RV function in congenital heart diseases and pulmonary hypertension

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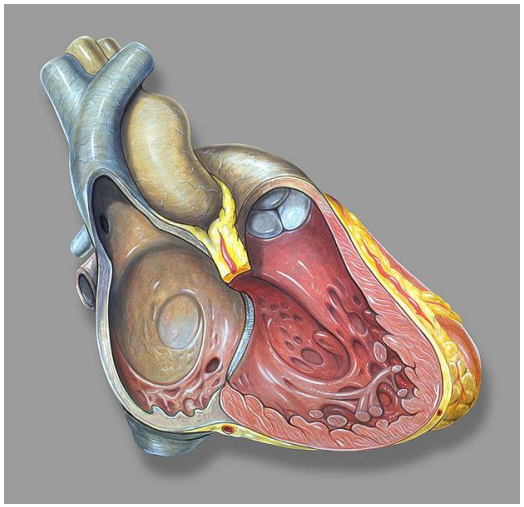
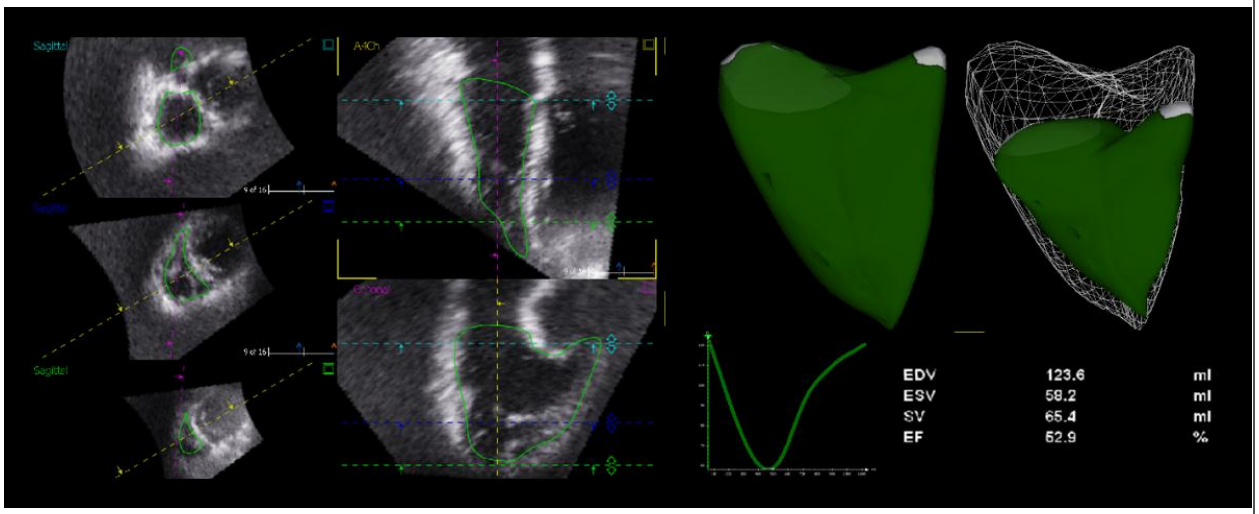
Declaration of conflict of interest: none to declare

Agenda

- **Background**
  - RV – complex anatomy & function
- **Specific question**
  - RV myocardial function in PH and congenital heart disease = RV in different loading conditions
    - deformation imaging and loading conditions
- **Take home messages**

RV remodeling





- The RV and LV differ markedly in their anatomy, mechanics, and loading conditions:
  - **Structure**: crescent-shaped, thin-walled RV
  - **Hemodynamics**: volume pump, ejecting in a low-resistance pulmonary arterial circulation.
- Special contraction pattern – peristaltic movement
  - 87% from the RV stroke volume – RV sinus (apical 4CV)
  - 80% from the RV stroke volume - longitudinal contraction

RV remodeling/failure and prognosis

- PHT and RV failure - strong **predictors of mortality** in LV failure, AMI and COPD
- **RV dysfunction is a strong prognostic factor** in:
  - PulmReg postrepair for Tetralogy of Fallot
  - systemic RV in TGA
  - PH (TAPSE only)…
- RV pressure overload associated with **pulmonary valve stenosis - better prognosis than PAH**

Load and contractility

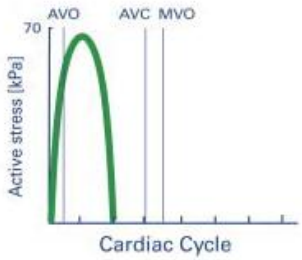
Elastic recoil

non-linear passive stress/strain relation

proportional to local deformation

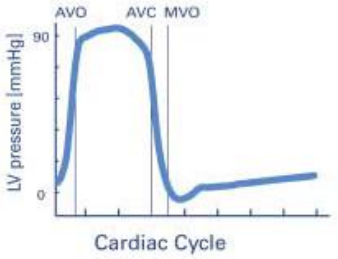
Active contraction

Intrinsic contractility



LV Pressure

Passive loading



Segment interaction

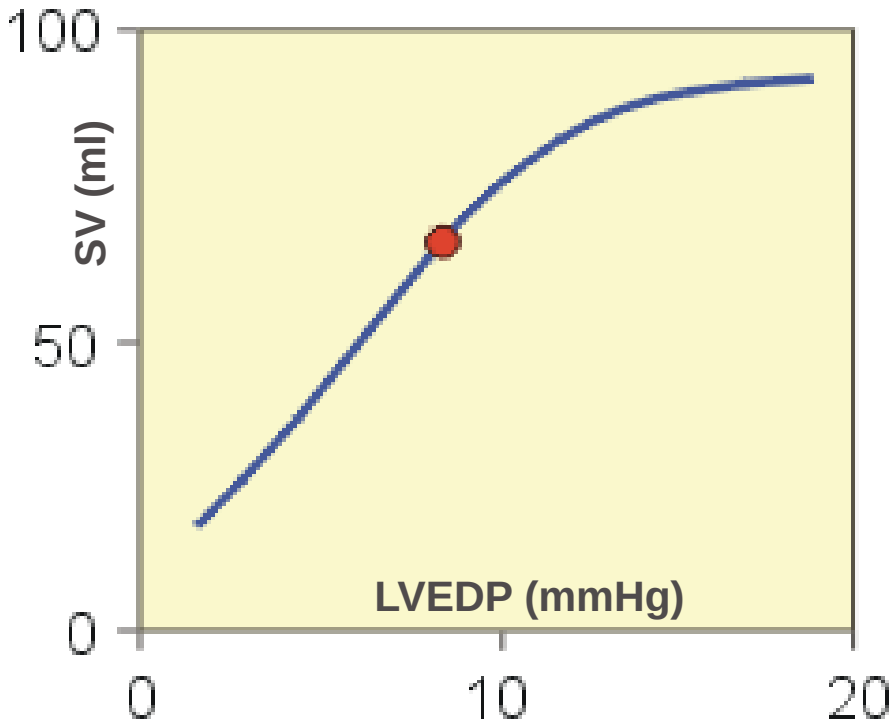
Passive loading

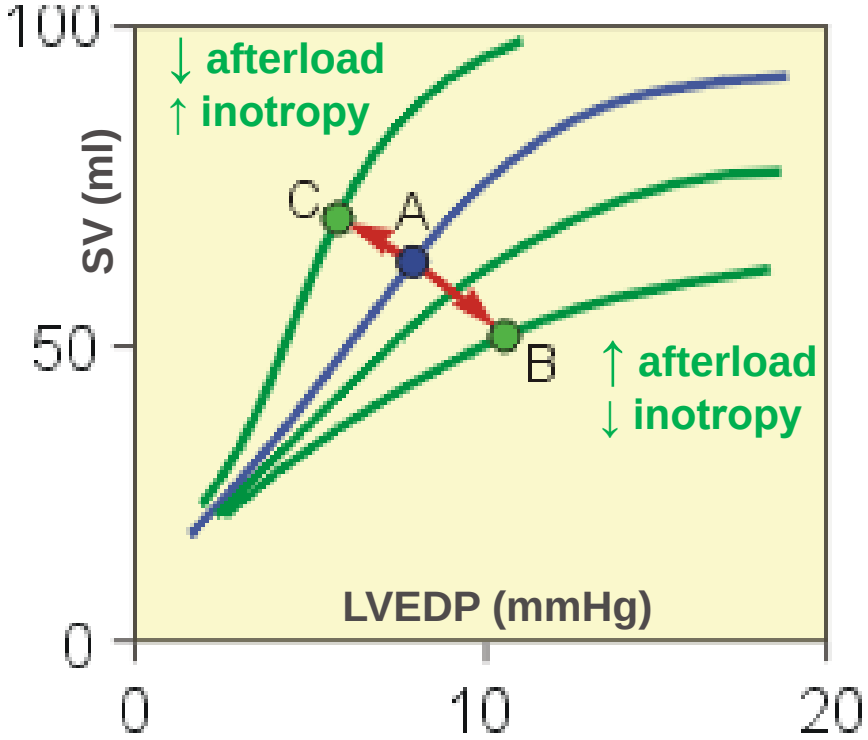
proportional to local deformation of neigbouring segment

Bijnens et al EJE 2008

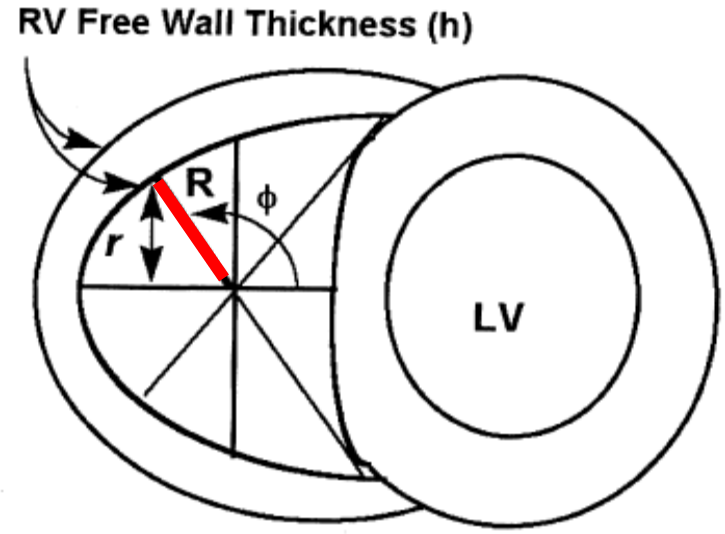
Cardiac mechanics – how is it balanced?

Frank Starling law





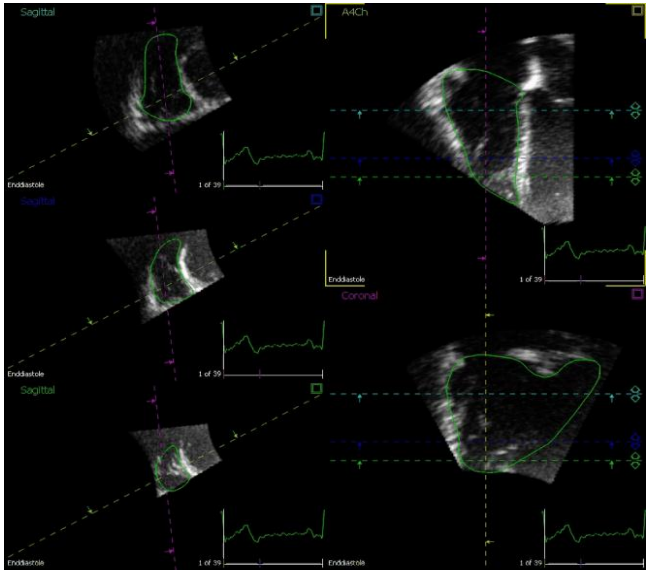
Load, geometry and contractility

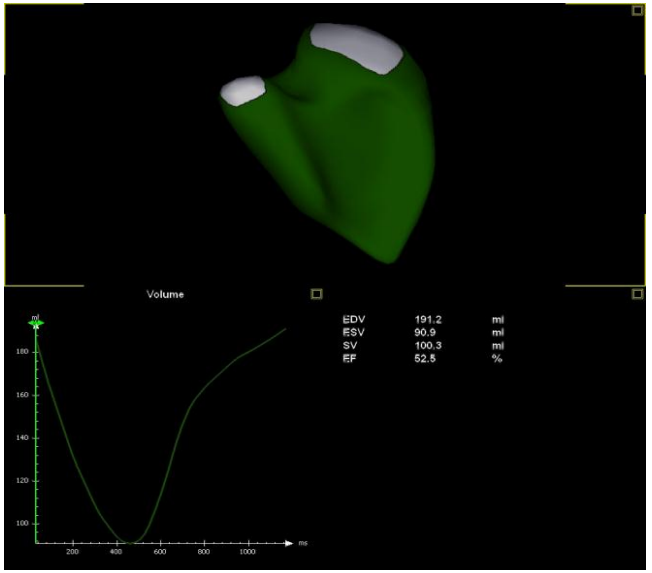


Relative Wall Stress = P x r / 2h

(P = RV peak systolic pressure)

