



HJÄRTCENTRUM

Universitetssjukhuset i Linköping

*Välkomna till  
PH/PAH-utbildning för  
ST-läkare i  
kardiologi och klinisk fysiologi  
i Sydöstra Sjukvårdsregionen*

Vimmerby 2022-10-05

JoannaMaria Papageorgiou  
David Kylhammar  
Kjell Jansson

# Dagen idag

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- 09.00-09.50 Översikt; definition/klassifikation
- 09.50-10.10 Fika
- 10.10-11.10 Diagnostik och differentialdiagnostik
- 11.10-11.15 Kort bensträckare
- 11.15-12.15 Hemodynamik; gruppövning
- 12.15-13.15 Lunch
- 13.15-13.50 Aspekter på behandling
- 13.50-13.55 Kort bensträckare
- 13.55-15.00 Fallpresentation och diskussion
- 15.00- Avslut och fika

Översikt; definition/klassifikation

# Diagnostik och differentialdiagnostik

# Hemodynamik

# TECKEN PÅ OBALANS

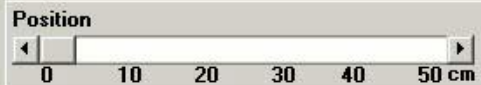
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Balansen i systemet kan beskrivas genom följande formel (med ursprung i Ohm's Lag):

$$\text{Resistens} = \frac{\text{Tryckdifferens}}{\text{Flöde}}$$

$$\text{PVR (Wood units)} = \frac{\text{mPAP (mmHg)} - \text{PCWP (mmHg)}}{\text{CO (l/min)}}$$

Swan-Ganz catheter 7.5 G



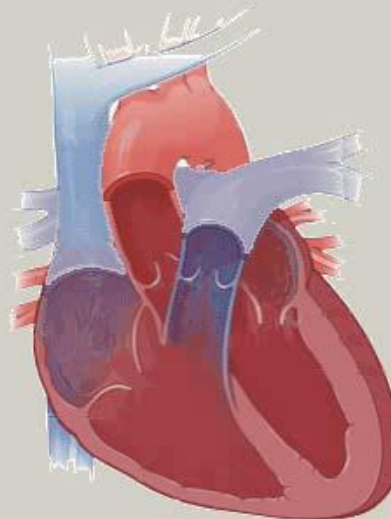
PCWP - If you push the button to the left the balloon on the tip of the catheter will be filled.

Saturation (%)

0

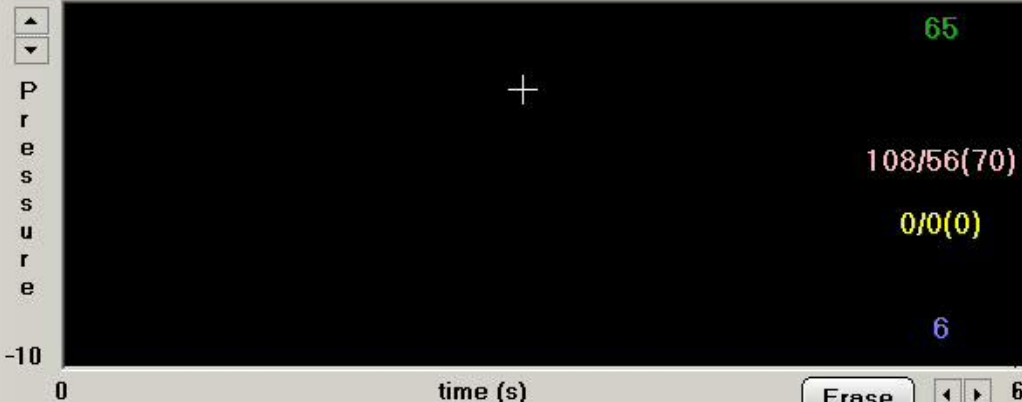
Pressure (mmHg)

0/0 (0)



Clinical monitoring

200 mmHg



- Aortic arterial pressure  Radial artery pressure  ECG
- Pulmonary artery catheter pressure  Right atrial pressure  Left atrial pressure

Global cardiac function

Cardiac output= 4,6 l/min  
Heart rate= 65 /min  
Effective stroke volume= 71 ml  
Effective LV ejection fraction= 62 %

Right ventricle

EDV= 112 ml  
ESV= 41 ml  
Stroke volume= 71 ml  
Ejection fraction= 63 %

Left ventricle

EDV= 113 ml  
ESV= 43 ml  
Stroke volume= 71 ml  
Ejection fraction= 62 %

SVR= 0,90

mmHg·s/ml

PVR= 0,07

mmHg·s/ml

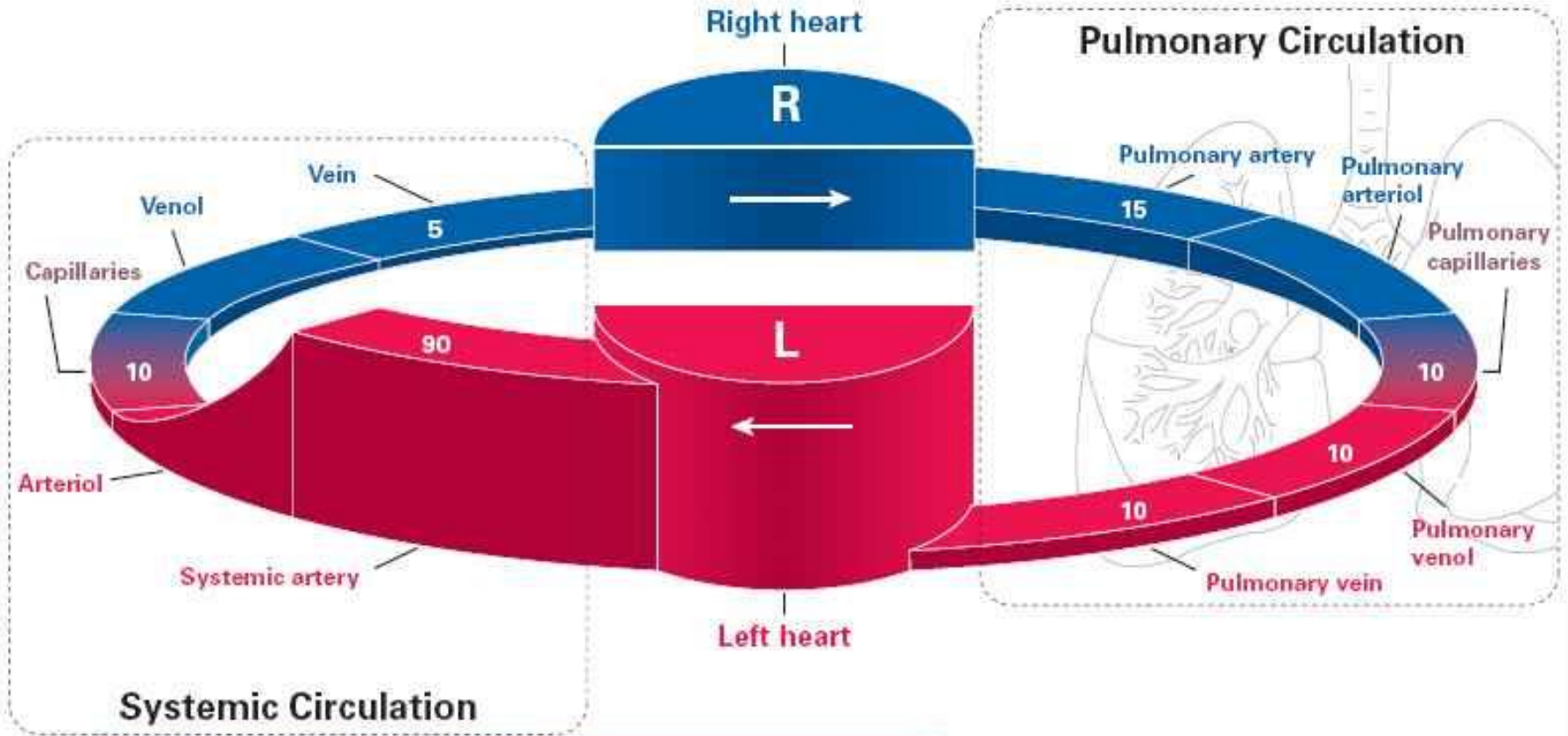
mmHg·s/ml

mmHg·min/l (Wood units)

