«Πνευμονική υπέρταση- Απεικόνιση Ι»
Μαγνητική τομογραφία καρδιάς- CMR in PAH.
Do we need it?

2ο ΠΑΝΕΛΛΗΝΙΟ ΣΥΝΕΔΡΙΟ ΠΝΕΥΜΟΝΙΚΗΣ ΥΠΕΡΤΑΣΗΣ
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ESC/ERS GUIDELINES

2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension

The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS)

1. Pulmonary arterial hypertension (PAH)

- 1.1 Idiopathic
- 1.2 Heritable
  - 1.2.1 BMPR2 mutation
  - 1.2.2 Other mutations
- 1.3 Drugs and toxins induced
- 1.4 Associated with:
  - 1.4.1 Connective tissue disease
  - 1.4.2 HIV infection
  - 1.4.3 Portal hypertension
  - 1.4.4 Congenital heart disease (Table 6)
  - 1.4.5 Schistosomiasis

Pulmonary Arterial Hypertension

Definition

mPAP >25 mmHg

+

PCWP, LAP, or LVEDP ≤15 mmHg

+

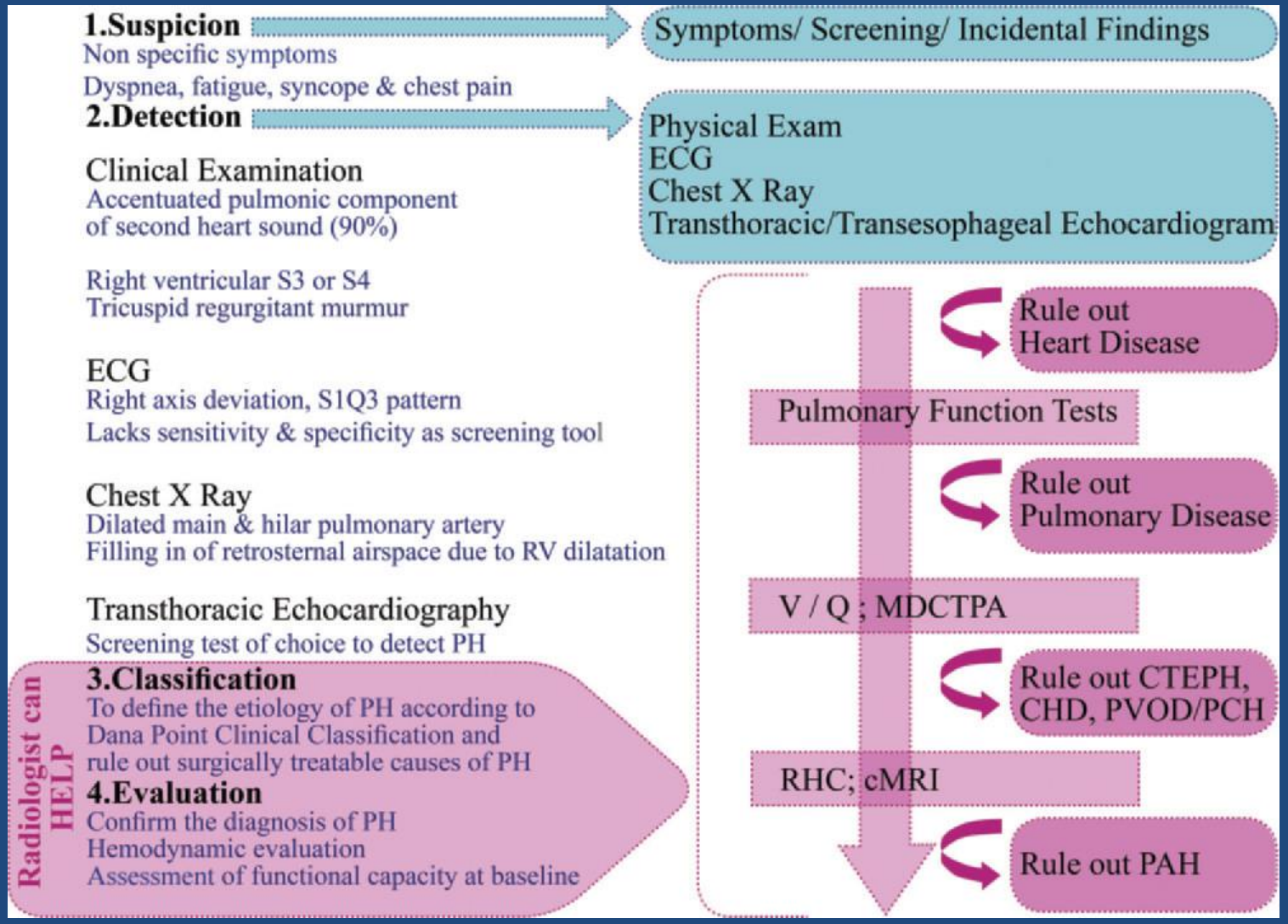
PVR >3 Wood Units

Table 12 Recommendations for diagnostic strategy

Recommendations	Class[a]	Level[b]	Ref.[c]
Echocardiography is recommended as a first-line non-invasive diagnostic investigation in case of suspicion of PH	I	C	
Ventilation/perfusion or perfusion lung scan is recommended in patients with unexplained PH to exclude CTEPH	I	C	47
Contrast CT angiography of the PA is recommended in the workup of patients with CTEPH	I	C	93
Routine biochemistry, haematology, immunology, HIV testing and thyroid function tests are recommended in all patients with PAH to identify the specific associated condition	I	C	
Abdominal ultrasound is recommended for the screening of portal hypertension	I	C	67
Lung function test with DLCO is recommended in the initial evaluation of patients with PH	I	C	36
High-resolution CT should be considered in all patients with PH	IIa	C	94
Pulmonary angiography should be considered in the workup of patients with CTEPH	IIa	C	
Open or thoracoscopic lung biopsy is not recommended in patients with PAH	III	C	

CT = computed tomography; CTEPH = chronic thromboembolic pulmonary hypertension; DLCO = diffusing capacity of the lung for carbon monoxide; PAH = pulmonary arterial hypertension; PH = pulmonary hypertension.

Diagnosis and assessment of PH



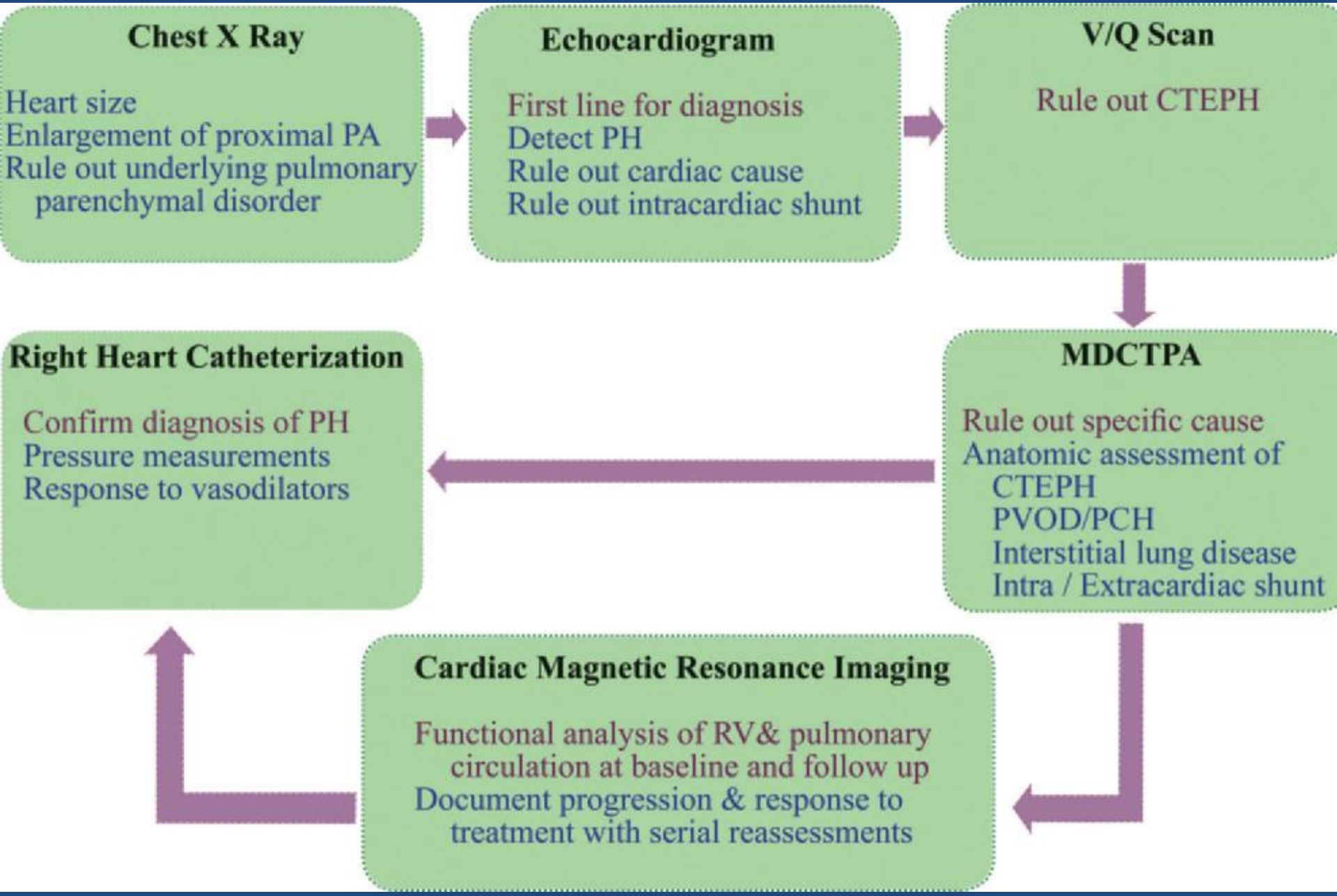

Chest X Ray
Heart size
Enlargement of proximal PA
Rule out underlying pulmonary parenchymal disorder
Echocardiogram
First line for diagnosis
Detect PH
Rule out cardiac cause
Rule out intracardiac shunt
V/Q Scan
Rule out CTEPH
MDCTPA
Rule out specific cause
Anatomic assessment of
CTEPH
PVOD/PCH
Interstitial lung disease
Intra / Extracardiac shunt
Cardiac Magnetic Resonance Imaging
Functional analysis of RV& pulmonary circulation at baseline and follow up
Document progression & response to treatment with serial reassessments
Right Heart Catheterization
Confirm diagnosis of PH
Pressure measurements
Response to vasodilators

