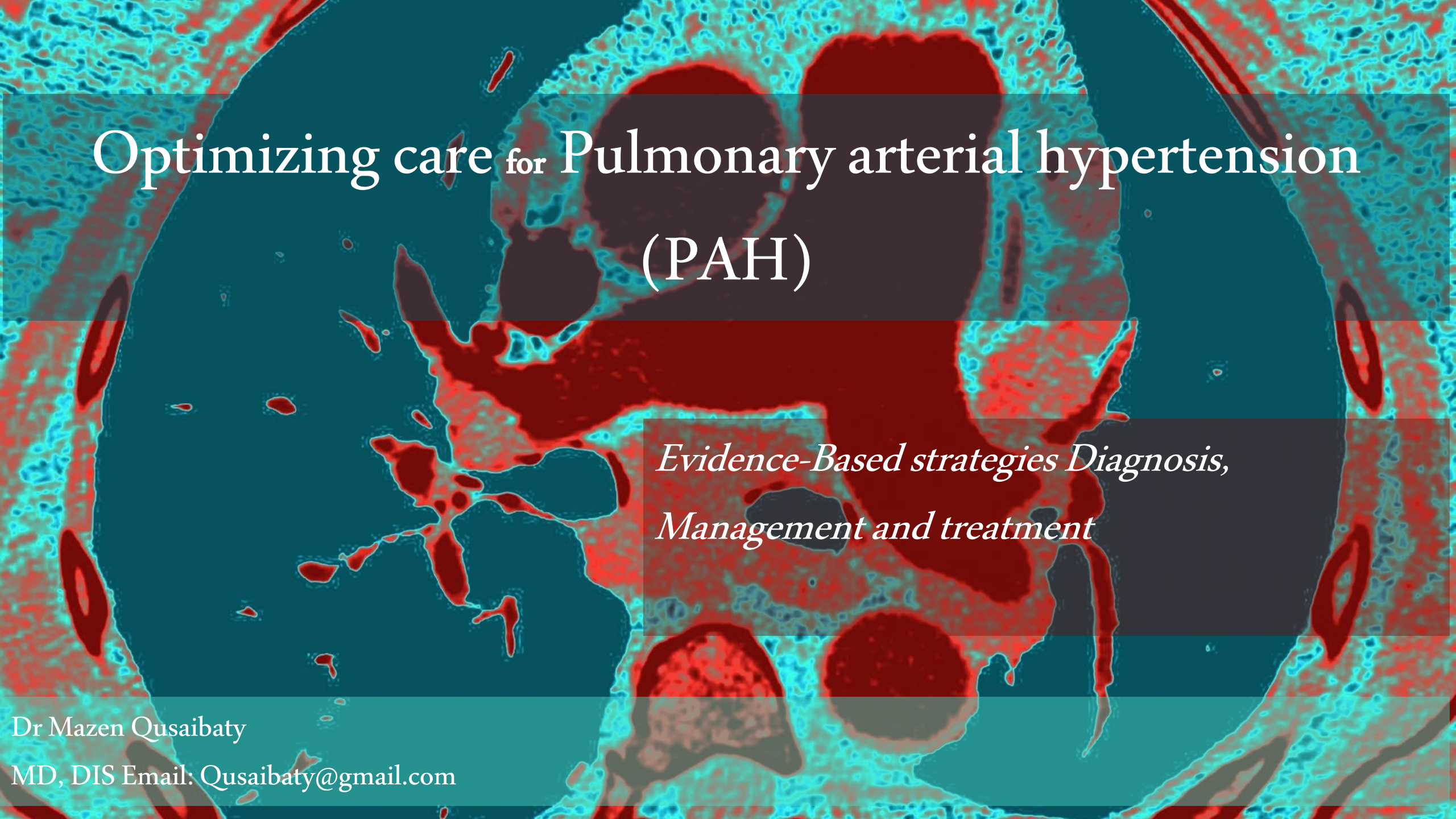


Optimizing care for Pulmonary arterial hypertension (PAH)

Evidence-Based strategies Diagnosis, Management and treatment

Dr Mazen Qusaibaty

MD, DIS Email: Qusaibaty@gmail.com

THANK YOU!

Thank You!

Thank You!

Thank You!

European Heart Journal (2022) 43, 3618–3731

ESC European Society of Cardiology

European Heart Journal (2022) 43, 3618–3731
https://doi.org/10.1093/eurheartj/ehac237

ESC/ERS GUIDELINES

2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension

Developed by the task force for the diagnosis and treatment of pulmonary hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS).

Endorsed by the International Society for Heart and Lung Transplantation (ISHLT) and the European Reference Network on rare respiratory diseases (ERN-LUNG).

Authors/Task Force Members: Marc Humbert (France), Gabor Kovacs (Austria), Marius M. Hoeper (Germany), Roberto Badagliacca (Italy), Rolf M.F. Berger (Netherlands), Margarita Brida (Croatia), Jørn Carlsen (Denmark), Andrew J.S. Coats (United Kingdom), Pilar Escribano-Subias (Spain), Pisana Ferrari (Italy), Diogenes S. Ferreira (Brazil), Hossein Ardeschir Ghofrani (Germany), George Giannakoulas (Greece), David G. Kiely (United Kingdom), Eckhard Mayer (Germany), Gergely Meszaros (Hungary), Blin Nagavci (Germany), Karen M. Olsson (Germany), Joanna Pepke-Zaba (United Kingdom), Jennifer K. Quint (United Kingdom), Göran Rådegran (Sweden), Gerald Simonneau (France), Olivier Sitbon (France), Thomy Tonia (Switzerland), Mark Toshner (United Kingdom), Jean-Luc Vachiery (Belgium), Anton Vonk Noordegraaf (Netherlands), Marion Delcroix *† (ERS Chairperson) (Belgium), Stephan Rosenkranz *† (ESC Chairperson) (Germany), and ESC/ERS Scientific Document Group

ESC
European Society of Cardiology

ERS
EUROPEAN RESPIRATORY SOCIETY
every breath counts

European Reference Networks

European Heart Journal (2022) 43, 3618–3731
https://doi.org/10.1093/eurheartj/ehac237

ESC
European Society of Cardiology

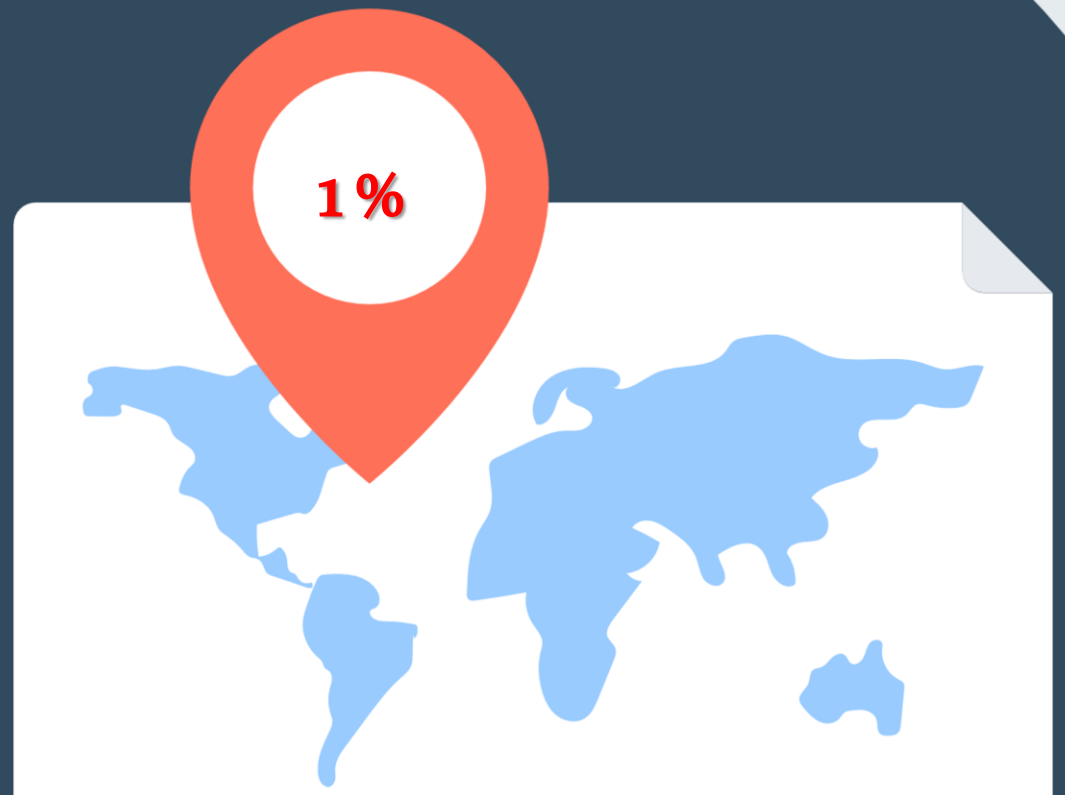
ERS
EUROPEAN RESPIRATORY SOCIETY
every breath counts

3728 pages

European Heart Journal (2022) 43, 3618–3731
https://doi.org/10.1093/eurheartj/ehac237

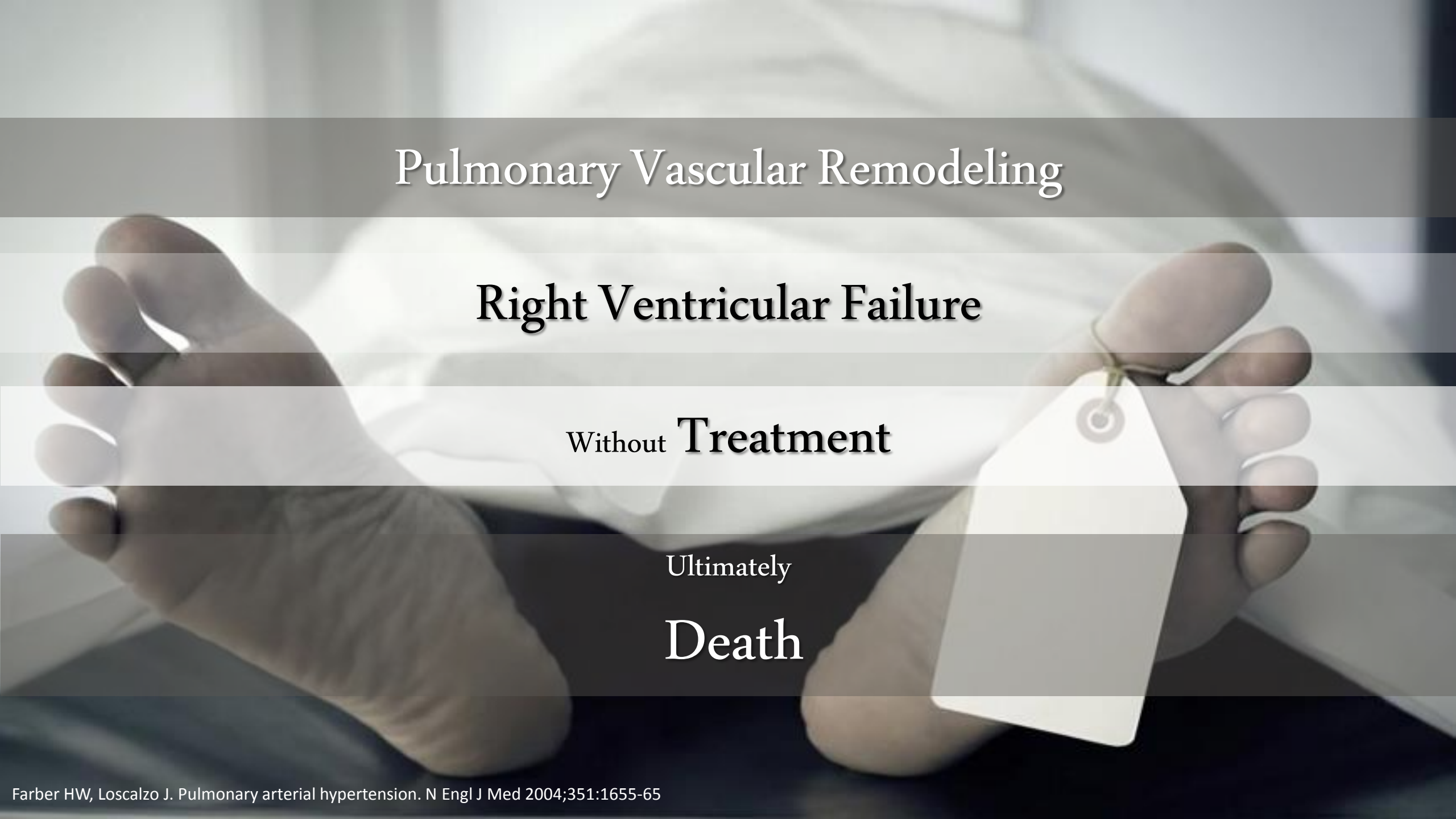
Epidemiology

Prevalence



Global population

Hoeper MM, Humbert M, Souza R, Idrees M, Kawut SM, Sliwa-Hahnle K, et al. A global view of pulmonary hypertension. Lancet Respir Med 2016; 4:306–322



Farber HW, Loscalzo J. Pulmonary arterial hypertension. N Engl J Med 2004;351:1655-65

The **Management** of **Pulmonary Hypertension**

SUCCESS

The management of Pulmonary Hypertension

1. Identify Groups

Pulmonary hypertension (Dana Point classification)

GROUP 1
PAH

- Idiopathic (IPAH)
- Heritable
- Drug- and toxin-induced
- Associated with other conditions (APAH)

Group 1'
- Pulmonary veno-occlusive disease
- Pulmonary capillary hemangiomatosis

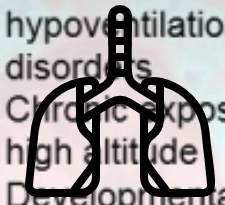
Group 1''
- Persistent pulmonary hypertension of the newborn (PPHN)

GROUP 2
Left-heart related

- Systolic dysfunction
- Diastolic dysfunction
- Valvular disease
- Congenital/acquired left heart inflow/ outflow tract obstruction and congenital cardiomyopathies
- Congenital/acquired pulmonary veins stenosis

GROUP 3
Lung/hypoxia related

- Chronic obstructive pulmonary disease (COPD)
- Interstitial lung disease (ILD)
- Other pulmonary diseases with mixed restrictive and obstructive pattern
- Sleep-disordered breathing
- Alveolar hypoventilation disorders
- Chronic exposure to high altitude
- Developmental lung diseases



GROUP 4
CTEPH and other pulmonary artery obstructions

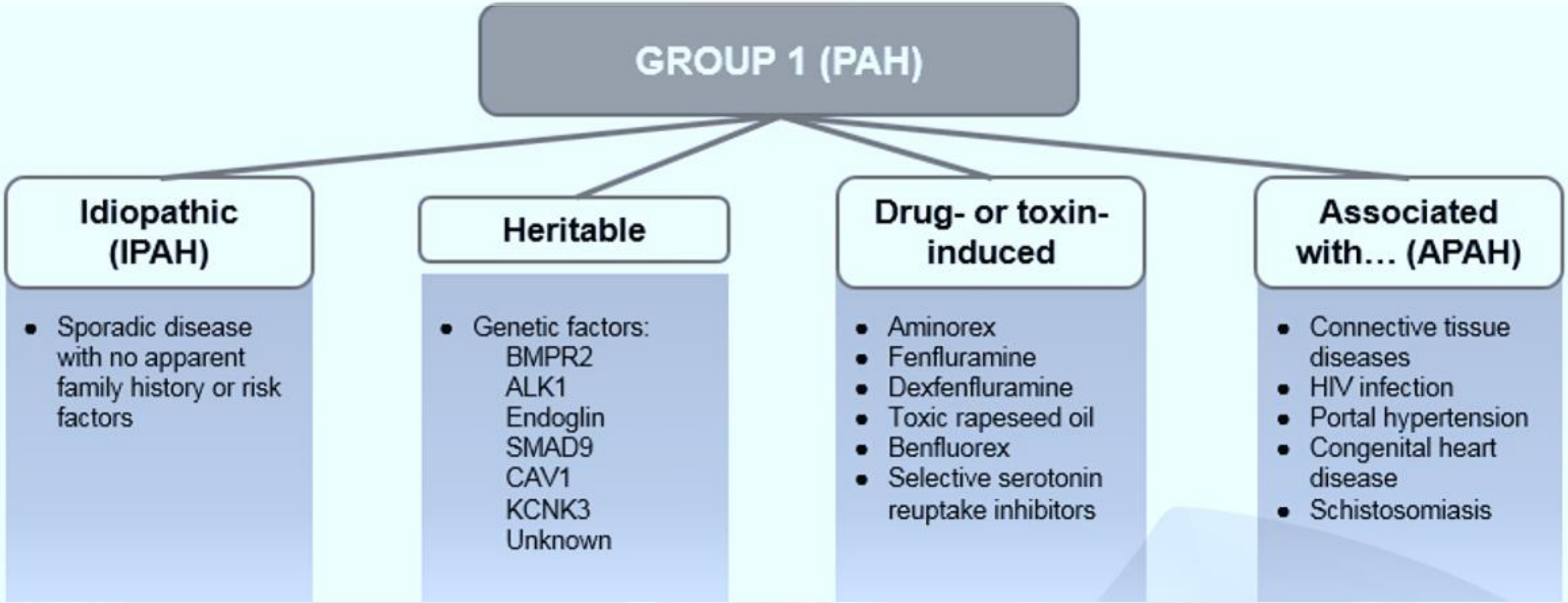
- CTEPH
- Other pulmonary artery obstructions

GROUP 5
Other

PH with unclear multifactorial mechanisms

Galiè N et al. Eur Respir J 2015;46:903–975.

PAH is a group of conditions with common symptoms and pathophysiology



ALK1, activin receptor-like kinase type 1; BMPR2, bone morphogenetic protein receptor type 2; CAV1, caveolin-1; HIV, human immunodeficiency virus; KCNK3, gene encoding potassium channel super family K member-3; SMAD9, mothers against decapentaplegic 9. Galiè N et al. Eur Respir J 2015;46:903–975.

SUCCESS

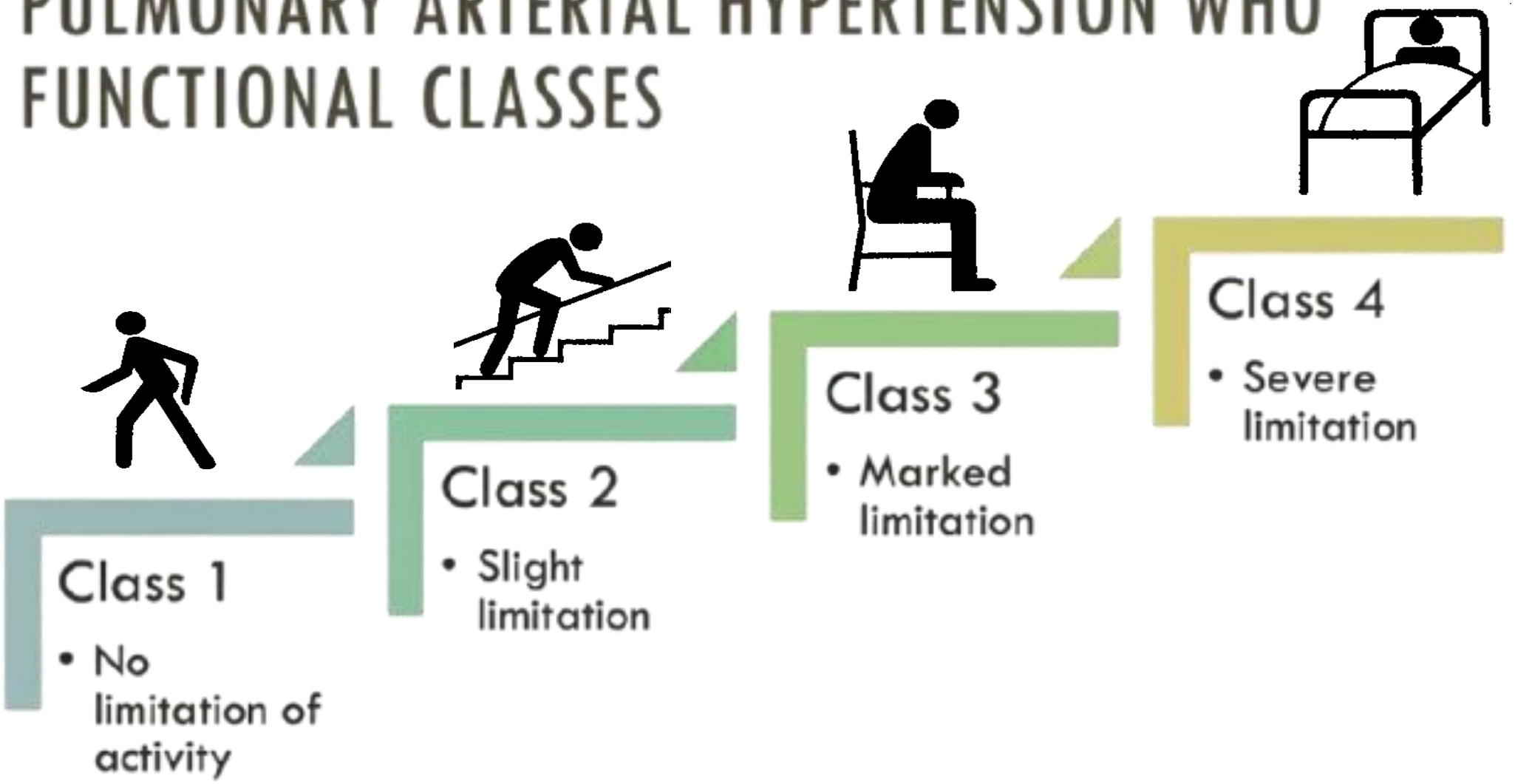
The management of Pulmonary Hypertension

1. Identify Groups
2. **Identify Functional Classes**

World Health Organization (WHO) Functional

Classification for pulmonary hypertension

PULMONARY ARTERIAL HYPERTENSION WHO FUNCTIONAL CLASSES

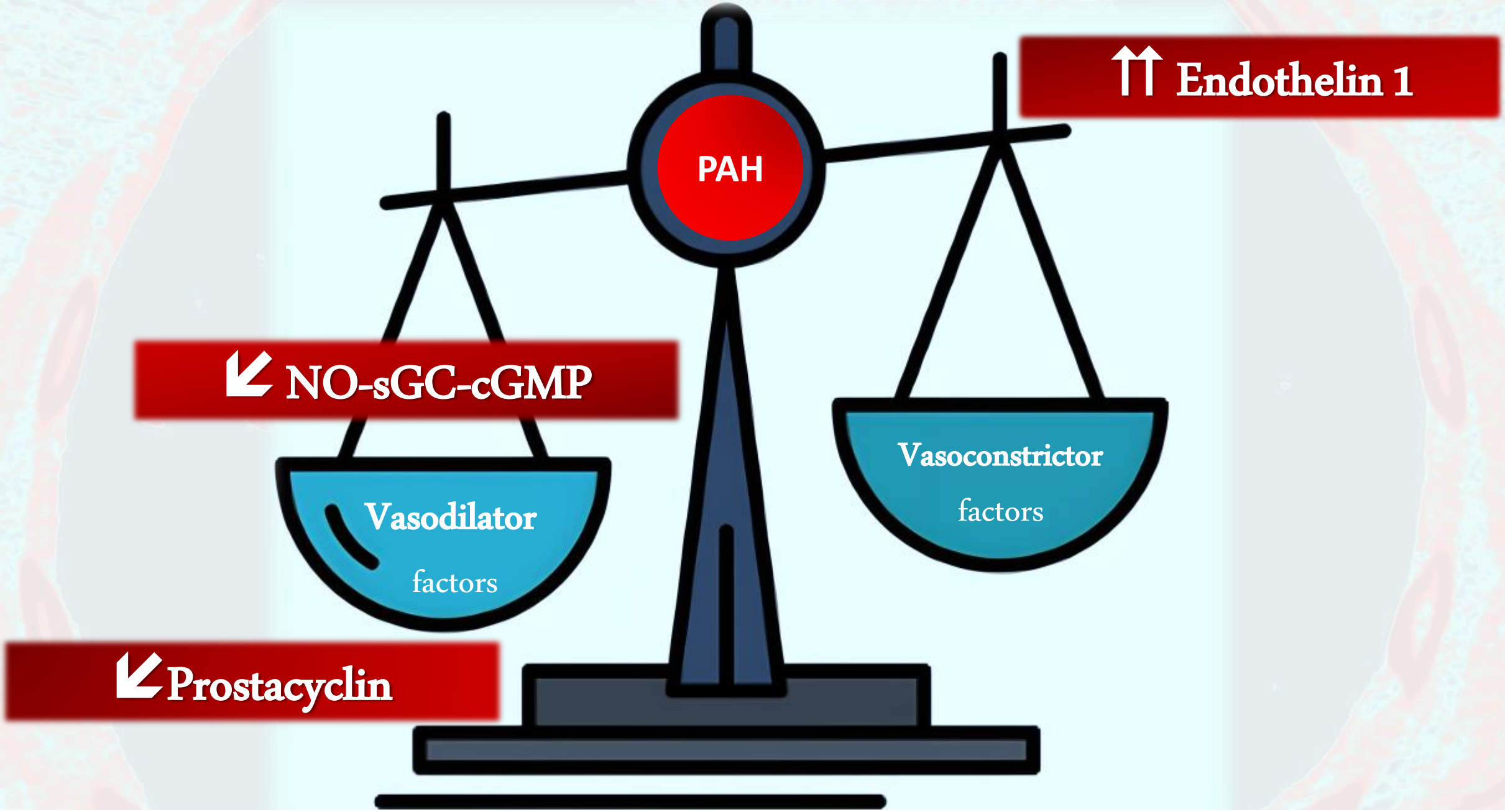


Chest. 2019 Mar;155(3):565-586. doi: 10.1016/j.chest.2018.11.030. Epub 2019 Jan 17. Erratum in: Chest. 2021 Jan;159(1):457. doi: 10.1016/j.chest.2020.11.021. PMID: 30660783.

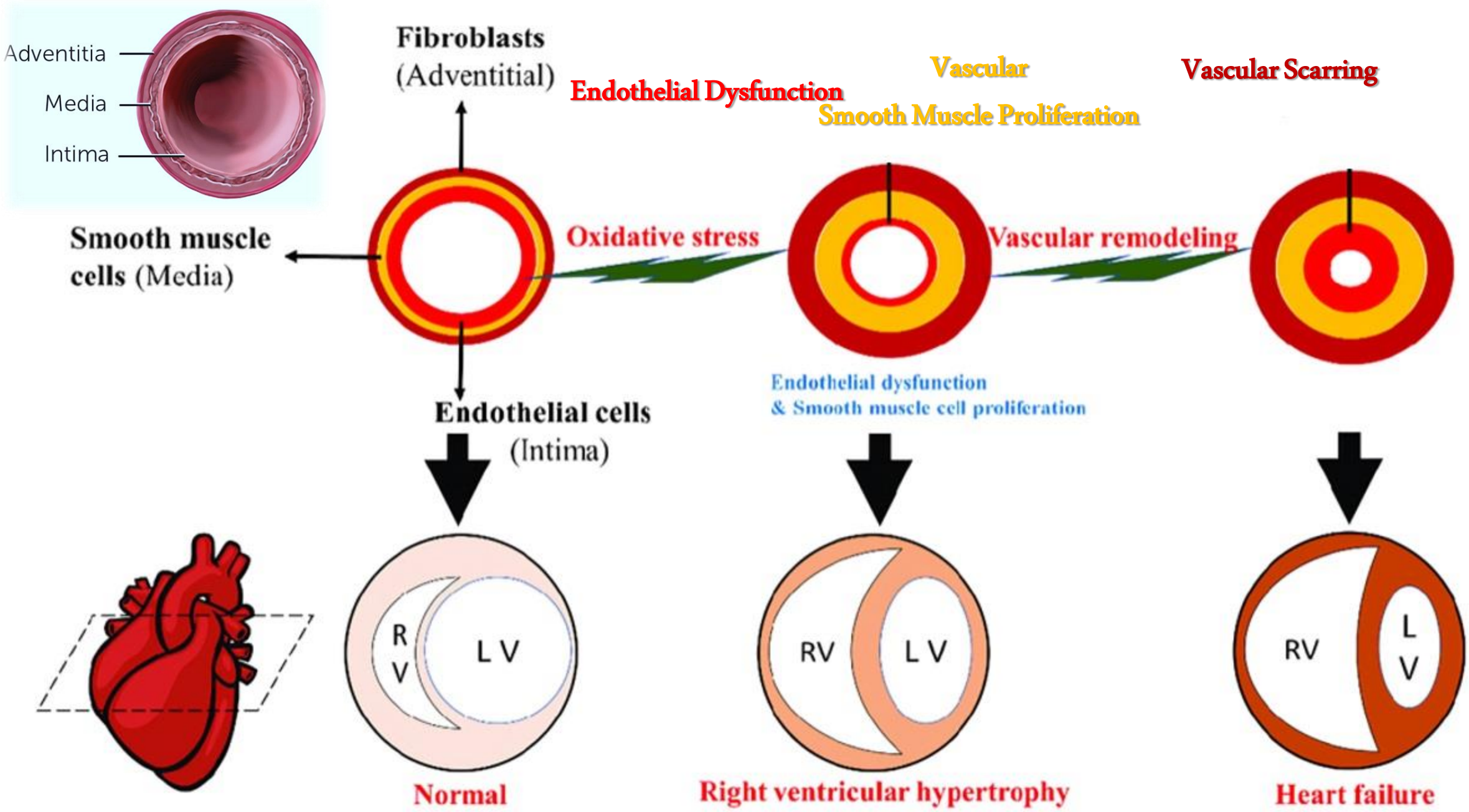
SUCCESS

The management of Pulmonary Hypertension

1. Identify Groups
2. Identify Functional Classes
3. **PAH-directed therapy**

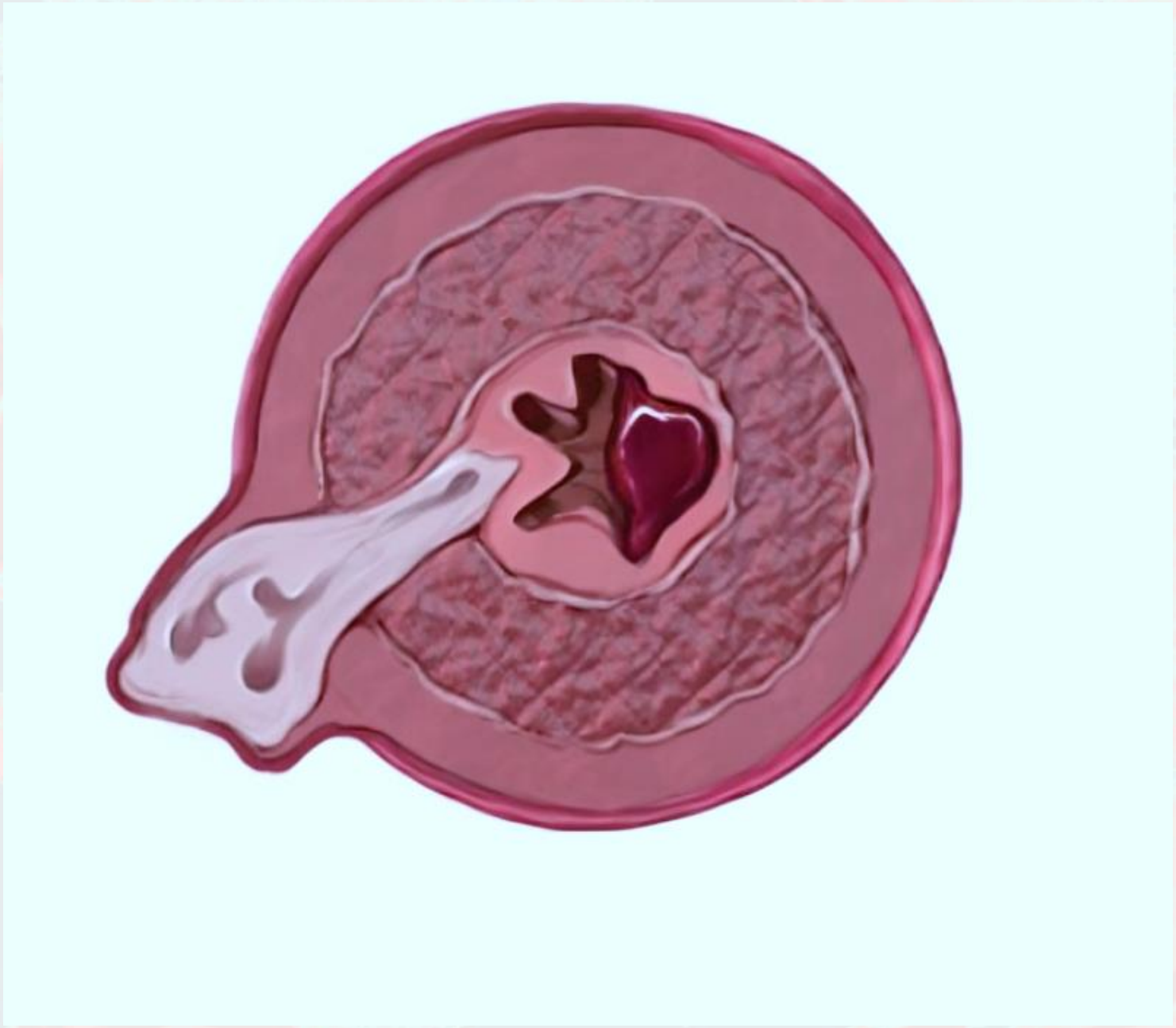


Barst RJ, Gibbs US, Ghofrani HA, et al. Updated evidence-based treatment algorithm in pulmonary arterial hypertension. J Am Coll Cardiol 2009; 54:S78.