dyne·s/cm<sup>5</sup>

# Normal Circulation

Flow 5 l/min

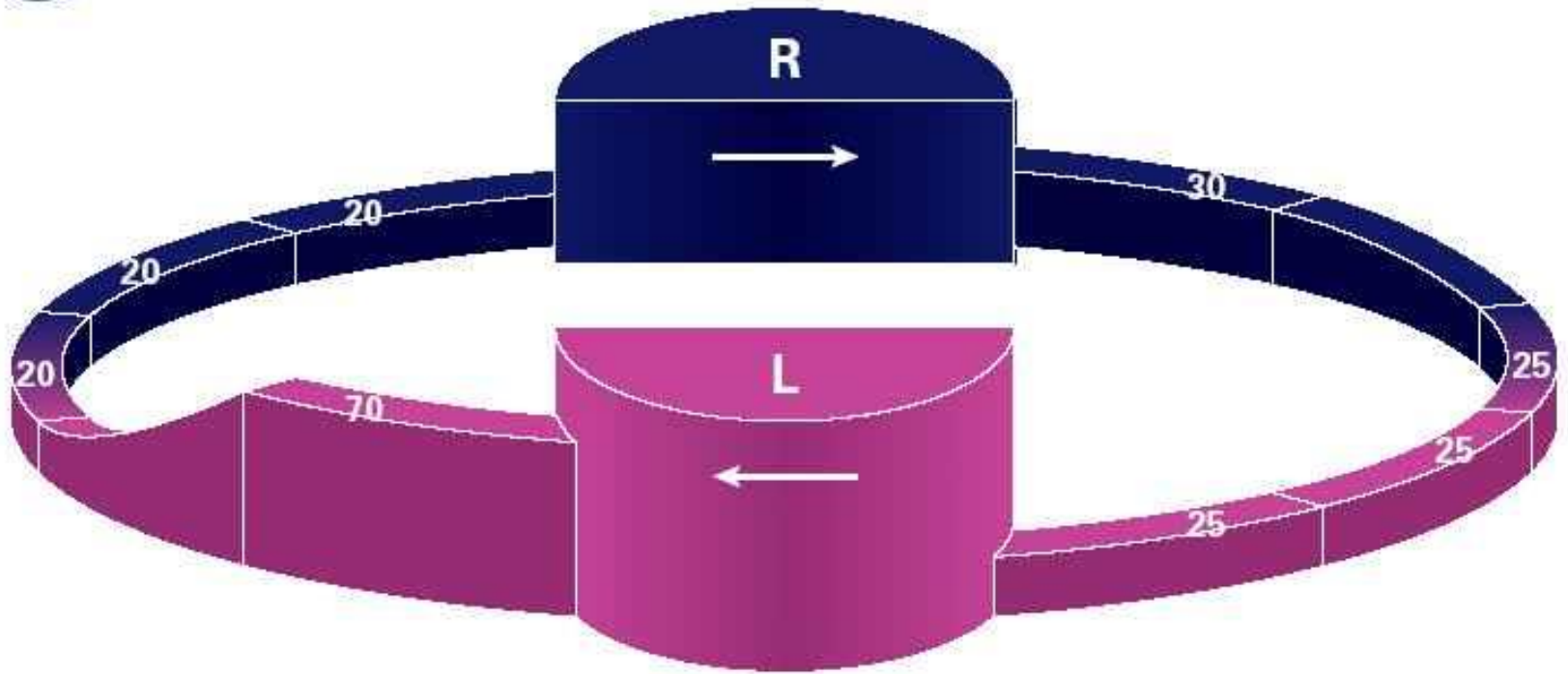


$$PVR = \frac{\text{mmHg}}{\text{l/min}} = \text{Wood unit}$$





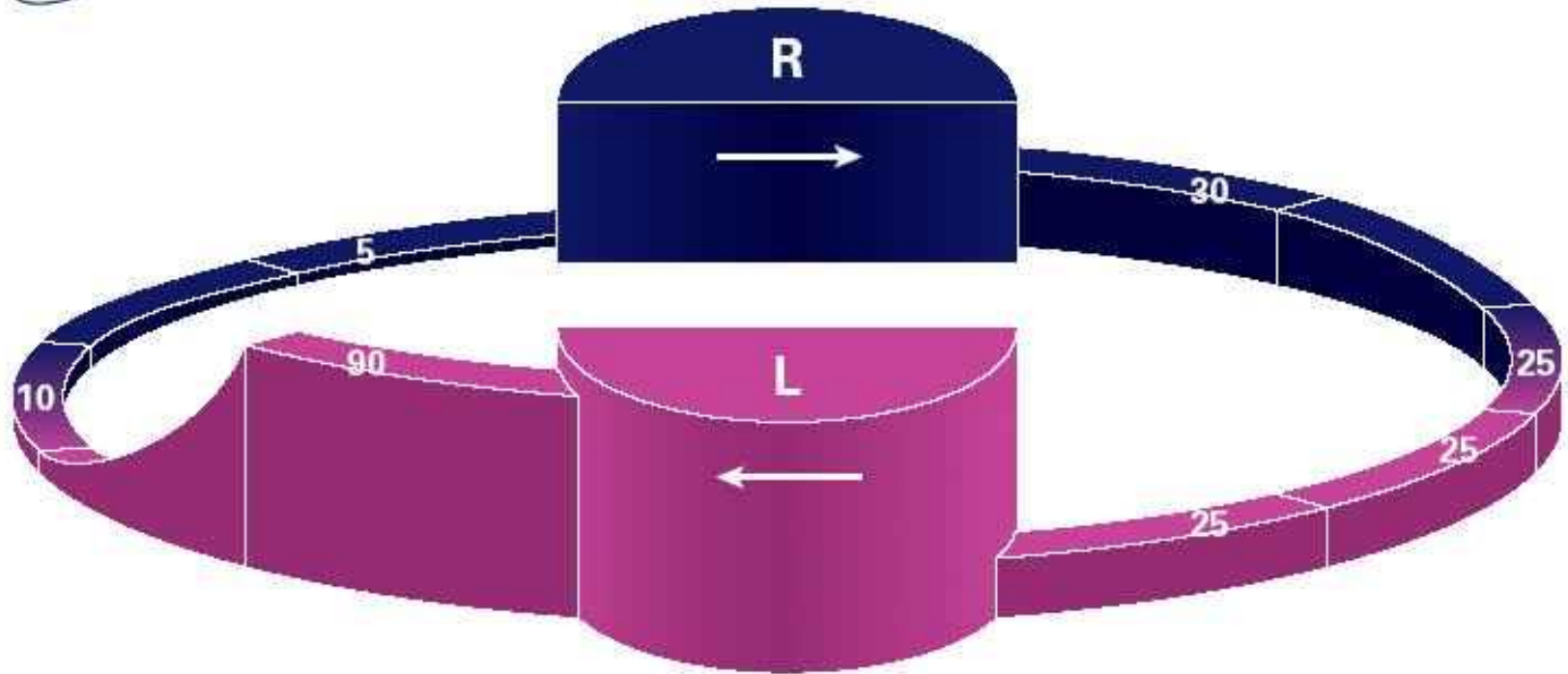
Flow 2.5 l/min



$$PVR = \frac{\text{---} - \text{---} \text{ mmHg}}{\text{---} \text{ l/min}} = \text{---} = \text{---} \text{ Wood unit(s)}$$



