31 GIORNATE CARDIOLOGICHE TORINESI

Heart-lung interaction:

From Right ventricle to pulmonary artery coupling

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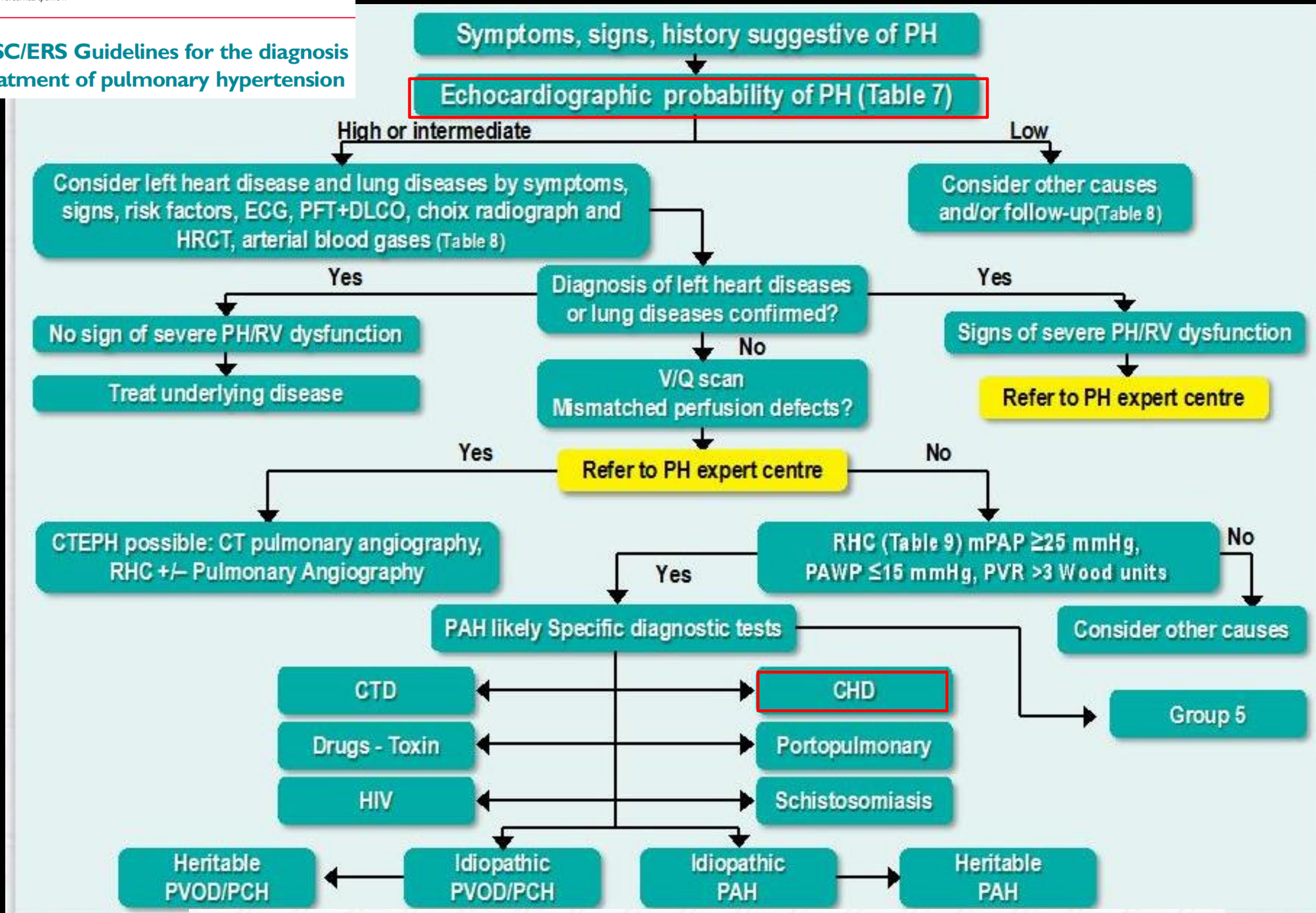
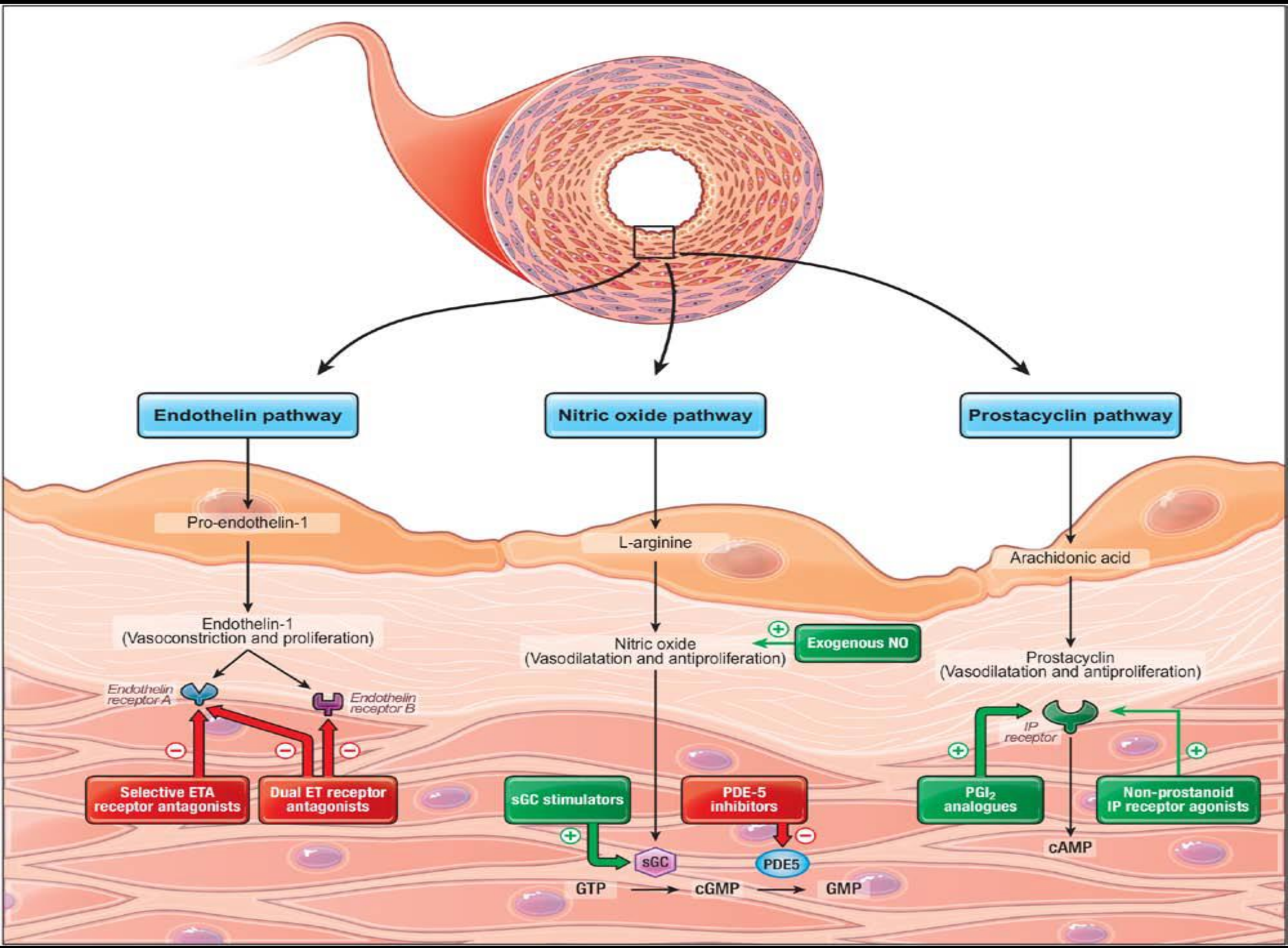
2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension



Recommendations	Class	Level
Echocardiography is recommended as a first-line non-invasive diagnostic investigation in case of suspicion of PH.	I	C

European Heart Journal (2016) 37, 67–119


Endothelin pathway
Nitric oxide pathway
Prostacyclin pathway
Pro-endothelin-1
L-arginine
Arachidonic acid
Endothelin-1
(Vasoconstriction and proliferation)
Nitric oxide
(Vasodilatation and antiproliferation)
Exogenous NO
Prostacyclin
(Vasodilatation and antiproliferation)
Endothelin receptor A
Endothelin receptor B
IP receptor
Selective ETA receptor antagonists
Dual ET receptor antagonists
sGC stimulators
PDE-5 inhibitors
PGI2 analogues
Non-prostanoid IP receptor agonists
sGC
PDE5
cAMP
GTP
cGMP
GMP

