

Research Article

Morphological and Clinicopathological Correlates Of Cor Pulmonale in Pulmonary Emphysema: An Anatomical Assessment

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ABSTRACT

Background: Pulmonary emphysema is characterized by irreversible destruction of alveolar walls and loss of the pulmonary capillary bed. Progressive pulmonary vascular abnormalities, hypoxic vasoconstriction, and increased pulmonary vascular resistance may impose chronic pressure overload on the right ventricle, resulting in right ventricular hypertrophy and, in advanced disease, cor pulmonale.

Objective: To assess the morphological and clinicopathological correlates of cor pulmonale in individuals with pulmonary emphysema, with emphasis on emphysema pattern, pulmonary vascular abnormalities, right ventricular hypertrophy, and selected clinical and pathological characteristics.

Methods: This analytical observational study included 160 individuals with histologically confirmed pulmonary emphysema. Clinical records and available cardiopulmonary findings were reviewed, followed by systematic gross and microscopic examination of pulmonary and cardiac specimens. Emphysema was classified as centrilobular, panlobular, paraseptal, or mixed. Pulmonary vascular abnormalities included vascular deformity, arteriolar narrowing, medial hypertrophy, intimal fibrosis, vascular compression, and thromboembolic lesions. Cor pulmonale was defined anatomically by right ventricular hypertrophy with or without right ventricular dilatation in the setting of pulmonary disease after exclusion of a primary left-sided cardiac cause.

Results: Cor pulmonale was identified in 118/160 (73.8%). Right ventricular hypertrophy was most frequent in mixed and centrilobular emphysema. Pulmonary vascular deformity, vascular compression, intimal fibrosis, and arteriolar narrowing were frequent and were more common among cases with cor pulmonale. Extensive emphysema and several pulmonary vascular abnormalities showed independent associations with cor pulmonale in the multivariable model.

Conclusion: Cor pulmonale in pulmonary emphysema appears to reflect combined parenchymal destruction, pulmonary vascular remodeling/deformation, and right ventricular adaptation. Integrated cardiopulmonary morphological assessment may improve understanding of the structural basis of right-sided cardiac remodeling.

Keywords: Pulmonary Emphysema, Cor Pulmonale, Right Ventricular Hypertrophy, Pulmonary Hypertension, Pulmonary Vasculature, Histopathology, Anatomical Pathology, Chronic Obstructive Pulmonary Disease.

INTRODUCTION

Pulmonary emphysema is an important structural component of chronic obstructive pulmonary disease (COPD) and is characterized

morphologically by abnormal permanent enlargement of airspaces distal to the terminal bronchioles accompanied by destruction of their walls. The resulting loss of alveolar-

capillary surface area contributes not only to airflow limitation and impaired gas exchange but also to significant alterations in the pulmonary circulation.

Cor pulmonale traditionally refers to structural and functional alteration of the right ventricle secondary to pulmonary disease producing increased pulmonary vascular resistance. Chronic hypoxic vasoconstriction, pulmonary vascular remodeling, destruction of the pulmonary vascular bed, and mechanical distortion of pulmonary vessels may increase right ventricular afterload.

The relationship between emphysematous destruction and pulmonary vascular disease is complex. Loss of alveolar walls directly reduces the pulmonary capillary vascular bed, while hypoxia promotes vasoconstriction and vascular remodeling. Endothelial dysfunction and abnormalities in vascular maintenance may also contribute to pulmonary vascular loss in emphysema.

Historical anatomical studies have demonstrated that pulmonary vascular deformity and compression of pulmonary arterial branches by enlarged emphysematous spaces may contribute substantially to increased pulmonary vascular resistance. Dunnill's classic postmortem study emphasized vascular distortion and mechanical pressure on pulmonary arteries as important anatomical factors in cor pulmonale associated with emphysema.

Pulmonary vascular remodeling may include medial hypertrophy, muscularization of small pulmonary arteries and arterioles, intimal fibrosis, and narrowing of the vascular lumen. These abnormalities may occur in parallel with destruction of the pulmonary microcirculation and can amplify the effects of hypoxic vasoconstriction.

The severity of pulmonary hypertension in COPD does not always correspond directly to spirometric impairment. Current pulmonary hypertension classifications recognize pulmonary hypertension associated with COPD and emphysema as a form of group 3 pulmonary hypertension related to lung disease and/or hypoxia.