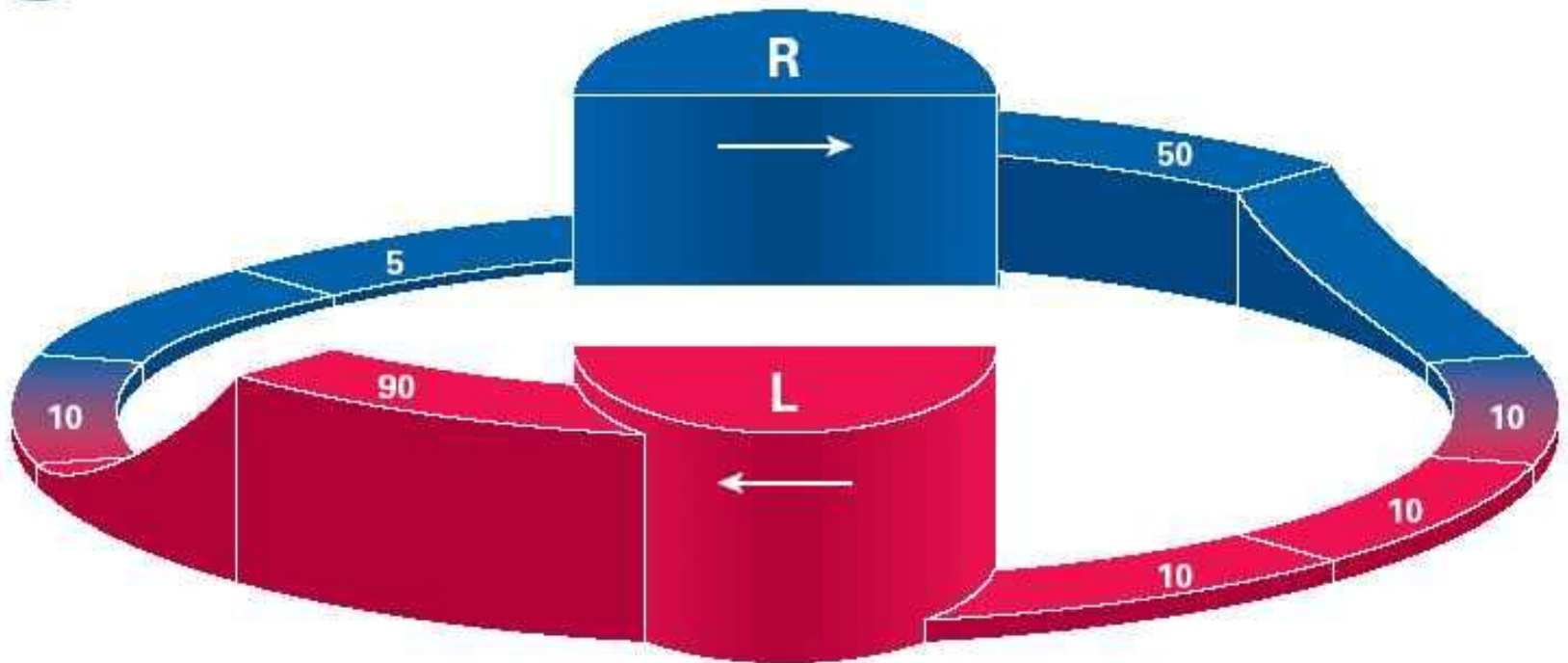
Flow 2.5 l/min



$$PVR = \frac{\text{mmHg}}{\text{l/min}} = \text{Wood unit(s)}$$

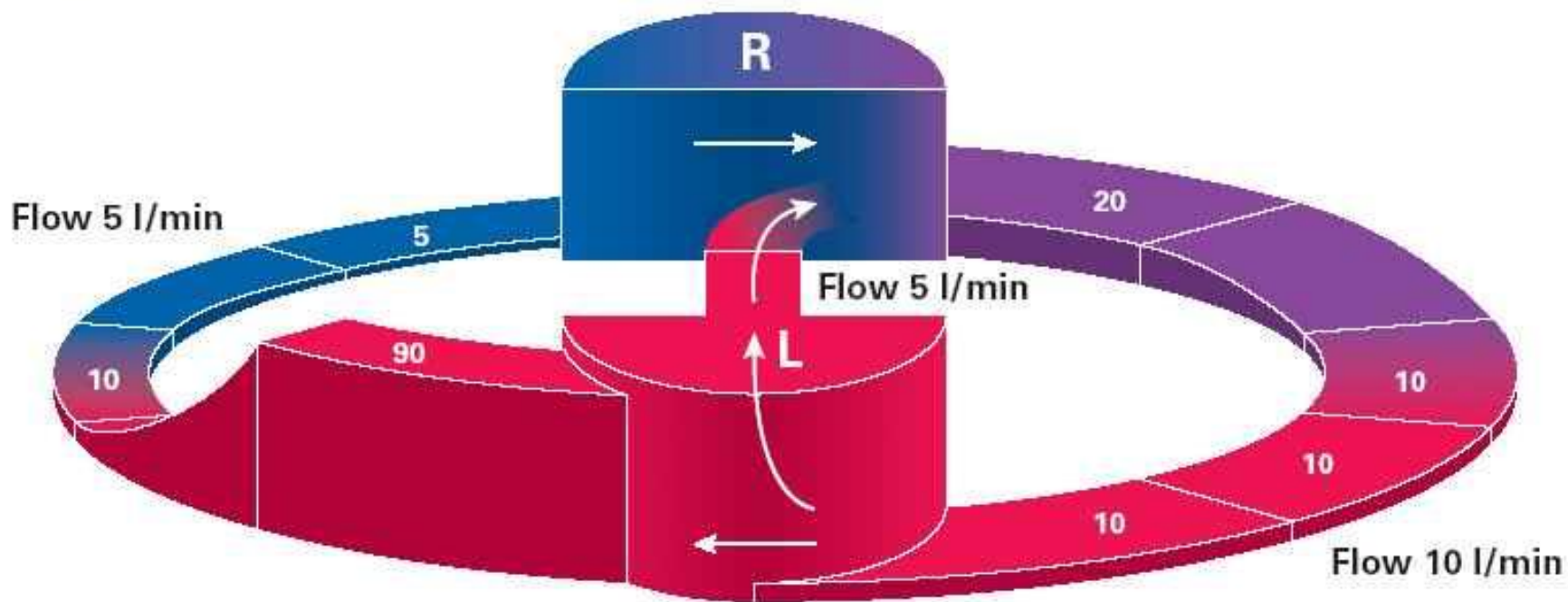


Flow 5 l/min



$$PVR = \frac{\text{mmHg}}{\text{l/min}} = \text{Wood unit(s)}$$

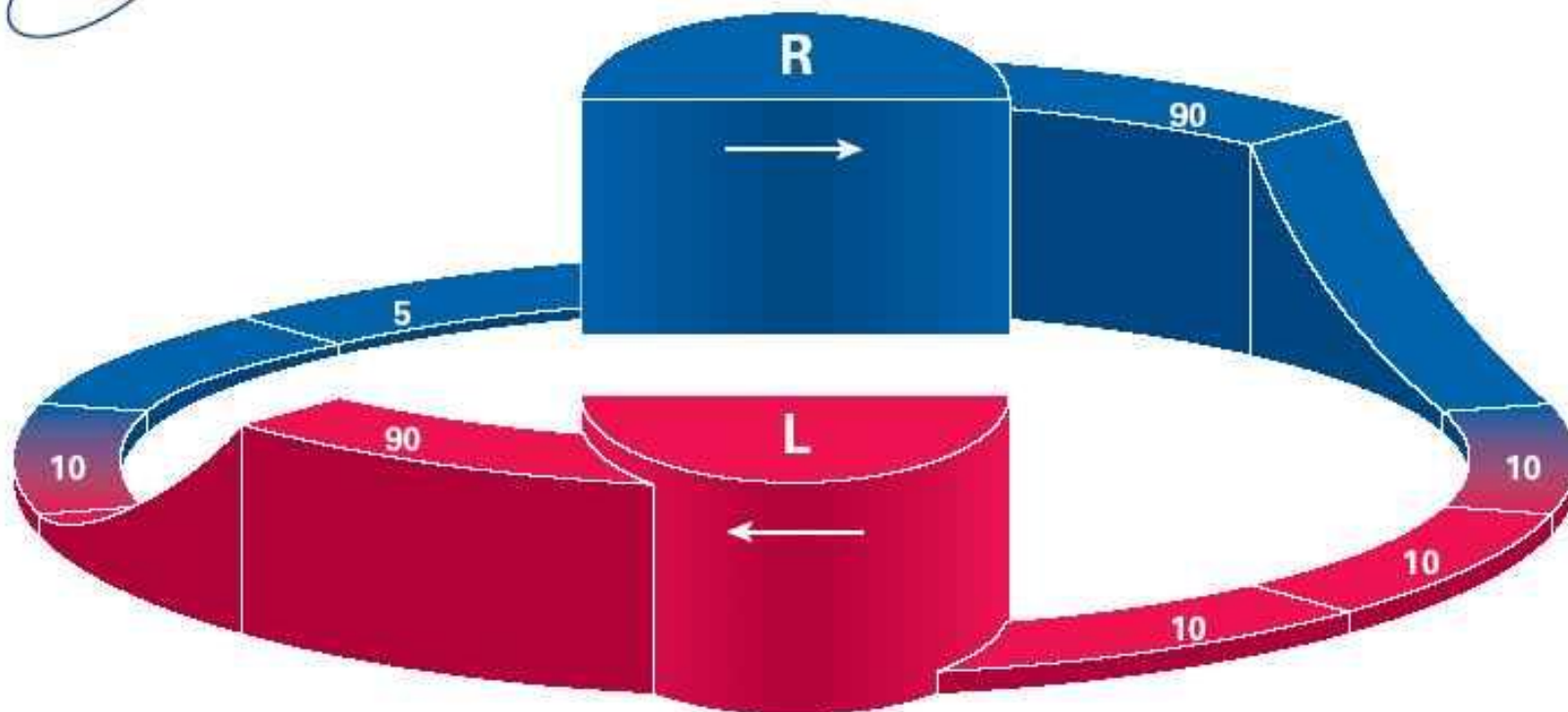




$$PVR = \frac{\text{---} - \text{---} \text{ mmHg}}{\text{---} \text{ l/min}} = \text{---} = \text{---} \text{ Wood unit(s)}$$