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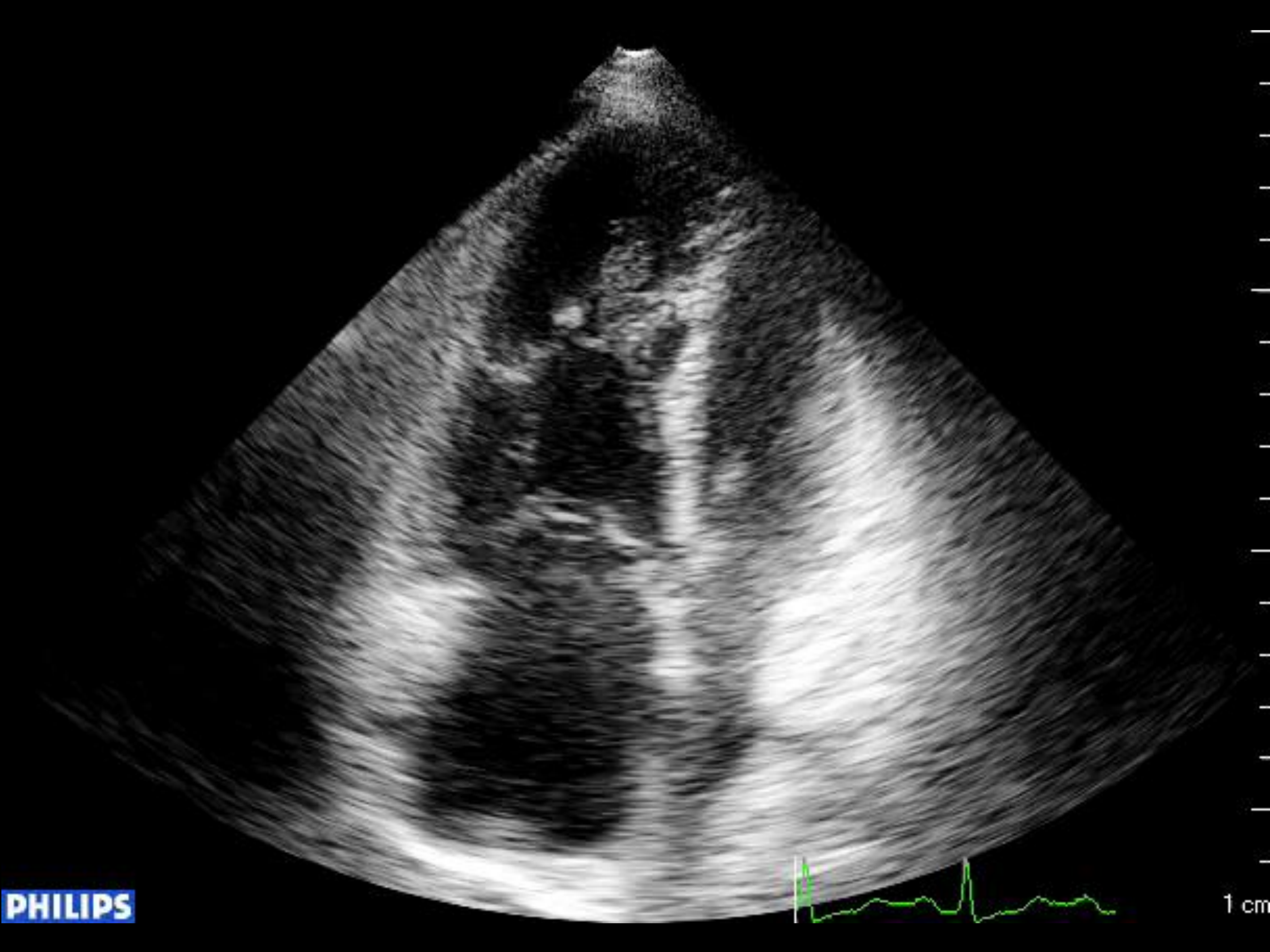
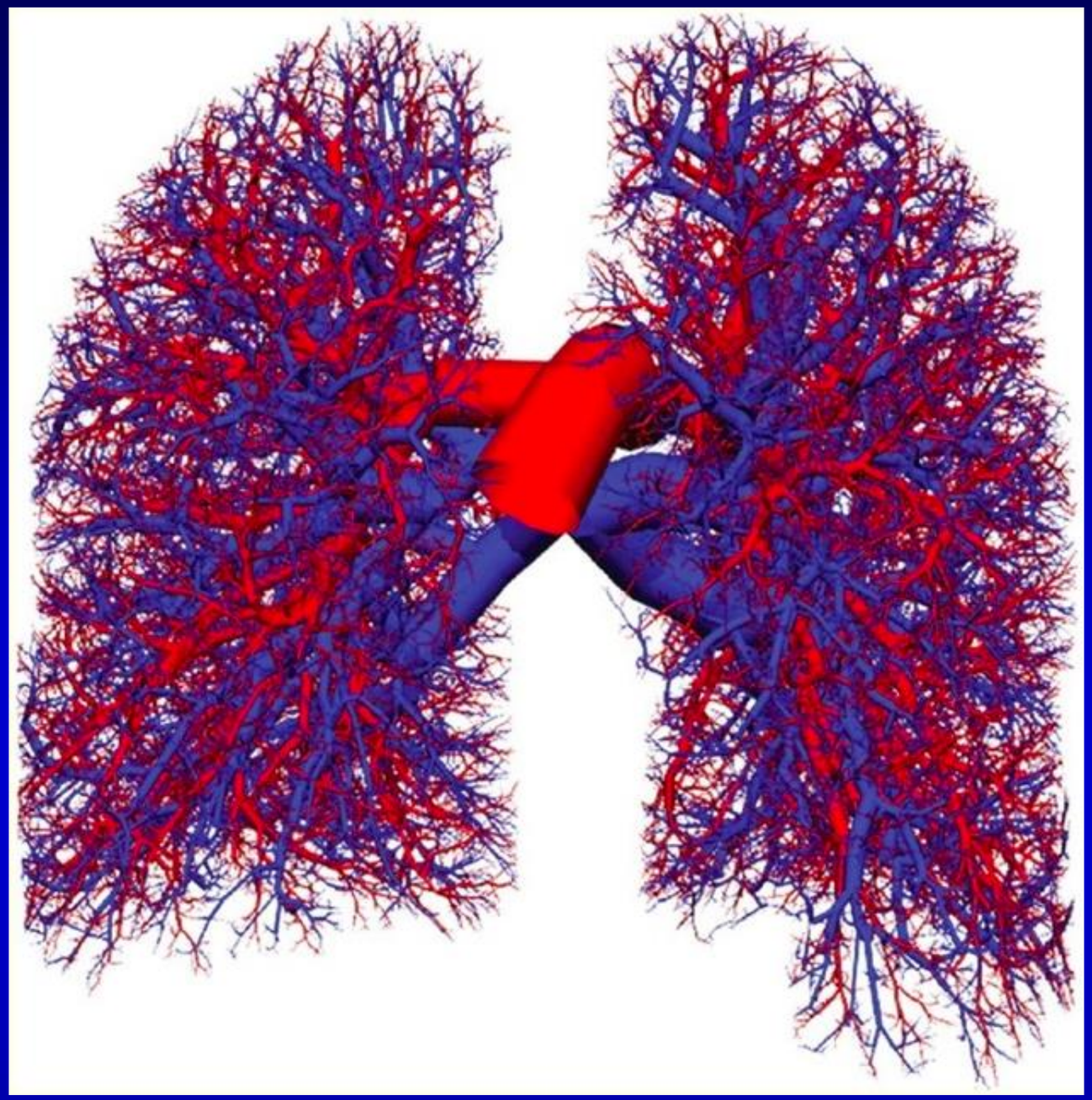
ESC/ERS GUIDELINES

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

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%


PHILIPS
1 cm



Right ventricle and pulmonary circulation are deeply different from the well-known systemic circulation

Pulmonary circulation is not the systemic circulation

Right ventricle is not the left ventricle

How do they interact?

Pulmonary artery circulation:

Not your typical circulation

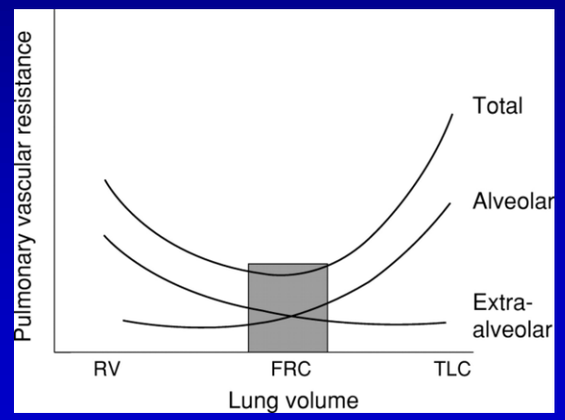
Normal flow but low pressures:
Low impedance
PVR = $(l \cdot \mu \cdot 8)/(\pi \cdot r^4)$

→

< length
>>> capillary bed
Limited arteriolar regulation

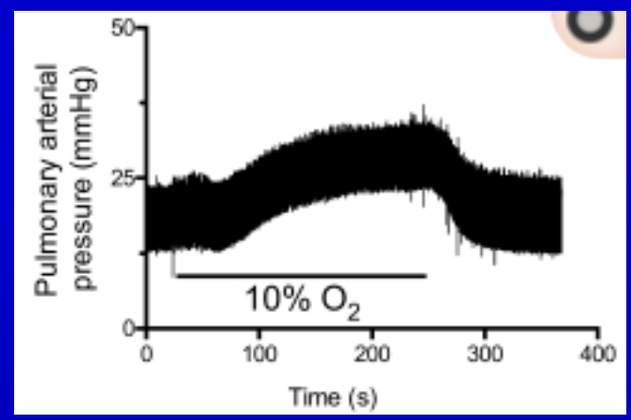
Strictly dependent from transmural pressure