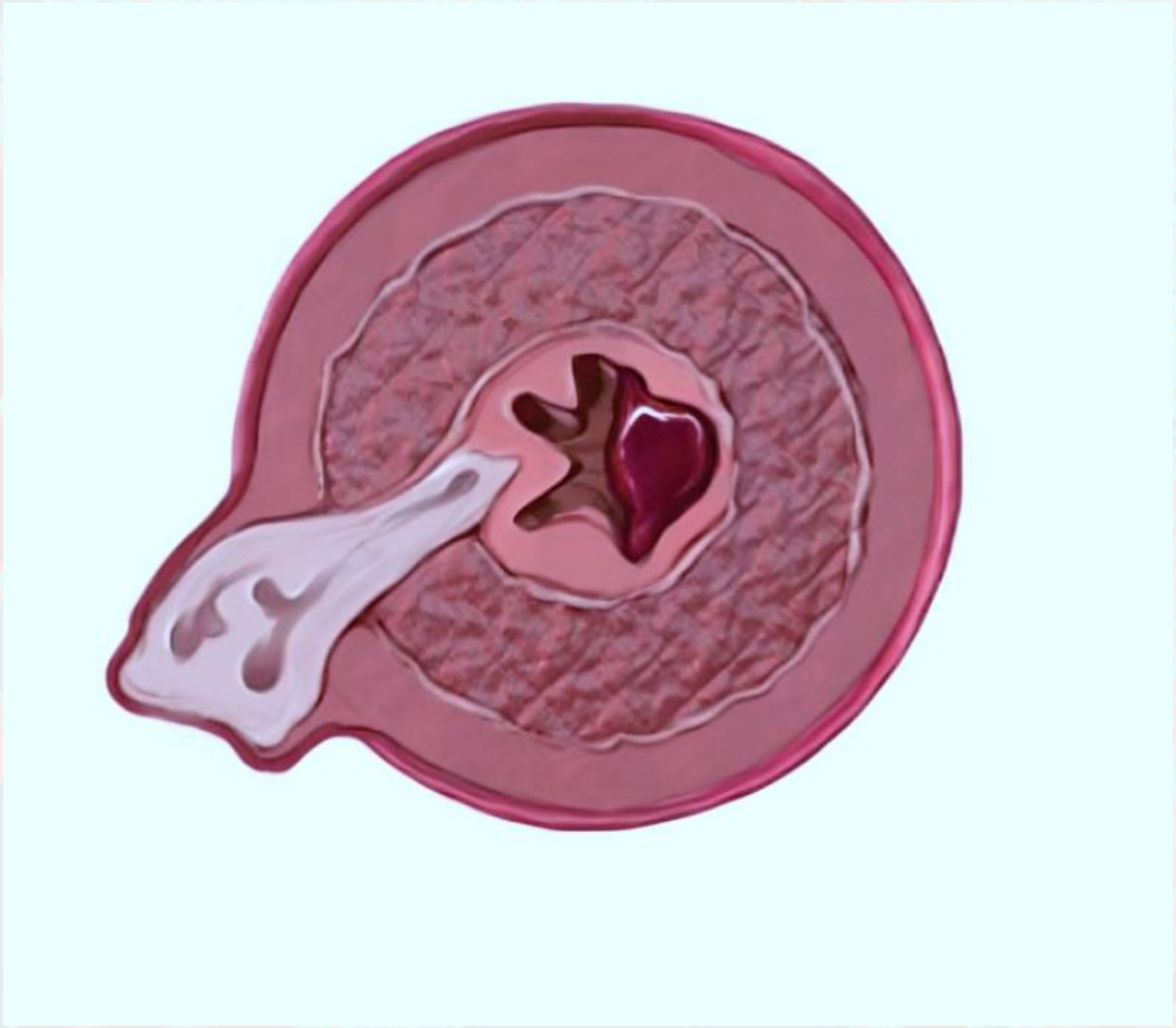
https://www.researchgate.net/figure/Schematic-progression-of-pulmonary-arterial-hypertension-Progressive-vascular-remodeling_fig1_361256722

Plexiform Lesions



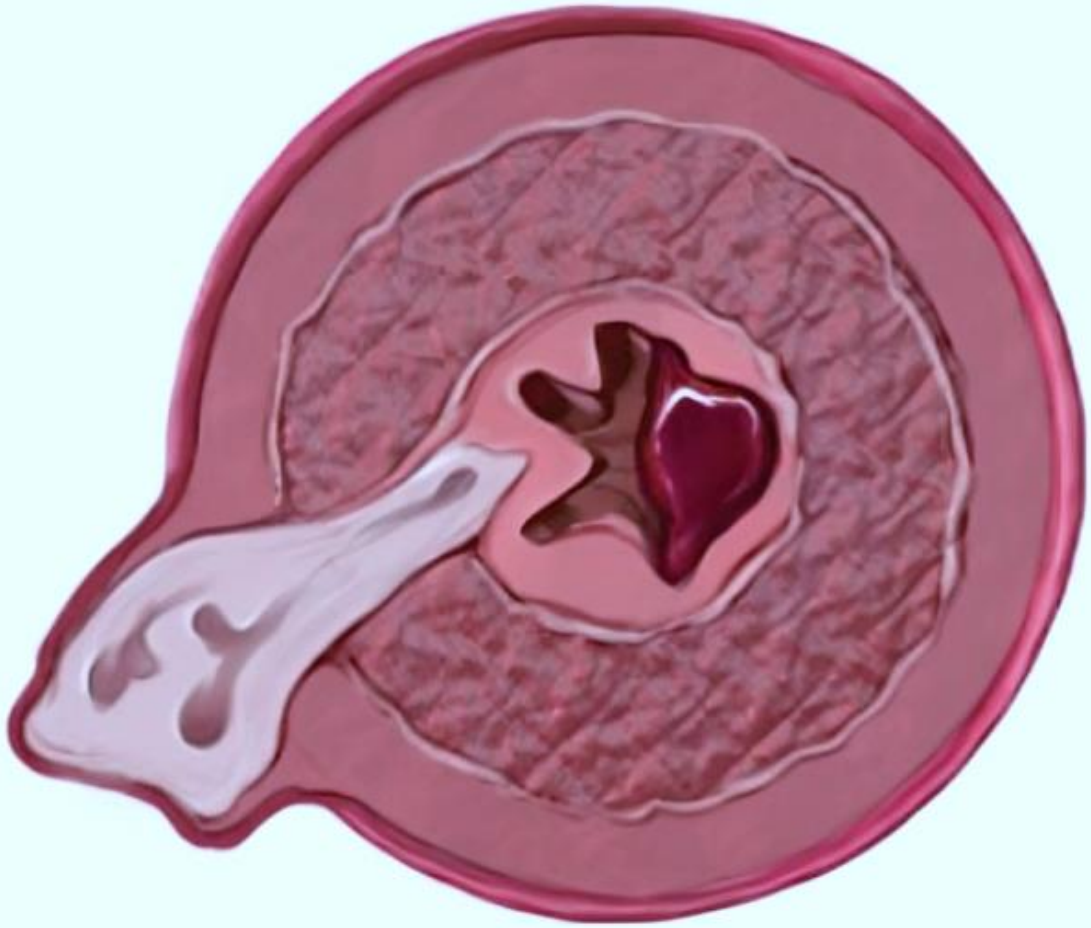
Plexiform Lesions

Thrombi form



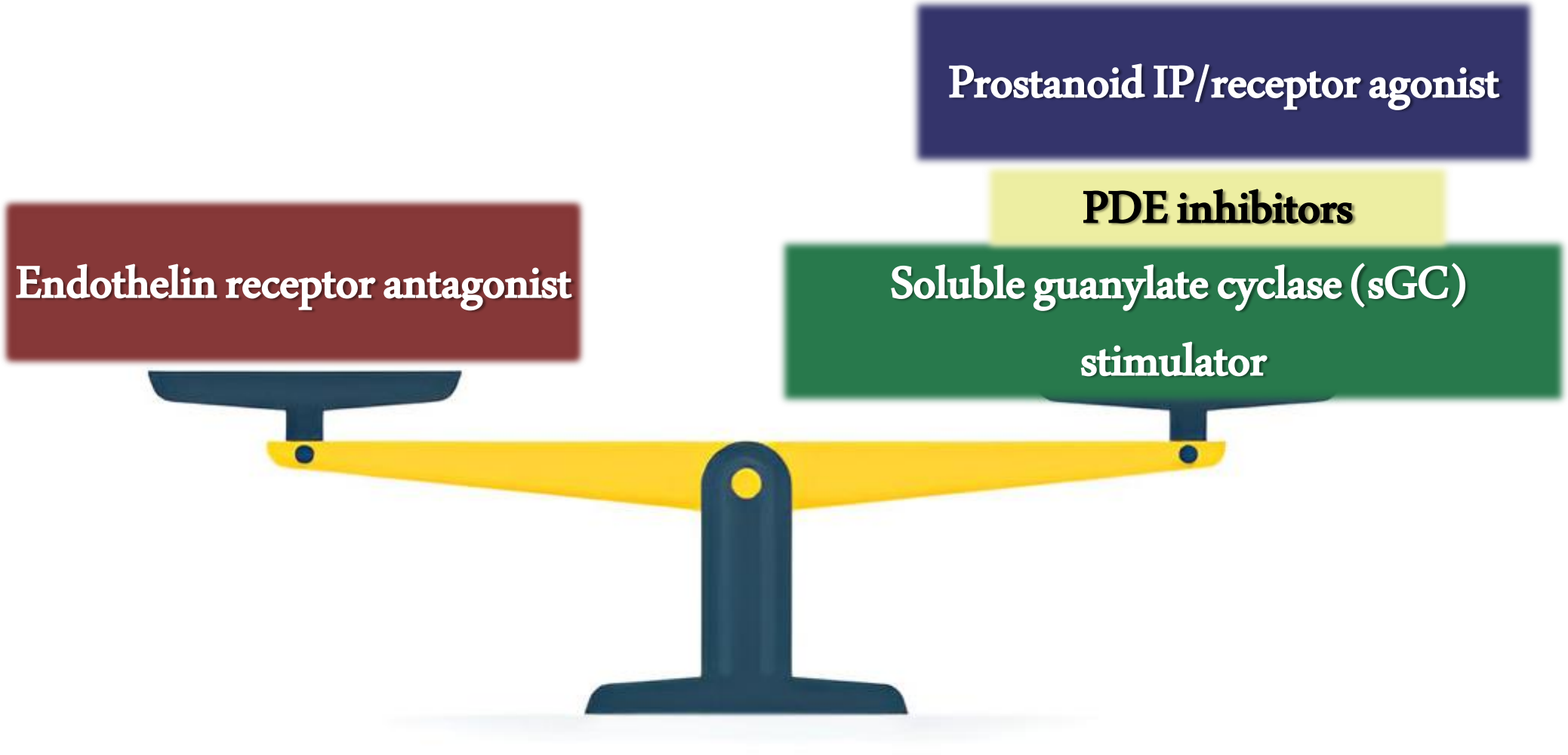
Plexiform Lesions

Thrombi form

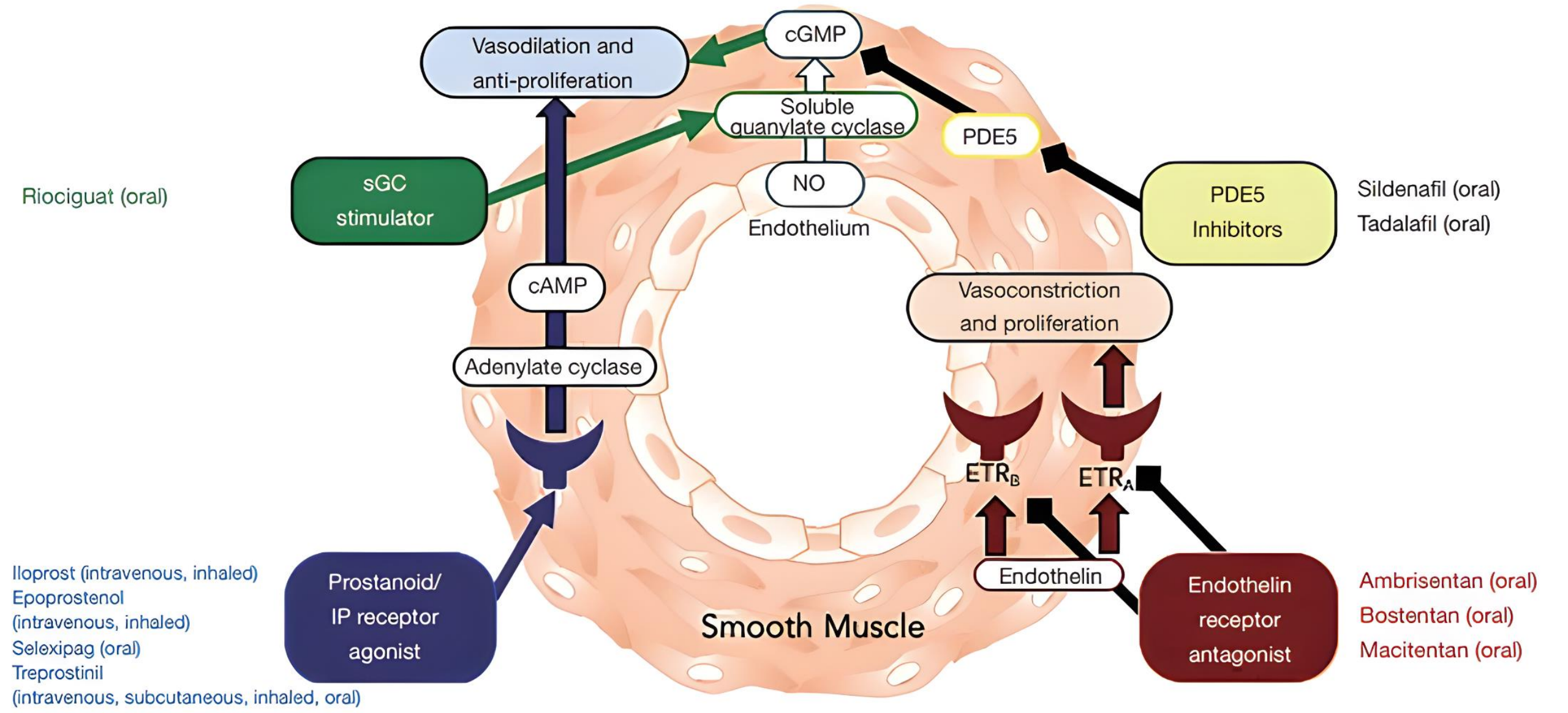


Severe PAH

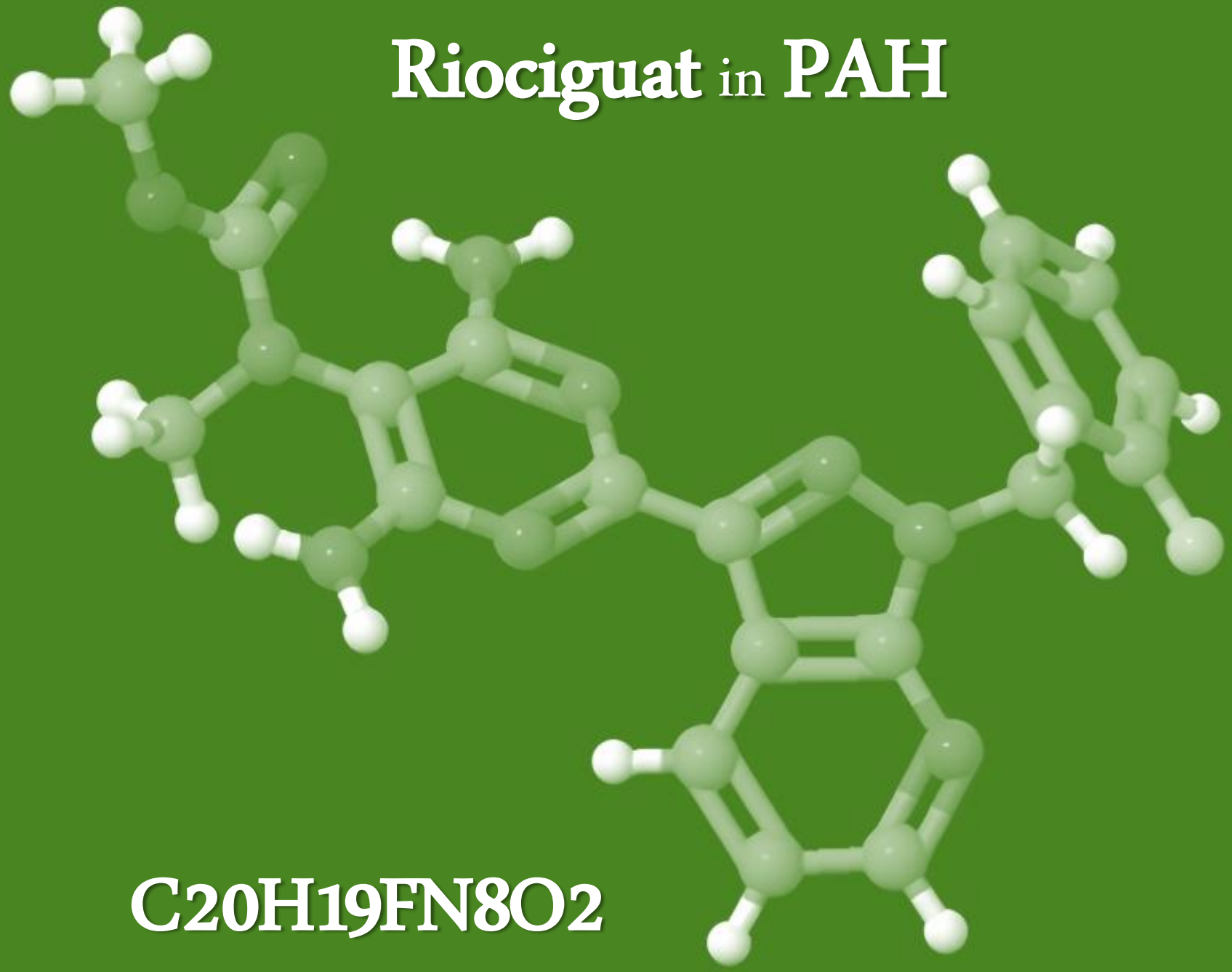
PAH-directed therapy



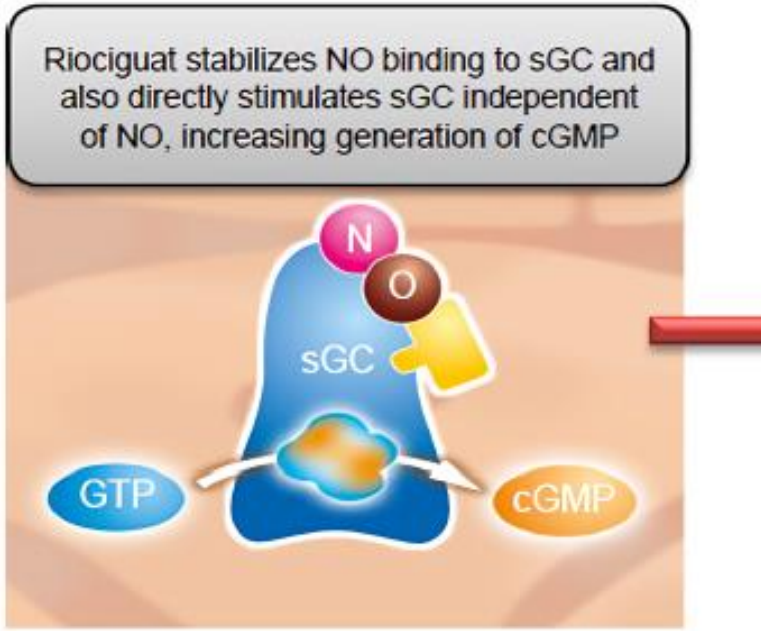
Barst RJ, Gibbs US, Ghofrani HA, et al. Updated evidence-based treatment algorithm in pulmonary arterial hypertension. J Am Coll Cardiol 2009; 54:S78.


Vasodilation and anti-proliferation
cGMP
Soluble guanylate cyclase
PDE5
NO
Endothelium
sGC stimulator
Riociguat (oral)
PDE5 Inhibitors
Sildenafil (oral)
Tadalafil (oral)
cAMP
Vasoconstriction and proliferation
Adenylate cyclase
ETR$_B$
ETR$_A$
Endothelin
Prostanoid/ IP receptor agonist
Iloprost (intravenous, inhaled)
Epoprostenol (intravenous, inhaled)
Selexipag (oral)
Treprostinil (intravenous, subcutaneous, inhaled, oral)
Smooth Muscle
Endothelin receptor antagonist
Ambrisentan (oral)
Bostentan (oral)
Macitentan (oral)

Riociguat in PAH



$C_{20}H_{19}FN_8O_2$



Chest, 151(2), Ghofrani HA, Humbert M, Langleben D, et al, Riociguat: mode of action and clinical development in pulmonary hypertension, 468–480, Copyright (2017), with permission from Elsevier.26

PATENT-1

PATENT-2

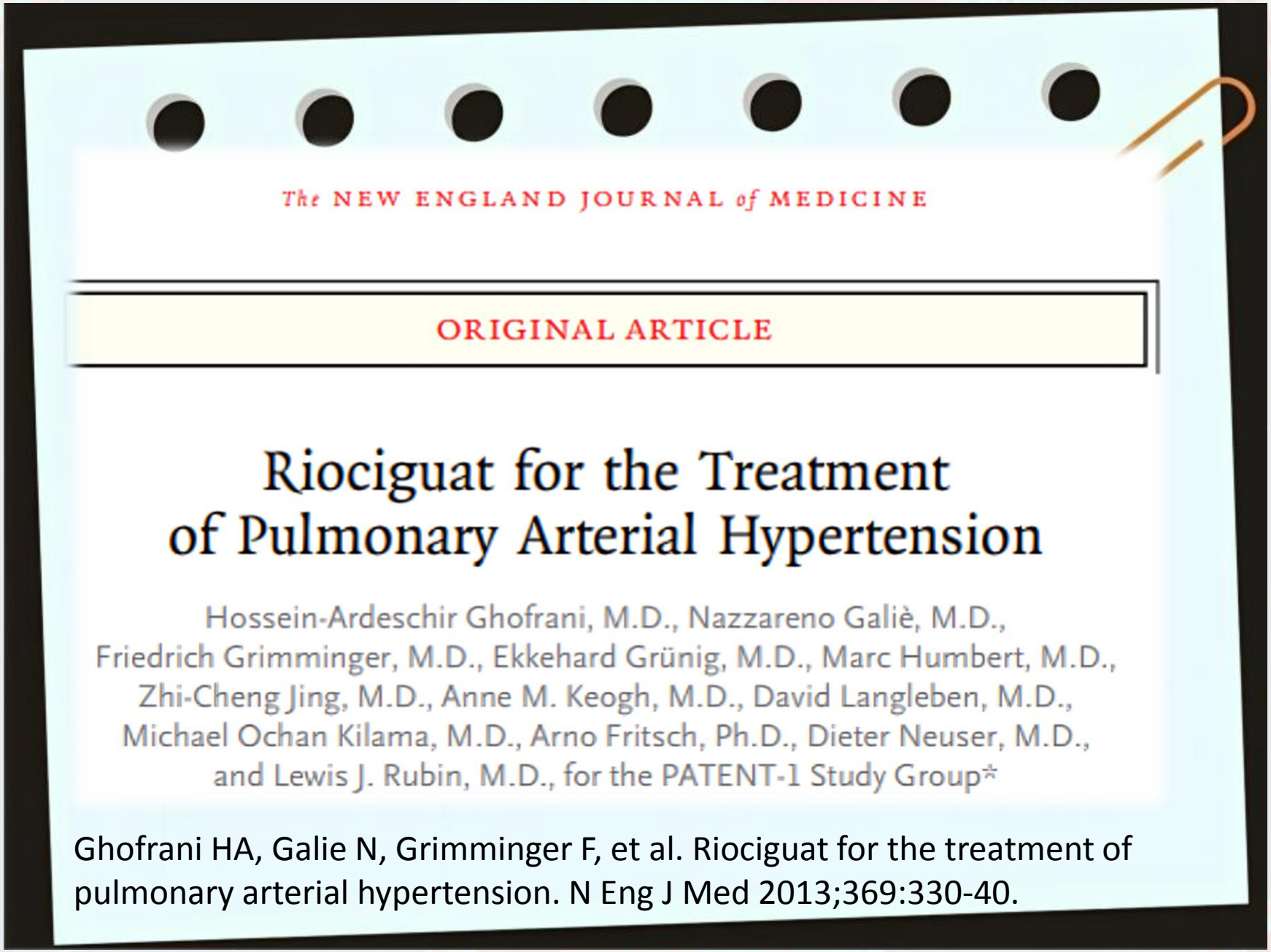
CHEST-1

CHEST-2

PATENT-1

Riociguat for the Treatment of Arterial Hypertension

The safety and efficacy of ***riociguat*** in PAH



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Riociguat for the Treatment of Pulmonary Arterial Hypertension

Hossein-Ardeschir Ghofrani, M.D., Nazzareno Galiè, M.D., Friedrich Grimminger, M.D., Ekkehard Grünig, M.D., Marc Humbert, M.D., Zhi-Cheng Jing, M.D., Anne M. Keogh, M.D., David Langleben, M.D., Michael Ochan Kilama, M.D., Arno Fritsch, Ph.D., Dieter Neuser, M.D., and Lewis J. Rubin, M.D., for the PATENT-1 Study Group*

Ghofrani HA, Galie N, Grimminger F, et al. Riociguat for the treatment of pulmonary arterial hypertension. N Eng J Med 2013;369:330-40.

PATENT-1 trial

PATENT
Pulmonary Arterial Hypertension sGC-Stimulator Trial
Riociguat

An international {30 countries}

Multicenter {24 centers}

Randomized

placebo controlled clinical trial.16

Ghofrani HA, Galie N, Grimminger F, et al. Riociguat for the treatment of pulmonary arterial hypertension. N Engl J Med 2013;369:330-40

Ghofrani HA, Galie N, Grimminger F, et al. Riociguat for the treatment of pulmonary arterial hypertension. N Engl J Med 2013;369:330-40

PATENT -1

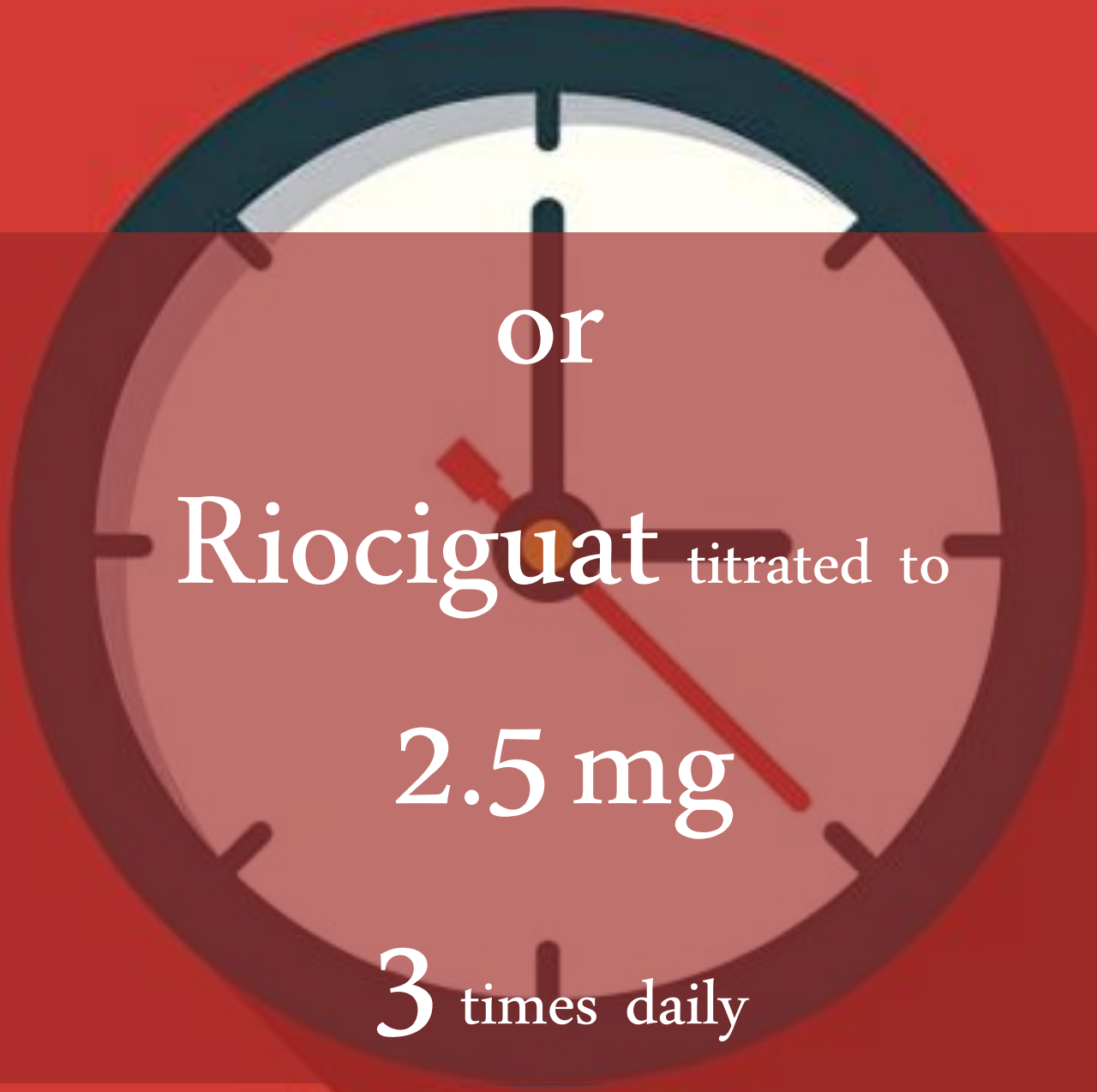
Riociguat titrated to

1.5 mg

3 times daily

Ghofrani HA, Galie N, Grimminger F, et al. Riociguat for the treatment of pulmonary arterial hypertension. N Engl J Med 2013;369:330-40

PATENT -1



or

Riociguat titrated to

2.5 mg

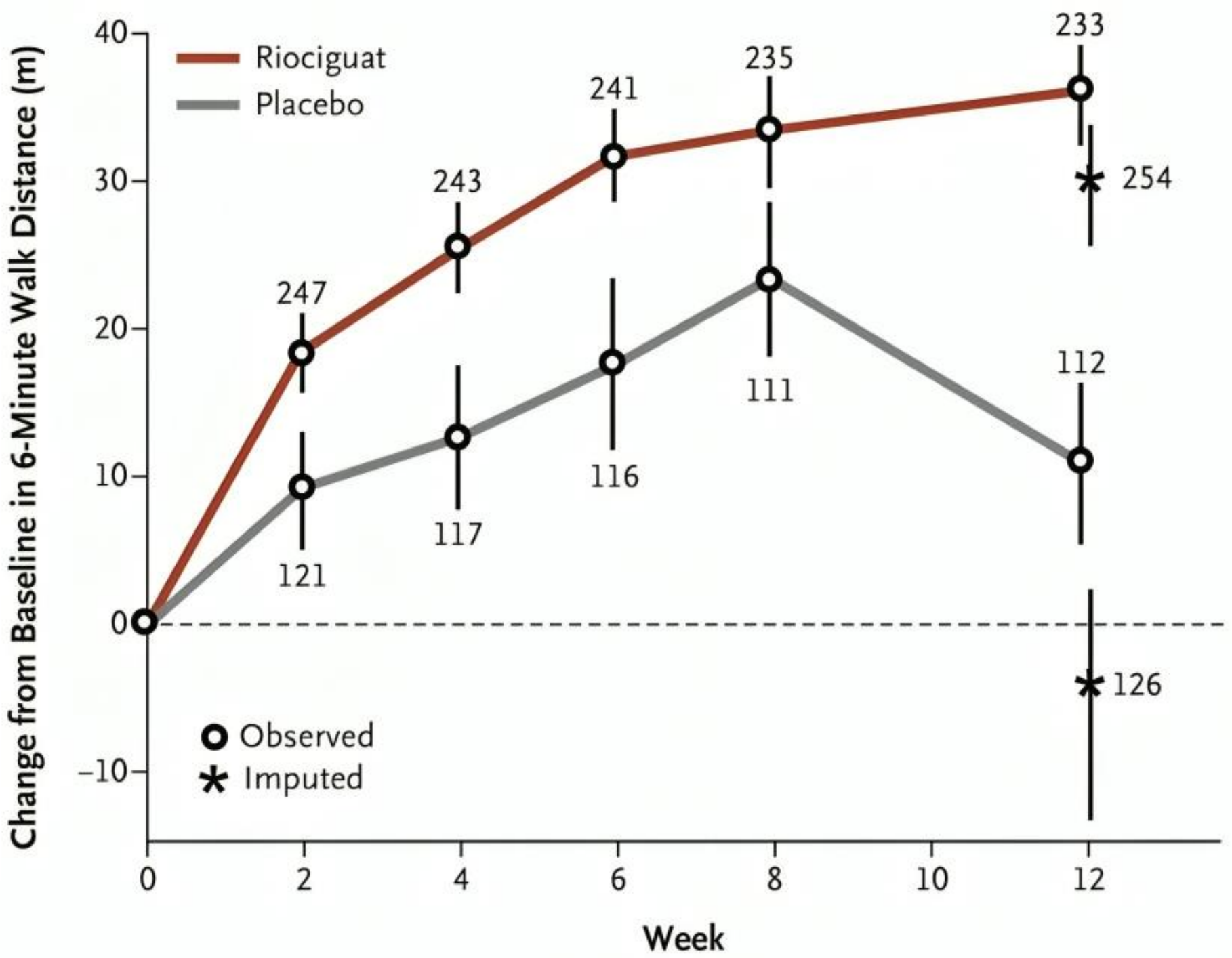
3 times daily

Ghofrani HA, Galie N, Grimminger F, et al. Riociguat for the treatment of pulmonary arterial hypertension. N Engl J Med 2013;369:330-40

PATENT -1

Increasing 6MWD

30 meters at 12 weeks



PATENT -1

Improvements in:

PVR

Ghofrani HA, Galie N, Grimminger F, et al. Riociguat for the treatment of pulmonary arterial hypertension. N Eng J Med 2013;369:330-40.

PATENT -1

Improvements in:

N-terminal pro—brain natriuretic

peptide (NT-pro-BNP)

Ghofrani HA, Galie N, Grimminger F, et al. Riociguat for the treatment of pulmonary arterial hypertension. N Eng J Med 2013;369:330-40.

PATENT -1

Improvements in:

Functional class

Ghofrani HA, Galie N, Grimminger F, et al. Riociguat for the treatment of pulmonary arterial hypertension. N Eng J Med 2013;369:330-40.