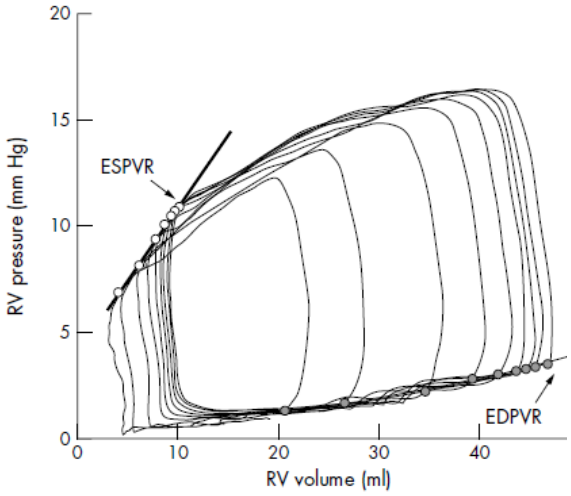
Laplace's law

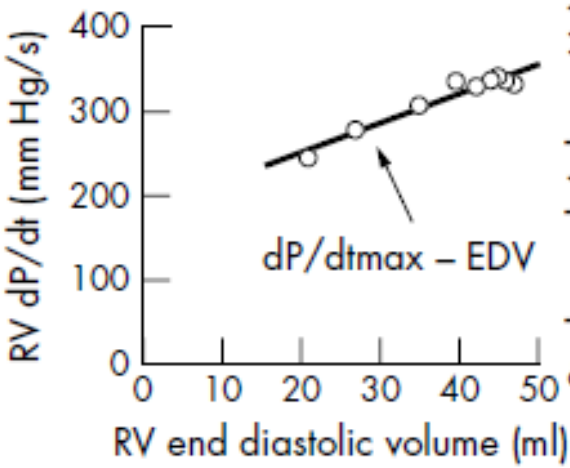


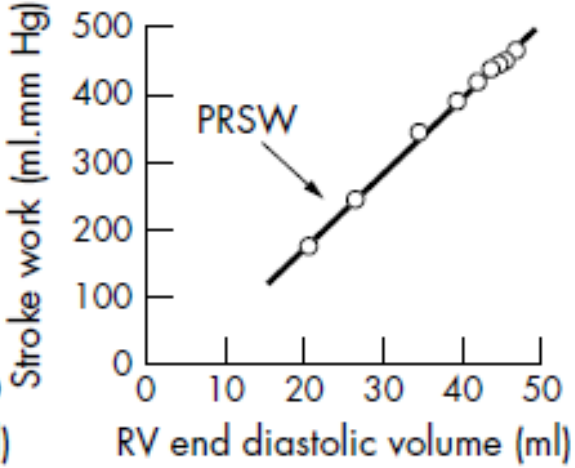


RV function assessment

Gold standard: pressure-volume loops



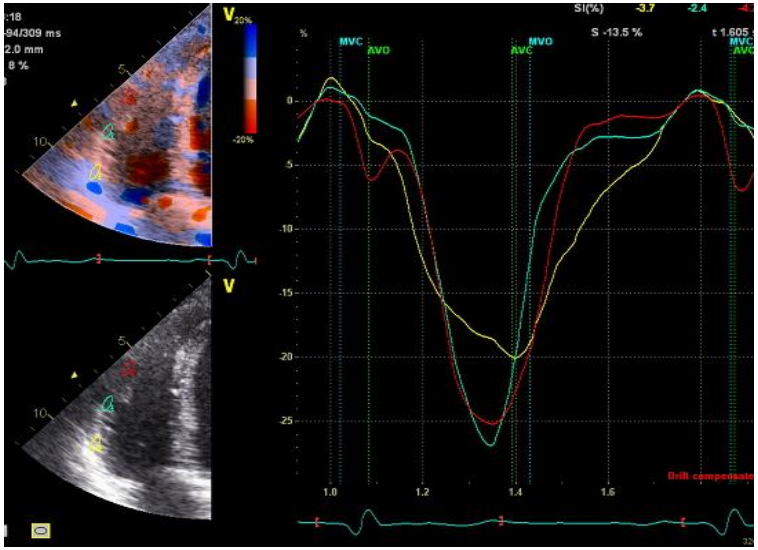


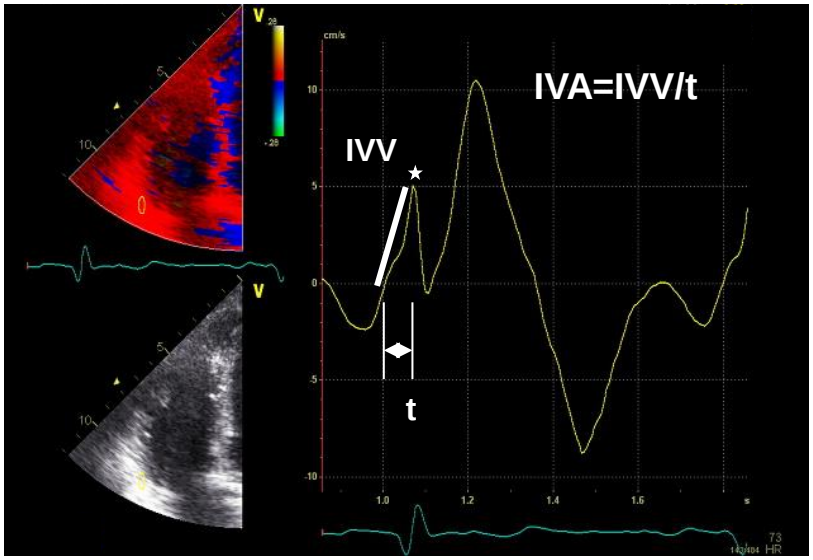


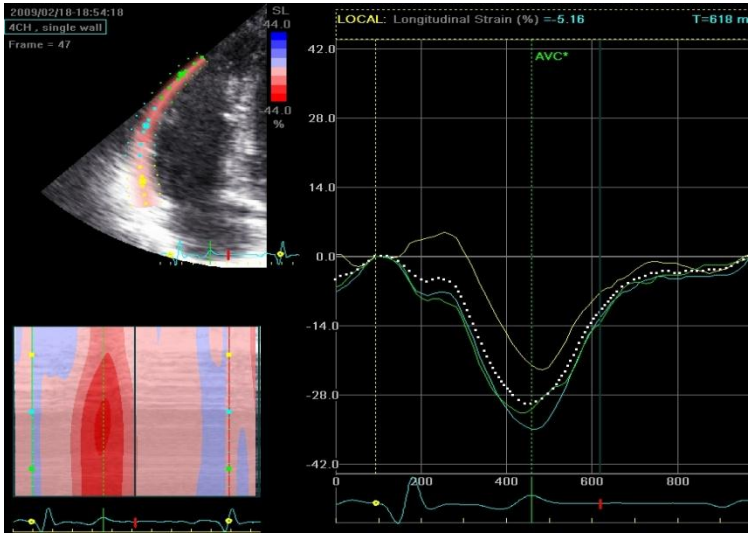
Load **dependence** of **dp/dt, stroke work**
Load **independence** of **end systolic elastance, PRSW**

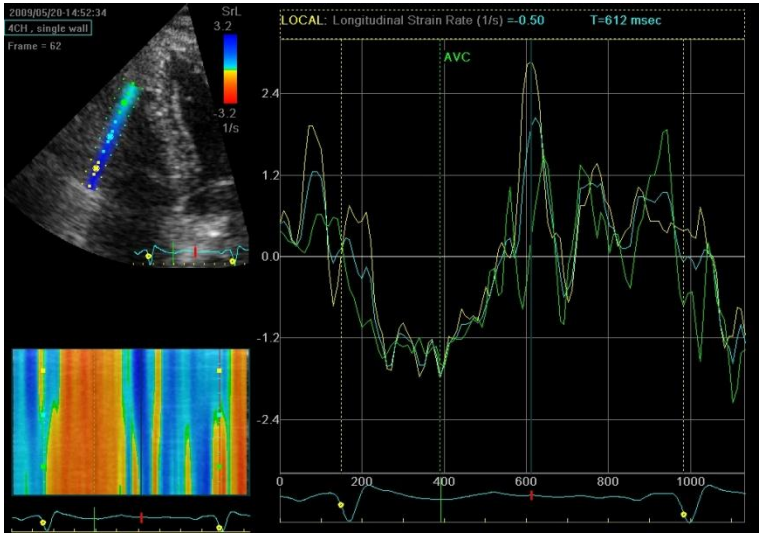
Bleeker, Heart 2006

Myocardial deformation imaging – several techniques, several parameters



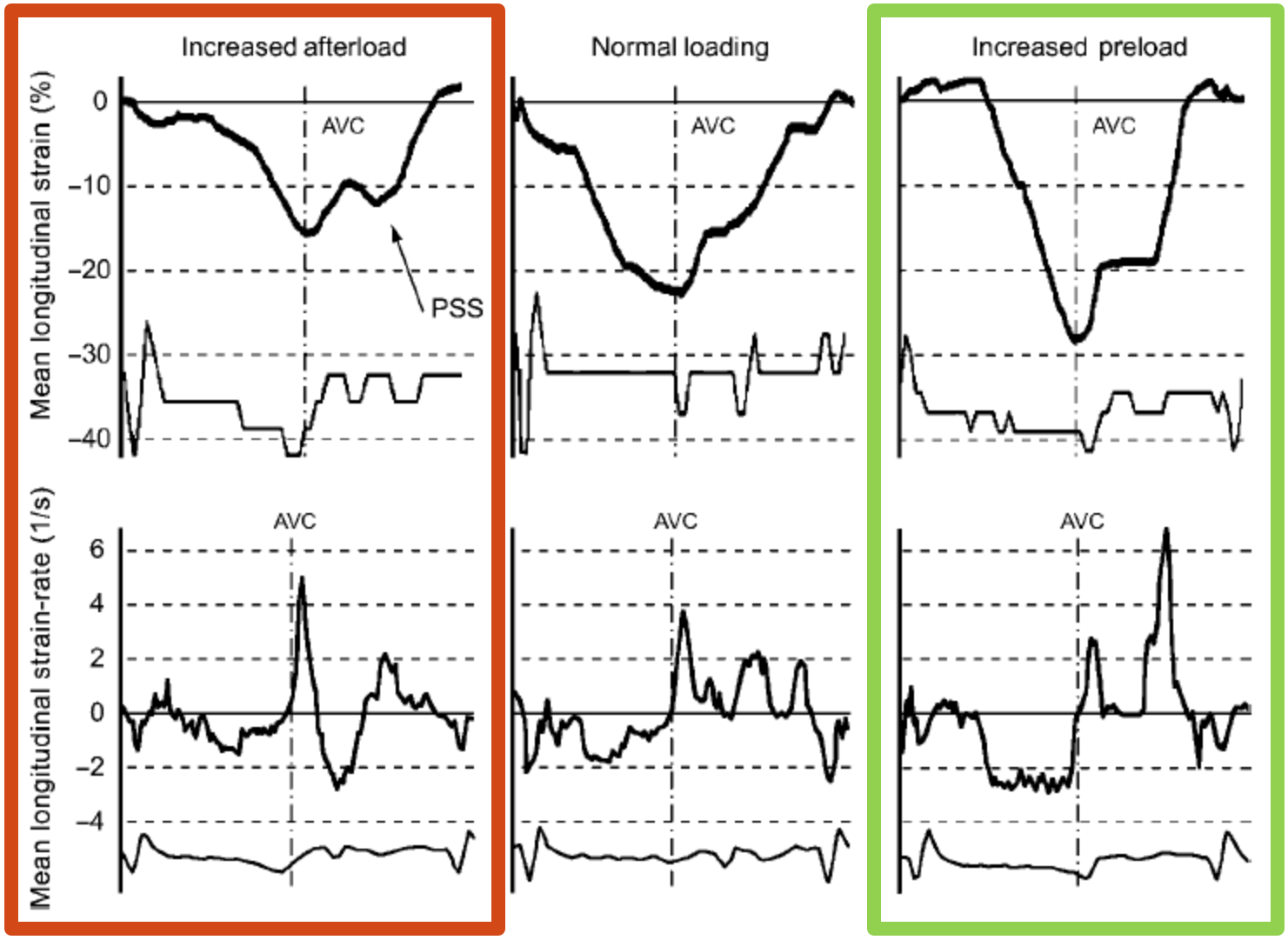






Jurcut et al, Eur J Echo 2010

Load and contractility – in practice



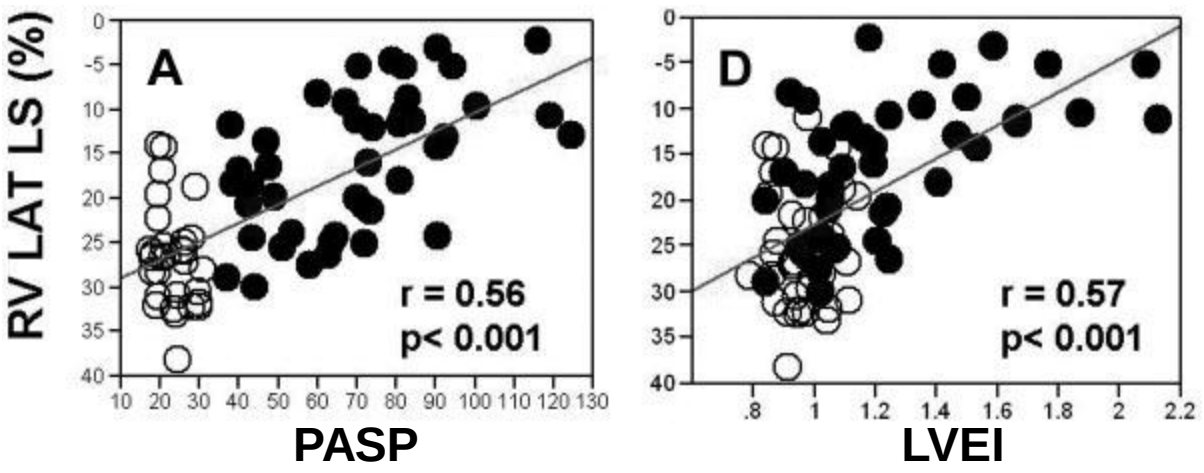
Rosner et al, EJE 2008

RV deformation

- **Afterload alterations**
  - Pulmonary hypertension
  - Pulmonary stenosis
  - Transposition of the great arteries
    ("systemic RV")

- **Preload alterations**
  - Atrial septal defect
  - Tricuspid regurgitation
  - Pulmonary regurgitation

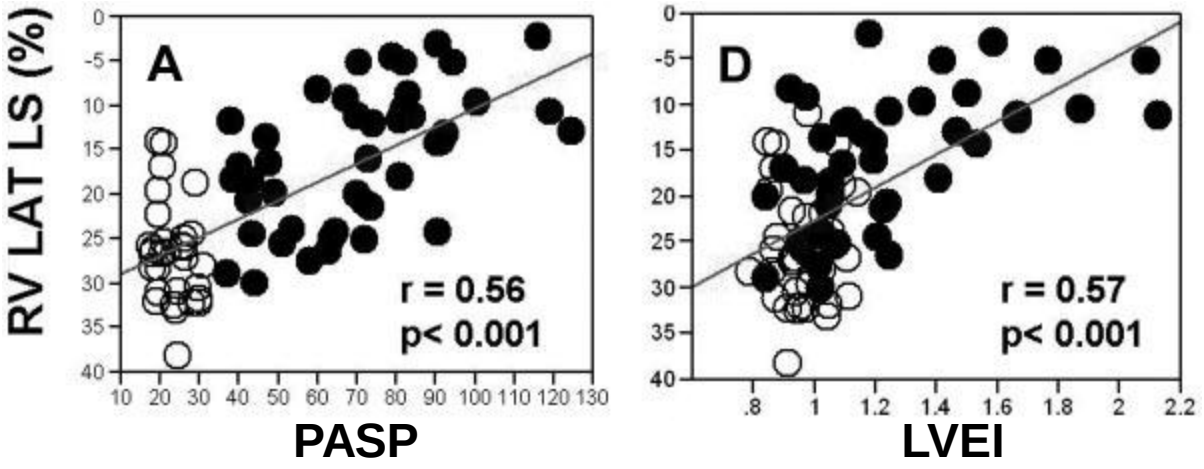
Pulmonary Hypertension



	Unadjusted	Adjusted for PASP	Adjusted for LV Eccentricity Index
LS, %			
RV LAT			
PH patients	−15.9±7.6*	−19.2±1.3	−17.1±1.1*
Control subjects	−25.5±6.1	−21.9±1.6	−24.0±1.1

