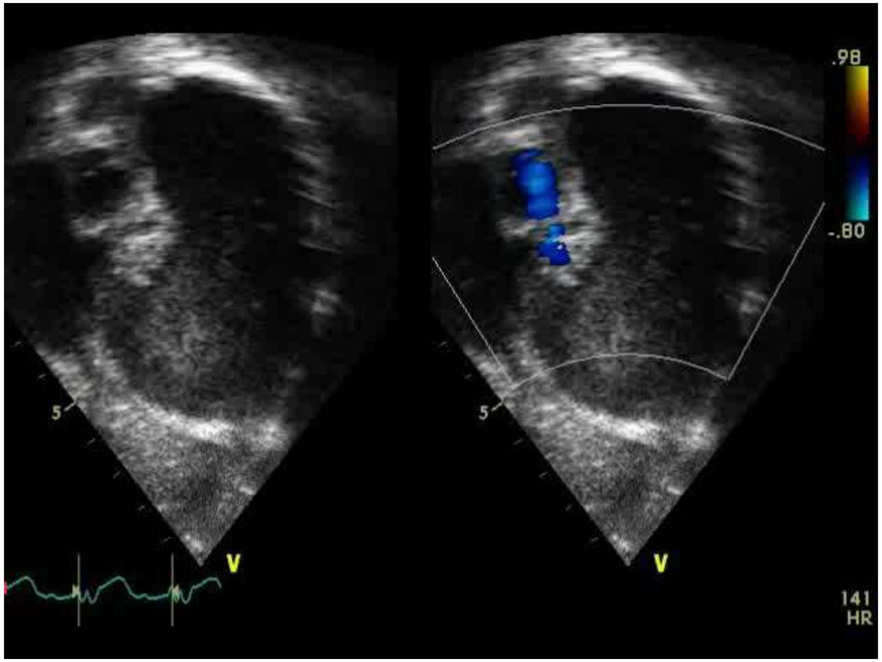


Ebstein`s anomaly: Cone operation

Day 1
Post cone

Day 10
Discharged

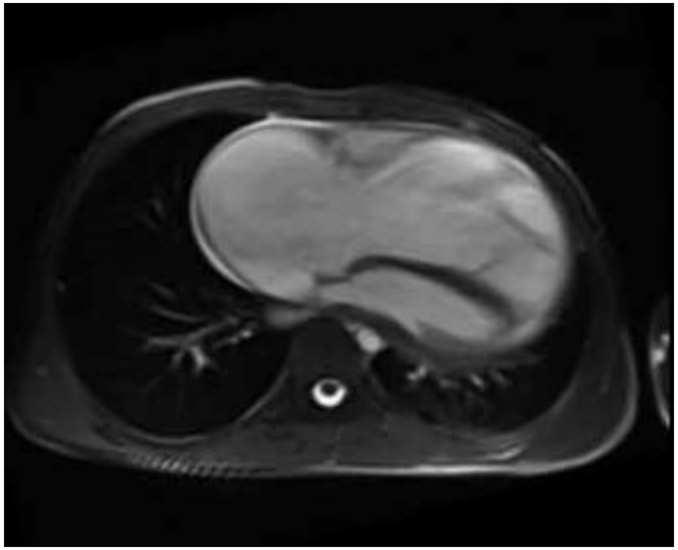
Day 14
Post cone

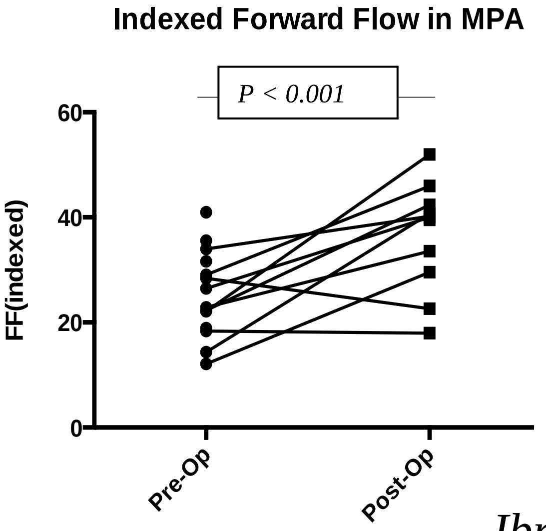


Parental consent

Reduced EF but increased Forward Flow

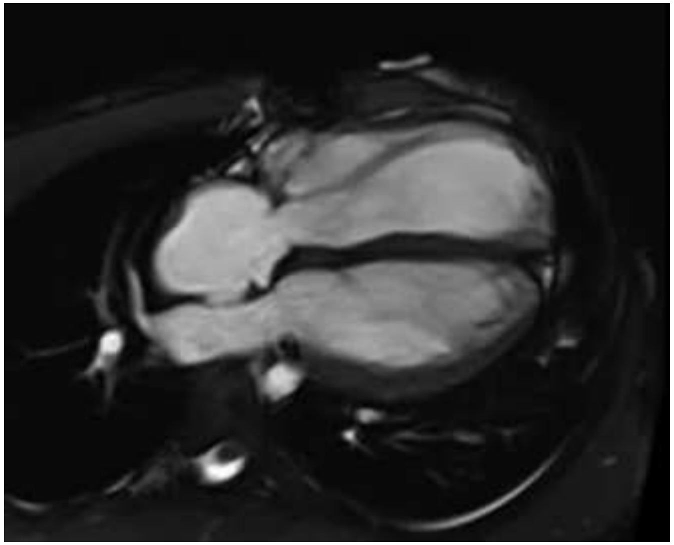
Before

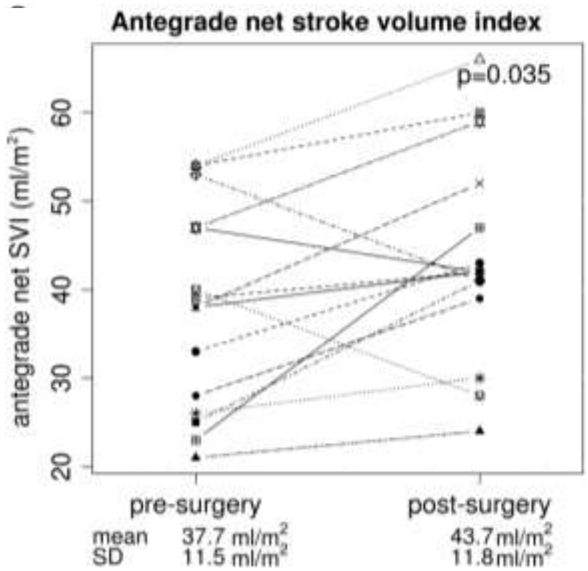




Ibrahim M, JTCS 2015

