How biology informs treatment decisions

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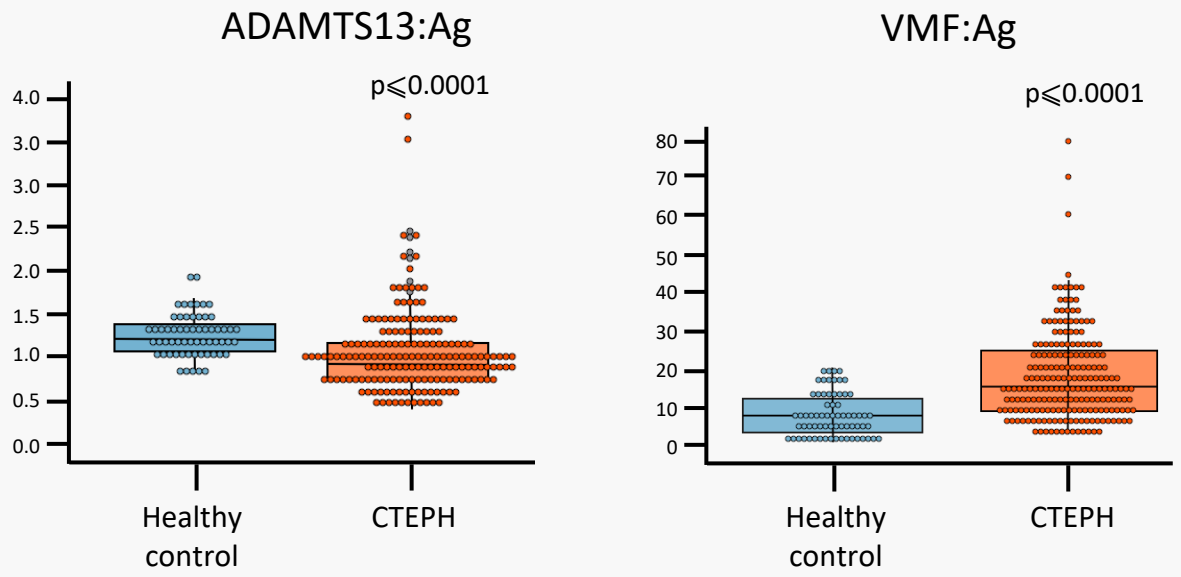
ADAMTS13–VMF axis is implicated in underlying CTEPH pathophysiology

Patients with CTEPH had decreased ADAMTS13 and increased VWF levels compared to healthy controls



Healthy control, n=68; CTEPH, n=208

- ✔ Plasma ADAMTS13 antigen levels are markedly decreased in CTEPH, independent of pulmonary hypertension, disease severity or systemic inflammation:[1]
  - ADAMTS13 levels remained low after reversal of pulmonary hypertension by PAE surgery
  - A genetic variant near the ADAMTS13 gene was associated with ADAMTS13 protein that accounted for ~8% of the variation in levels
- ✔ An earlier study did not demonstrate decreased ADAMTS13 activity in CTEPH versus PH[2]

Ag, antigen; CTEPH, chronic thromboembolic pulmonary hypertension; PAE, pulmonary endarterectomy; PH, pulmonary hypertension; VMF, von Willebrand factor.