PATENT -1

Improvements in:

Time to clinical worsening at 12 week

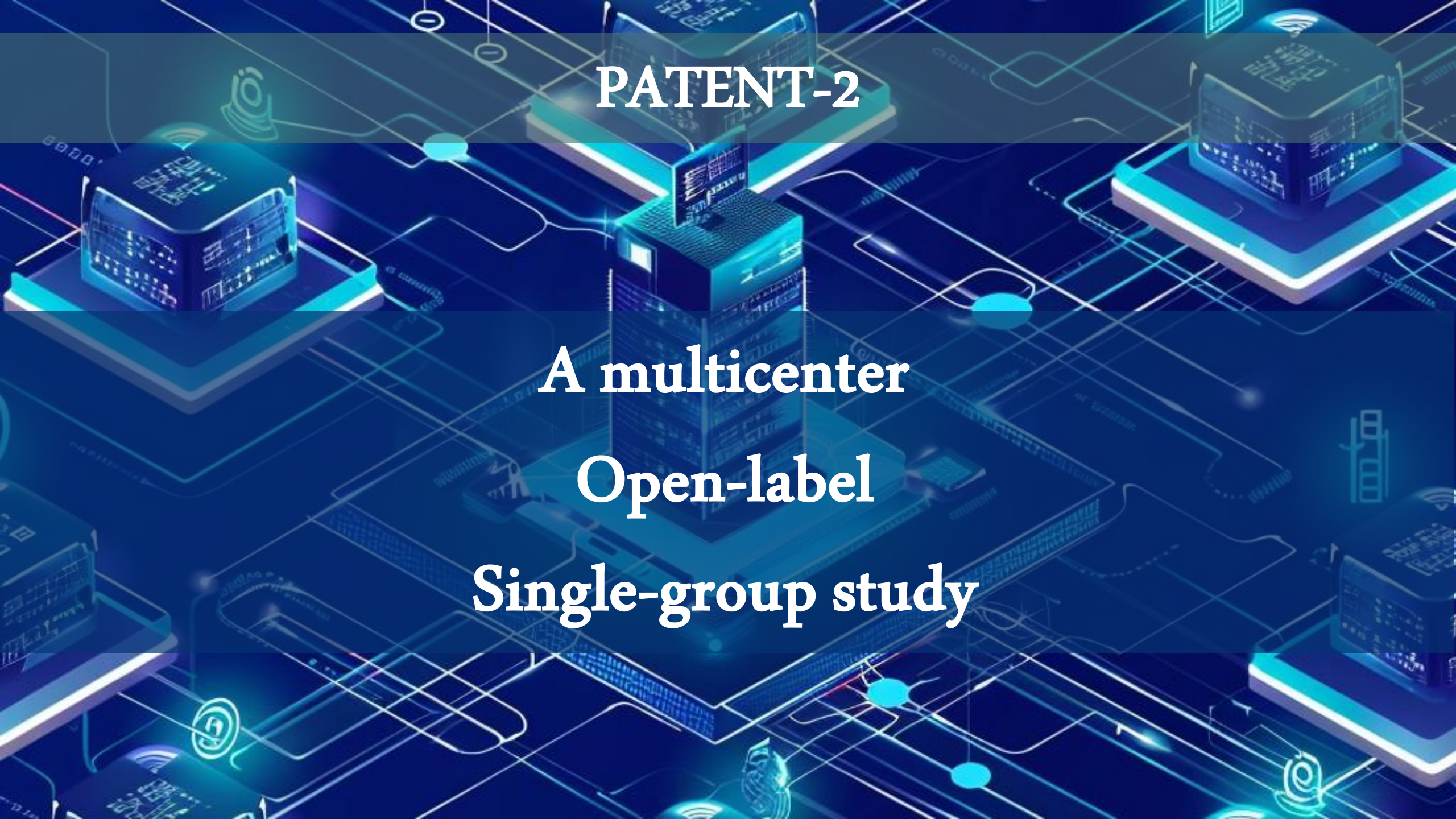
Ghofrani HA, Galie N, Grimminger F, et al. Riociguat for the treatment of pulmonary arterial hypertension. N Eng J Med 2013;369:330-40.

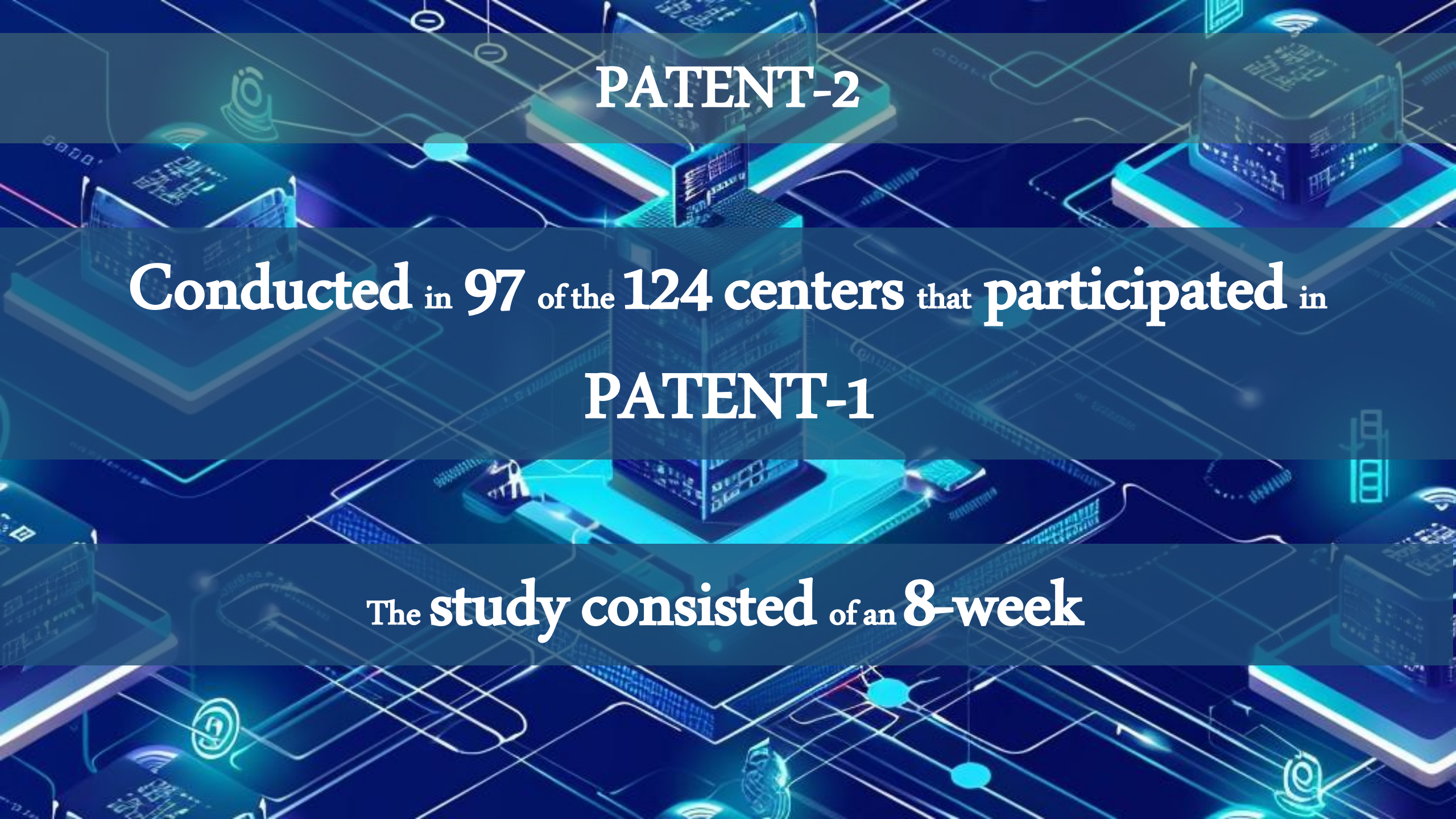
PATENT-2

Riociguat for the treatment of pulmonary arterial hypertension: a long-term extension study (PATENT-2)

Lewis J. Rubin[1], Nazzareno Galiè[2], Friedrich Grimminger[3,4], Ekkehard Grünig[5], Marc Humbert[6,7,8], Zhi-Cheng Jing[9], Anne Keogh[10], David Langleben[11], Arno Fritsch[12], Flavia Menezes[13], Neil Davie[12] and Hossein-Ardeschir Ghofrani[3,4,14]

European Respiratory Journal 2015 45: 1303-1313; **DOI:** 10.1183/09031936.00090614

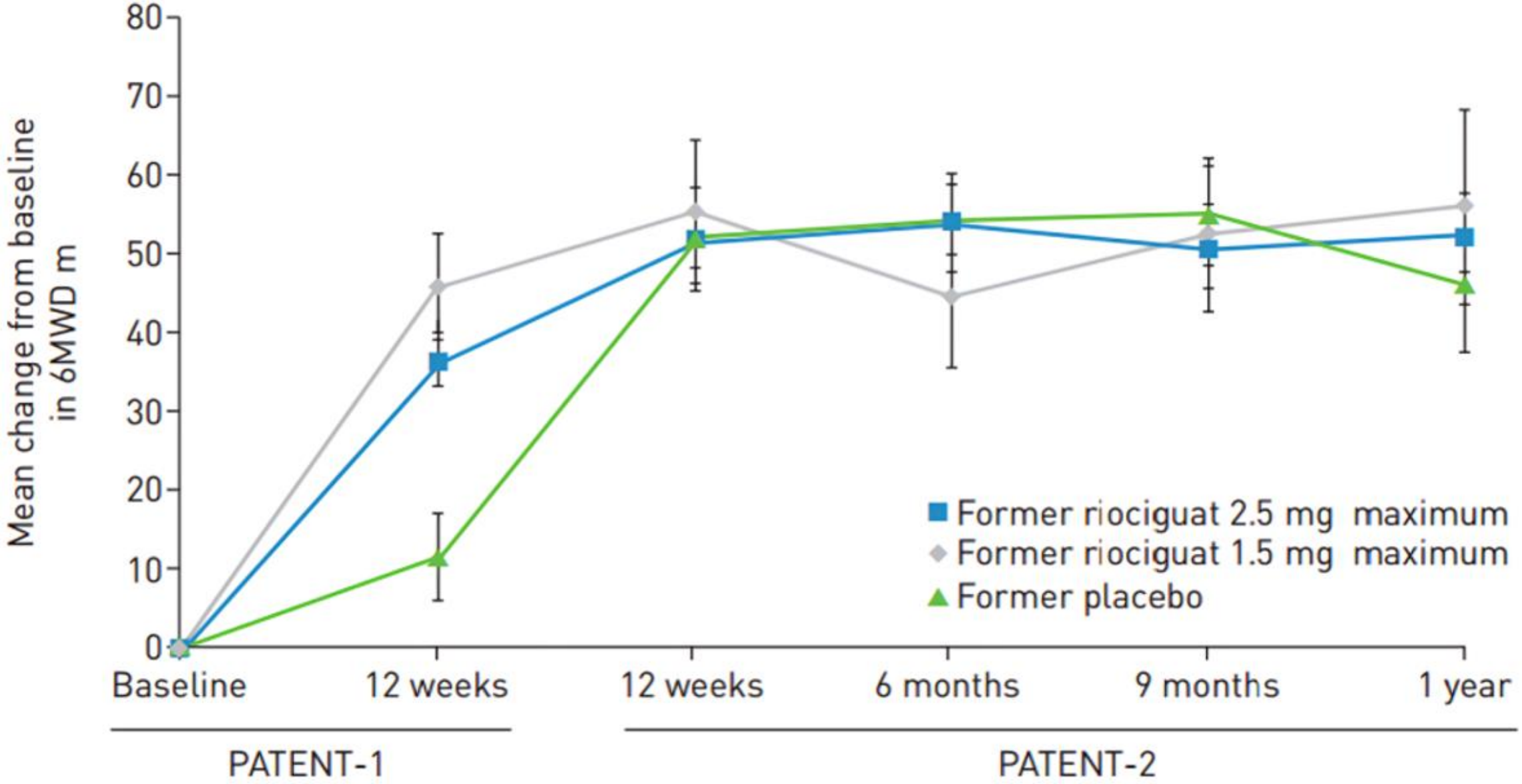

PATENT-2
A multicenter
Open-label
Single-group study


PATENT-2
Conducted in 97 of the 124 centers that participated in
PATENT-1
The study consisted of an 8-week

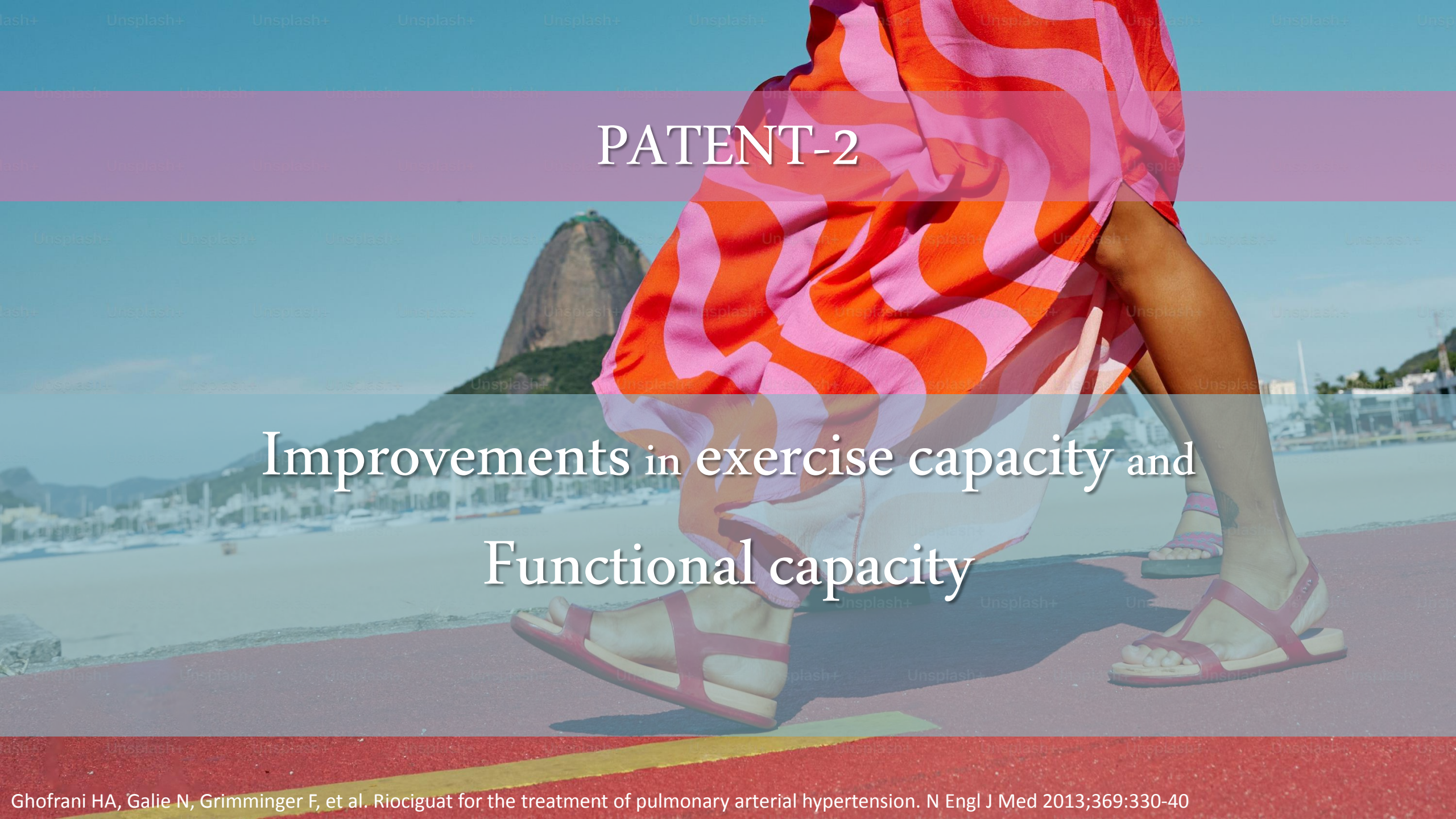
PATENT 2

6MWD

Ghofrani HA, Galie N, Grimminger F, et al. Riociguat for the treatment of pulmonary arterial hypertension. N Engl J Med 2013;369:330-40



European Respiratory Journal 2015 45: 1303-1313; **DOI:** 10.1183/09031936.00090614



PATENT-2

Improvements in exercise capacity and Functional capacity

Ghofrani HA, Galie N, Grimminger F, et al. Riociguat for the treatment of pulmonary arterial hypertension. N Engl J Med 2013;369:330-40

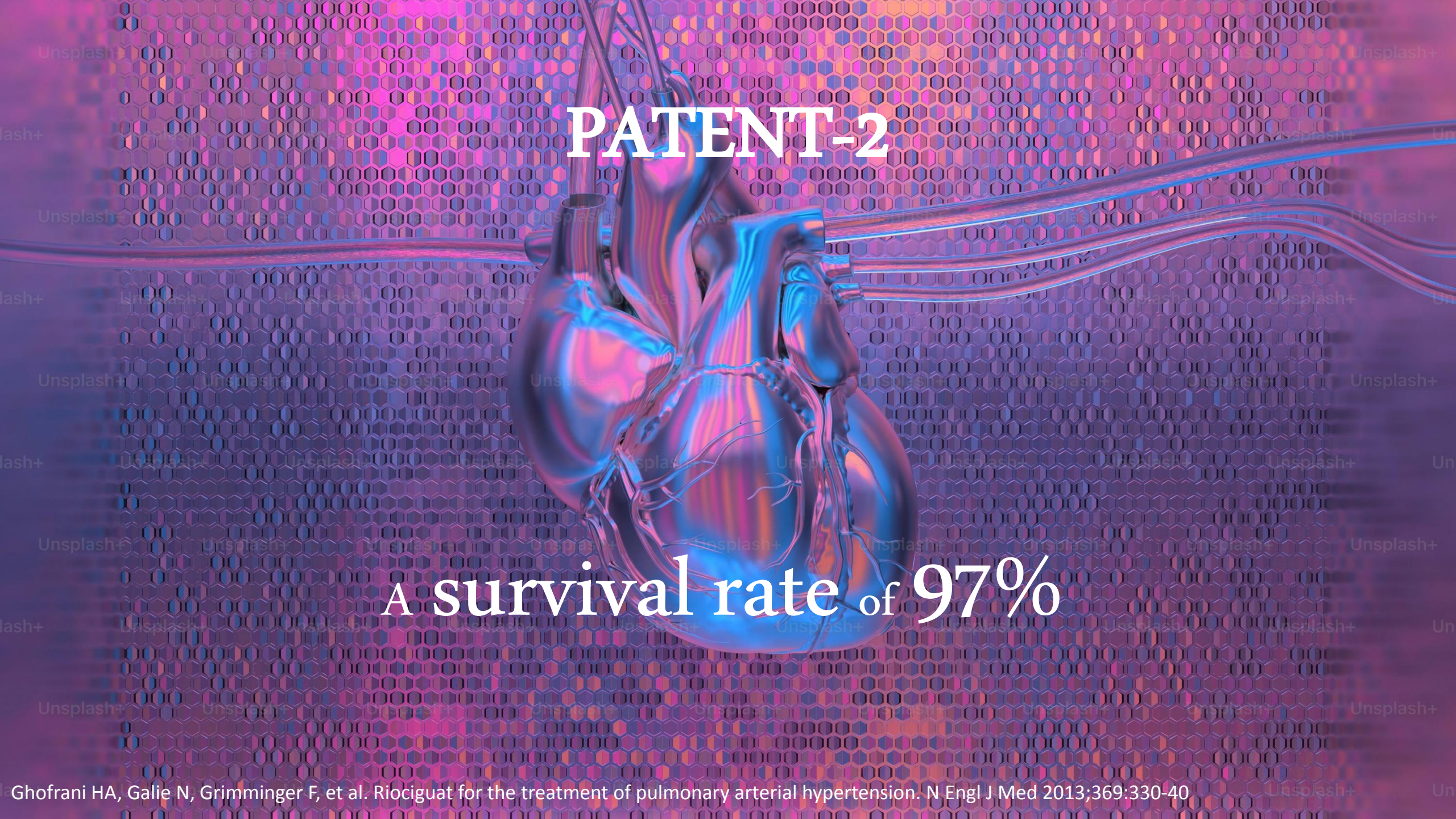
PATENT-2

Improvement in 6MWD at 24 weeks

Maintained for up to 1 year of in the long-term extension study

Ghofrani HA, Galie N, Grimminger F, et al. Riociguat for the treatment of pulmonary arterial hypertension. N Engl J Med 2013;369:330-40

PATENT-2



A survival rate of 97%

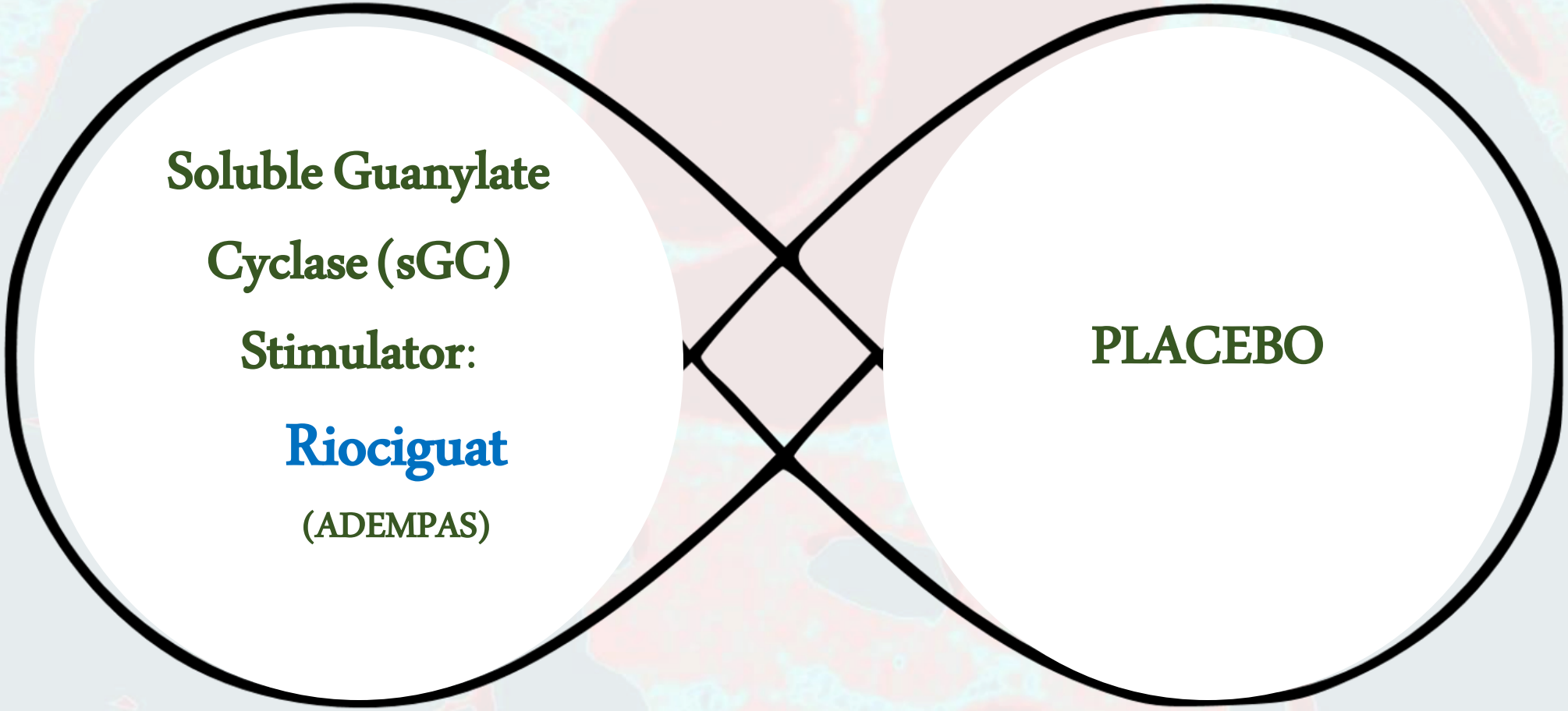
Ghofrani HA, Galie N, Grimminger F, et al. Riociguat for the treatment of pulmonary arterial hypertension. N Engl J Med 2013;369:330-40

ELSEVIER

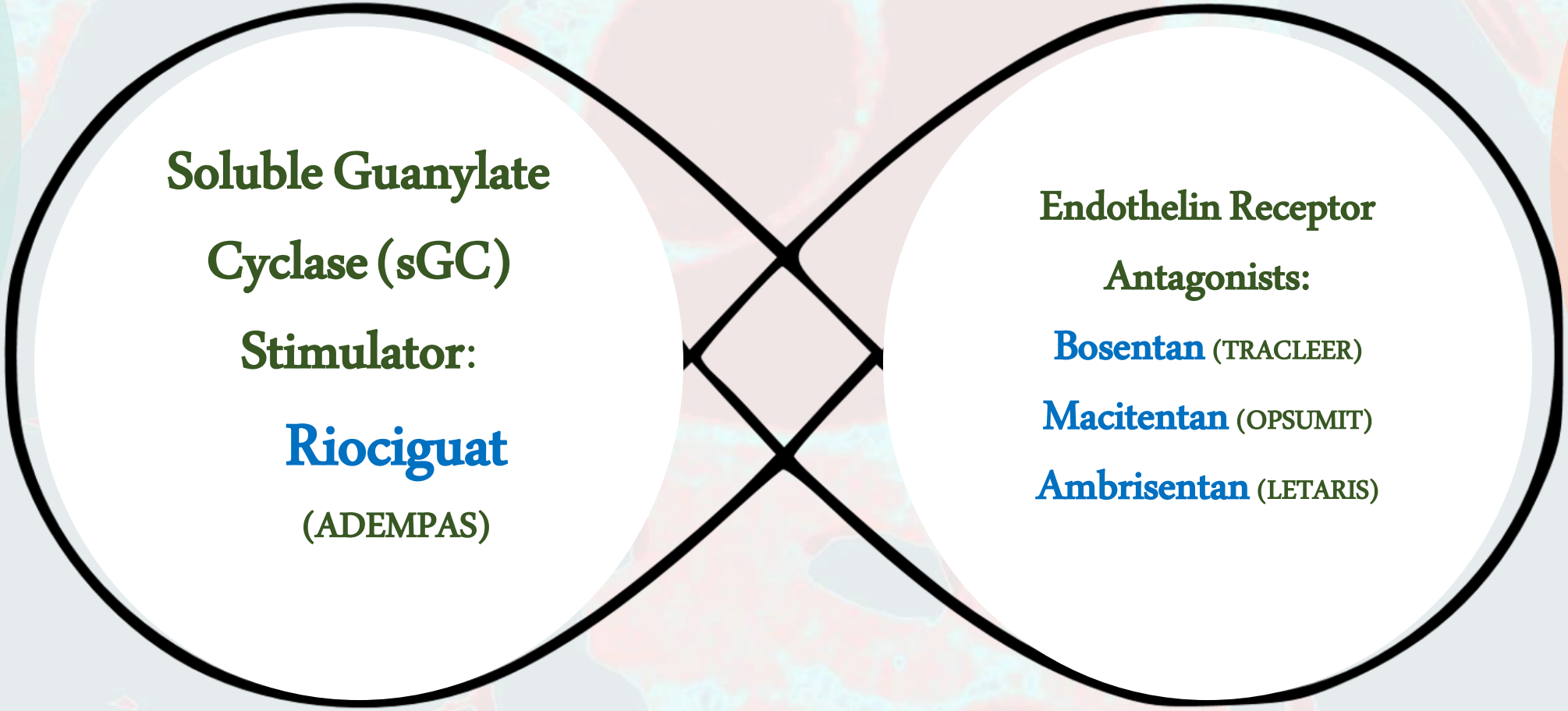
The Journal of Heart and Lung Transplantation
http://www.jhltonline.org

Comparison of hemodynamic parameters in treatment-naïve and pre-treated patients with pulmonary arterial hypertension in the randomized phase III PATENT-1 study

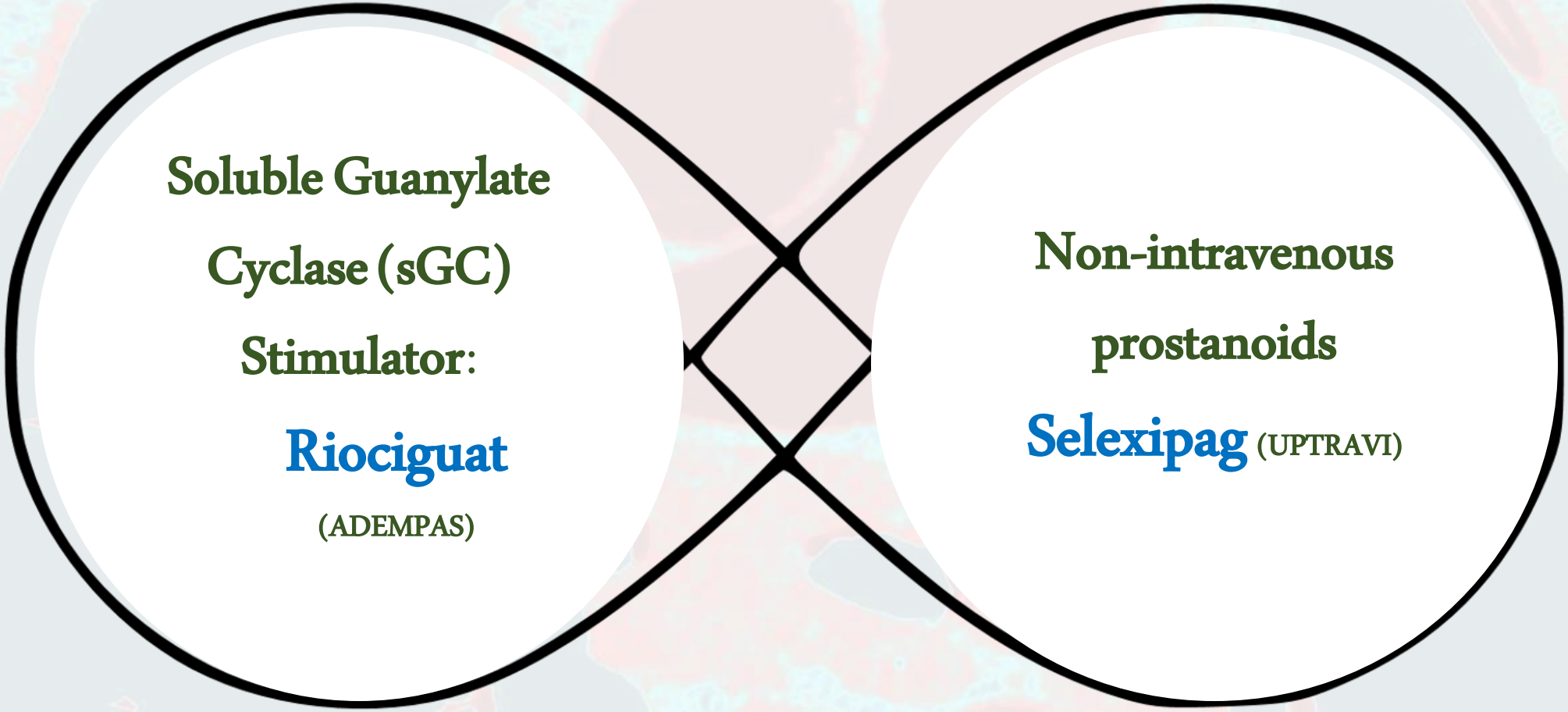
Nazzareno Galiè, MD,[a] Friedrich Grimminger, MD, PhD,[b] Ekkehard Grünig, MD,[c] Marius M. Hoeper, MD,[d] Marc Humbert, MD, PhD,[e] Zhi-Cheng Jing, MD,[f] Anne M. Keogh, PhD,[g] David Langleben, MD,[h] Lewis J. Rubin, MD,[i] Arno Fritsch, PhD,[j] Neil Davie, PhD,[j] and Hossein-Ardeschir Ghofrani, MD[b,k]



N. Gali`e, F. Grimminger, E. Grünig, et al., Comparison of hemodynamic parameters in treatment-naïve and pre-treated patients with pulmonary arterial hypertension in the randomized phase III PATENT-1 study, J. Heart Lung Transplant. 36 (5) (2017) 509–519.

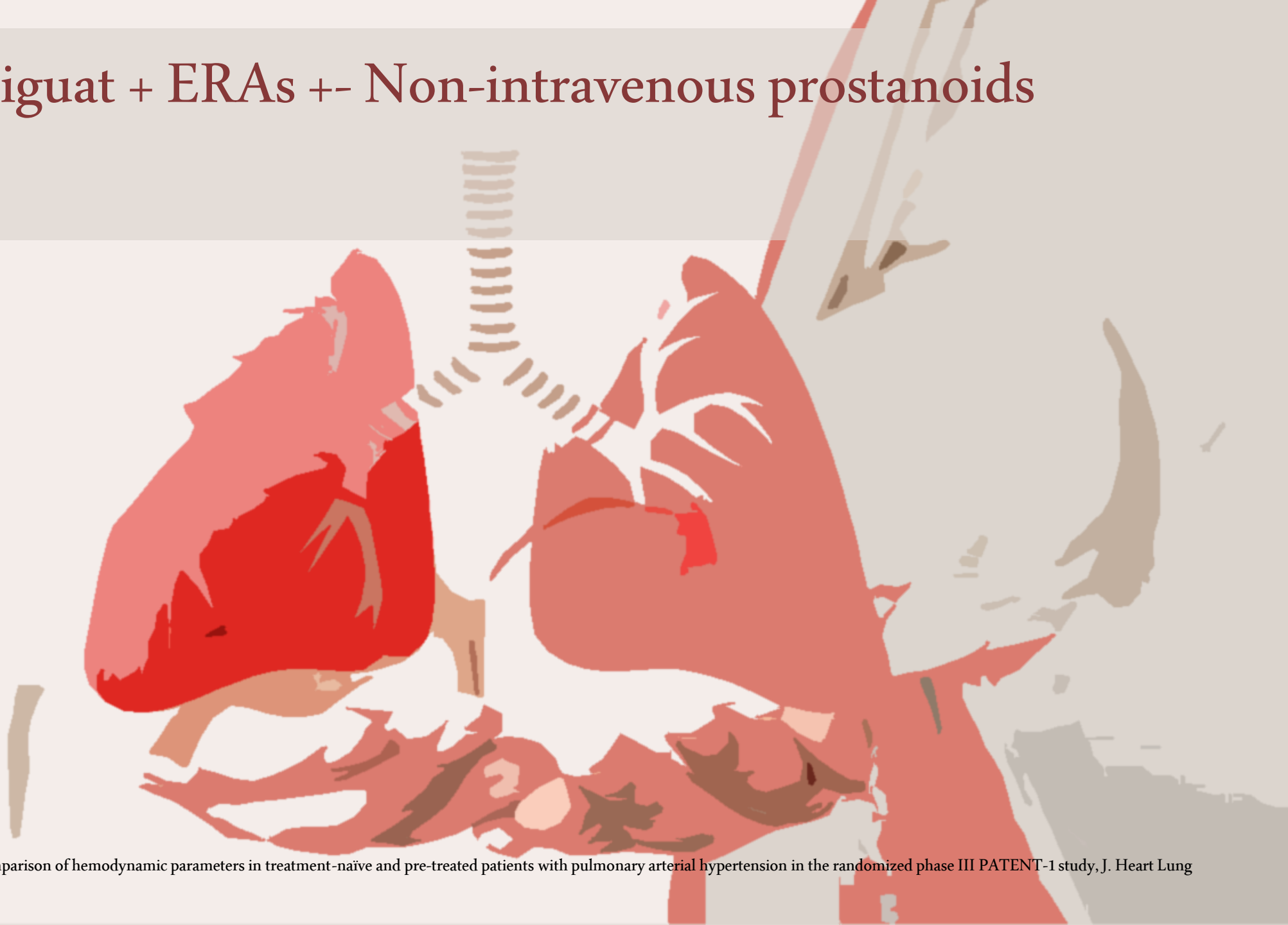


N. Gali`e, F. Grimminger, E. Grünig, et al., Comparison of hemodynamic parameters in treatment-naïve and pre-treated patients with pulmonary arterial hypertension in the randomized phase III PATENT-1 study, J. Heart Lung Transplant. 36 (5) (2017) 509–519.



N. Gali`e, F. Grimminger, E. Grünig, et al., Comparison of hemodynamic parameters in treatment-naïve and pre-treated patients with pulmonary arterial hypertension in the randomized phase III PATENT-1 study, J. Heart Lung Transplant. 36 (5) (2017) 509–519.

Riociguat + ERAs +- Non-intravenous prostanoids



N. Gali` e, F. Grimminger, E. Grünig, et al., Comparison of hemodynamic parameters in treatment-naïve and pre-treated patients with pulmonary arterial hypertension in the randomized phase III PATENT-1 study, J. Heart Lung Transplant. 36 (5) (2017) 509–519.