Puwanant et al, Circulation 2010

Pulmonary Hypertension



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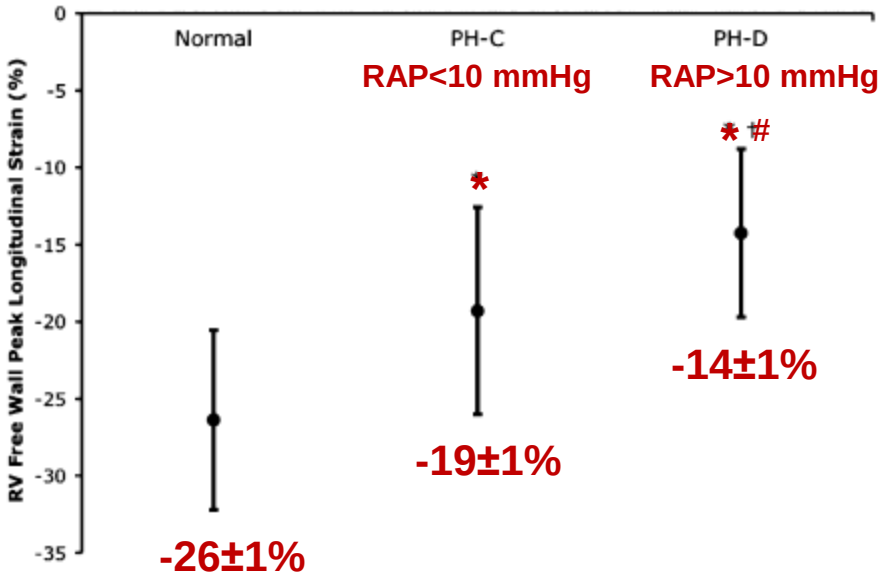
Pulmonary Hypertension

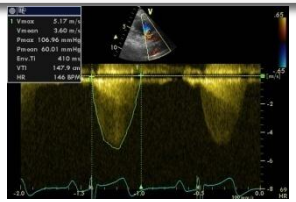
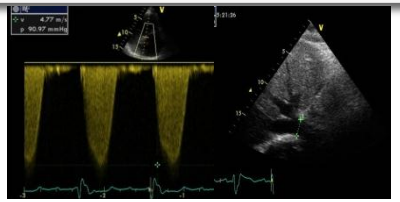


Study group	RV FW LS ROC curve cutoff	Sn	Sp
Normal PAPs	**≤ -27.2%**	70%	93.5%
PH compensated vs decompensated	**≥ -14.9%**	61.5%	85%

Simon et al, Congest Heart Fail 2009

Increased afterload: PHT vs PStenosis

62 patients

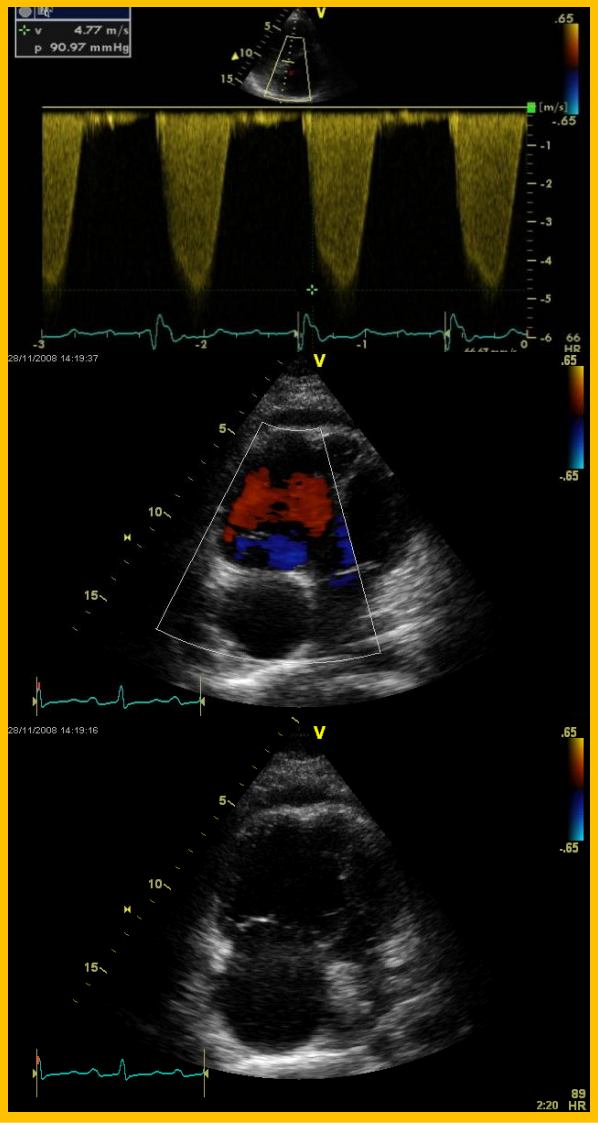
PulmSten	aPHT	Control
19 pts	22 pts	21 pts
37±16 y	44 ± 16 y	38 ± 12 y
		
RVP 73±34 mmHg	RVP 88±31 mmHg	RVP 25±4 mmHg

p = 0.37

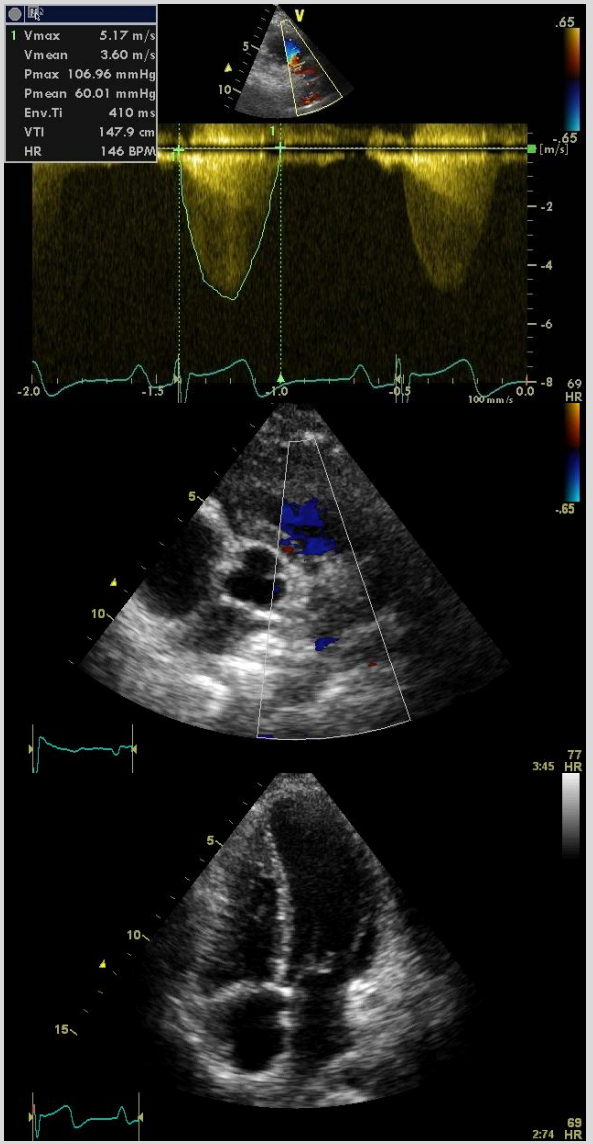
p<0.001

Jurcut et al, JASE 2011

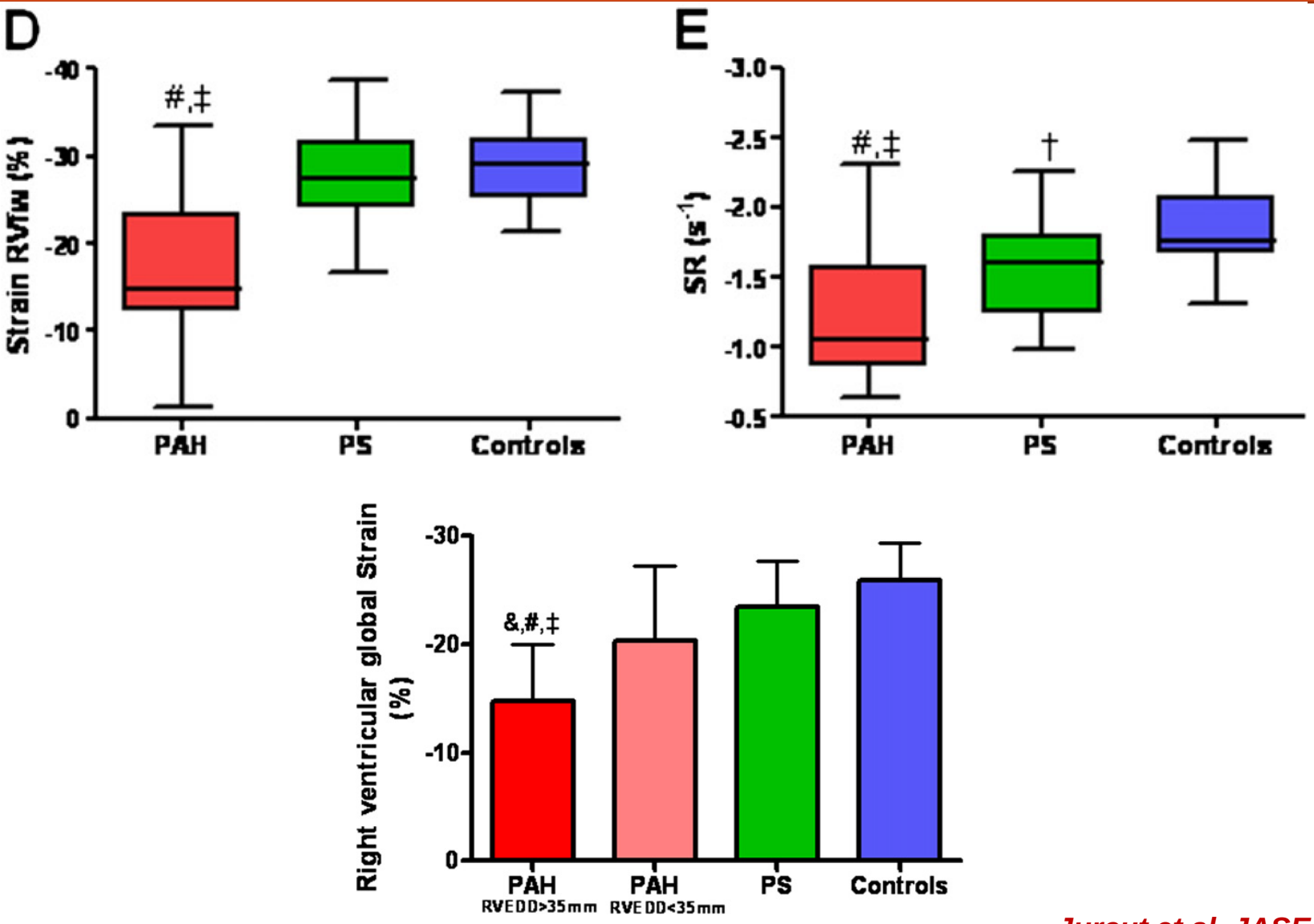
Arterial PHT
F, 25 years
RVP = 100 mmHg



Pulmonary stenosis
F, 27 years
RVP = 106 mmHg



Increased afterload: PHT vs PStenosis



Jurcut et al, JASE 2011

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

Chronic Pulmonary Artery Pressure Elevation Is Insufficient to Explain Right Heart Failure

Harm J. Bogaard, Ramesh Natarajan, Scott C. Henderson, Carlin S. Long, Donatas Kraskauskas, Lisa Smithson, Ramzi Ockaili, Joe M. McCord and Norbert F. Voelkel

Circulation 2009;120:1951-1960; originally published online Nov 2, 2009;

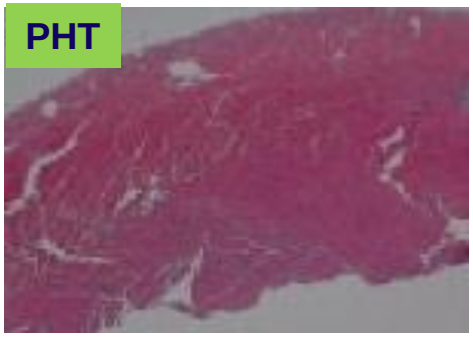
Pulmonary artery banding ~ PulmSten

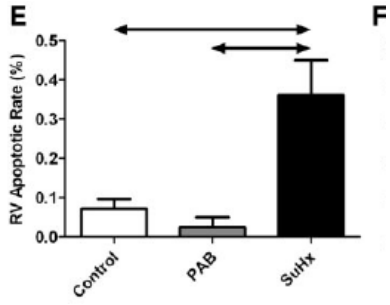
Angioproliferative pulmonary vascular remodeling ~ aPHT

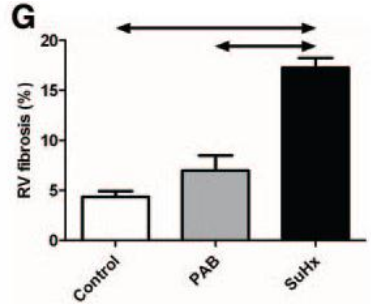
	BW, g	RV, mg	RV/LV+S	TAPSE, mm	HR, bpm	SV, μL	CO, mL/min
Controls (n=6)	362±14	202±19	0.24±0.02	3.5±0.2	312±15	206±46	62.2±5.2
PAB (n=8)	357±25*	451±71†‡	0.52±0.07†‡	2.6±0.7§‡	297±12	199±25‖	59.7±7.1‖
SuHx (n=8)	324±34†	663±146†	0.76±0.17†	1.5±0.5†	292±15	127±22#	37.3±6.3#