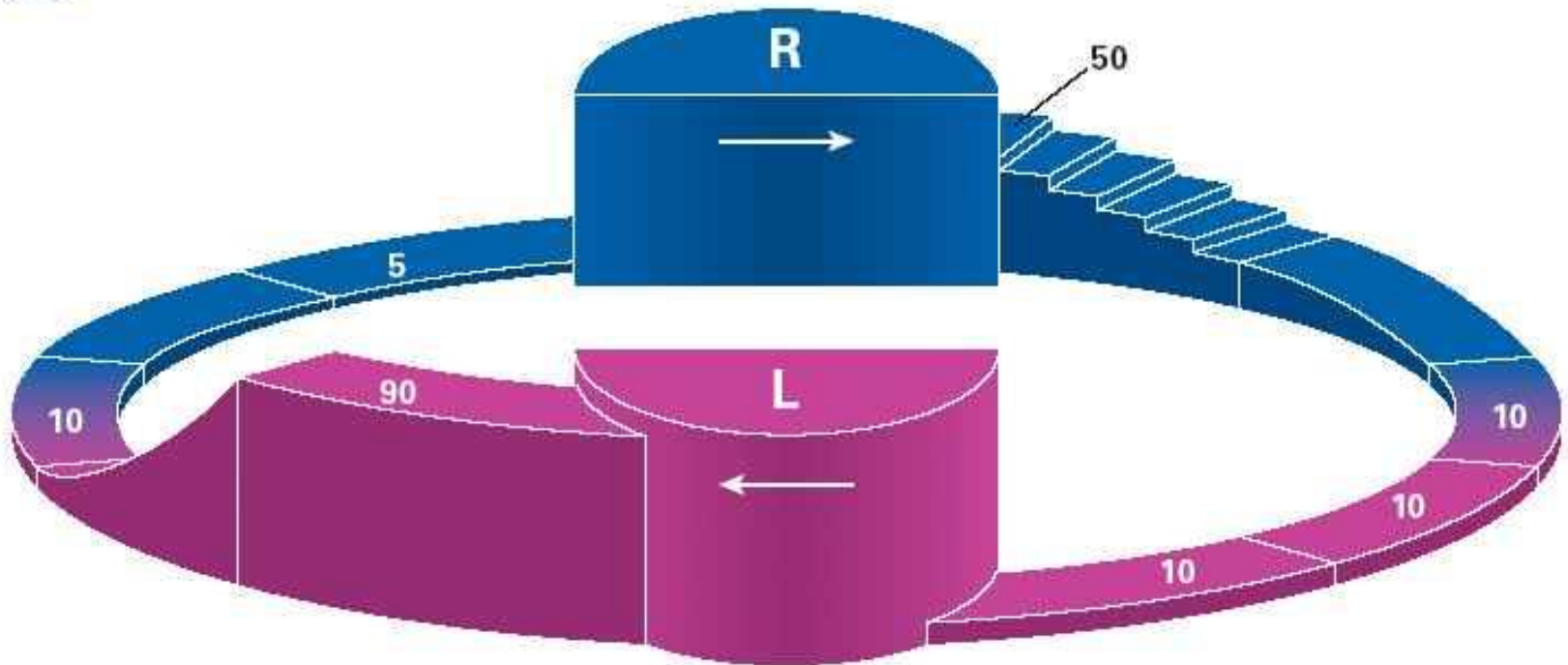
Flow 5 l/min



$$PVR = \frac{\text{.....} - \text{.....} \text{ mmHg}}{\text{.....} \text{ l/min}} = \text{.....} = \text{.....} \text{ Wood unit(s)}$$