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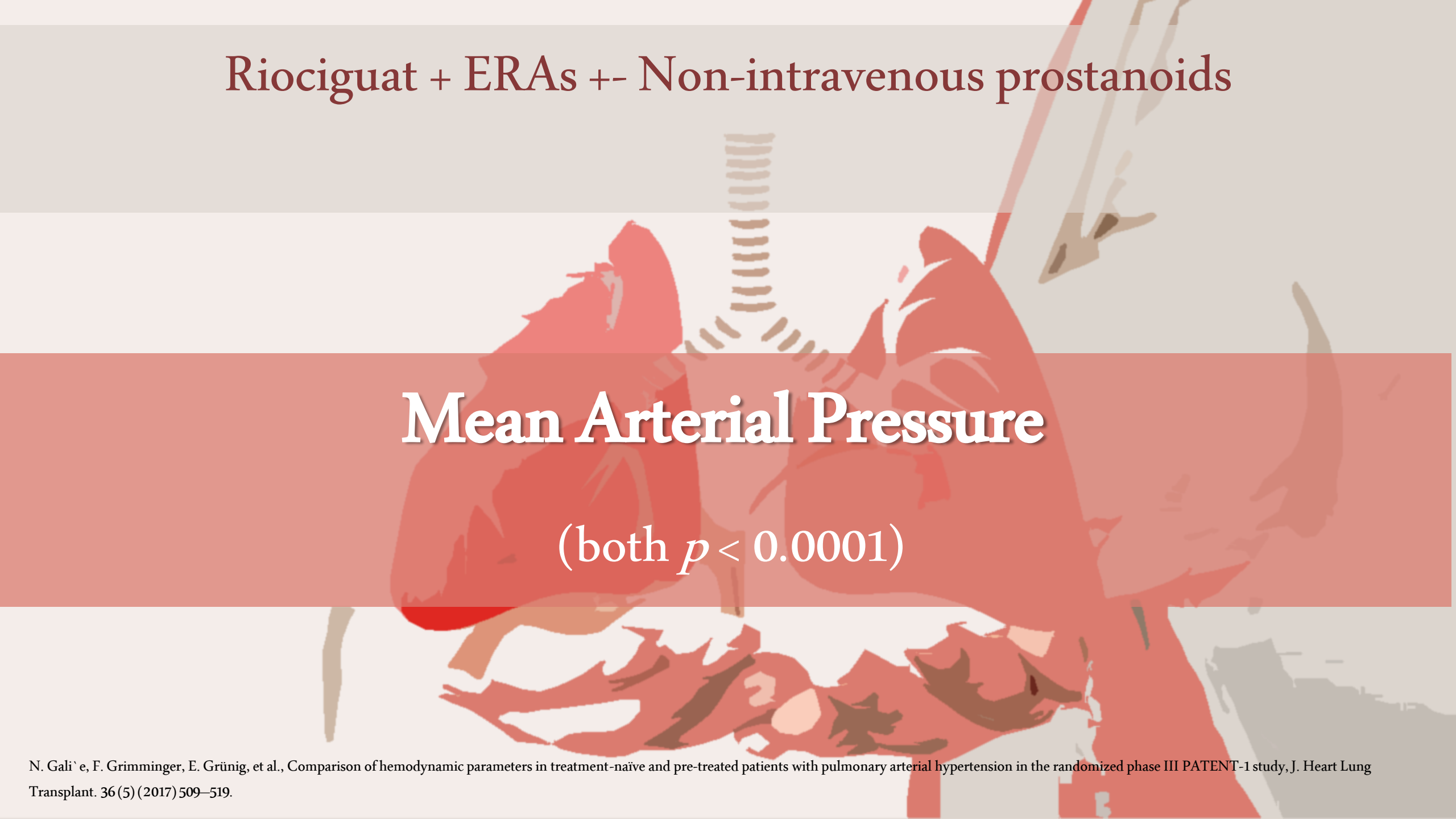


Mean Arterial Pressure

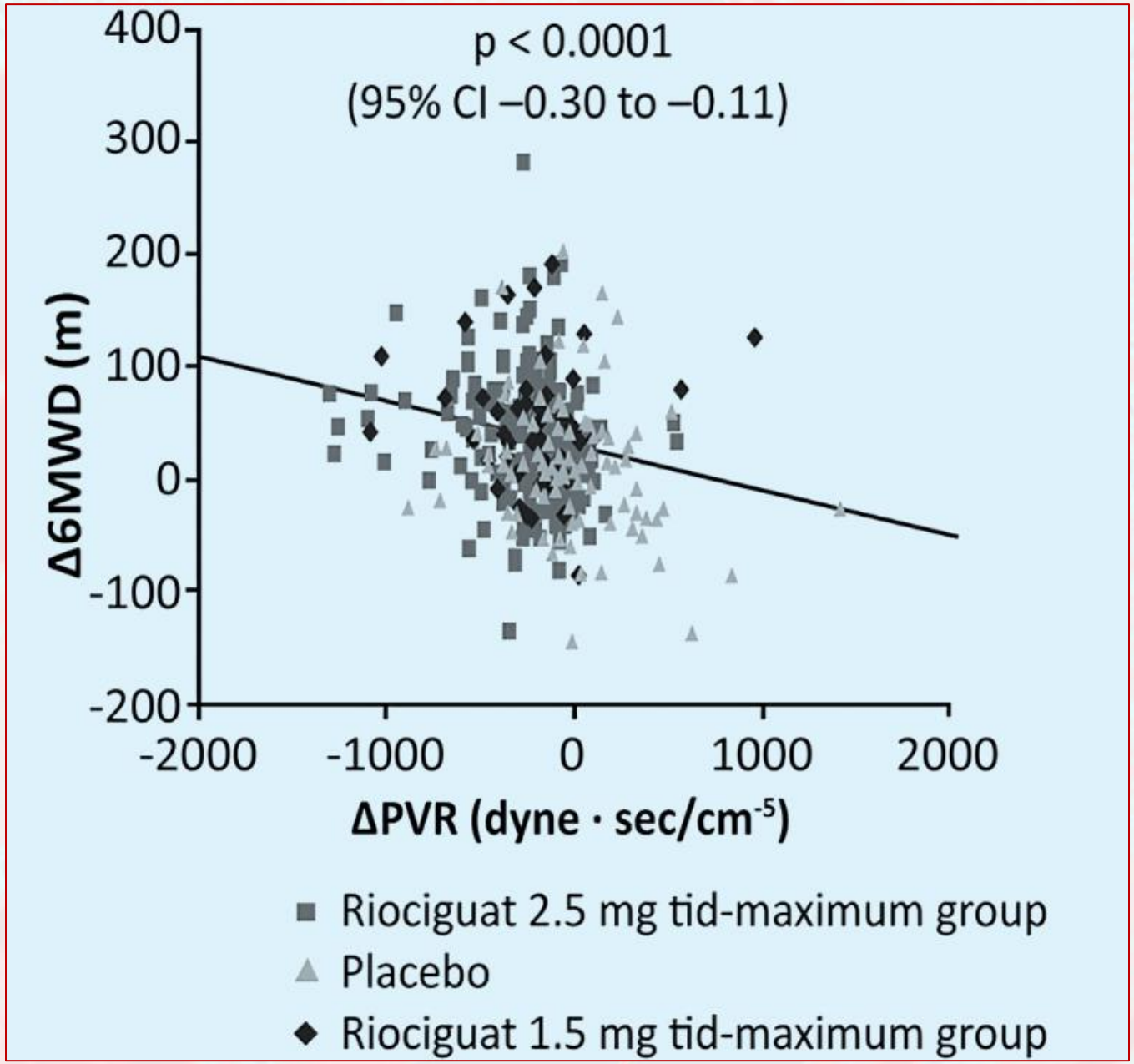
(both $p < 0.0001$)

N. Gali` e, F. Grimminger, E. Grünig, et al., Comparison of hemodynamic parameters in treatment-naïve and pre-treated patients with pulmonary arterial hypertension in the randomized phase III PATENT-1 study, J. Heart Lung Transplant. 36 (5) (2017) 509–519.

Riociguat + ERAs +- Non-intravenous prostanoids

⬇⬇

Pulmonary vascular resistance(PVR)

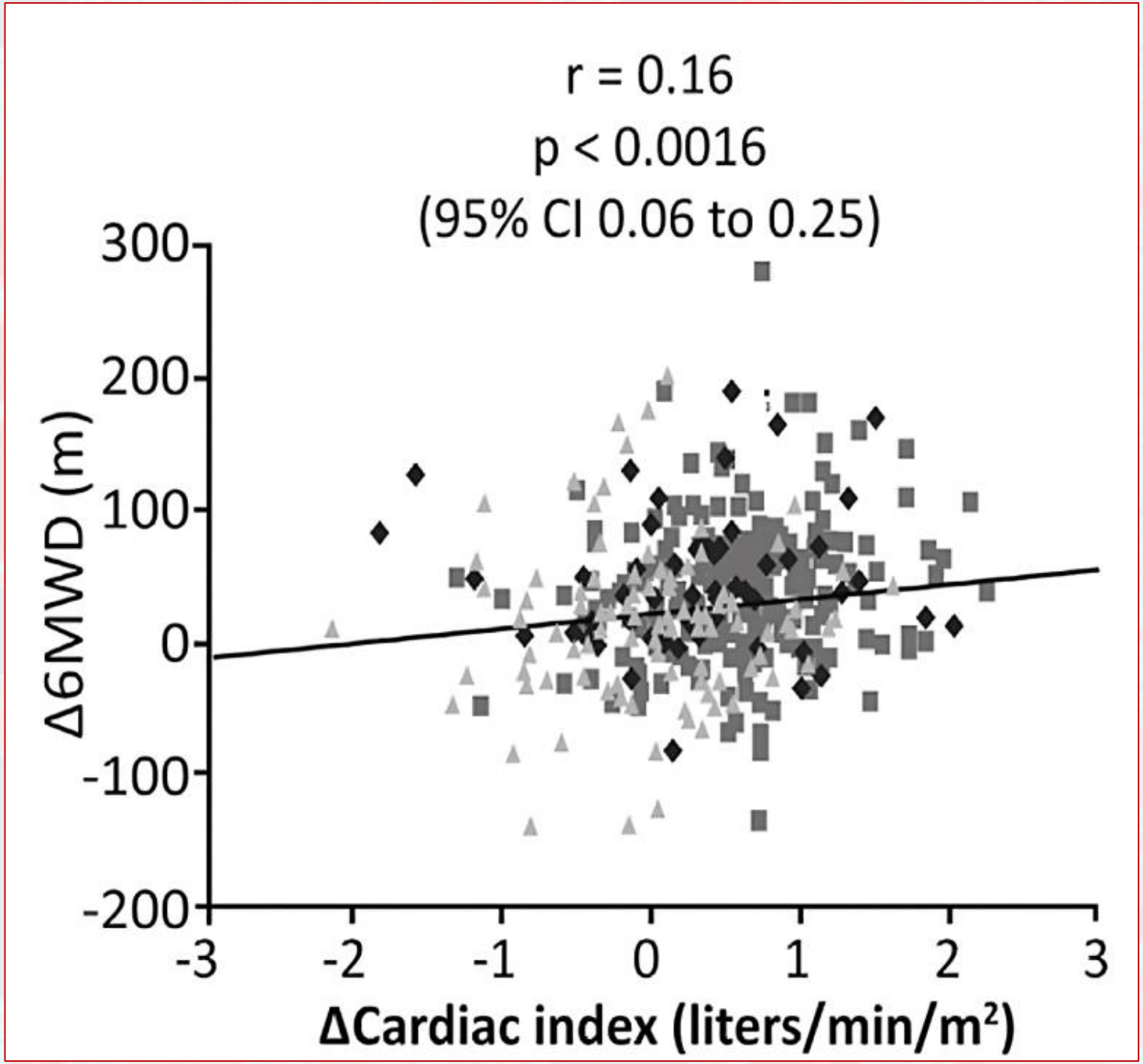


N. Gali`e, F. Grimminger, E. Grünig, et al., Comparison of hemodynamic parameters in treatment-naïve and pre-treated patients with pulmonary arterial hypertension in the randomized phase III PATENT-1 study, J. Heart Lung Transplant. 36 (5) (2017) 509–519.

Cardiac Index

↑↑

Riociguat + ERAs +- Non-intravenous prostanoids



N. Gali`e, F. Grimminger, E. Grünig, et al., Comparison of hemodynamic parameters in treatment-naïve and pre-treated patients with pulmonary arterial hypertension in the randomized phase III PATENT-1 study, J. Heart Lung Transplant. 36 (5) (2017) 509–519.

PATENT-2

Riociguat is

An effective long term

treatment for PAH

as a Monotherapy or Combination

therapy

CHEST-1

Riociguat for the treatment of chronic thromboembolic pulmonary Ghofrani HA, D'Armini AM, Grimminger F, Hoeper MM, Jansa P, Kim NH, Mayer E, Simonneau G, Wilkins MR, Fritsch A, Neuser D, Weimann G, Wang C, CHEST-1 Study Group Engl J Med. 2013 Jul;369(4):.31929 hypertension.

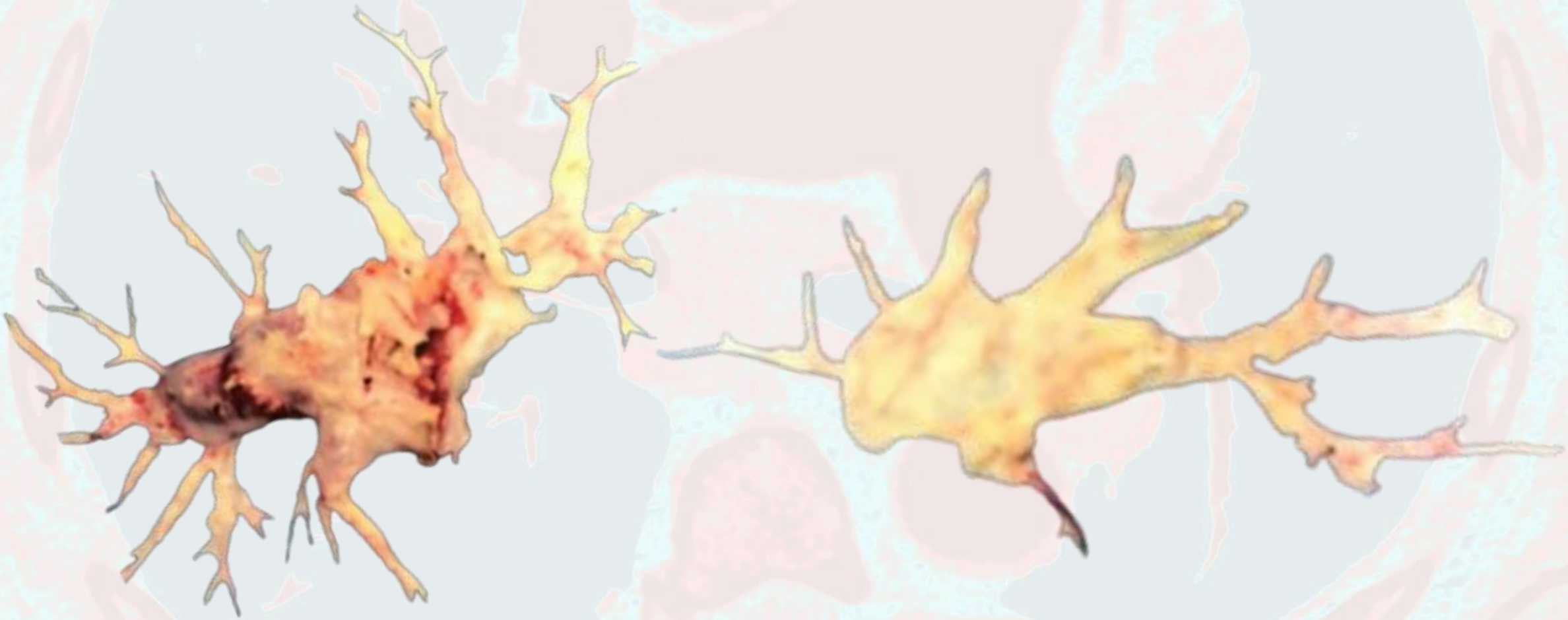
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

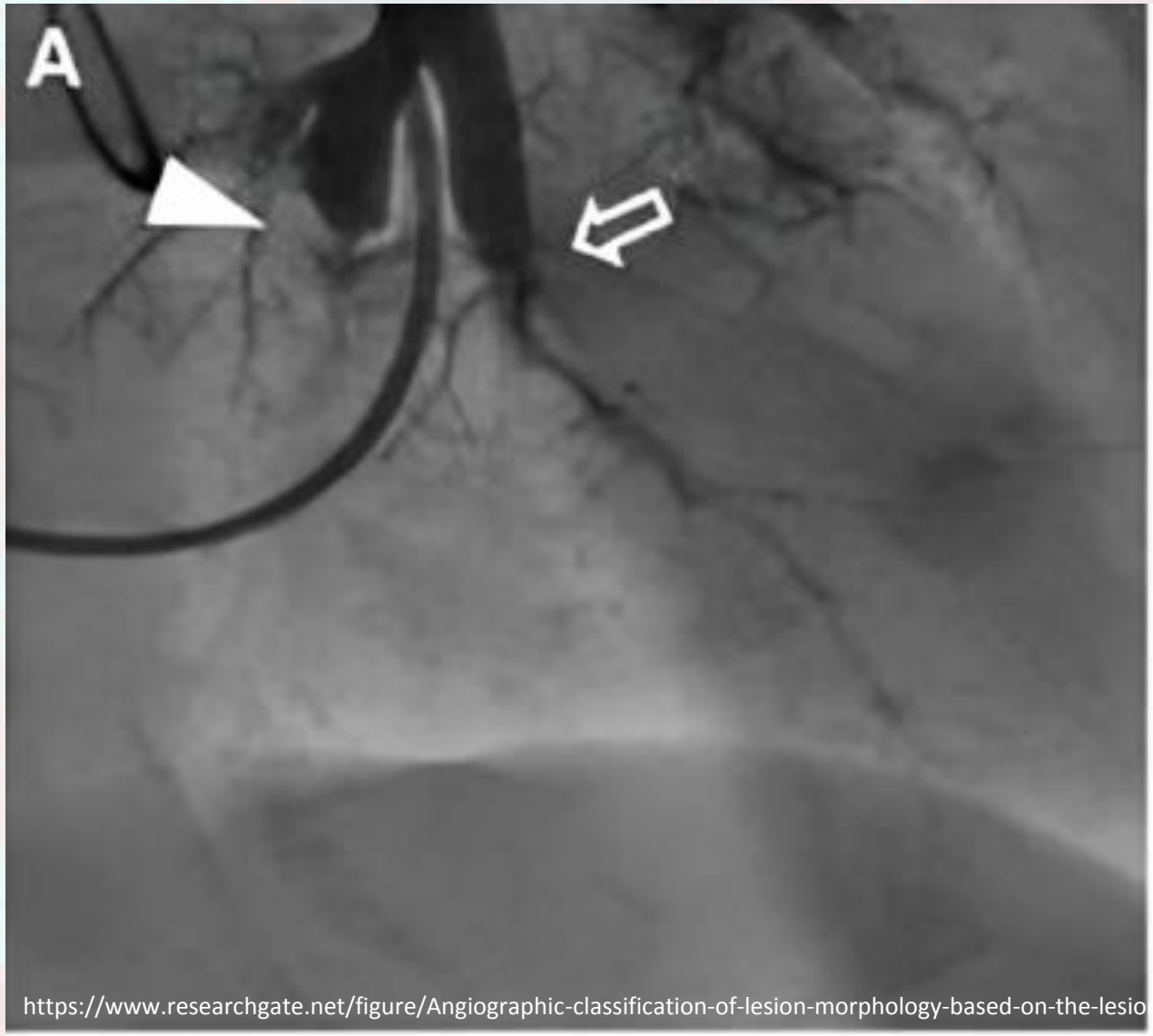
Riociguat for the Treatment of Chronic Thromboembolic Pulmonary Hypertension

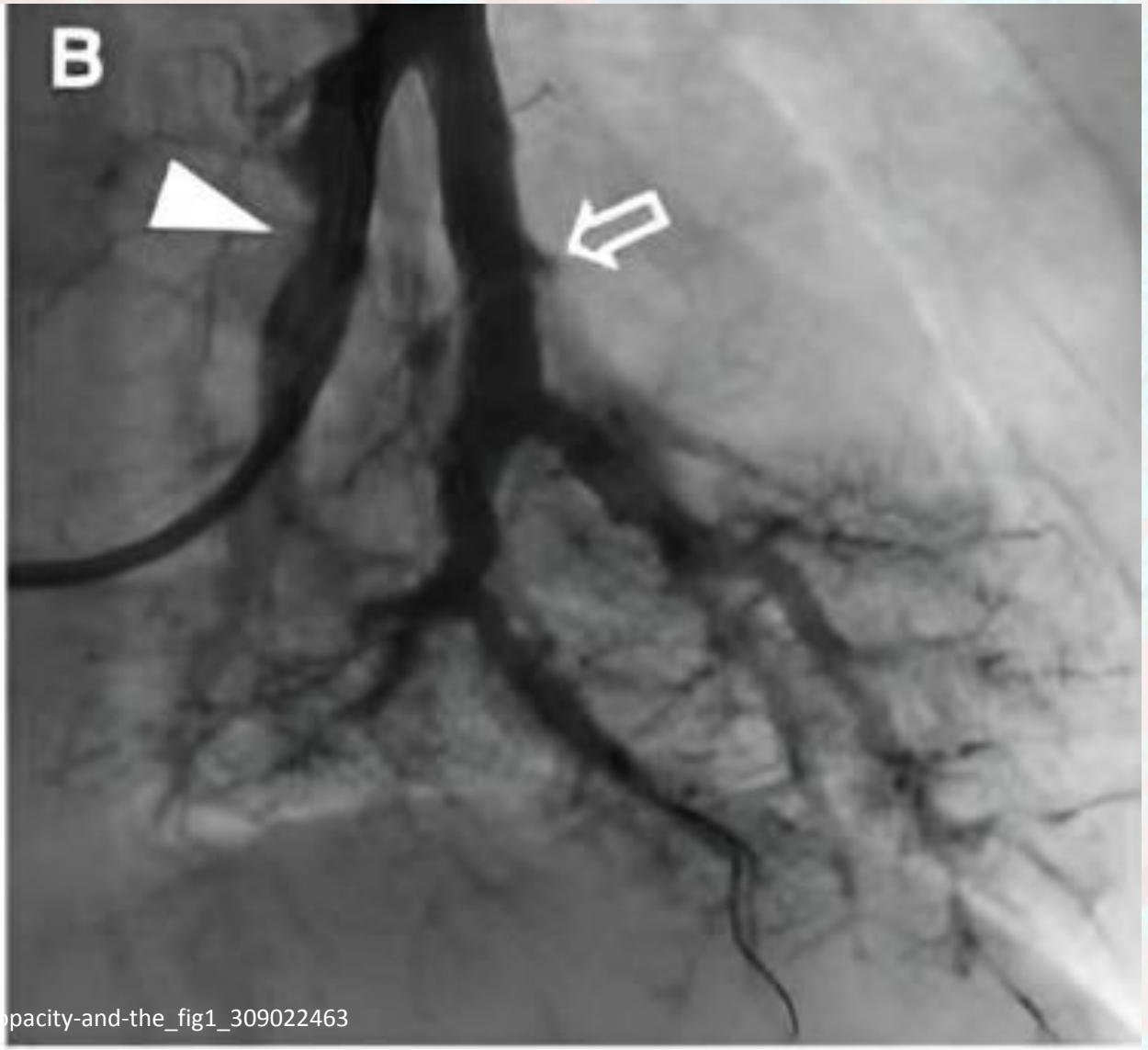
Hossein-Ardeschir Ghofrani, M.D., Andrea M. D'Armini, M.D., Friedrich Grimminger, M.D., Marius M. Hoeper, M.D., Pavel Jansa, M.D., Nick H. Kim, M.D., Eckhard Mayer, M.D., Gerald Simonneau, M.D., Martin R. Wilkins, M.D., Arno Fritsch, Ph.D., Dieter Neuser, M.D., Gerrit Weimann, M.D., and Chen Wang, M.D., for the CHEST-1 Study Group*

Pulmonary Thromboendarterectomy (PTE)



Balloon Pulmonary Angioplasty

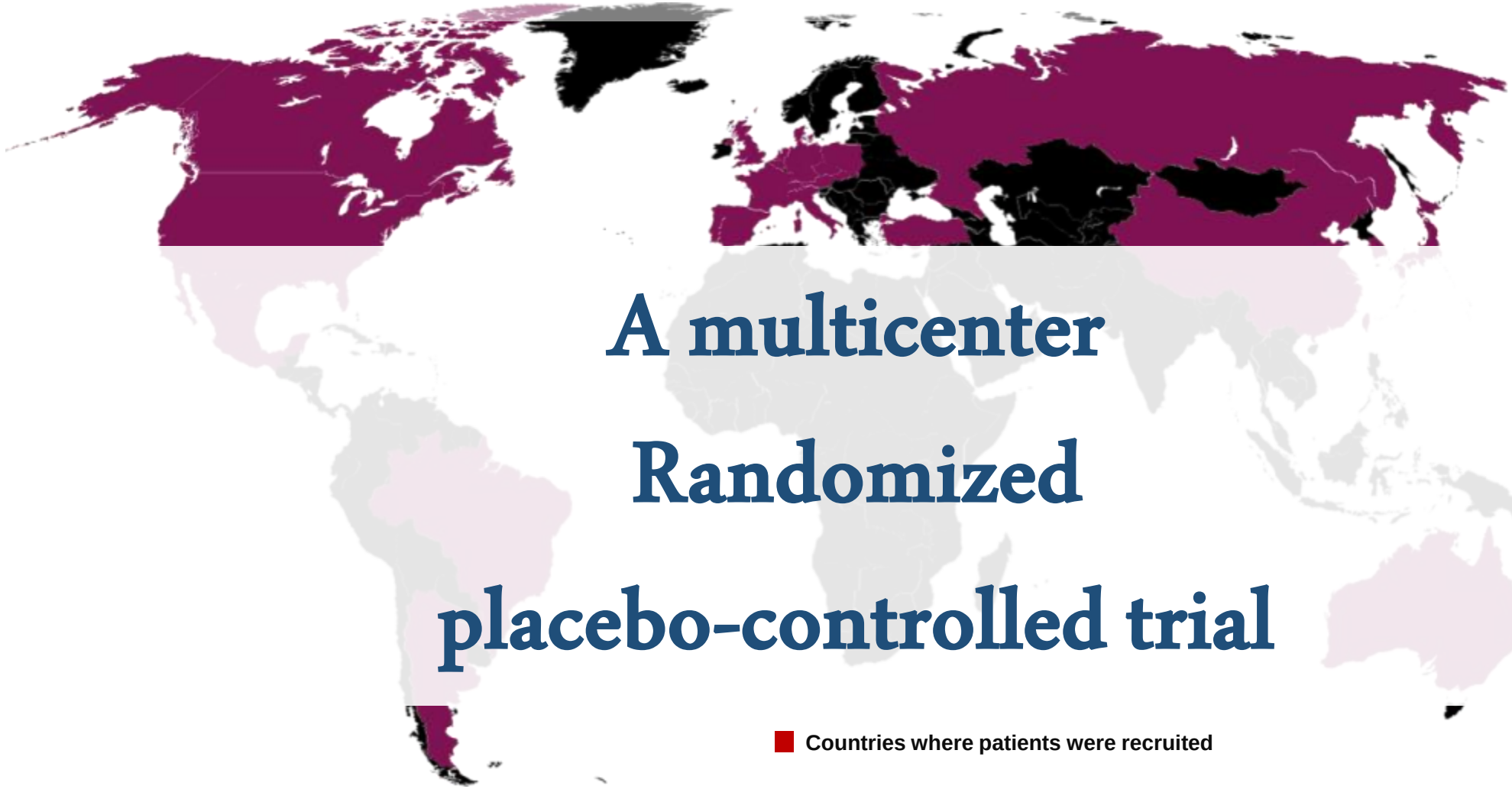




https://www.researchgate.net/figure/Angiographic-classification-of-lesion-morphology-based-on-the-lesio pacity-and-the_fig1_309022463

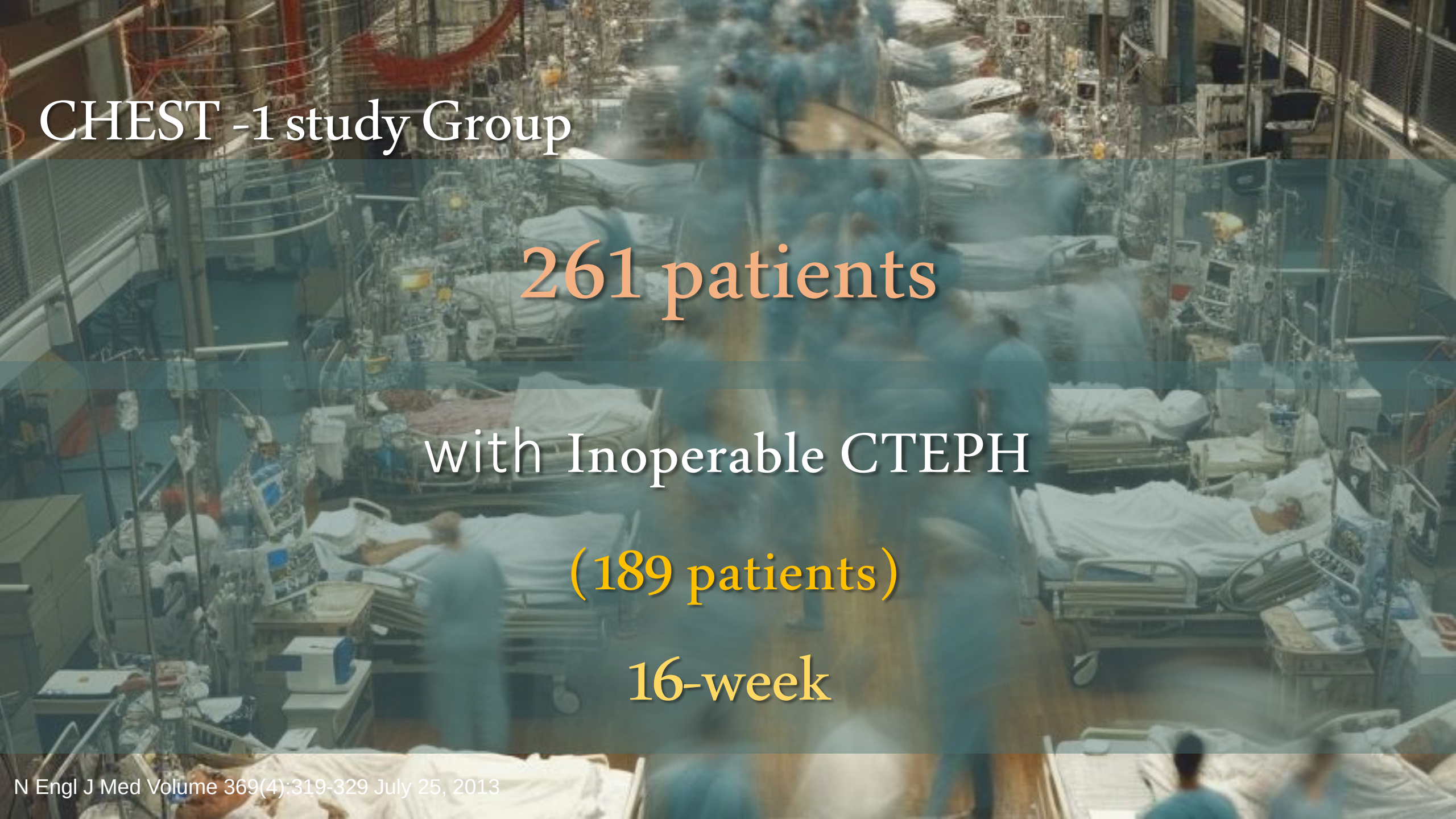
CHEST -1 study Group

CHEST
Chronic Thromboembolic Pulmonary Hypertension sGC-Stimulator Trial
Riociguat