→



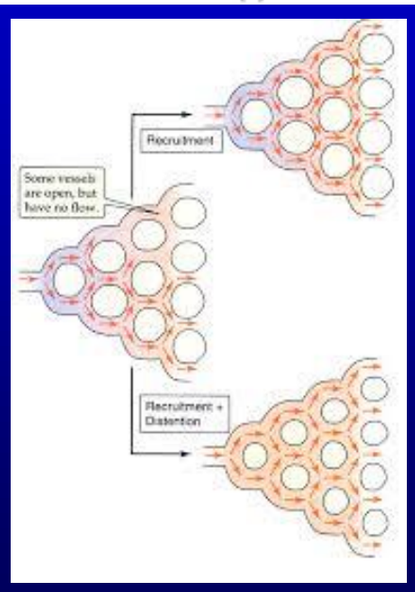
<u>Hypoxic</u> vasoconstriction

→



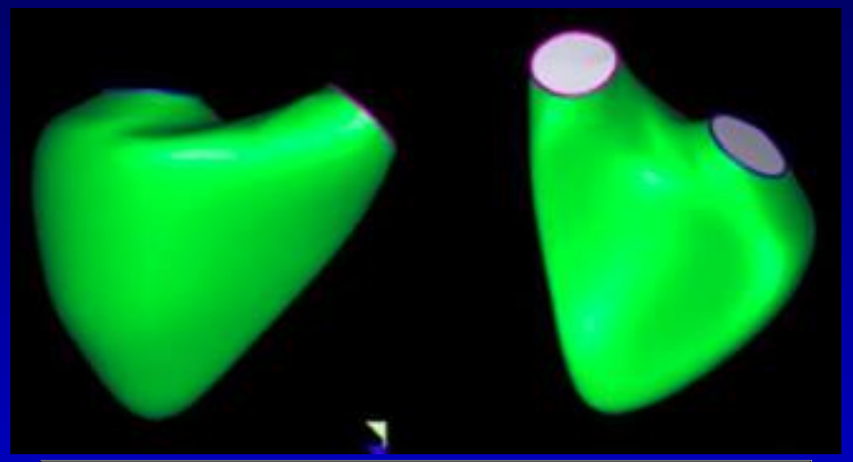
Recruitment/distension phenomenon

→

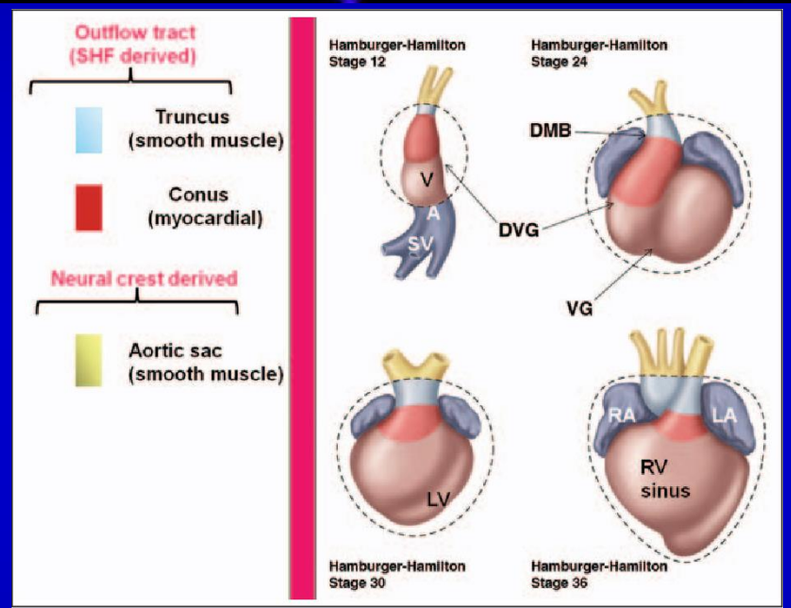


Right ventricle:

Not your typical ventricle



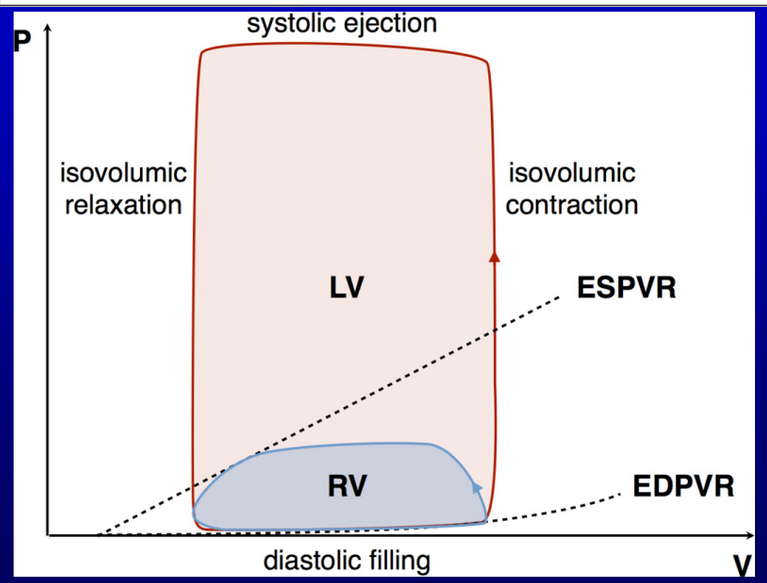
Different anatomy



Different embryology (RVOT)

Different physiology:

Low impedance
Preload dependency
Afterload dependency



Assessment of the pulmonary circulation is <u>complex</u>
For example, no direct access to arterial pressures

Right ventricle

RV-FAC

3D RV EF

TAPSE

RV TDI S’

MPI

IVRT

RVCPI

RV EDP

RV ESP

CO, CI, SV

RVSWI

Pre/afterload dependency

Pulmonary circulation

PVR = TRV/TVIRVOT × 10 + 0.16

o sPAP/(HR × TVIrvot)

sPAP = 4 * TRV^2

Pulmonary flow acceleration time

dPAP = 4 * PR^2 + RAP

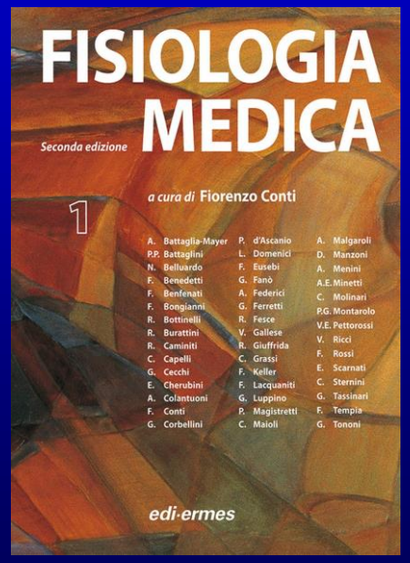
mPAP = 4 * PR^2 + RAP

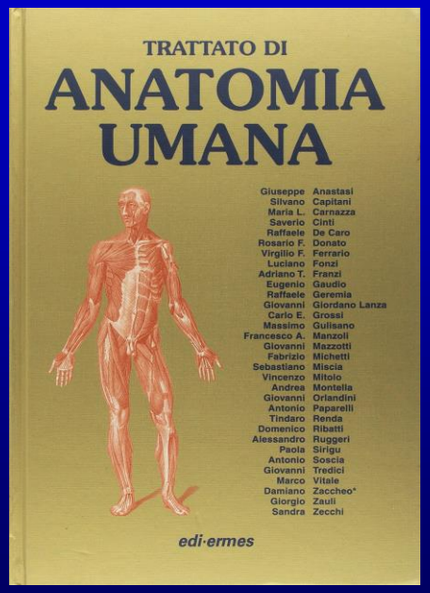
How can we put together RV physiology with pulmonary circulation?

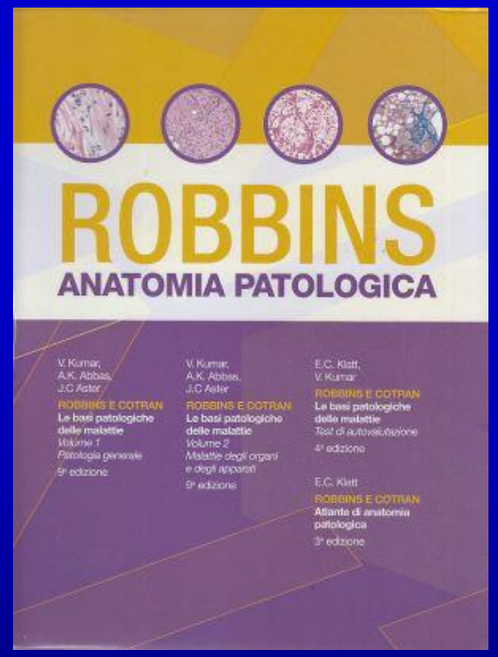
Is it really so hard to couple RV function to pulmonary artery?