Cardiac remodeling in emphysema may also be more complex than the traditional concept of progressive right ventricular enlargement. Contemporary imaging studies have demonstrated that some patients with emphysema may have reduced right ventricular volume, possibly reflecting pulmonary vascular

pruning and reduced pulmonary blood flow rather than classical right ventricular dilatation. Clinicopathological studies have demonstrated imperfect correlations between pulmonary physiology, macroscopic emphysema severity, pulmonary hypertension, and right ventricular hypertrophy. These observations emphasize the importance of directly examining pulmonary and cardiovascular morphology when investigating cor pulmonale.

The present study was designed to assess the morphological and clinicopathological correlates of cor pulmonale in pulmonary emphysema. The primary objective was to determine the association between pulmonary emphysema pattern, pulmonary vascular abnormalities, and right ventricular hypertrophy. Secondary objectives were to evaluate the relationship between the extent of emphysematous destruction and cardiac remodeling and to identify pathological features independently associated with cor pulmonale.

MATERIALS AND METHODS

Study Design and Setting

This was designed as an analytical observational clinicopathological study Conducted at Frontier Medical College Abbottabad involving 160 individuals with pulmonary emphysema.

Study Population

The study population consisted of adults with histologically confirmed pulmonary emphysema for whom adequate pulmonary tissue and cardiac morphological information were available.

Inclusion Criteria

Histologically confirmed emphysema; adequate lung tissue; adequate cardiac examination; available clinical information; and sufficient pathological material for vascular assessment.

Exclusion Criteria

Primary congenital heart disease; significant primary left-sided valvular or myocardial disease sufficient to explain right ventricular hypertrophy; chronic thromboembolic disease as the dominant cause; inadequate tissue preservation; or incomplete pathological examination.

Morphological Assessment

Representative lung sections were examined using hematoxylin and eosin staining. Emphysema was classified as centrilobular, panlobular, paraseptal, or mixed. Pulmonary

vascular deformity, arteriolar narrowing, medial hypertrophy, intimal fibrosis, vascular compression, bronchopulmonary vascular changes, and thromboembolic lesions were recorded.

Assessment of Right Ventricular Morphology

Right ventricular wall thickness, hypertrophy, dilatation, gross cardiac enlargement, and right-to-left ventricular morphological relationships were assessed. Cor pulmonale was considered present when right ventricular hypertrophy and/or dilatation occurred in

association with pulmonary emphysema and there was no alternative primary cardiac cause.

Statistical Analysis

Continuous variables were expressed as mean $\pm$ standard deviation and categorical variables as frequencies and percentages. Chi-square/Fisher exact tests and independent-samples t tests or Mann-Whitney U tests were used as appropriate. Multivariable logistic regression was planned to identify independent predictors of cor pulmonale. A p value <0.05 was considered statistically significant.

RESULTS

Table 1. Demographic and clinical characteristics of the study population.

Variable	Total (n=160)
Age, years, mean $\pm$ SD	63.4 $\pm$ 9.8
Male sex	119 (74.4%)
Female sex	41 (25.6%)
Current/former smokers	122 (76.3%)
Long-standing respiratory disease	127 (79.4%)
Documented hypoxemia	96 (60.0%)
Cor pulmonale	118 (73.8%)
Right ventricular hypertrophy	121 (75.6%)
Right ventricular dilatation	87 (54.4%)

Table 1 summarizes the demographic and clinical profile of the cohort. The mean age was 63.4 years, and males constituted approximately three-quarters of participants. A history of current or former smoking was

reported in 76.3%, while 60.0% had documented hypoxemia. Right ventricular hypertrophy was present in 75.6% and right ventricular dilatation in 54.4%. Cor pulmonale was identified in 73.8% of the population.

Table 2. Distribution of emphysema patterns.

Emphysema pattern	n (%)
Centrilobular	72 (45.0%)
Panlobular	38 (23.8%)
Paraseptal	18 (11.3%)
Mixed	32 (20.0%)
Total	160 (100%)

Table 2 demonstrates that centrilobular emphysema was the most frequent morphological pattern, accounting for 45.0% of cases, followed by panlobular emphysema (23.8%), mixed emphysema (20.0%), and

paraseptal emphysema (11.3%). The predominance of centrilobular disease is compatible with the common association between smoking-related lung injury and centrilobular structural destruction.