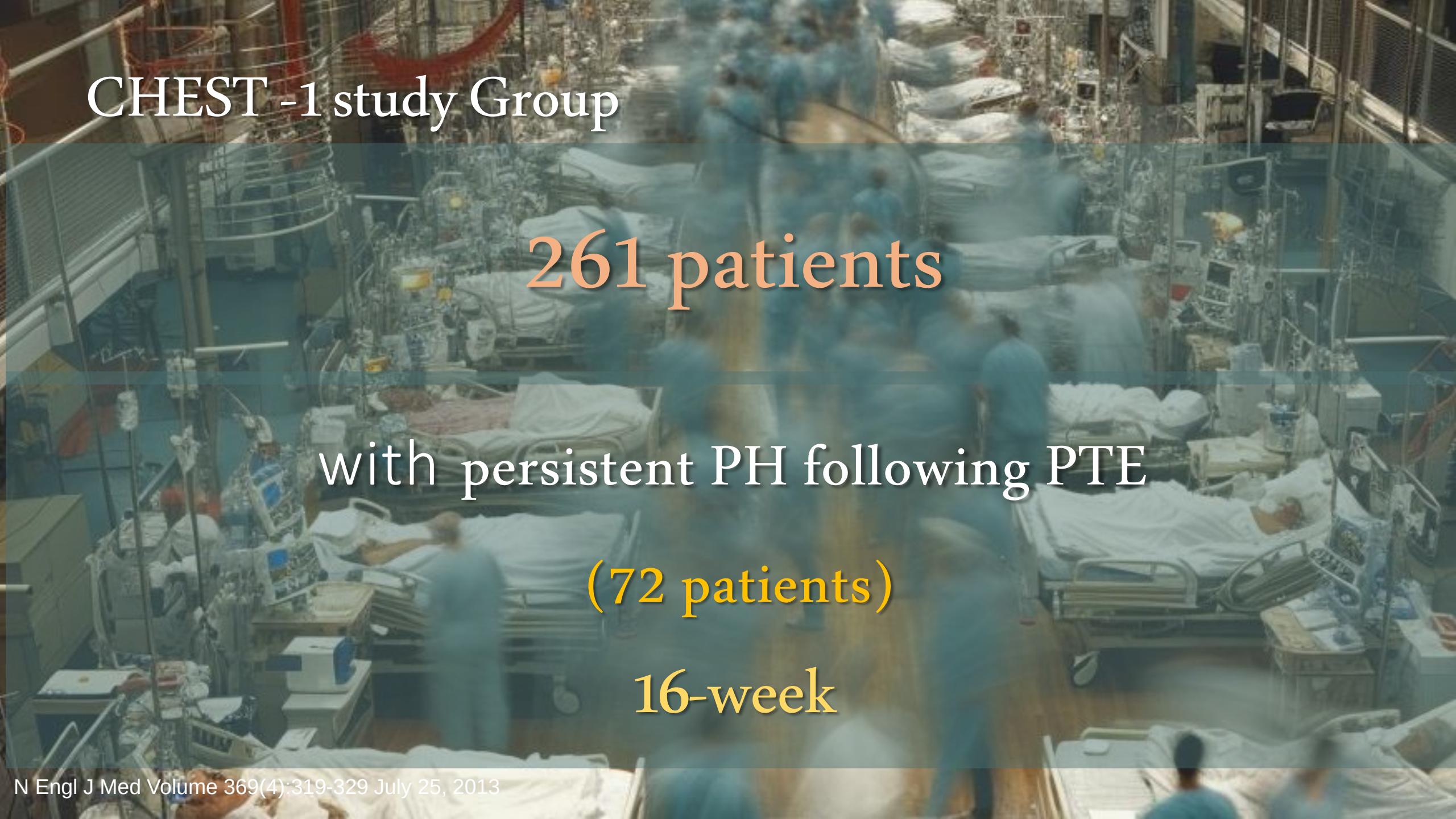


A multicenter Randomized placebo-controlled trial

Ghofrani H-A *et al. N Engl J Med* 2013;369:319–29



N Engl J Med Volume 369(4):319-329 July 25, 2013



CHEST -1 study Group

261 patients

with persistent PH following PTE

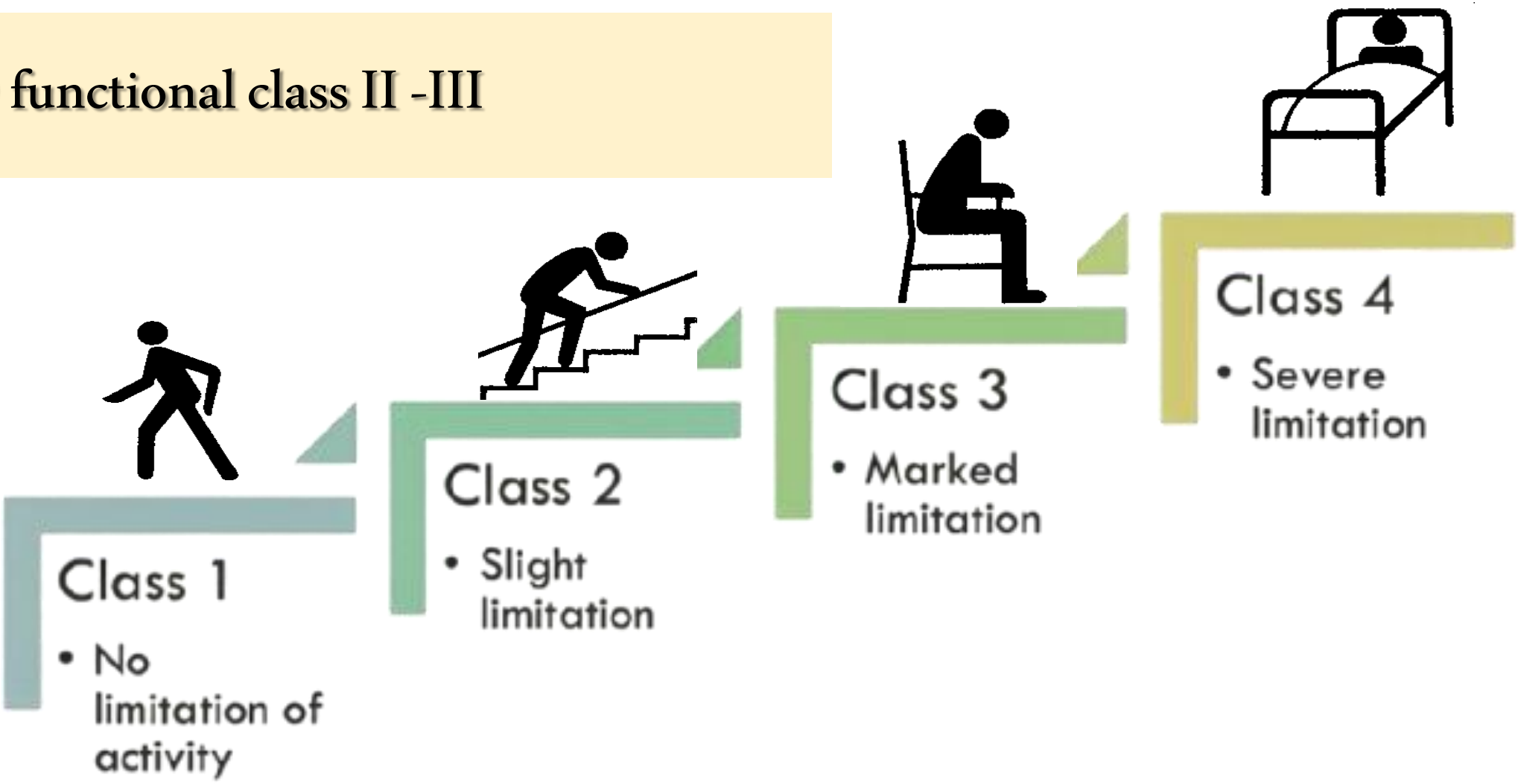
(72 patients)

16-week

N Engl J Med Volume 369(4):319-329 July 25, 2013

CHEST -1 study Group

WHO functional class II -III

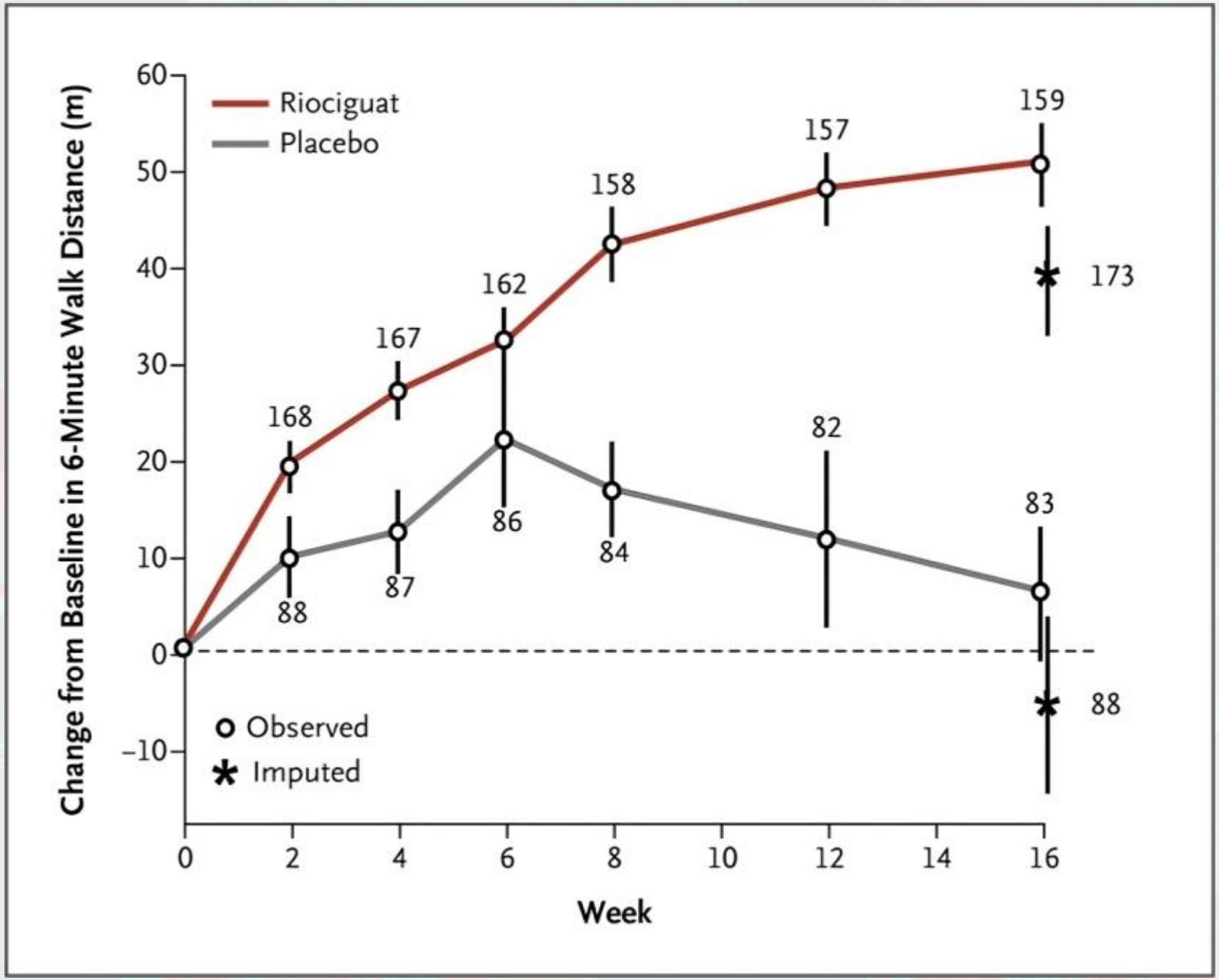


N Engl J Med Volume 369(4):319-329 July 25, 2013

CHEST -1 study Group

Mean Change from Baseline in the 6-Minute Walk Distance

6MWD increased 39 m



Ghofrani H-A et al. N Engl J Med 2013;369:319-329

CHEST -1 study Group

Pulmonary hemodynamics

PVR

↓↓ [2.8 Wood units]

Ghofrani H-A et al. N Engl J Med 2013;369:319-329

CHEST-2

CHEST-2 : Predictors of long-term outcomes

Lancet Respir Med. 2016;4(5):372. Epub 2016 Apr 8.

CHEST-2 : Predictors of long-term outcomes

Patients treated with Riociguat

for

Chronic Thromboembolic Pulmonary Hypertension

Lancet Respir Med. 2016;4(5):372. Epub 2016 Apr 8.

CHEST-2

Open-label

Randomized

Long-term extension trial

Lancet Respir Med. 2016;4(5):372. Epub 2016 Apr 8.

A follow-up long-term extension study (CHEST-2) reported that…

Prolonged therapy for up to two years with Riociguat

resulted in a

similar efficacy and safety profile

Lancet Respir Med. 2016;4(5):372. Epub 2016 Apr 8.


SUMMARY

High Quality evidence…

Riociguat

Group 01

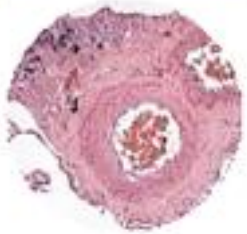
PAH

Group IV

CTPAH

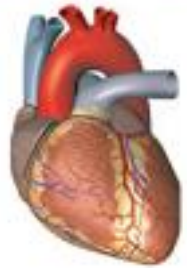
Clinical Classification

Pulmonary arterial hypertension (PAH)



- Idiopathic/heritable
- Associated conditions

PH associated with left heart disease

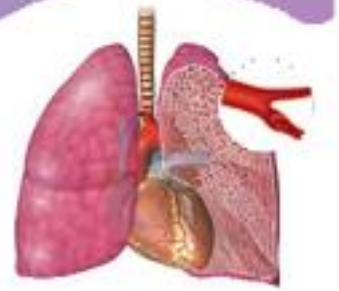


- IpcPH
- CpcPH

PH associated with lung disease

- Non-severe PH
- Severe PH

PH associated with pulmonary artery obstructions



- CTEPH
- Other pulmonary obstructions

PH with unclear and/or multifactorial mechanisms

- Haematological disorders
- Systemic disorders

Therapeutic Strategies

Medical therapy
- PAH drugs
- CCB in responders

Lung transplantation

IpcPH:
- Treatment of LHD[a]

CpcPH:
- Treatment of LHD[a]
- Potentially: PAH drugs (trials)

PH-lung disease:
- Optimized care of underlying lung disease

Severe PH:
- Potentially: PAH drugs (trials)

Surgical therapy:
- PEA

Interventional:
- BPA

Medical therapy:
- PH drugs

Optimized treatment of underlying disease
- Potentially: PAH drugs (trials)

ESC ERS

WHO functional class I

Monotherapy with a PAH-specific agent

PDE5I

ERA

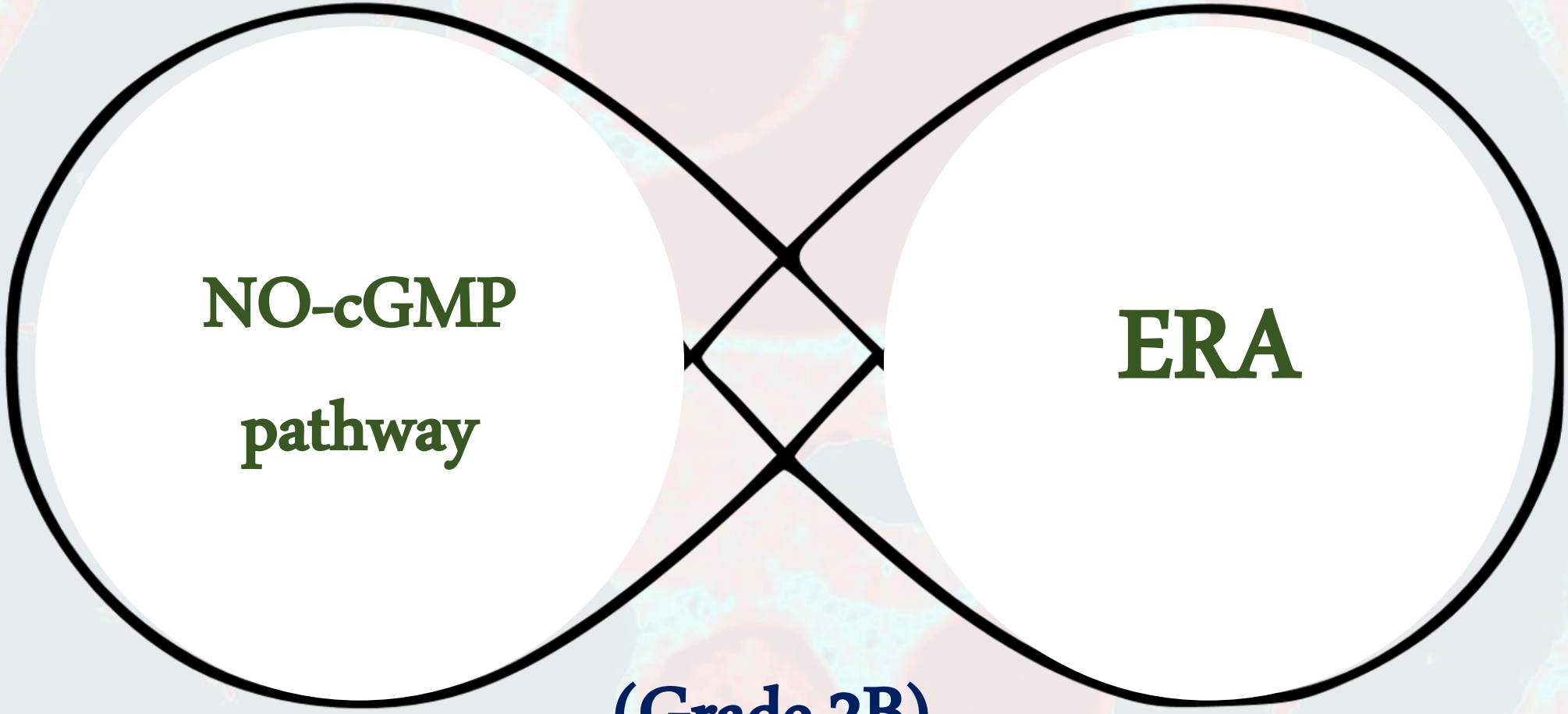
Riociguat

(Grade 2C)

rather than no **treatment**

Barst RJ, Gibbs US, Ghofrani HA, et al. Updated evidence-based treatment algorithm in pulmonary arterial hypertension. J Am Coll Cardiol 2009; 54:S78.

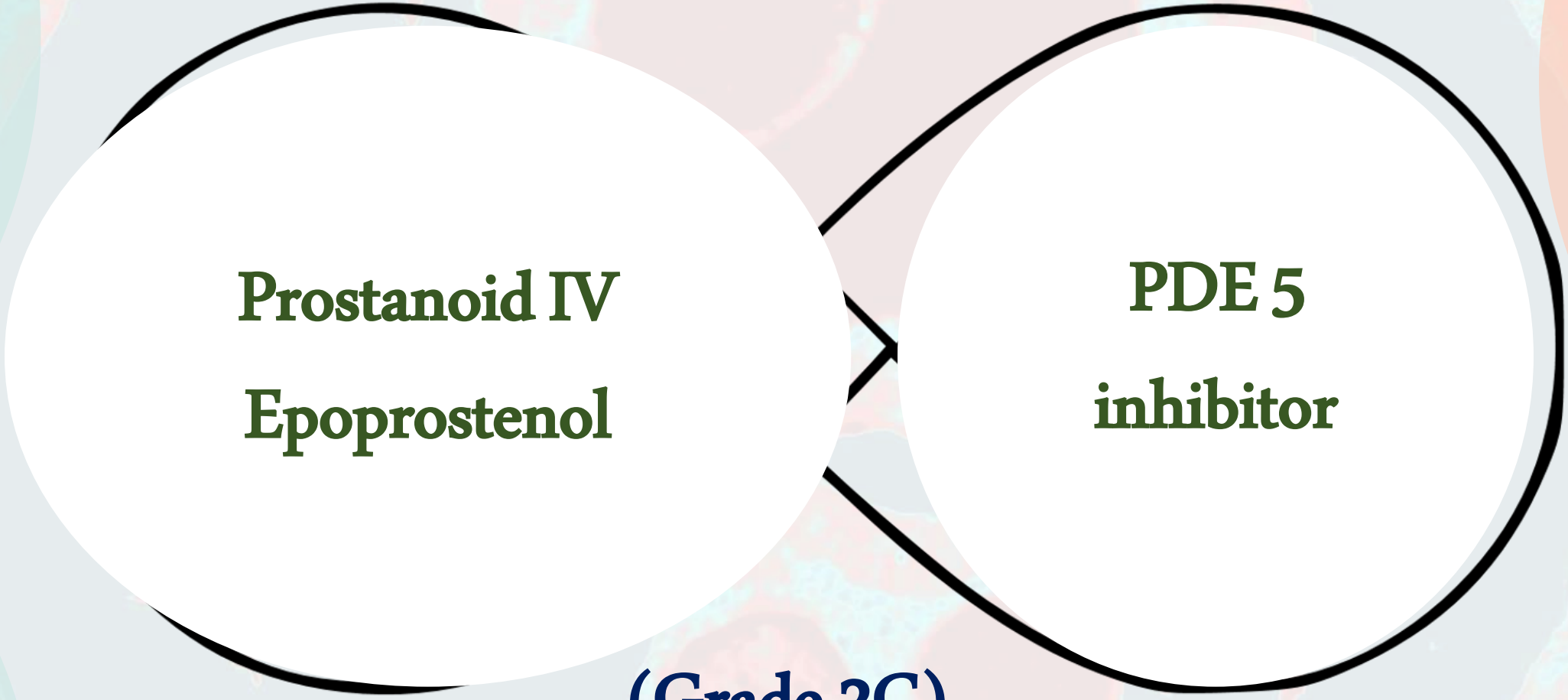
WHO functional class II/III



(Grade 2B)

Barst RJ, Gibbs US, Ghofrani HA, et al. Updated evidence-based treatment algorithm in pulmonary arterial hypertension. J Am Coll Cardiol 2009; 54:S78.

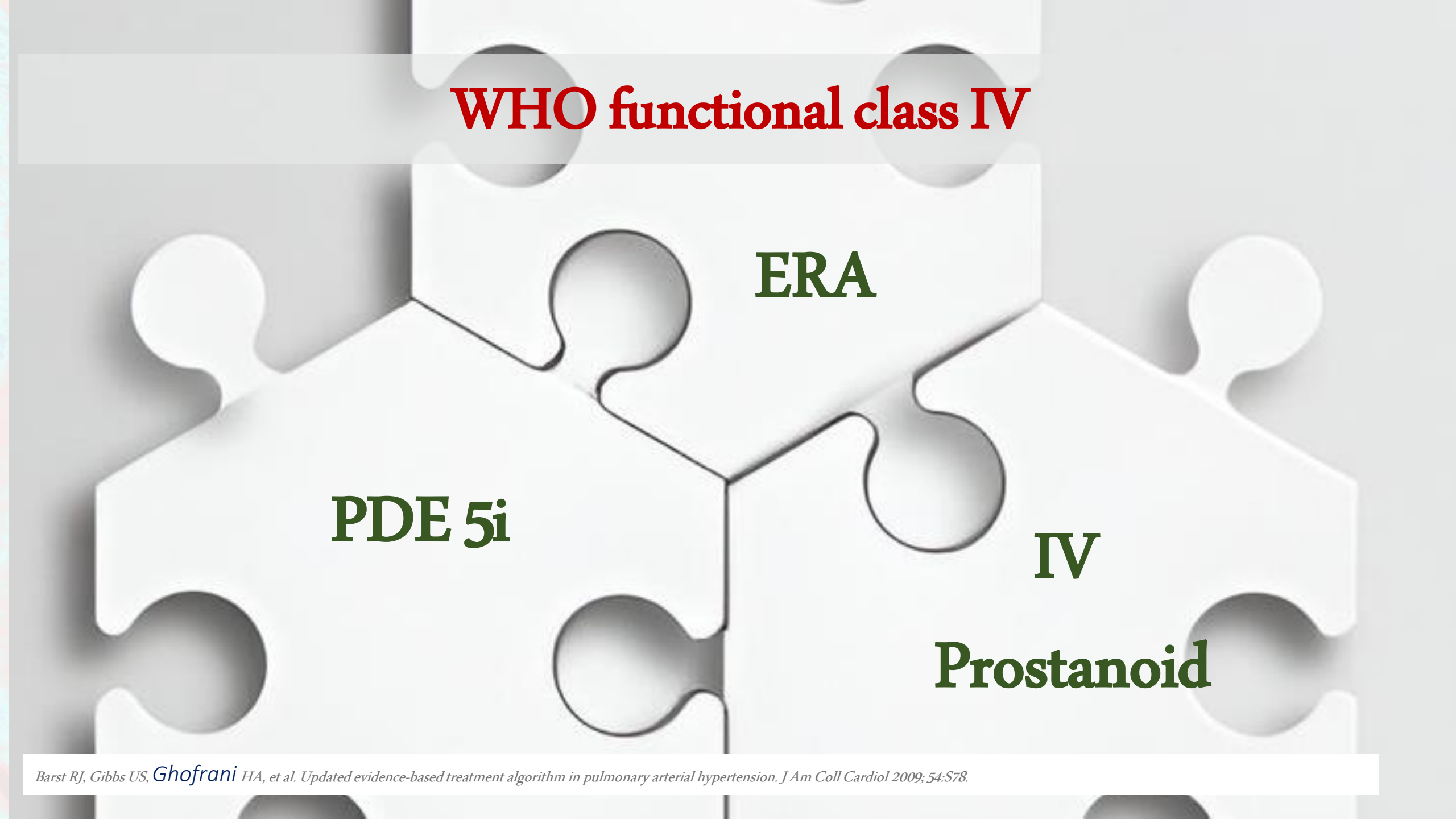
WHO functional class IV



(Grade 2C)

Barst RJ, Gibbs US, Ghofrani HA, et al. Updated evidence-based treatment algorithm in pulmonary arterial hypertension. J Am Coll Cardiol 2009; 54:S78.

WHO functional class IV



Barst RJ, Gibbs US, Ghofrani HA, et al. Updated evidence-based treatment algorithm in pulmonary arterial hypertension. J Am Coll Cardiol 2009; 54:S78.

SUCCESS

The management of Pulmonary Hypertension

1. Identify Groups
2. Identify Classes
3. PAH-directed therapy

4. Supportive therapy

Supportive Therapy

Oral Anticoagulants

Diuretics

Digoxin

Exercise rehabilitation

1A

حدد الخيار الخطأ فيما يلي:

A. فائدة تمارين اللياقة البدنية في مرضي ارتفاع ضغط الشريان الرئوي المستقرين على العلاج الدوائي كبيرة

B. ينبغي الانتباه للأمراض القلبية المرافقة للمرضى المصابين بارتفاع ضغط الشريان الرئوي من حيث التشخيص والعلاج.

C. ينبغي تقديم العلاج القلبي المثالي لمرضى المجموعة الثانية قبل أن يتم النظر في تقييم ارتفاع ضغط الدم الرئوي لديهم.

D. يستطب إعطاء PDE5i في مرضي قصور القلب المحافظ على الجزء المقذوف بشكل جيد Heart failure with preserved ejection fraction ولديهم ارتفاع بضغط الشريان الرئوي

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A	10
B	0
C	12
D	22

Clinical classification of PH

(updated)

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[a]

1.3 Associated with drugs and toxins[a]

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

European Respiratory Journal Jan 2022, 2200879; **DOI:** 10.1183/13993003.00879-2022

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

European Respiratory Journal Jan 2022, 2200879; **DOI:** 10.1183/13993003.00879-2022

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

(LAM)

European Respiratory Journal Jan 2022, 2200879; **DOI:** 10.1183/13993003.00879-2022

GROUP 5 PH with unclear and/or multifactorial 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

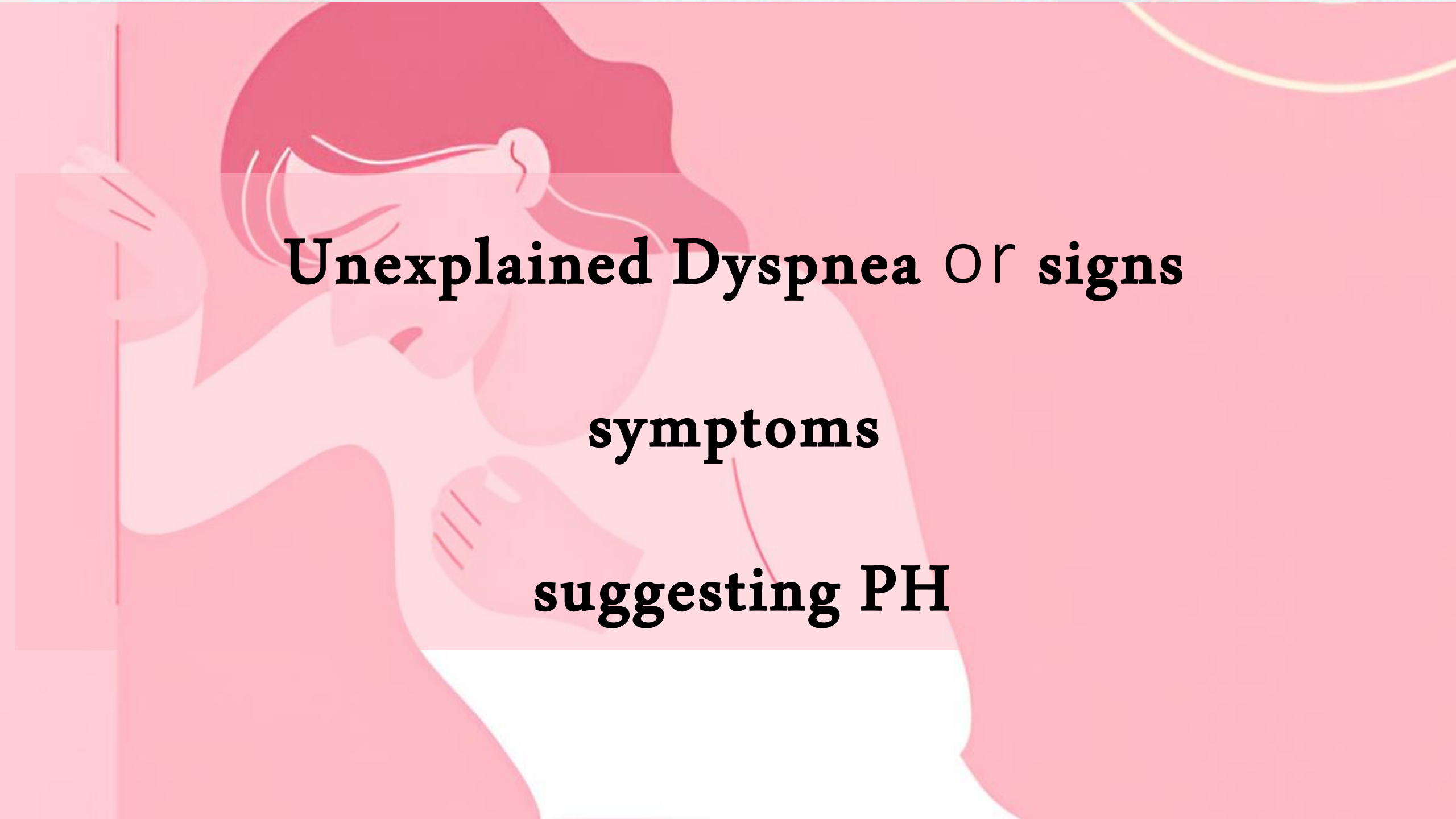
5.6 Fibrosing mediastinitis

European Respiratory Journal Jan 2022, 2200879; **DOI:** 10.1183/13993003.00879-2022

Diagnostic algorithm steps for PH

Step 1

Suspicion



Unexplained Dyspnea or signs

symptoms

suggesting PH

Early

Late

Symptoms

- Dyspnoea on exertion (WHO-FC)
- Fatigue and rapid exhaustion
- Dyspnoea when bending forward (bendopnoea)
- Palpitations
- Haemoptysis
- Exercise-induced abdominal distension and nausea
- Weight gain due to fluid retention
- Syncope (during or shortly after physical exertion)

Rare symptoms due to pulmonary artery dilation[a]

- Exertional chest pain:
  dynamic compression of the left main coronary artery
- Hoarseness (dysphonia):
  compression of the left laryngeal recurrent nerve
  (cardiovocal or Ortner´s syndrome)
- Shortness of breath, wheezing, cough, lower respiratory tract infection, atelectasis:
  compression of the bronchi

ESC ERS

Signs of PH

- Central, peripheral, or mixed cyanosis
- Accentuated pulmonary component of the second heart sound
- RV third heart sound
- Systolic murmur of tricuspid regurgitation
- Diastolic murmur of pulmonary regurgitation

Signs of RV backward failure

- Distended and pulsating jugular veins
- Abdominal distension
- Hepatomegaly
- Ascites
- Peripheral oedema

Signs pointing towards underlying cause of PH

- Digital clubbing: Cyanotic CHD, fibrotic lung disease, bronchiectasis, PVOD, or liver disease
- Differential clubbing/cyanosis: PDA/Eisenmenger's syndrome
- Auscultatory findings (crackles or wheezing, murmurs): lung or heart disease
- Sequelae of DVT, venous insufficiency: CTEPH
- Telangiectasia: HHT or SSc
- Sclerodactyly, Raynaud's phenomenon, digital ulceration, GORD: SSc

Signs of RV forward failure

- Peripheral cyanosis (blue lips and tips)
- Dizziness
- Pallor
- Cool extremities
- Prolonged capillary refill

ESC ERS

Prognosis


Prognosis
Estimated
one year - Mortality

Determinants of prognosis (estimated 1-year mortality)	Low risk (5%)	Intermediate risk (5–20%)	High risk (20%)
Clinical observations and modifiable variables			

Eur Respir Rev 2013; 22: 526–534 | DOI: 10.1183/09059180.00006313

Determinants of prognosis (estimated 1-year mortality)	Low risk (5%)	Intermediate risk (5–20%)	High risk (20%)
Clinical observations and modifiable variables			
Signs of right HF	Absent	Absent	Present
Progression of symptoms and clinical manifestations	No	Slow	Rapid

Eur Respir Rev 2013; 22: 526–534 | DOI: 10.1183/09059180.00006313

Determinants of prognosis (estimated 1-year mortality)	Low risk (5%)	Intermediate risk (5–20%)	High risk (20%)
Clinical observations and modifiable variables			
Syncope	No	Occasional syncope	Repeated syncope
WHO-FC	I, II	III	IV
6MWDC	>440 m	165-440 m	<165 m
CPET	Peak VO2 >15 mL/min/kg (>65% pred.) VE/CO2 slope <36	Peak VO2 11-15 mL/min/kg (35-65% pred.) VE/CO2 slope 36-44	Peak VO2 <11 mL/min/kg (<35% pred.) VE/VCO2 slope >44

Eur Respir Rev 2013; 22: 526–534 | DOI: 10.1183/09059180.00006313

حدد الخيار الخطأ فيما يلي: ارتفاع ضغط الشريان الرئوي

A. يفيد استجواب المريض عن حالة الغشي syncope في تقدير تطور اصابته

B. لا يعتبر اختبار المشي 6 دقائق 6MWD معيارا مهما في تقييم شدة الاصابة ولا يفيد في مناطرة المريض المصاب.

C. يصنف المريض الذي يشكو من زلة تنفسية أثناء الراحة [class IV] من المرضى عالي الخطورة

D. يفيد إيكو القلب الدوري في متابعة تطور حالة المريض

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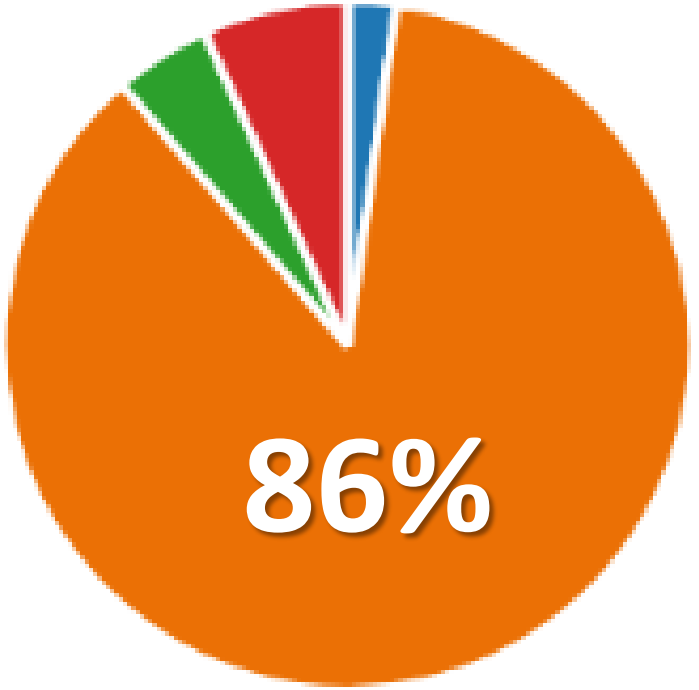
لا يعتبر اختبار المشي 6 دقائق 6MWD معيارا مهما في تقييم شدة الاصابة ولا يفيد في مناطرة المريض المصاب.