After



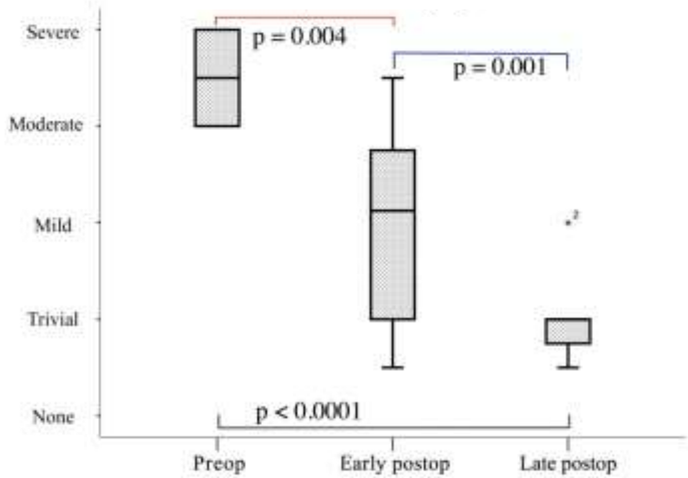


Lange R, Eur J Cardiothorac Surg 2015

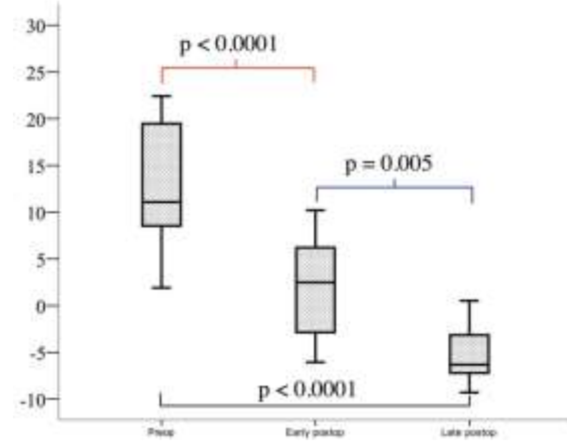
Ebstein's: Myocardial function

Recent GOSH data: Mean FU is 26.9 months (range 1-77 months)

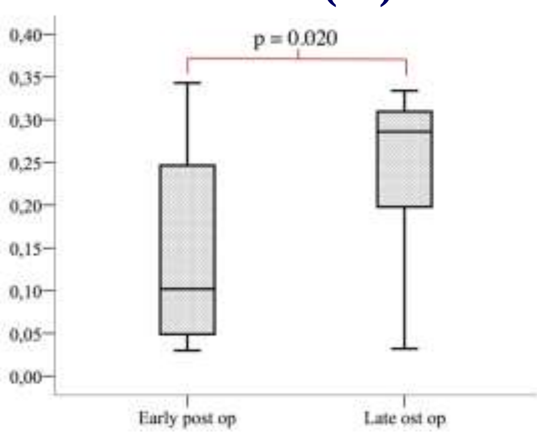
Tricuspid regurgitation



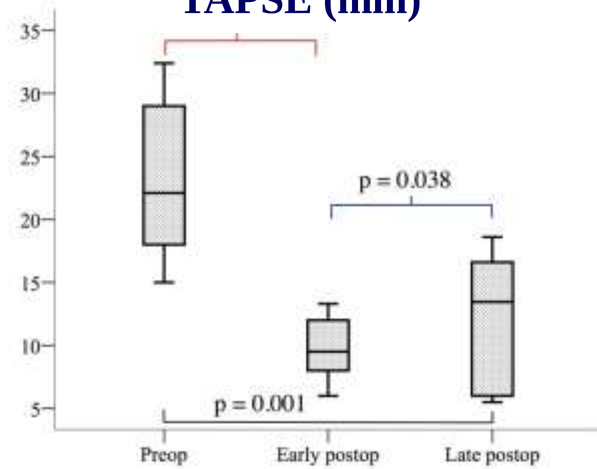
Tricuspid annulus (Z-score)



RV FAC (%)