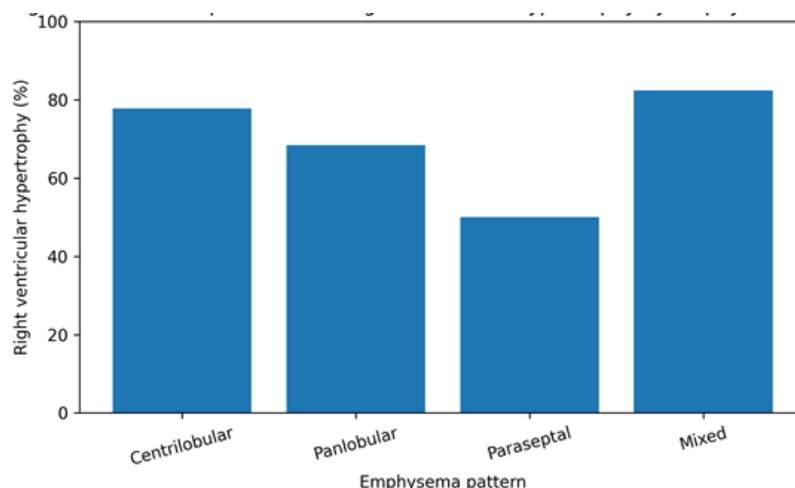


Figure 1. Prevalence of right ventricular hypertrophy according to emphysema pattern

Figure 1 illustrates the frequency of right ventricular hypertrophy across emphysema patterns. The highest proportion was observed in mixed emphysema (82.4%), followed by

centrilobular emphysema (77.8%). Panlobular emphysema showed a frequency of 68.4%, whereas paraseptal emphysema showed 50.0%.

Table 3. Pulmonary vascular morphological abnormalities.

Morphological abnormality	n (%)
Pulmonary vascular deformity	112 (70.0%)
Vascular compression by emphysematous spaces	101 (63.1%)
Intimal fibrosis	99 (61.9%)
Arteriolar narrowing	88 (55.0%)
Medial hypertrophy	83 (51.9%)
Bronchopulmonary vascular anastomotic changes	42 (26.3%)
Thromboembolic lesions	18 (11.3%)

Table 3 shows the distribution of pulmonary vascular lesions. Vascular deformity was the most common abnormality (70.0%), followed by vascular compression (63.1%) and intimal fibrosis (61.9%). Arteriolar narrowing and medial hypertrophy were also frequent.

Thromboembolic lesions were less frequent, occurring in 11.3%. Collectively, these findings illustrate how parenchymal destruction may coexist with both mechanical and remodeling-related abnormalities of the pulmonary vascular bed.

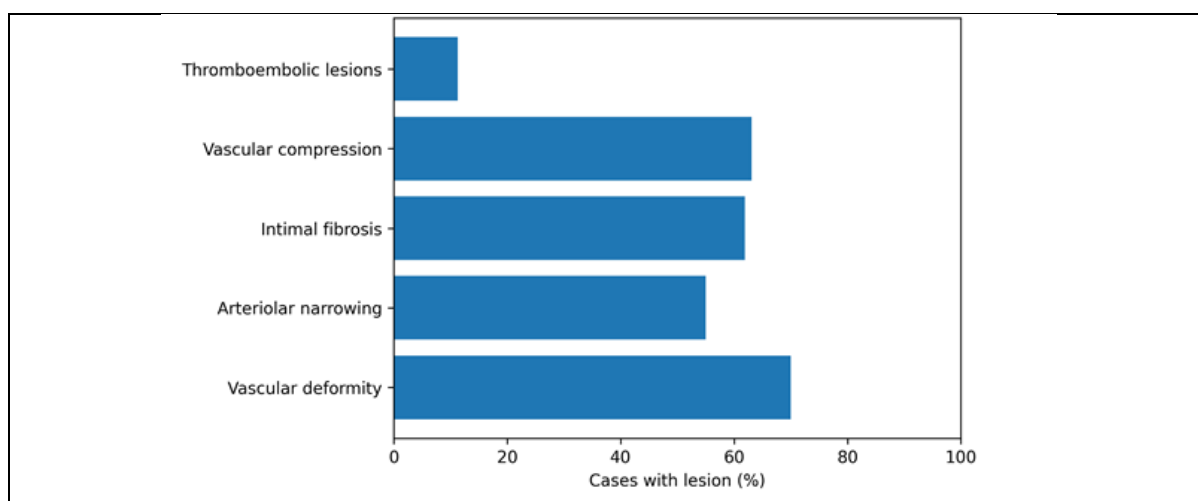


Figure 2. Prevalence of pulmonary vascular morphological lesions

Figure 2 provides a visual representation of the pulmonary vascular abnormalities listed in Table 3. The predominance of vascular deformity and compression emphasizes the potential mechanical contribution of

emphysematous destruction to increased pulmonary vascular resistance. Intimal fibrosis and arteriolar narrowing represent additional remodeling mechanisms that can reduce vascular caliber.