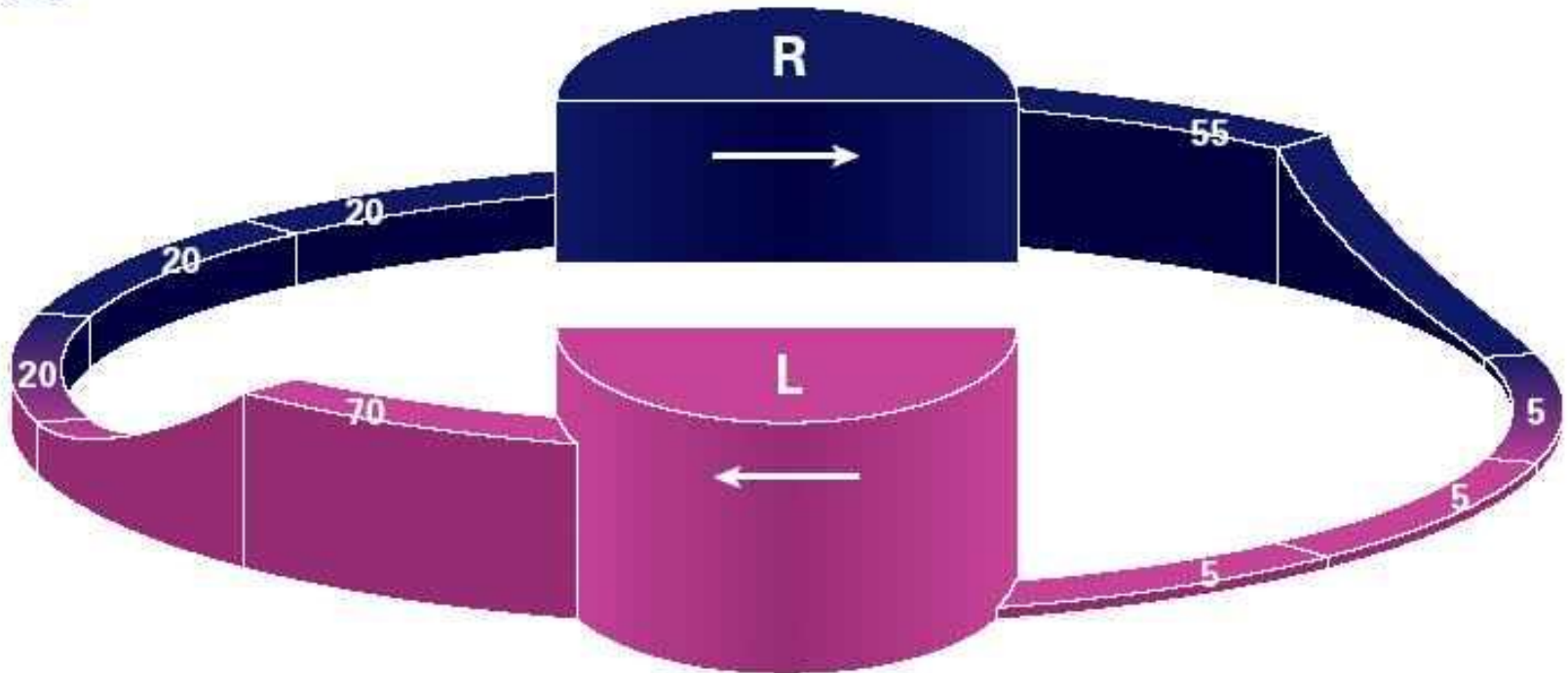
Flow 5 l/min



$$PVR = \frac{\text{mmHg}}{\text{l/min}} = \text{Wood unit(s)}$$

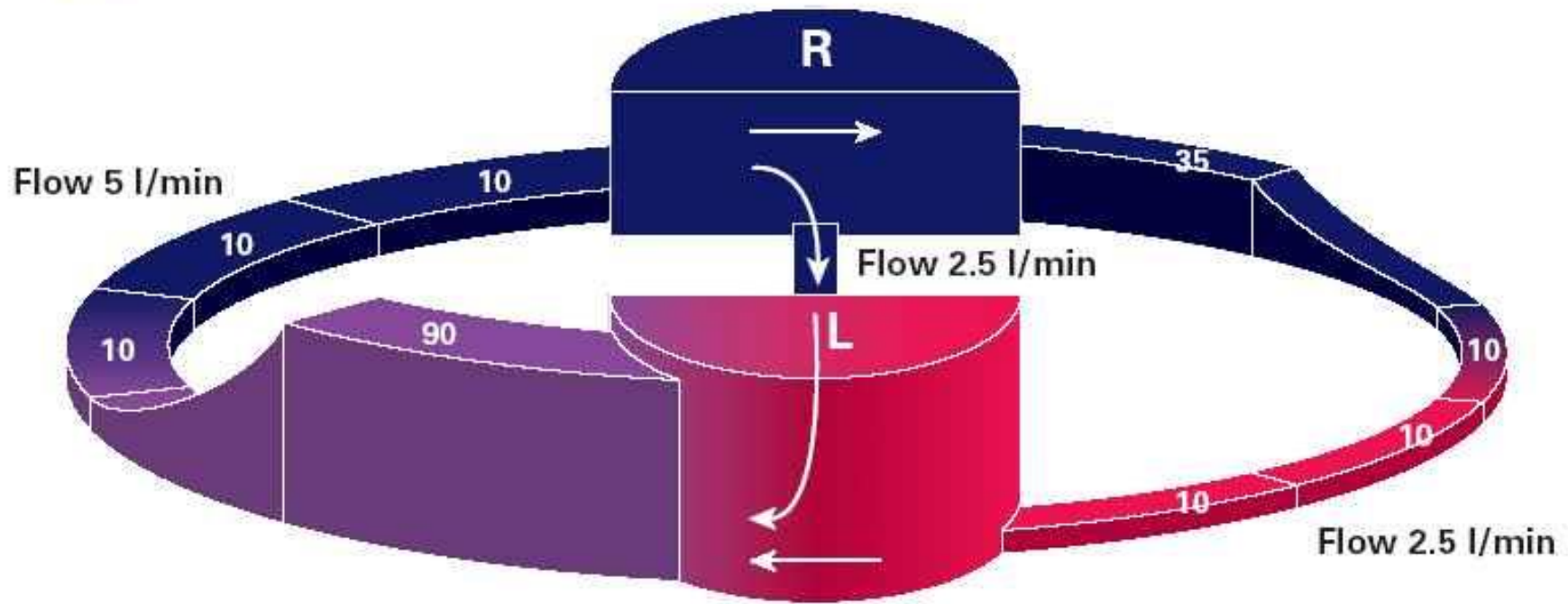


Flow 2.5 l/min



$$PVR = \frac{70 - 5 \text{ mmHg}}{2.5 \text{ l/min}} = \frac{65}{2.5} = 26 \text{ Wood unit(s)}$$





$$PVR = \frac{\text{mmHg}}{\text{l/min}} = \text{Wood unit(s)}$$





# Jämförelse

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Vilken patient är "sjukast"?

- C?
- E?
- G?

Pressure is not the target;  
flow should be the target!

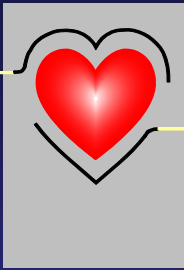
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Jay N Cohn

Editorial in JACC 2004 vol 43

No 8 1430-31.

Lunch!



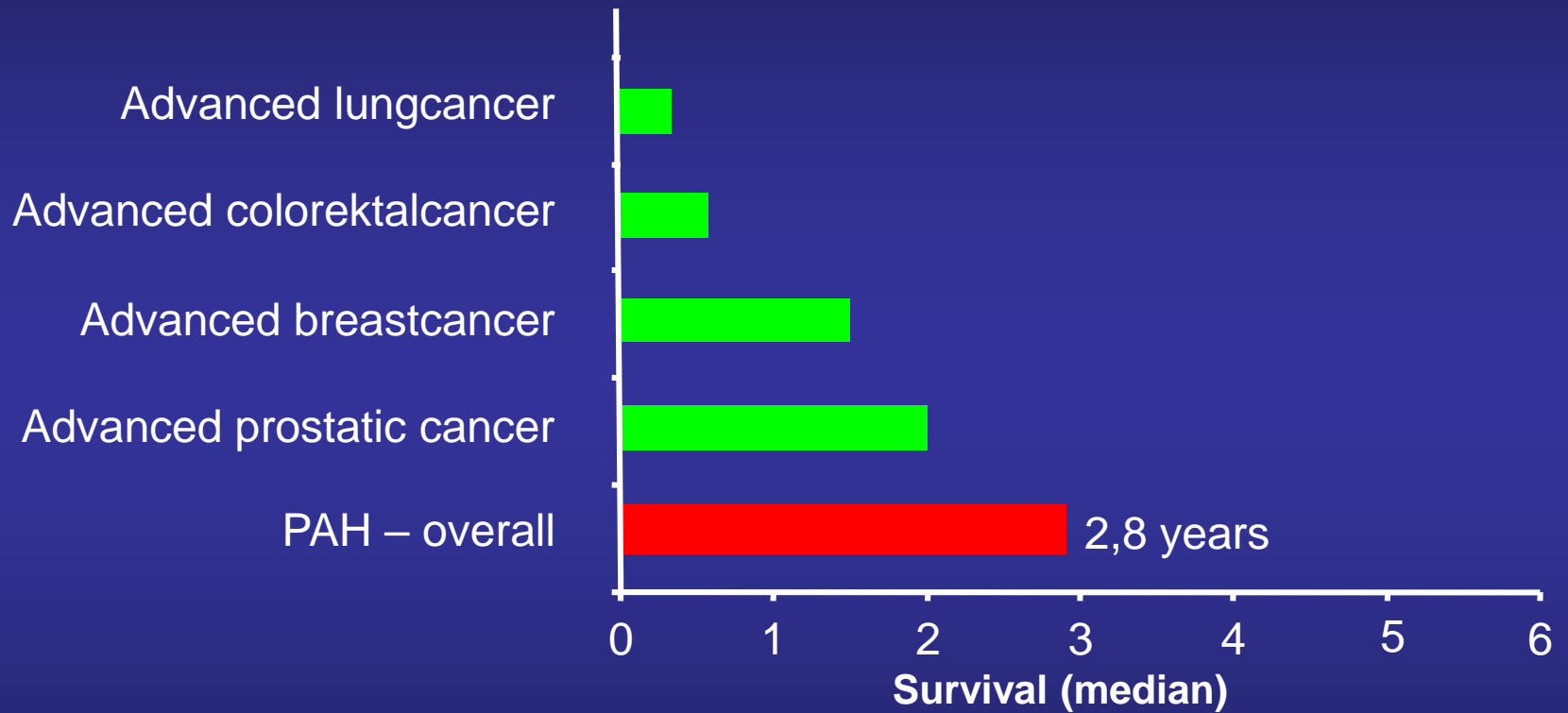
FYSIOLOGISKA KLINIKEN

Universitetssjukhuset i Linköping

# Behandling vid Pulmonell Arteriell Hypertension

# Prognosis in PAH

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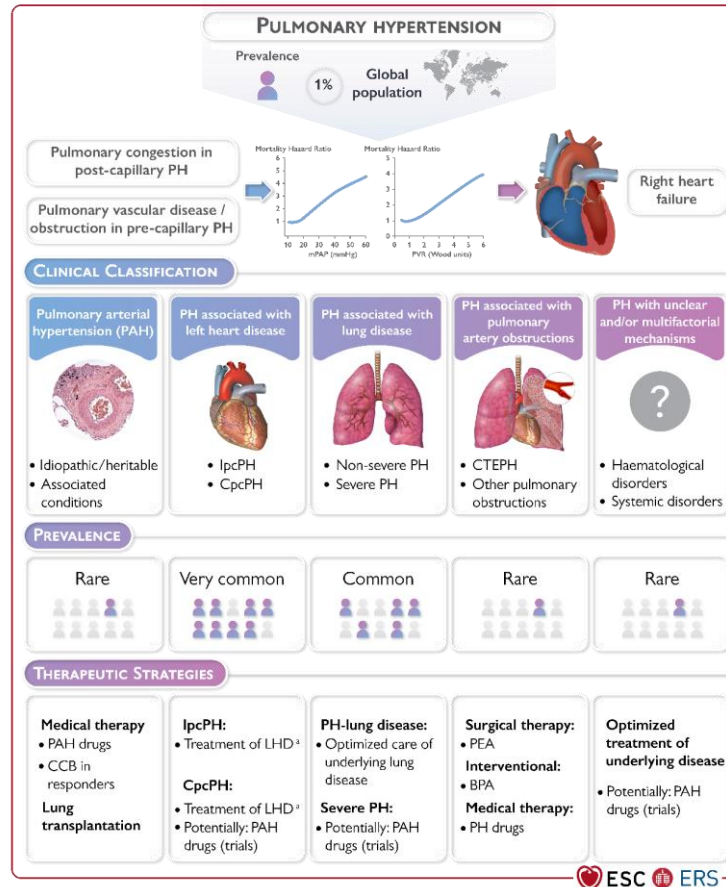
<sup>1</sup> D'Alonzo et al, *Ann Internal Med* 1991; 115; 5: 343-9