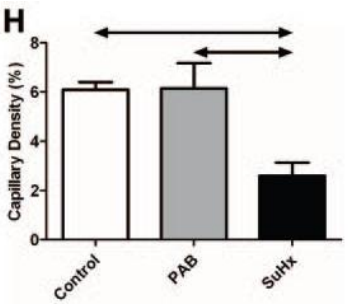
PS

PHT



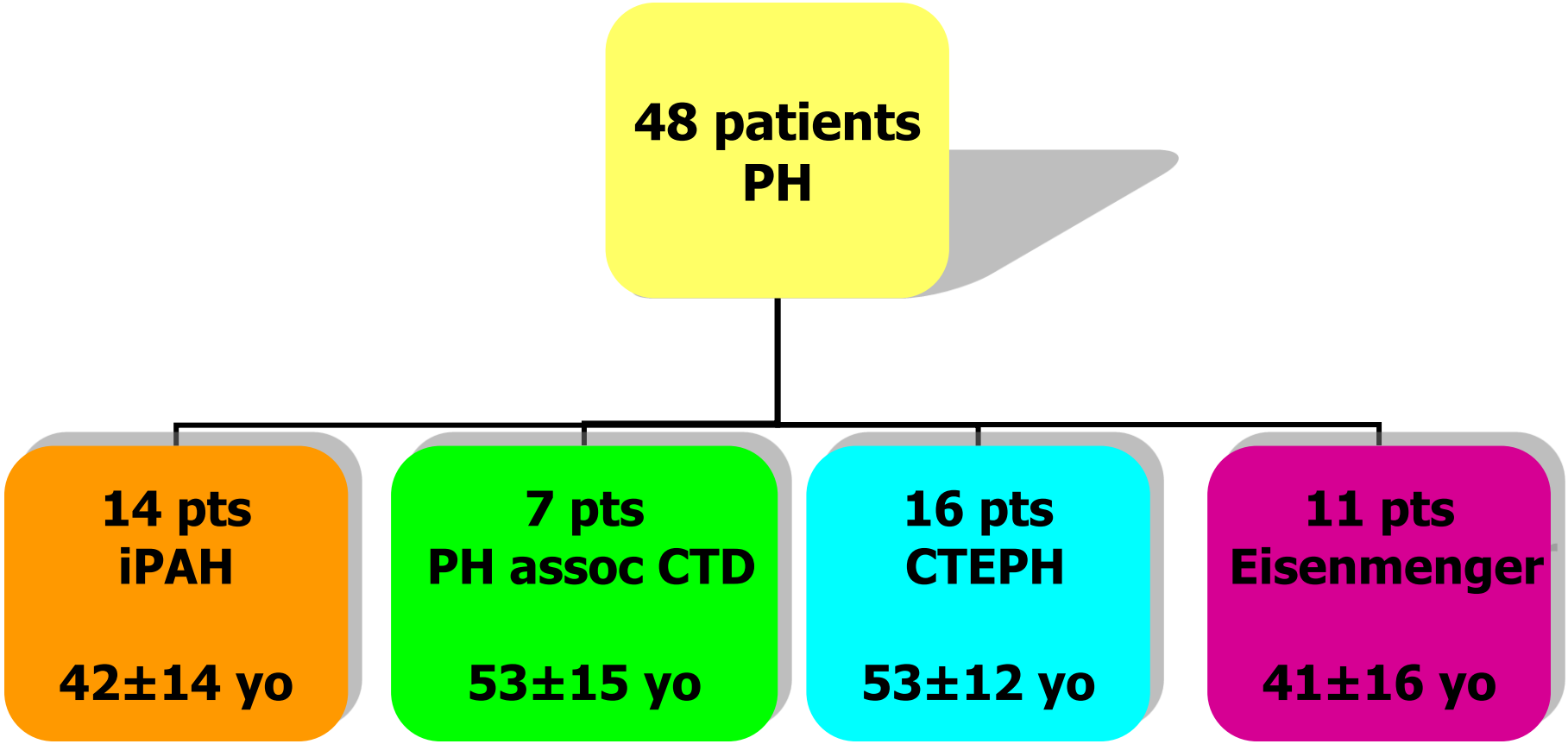






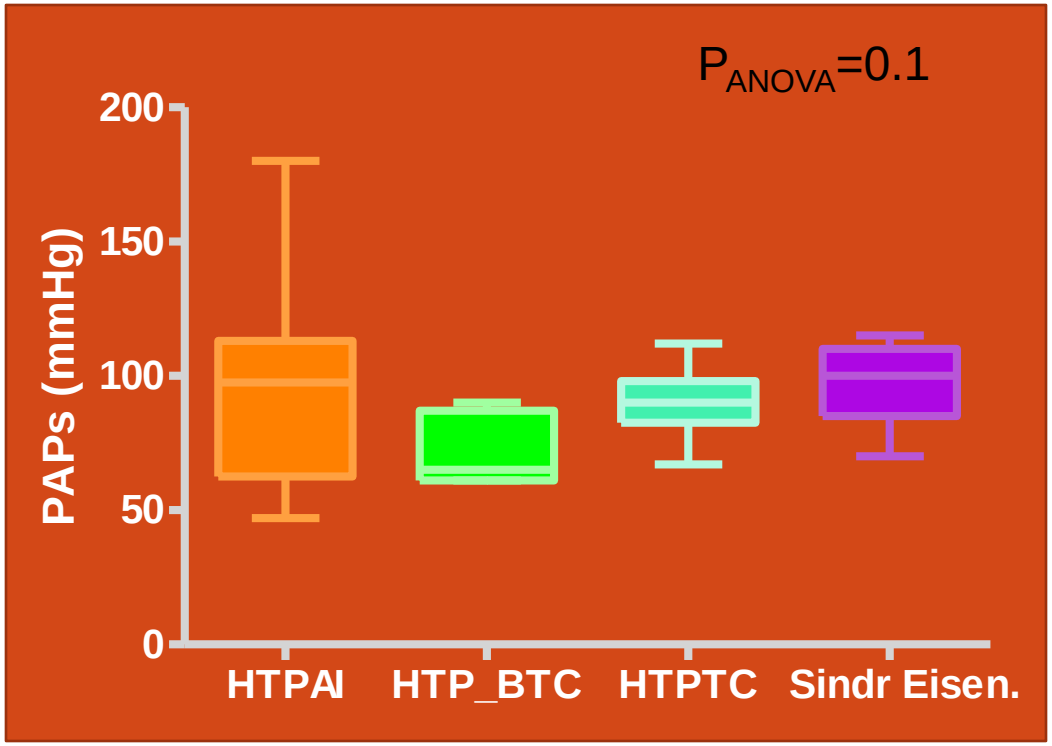
Bogaard et al, Circulation 2009

RV and PH etiology – does it matter?



Giusca, Jurcut et al, data on file

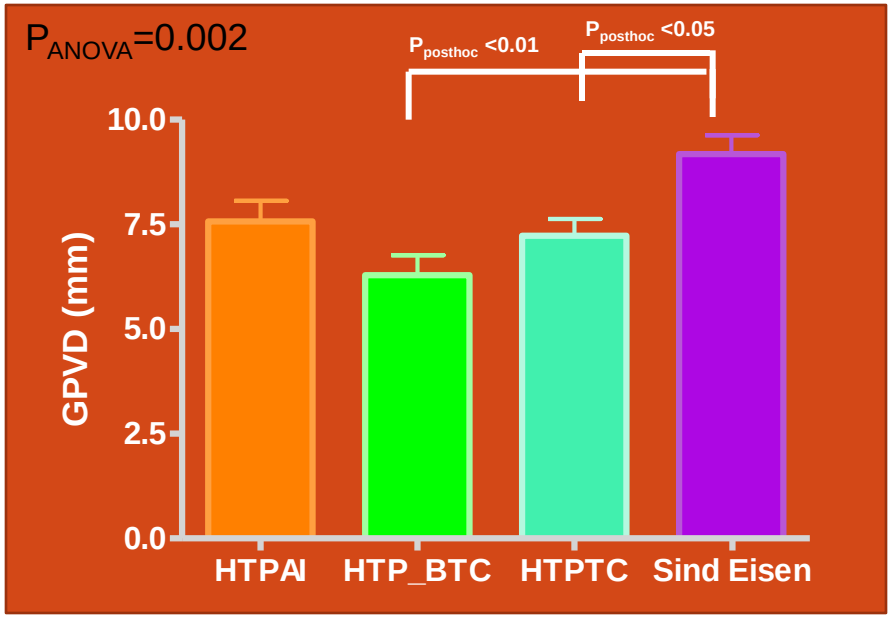
Similar sPAP…

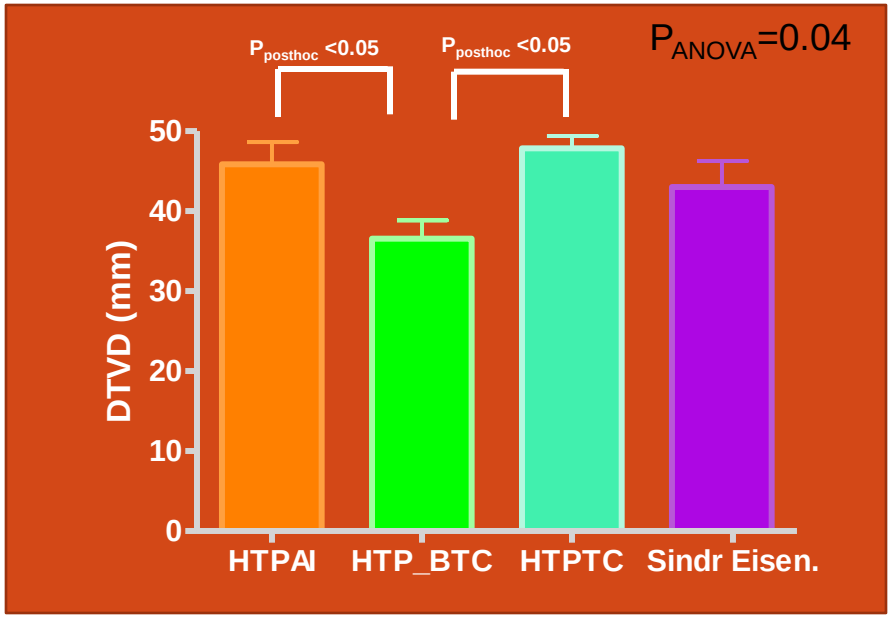


	iPAH	PH_CTD	CTEPH	EisenSy
sPAP (mmHg)	96±36	72±12.5	89±12	96±14

Giusca, Jurcut et al, data on file

…but different RV morphology…



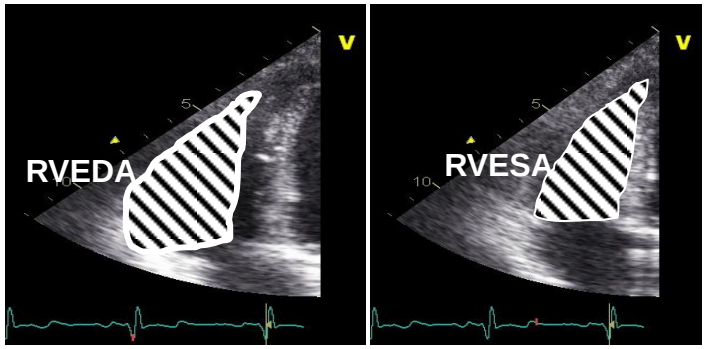


RVfw	7,6±1,8	6,2±1,2	7,2±1,4	9,2±1,5

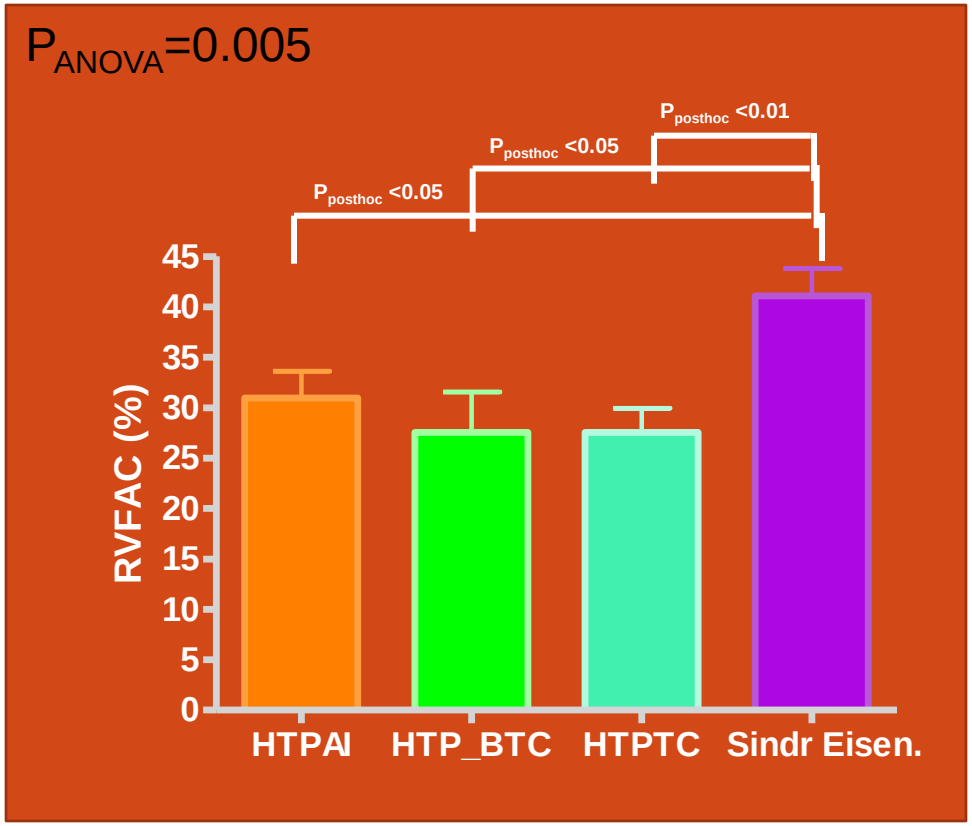
RVEDD	45,9±10	36,6±6	47,9±6	43±10,8

Giusca, Jurcut et al, data on file

…and different RV function



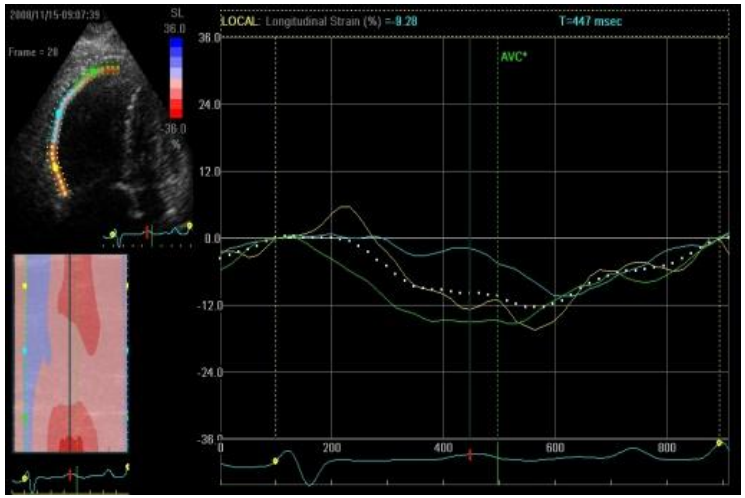
$$RVFAC = \frac{RV\ enddiastolic\ area - RV\ endsystolic\ area}{RV\ enddiastolic\ area}$$