Probably no

I mean, not SO hard







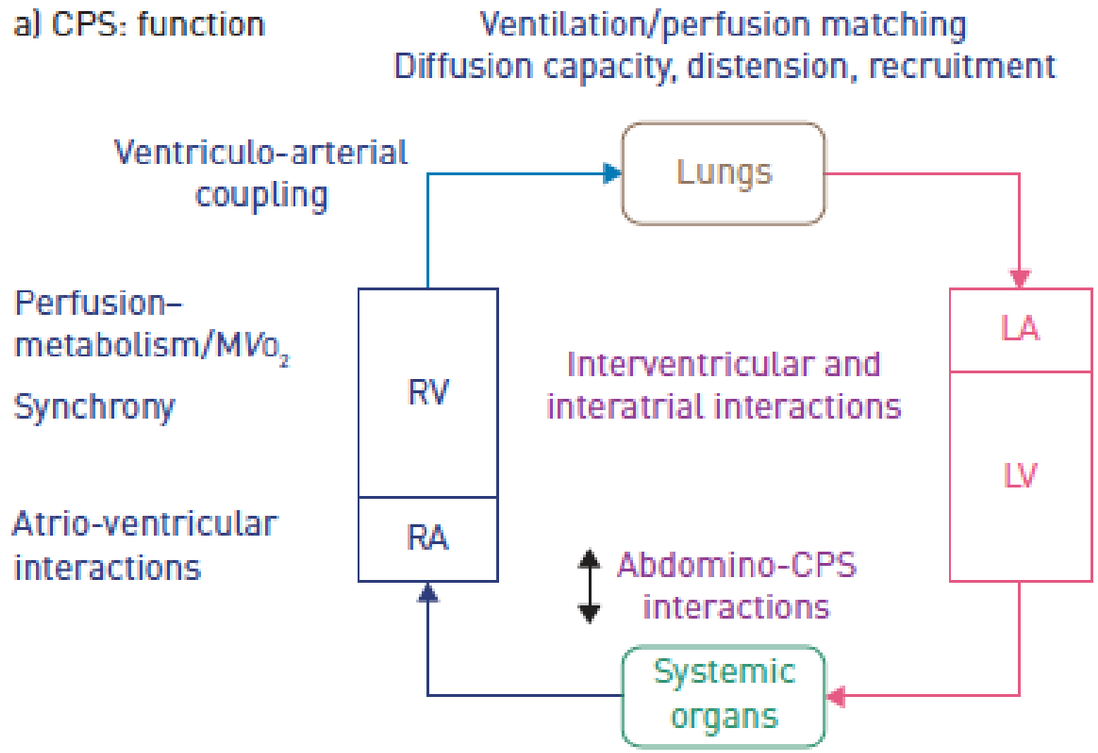
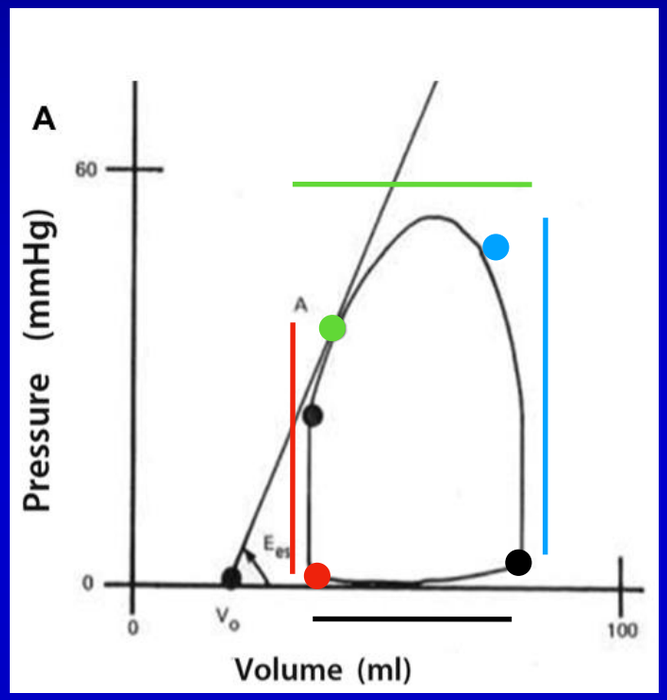


FIGURE 1 The cardiopulmonary system (CPS): a) function and b) characterisation. MVo_2: myocardial oxygen consumption; RV: right ventricle; RA: right atrium; LA: left atrium; LV: left ventricle; E_{es}: end-systolic elastance; τ: time constant of ventricular relaxation; E_{ed}: end-diastolic elastance; PVR: pulmonary vascular resistance; PAC: pulmonary arterial compliance; E_a: arterial elastance; PAP: pulmonary arterial pressure; PAWP: pulmonary arterial wedge pressure; EF: ejection fraction; CO: cardiac output. Subsystems (or units: heart, respectively its load) are characterised by their intrinsic function, which can be derived from the ventricular pressure–volume relationship and the pulmonary pressure–flow relationship. The system parameters result from cardiopulmonary interaction.

Back to physiology:

First step:

RV pressure/volume loop



Red: diastasis, isovolumetric relaxation

Black: early + late diastole

Blue: isovolumetric contraction

Green: systole

Red: tricuspid valve opening

Black: tricuspid valve closure

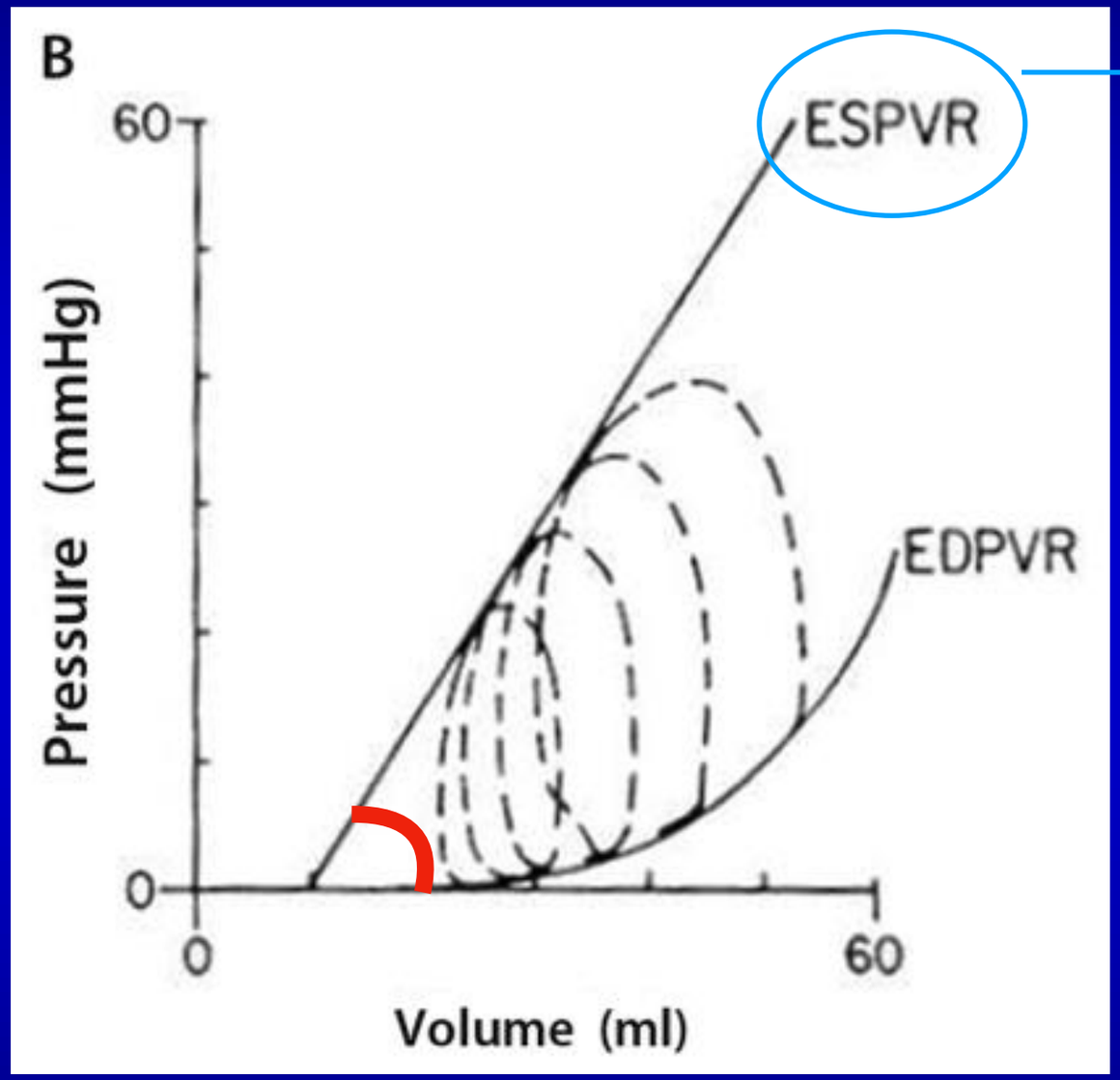
Blue: pulmonary valve opening

Green: pulmonary valve closure

Back to physiology:

Second step:

Let's play with preload (by inflating a balloon in inferior vena cava)



End systolic pressure volume relationship =
intercept of multiple P/V curves under different preload condition

What can we observe:

1) **linearity**
2) **slope of the intercept is constant**

So, let's measure the angle of the intercept: Ees

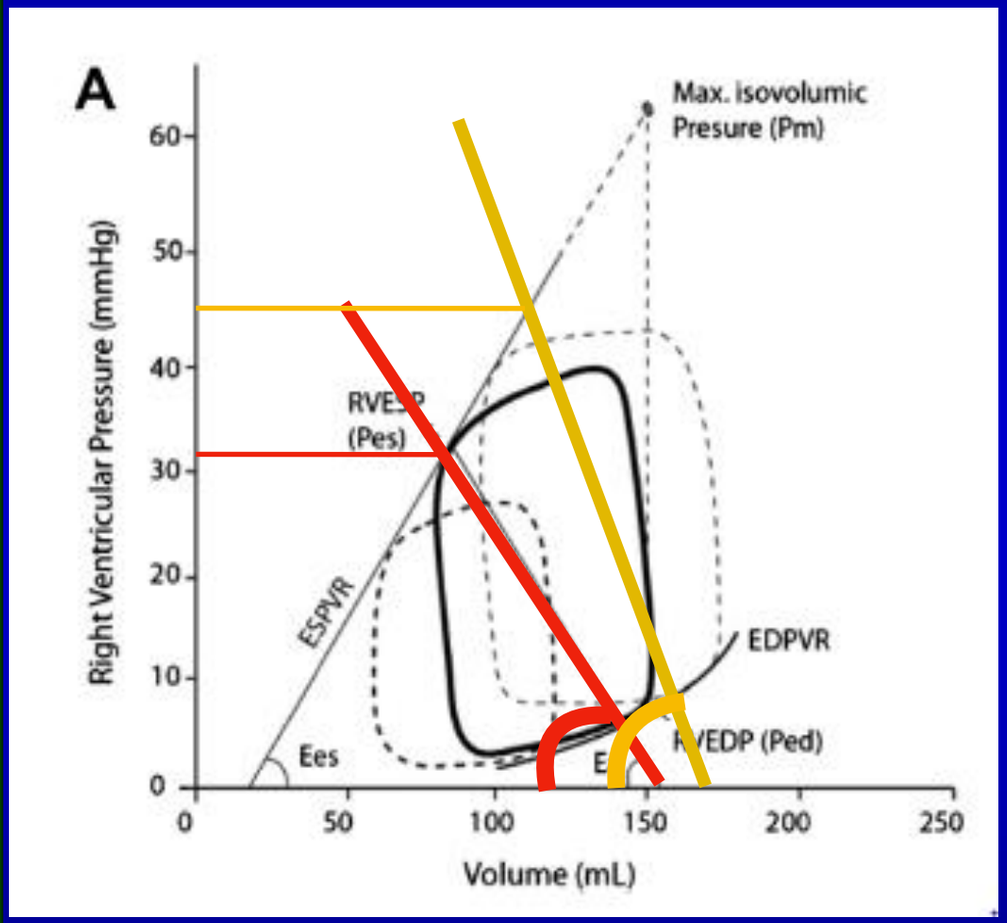
Ees represent the RV end systolic elastance, which is a direct measure of RV inotropism; moreover, it is preload independent (since it is linear)

The greater, the better.

Back to physiology:

Third step:

Focus on the pulmonary circulation side



How can we assess pulmonary impedance?

Trace a line between end-diastolic volume and P/V status at end systole
(basically, pulsatory pressure/end systolic RV pressure)

The slope define Ea, which is pulmonary artery elastance (resistive + pulsatile)

Let's try to increase PVR:

- **higher RV end diastolic volume and pressure**
- **higher RV end systolic volume and pressure**
- **higher Ea**

The lower Ea, the better

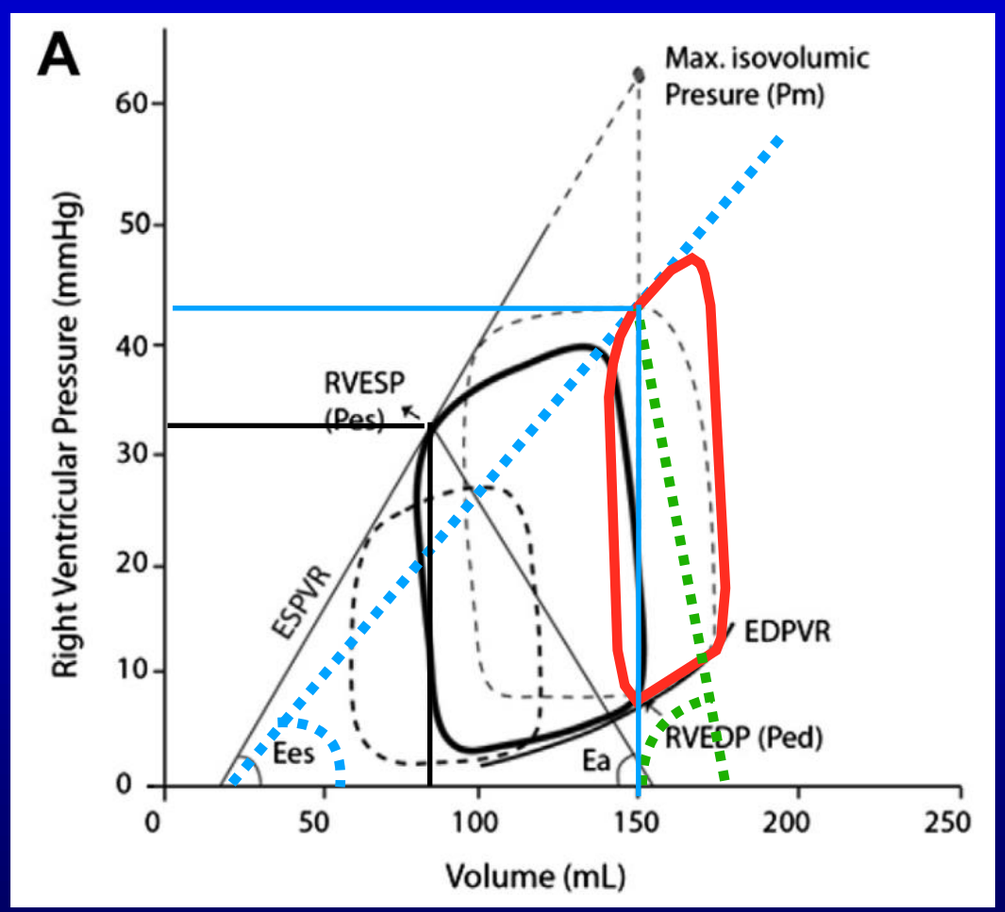
Back to physiology:

Forth step:

Put the data together!

That means, calculate Ees/Ea:
end systolic RV elastance/pulmonary artery elastance

With a simple number, we know how the ventricle react to the after load, independently from the preload



Baseline P/V loop (black)

Let's raise PVR:

P/V loop shift to right
Higher RV end systo/diastolic pressures
Higher RV end systo/diastolic volumes
Lower pulsatory pressure

But most importantly:
Lower Ees, higher Ea → **lower Ees/Ea**
RV uncoupling

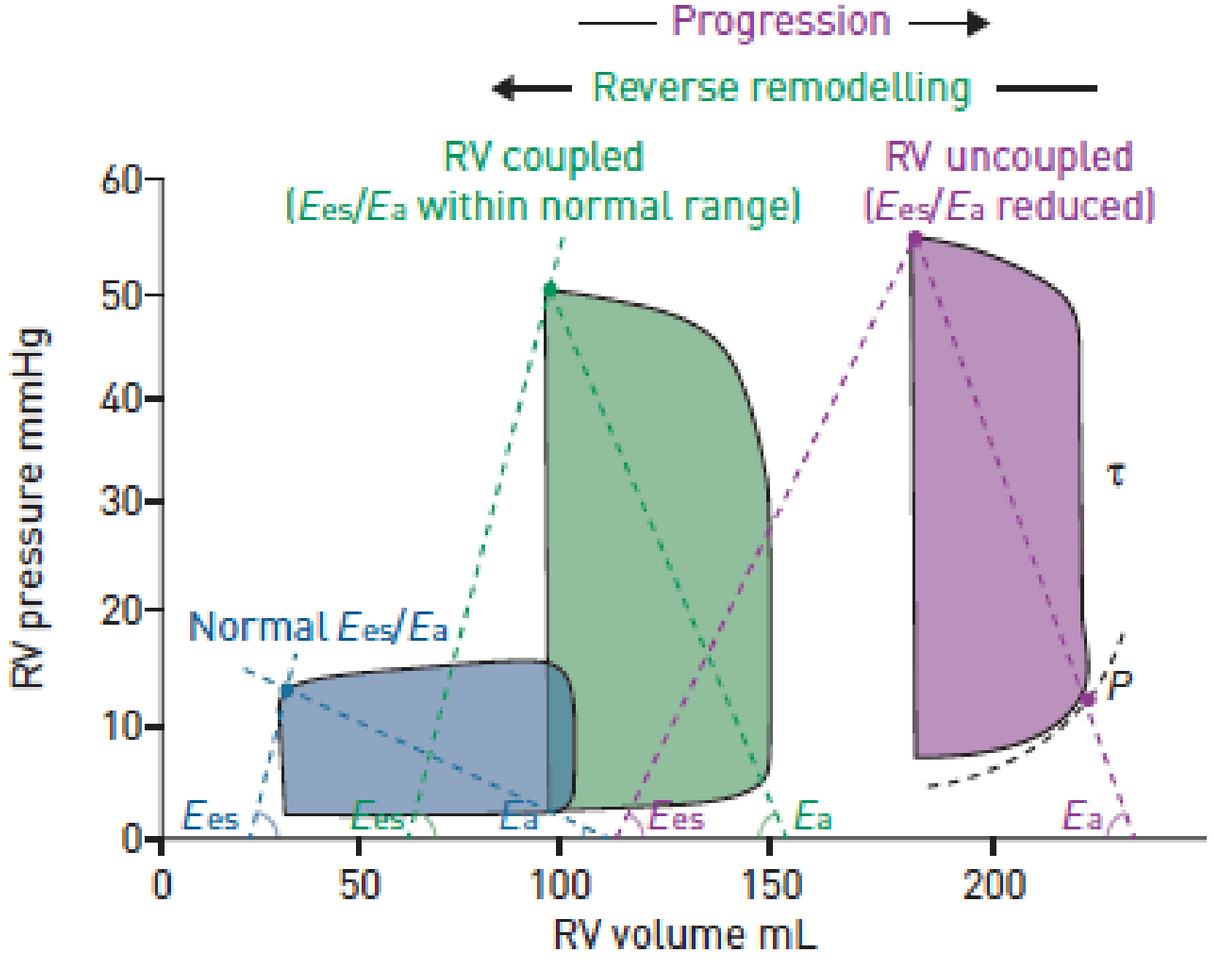


FIGURE 2 Right ventricular (RV) pressure–volume analysis. Pressure–volume loops at three different stages: normal (blue), pulmonary hypertension (green) and right ventricular failure (purple). E_{es}: end-systolic elastance; E_a: arterial elastance; τ: time constant of ventricular relaxation. $P=\alpha(e^{\beta V}-1)$ describes the diastolic pressure–volume relation. Reproduced and modified from [11] with permission.