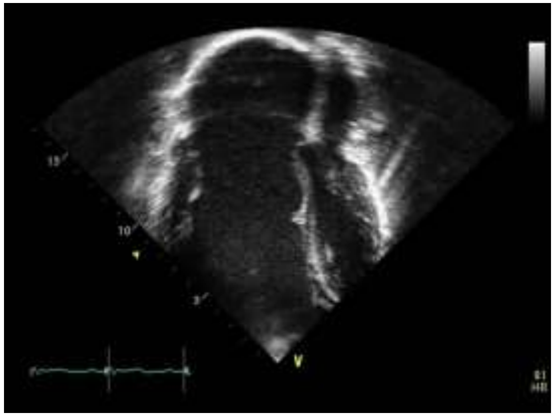
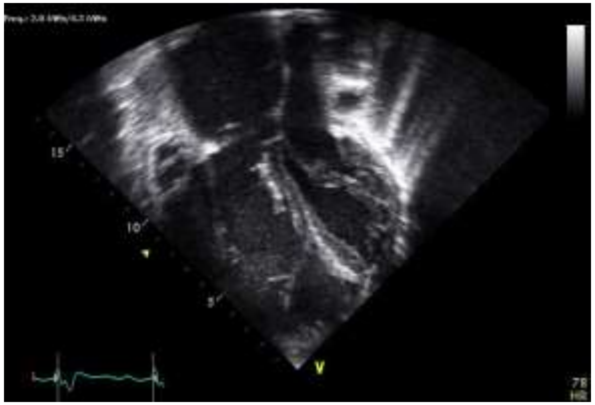
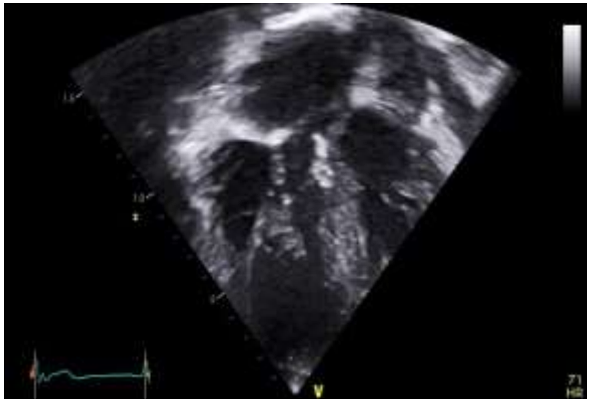


TAPSE (mm)



Perdreau E, manuscript

Why does RVEF decrease after surgery?

Pre-operative	Post-operative 1 week	Post-operative 4 years
		

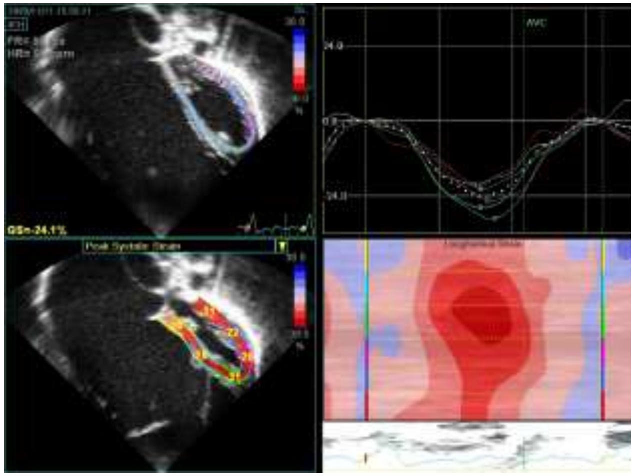
- **Competent valve**

  Decreased stroke volume & ejection fraction

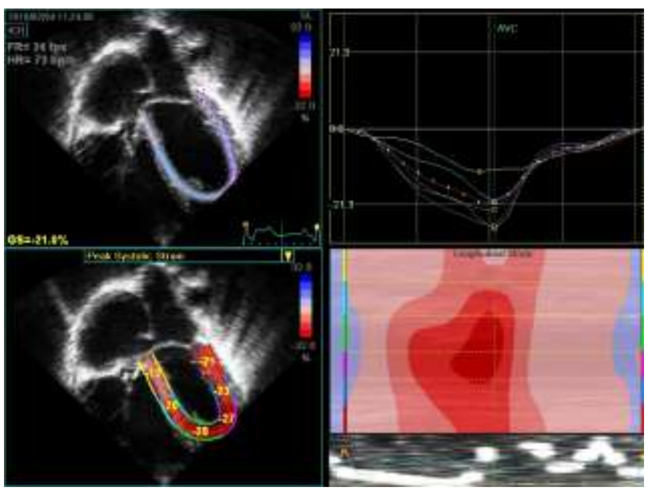
  Increased afterload
- **“Re-ventricularised” myocardial wall**
- **Remodelation** or **Intrinsic Cardiomyopathy**?