Table 4. Relationship between pulmonary vascular abnormalities and cor pulmonale.

Variable	Cor pulmonale (n=118)	No cor pulmonale (n=42)	p value
Vascular deformity	91 (77.1%)	21 (50.0%)	0.001
Vascular compression	81 (68.6%)	20 (47.6%)	0.018
Intimal fibrosis	78 (66.1%)	21 (50.0%)	0.068
Arteriolar narrowing	73 (61.9%)	15 (35.7%)	0.004
Medial hypertrophy	68 (57.6%)	15 (35.7%)	0.019
Thromboembolic lesions	15 (12.7%)	3 (7.1%)	0.326

Table 4 compares pulmonary vascular abnormalities between cases with and without cor pulmonale. Vascular deformity, vascular compression, arteriolar narrowing, and medial hypertrophy occurred more frequently in the cor pulmonale group, with statistically significant differences for several variables. Intimal fibrosis showed a numerical difference

but did not reach the predefined significance threshold in this model. Thromboembolic lesions were uncommon and did not show a statistically significant association. These results support a model in which pulmonary vascular remodeling and mechanical distortion contribute to right ventricular pressure loading.

Table 5. Cardiac morphological characteristics according to cor pulmonale status.

Variable	Cor pulmonale	No cor pulmonale	p value
RV wall thickness (mm), mean $\pm$ SD	7.4 $\pm$ 1.3	4.9 $\pm$ 0.8	<0.001
RV hypertrophy	113 (95.8%)	8 (19.0%)	<0.001
RV dilatation	76 (64.4%)	11 (26.2%)	<0.001
Gross cardiac enlargement	69 (58.5%)	9 (21.4%)	<0.001

Table 5 demonstrates the differences in right-sided cardiac morphology. Mean right ventricular wall thickness was higher in the cor pulmonale group, and right ventricular hypertrophy was present in nearly all cor pulmonale cases. Right ventricular dilatation

and gross cardiac enlargement were also more frequent. The pattern is consistent with chronic right ventricular pressure overload leading initially to hypertrophic remodeling and, in a subset, subsequent chamber dilatation.

Table 6. Multivariable logistic regression analysis for cor pulmonale.

Predictor	Adjusted OR	95% CI	p value
Extensive emphysema	2.86	1.42–5.77	0.003
Pulmonary vascular deformity	3.12	1.55–6.28	0.002
Arteriolar narrowing	2.41	1.18–4.91	0.016
Vascular compression	2.18	1.09–4.36	0.028
Intimal fibrosis	1.87	0.94–3.72	0.074
Current/former smoking	1.39	0.68–2.85	0.361
Age >65 years	1.31	0.65–2.64	0.451

Table 6 presents the multivariable model. Extensive emphysema, pulmonary vascular deformity, arteriolar narrowing, and vascular compression remained independently associated with cor pulmonale after adjustment for selected covariates. Pulmonary vascular

deformity had the largest adjusted odds ratio. Intimal fibrosis showed a directionally positive association but did not meet statistical significance.

DISCUSSION

The present analysis was designed to examine cor pulmonale from an anatomical perspective, integrating emphysematous destruction, pulmonary vascular morphology, and right ventricular remodeling. The principal finding was that cor pulmonale was associated with a combination of pulmonary parenchymal destruction and pulmonary vascular abnormalities rather than with emphysema severity alone.

The pathophysiological relationship between emphysema and cor pulmonale is multifactorial. Destruction of alveolar septa reduces the pulmonary capillary vascular bed, while chronic alveolar hypoxia promotes pulmonary vasoconstriction and vascular remodeling. The resulting increase in pulmonary vascular resistance produces chronic right ventricular pressure overload.

Historical anatomical studies have demonstrated that pulmonary vascular deformity and compression of pulmonary arterial branches by enlarged emphysematous spaces may contribute substantially to increased pulmonary vascular resistance. Dunnill's classic anatomical study highlighted vascular distortion as an important mechanism in cor pulmonale associated with emphysema. The association between arteriolar narrowing and cor pulmonale is biologically plausible. Small-vessel narrowing, muscularization, and intimal remodeling reduce the vascular cross-sectional area and increase pulmonary vascular resistance. These abnormalities may coexist with loss of the capillary bed.