A	1
B	38
C	2
D	3

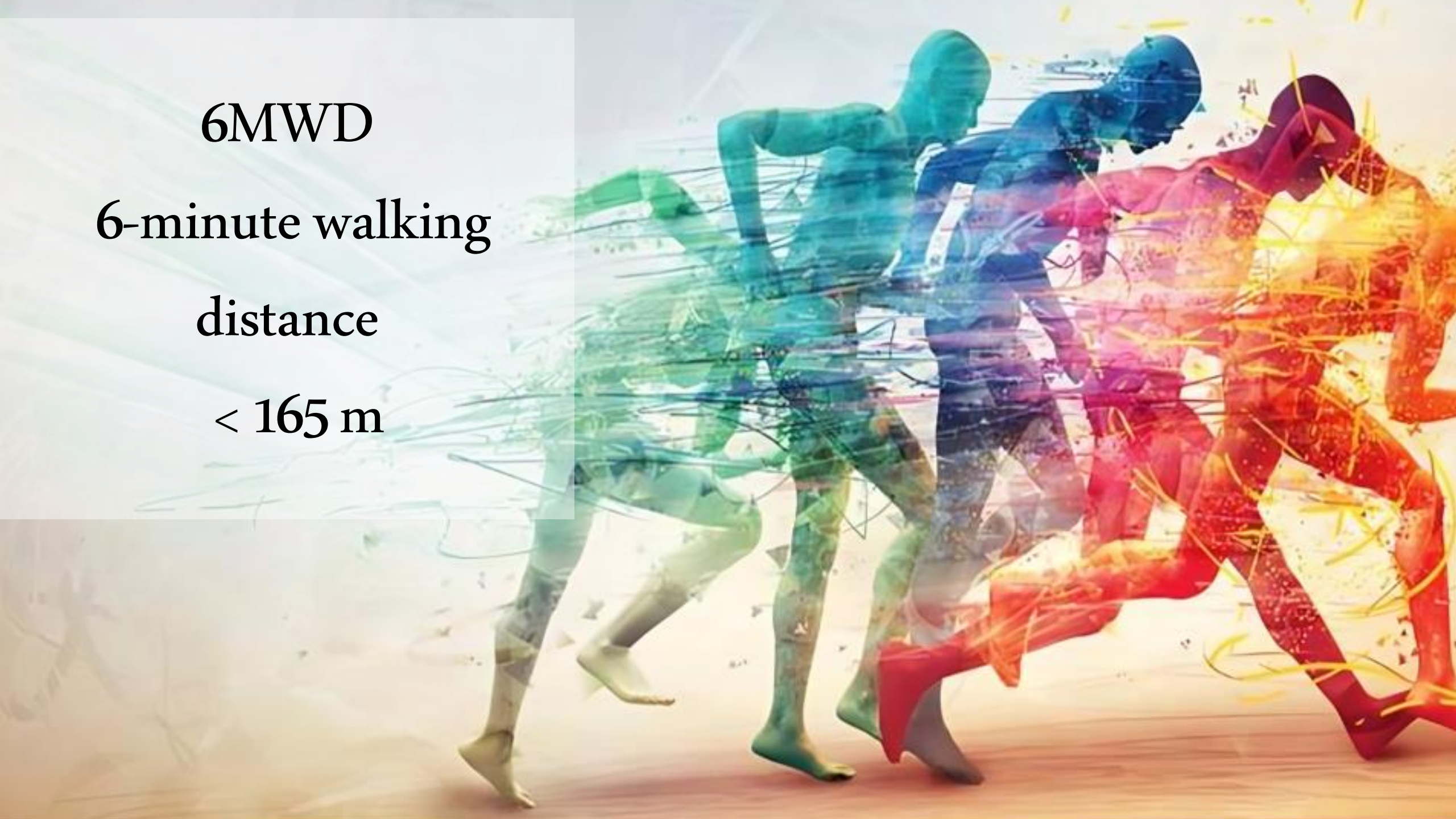


6MWD

6-minute walking

distance

< 165 m

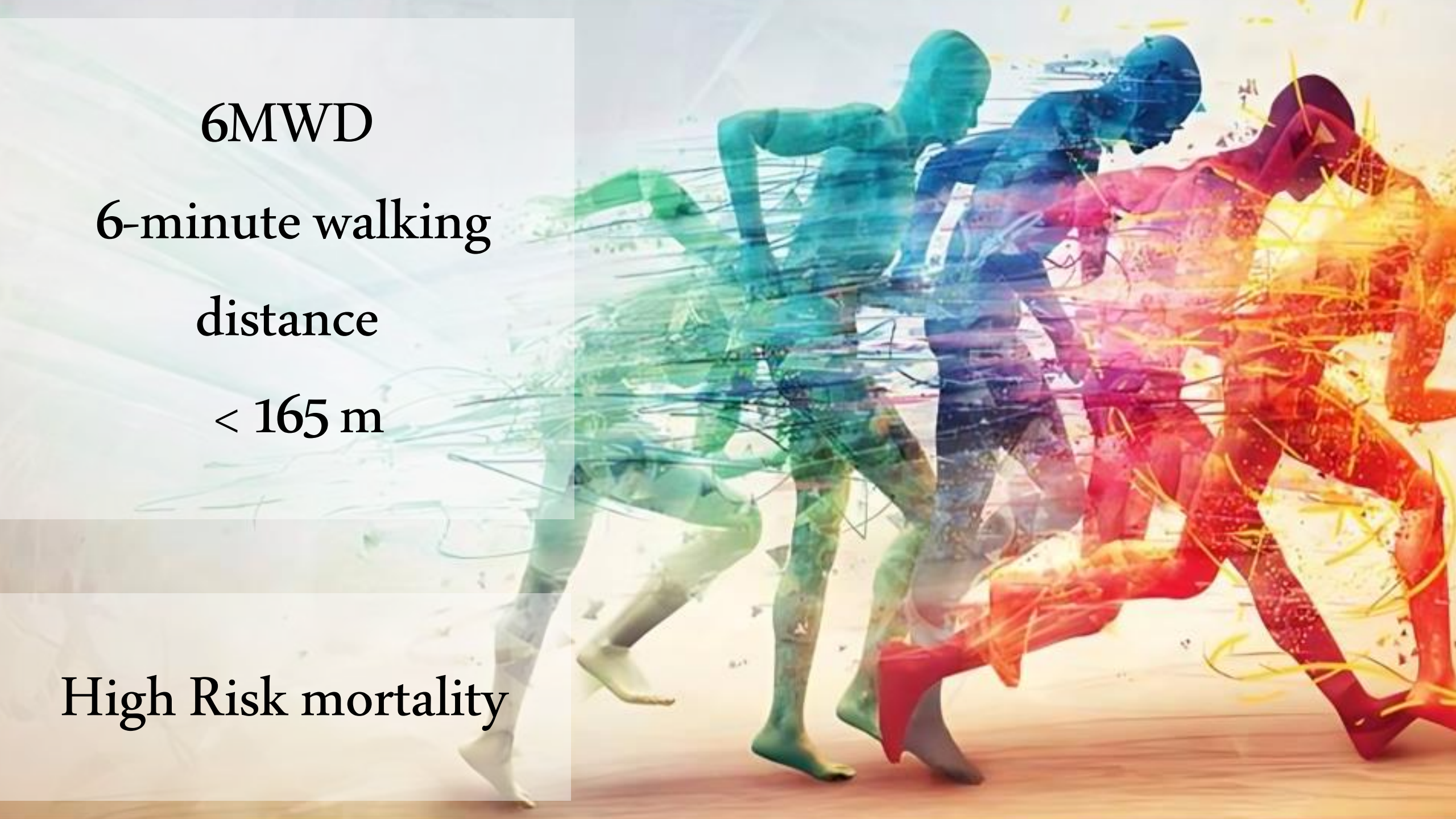


6MWD

6-minute walking

distance

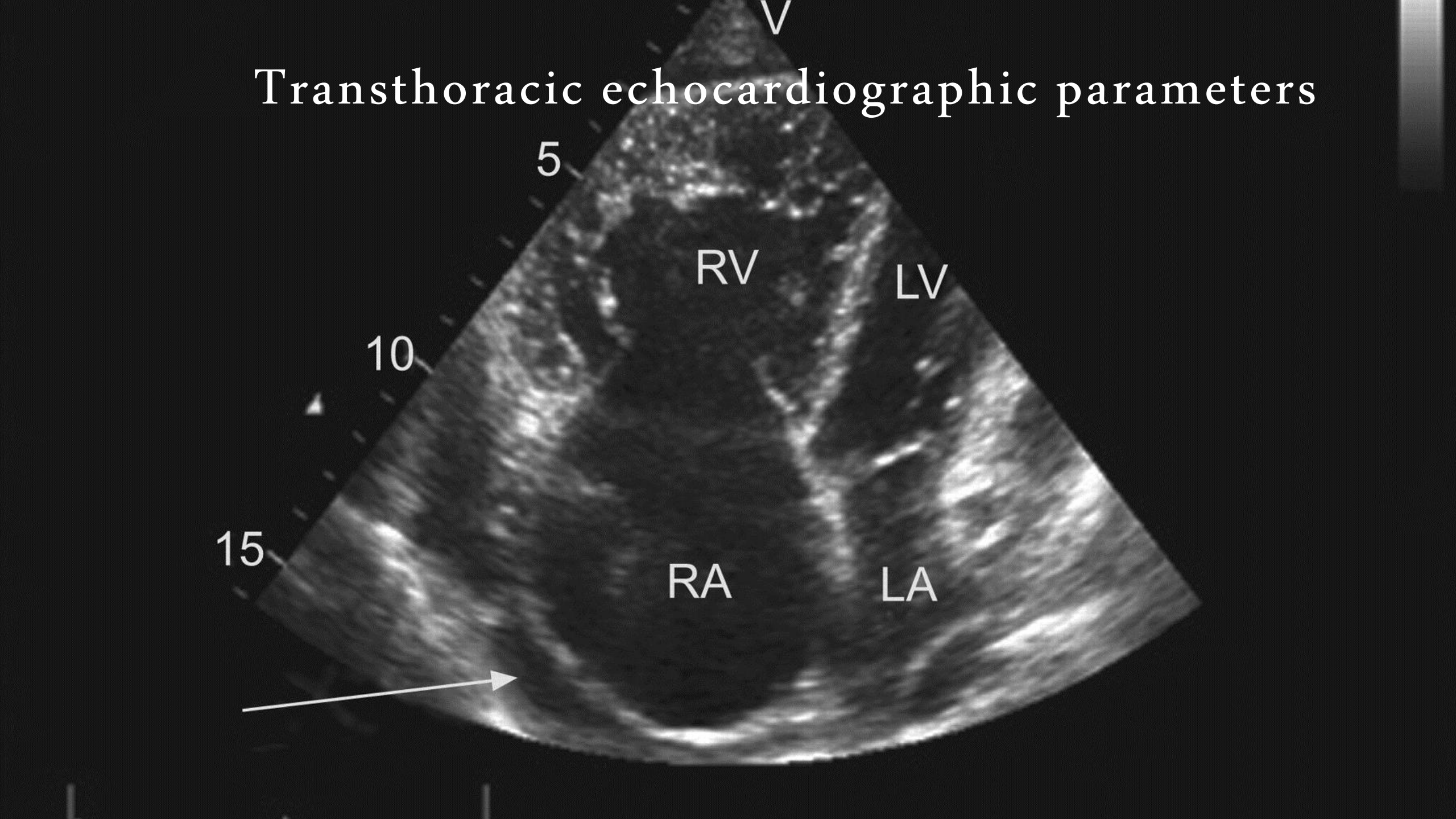
< 165 m



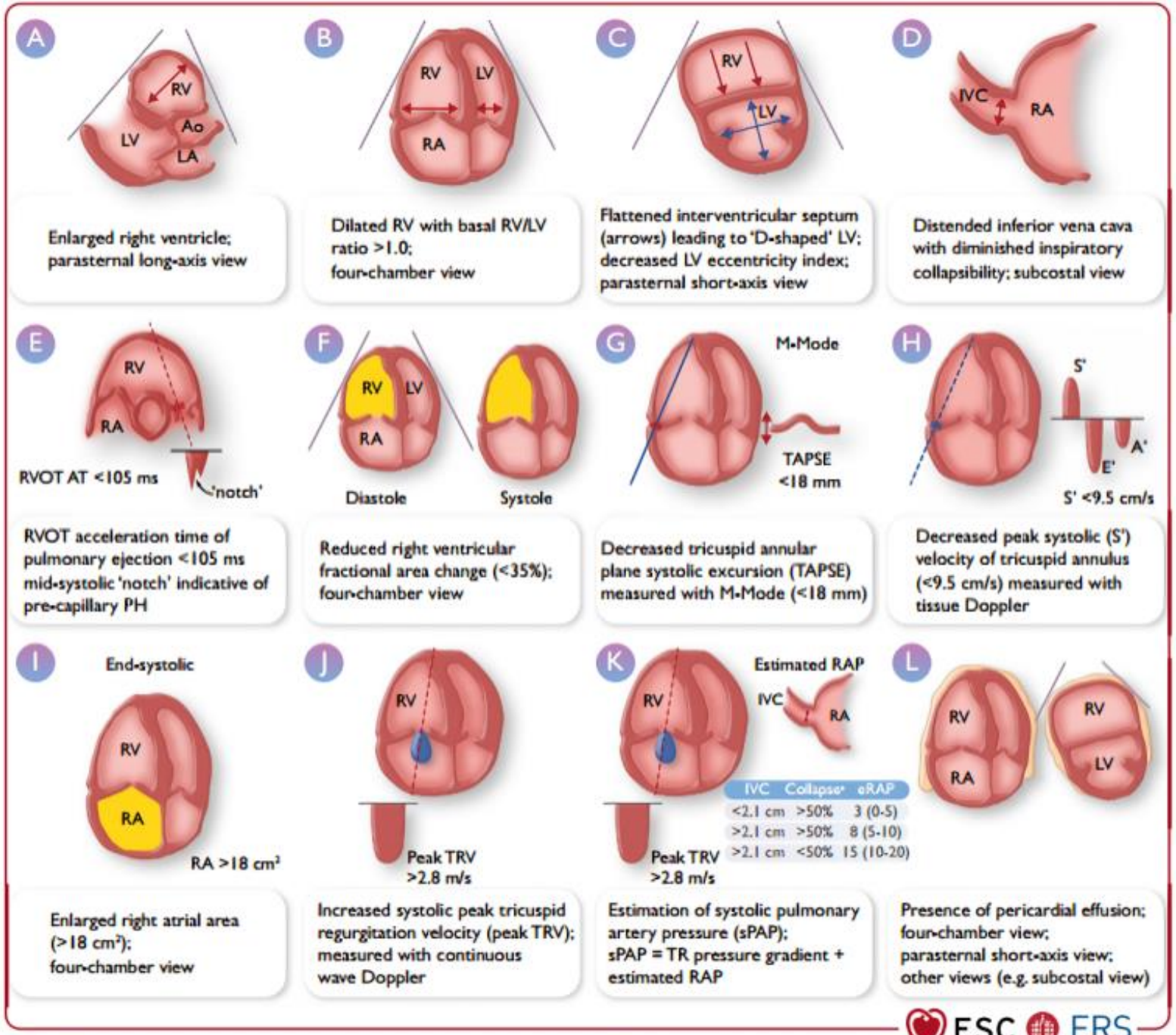
High Risk mortality

Step 2 Detection

Transthoracic echocardiographic parameters



Echo


A
RV
Ao
LV
LA
Enlarged right ventricle; parasternal long-axis view
B
RV
LV
RA
Dilated RV with basal RV/LV ratio >1.0; four-chamber view
C
RV
LV
Flattened interventricular septum (arrows) leading to 'D-shaped' LV; decreased LV eccentricity index; parasternal short-axis view
D
IVC
RA
Distended inferior vena cava with diminished inspiratory collapsibility; subcostal view
E
RV
RA
RVOT AT <105 ms
'notch'
RVOT acceleration time of pulmonary ejection <105 ms mid-systolic 'notch' indicative of pre-capillary PH
F
RV
LV
RA
Diastole
Systole
Reduced right ventricular fractional area change (<35%); four-chamber view
G
M-Mode
TAPSE
<18 mm
Decreased tricuspid annular plane systolic excursion (TAPSE) measured with M-Mode (<18 mm)
H
S'
E'
A'
S' <9.5 cm/s
Decreased peak systolic (S') velocity of tricuspid annulus (<9.5 cm/s) measured with tissue Doppler
I
End-systolic
RV
RA
RA >18 cm²
Enlarged right atrial area (>18 cm²); four-chamber view
J
RV
Peak TRV
>2.8 m/s
Increased systolic peak tricuspid regurgitation velocity (peak TRV); measured with continuous wave Doppler
K
RV
Estimated RAP
IVC
RA
IVC Collapse eRAP
<2.1 cm >50% 3 (0-5)
>2.1 cm >50% 8 (5-10)
>2.1 cm <50% 15 (10-20)
Peak TRV
>2.8 m/s
Estimation of systolic pulmonary artery pressure (sPAP); sPAP = TR pressure gradient + estimated RAP
L
RV
RA
RV
LV
Presence of pericardial effusion; four-chamber view; parasternal short-axis view; other views (e.g. subcostal view)
ESC ERS

Echo

Determinants of prognosis (estimated 1-year mortality)		
Low risk (5%)	Intermediate risk (5–20%)	High risk (20%)

Eur Respir Rev 2013; 22: 526–534 | DOI: 10.1183/09059180.00006313

	Determinants of prognosis (estimated 1-year mortality)		
	Low risk (5%)	Intermediate risk (5–20%)	High risk (20%)
Echo ♥	RA area 18 cm2	RA area 18–26 cm2	RA area 26 cm2

Eur Respir Rev 2013; 22: 526–534 | DOI: 10.1183/09059180.00006313

Echo

Determinants of prognosis (estimated 1-year mortality)		
Low risk (5%)	Intermediate risk (5–20%)	High risk (20%)
RA area:18 cm2	RA area 18–26 cm2	RA area .26 cm2
TAPSE/sPAP 0.32 mm/mmHg	TAPSE/sPAP 0.19–0.32 mm/mmHg	TAPSE/sPAP 0.19 mm/mmHg

Eur Respir Rev 2013; 22: 526–534 | DOI: 10.1183/09059180.00006313

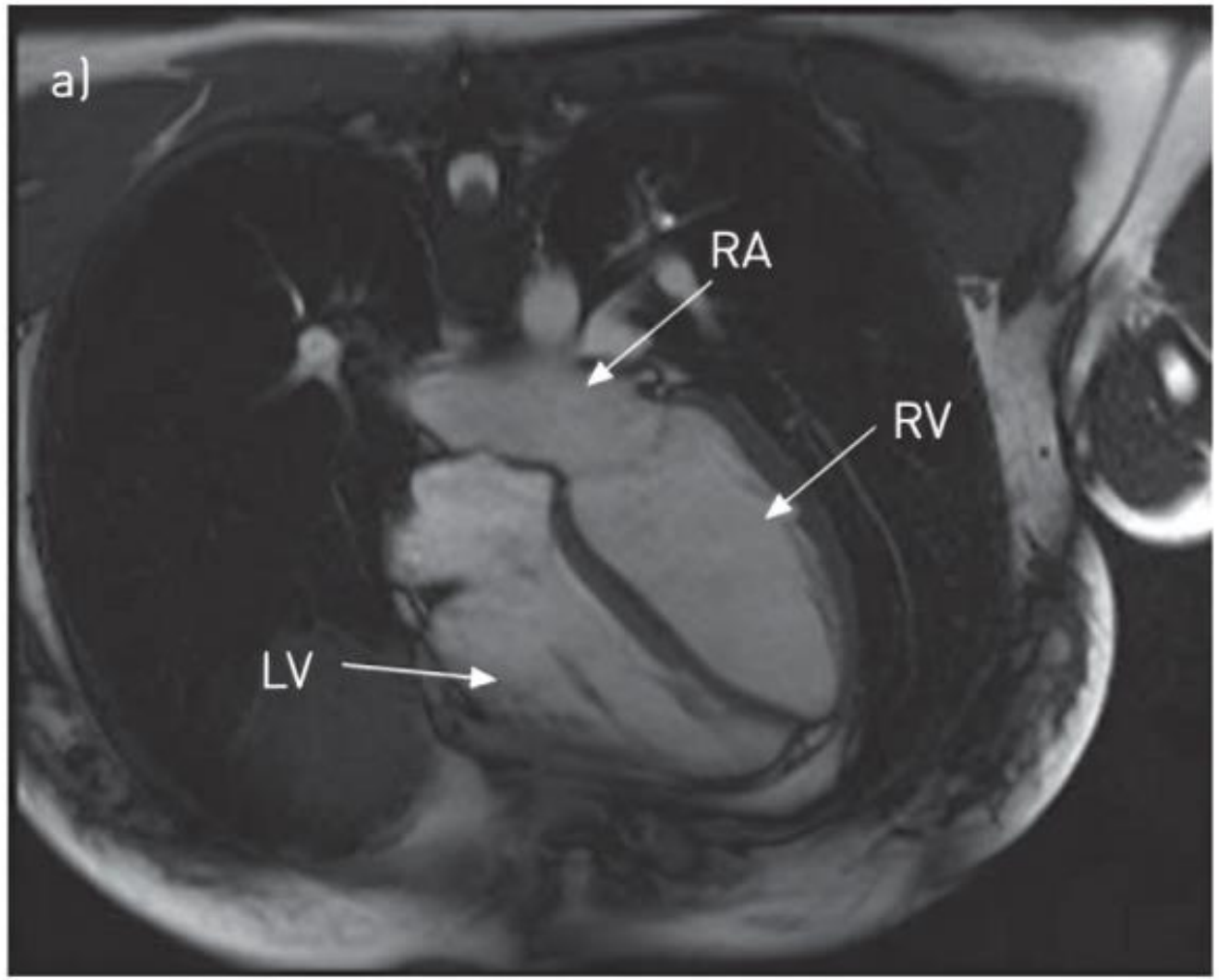
	Determinants of prognosis (estimated 1-year mortality)		
	Low risk (5%)	Intermediate risk (5–20%)	High risk (20%)
Echo ♥	RA area:18 cm2	RA area 18–26 cm2	RA area .26 cm2
	TAPSE/sPAP 0.32 mm/mmHg	TAPSE/sPAP 0.19–0.32 mm/mmHg	TAPSE/sPAP 0.19 mm/mmHg
	No pericardial effusion	Minimal pericardial effusion	Moderate or large pericardial effusion

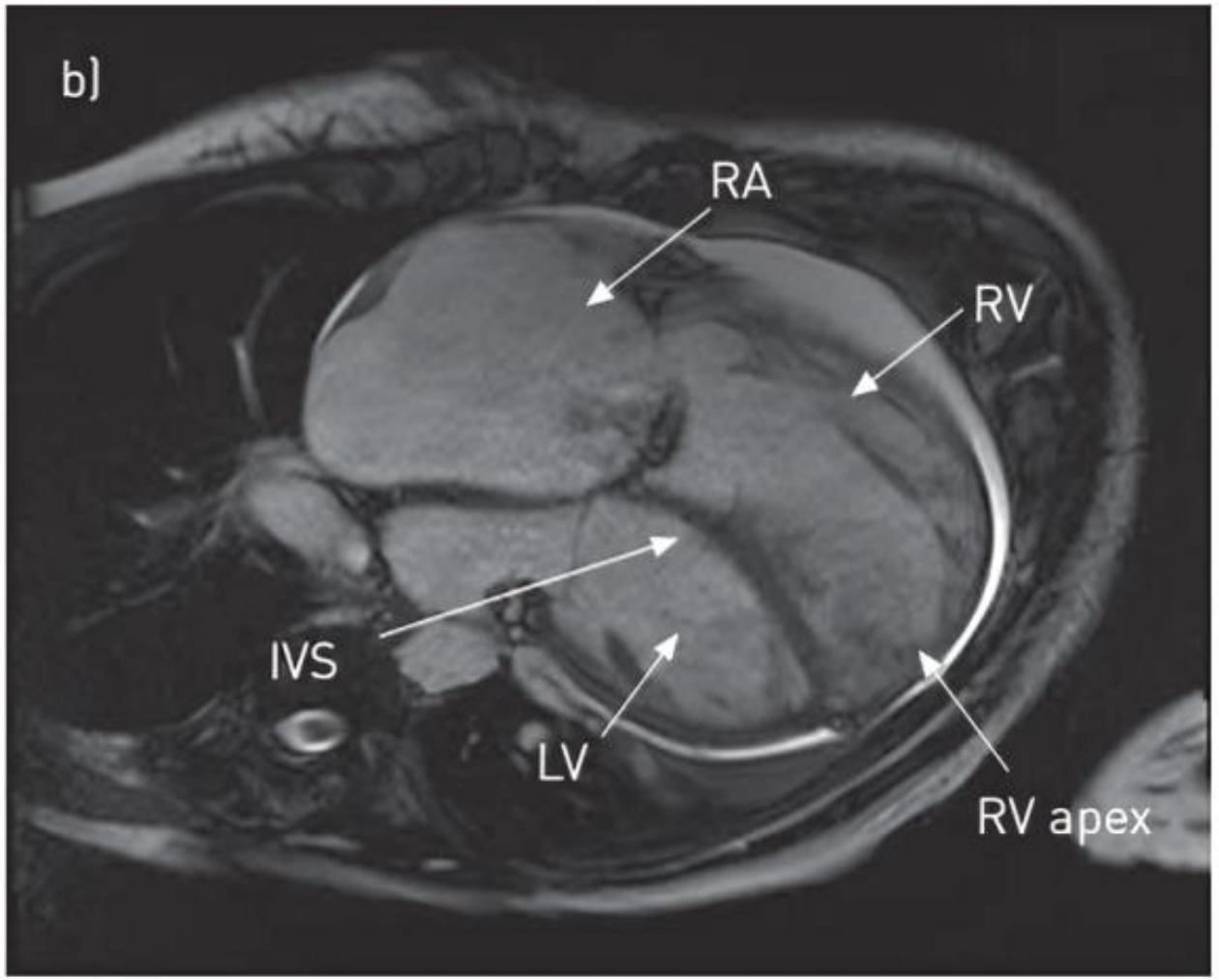
Eur Respir Rev 2013; 22: 526–534 | DOI: 10.1183/09059180.00006313

Cardiac magnetic resonance imaging

Eur Respir Rev 2013; 22: 526–534 | DOI: 10.1183/09059180.00006313

Cardiac magnetic resonance imaging





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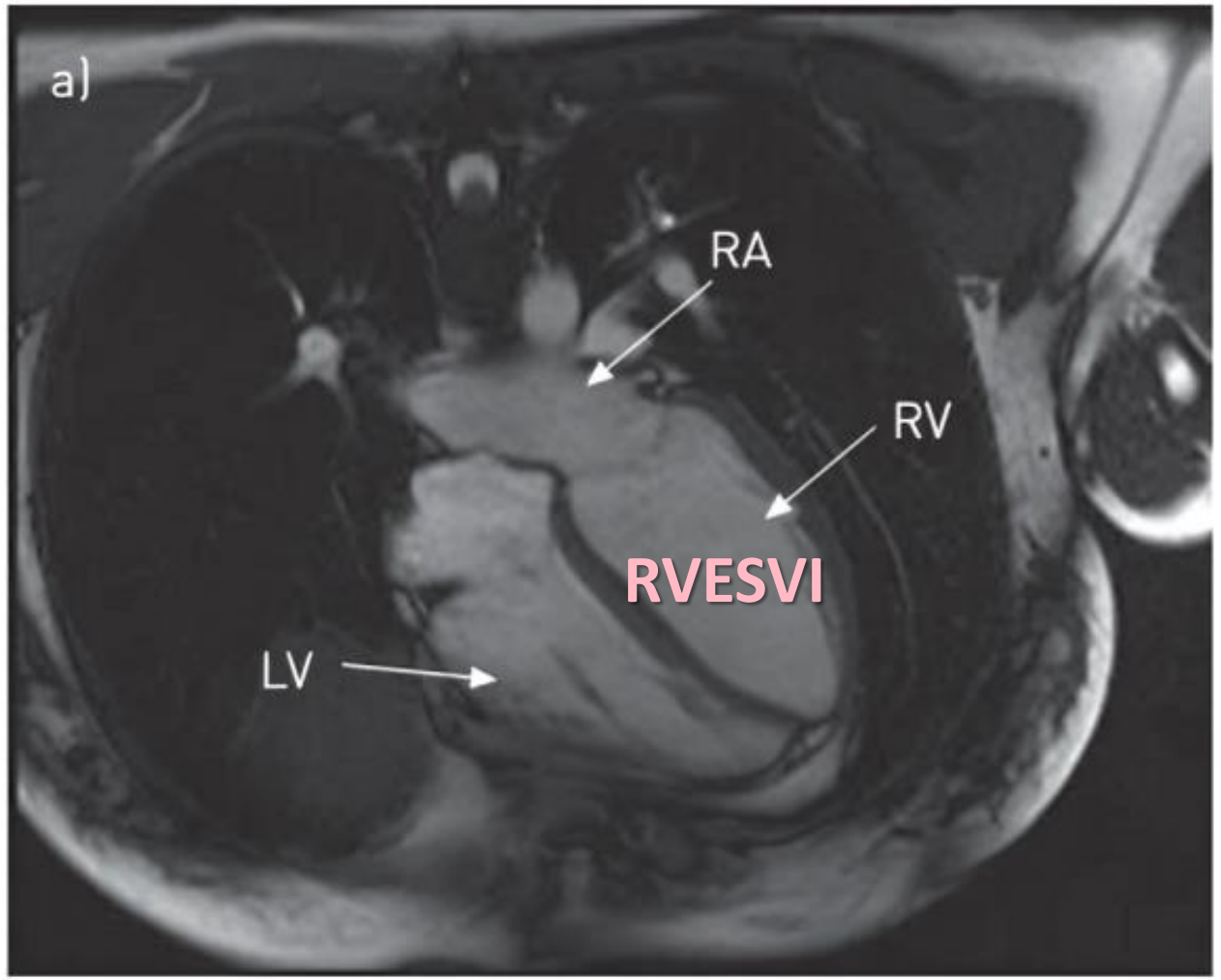
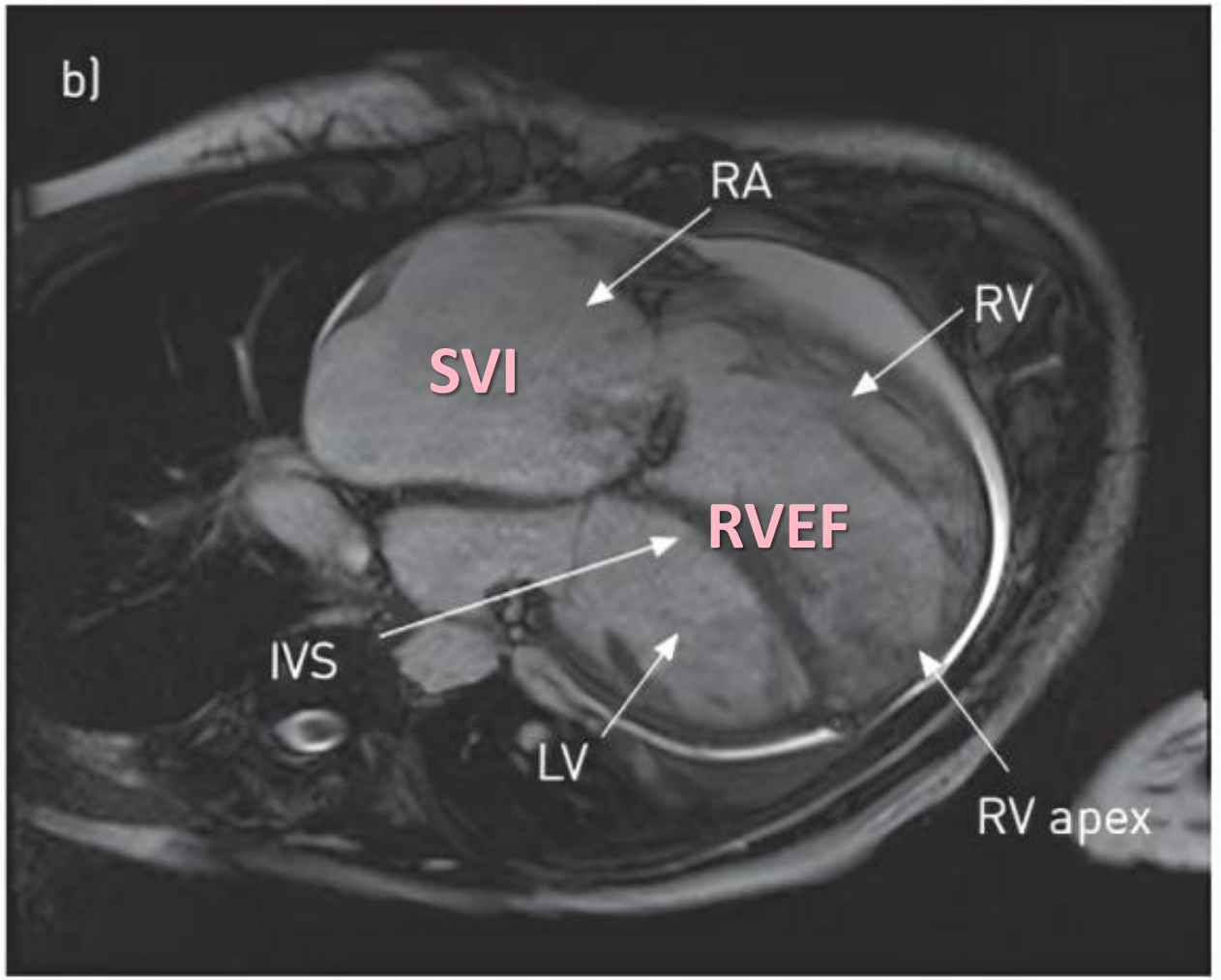
Cardiac magnetic resonance imaging





Eur Respir Rev 2013; 22: 526–534 | DOI: 10.1183/09059180.00006313

	Determinants of prognosis (estimated 1-year mortality)		
cMRI	Low risk (5%)	Intermediate risk (5–20%)	High risk (20%)
	RVEF : 54%	**RVEF: 37–54%**	**RVEF: 37%**
	SVI:40 mL/m2	**SVI: 26–40** mL/m2	**SVI: 26** mL/m2
	RVESVI: 42 mL/m2	**RVESVI 42–54** mL/m2	**RVESVI: 54** mL/m2

Eur Respir Rev 2013; 22: 526–534 | DOI: 10.1183/09059180.00006313

حدد الخيار الصحيح فيما يلي: ارتفاع ضغط الشريان الرئوي:

A. لا يوجد استطباب لمرنان القلب المغناطيسي CMRI في متابعة تطور حالة المريض ومناطرته

B. ليس لقثطرة القلب الأيمن دورا في مناطرة المريض المصاب

C. لا يؤثر تطور انصباب تامور على إنذار المريض

D. لا يفيد معايرة NT-proBNP في مناطرة المريض المصاب

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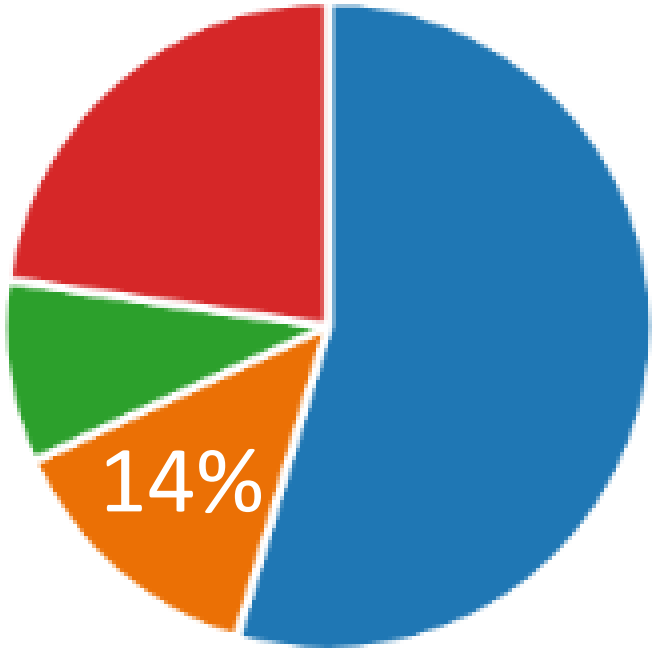
D. لا يفيد معايرة NT-proBNP في مناطرة المريض المصاب