Table 13 Risk assessment in pulmonary arterial hypertension

Determinants of prognosis[a] (estimated 1-year mortality)	Low risk <5%	Intermediate risk 5–10%	High risk >10%
Clinical signs of right heart failure	Absent	Absent	Present
Progression of symptoms	No	Slow	Rapid
Syncope	No	Occasional syncope[b]	Repeated syncope[c]
WHO functional class	I, II	III	IV
6MWD	>440 m	165–440 m	<165 m
Cardiopulmonary exercise testing	Peak VO_2 >15 ml/min/kg (>65% pred.) VE/VCO_2 slope <36	Peak VO_2 11–15 ml/min/kg (35–65% pred.) VE/VCO_2 slope 36–44.9	Peak VO_2 <11 ml/min/kg (<35% pred.) VE/VCO_2 slope ≥45
NT-proBNP plasma levels	BNP <50 ng/l NT-proBNP <300 ng/l	BNP 50–300 ng/l NT-proBNP 300–1400 ng/l	BNP >300 ng/l NT-proBNP >1400 ng/l
Imaging (echocardiography, CMR imaging)	RA area <18 cm^2 No pericardial effusion	RA area 18–26 cm^2 No or minimal, pericardial effusion	RA area >26 cm^2 Pericardial effusion
Haemodynamics	RAP <8 mmHg CI ≥2.5 l/min/m^2 SvO_2 >65%	RAP 8–14 mmHg CI 2.0–2.4 l/min/m^2 SvO_2 60–65%	RAP >14 mmHg CI <2.0 l/min/m^2 SvO_2 <60%

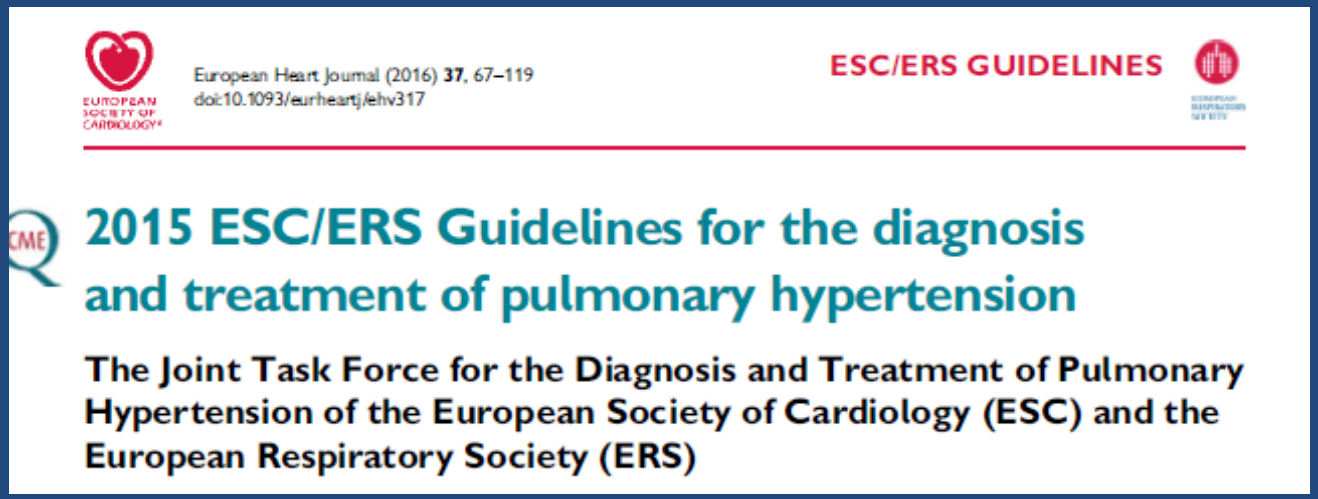
6MWD = 6-minute walking distance; BNP = brain natriuretic peptide; CI = cardiac index; CMR = cardiac magnetic resonance; NT-proBNP = N-terminal pro-brain natriuretic peptide; pred. = predicted; RA = right atrium; RAP = right atrial pressure; SvO_2 = mixed venous oxygen saturation; VE/VCO_2 = ventilatory equivalents for carbon dioxide; VO_2 = oxygen consumption; WHO = World Health Organization.

[a]Most of the proposed variables and cut-off values are based on expert opinion. They may provide prognostic information and may be used to guide therapeutic decisions, but application to individual patients must be done carefully. One must also note that most of these variables have been validated mostly for IPAH and the cut-off levels used above may not necessarily apply to other forms of PAH. Furthermore, the use of approved therapies and their influence on the variables should be considered in the evaluation of the risk.

[b]Occasional syncope during brisk or heavy exercise, or occasional orthostatic syncope in an otherwise stable patient.

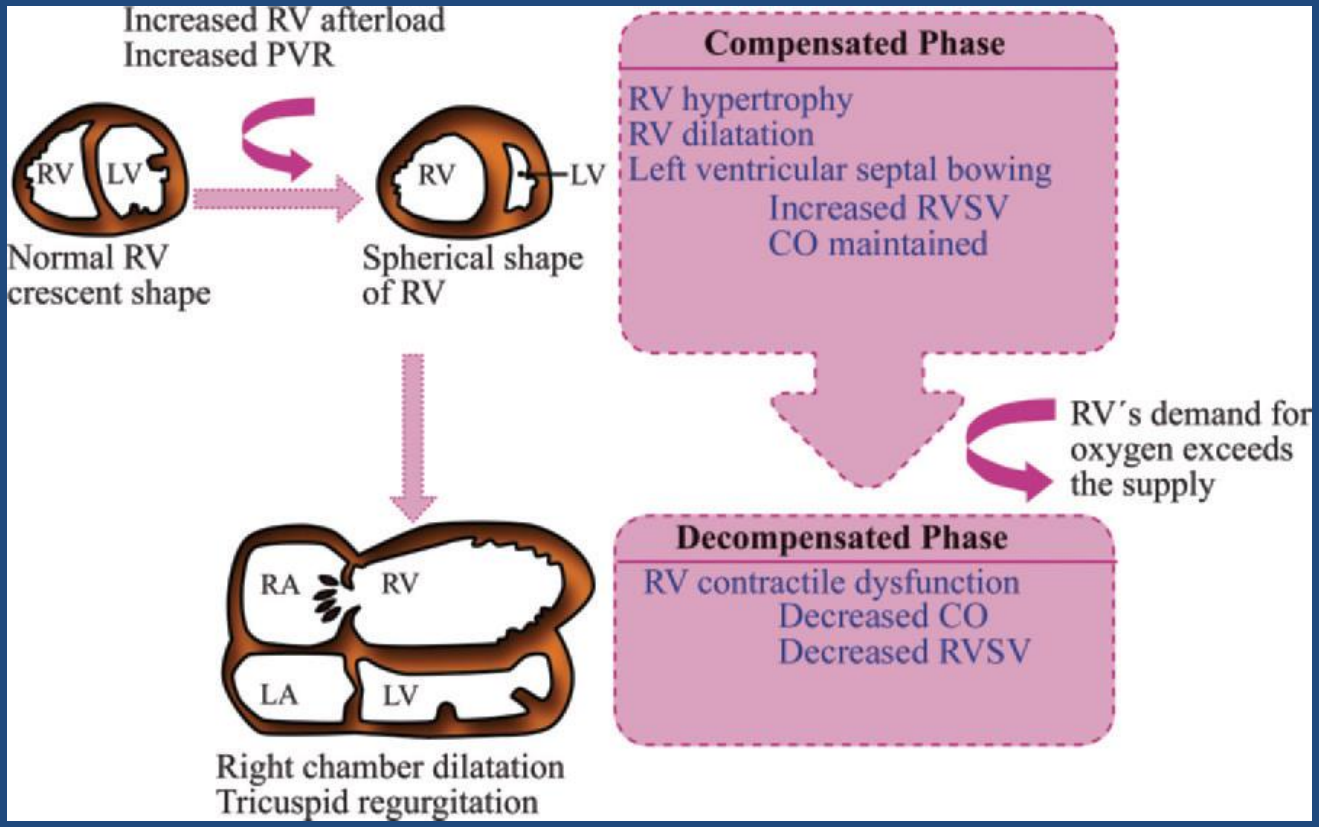
[c]Repeated episodes of syncope, even with little or regular physical activity.

Role of CMR in PH guidelines



- Accurate and reproducible in the assessment of RV size, morphology and function
- Non-invasive assessment of blood flow, SV, CO, pulmonary arterial dispensibility, RV mass
- LGE
- Diagnosis of CHD
- MRA for the diagnosis of CTEPH
- Prognostic information in pts PAH at baseline and follow up
- Identifying RV failure prior to the development of clinical features

Structural RA/RV changes in PAH



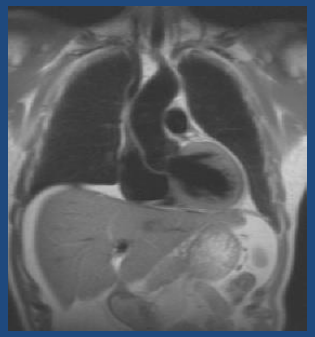
Cardiac MRI in PH

Is it more than just nice images?

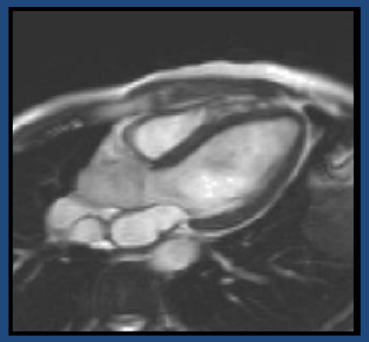
CMR is Versatile

"able to be adapted to many different functions"

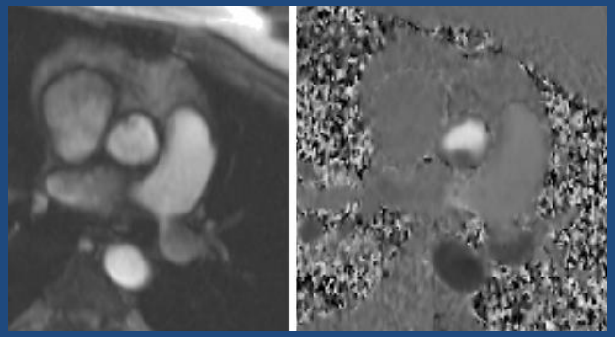
Different sequences/techniques for different clinical questions



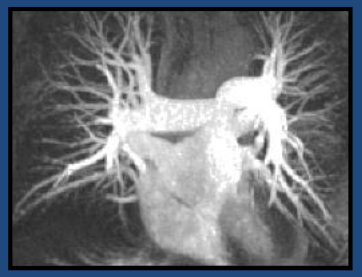
Anatomical images



Function-cine

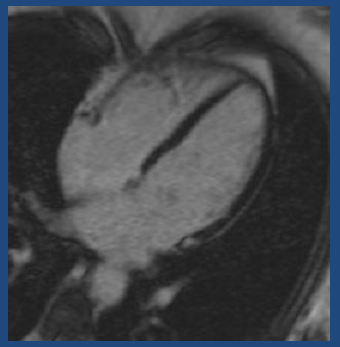


Flow mapping



Contrast angiography

- What are the sequences showing
- What can I expect as a clinician

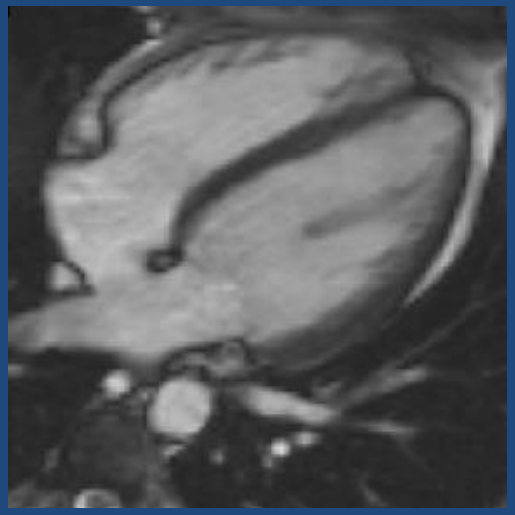


Late gadolinium

MR - Tissue characterisation

CMR: Excellent tissue characterisation

→differentiation of blood-myocardium



Confirming the diagnosis- providing prognostic information

- Patient referrals
  - with established diagnosis
  - Requiring clarification
  - With unknown aetiology
  - With other indication for MRI scan (left heart disease/ARVC?)