<sup>2</sup> Kato et al, *Cancer* 2001; 92: 8: 2211-2219

# Risk-stratifying vid PAH

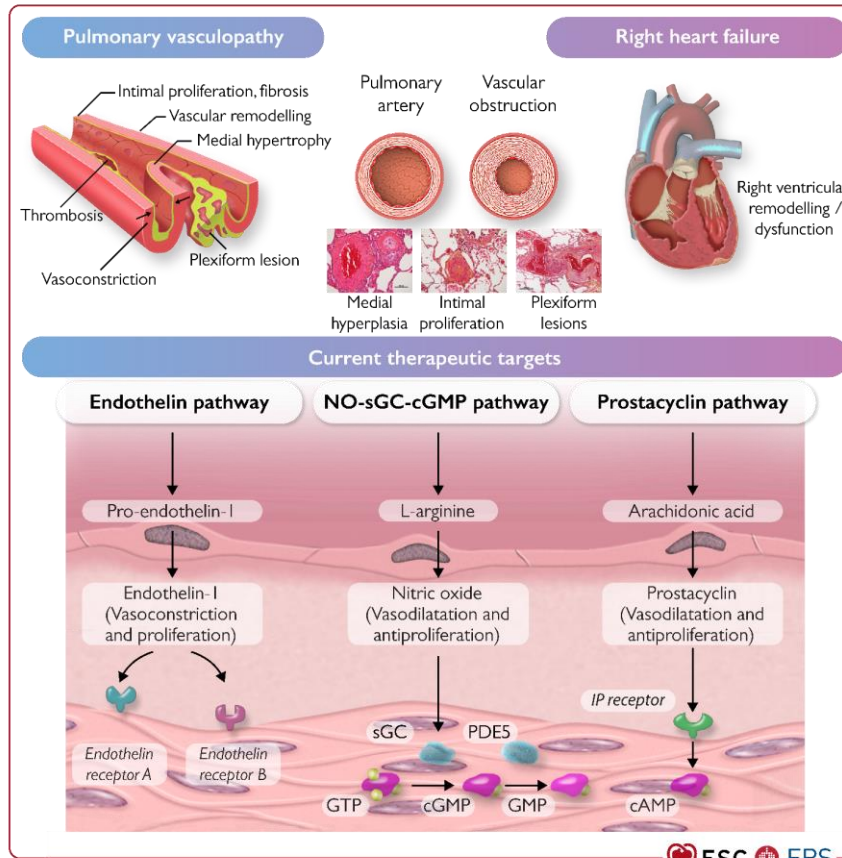
Determinants of prognosis <sup>a</sup> (estimated 1-year mortality)	Low risk <5%	Intermediate risk 5–10%	High risk >10%
Clinical signs of right heart failure	Absent	Absent	Present
Progression of symptoms	No	Slow	Rapid
Syncope	No	Occasional syncope <sup>b</sup>	Repeated syncope <sup>c</sup>
WHO functional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

**Figure 1**  
**Central illustration**



**Figure 7**

**Pathophysiology and current therapeutic targets of pulmonary arterial hypertension (group 1)**



©ESC/ERS



# Clinical classification of pulmonary hypertension (1)

## GROUP 1 Pulmonary arterial hypertension (PAH)

### 1.1 Idiopathic

1.1.1 Non-responders at vasoreactivity testing

1.1.2 Acute responders at vasoreactivity testing

### 1.2 Heritable

### 1.3 Associated with drugs and toxins

### 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

1.4.5 Schistosomiasis

### 1.5 PAH with features of venous/capillary (PVOD/PCH) involvement

### 1.6 Persistent PH of the newborn

# Stödjande behandling vid PAH

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- Antikoagulation (?)
- Syrgas
- Diuretika, MRA
- Fysisk träning

# Specifik farmakologisk behandling av PAH (1)

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## Responders (positivt vasoreaktivitetstest)

- Calciumflödeshämmare (CCB)
  - nifedipine (Adalat®)
  - diltiazem
  - amlodipin, felodipin

# Specifik farmakologisk behandling av PAH (2)

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- Endothelin receptor antagonist (ERA)
  - bosentan, ambrisentan, macicentan
- Fosfodiesteras-5 hämmare (PDEI)
  - sildenafil, tadalafil
- Adenylatcyklas-stimulering (sGCS)
  - riociguat
- Prostacyclin analoger
  - epoprostenol, ilomedin, treprostenil
  - selexipag (Uptravi®)

## Clinical classification of pulmonary hypertension (2)

### **GROUP 2 PH associated with left heart disease**

#### 2.1 Heart failure:

2.1.1 with preserved ejection fraction

2.1.2 with reduced or mildly reduced ejection fraction

#### 2.2 Valvular heart disease

#### 2.3 Congenital/acquired cardiovascular conditions leading to post-capillary PH

### **GROUP 3 PH associated with lung diseases and/or hypoxia**

3.1 Obstructive lung disease or emphysema

3.2 Restrictive lung disease

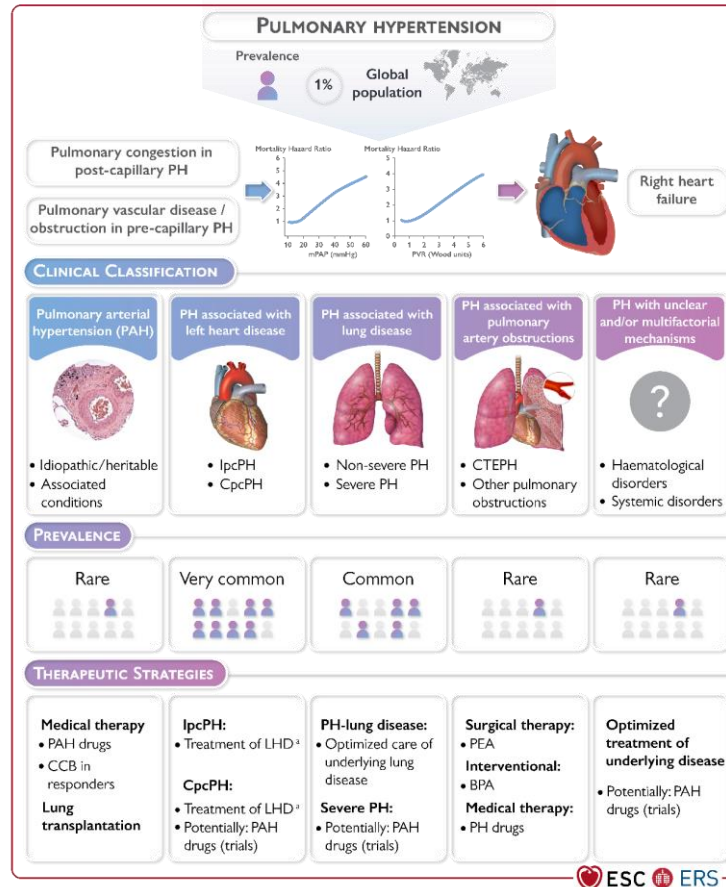
3.3 Lung disease with mixed restrictive/obstructive pattern

3.4 Hypoventilation syndromes

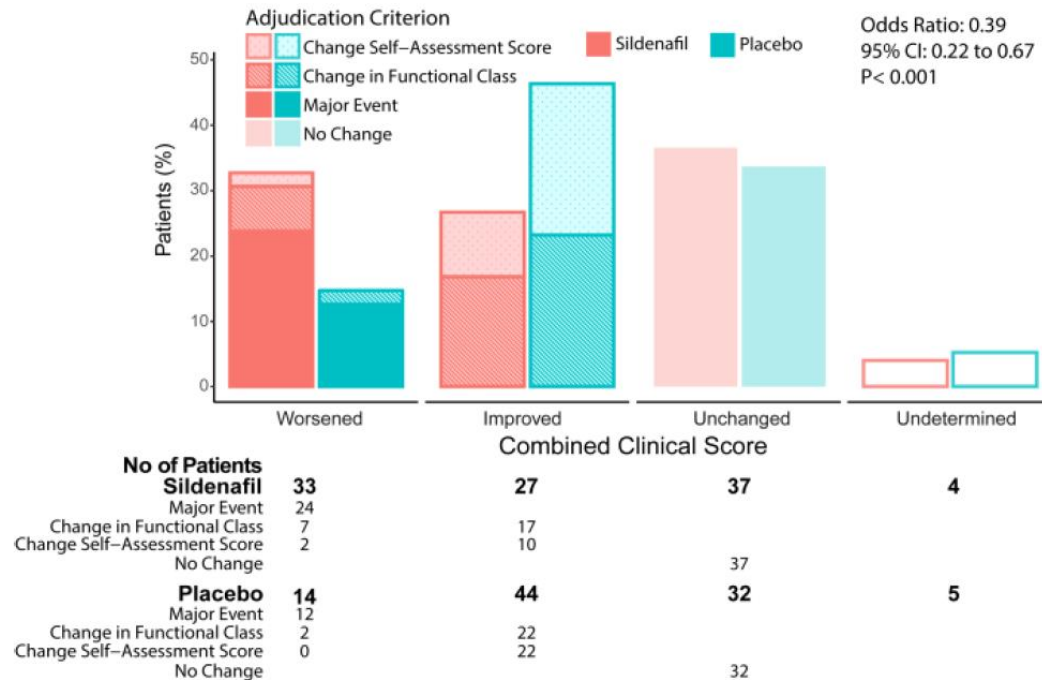
3.5 Hypoxia without lung disease (e.g. high altitude)

3.6 Developmental lung disorders

**Figure 1**  
**Central illustration**



# Primary Endpoint



## Sildenafil should be avoided in valve disease with residual pulmonary hypertension (SIOVAC)

28 Aug 2017

**Barcelona, Spain - 28 Aug 2017:** Sildenafil should not be used to treat residual hypertension in patients with valvular heart disease, according to late-breaking results from the SIOVAC trial presented today in a Hot Line LBCT Session at ESC Congress. (1) The off-label use of the drug led to worse clinical outcomes including a doubled risk of hospitalisation compared to placebo.