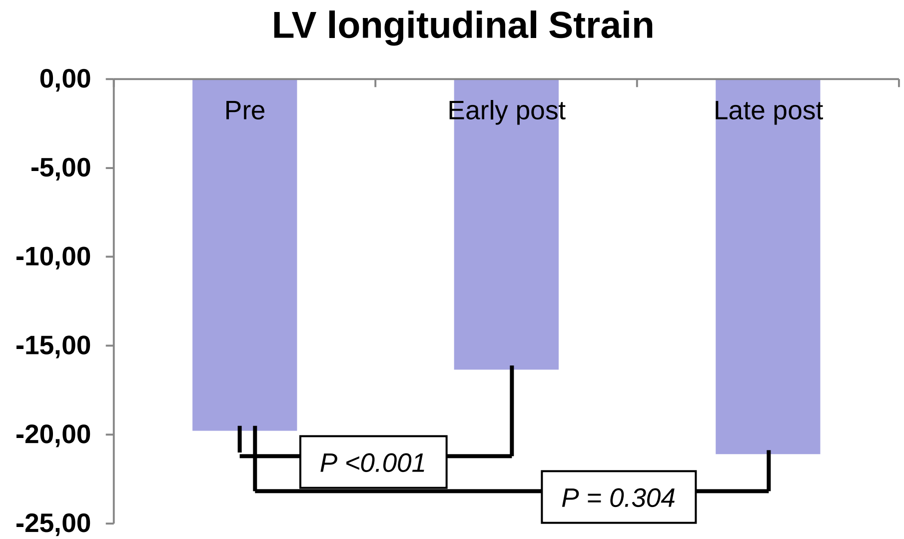
Ebstein's: LV function

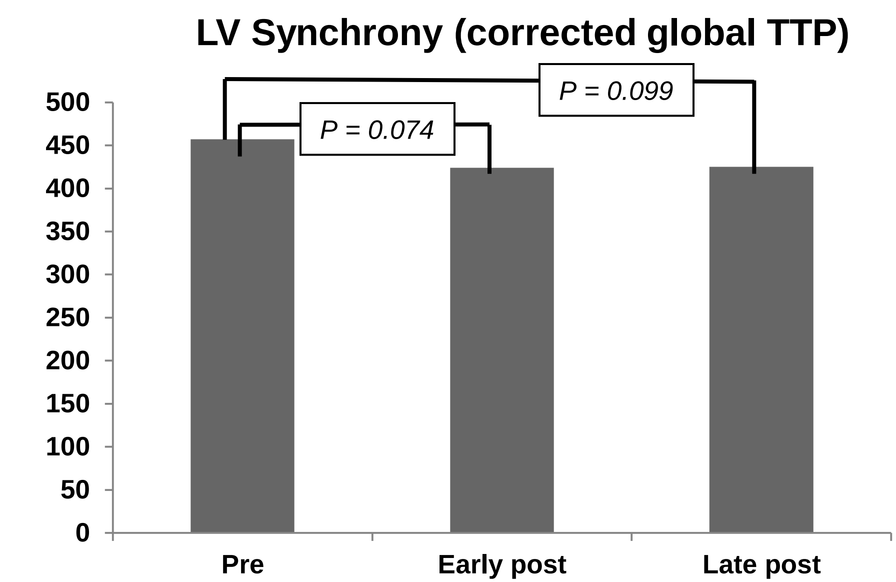
Before Cone



After Cone







Perdreau E, manuscript

Right Ventricle

Exposed to High Atferload:

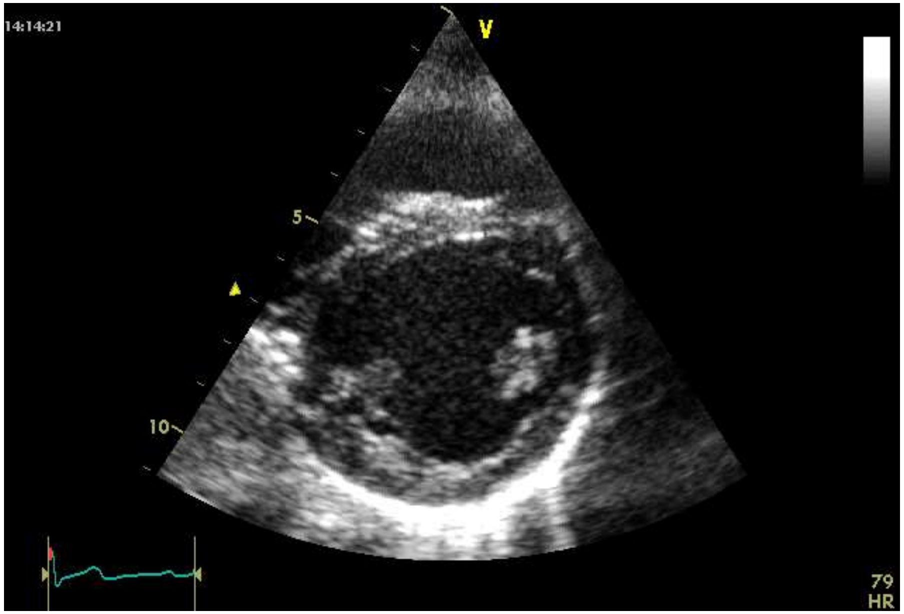
Ventricular Interdependence

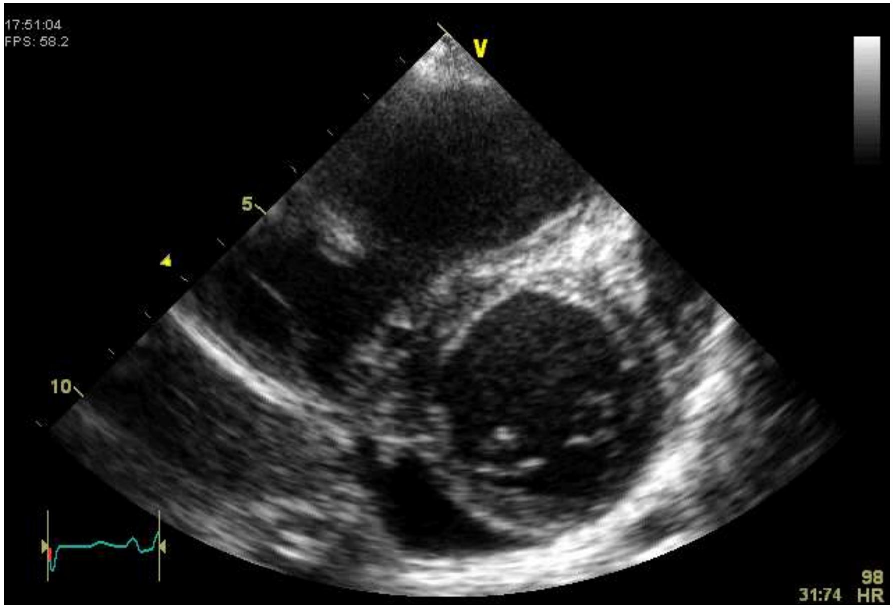
&

Role of Septum

Ventricular Interdependence & Role of Septum

Pulmonary arterial hypertension



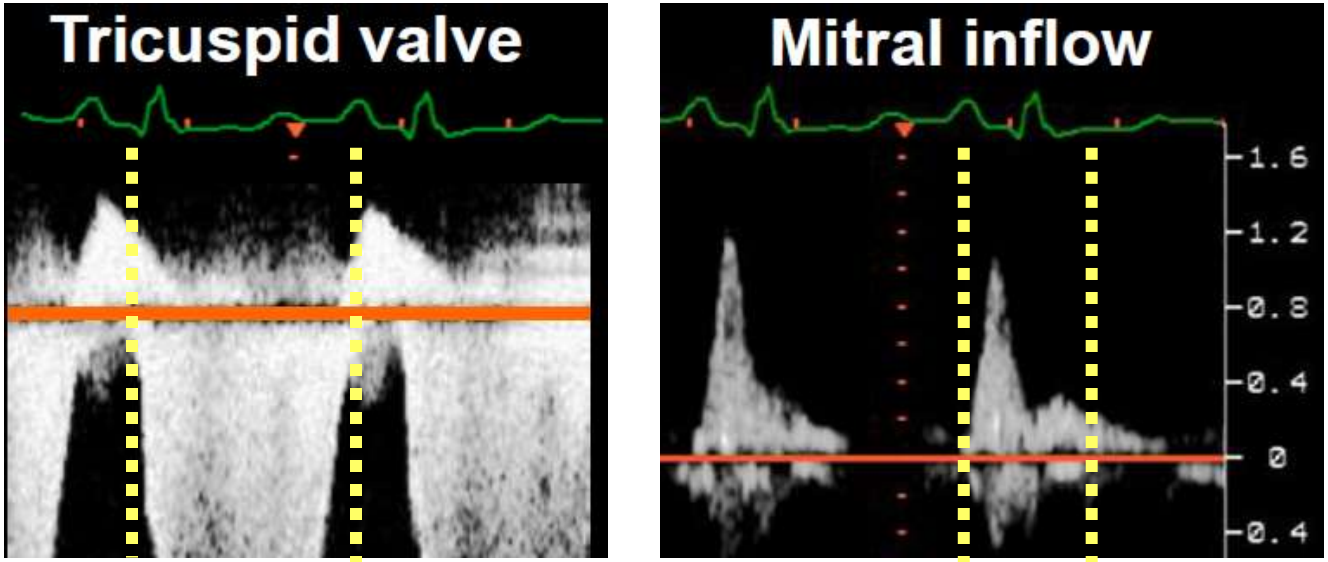


Low PAp

High PAp

RV dyssynchrony & RV-LV interaction in PAH

S:D Ratio

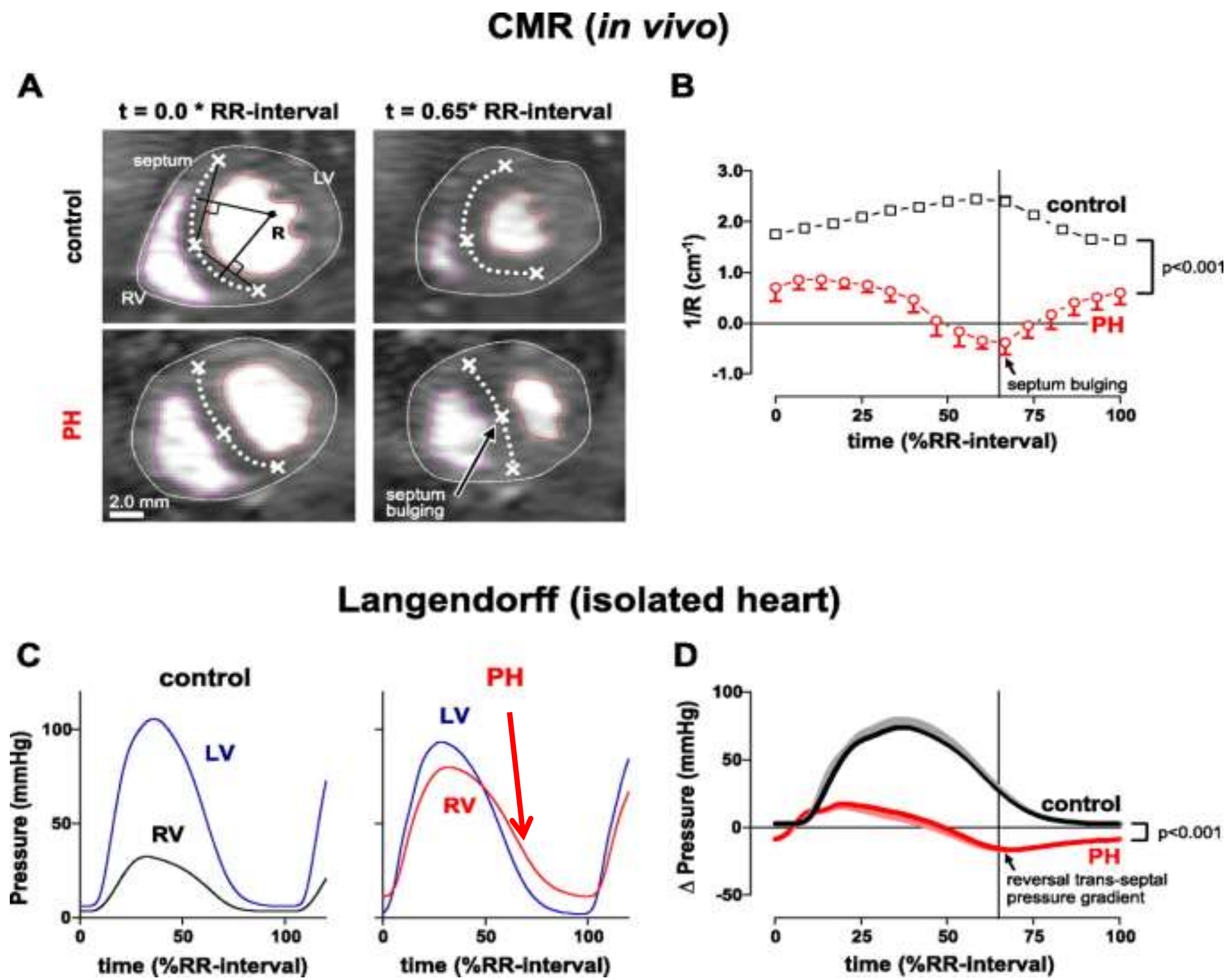