1. Newham M, et al. *Eur Respir J* 2019:**53**:1801805; 2. Pazenboeck A, et al. *Eur Heart J* 2018;**39**:P1621.

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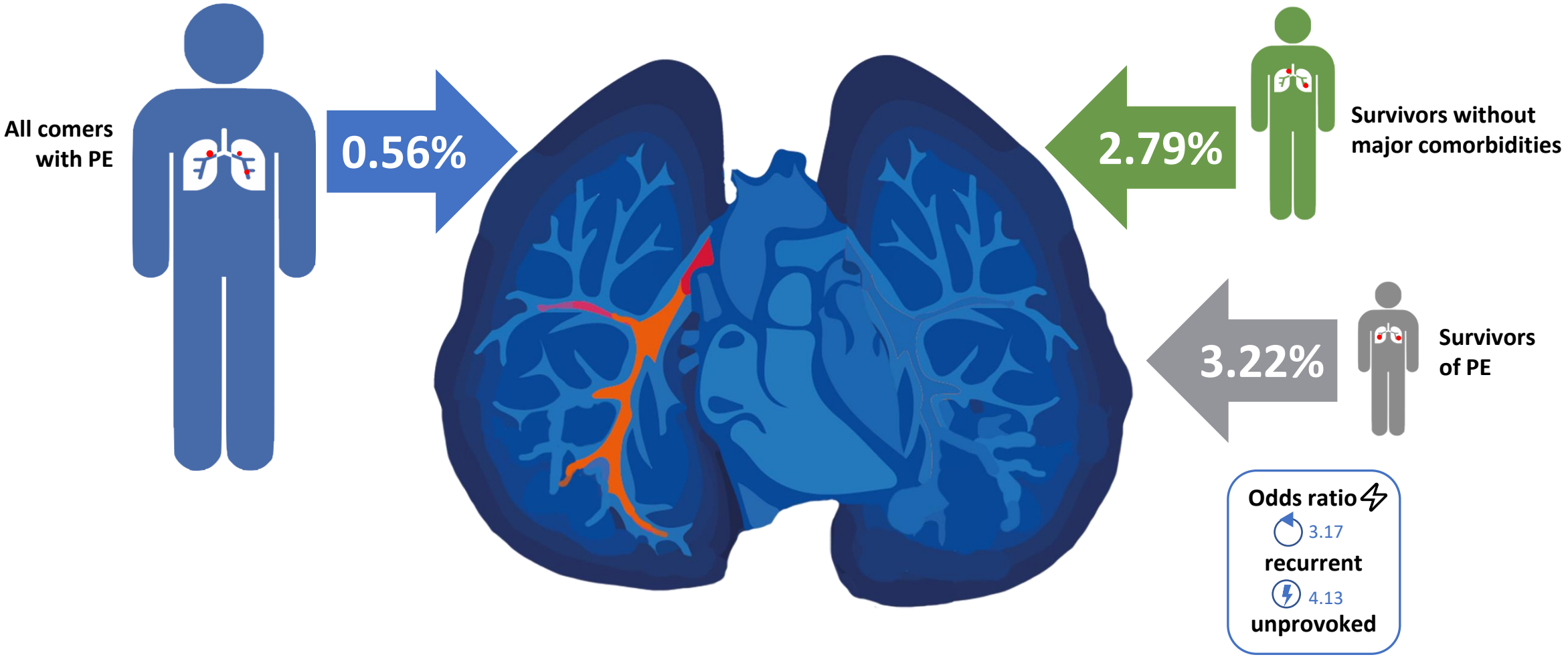
Incidence of CTEPH after acute pulmonary embolism