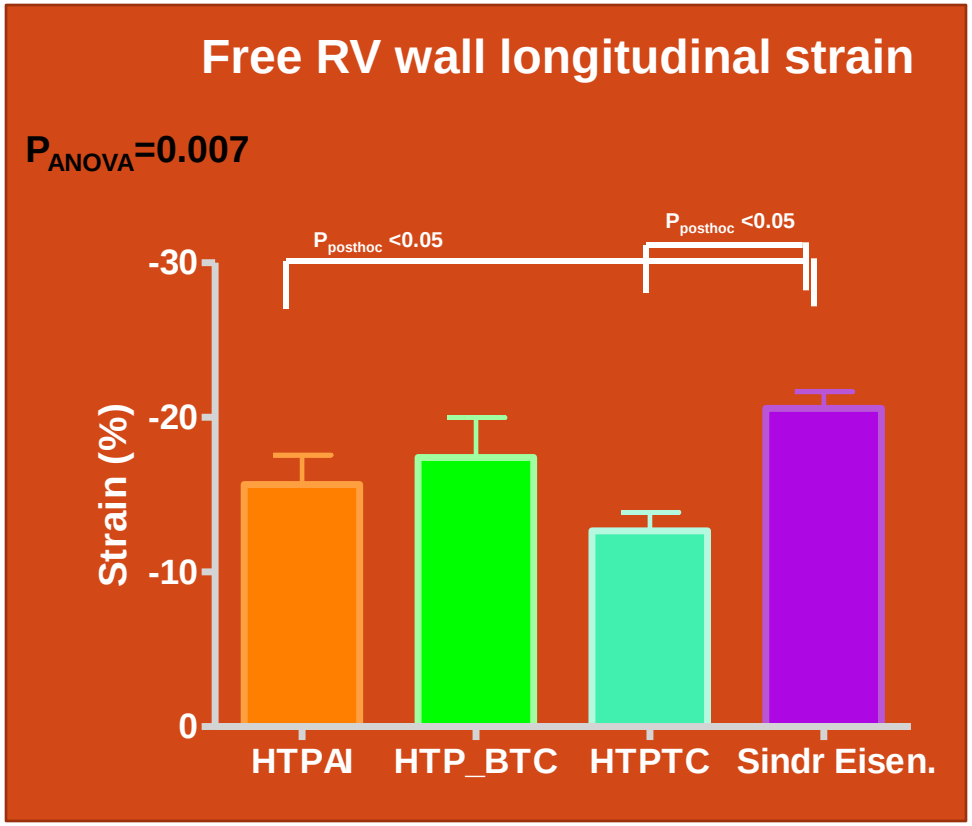


RVFAC	30,9±10	27,5±11	27,5±9,5	41±8,9

Giusca, Jurcut et al, data on file

…and different RV function



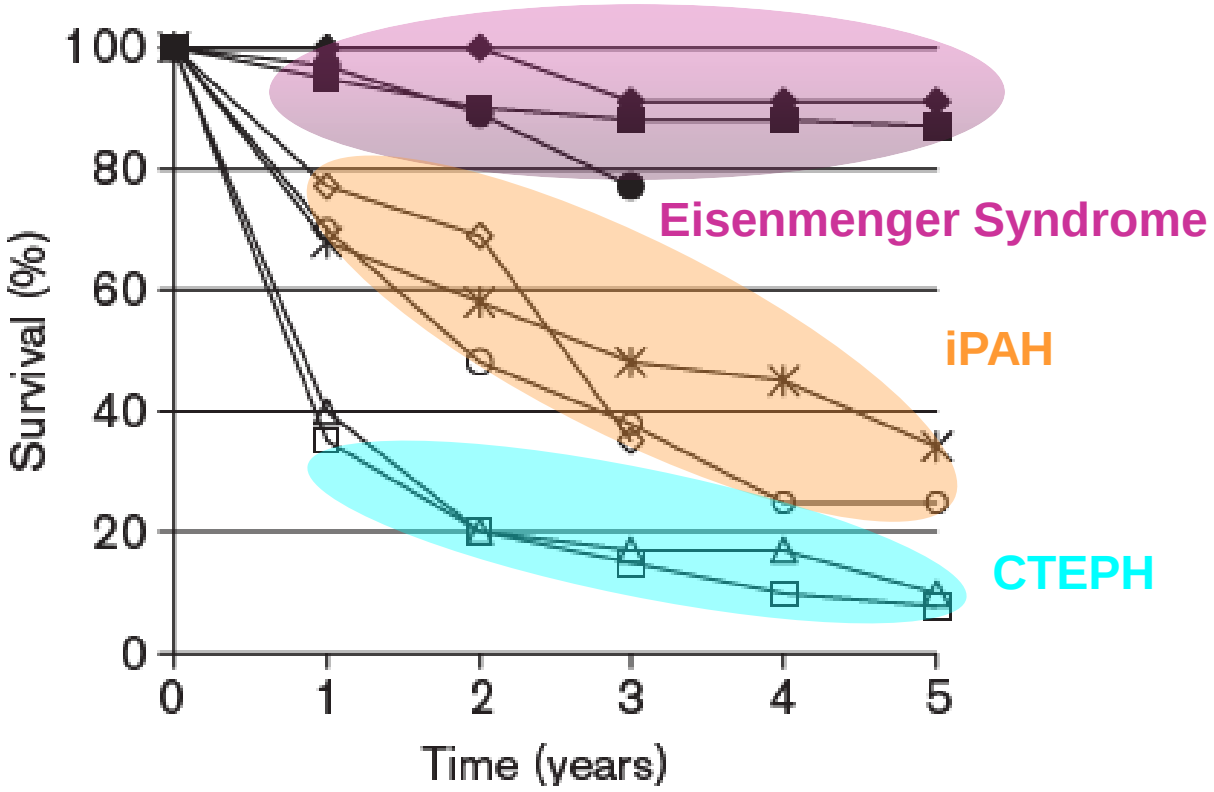


Long S (%)	**-15,6±6,8**	**-17,4±6,8**	**-12,6±4,8**	**-20,6±3,5**

Giusca, Jurcut et al, data on file

So…

- Is RV adaptation/remodeling identical for all PH forms? And what does it mean?



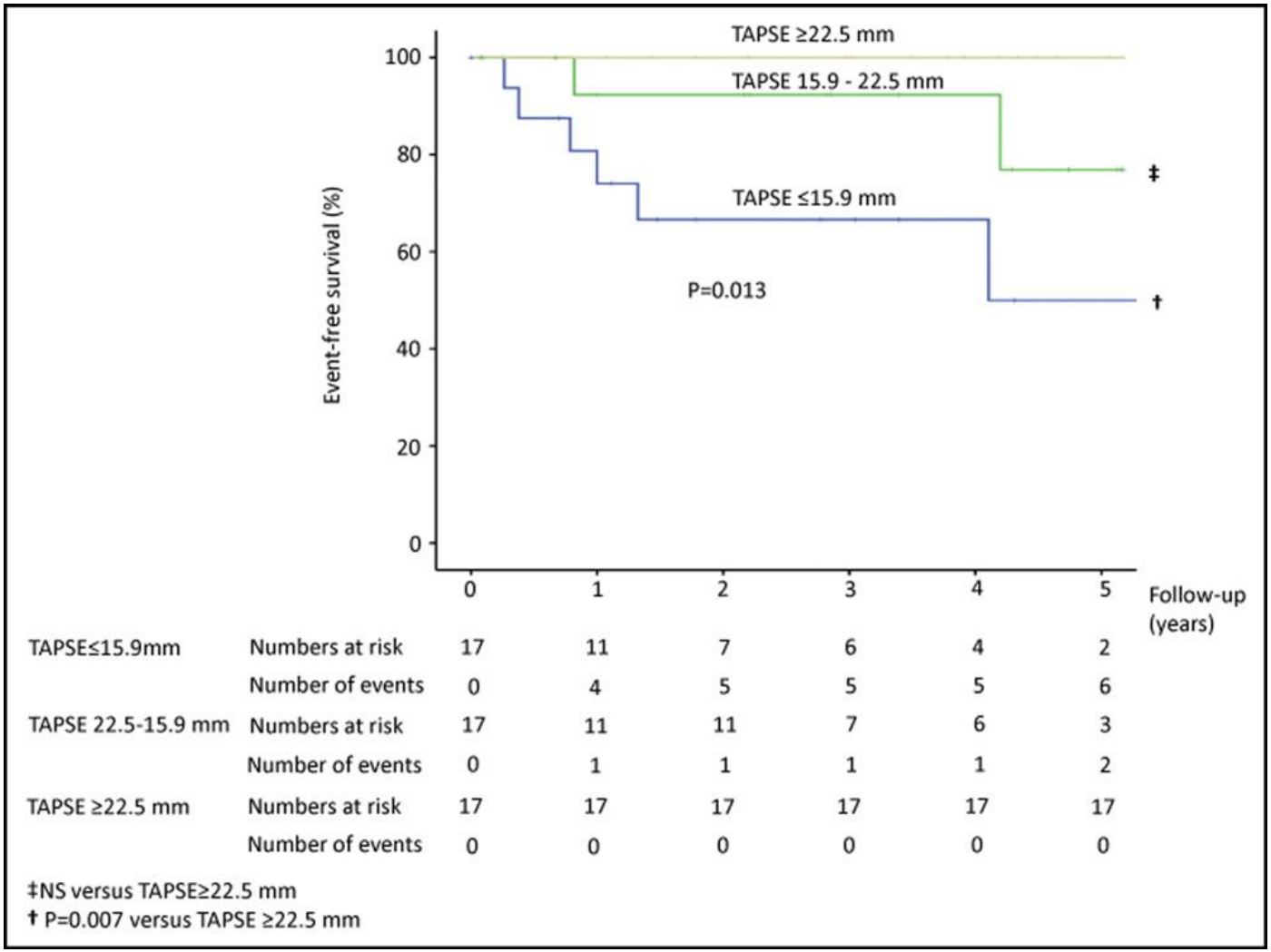
Hopkins et al, Coronary Artery Disease 2005

However, also in Eisenmenger syndrome…

Variable	Simple Pretricuspid (n = 9)	Simple Post Tricuspid (n = 26)	Combined (n = 23)	p Value*
Left atrium parasternal (mm)	46.9 ± 8.5	31.9 ± 6.7	30.0 ± 8.6	<0.0001
Left atrium apical (mm)	56.2 ± 9.1	42.8 ± 8.2	42.6 ± 7.9	<0.0001
Right atrium apical (mm)	59.4 ± 7.1	44.1 ± 7.9	45.7 ± 6.4	<0.0001
Left ventricle transverse (mm)	38.4 ± 9.9	36.3 ± 7.7	36.1 ± 7.0	0.744
Right ventricle transverse (mm)	48.7 ± 11.3	37.8 ± 9.9	34.6 ± 8.1	0.002
Eccentricity index	0.9 ± 0.4	1.0 ± 0.4	1.1 ± 0.3	0.248
Interventricular septum (mm)	11.1 ± 1.8	10.5 ± 3.1	12.0 ± 2.8	0.195
Left ventricular ejection fraction (%)	65.3 ± 10.6	63.4 ± 7.4	68.2 ± 10.2	0.191
Right ventricular function	2.0 ± 1.0	1.6 ± 0.8	1.4 ± 0.5	0.111
Mitral inflow E/A ratio	0.77 ± 0.25	1.17 ± 0.41	1.41 ± 0.36	0.001
Pulmonary acceleration time (ms)	73.2 ± 19.0	72.4 ± 22.3	81.4 ± 18.0	0.337
Tricuspid annular plane systolic excursion (mm)	18.0 ± 4.0	17.2 ± 4.1	19.3 ± 4.0	0.222
Mitral regurgitation (n/4)	1.3 ± 0.5	1.1 ± 1.0	—	0.459
Tricuspid regurgitation (n/4)	2.7 ± 0.9	1.7 ± 0.9	—	0.012
Atrioventricular valve regurgitation (n/4)	—	—	1.7 ± 1.2	—
Aortic regurgitation (n/4)	0.1 ± 0.3	0.3 ± 0.5	0.1 ± 0.2	0.132
Pulmonary regurgitation (n/4)	1.4 ± 0.5	1.1 ± 0.8	0.9 ± 0.7	0.187
Systolic pulmonary artery pressure (mm Hg)	86.0 ± 18.3	91.6 ± 31.6	74.7 ± 16.4	0.259

Van de Bruaene et al, Am J Cardiol 2012

Eisenmenger syndrome – linking echo to prognosis

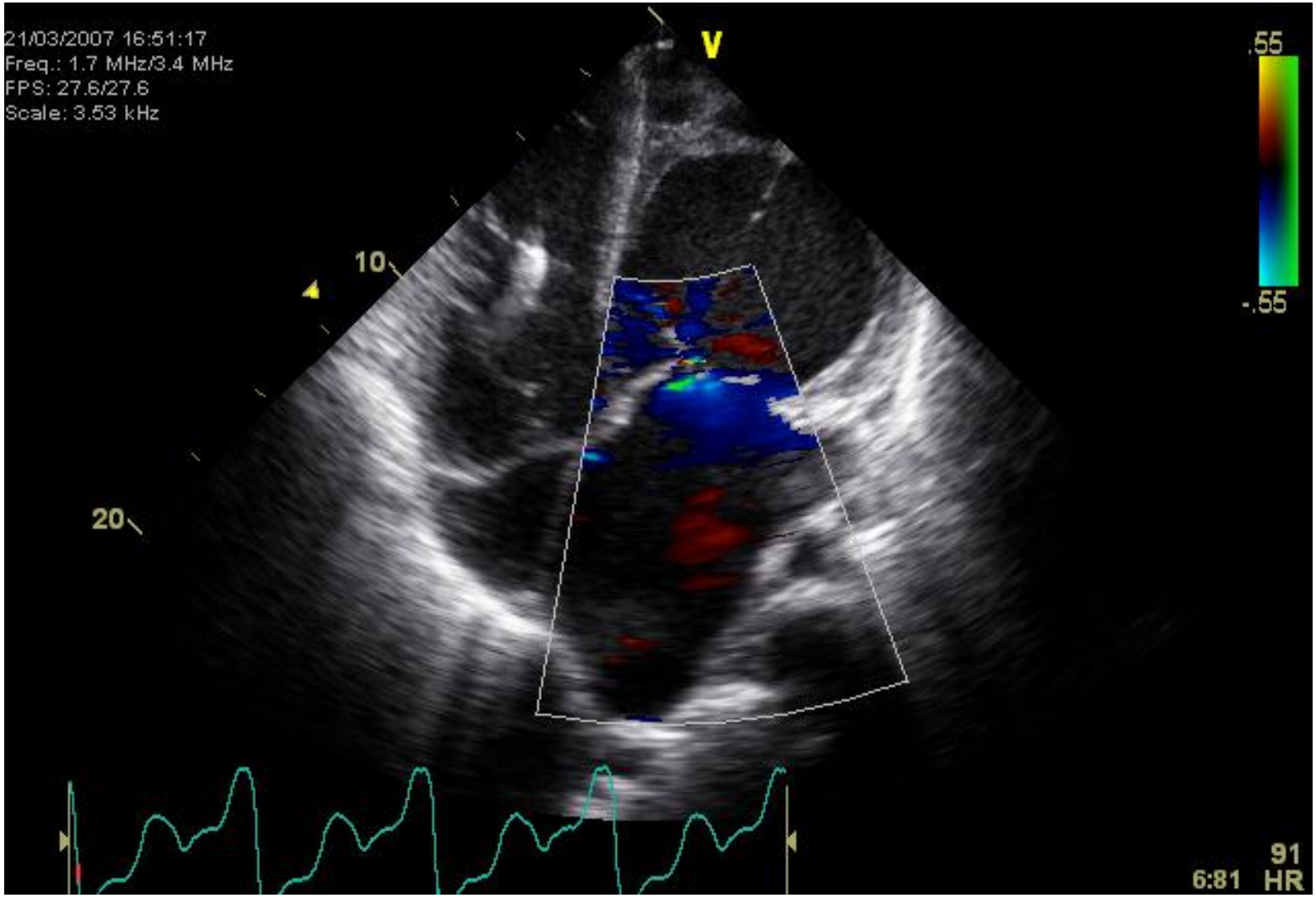


TAPSE≤15.9mm	Numbers at risk	17	11	7	6	4	2
	Number of events	0	4	5	5	5	6
TAPSE 22.5-15.9 mm	Numbers at risk	17	11	11	7	6	3
	Number of events	0	1	1	1	1	2
TAPSE ≥22.5 mm	Numbers at risk	17	17	17	17	17	17
	Number of events	0	0	0	0	0	0