Friedberg M, JASE 2007

- Correlates with worse outcome, exercise tolerance, haemodynamics and pulmonary resistance
- Associated with risk for lung transplantation or death (hazard ratio 1.13, p <0.001).

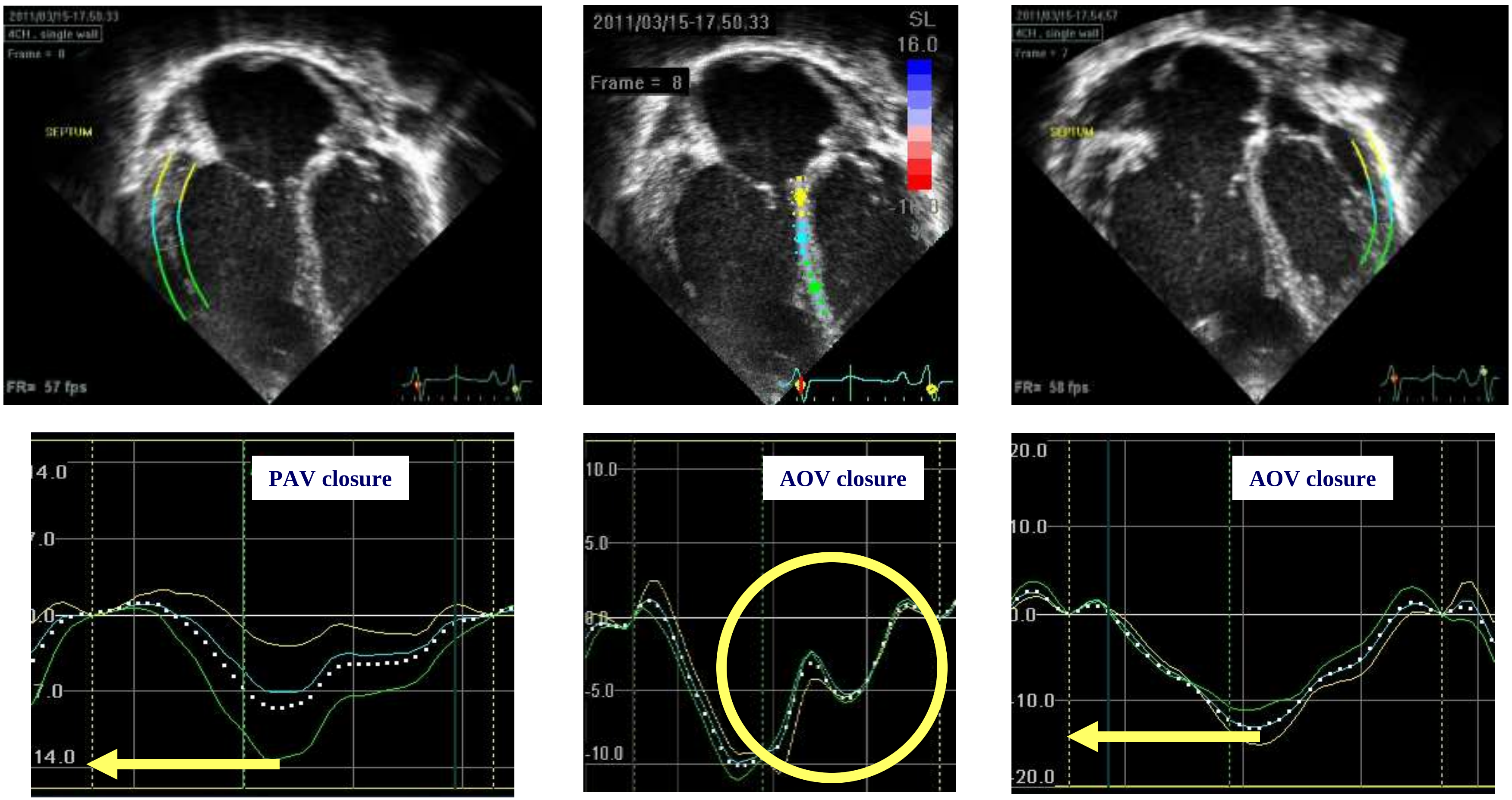
Alkon J, Am J Cardiol 2010

PH-related ventricular dyssynchrony in Experimental model (monocrotaline-treated rats)