Table 2 Right Heart Changes in Pulmonary Hypertension
RV hypertrophy involving the papillary muscles, trabeculations and interventricular septum [72]. Asymmetric septal hypertrophy may be present [73-75]
Progressive RV dilatation until it becomes the dominant, apex-forming ventricle
Abnormal interventricular septal motion
Tricuspid regurgitation as a consequence of RV dilatation and stretching of the valve annulus
Interatrial septum becomes convex leftwards reflecting elevated RA pressures
Dilated RA
Plethoric vena cavae
Pericardial effusion

Essential CMR Protocol in PHT

1-Anatomical images

2-Cine images

3-Flow studies

4-MR angiography

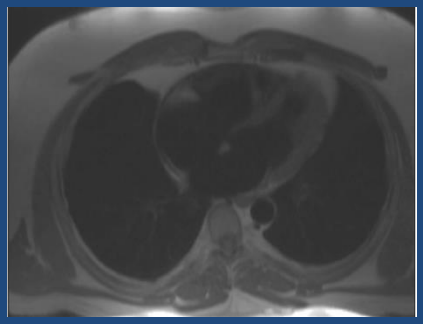
- Late gadolinium
- STIR-T2
- 3D noncontrast volumetric acquisition

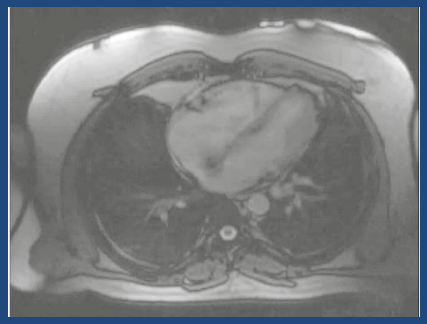
research

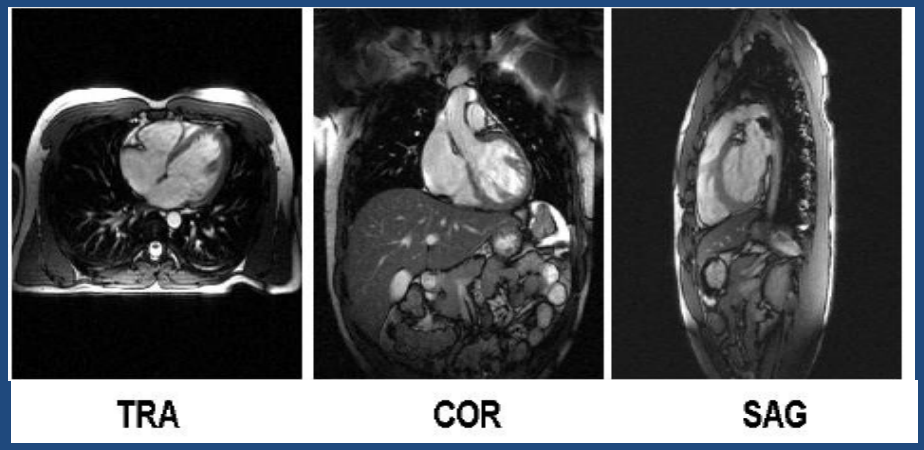
- Tagging, feature tracking
- 4D flow
- Myocardial DTI
- 3D Late gadolinium
- Perfusion
- RV T1 mapping

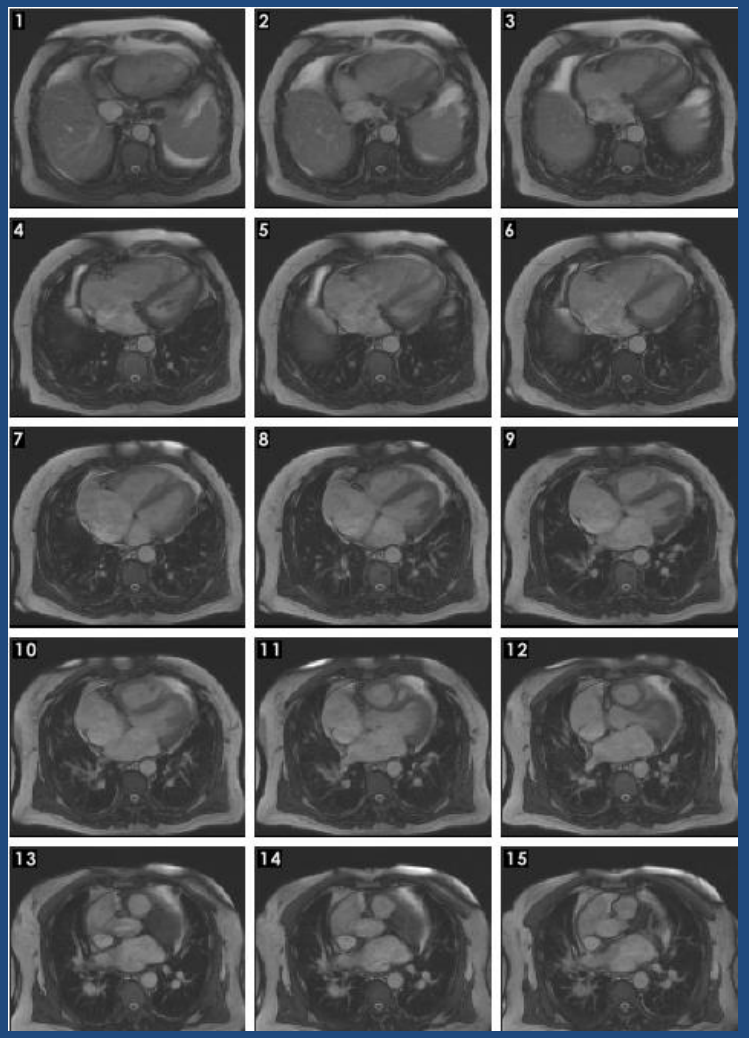
Static anatomical images

Black blood and white blood









RV, PA size, vascular connections

Cine Images

- Assessment of RV and LV

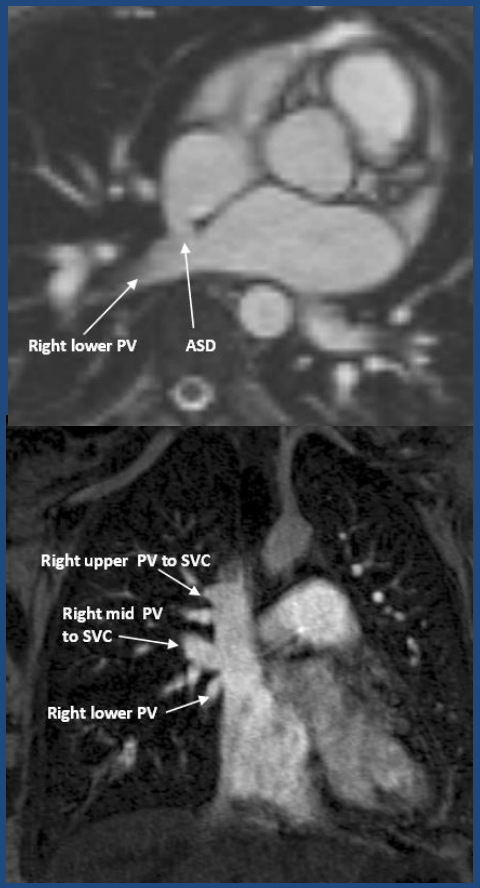
  Volumetric analysis with no geometric assumptions
- Pulmonary arteries
- Shunts, ASD

CMR - Large field of view and unlimited image planes

- Large FoV

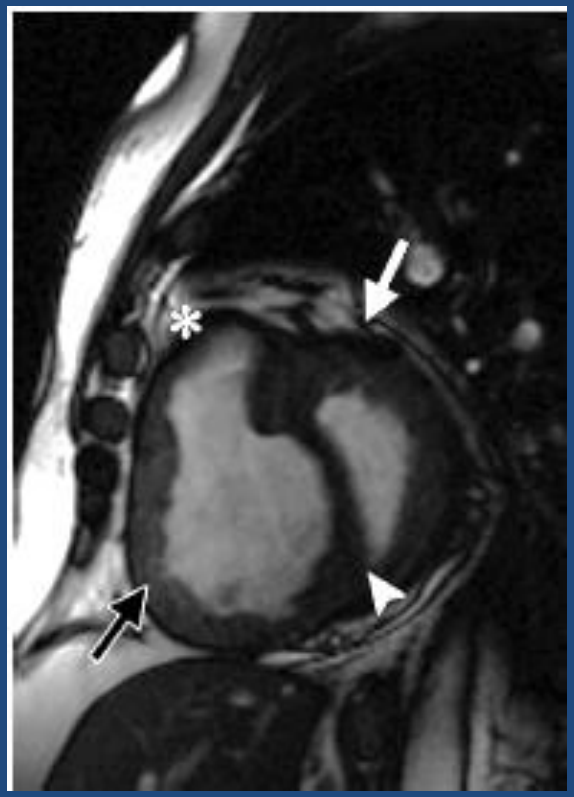
  Heart + thorax + vessels

- Unlimited image planes



CMR in PAH- Functional evaluation

- Assessment of
  - ventricular volumes
  - RA/RV Morphologic characteristics (RV shape and dilatation, RVH, RA enlargement, flattening of the IVS, TR)
  - RV mass and function
  - Pulmonary arteries (size and pulsalitility)