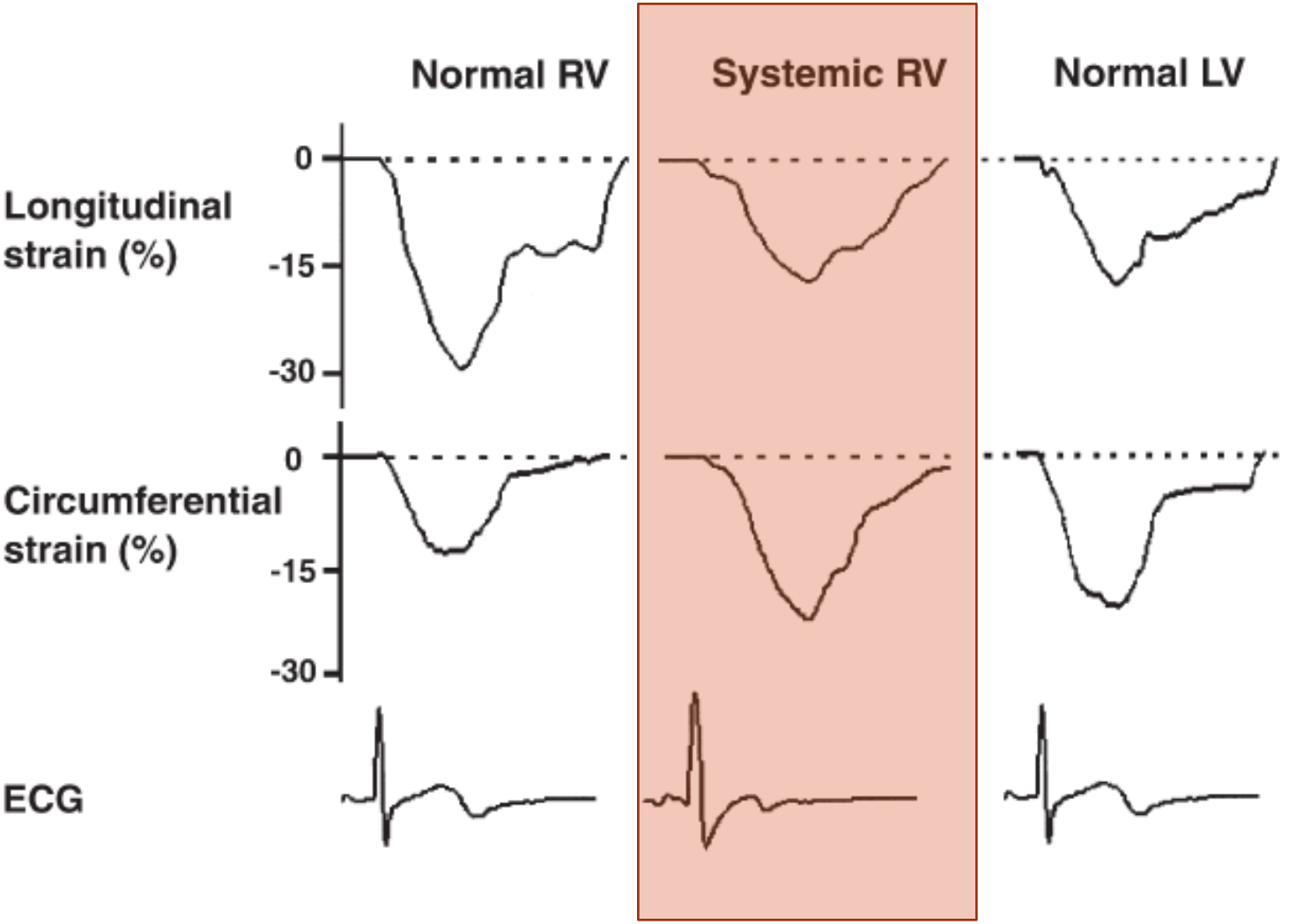
‡NS versus TAPSE≥22.5 mm
† P=0.007 versus TAPSE ≥22.5 mm

Van de Bruaene et al, Am J Cardiol 2012

TGA – the “systemic right ventricle”



TGA – the “systemic right ventricle”

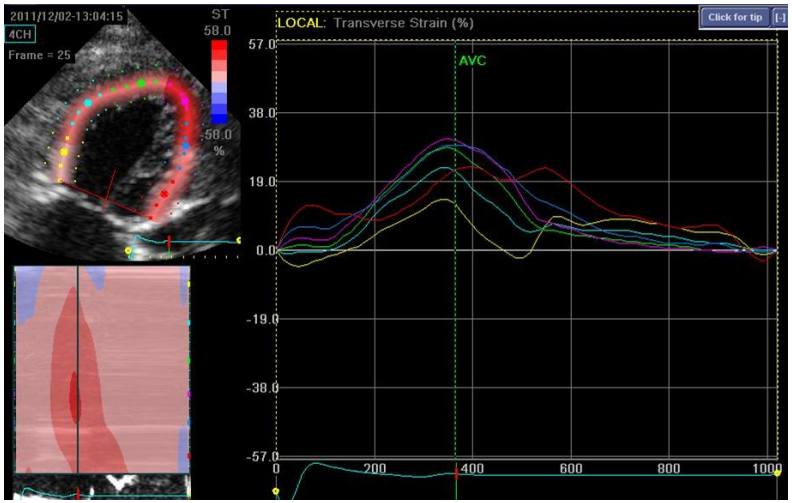


Pettersen et al, JACC 2007

TGA – the "systemic right ventricle"

	Controls ($n=24$)	AS-TGA patients ($n=26$)	*P* value
RV longitudinal 2D strain			
Basal segment	-33 ± 6	-13 ± 4	0.0001
Mid segment	-29 ± 6	-14 ± 4	0.0001
Apical segment	-26 ± 6	-13 ± 3	0.0001
Average	-29 ± 6	-13 ± 3	0.0001
RV transverse 2D strain			
Basal segment	26 ± 6	26 ± 19	0.0001
Mid segment	26 ± 6	30 ± 18	0.01
Apical segment	20 ± 9	28 ± 15	0.02
Average	27 ± 6	28 ± 16	0.0001

	Coefficient	Standard error	Standard coeff.	*T* value	*P* value
Terme cst.	7.245	5.056	7.245	1.433	.1691
Average transverse strain	.094	.018	.828	5.148	<.0001
Average longitudinal strain	−.037	.088	−.063	−.422	.6781
Age	−.005	.057	−.017	−.093	.9266
BSA	.270	1.283	.033	.210	.8359
Degree TR	.323	.299	.174	1.081	.2940
TAPSE	.134	.306	.070	.438	.6669
RV EF	−.023	.073	−.046	−.316	.7554
RV FAC	−.031	.075	−.057	−.408	.6882



Di Salvo et al, Int J Cardiol 2010

TGA – the "systemic right ventricle"

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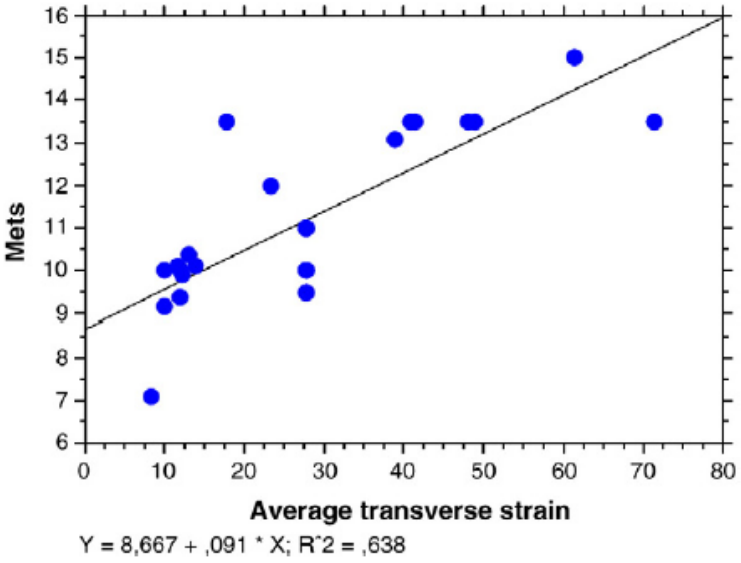
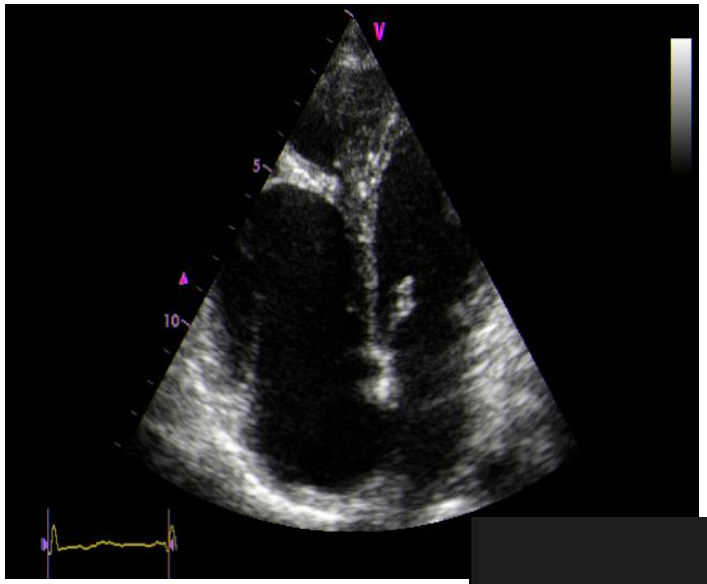
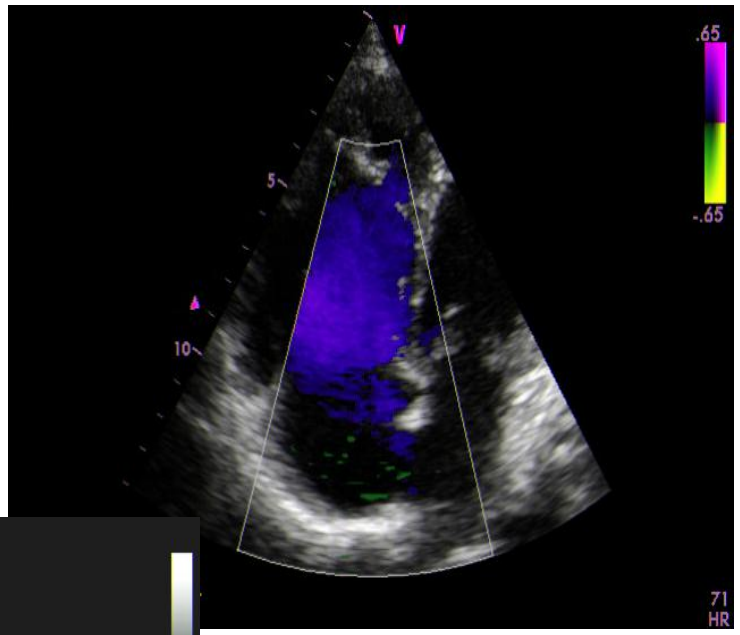
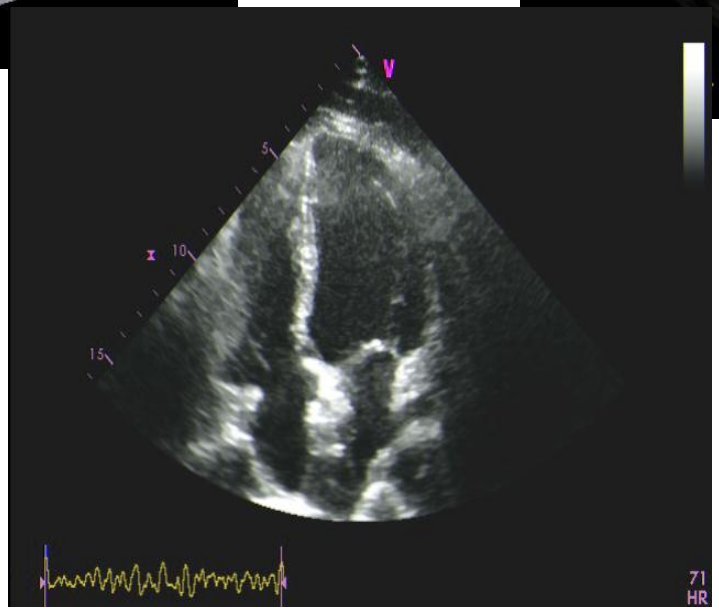