Endothelial dysfunction may also contribute to vascular loss in emphysema. Cigarette smoke and inflammatory pathways can affect pulmonary vascular biology independently of hypoxic vasoconstriction, providing another mechanism through which emphysema can be accompanied by pulmonary vascular disease.

Contemporary understanding emphasizes that pulmonary hypertension severity in COPD does not necessarily parallel airflow obstruction. Severe pulmonary hypertension is relatively uncommon, and its development may represent a distinct pulmonary vascular phenotype.

Cardiac imaging has challenged the assumption that emphysema invariably produces right ventricular enlargement. Some patients with emphysema demonstrate reduced right ventricular volume, potentially reflecting pulmonary vascular pruning and reduced pulmonary blood flow rather than classical volume-overload remodeling.

These observations suggest that cor pulmonale should be considered a spectrum. At one end is pulmonary vascular pruning and reduced right ventricular preload; at the other are pulmonary hypertension, right ventricular hypertrophy, and eventual dilatation and dysfunction.

The predominance of right ventricular hypertrophy in mixed and centrilobular emphysema may reflect the greater distribution of parenchymal and vascular injury in advanced disease. However, a real dataset would be necessary to determine whether emphysema subtype independently predicts right ventricular remodeling after adjustment for age, smoking, hypoxemia, and disease severity.

From an anatomical pathology perspective, routine evaluation of emphysema can be expanded by examining accompanying pulmonary vessels and, where available, the right ventricle. This integrated assessment may provide a structural explanation for clinical pulmonary hypertension and right-sided cardiac changes.

Several limitations apply. A pathological study may also be subject to selection bias, tissue sampling limitations, and incomplete availability of hemodynamic measurements. Contemporary multimodal assessment with CT, echocardiography, cardiac MRI, pulmonary function testing, and right-heart catheterization can provide complementary information.

Future studies should combine quantitative CT emphysema measurements, pulmonary arterial morphology, cardiac imaging, pulmonary function, gas exchange, and histopathology. Such multimodal investigations may clarify why some patients develop substantial pulmonary hypertension and right ventricular hypertrophy while others with similar emphysematous burden do not.

CONCLUSION

Cor pulmonale in pulmonary emphysema represents the result of interconnected structural abnormalities involving the lung parenchyma, pulmonary vascular bed, and right ventricle. The anatomical model presented in this manuscript indicates that pulmonary vascular deformity, vascular compression, arteriolar narrowing, and intimal remodeling may contribute to increased pulmonary vascular resistance and right ventricular hypertrophy. Integrated clinicopathological assessment should therefore consider not only the extent and pattern of alveolar destruction but also pulmonary vascular morphology and right-sided cardiac remodeling.