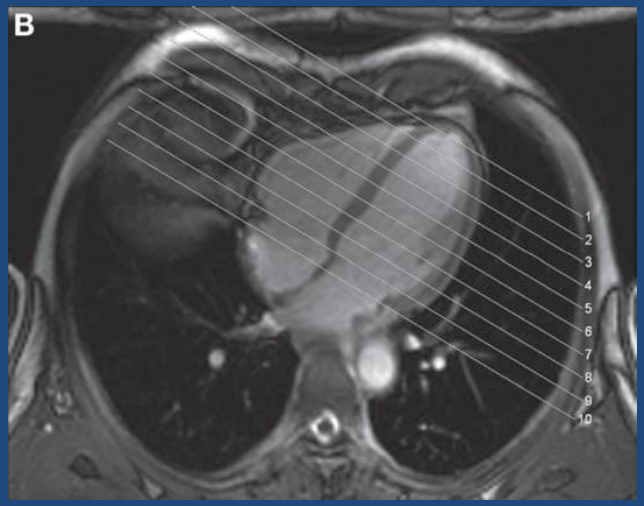


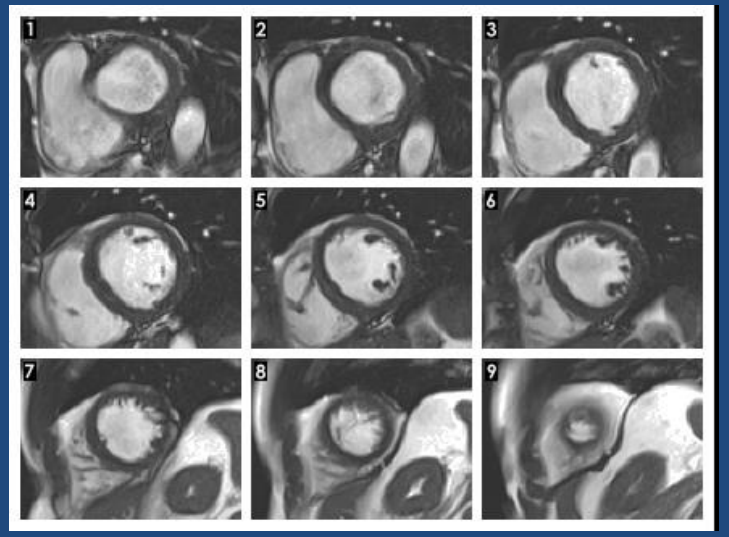
RV -cine

- Reproducible assessment of RV volume, function and mass
- Assessment of RWMA
- Increased RVEDV and RVESV, decreased RVSV and RVCO, decreased RVEF

- Treatment failure/mortality

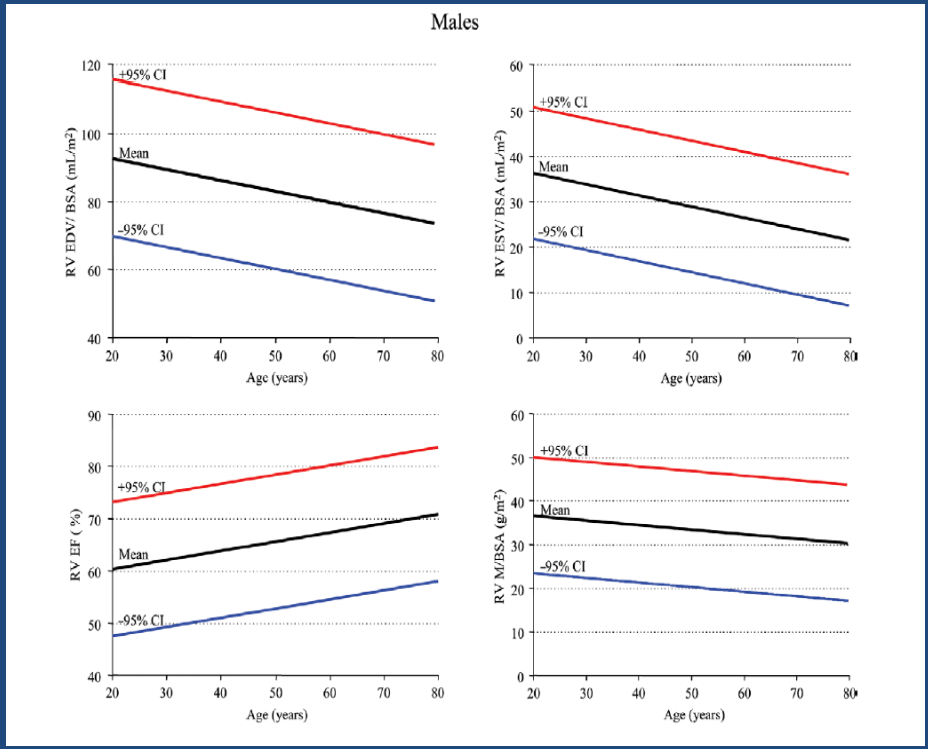
Ventricular Volumetric analysis

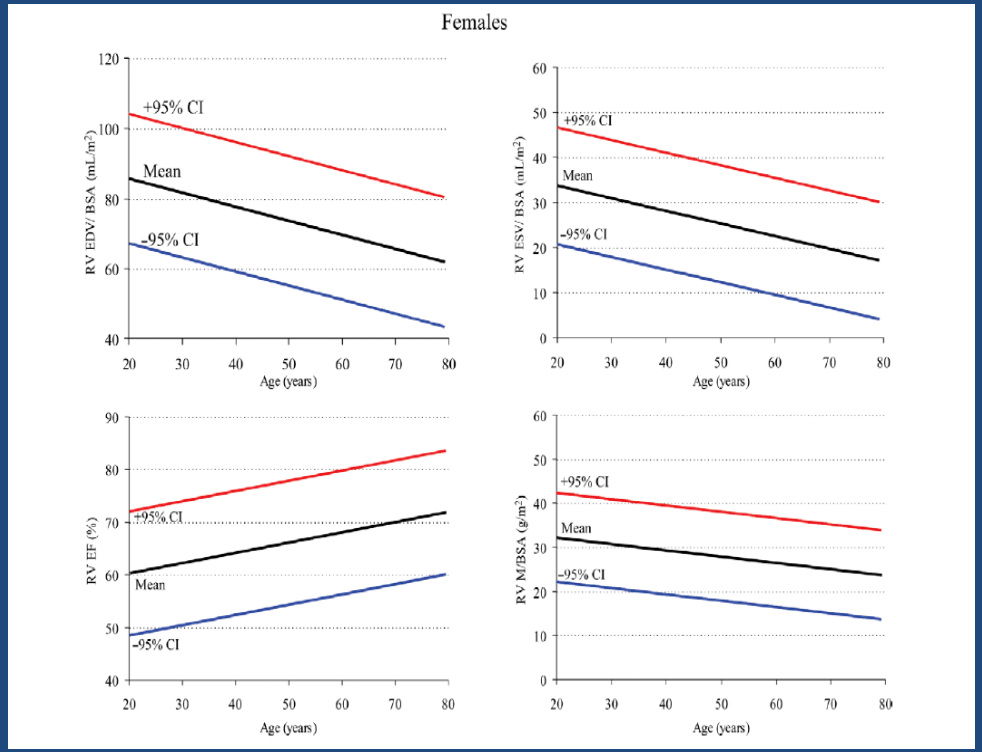




	EDV (mL)	ESV (mL)	SV (mL)	EF (%)	Mass index (g/m^2)
LV	167	54	113	67	121
RV	144	38	106	73	18

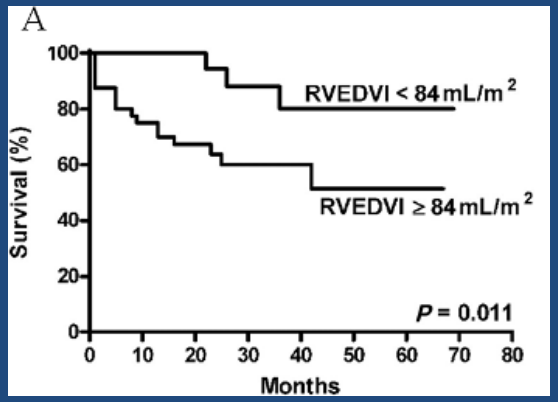
RV Volumes and function; normal ranges (95% CI) indexed for BSA

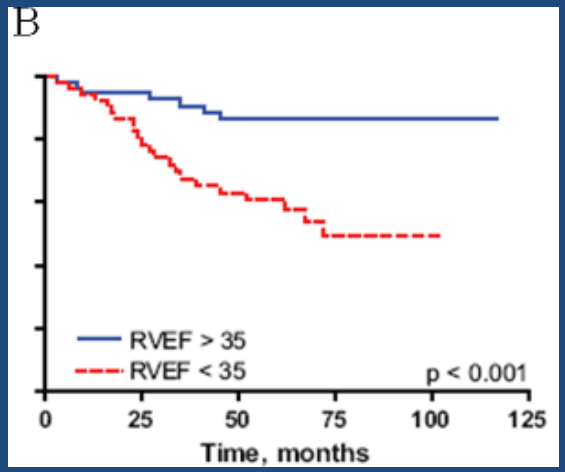


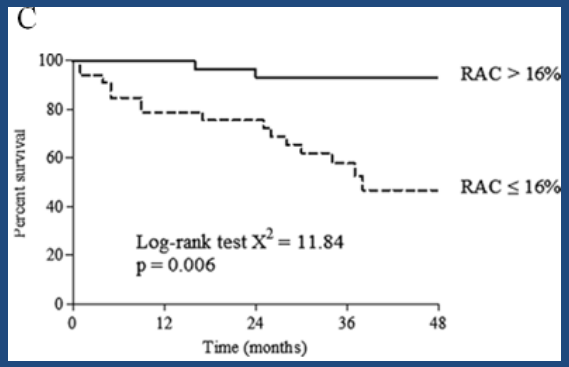


Maceira AM et al. Eur Heart J (2006) 27, 2879-2888

PAH – prognosis CMR







Changes in Right Ventricular Function Measured by Cardiac Magnetic Resonance Imaging in Patients Receiving Pulmonary Arterial Hypertension–Targeted Therapy