Di Salvo et al, Int J Cardiol 2010

Atrial septal defect

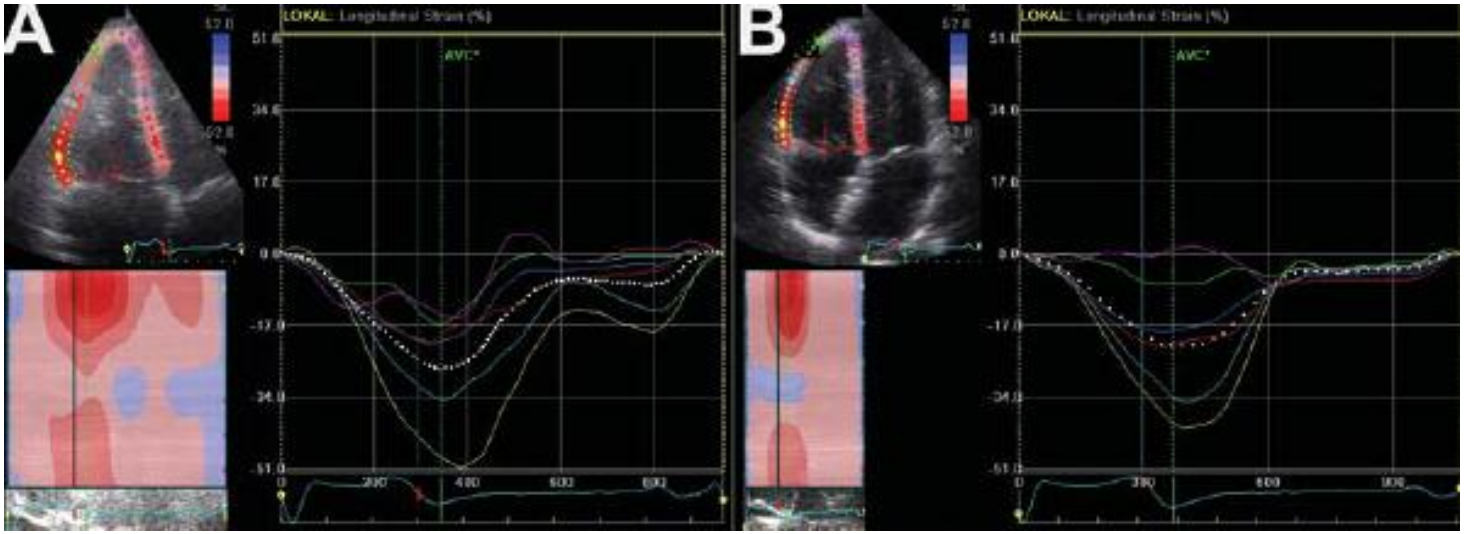






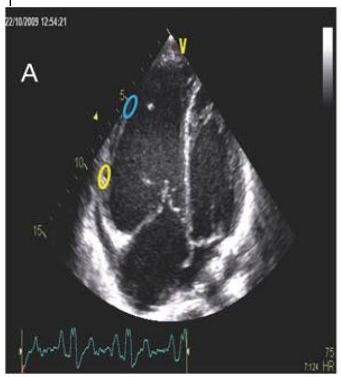
Open atrial septal defect

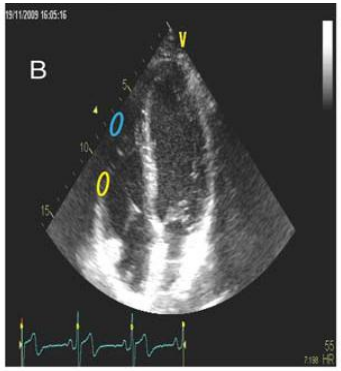
	Control group	Pre
Global strain	−21.6 ± 4.9	−23.4 ± 4.5 *
Lateral basal	−28.7 ± 8.8	−28.2 ± 9.8
Lateral mid	−28.6 ± 7.8	−29.4 ± 7.7
Lateral apical	−23.6 ± 7.6	−27.0 ± 6.7
Septal apical	−15.7 ± 7.7	−21.2 ± 7.4
Septal mid	−17.9 ± 3.7	−20.2 ± 4.7
Septal basal	−18.7 ± 3.5	−18.5 ± 3.8
Global strain rate	−1.11 ± 0.18	−1.25 ± 0.18

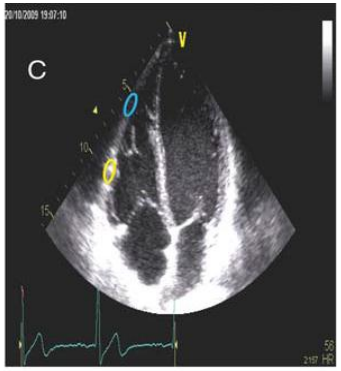


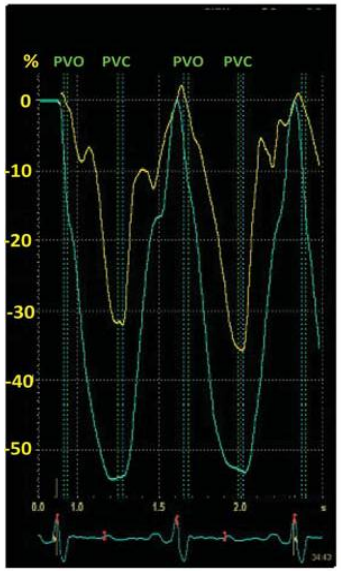
Jategaonkar et al, EJE 2009

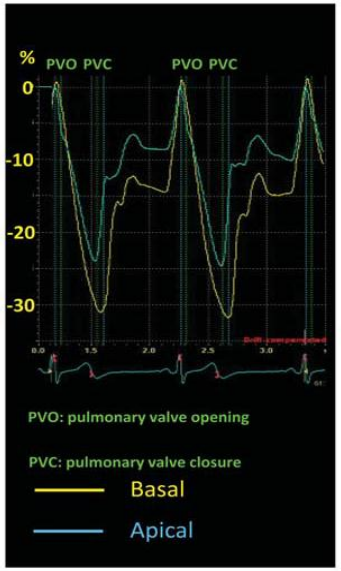
Atrial septal defect – open vs closed

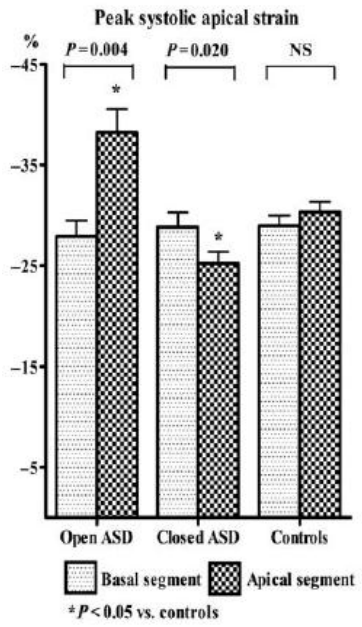


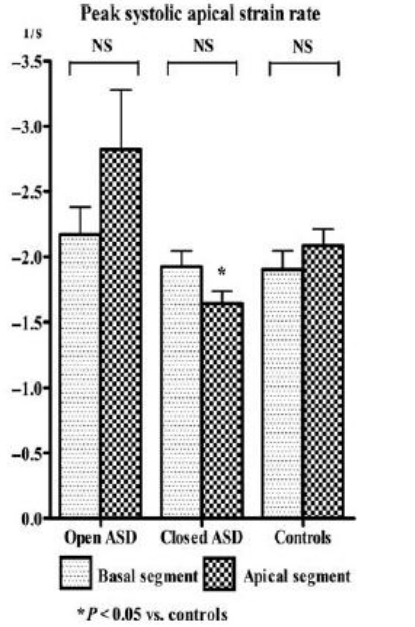


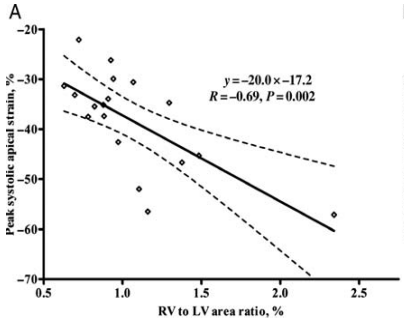


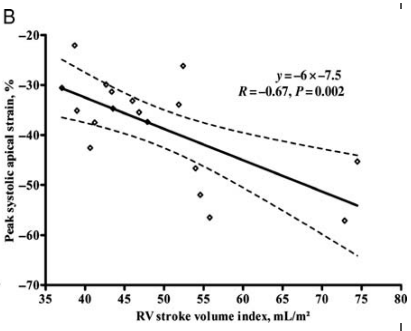






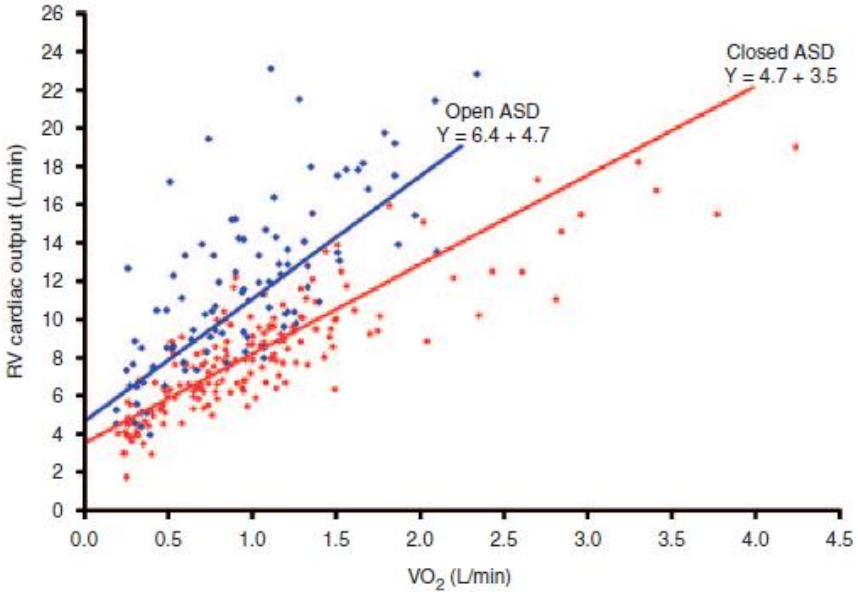


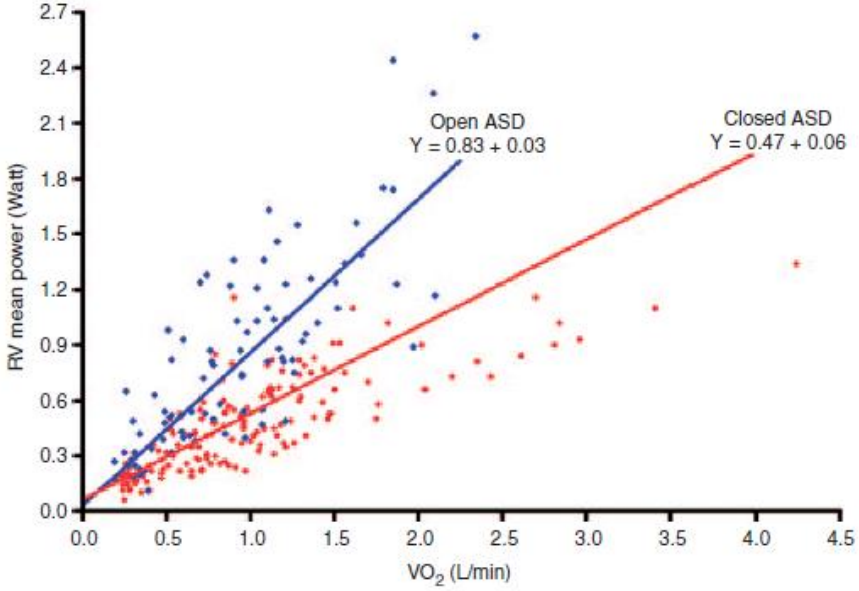




Van de Bruaene et al, EJE 2011

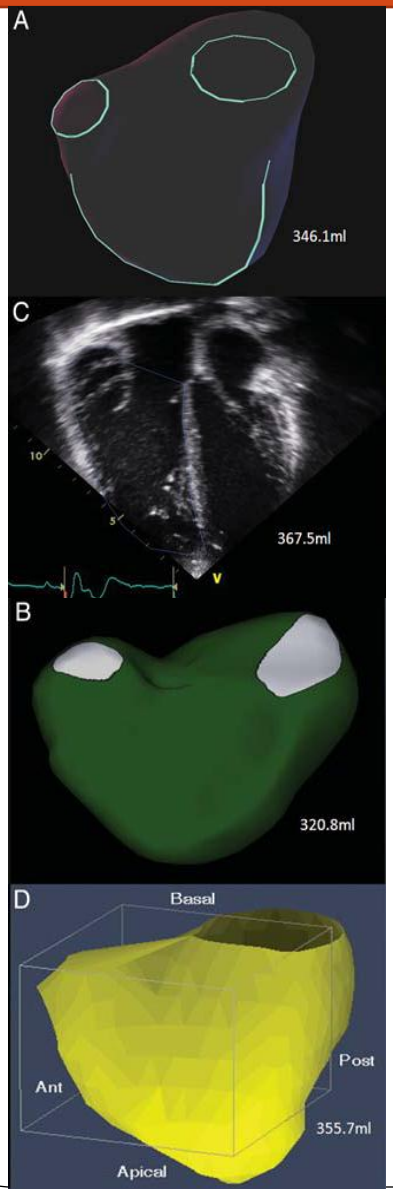
Atrial septal defect – exercise physiology