Awesome, but how we measure Ees/Ea in the real world?

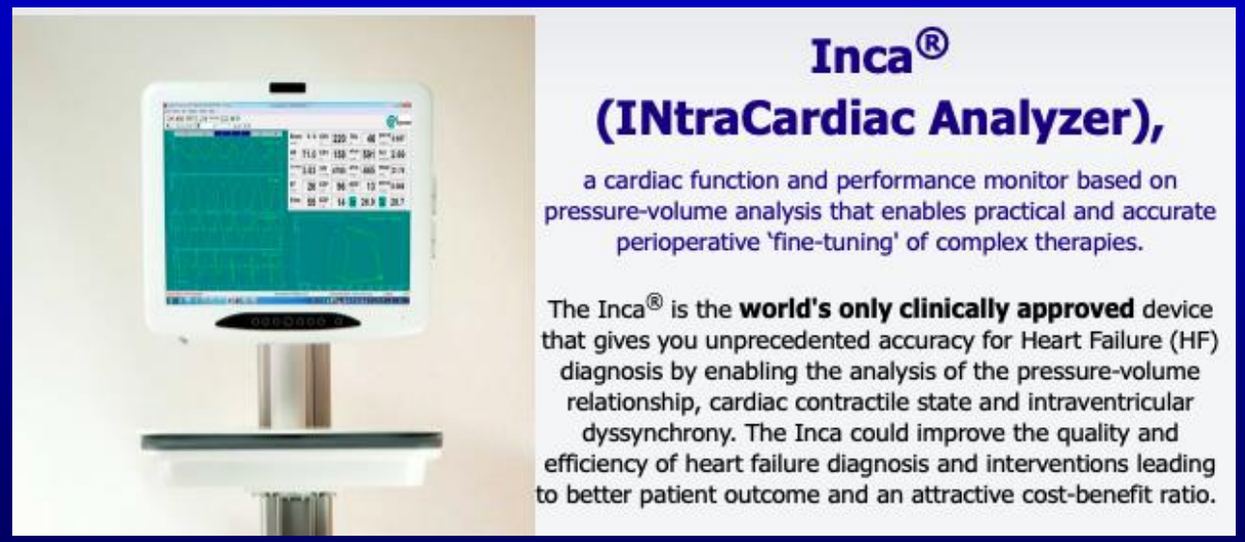
First, we have pressure curve all around the cardiac cycle with right heart catheterization

But, we need to know how volume changes during cardiac cycles

Not so easy

Possible solutions:

1. **Cardiac magnetic resonance** (validated multiple times)
2. **3D echo reconstruction of RV volume changes** (not so used in literature)
3. **P/V catheters** (validated multiple times)



Second, we need **multiple beats** with different preload condition to derive **Ees** (Ea is quite simple to obtain)

Not that easy (nor ethic)

Possible solution:

$$Emax(SB)=Pes/[Ves-Vo(SB)]$$

$$Vo(SB) = [EN(tN)\times P(tmax)\times V(tN)-P(tN)\times V(tmax)]/[EN(tN)\times P(tmax)-P(tN)] \text{ and}$$

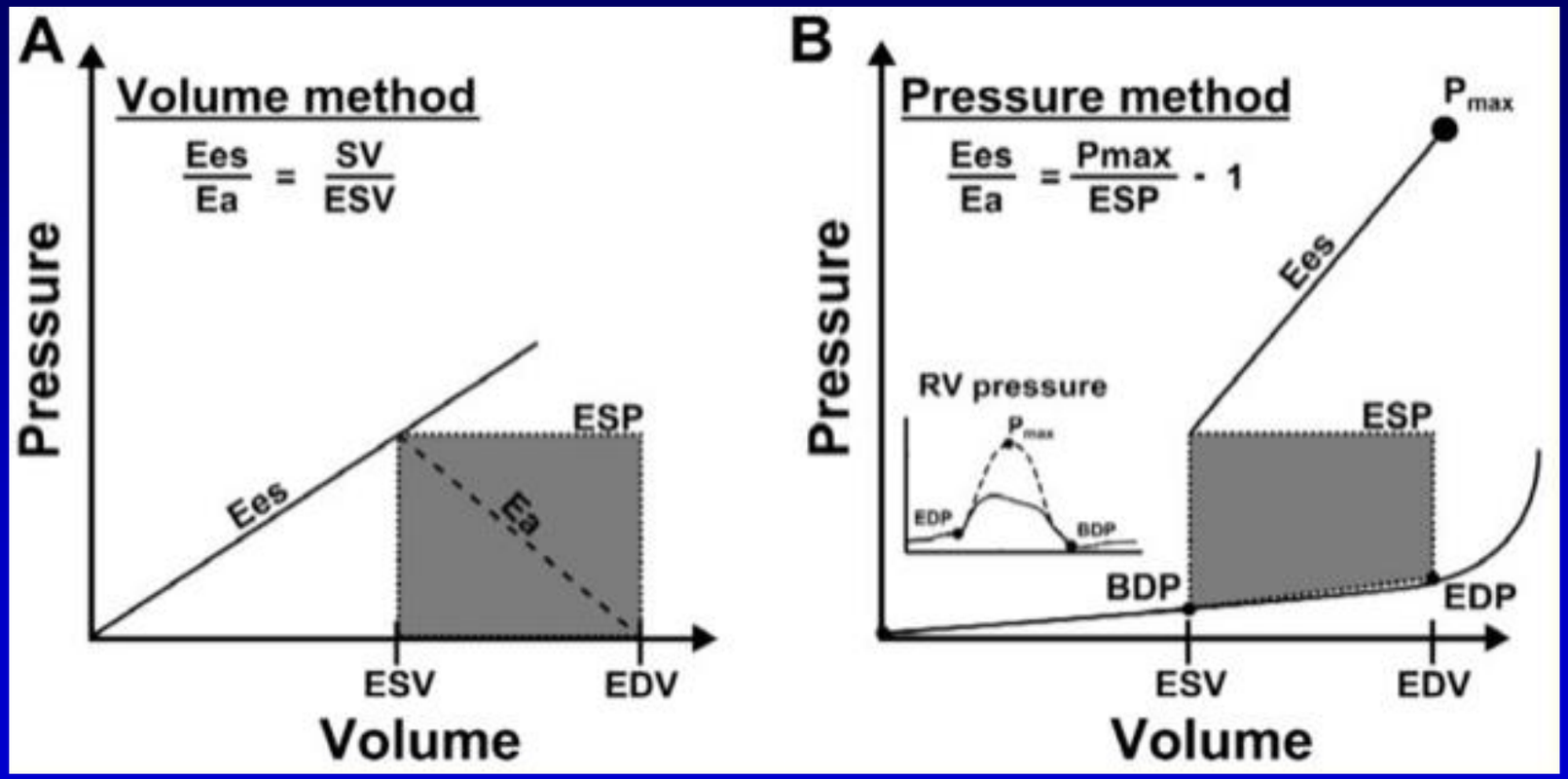
Is it really so hard to couple RV function to pulmonary artery?
Maybe **a little**

So, RV Ees/Ea can be calculated, only in this cases:

1. we have P/V catheter - simplest and gold-standard solution, but requires money and experienced operators
2. we have have access to MRI <24h from right heart catheterization - not so feasible; and we still need multiple beats OR complex mathematical equations
3. we have a proper post-processing software of 3D acquisitions of RV echocardiography - feasible! - still need complex mathematical equations

Luckily, we have some good alternatives to calculate Ees/Ea

Two alternatives (both have significant defects, but they still work):

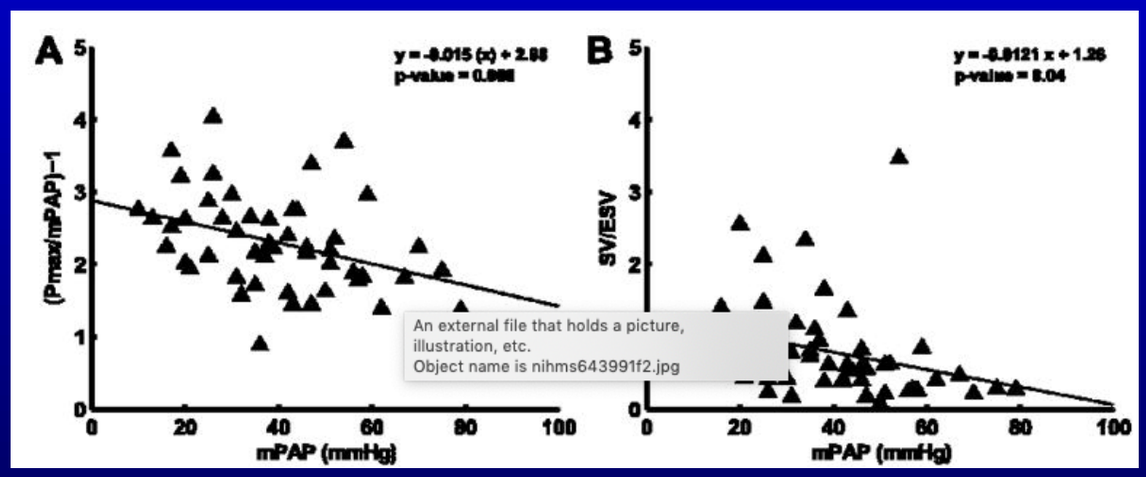


1. The volumetric way:

Ees/Ea ≈ SV/ESV

2. The pressure way:

Ees/Ea ≈ (Pmax/ESP)-1



Heart. 2015 Jan;101(1):37-43. doi: 10.1136/heartjnl-2014-306142. Epub 2014 Sep 11.
RV-pulmonary arterial coupling predicts outcome in patients referred for pulmonary hypertension.
Vanderpool RR

Still, not so feasible bedside (need 3D echo and still need some math competency)

BUT:

Am J Physiol Heart Circ Physiol 305: H1373–H1381, 2013.
First published August 30, 2013; doi:10.1152/ajpheart.00157.2013.