The EURO-MR Study

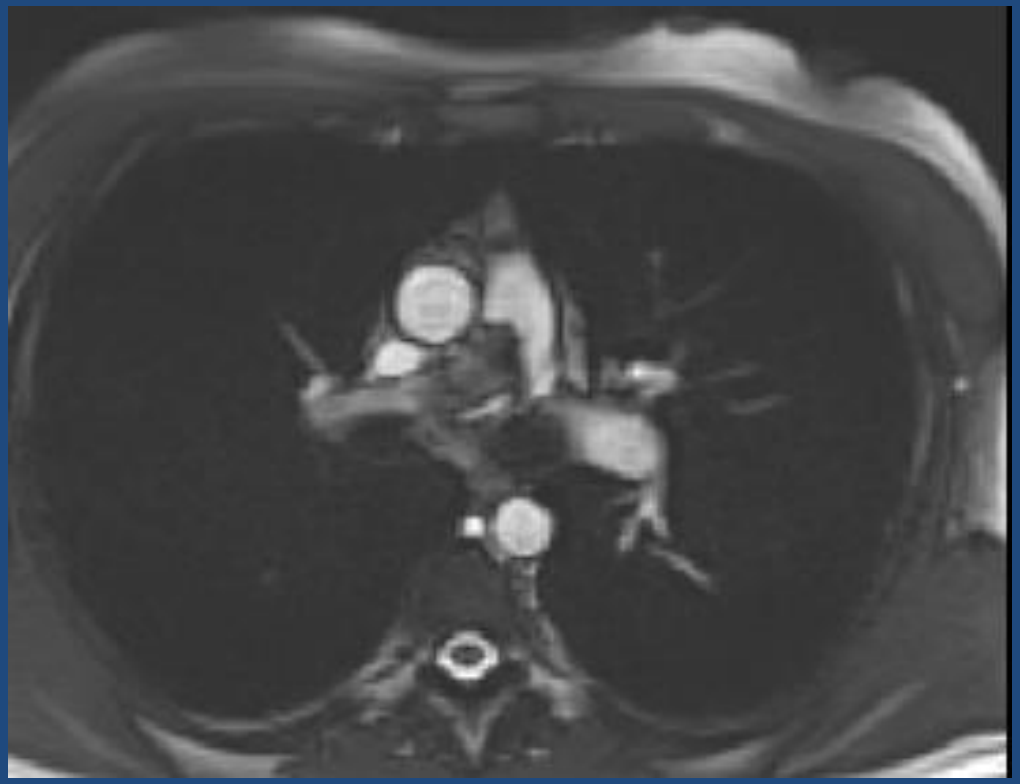
Right ventricular function has been shown to play a key role in the survival of patients with pulmonary arterial hypertension (PAH). However, little information is available about the impact that PAH-specific therapy has on right ventricular function. Although cardiac MRI provides a comprehensive picture of right ventricular structure and function, its use in clinical practice is limited, which may result, at least in part, from the lack of published data on patients with PAH. The multicentre pan-European study described here is the most comprehensive to date, investigating the use of cardiac MRI during treatment of patients with PH. It demonstrates that cardiac MRI variables (stroke volume index, cardiac index, and ejection fraction) are significantly associated with response to PAH-specific therapy. The study describes the detailed assessments required at baseline and during follow-up in this cohort of patients. We think that these data should be considered when designing future trials of PAH-specific therapy so that cardiac MRI variables are included as a marker of therapeutic response.

Peacock et al (*Circ Cardiovasc Imaging*. 2014;7:107-114.)

Studies by Vonk-Noordegraaf Group

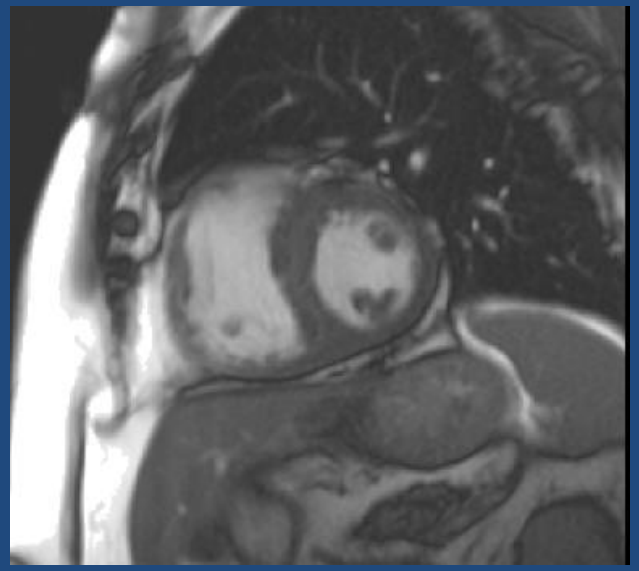
Cine - pulmonary arteries

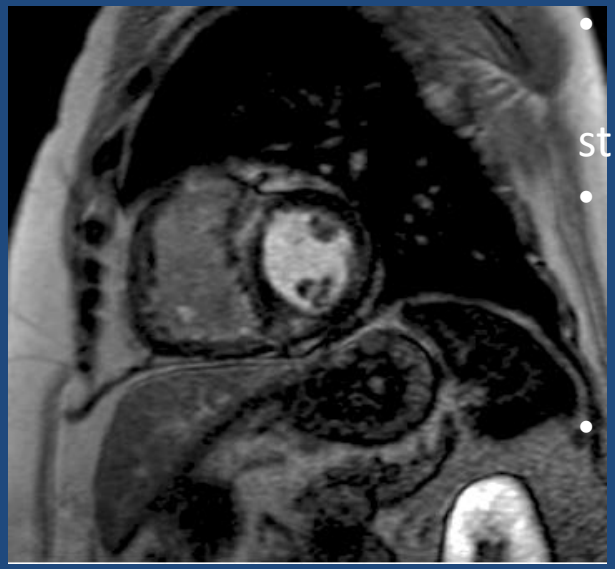
- Cines main and branch PAs



- expansibility

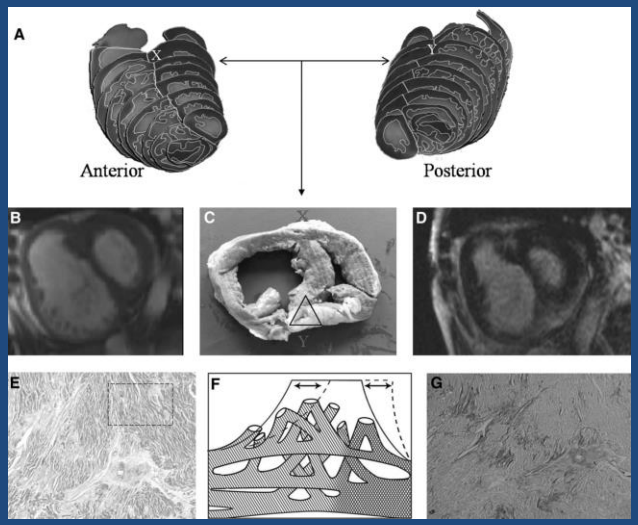
Late gadolinium enhancement





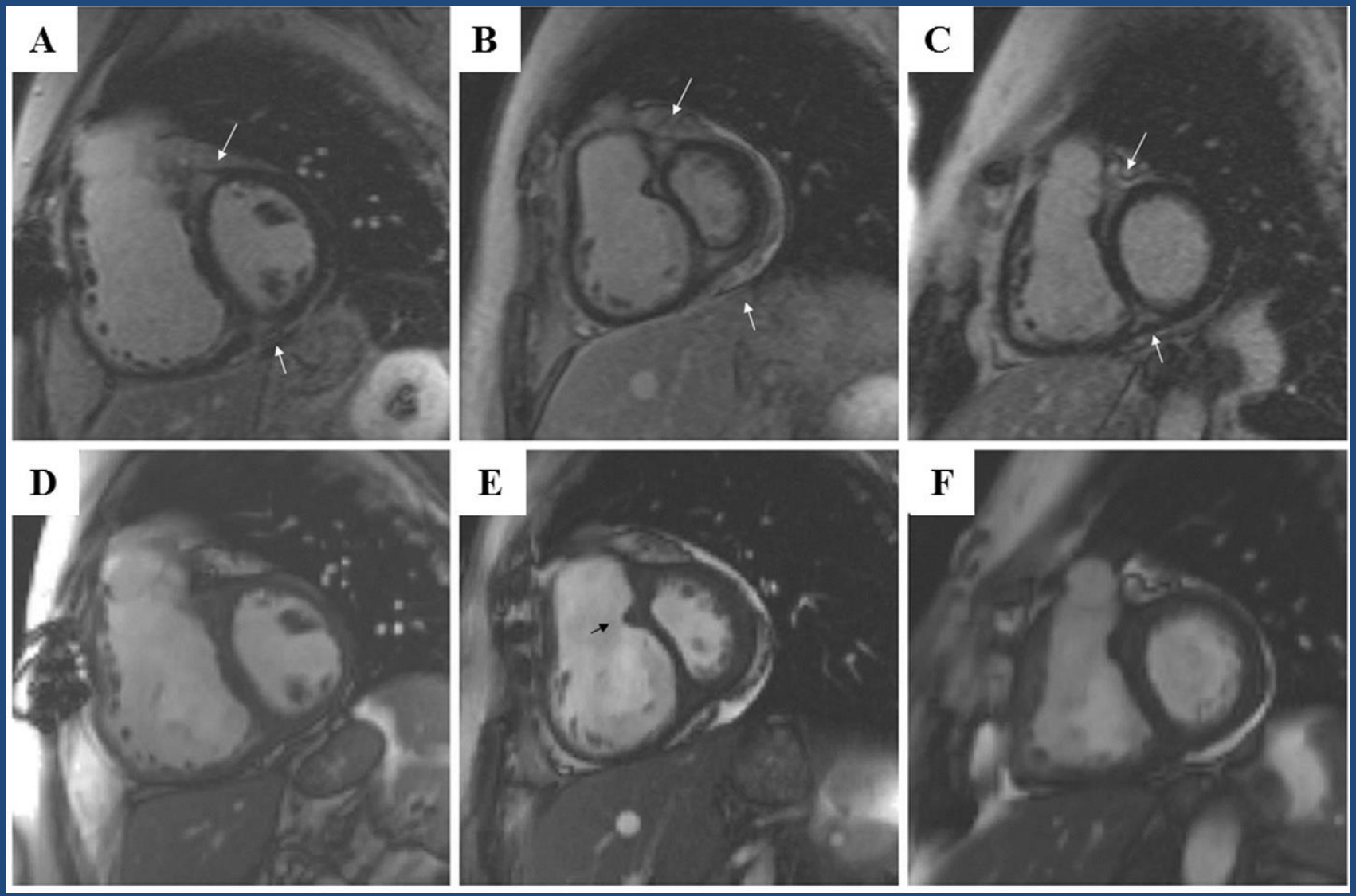
Ventricular insertion point LGE

- indicative of increased mechanical stress in these areas;
- Elevated RVSP -> tissue abnormalities (fibrosis, myocardial disarray, and inflammation).
- systolic pulmonary pressure is the only tool that may help predict LGE



Bradlow et al., *Circulation CV 2010*
Am J Cardiol 2007;100(4):731–735.