Van de Bruaene et al, Eur J Prev Cardiol 2012

RV function after ToF repair



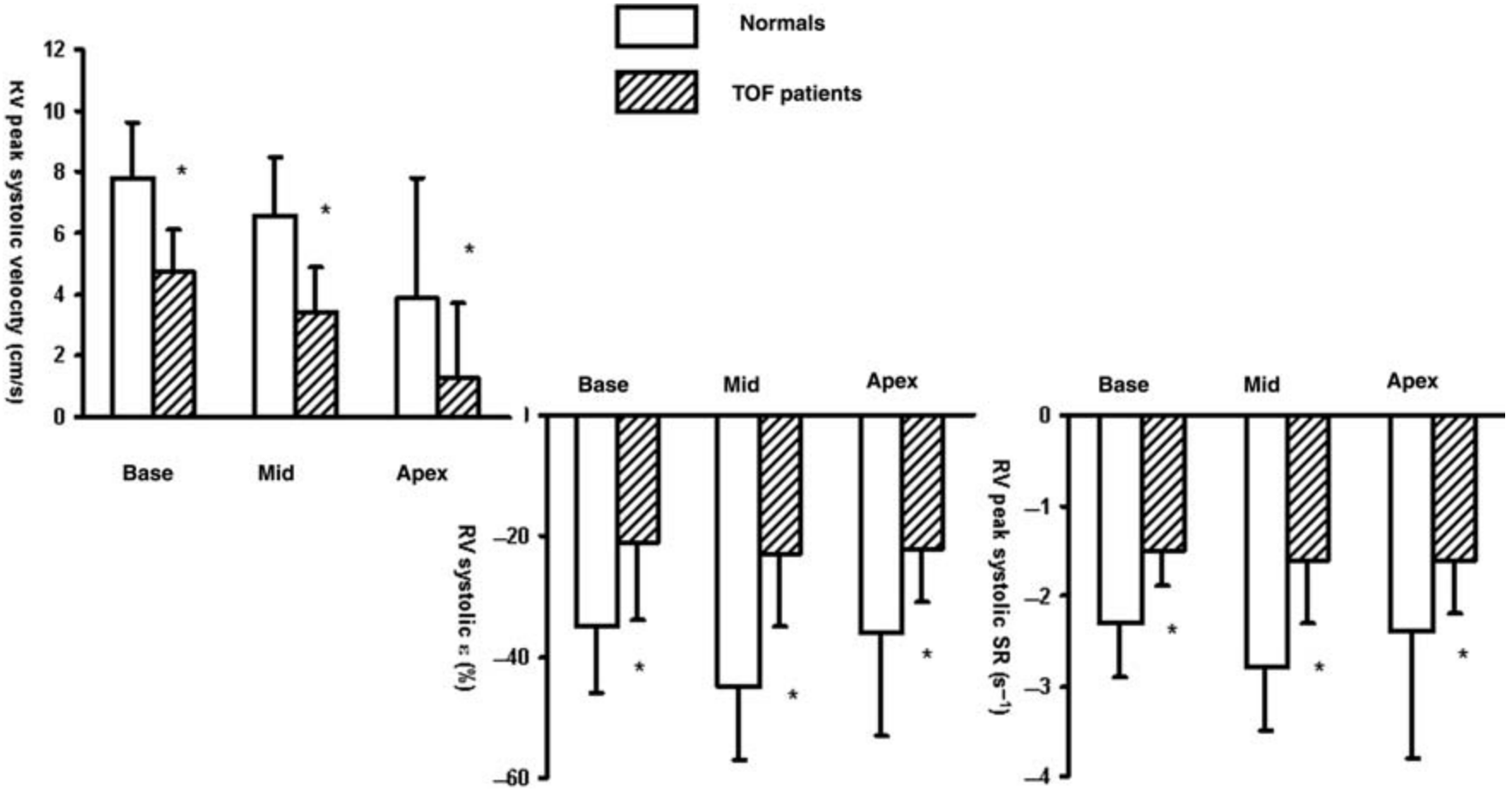
•Different echocardiographic techniques have become available that allow to reliably and accurately assess RV volumes and function.

• Both 3D an 3DR can be used in postoperative pediatric patients after TOF correction.

• Cardiac MRI currently still is the reference technique.

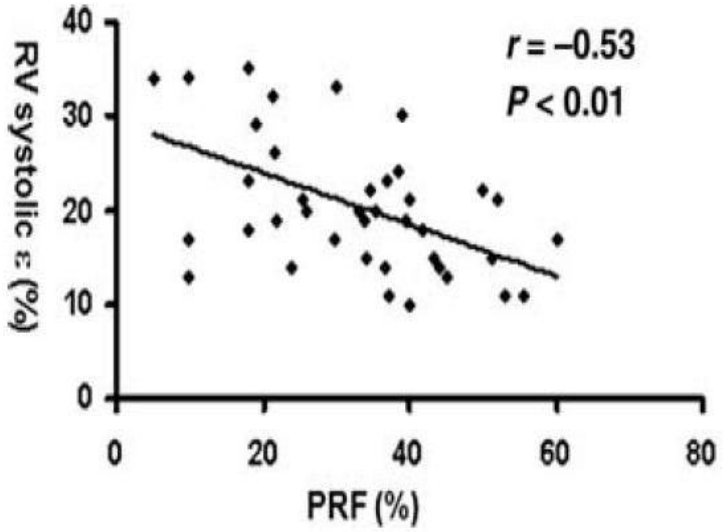
Dragulescu et al, Eur J Echo 2011

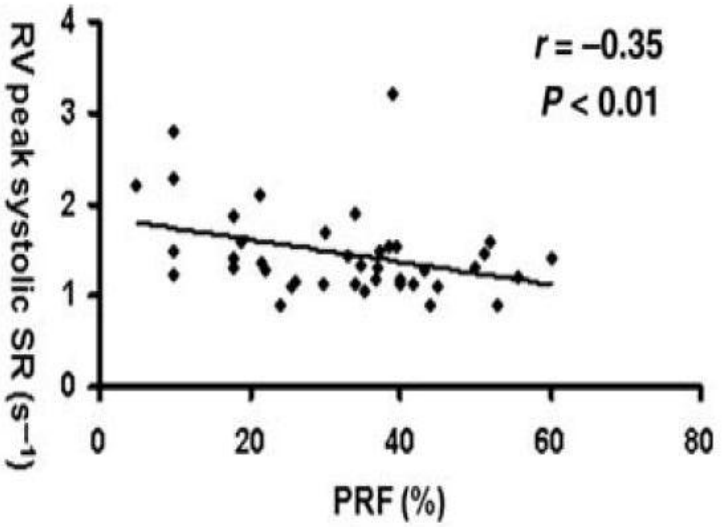
RV function after ToF repair



Eyskens et al, Eur J Echocard 2010

RV function after ToF repair

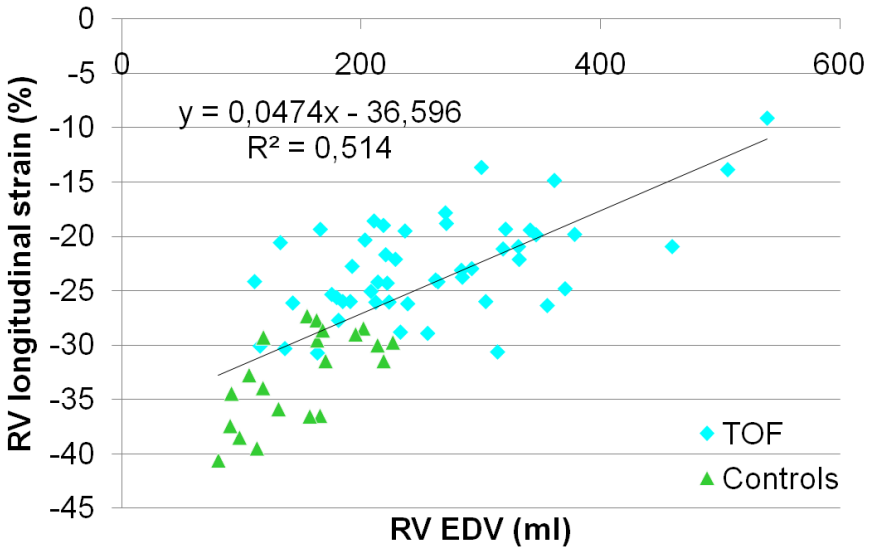


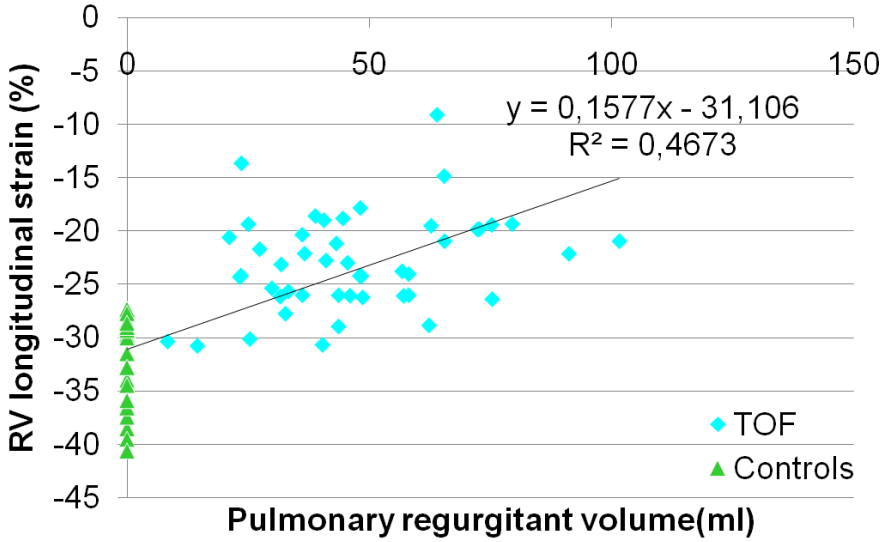


Variable	PRF > 30% (*n* = 22)	PRF < 30% (*n* = 18)	P-value
PRF (%)	42.5 ± 7.8*	19.9 ± 8.0*	<0.0001
RVEDV (mL/m^2)	123.1 ± 18.8*	99.2 ± 20.4*	0.001
RVSV (mL/m^2)	66.1 ± 13.1*	58.1 ± 0.1*	0.06
RVEF (%)	53.7 ± 7.3*	58.5 ± 8.2*	0.09
RVEF$_\varepsilon$ (%)	31.7 ± 5.6*	46.3 ± 9.7*	<0.0001
Peak S vel (cm/s)	4.5 ± 1.5*	4.8 ± 0.9*	0.56
Systolic ε (%)	−17.0 ± 4.3*	−24.6 ± 7.1*	<0.001
Peak systolic SR (s^{-1})	−1.29 ± 0.23*	−1.59 ± 0.45*	0.02
Heart rate (bpm)	76 ± 10	72 ± 17	0.3
QRS duration (ms)	132.9 ± 19.6*	127.4 ± 9.7*	0.28

Eyskens et al, Eur J Echocard 2010

RV function after ToF repair

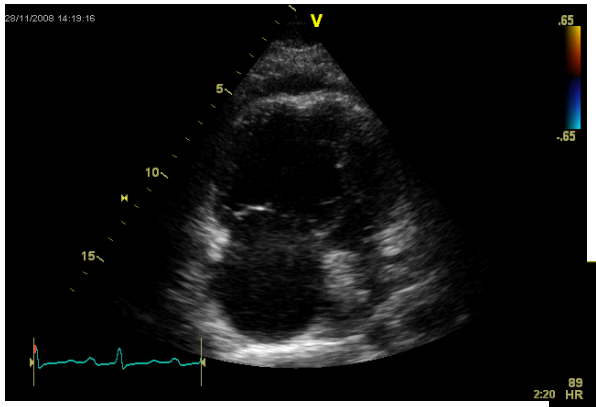


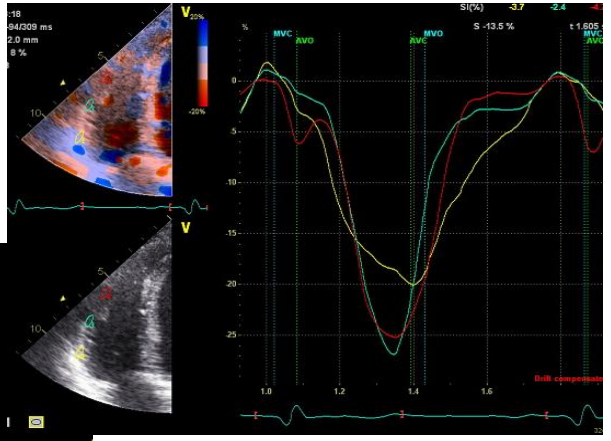


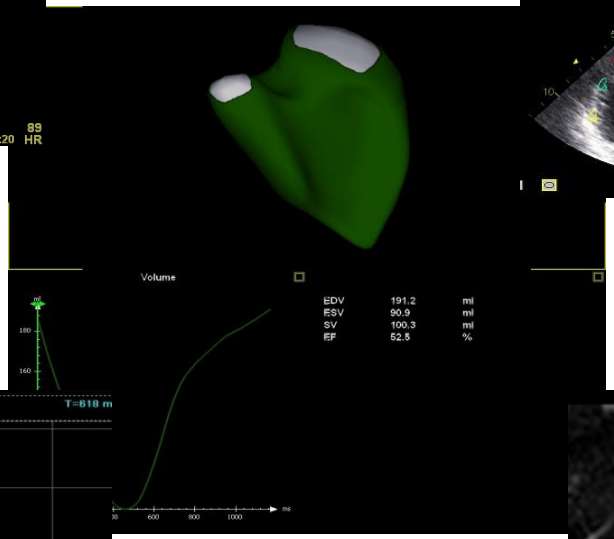
In patients after ToF repair, RV dilatation due to chronic Pulm Reg is associated with reduced strain.

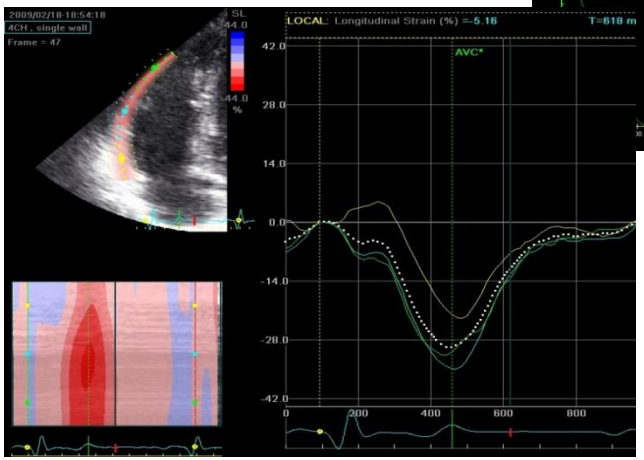
Dragulescu et al, Euroecho 2011

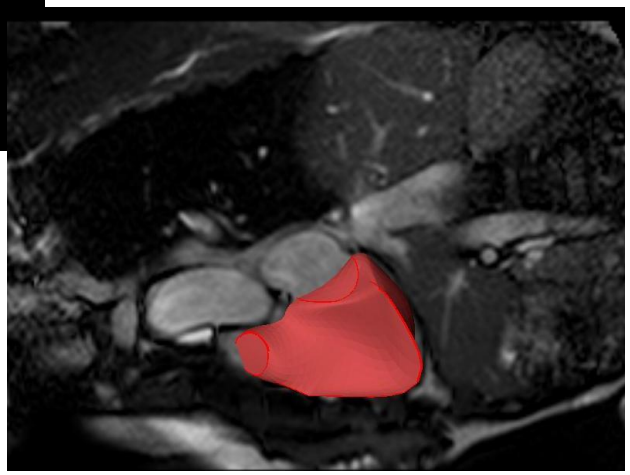
Take home messages











Take home messages

- **Interpretation of MDI parameters must always incorporate loading conditions**:
  - Influence of volume vs pressure overload
  - Influence of geometrical changes (e.g.RV dilation)
- **RV function may not be adequately described by longitudinal function alone.**
- **RV myocardial adaptation to load in different conditions:**
  - RV wall transverse fibers hypertrophy with increased afterload
  - Different cellular and molecular adaptation mechanisms to pressure overload (e.g. PS vs PHT)