ليس لقثطرة القلب الأيمن دورا في مناطرة المريض المصاب

A	24
B	6
C	4
D	10



	Determinants of prognosis (estimated 1-year mortality)		
Biomarkers: BNP or NT-proBNP	**Low risk (5%)**	**Intermediate risk (5–20%)**	**High risk (20%)**

Kylhammar D, Hesselstrand R, Nielsen S, Scheele C, Radegran G. Angiogenic and inflammatory biomarkers for screening and follow-up in patients with pulmonary arterial hypertension. Scand J Rheumatol 2018; 47:319–324

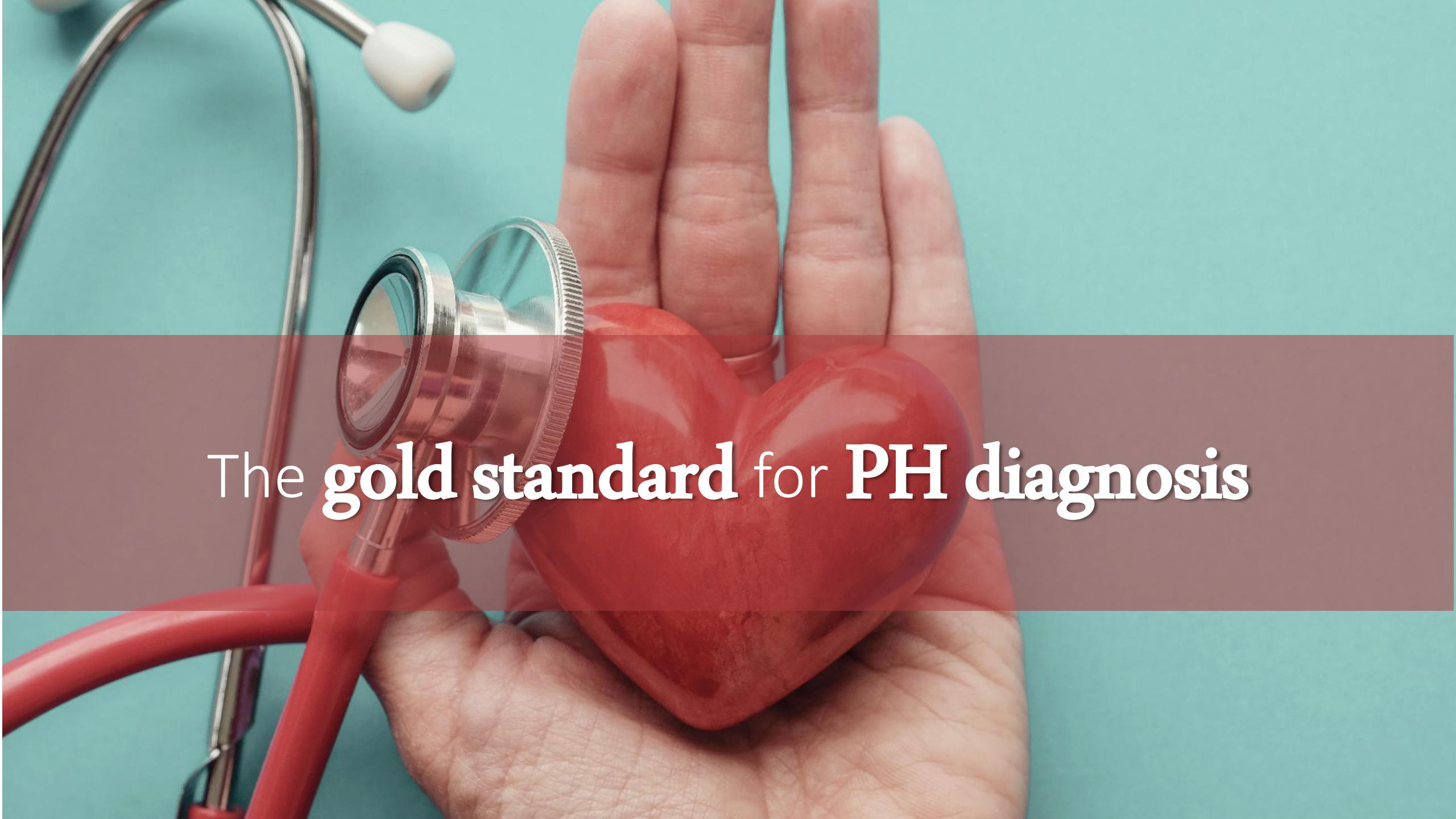
	Determinants of prognosis (estimated 1-year mortality)		
Biomarkers: BNP or NT-proBNP	**Low risk (5%)**	**Intermediate risk (5–20%)**	**High risk (20%)**
	BNP 50 ng/L	**BNP 50–800 ng/L**	**BNP > 800 ng/L**

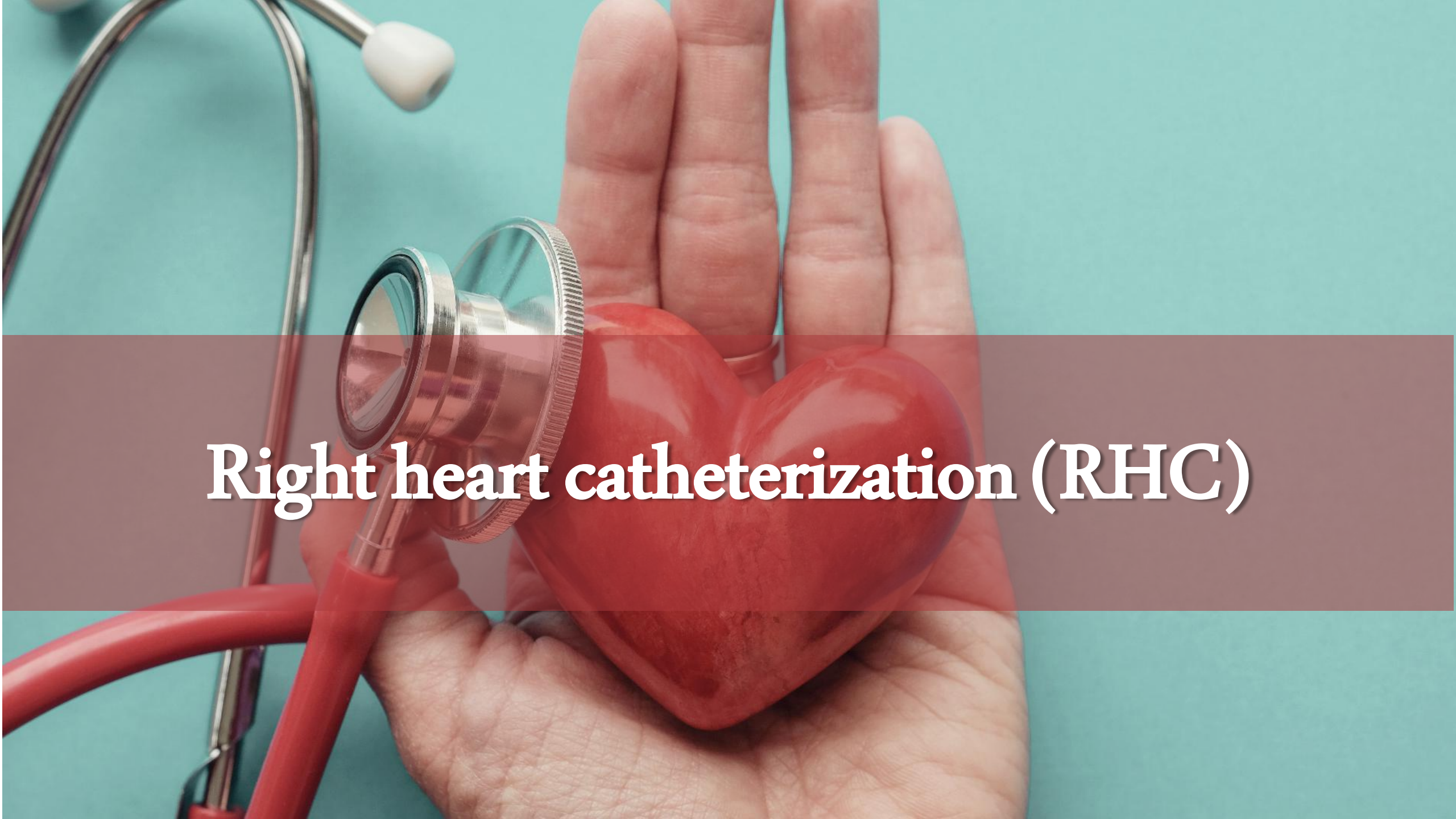
Kylhammar D, Hesselstrand R, Nielsen S, Scheele C, Radegran G. Angiogenic and inflammatory biomarkers for screening and follow-up in patients with pulmonary arterial hypertension. Scand J Rheumatol 2018; 47:319–324

	Determinants of prognosis (estimated 1-year mortality)		
Biomarkers: BNP or NT-proBNP	**Low risk (5%)**	**Intermediate risk (5–20%)**	**High risk (20%)**
	BNP 50 ng/L	**BNP 50–800 ng/L**	**BNP > 800 ng/L**
	NT-proBNP < 300 ng/L	**NT-proBNP 300–1100 ng/L**	**NT-proBNP >1100 ng/L**

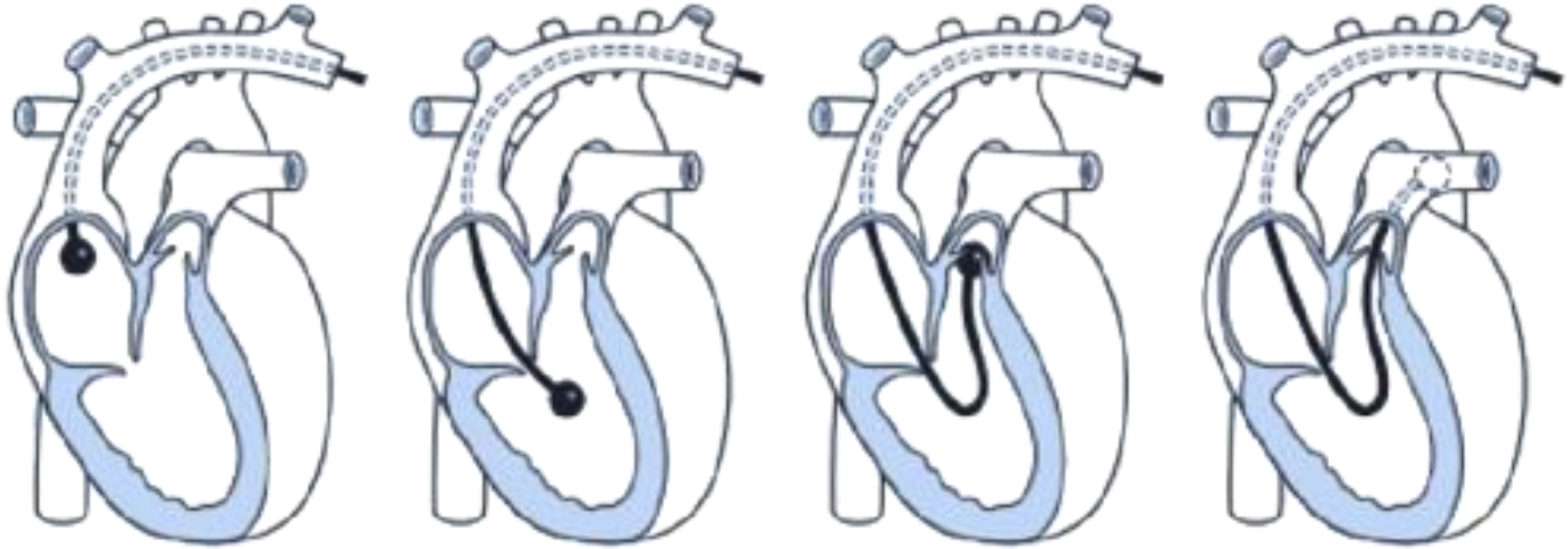
Kylhammar D, Hesselstrand R, Nielsen S, Scheele C, Radegran G. Angiogenic and inflammatory biomarkers for screening and follow-up in patients with pulmonary arterial hypertension. Scand J Rheumatol 2018; 47:319–324

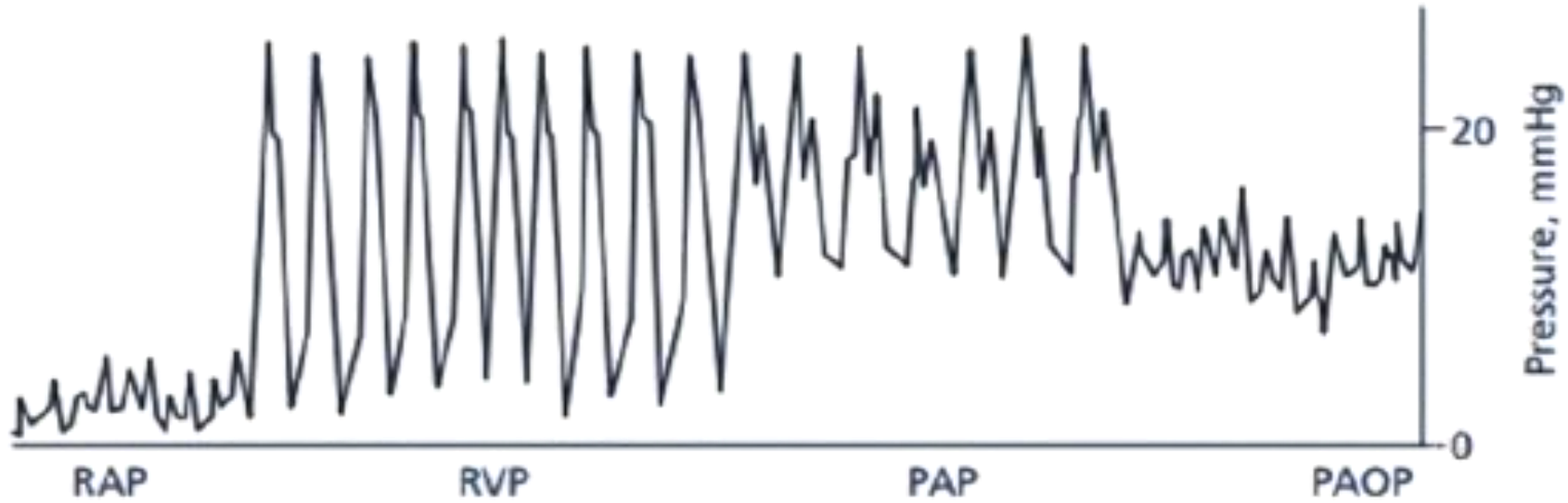
Step 3 Confirmation


The gold standard for PH diagnosis



Right heart catheterization (RHC)


Right atrium
Right ventricle
Pulmonary artery
Occluded pulmonary artery


20
0
Pressure, mmHg
RAP
RVP
PAP
PAOP

RHC: Recommendation

Confirming the diagnosis of PH

RHC: Recommendation

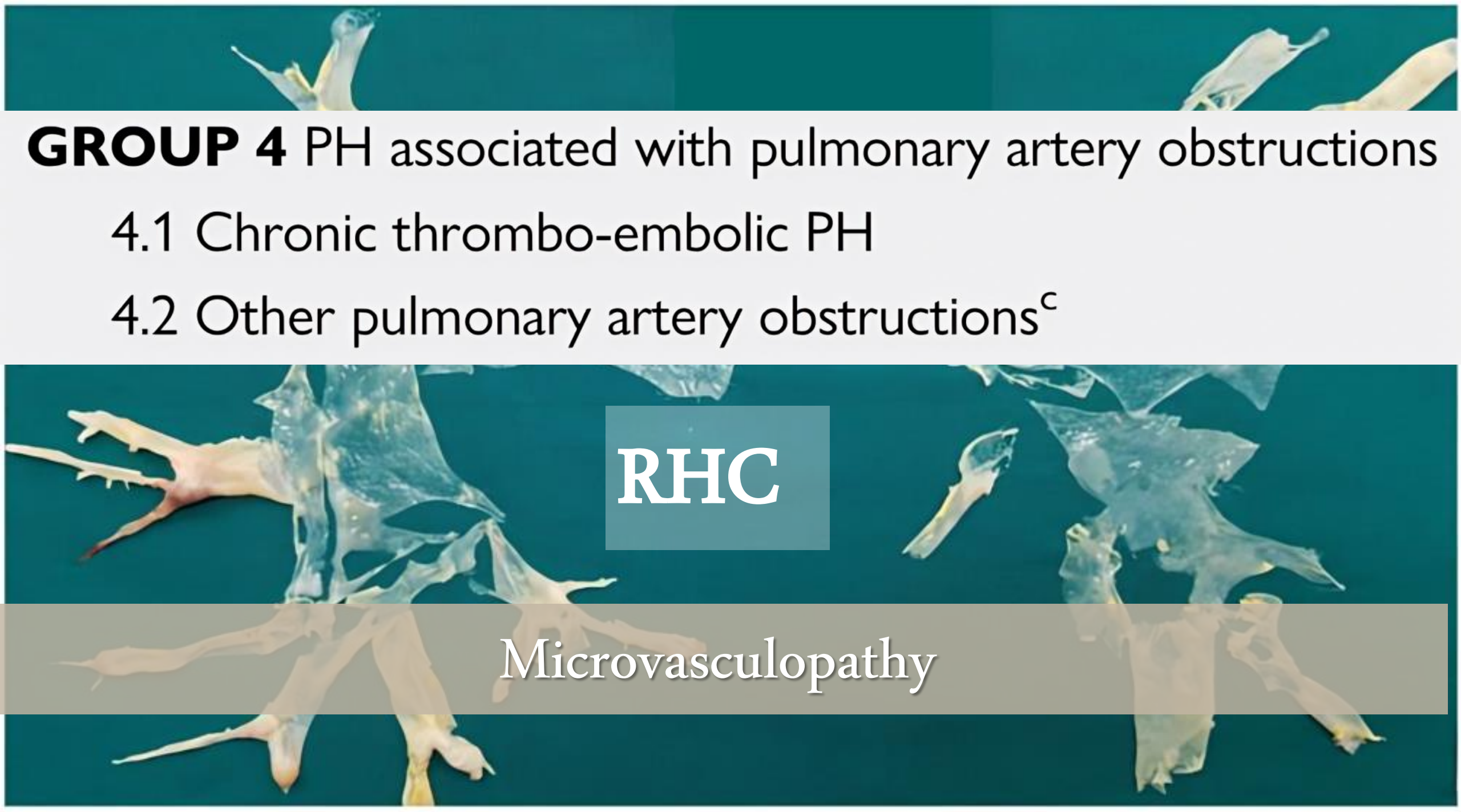
Confirming the diagnosis of PH

Support treatment decisions

GROUP 1 Pulmonary arterial hypertension (PAH)

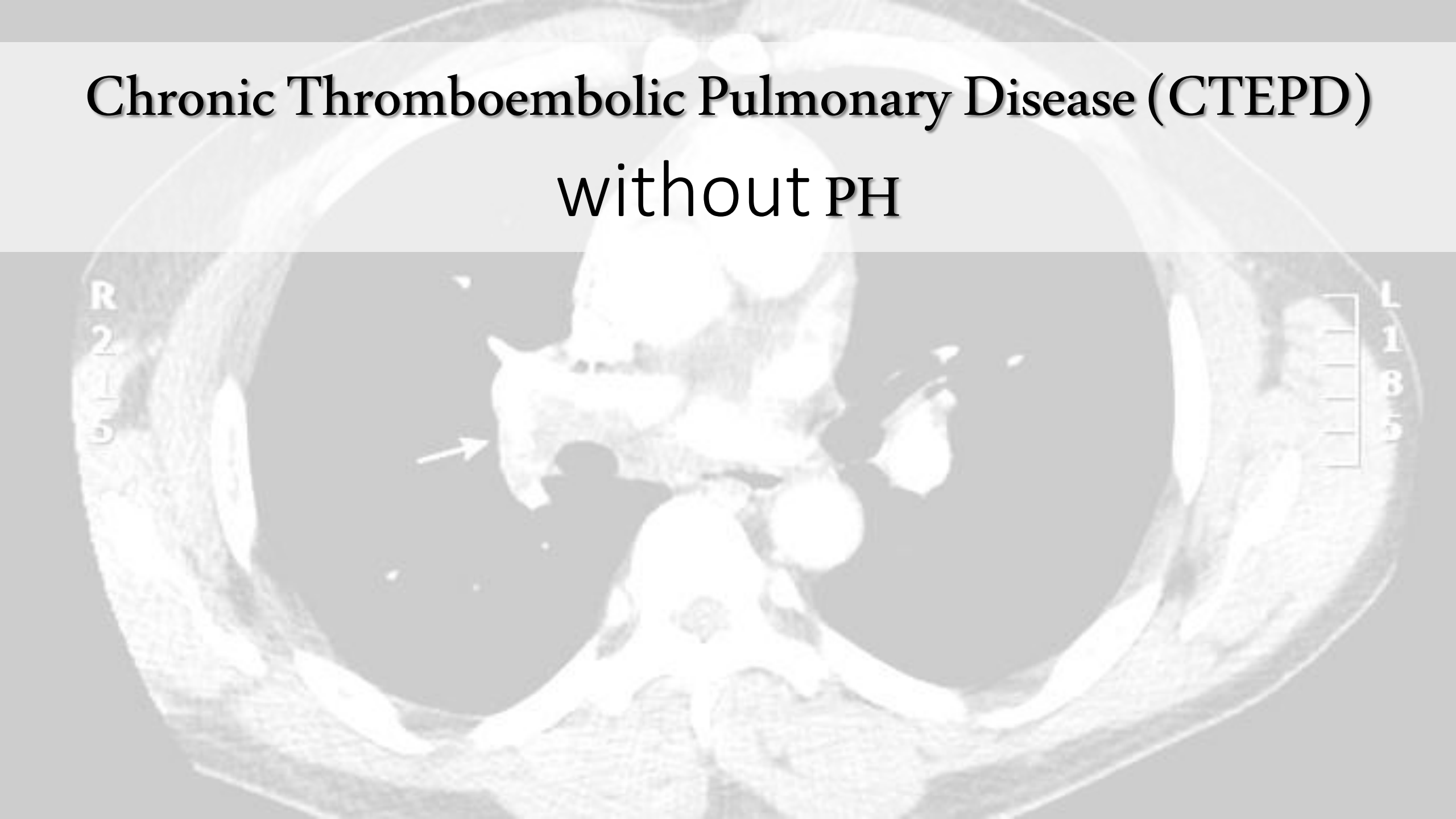
- 1.1 Idiopathic
  - 1.1.1 Non-responders at vasoreactivity testing
  - 1.1.2 Acute responders at vasoreactivity testing
- 1.2 Heritable[a]
- 1.3 Associated with drugs and toxins[a]
- 1.4 Associated with:
  - 1.4.1 Connective tissue disease
  - 1.4.2 HIV infection
  - 1.4.3 Portal hypertension
  - 1.4.4 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

RHC


GROUP 4 PH associated with pulmonary artery obstructions
4.1 Chronic thrombo-embolic PH
4.2 Other pulmonary artery obstructions[c]
RHC
Microvasculopathy

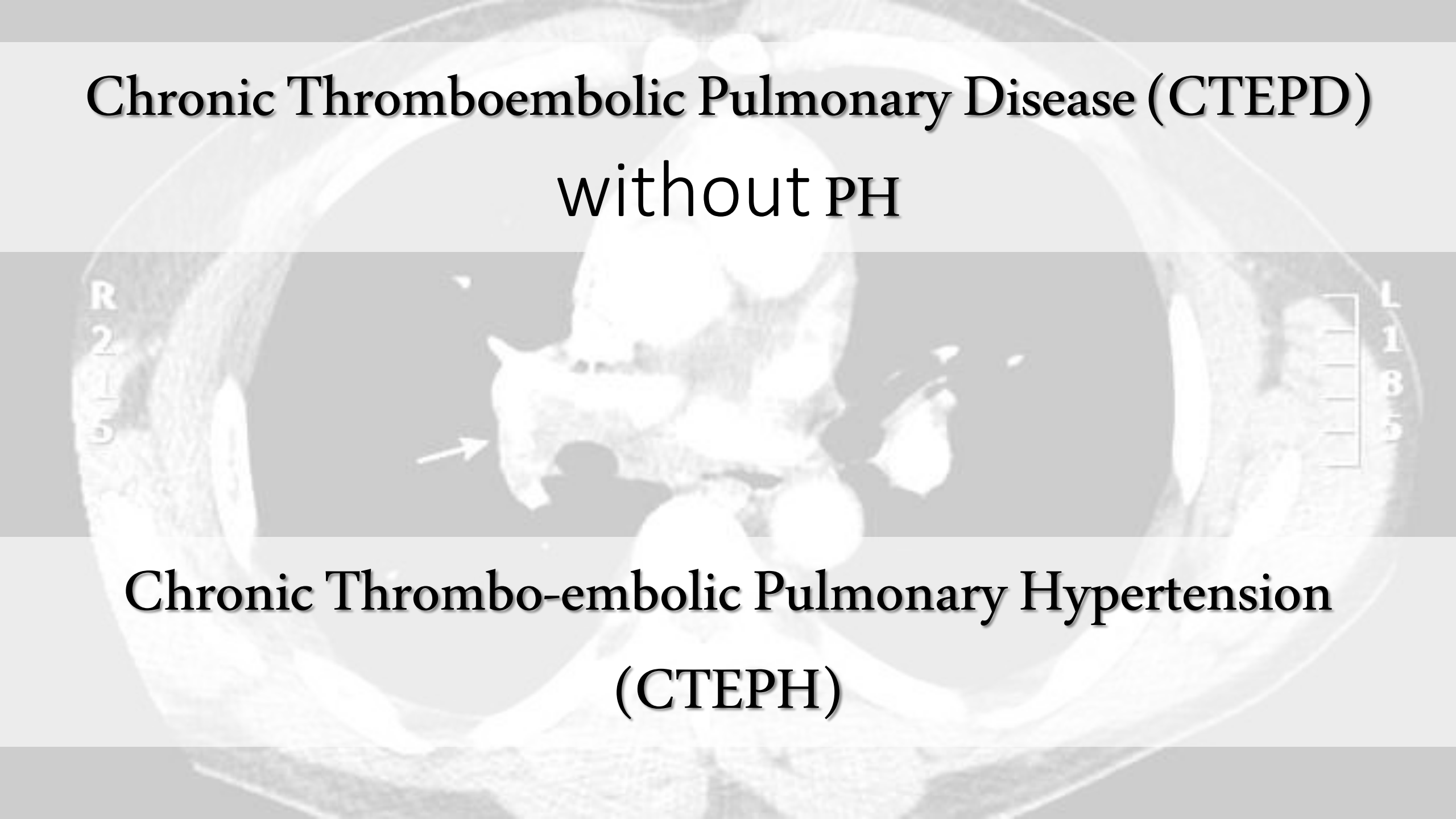
Chronic Thromboembolic Pulmonary Disease (CTEPD)

without PH



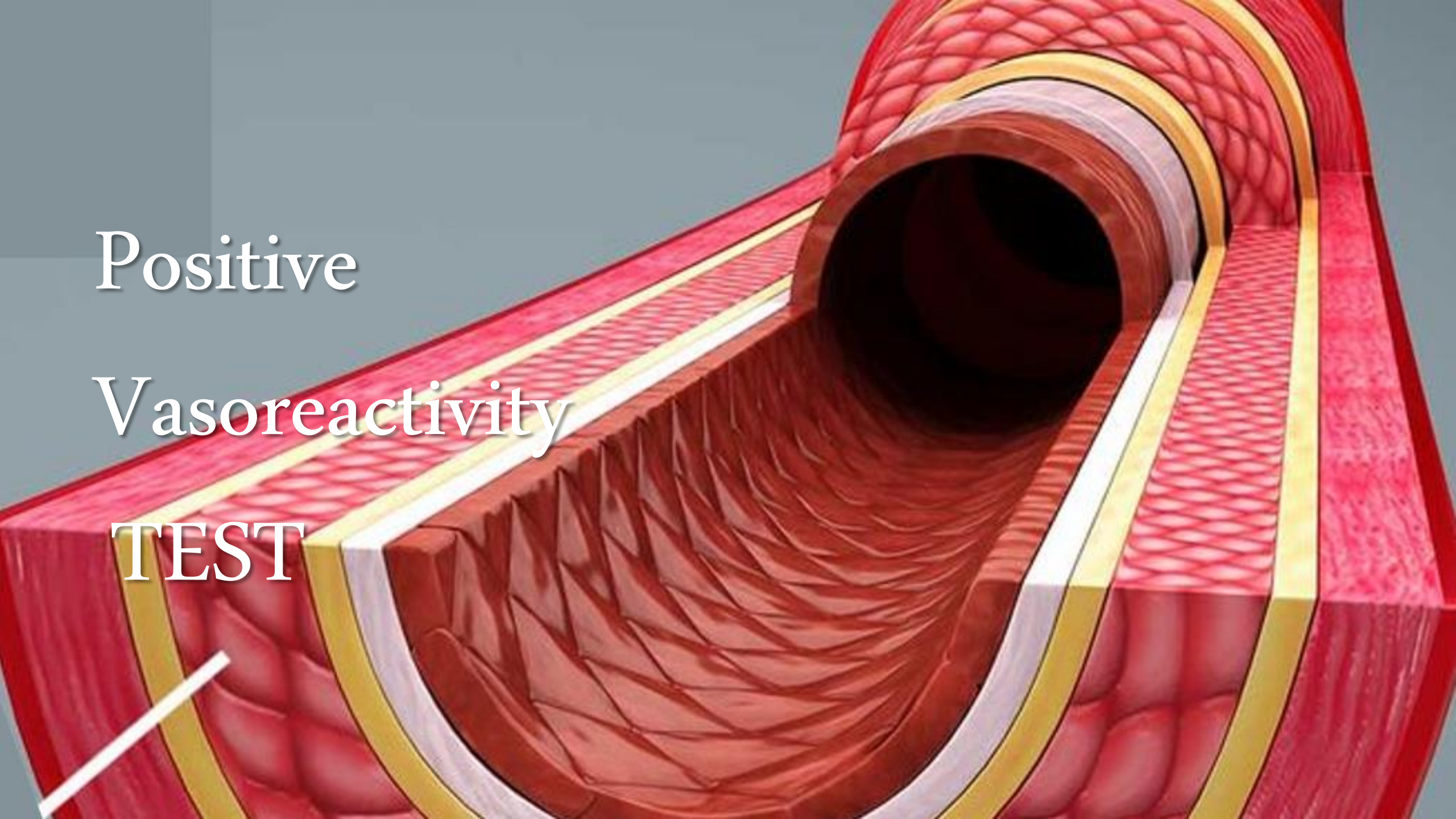
Chronic Thromboembolic Pulmonary Disease (CTEPD)

without PH



Chronic Thrombo-embolic Pulmonary Hypertension (CTEPH)

Positive Vasoreactivity TEST



Nitric Oxide

the miracle molecule

Acute challenge with a vasodilator

(preferably 10–20 ppm NO)

Galiè N et al. Eur Respir J 2015;46:903–975.

A positive acute response of a vasoreactivity

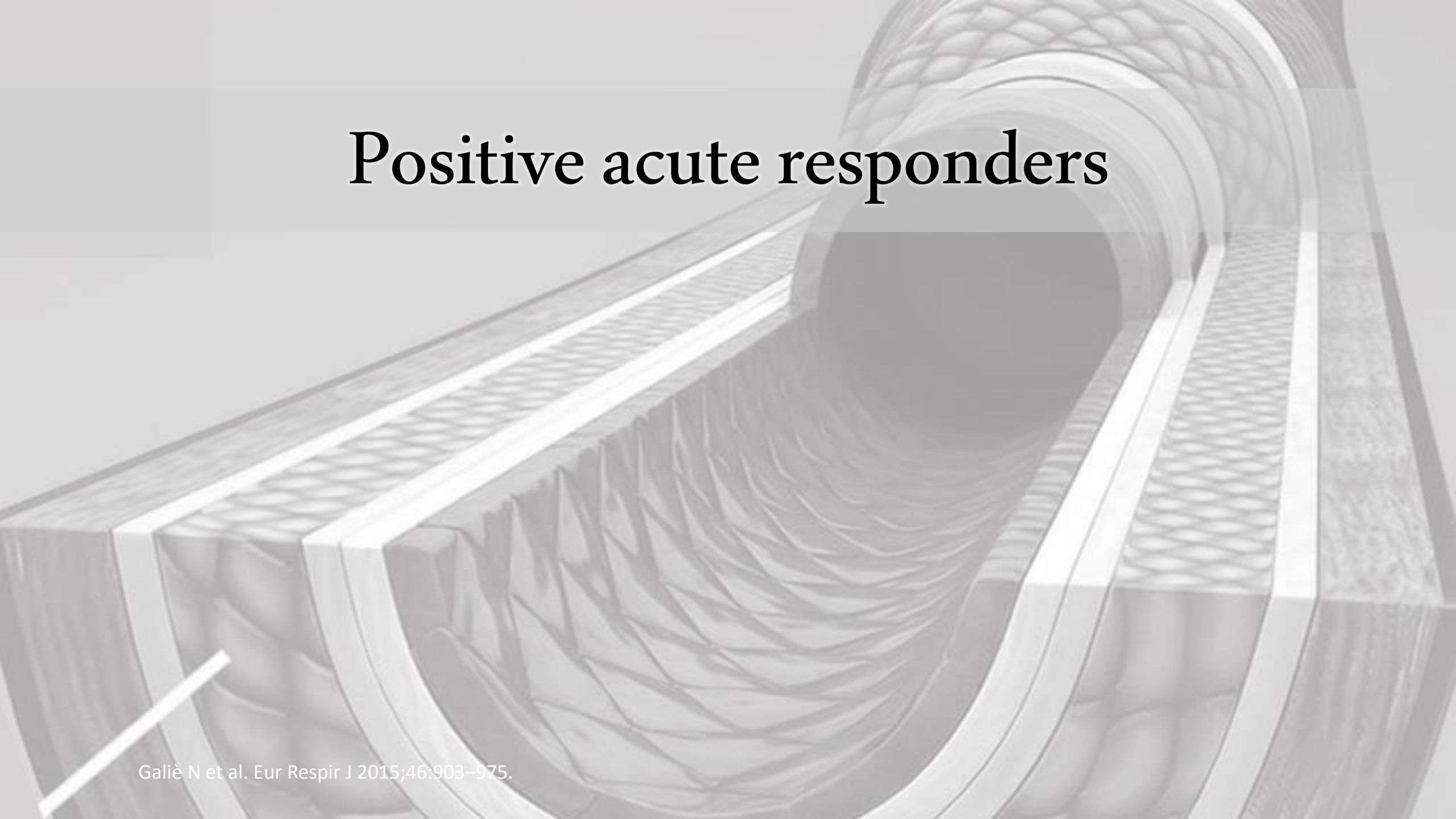
↓ mPAP by ≥10 mmHg to reach an absolute value ≤40 mmHg

with

Increased or unchanged CO

Galiè N et al. Eur Respir J 2015;46:903–975.