"Valvular disease is considered the next cardiac epidemic because of its strong association with age and the

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## ÖVERSIKT

# Pulmonell hypertension vanligt vid kronisk lungsjukdom

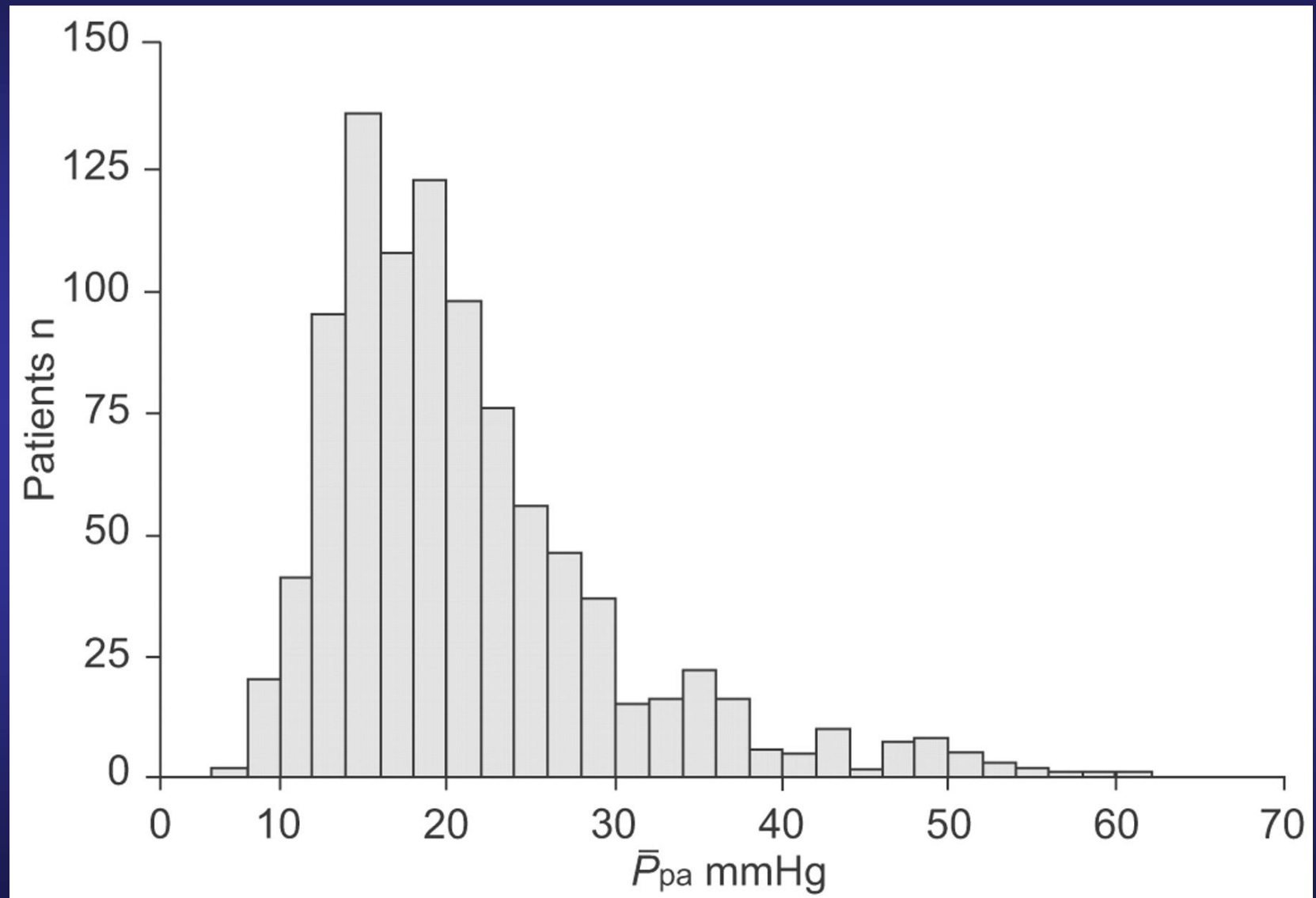
## Europeiska riktlinjer kring utredning och behandling

David Kylhammar, med dr, ST-läkare, fysiologiska kliniken, Universitetssjukhuset, Linköping

[david.kylhammar@regionostergotland.se](mailto:david.kylhammar@regionostergotland.se)

Göran Rådegran, docent, överläkare, ordförande i Svensk förening för pulmonell hypertension; båda sektionen för hjärtsvikt- och klaffsjukdomar, VO hjärt- och lungmedicin, Skånes universitetssjukhus; avdelningen för kardiologi, institutionen för kliniska vetenskaper Lund, Lunds universitet, Lund

# PA-medel vid COPD



# Huvudbudskap

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- Samsjuklighet förekommer, men ...

Behandling med läkemedel specifika för pulmonell hypertension rekommenderas inte vid pulmonell hypertension sekundär till lungsjukdom. Lungsjukdomen ska behandlas optimalt inklusive långtidsbehandling med syrgas vid kronisk hypoxemi.

## Clinical classification of pulmonary hypertension (3)

### **GROUP 4 PH associated with pulmonary artery obstructions**

4.1 Chronic thrombo-embolic PH

4.2 Other pulmonary artery obstructions

### **GROUP 5 PH with unclear and/or multi-factorial mechanisms**

5.1 Haematological disorders

5.2 Systemic disorders

5.3 Metabolic disorders

5.4 Chronic renal failure with or without haemodialysis

5.5 Pulmonary tumour thrombotic microangiopathy

5.6 Fibrosing mediastinitis

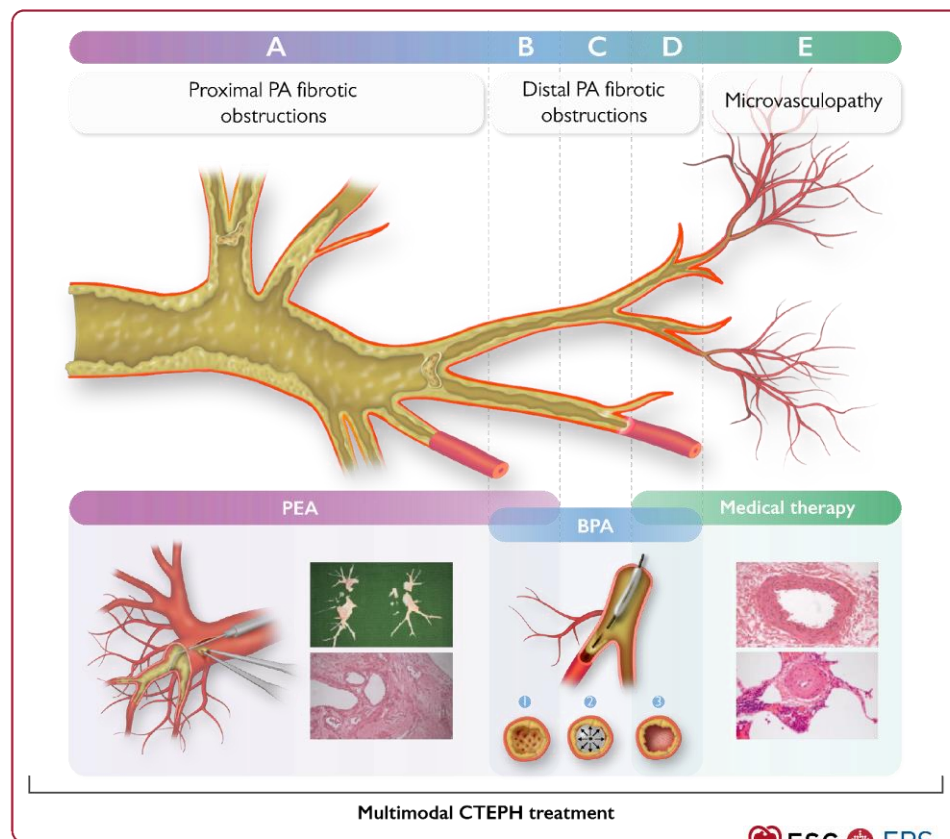
# Specifik behandling (3)

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- Vid CTEPH
  - antikoagulation (warfarin)
  - PEA
  - BPA
- Läkemedel(?)