Tricuspid annular plane systolic excursion and pulmonary arterial systolic pressure relationship in heart failure: an index of right ventricular contractile function and prognosis

M. Guazzi,[1] F. Bandera,[1] G. Pelissero,[1] S. Castelvecchio,[1] L. Menicanti,[2] S. Ghio,[3] P. L. Temporelli,[4] and R. Arena[5]

TAPSE/PAPs:

- simple
- bedside disposable
- estimate accurately RV-PA coupling
- validated multiple times
- predict prognosis

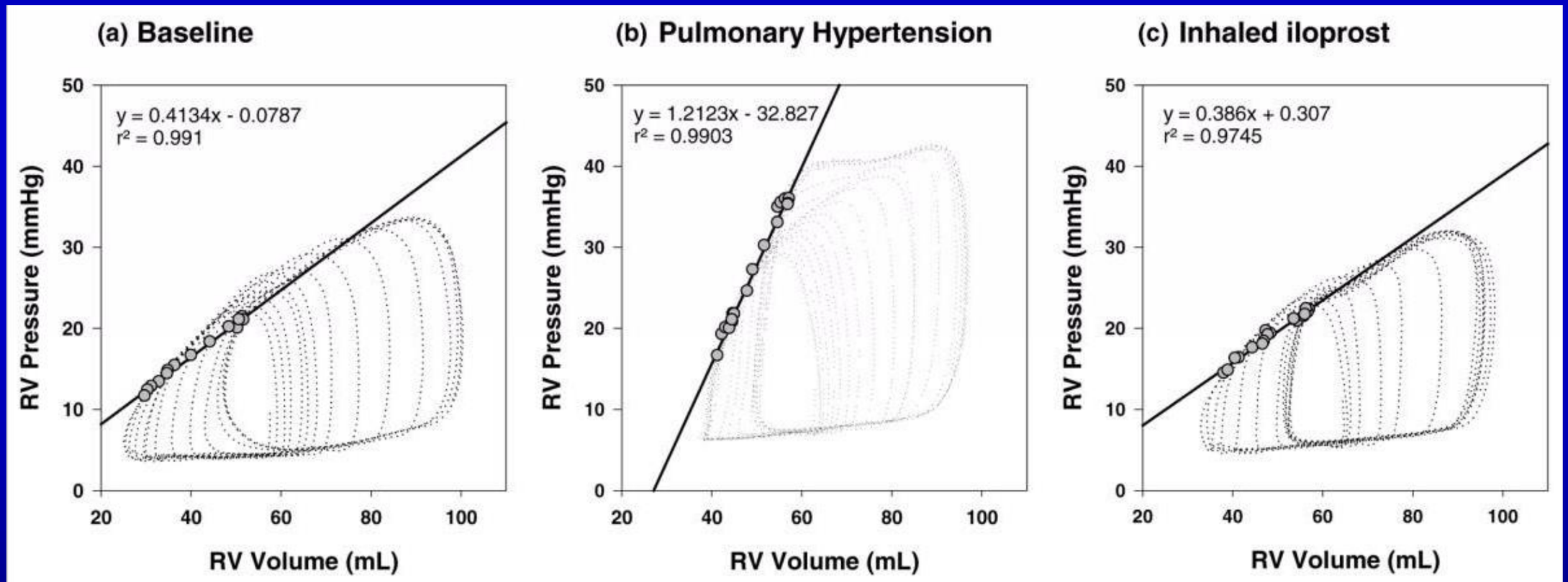
Use of Tricuspid Annular Plane Systolic Excursion/Pulmonary Artery Systolic Pressure As a Non-Invasive Method to Assess Right Ventricular-PA Coupling in Patients With Pulmonary Hypertension

A Routine Measurement in Pulmonary Hypertension?

Back to clinical:

Why should we measure Ees/Ea in the setting of pulmonary hypertension (either idiopathic or in HFp/rEF)?

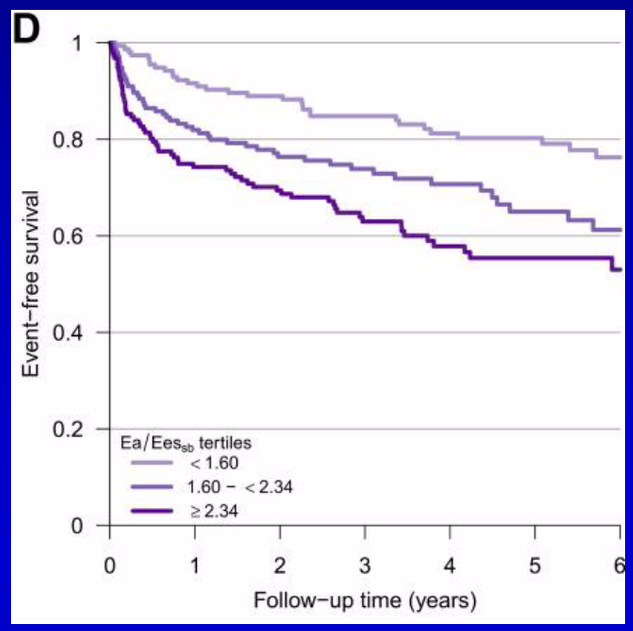
1. because it tells us how RV works, facing high pulmonary artery impedance, independently from preload



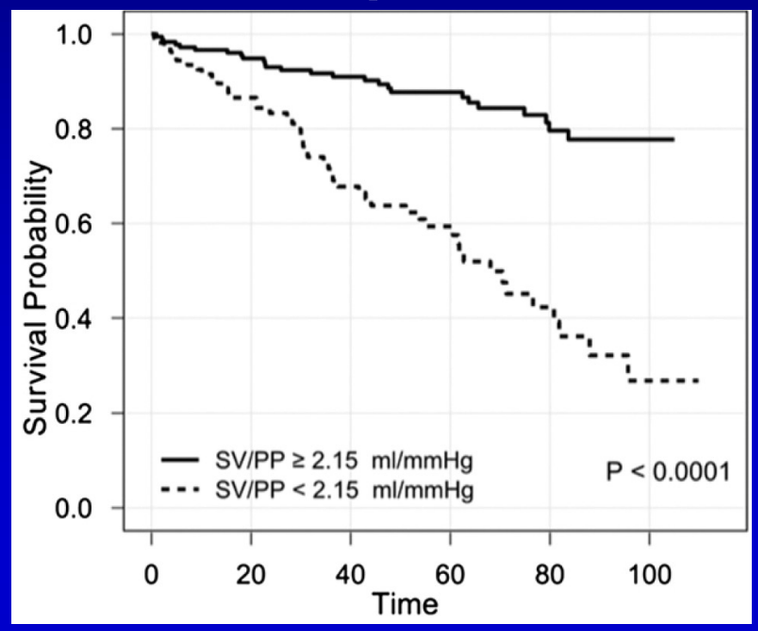
Back to clinical:

2. because it predicts prognosis in complex patients

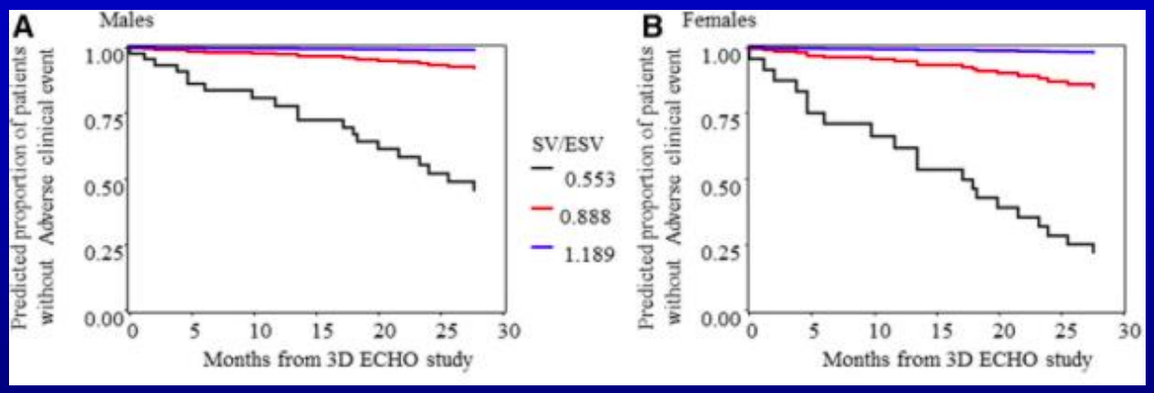
HFrEF



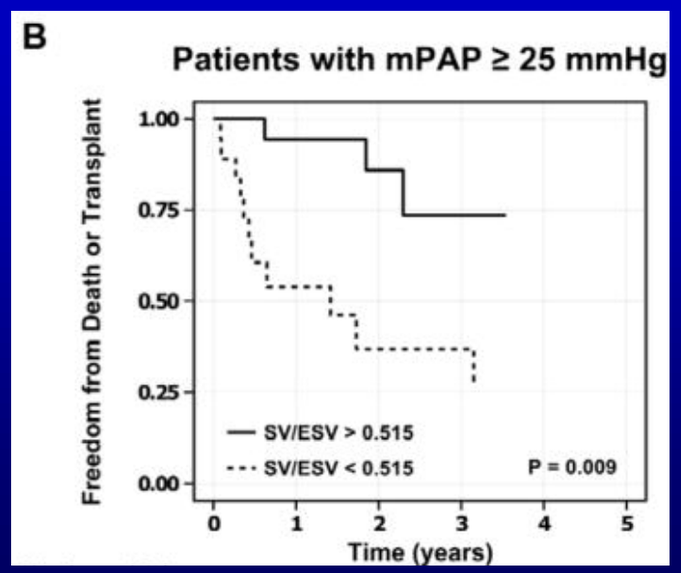
HFpEF



Pediatric pulmonary hypertension



Idiopathic pulmonary hypertension

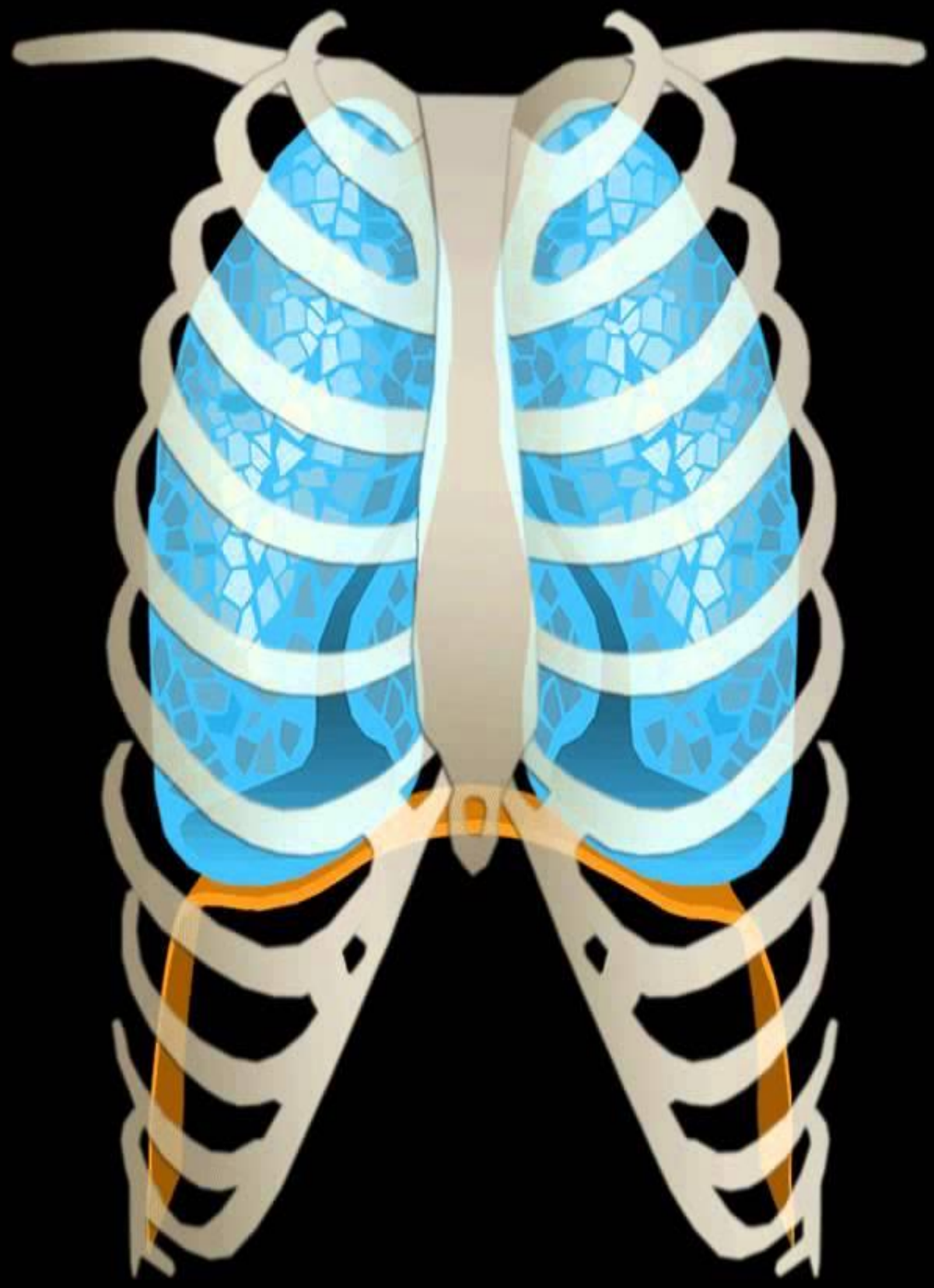


So what?

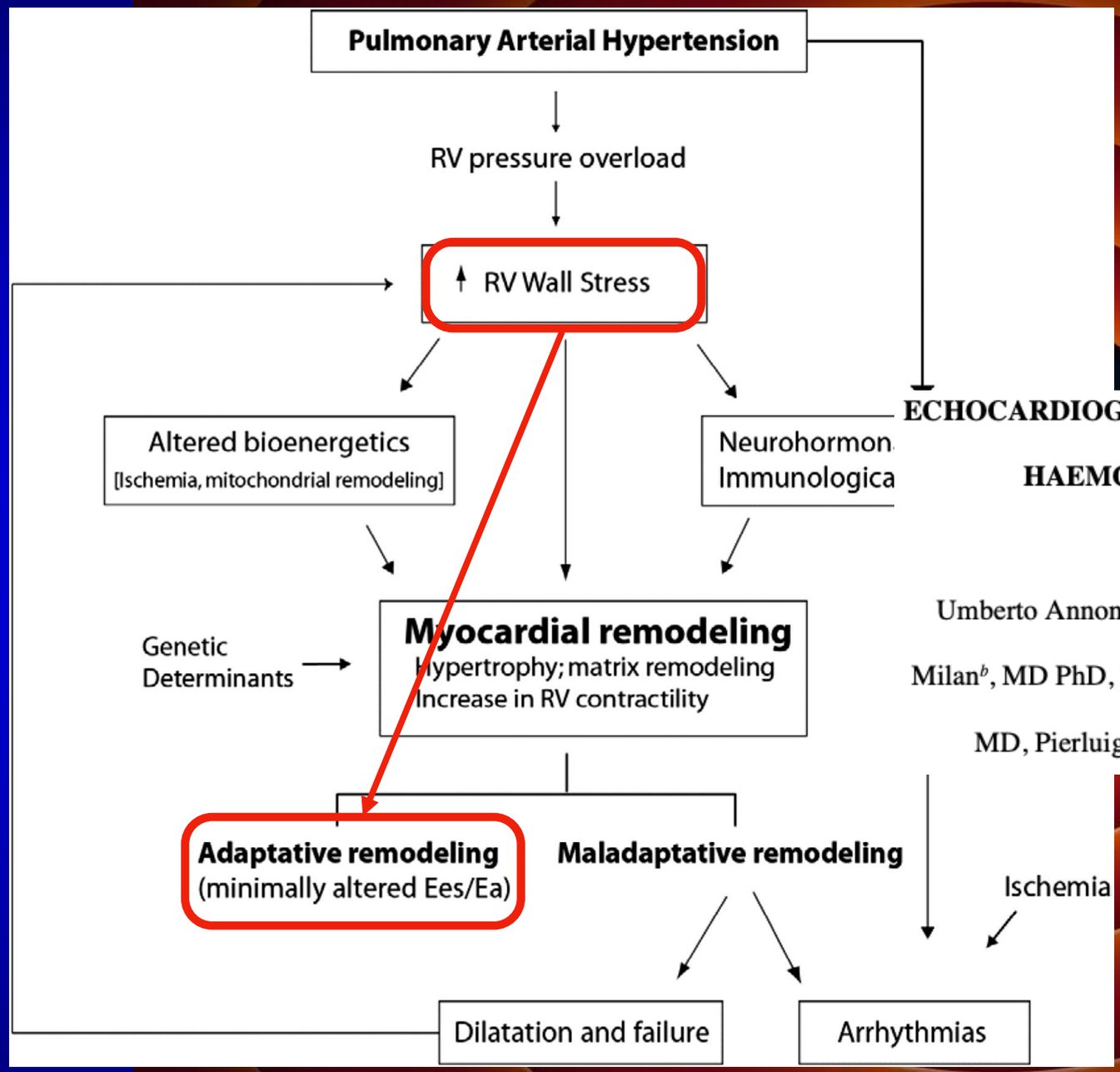
We suggest to use simple methods like TAPSE/PAPs (or SV/ESV) to estimate RV to PA coupling in patients with mild-moderate pulmonary hypertension **independently** from its ethiology

Because it is able to estimate adequately the status of the **whole pulmonary circulation**, detaching from a "RV focused" evaluation

Furthermore, Ees/Ea, estimated with any method, it is able to **predict prognosis**, sometimes even better that canonical RV function parameters, in multiple clinical landscapes.



Or maybe not?



RV wall stress/tension precedes RV uncoupling

ECHOCARDIOGRAPHIC ESTIMATION OF RIGHT VENTRICULAR WALL TENSION:

HAEMODYNAMIC COMPARISON AND LONG-TERM FOLLOW-UP

Umberto Annone[a], MD, Pier Paolo Bocchino[a], MD, Walter Grosso Marra[a], MD PhD, Alberto Milan[b], MD PhD, Fabrizio D'Ascenzo[a], MD PhD, Corrado Magnino[b], MD, Antonio Montefusco[a], MD, Pierluigi Omedè[a], MD, Franco Veglio[b], MD PhD, Gaetano Maria de Ferrari[a], MD

Grazie a tutti ma soprattutto ad Umberto Annone