LGE in PH



Bradlow et al. Journal of Cardiovascular Magnetic Resonance 2012, 14:6

Contrast MR angiography

3D SSFP angiography

from S Babu-Narayan

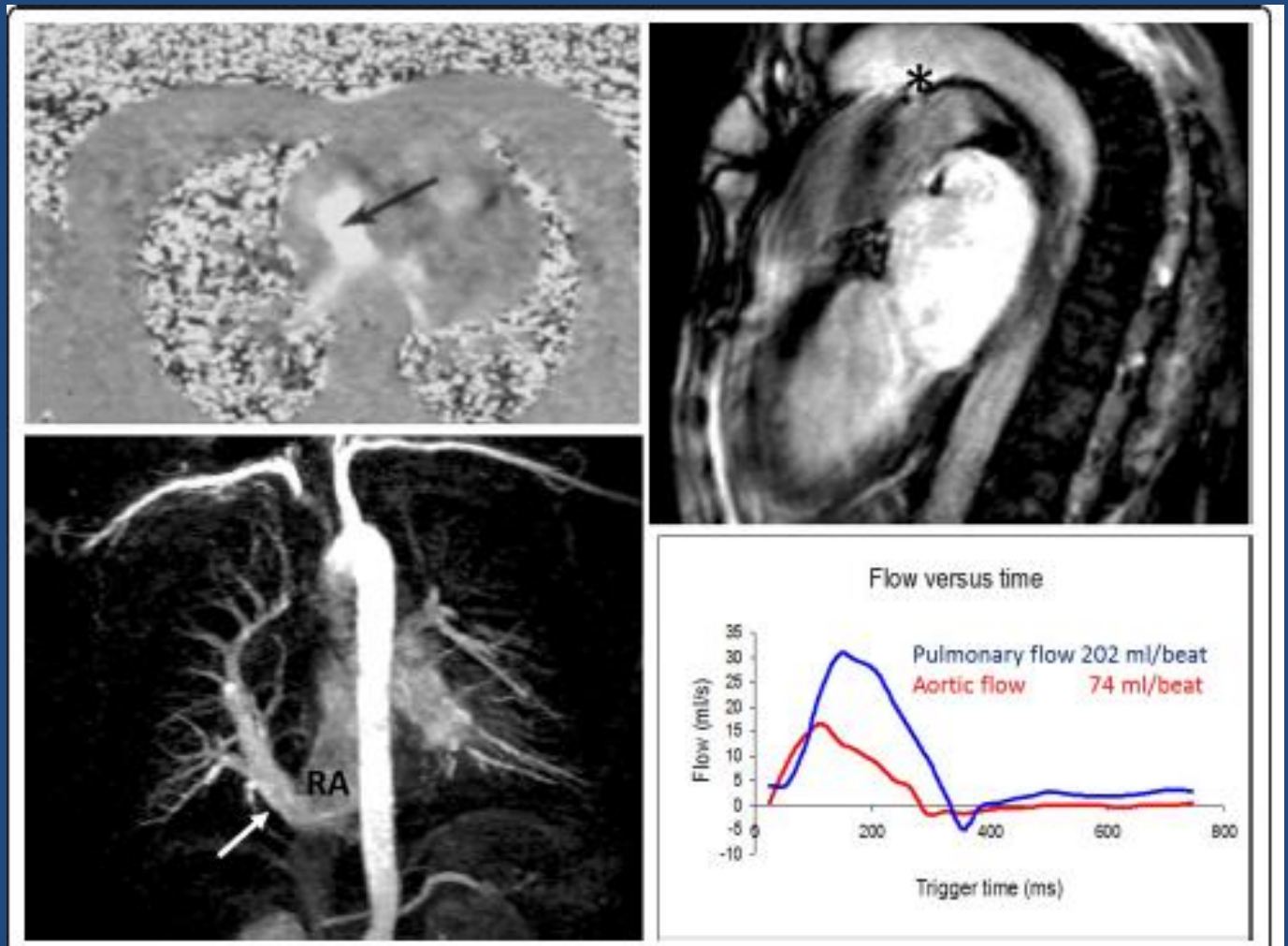
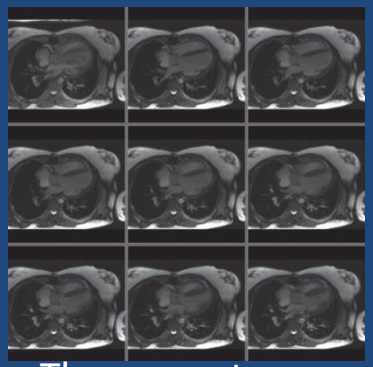
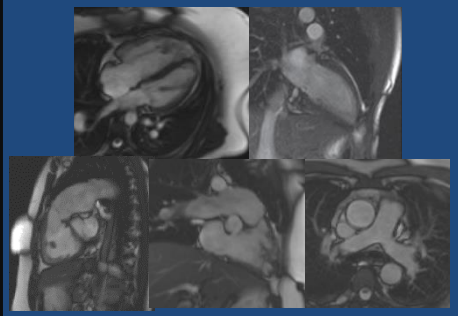


Figure 1 Cardiovascular Magnetic Resonance in Group 1 PAH due to Congenital Heart Disease. Top left, In plane flow mapping demonstrating flow between left and right atrium (arrow) through an atrial septal defect; Top right, a steady state free procession cine showing flow (asterisk) from descending aorta to pulmonary artery via a persistent ductus arteriosus; Bottom left, Magnetic Resonance Angiography of an aberrant pulmonary vein (arrow) draining into the right atrium (RA); Bottom right, flow mapping in this patient in the main pulmonary artery and aorta allowed a QpQs of 2.7 to be derived.

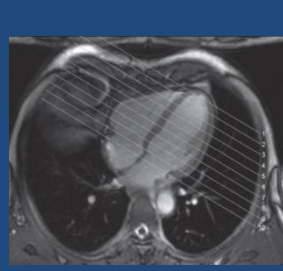
PAH -essential CMR

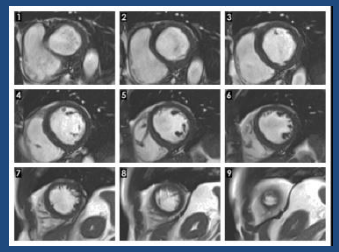


Thorax anatomy

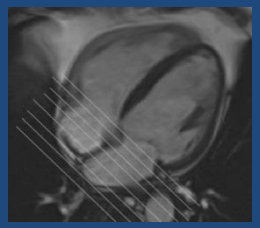


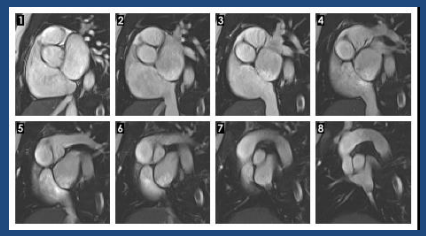
Ventricular Long axis cines
PA cines, transaxial cines





SAX cines,
Ventricular Vols
and EF



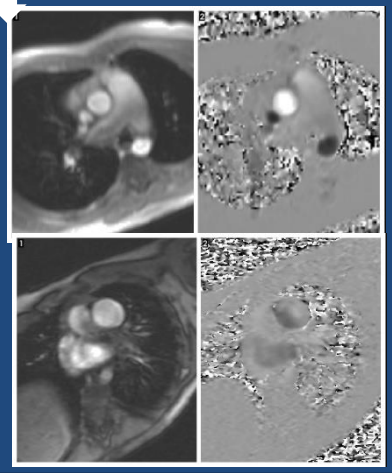


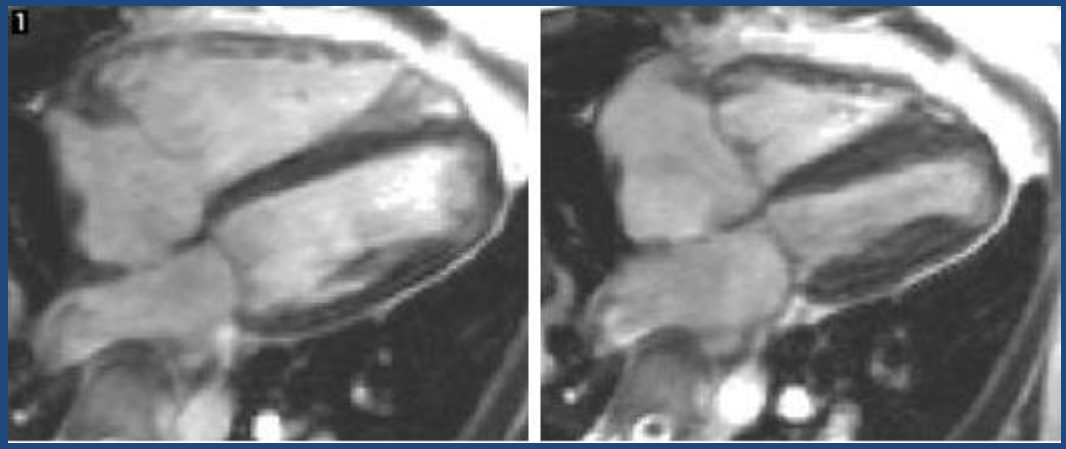
Atrial SAX rule out ASD

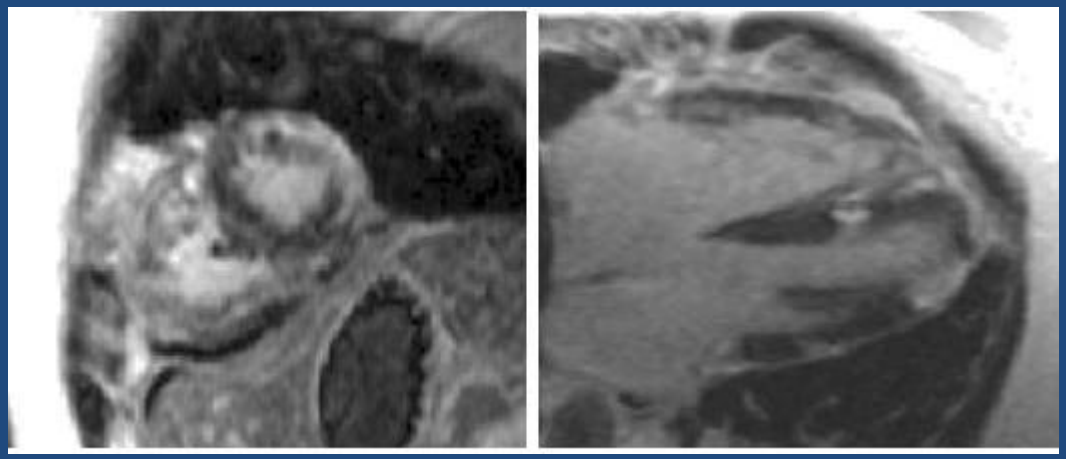
~30 mins

- **Confirmation of diagnosis**
- **Exclusion of shunts**
- **Prognostic markers**

Cardiac output:
PA flow
Ao flow
Qp/Qs







64years old female
Significantly dilated RV/RA
Mild TR
Dilated MPA and PA branches
(MPA 34mm, RPA 26mm, LPA 31mm)
Pulmonary and Cardiac sarcoid
Secundum ASD (Qp:Qs 2.08)
LGE positive

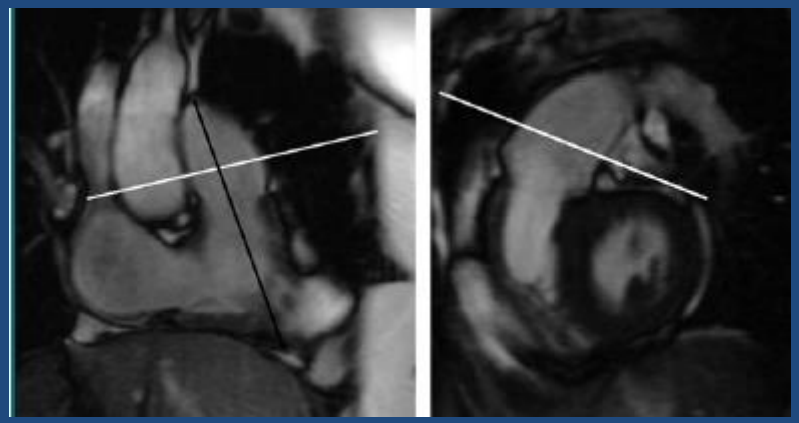
	EDV (mL)	ESV (mL)	SV (mL)	EF (%)	Mass index (g/m^2)
LV	137	62	75	55	71
RV	265 (58-154)	108 (12-68)	158 (35-98)	59 (47-80)	