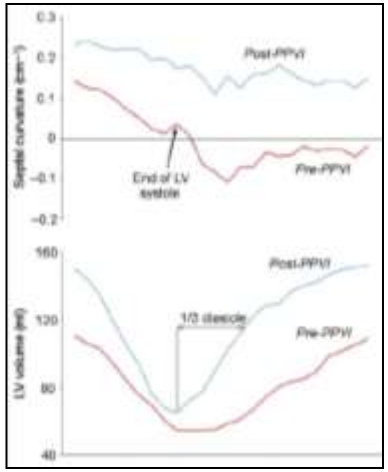
Handoko M L et al. Am J Physiol Heart Circ Physiol 2009

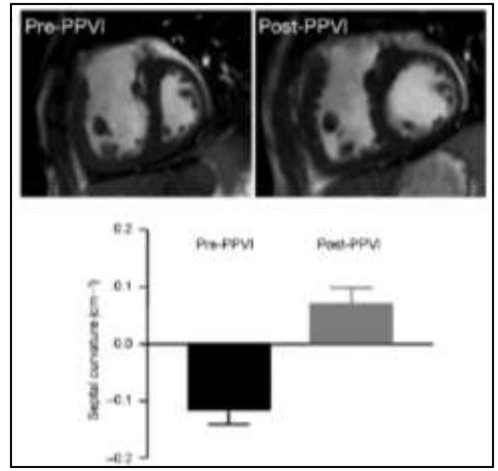
RV dyssynchrony & RV-LV interaction in PAH

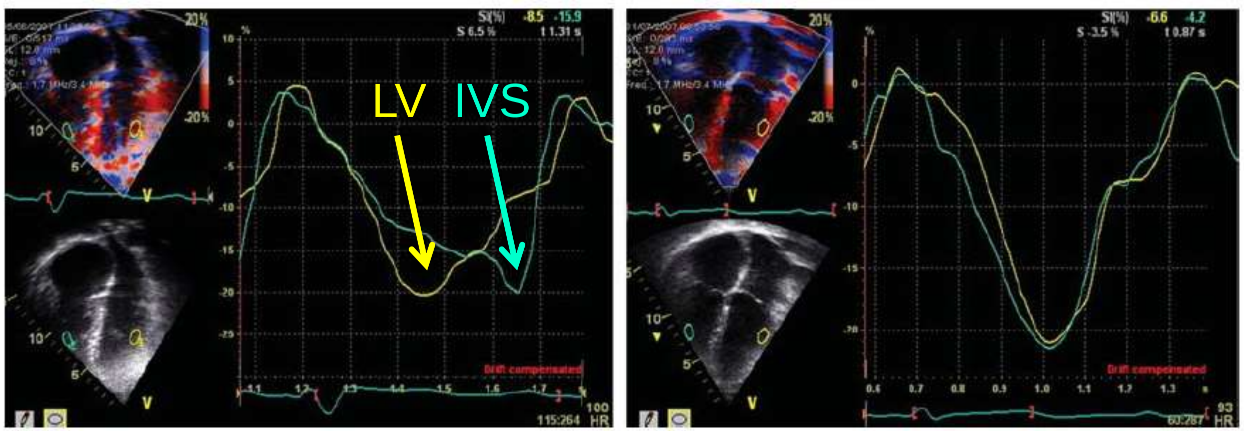


Important intra- (RVFW and IVS) &
inter-ventricular (RVFW and LVFW) mechanical delay

RV dyssynchrony & RV-LV interaction in post repaired TOF with # ↑RVOTO



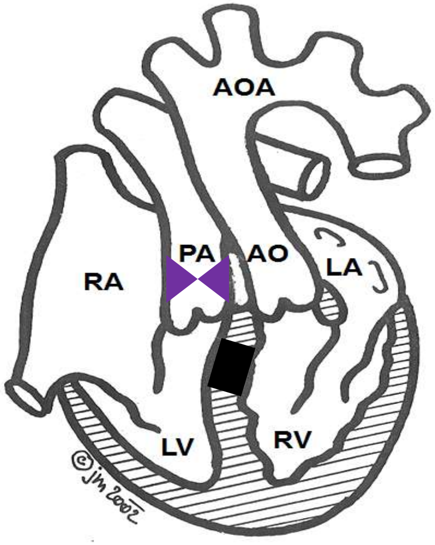




Increase in early LV diastolic filling correlated with the reduction in RV to LV mechanical delay (r ¼ 20.68; P ¼ 0.001) and change in septal curvature (r ¼ 0.71; P , 0.001)