**Figure 15**

**Overlap in treatments/multi-modality approach in chronic thrombo-embolic pulmonary hypertension**



# CTEPH-kirurgi

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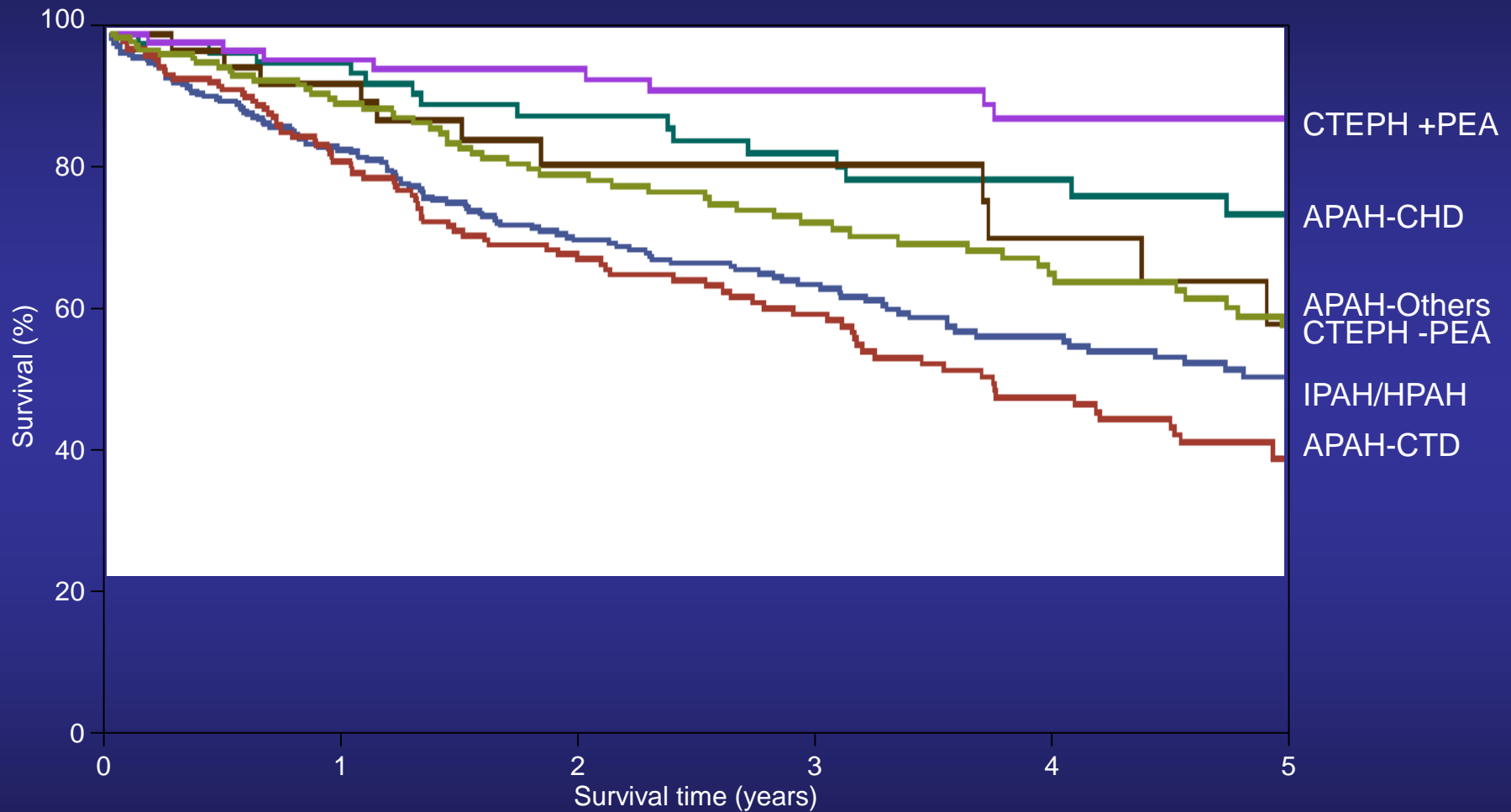
Højre



Venstre

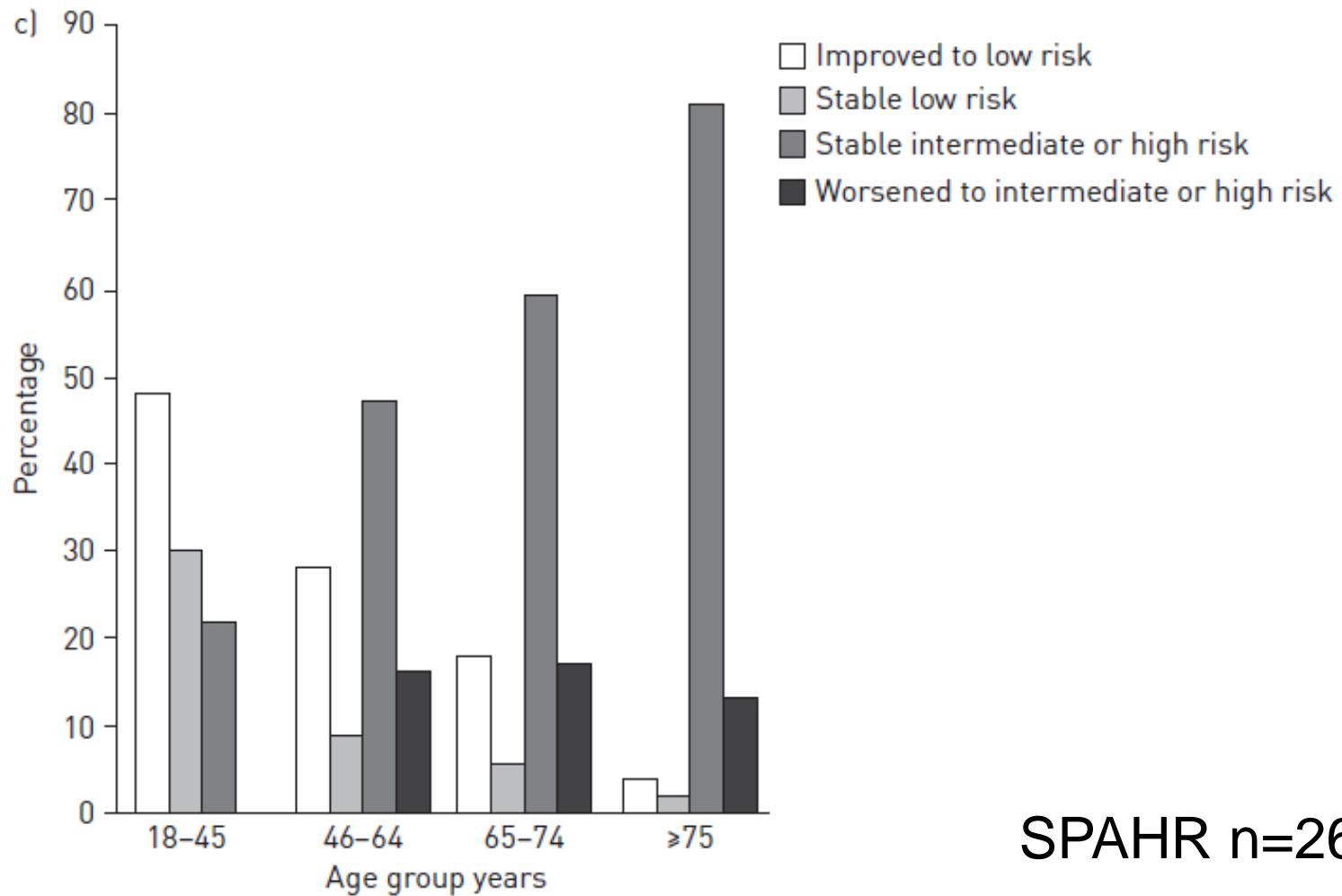


# Överlevnad (ur SPAHR)





# Behandling och ålder (comorbiditet)



Något ytterligare?

Lungtransplantation!

# Patient uppföljning

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	Baseline	6 månader
CVP (mm Hg)	7	3
PA-syst (mm Hg)	68	71
PA-medel (mm Hg)	45	41
PACW (mm Hg)	7	8
CO (l/min)	3,9	5,7
PVR (Wood)	9,7	5,8
Nt-proBNP (ng/l)	1400	660

Pressure is not the target;  
flow should be the target!

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Jay N Cohn

Editorial in JACC 2004 vol 43

No 8 1430-31.

# Falldiskussion