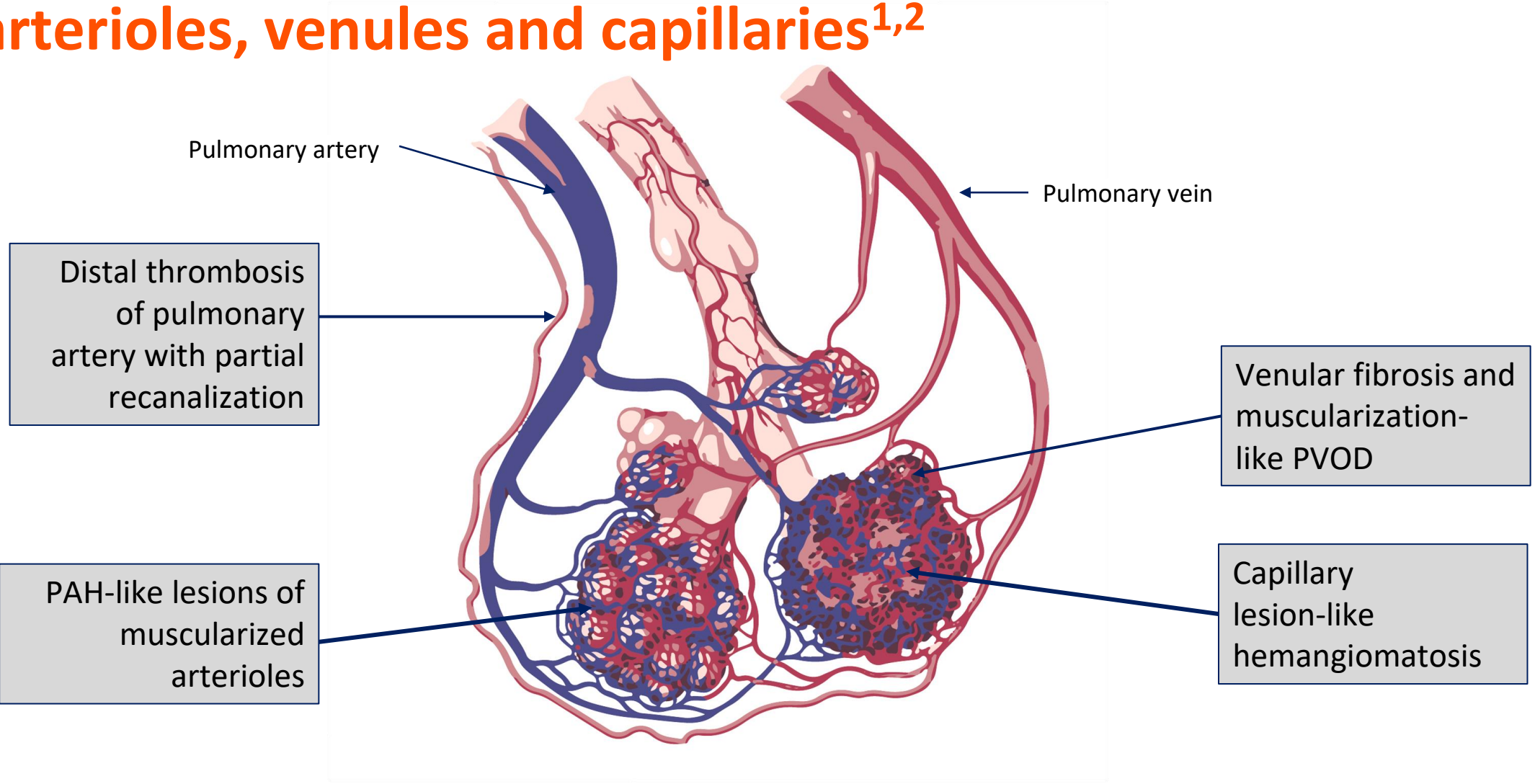


Percentages show pooled incidence of PE (n=4,047). All comers were defined as unselected consecutive PE patients, survivors as PE patients who survived the first 3 to 6 months after diagnosis, and survivors without comorbidities as survivors without cardiopulmonary, malignant and/or other severe comorbidities.

CTEPH, chronic thromboembolic pulmonary hypertension; PE, pulmonary embolism.

Klok FA, et al. *J Thromb Haem* 2018;**16**:1040–1051.

Microvasculopathy in CTEPH involving pulmonary arterioles, venules and capillaries[1,2]



CTEPH, chronic thromboembolic pulmonary hypertension; PAH, pulmonary arterial hypertension; PVOD, pulmonary veno-occlusive disease.

1. Dorfmuller P, et al. *Eur Respir J* 2014;**44**:1275–1288; 2. Simonneau G, et al. *Eur Respir Rev* 2017;**26**:160112.