Positive acute responders

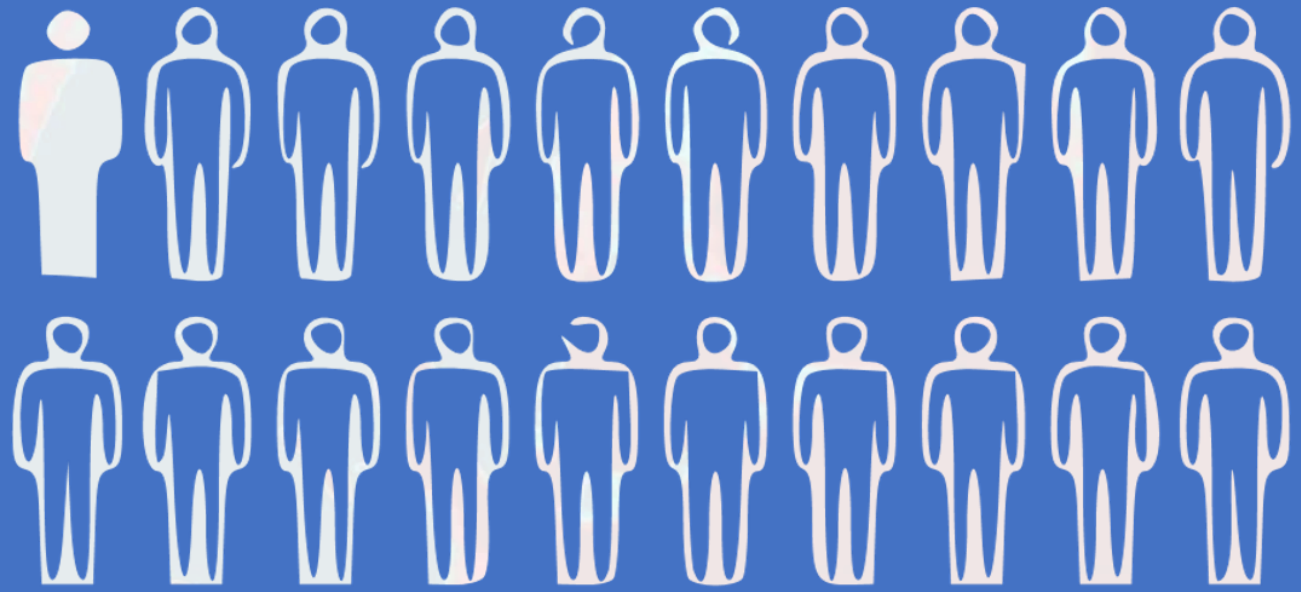


Galiè N et al. Eur Respir J 2015;46:903–975.

Positive acute responders

May be **eligible** for **treatment** with **calcium channel blockers (CCBs)**

Galiè N et al. Eur Respir J 2015;46:903–975.



1 in 20

Shows a long-term response to CCB therapy

Galiè N et al. Eur Respir J 2015;46:903–975.

The **hemodynamic definition** of **PH** has **been updated**

Definition	Haemodynamic characteristics
PH	mPAP >20 mmHg
Pre-capillary PH	mPAP >20 mmHg PAWP ≤15 mmHg PVR >2 WU

حدد الخيار الخطأ فيما يلي:

A. يتراوح ضغط الشريان الرئوي الوسطي الطبيعي mean PAP بين 15 إلى 20 ملم/زئبق

B. يقيس الضغط الإسفيني الرئوي Pulmonary Arterial Wedge Pressure – PAWP الضغط في الشعيرات الرئوية وهذا يعادل الضغط في الأذينة اليسرى

C. يعبر قياس مقاومة تدفق الدم عبر الأوعية الدموية الرئوية PVR عن صعوبة ضخ الدم إلى الرئتين من البطين الأيمن بعد امتلاءه ويحسب بمعرفة الضغط الانقباضي والانبساطي للشريان الرئوي وكذلك بقياس نتاج القلب

D. أي عامل يحرض cAMP سيؤدي إلى انخفاض مقوية العضلات الملساء الدم للشرينات الرئوية مما يؤدي إلى انخفاض ضغط الشريان الرئوي المرتفع

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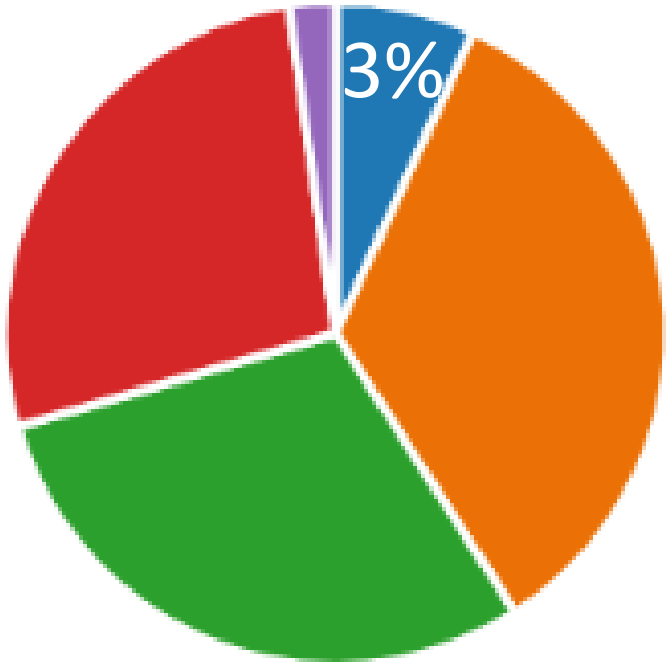
يتراوح ضغط الشريان الرئوي الوسطي الطبيعي mean PAP بين 15 إلى 20 ملم/زئبق

A	3
B	15
C	13
D	12
Other	1



ما هي المعايير التشخيصية الديناميكية الدموية لارتفاع ضغط دم الشريان الرئوي (PAH) بناءً على إرشادات ERS/ESC المحدثة لعام 2022؟

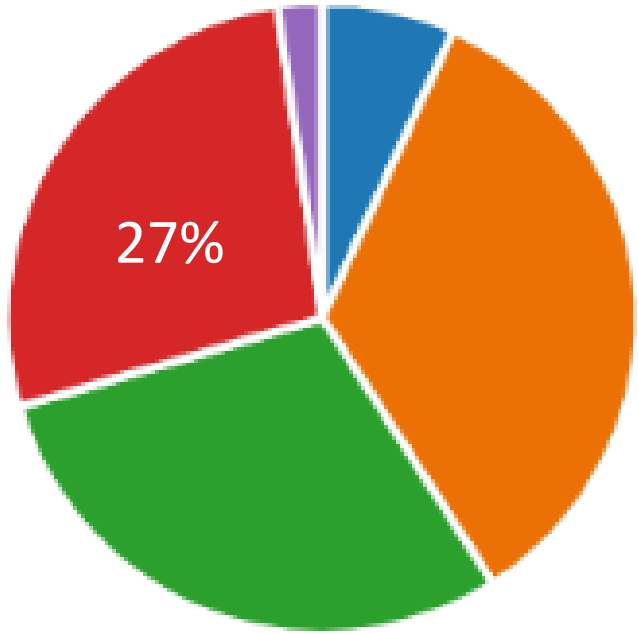
A. Echocardiogram with pulmonary pressure $\geq$ 50 mmHg
B. Echocardiogram with pulmonary pressure $\geq$ 55 mmHg
C. RHC with mean PAP $\geq$ 25, wedge $\leq$ 10, PVR > 2 WU
D. RHC with mean PAP $\geq$ 20 at rest, wedge $\leq$ 15, PVR > 2 WU
E. RHC with mean PAP $\geq$ 20, wedge $\leq$ 10, PVR > 3 WU

ما هي المعايير التشخيصية الديناميكية الدموية لارتفاع ضغط دم الشريان الرئوي (PAH) بناءً على إرشادات ERS/ESC المحدثة لعام 2022؟

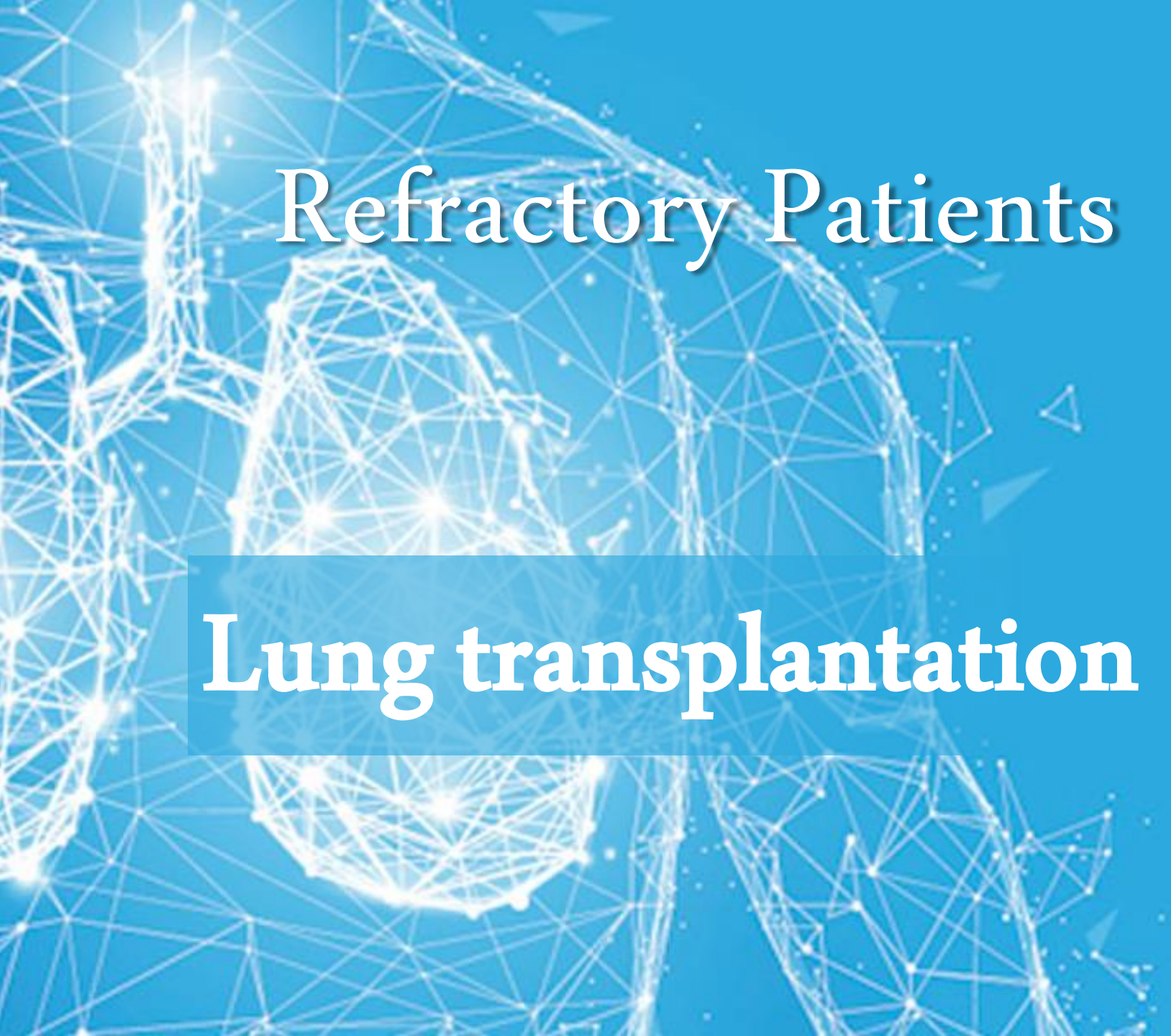
A. Echocardiogram with pulmonary pressure $\geq$ 50 mmHg
B. Echocardiogram with pulmonary pressure $\geq$ 55 mmHg
C. RHC with mean PAP $\geq$ 25, wedge $\leq$ 10, PVR > 2 WU
D. RHC with mean PAP $\geq$ 20 at rest, wedge $\leq$ 15, PVR > 2 WU
E. RHC with mean PAP $\geq$ 20, wedge $\leq$ 10, PVR > 3 WU

RHC with mean PAP ≥ 20 at rest, wedge ≤ 15, PVR > 2 WU

A	3
B	15
C	13
D	12
Other	1



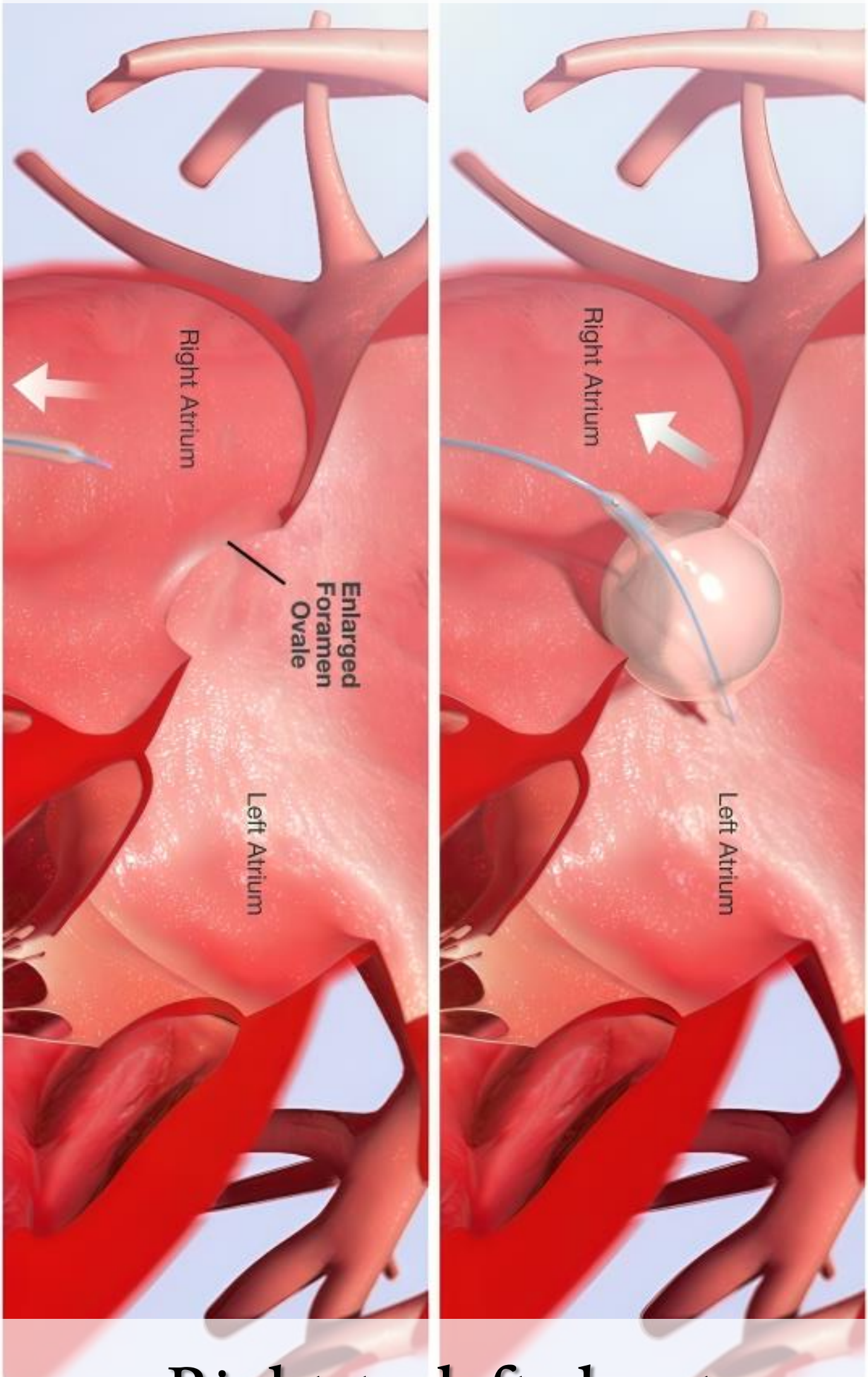
Refractory Patients



Refractory Patients

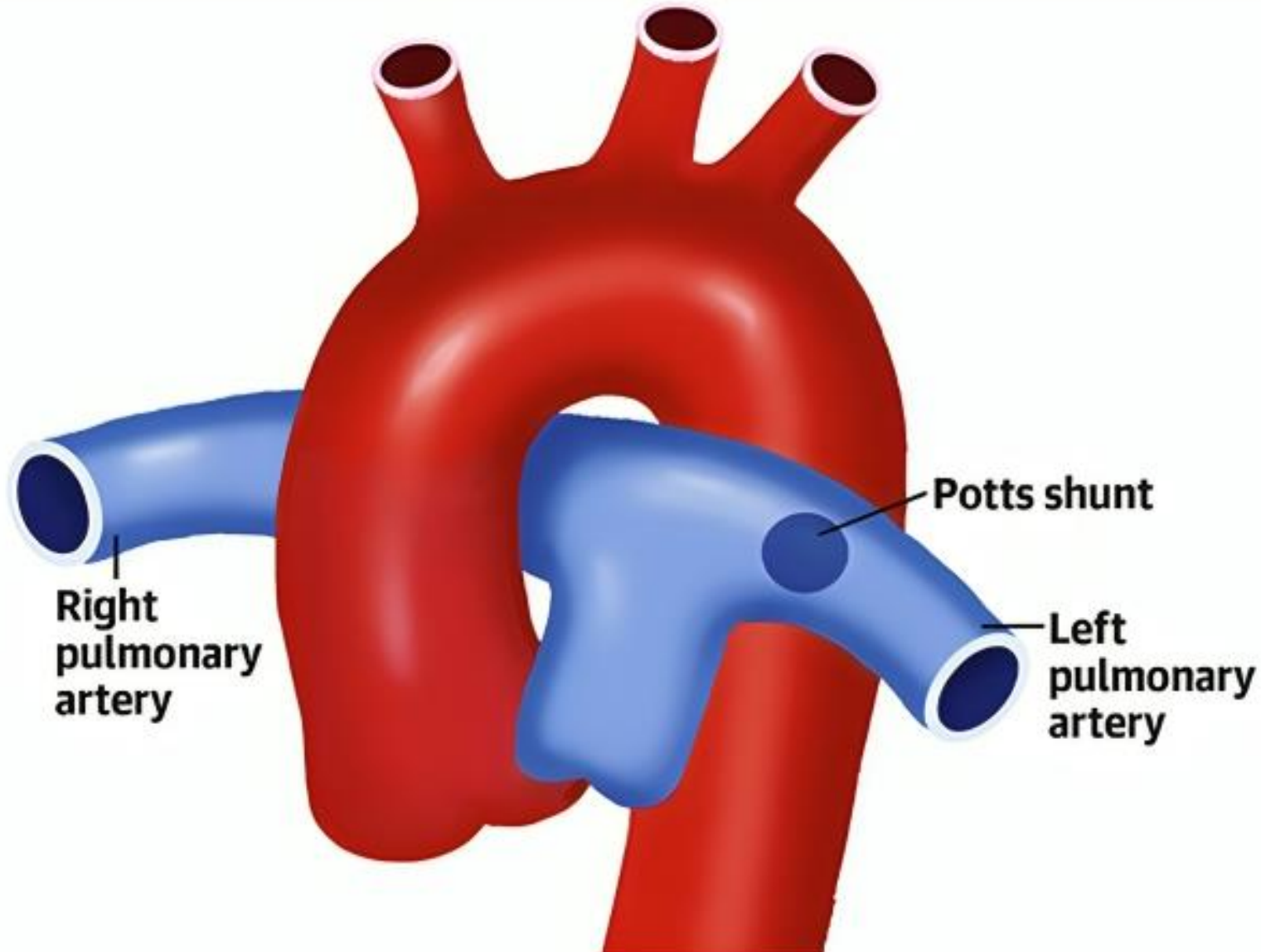
Lung transplantation

Atrial septostomy



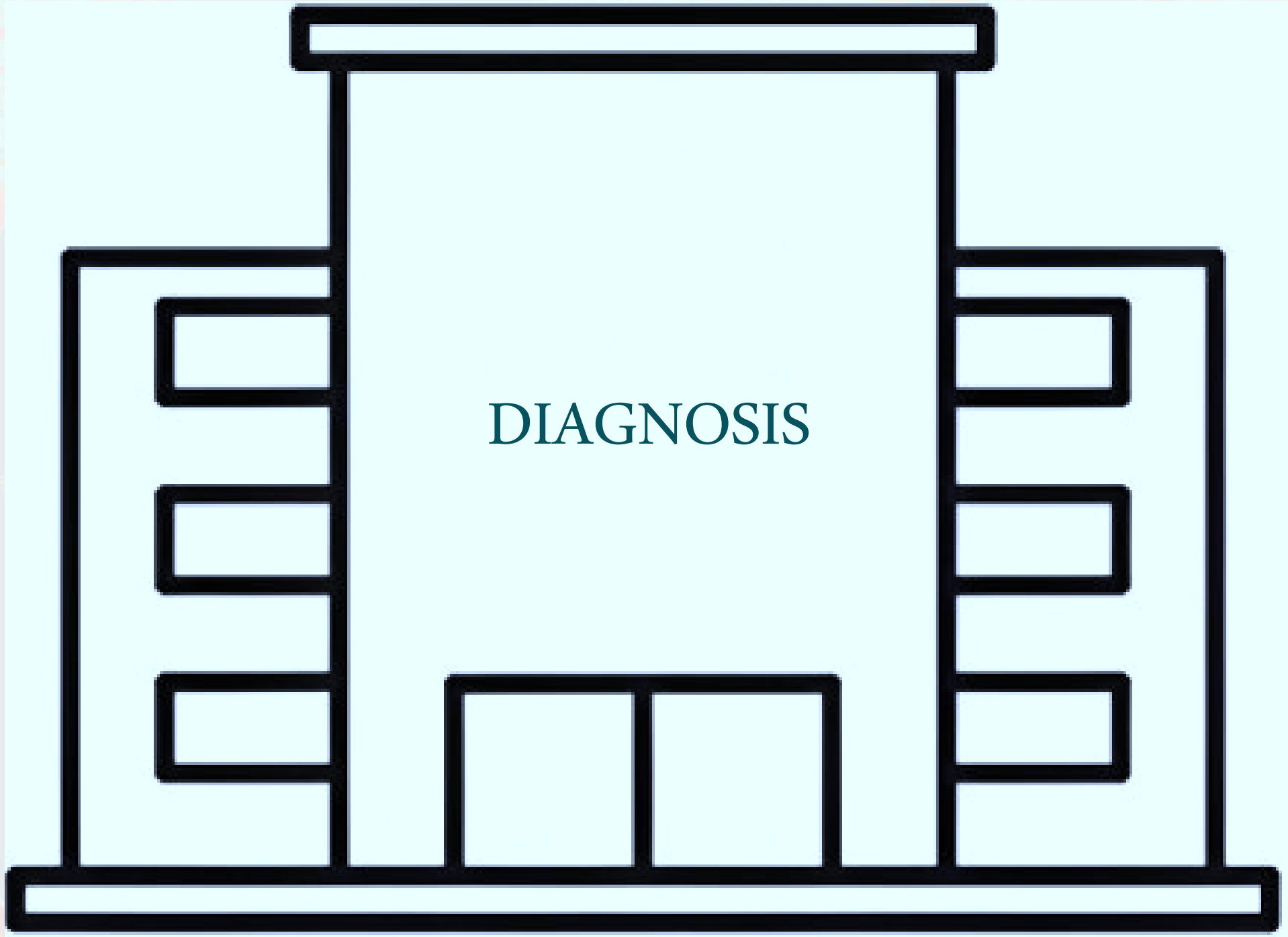
Right-to-left shunt

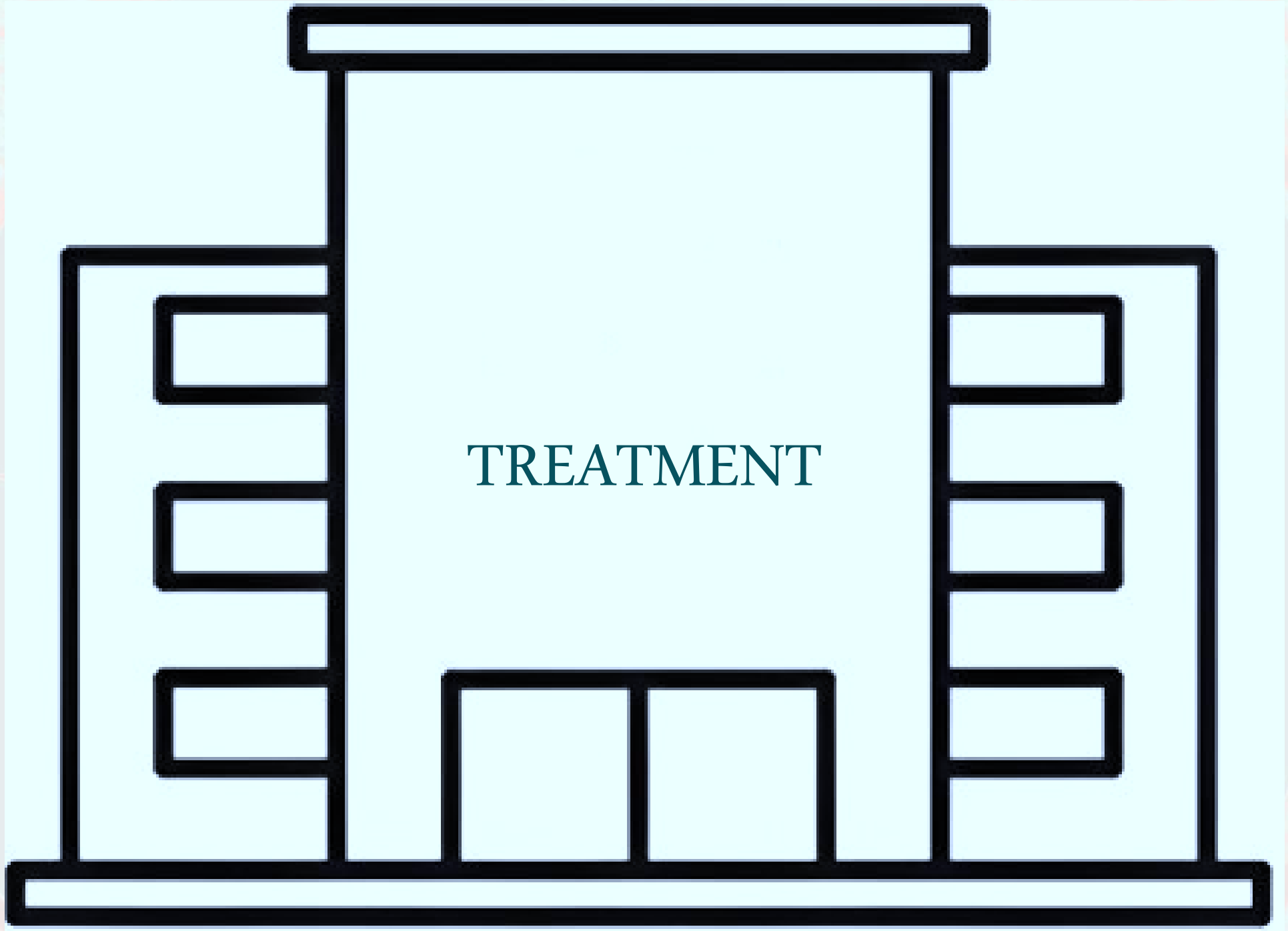
Potts Shunt and Pulmonary Hypertension

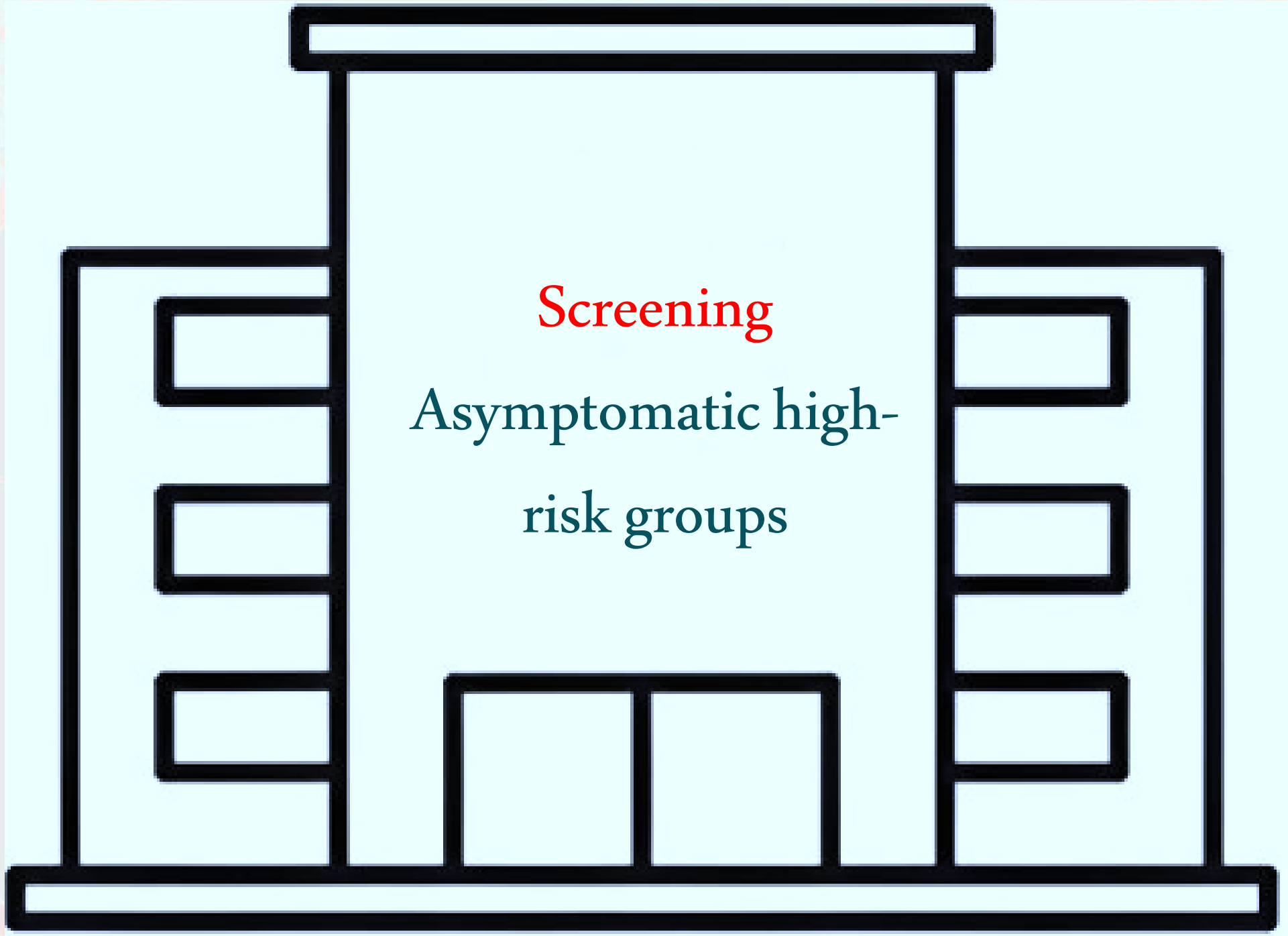


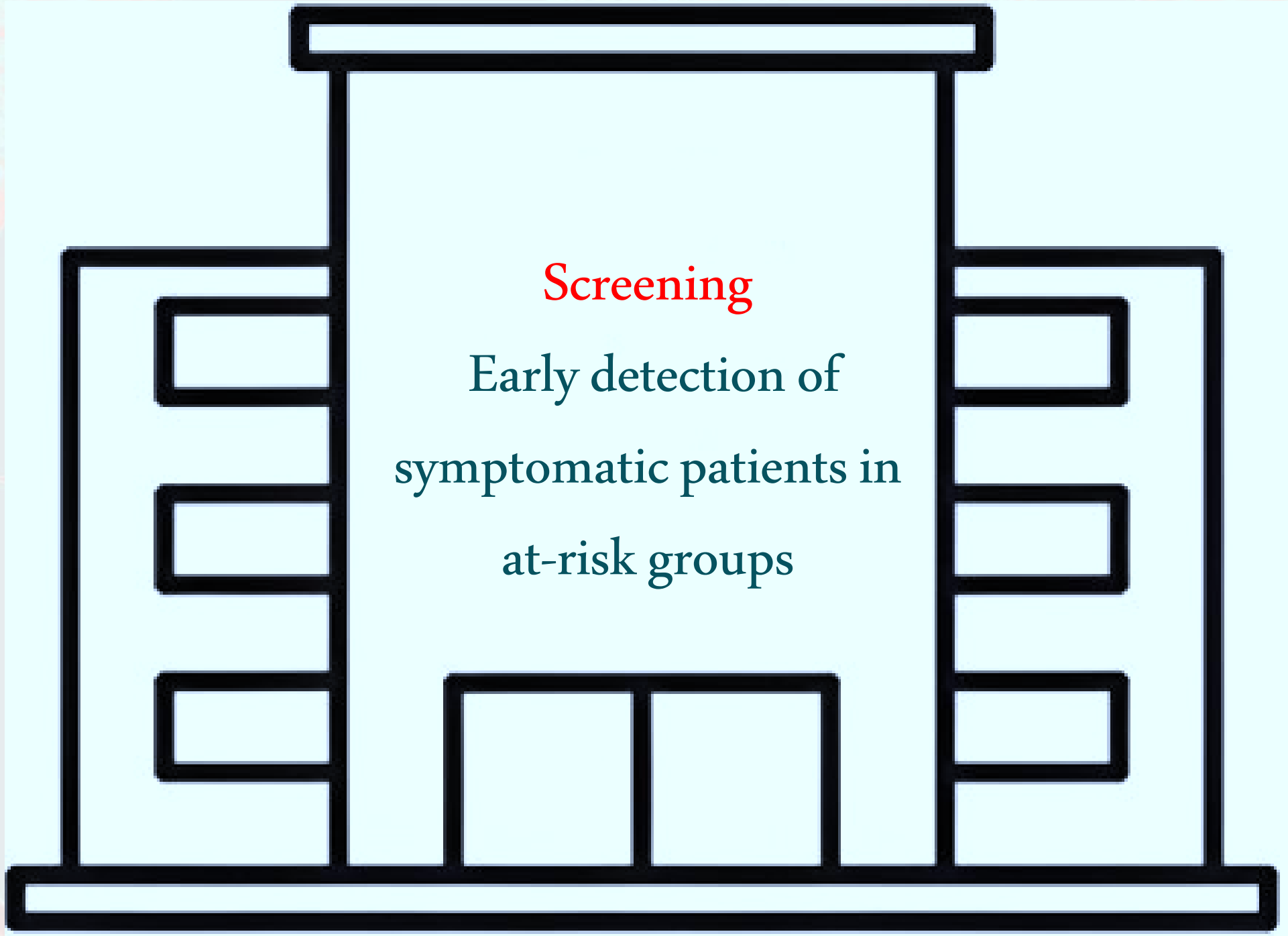

Geissmann-
Evangelium
Vol. 3
Geissmann


PH
CENTRE


DIAGNOSIS


TREATMENT


Screening
Asymptomatic high-risk groups


Screening
Early detection of
symptomatic patients in
at-risk groups


thank you