Research

INSIGHT	CMR METHOD	REF#
Early Changes		
PA stiffens before pulmonary artery pressure increase at rest	Distensibility of pulmonary arteries	[42]
Ventricular Remodeling and Dysfunction		
LV mass is lower in patients with chronic thromboembolic disease but normalizes post-pulmonary endarterectomy	LV mass	[62]
Interventricular dyssnchrony and septal bowing in PAH is due to slower contraction for the RV than LV	Tagging	[63]
Cardiac Ischemia		
Both ventricles display attenuated vasoreactivity proportional to mPAP	Adenosine Stress Perfusion	[64]

Pulmonary Arterial Hypertension: Noninvasive Detection with Phase-Contrast MR Imaging[1]

Radiology



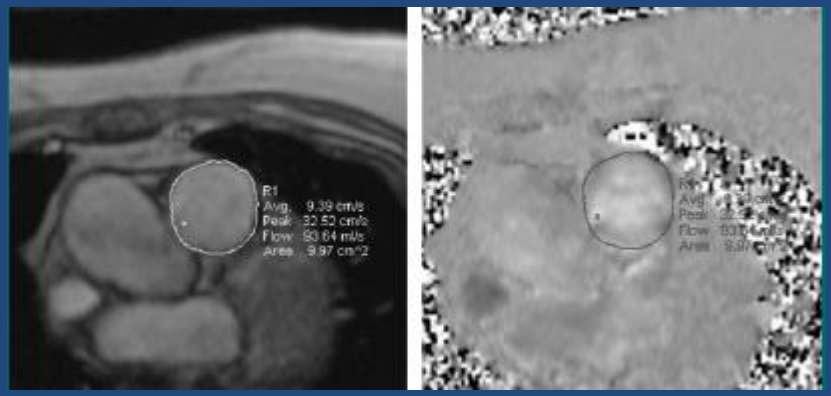


Table 1

Patient Subgroups according to Presence or Absence of PAH and Underlying Cause

Subgroup*	No. of Patients
Group 1—PAH and collagen-vascular disease	13
Scleroderma	8
Lupus erythematosus	4
Rheumatoid arthritis	1
Group 2—PAH and human immunodeficiency virus or portopulmonary syndrome	16
Human immunodeficiency virus	13 (five with advanced liver disease)
Portopulmonary syndrome	3
Group 3—idiopathic PAH	13
Group 4—normal pulmonary pressures†	17
Total	59

* Categories are based on the revised *Clinical Classification of Pulmonary Hypertension* (1).

† Reasons for evaluation in Group 4 included collagen-vascular disease ($n = 4$), human immunodeficiency virus infection ($n = 1$), corrected cardiac shunt ($n = 1$), end-stage liver disease ($n = 2$), use of anorexigens ($n = 2$), left-sided heart disease ($n = 2$), alveolar hypoventilation ($n = 2$), chronic thromboembolic disease ($n = 1$), and symptoms of unexplained origin (shortness of breath or ascites) ($n = 2$).

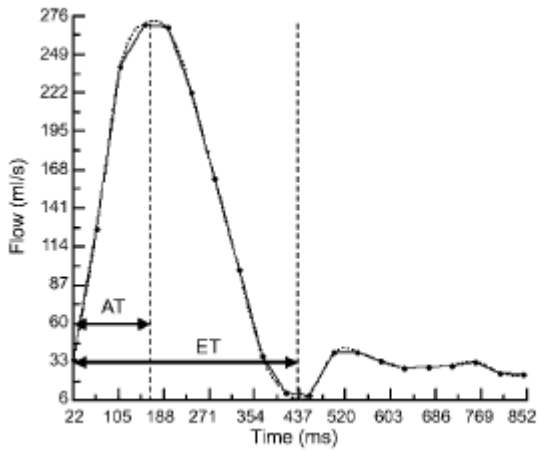


Figure 3: Flow curve of PA. AT and ET as quantified in our study are shown. Left dotted vertical line = time of peak systolic flow. Right dotted vertical line = time of end of ejection.

Radiology 2007;243:70-79

Pulmonary Arterial Hypertension: Noninvasive Detection with Phase-Contrast MR Imaging[1]

Radiology

Figure 4

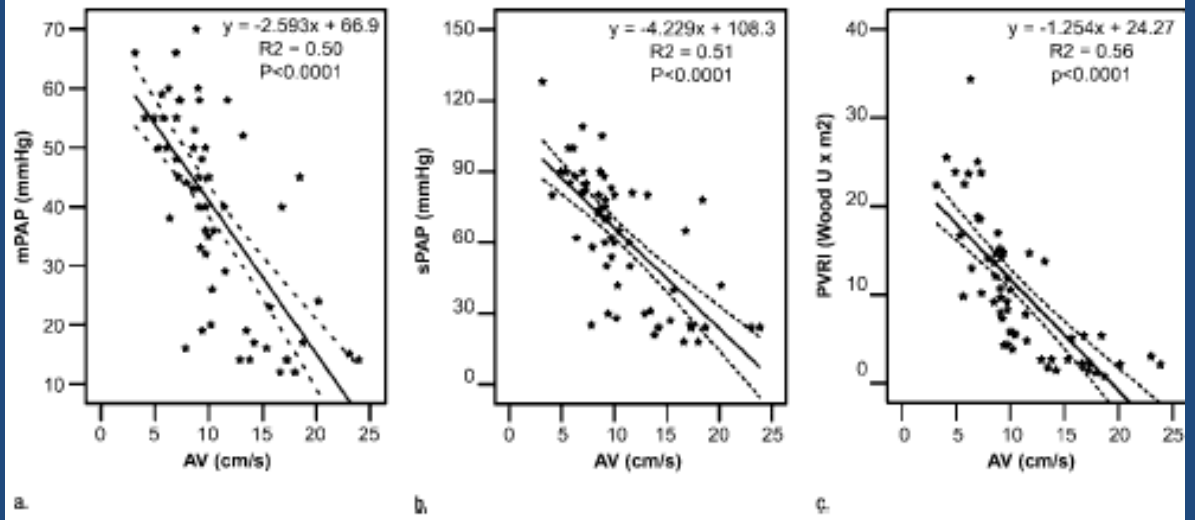


Figure 4: Graph shows results of regression analysis in whole study group between pulmonary average velocity *(AV)* and (a) mPAP, (b) sPAP, and (c) PVRI. Curve CIs of the mean.

Figure 6

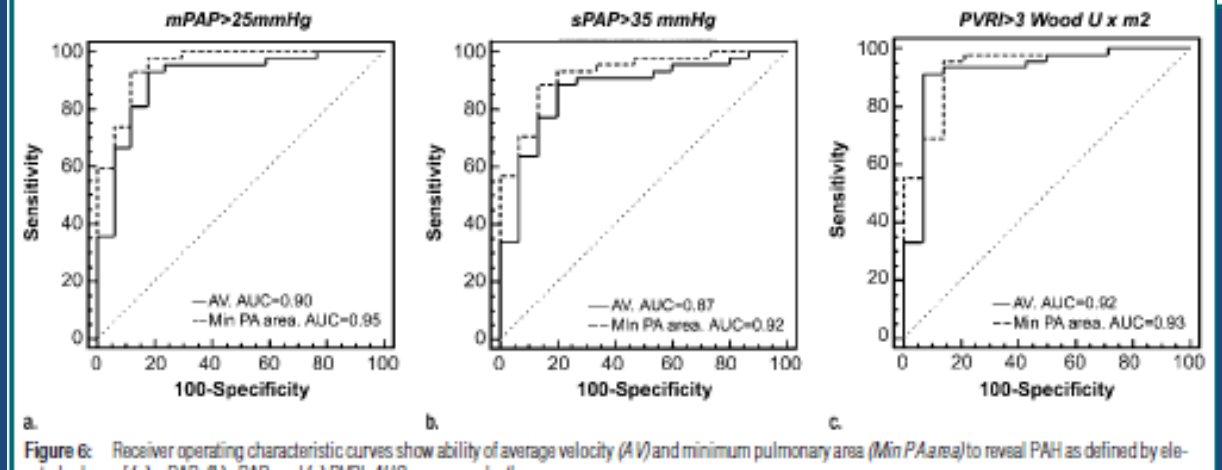
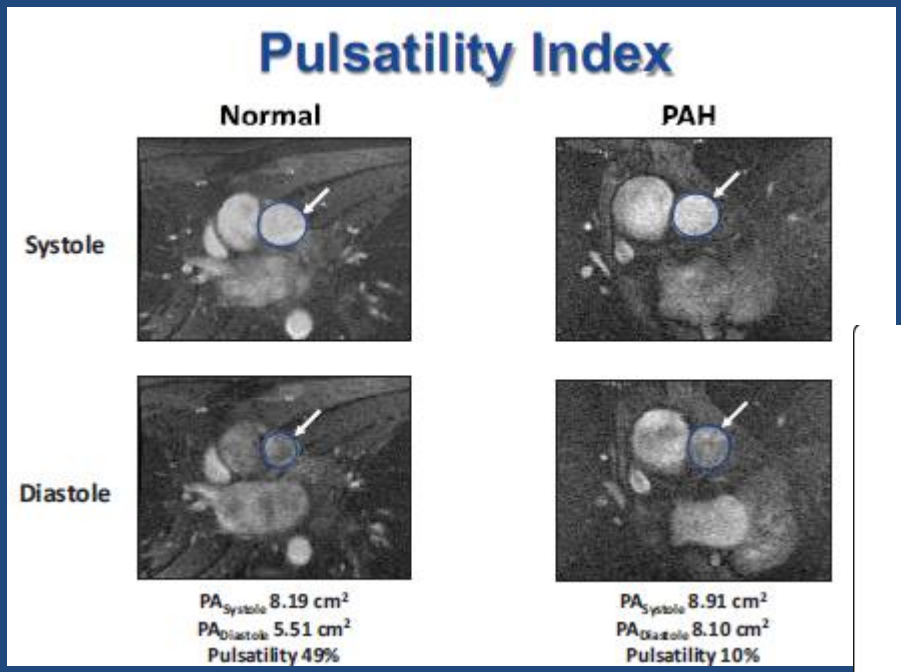


Figure 6: Receiver operating characteristic curves show ability of average velocity *(AV)* and minimum pulmonary area *(Min PA area)* to reveal PAH as defined by ele-