Risk–benefit assessment for surgery

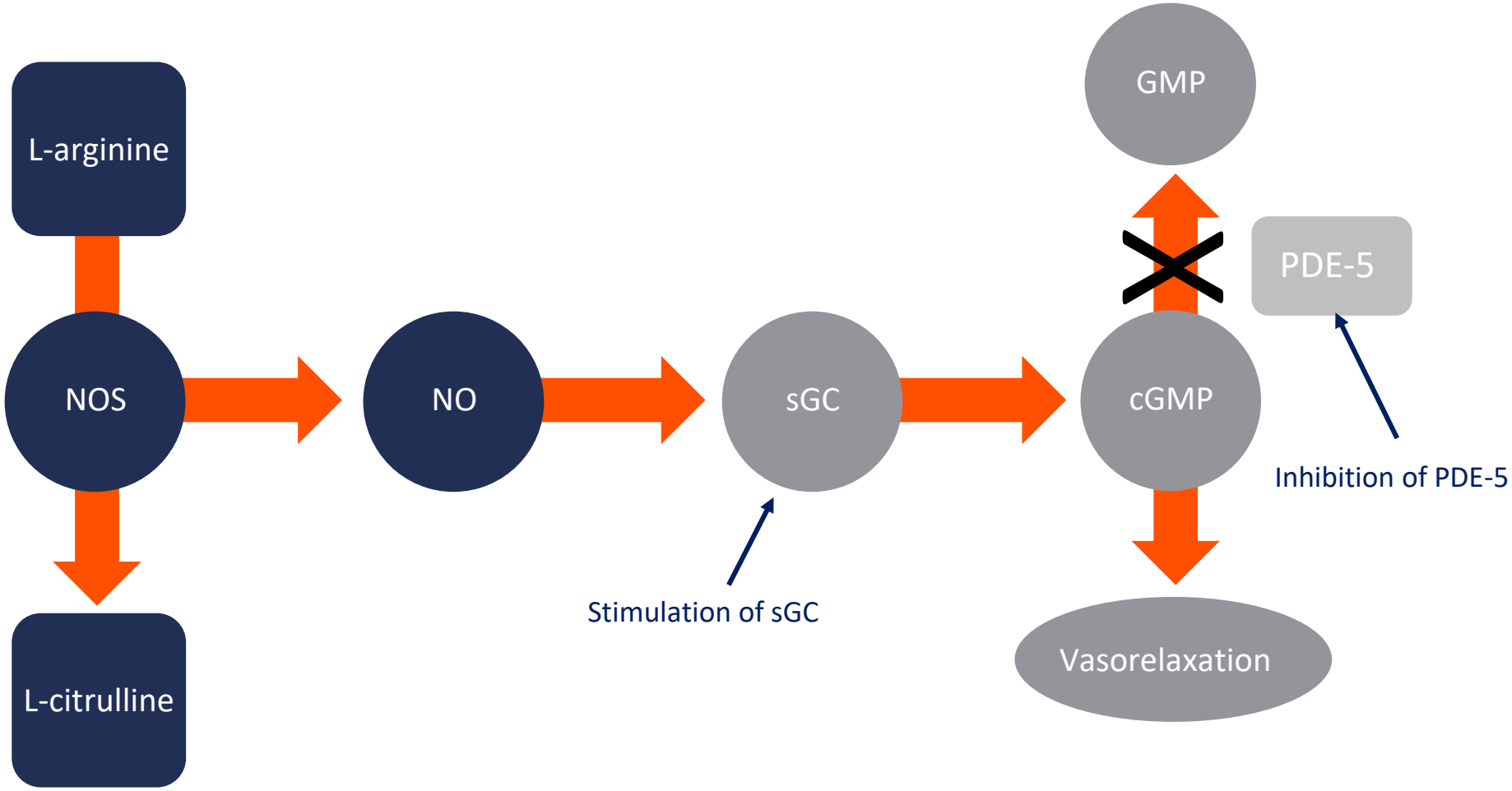
Lower risk with predictable good long-term outcome
History of DVT/PE
No signs of right heart failure
No comorbidities
Functional limitation: class II or III
Clear disease concordant on all images
Bilateral lower lobe disease
PVR<1000 dyn·s·cm^{-5} in proportion to site and number of obstructions on imaging, higher PA pulse pressure

Higher risk with less predictable long-term outcome*
No history of DVT/PE
Signs of right heart failure
Significant concomitant lung or left heart disease
Functional limitation: class IV
Inconsistency of imaging modalities
No disease appreciable in lower lobes
PVR<1200 dyn·s·cm^{-5} out of proportion to site and number of obstructions on imaging, higher PA diastolic pressure

* Not contraindications.
DVT, deep vein thrombosis; PA, pulmonary artery; PE, pulmonary embolism; PVR, pulmonary vascular resistance.

Kim NH, et al. *Eur Respir J* 2019;**53:**1801915.

NO-sGC-cGMP pathway in PH: A new therapeutic target



NO-sGC-cGMP, nitric oxide (NO)-soluble guanylate cyclase (sGC)-cyclic guanosine monophosphate (cGMP); NOS, NO synthase; PDE-5, phosphodiesterase-5; PH, pulmonary hypertension.

Kim NH. *Eur Respir Rev* 2010;**19**:69–71.