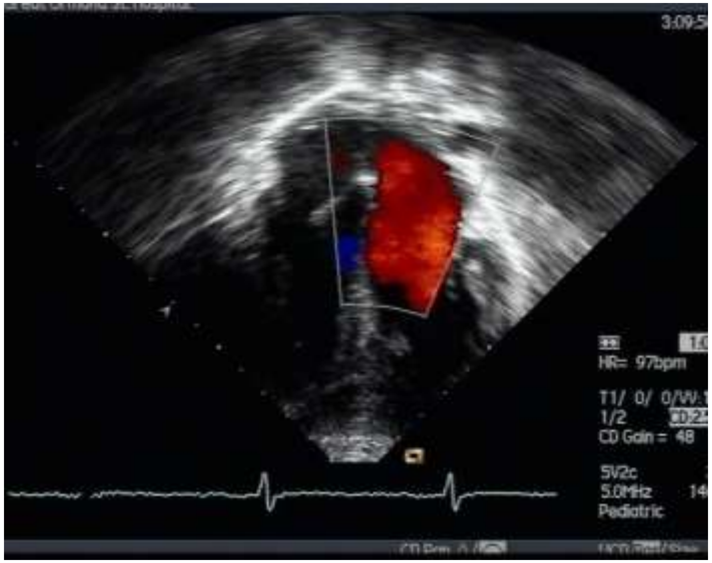
Lurz P, Eu Heart J 2009

CcTGA: ventricular interdependence



30-y old, CcTGA/VSD/AVBIII
VSD closure
S/P VVI pacing (LV)
Systemic RV, TR
S/P PA Banding

PA Band OFF



PA Band ON

CcTGA: ventricular interdependence

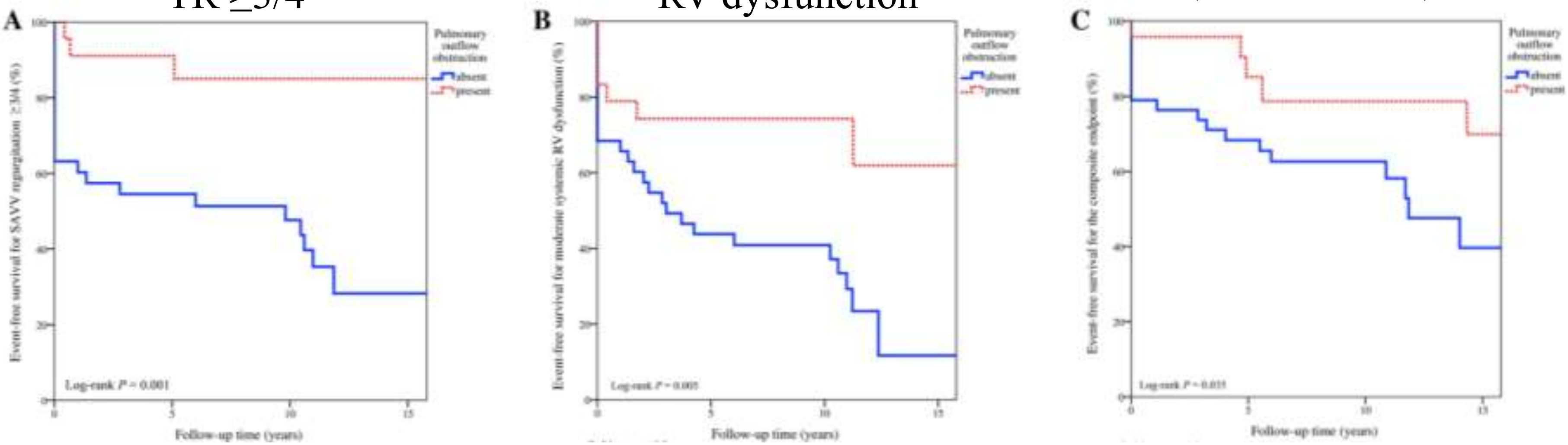
Effect of **native or surgically induced LVOTO** on event-free survival

TR ≥3/4

RV dysfunction

Composite endpoint

(death, HTx, CHF)



Patients with LVOTO had:

- **Lower risk for developing systemic TR ≥3/4** (P = 0.004)
- **Moderate systemic RV dysfunction** (P = 0.011)
- **Longer progression-free interval for the composite endpoint** (from 11.2 to 18.1yrs; P=0.035)

Helsen F, Int J Cardiol. 2015

Summary I.

- Different RV response to loading conditions among different acquired and different congenital heart lesions

- Weak understanding of differences among patients with same substrate and same starting point of disease

- Likely different genetic substrate driving up-regulation of myocardial response in CHD

"Fetal gene program"

Summary II.

- Majority of parameters/indices sensitive to loading conditions
  - No golden standard
  - Some indices (TAPSE, MPI, S:D) applicable with high predicting value where RV exposed to high afterload

- Ventricular interdependence has major impact on pump efficiency
  - "Optimising" loading conditions to achieve mechanical synchrony

Echocardiography & Prenatal Cardiology

Director Jan Marek

Clinical ECHO Consultants

Michelle Carr

Ram Awat

Georgi Christov

Clinical Prenatal Cardiology Consultants

Ian Sullivan

Robert Yates

Shankar Sridharan

Rachel Andrews

Fetal Sonographers

Jo Wolfenden

Nicola Callaghan

Cardiac Sonographers

Gill Riley

Rebecca Banks

Sarla Kataria

Kalaiiarasi Janagarajan

Jabeen Bibi

Sally Punzal

Sharmila Govinde

Emma Chokdar

Victoria Cable

ECHO Research Fellows

Beatrice Bonnello

Elodie Perdreau

Ilaria Bo

Anna Argiolas

Specialists Registrars

William Regan

Filip Kucera

Sadia Qyam

Salim Jivanji

Corina Pauls

William Regan

Gabrielle Norish