Radiology 2007;243:70-79

Pulmonary artery stiffness



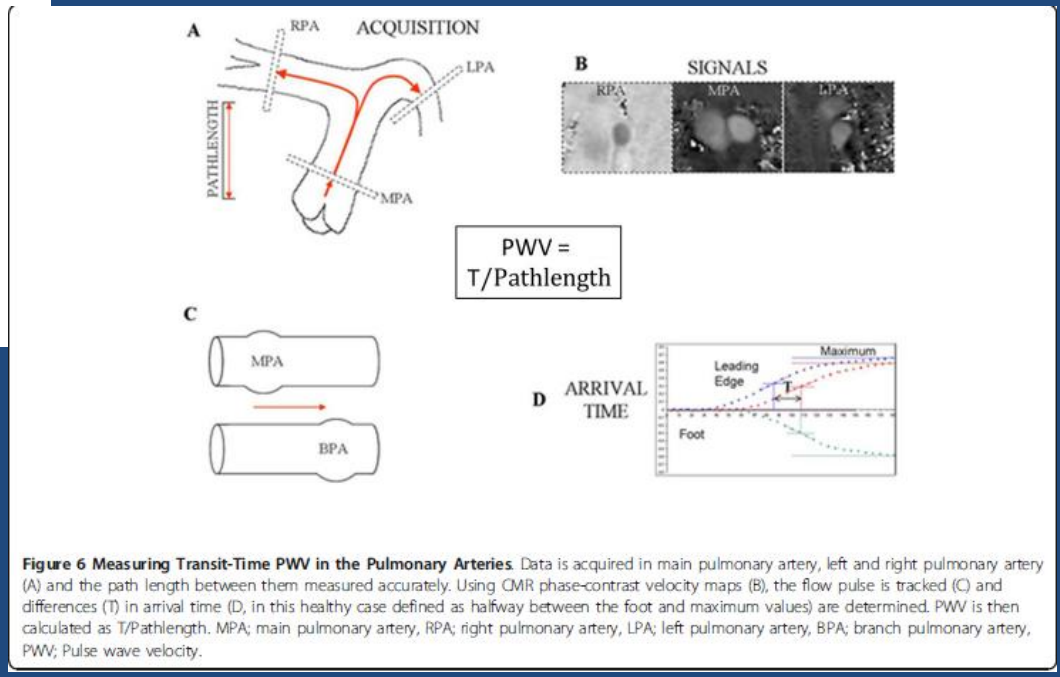
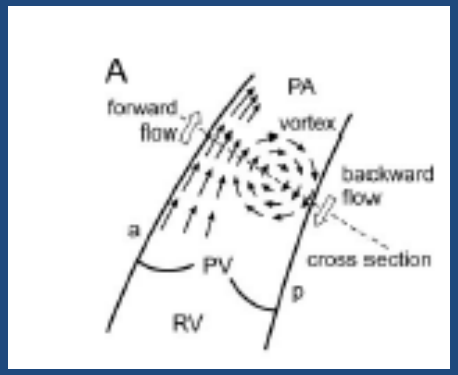


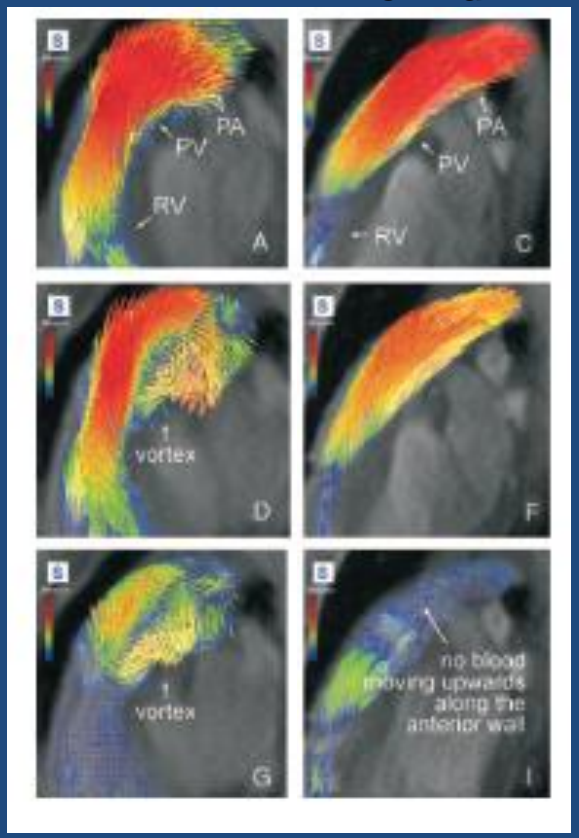
Figure 6 Measuring Transit-Time PWV in the Pulmonary Arteries. Data is acquired in main pulmonary artery, left and right pulmonary artery (A) and the path length between them measured accurately. Using CMR phase-contrast velocity maps (B), the flow pulse is tracked (C) and differences (T) in arrival time (D, in this healthy case defined as halfway between the foot and maximum values) are determined. PWV is then calculated as T/Pathlength. MPA; main pulmonary artery, RPA; right pulmonary artery, LPA; left pulmonary artery, BPA; branch pulmonary artery, PWV; Pulse wave velocity.

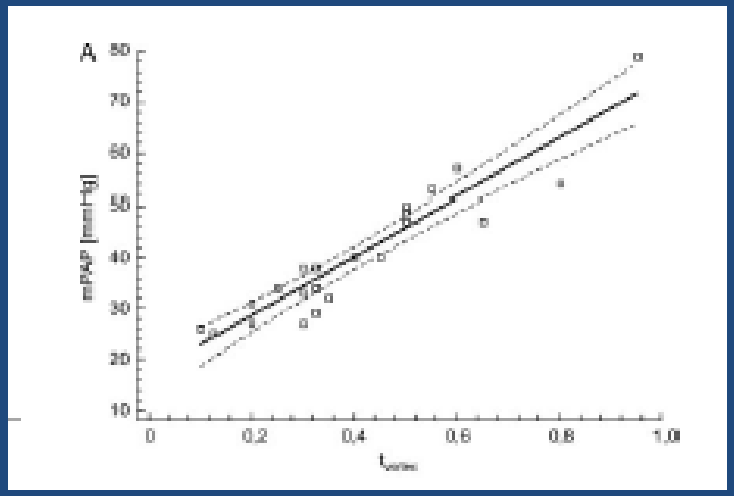
Bradlow et al. Journal of Cardiovascular Magnetic Resonance 2012, 14:6

4D flow mapping

Pulmonary artery flow profiles

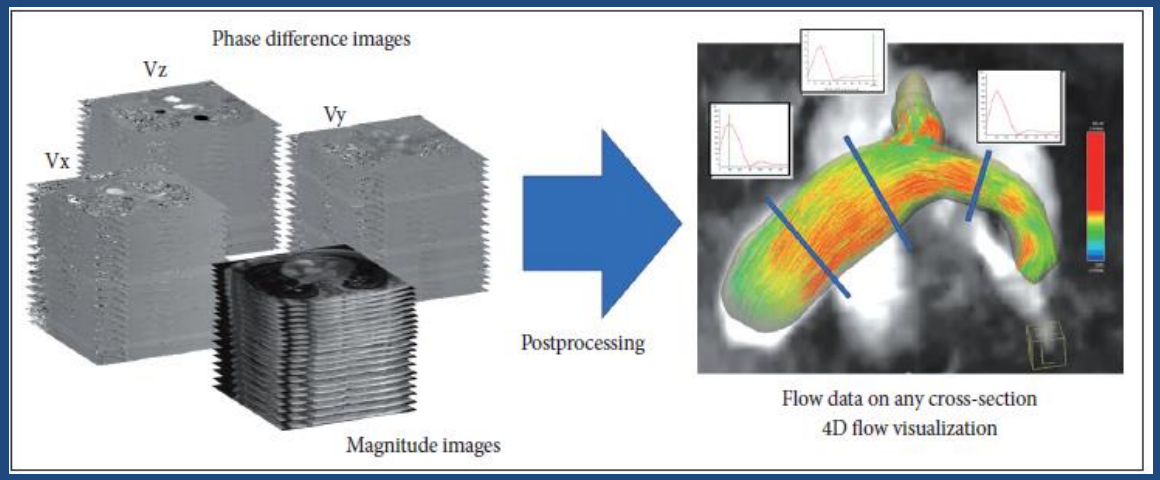




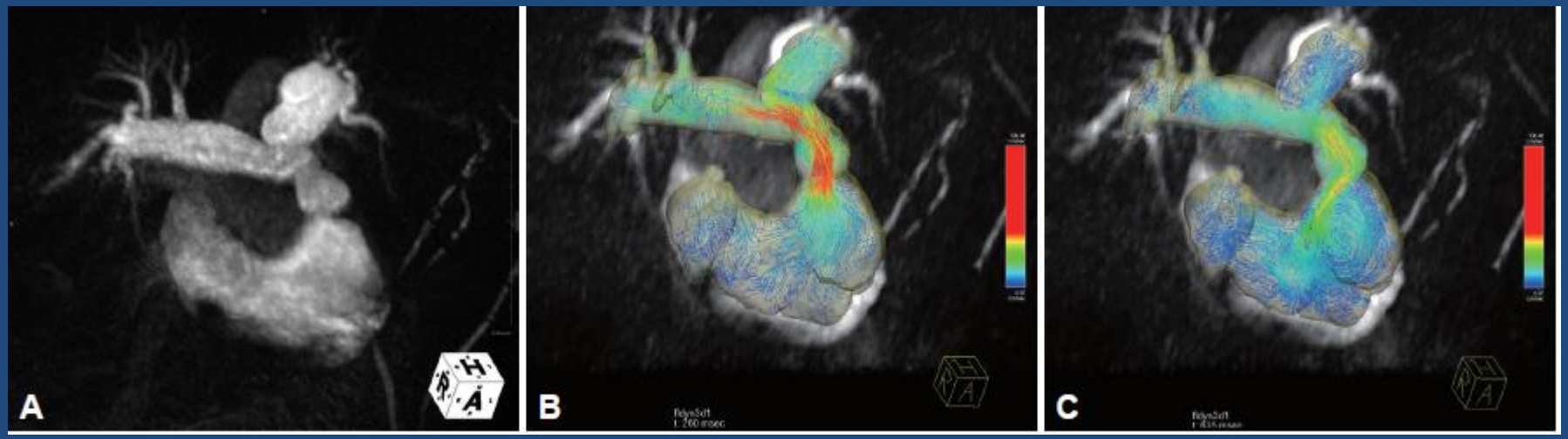


Reiter. Cir CV Imaging 2008

Future directions-4Dflow



- Characteristics of PH
- vortex flow formation
- wall shear stress
- correlation with mPAP



Odagiri K et al. Springer plus 2016;5:1071
Hideki et al, CVIA 2018;2(2): 85-96

Pros and cons of CMR

- Gold standard for RV ventricular size , function and mass
- Superior image quality (no limitations to acoustic windows and body habitus)
- Ver y low inter-observer variability
- Anatomic and functional assessment of PAs (size, pulsaliility)
- Tissue characterization
- No radiation

- Long scanning time
- Claustrophobia
- Motion and arrhythmia artefacts
- Breath holding
- Cost
- Nephrogenic systemic fibrosis in patients with severely impaired renal function
- Ferromagnetic materials and devices

Key messages

- Multimodality imaging is essential for diagnosis and management of patients with PH
- CMR is gold standard for assessment of RV size, function and mass
- CMR provides important information for diagnosis, classification and follow up of patients with PAH

Thank you very much