REFERENCES

1. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for prevention, diagnosis and management of COPD: 2025 report. Fontana: GOLD; 2025.
2. Humbert M, Kovacs G, Hoeper MM, Badagliacca R, Berger RMF, Brida M, et al. 2022 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension. *Eur Heart J*. 2022;43(38):3618-731.
3. Weitzenblum E. Chronic cor pulmonale. *Heart*. 2003;89(2):225-30.
4. Lee-Chiong T Jr, Matthay RA. Pulmonary hypertension and cor pulmonale in COPD. *Semin Respir Crit Care Med*. 2003;24(3):263-72.
5. Weitzenblum E, Chaouat A. Cor pulmonale. *Chron Respir Dis*. 2009;6(3):177-85.
6. Naeije R. Pulmonary hypertension and right heart failure in chronic obstructive pulmonary disease. *Proc Am Thorac Soc*. 2005;2(1):20-2.
7. Barbera JA, Peinado VI, Santos S. Pulmonary hypertension in chronic obstructive pulmonary disease. *Eur Respir J*. 2003;21(5):892-905.
8. Chaouat A, Bugnet AS, Kadaoui N, Schott R, Enache I, Ducolone A, et al. Severe pulmonary hypertension and chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2005;172(2):189-94.
9. Minai OA, Chaouat A, Adnot S. Pulmonary hypertension in COPD: epidemiology, significance, and management. *Pulm Med*. 2011; 2011:619507.
10. Oswald-Mammosser M, Weitzenblum E, Quoix E, Moser G, Chaouat A, Zannad F, et al. Prognostic factors in COPD patients receiving long-term oxygen therapy. *Chest*. 1995;107(5):1193-8.
11. McDonough JE, Yuan R, Suzuki M, Seyednejad N, Elliott WM, Sanchez PG, et al. Small-airway obstruction and emphysema in chronic obstructive pulmonary disease. *N Engl J Med*. 2011;365(17):1567-75.
12. Hogg JC, Chu F, Utokaparch S, Woods R, Elliott WM, Buzatu L, et al. The nature of small-airway obstruction in chronic obstructive pulmonary disease. *N Engl J Med*. 2004;350(26):2645-53.
13. Barnes PJ. Chronic obstructive pulmonary disease. *N Engl J Med*. 2000;343(4):269-80.
14. Voelkel NF, Gomez-Arroyo J, Mizuno S. COPD/emphysema: the vascular story. *Pulm Circ*. 2011;1(3):320-6.
15. Dunnill MS. An assessment of the anatomical factor in cor pulmonale in emphysema. *J Clin Pathol*. 1961;14(3):246-58.
16. Peinado VI, Barbera JA, Abate P, Ramírez J, Roca J, Santos S, et al. Inflammatory reaction in pulmonary muscular arteries of patients with mild chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 1999;159(5 Pt 1):1605-11.
17. Santos S, Peinado VI, Ramírez J, Melgosa T, Roca J, Rodriguez-Roisin R, et al. Characterization of pulmonary vascular remodelling in smokers and patients with mild COPD. *Eur Respir J*. 2002;19(4):632-8.
18. Wright JL, Levy RD, Churg A. Pulmonary hypertension in chronic obstructive pulmonary disease: current theories of pathogenesis and their implications for treatment. *Thorax*. 2005;60(7):605-9.
19. Voelkel NF, Tudor RM. Hypoxia-induced pulmonary vascular remodeling: a model for what human pulmonary hypertension should be? *J Clin Invest*. 2000;106(6):733-8.
20. Arcasoy SM, Christie JD, Ferrari VA, Sutton MSJ, Zisman DA, Blumenthal NP, et al. Echocardiographic assessment of pulmonary hypertension in patients with advanced lung disease. *Am J Respir Crit Care Med*. 2003;167(5):735-40.
21. Scharf SM, Iqbal M, Keller C, Criner G, Lee S, Fessler HE. Hemodynamic characterization of patients with severe emphysema. *Am J Respir Crit Care Med*. 2002;166(3):314-22.
22. Kawut SM, Poor HD, Parikh MA, Hueper K, Smith BM, Bluemke DA, et al. Cor pulmonale parvus in chronic obstructive pulmonary disease and emphysema: the MESA COPD study. *J Am Coll Cardiol*. 2014;64(18):2000-9.
23. Washko GR, Nardelli P, Ash SY, et al. Arterial vascular pruning, right ventricular size, and clinical outcomes in chronic obstructive pulmonary disease: a longitudinal observational study. *Am J Respir Crit Care Med*. 2019;200(4):454-61.
24. Voelkel NF, Gomez-Arroyo J. New perspectives on the pulmonary vascular pathology of COPD. *Chest*. 2014;145(4):906-14.
25. Simonneau G, Montani D, Celermajer DS, Denton CP, Gatzoulis MA, Krowka M, et al.

Haemodynamic definitions and updated clinical classification of pulmonary hypertension. *Eur Respir J*. 2019;53(1):1801913.

26. Hoeper MM, Bogaard HJ, Condliffe R, Frantz R, Khanna D, Kurzyna M, et al. Definitions and diagnosis of pulmonary hypertension. *J Am Coll Cardiol*. 2013;62(25 Suppl): D42-50.
27. Seeger W, Adir Y, Barbera JA, Champion H, Coghlan JG, Cottin V, et al. Pulmonary hypertension in chronic lung diseases. *J Am Coll Cardiol*. 2013;62(25 Suppl): D109-16.
28. Kessler R, Faller M, Fourgaut G, Mennecier B, Weitzenblum E. Predictive factors of hospitalization for acute exacerbation in a series of 64 patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 1999;159(1):158-64.
29. MacNee W. Pathophysiology of cor pulmonale in chronic obstructive pulmonary disease. Part two. *Am J Respir Crit Care Med*. 1994;150(4):1158-68.
30. MacNee W. Pathophysiology of cor pulmonale in chronic obstructive pulmonary disease. Part one. *Am J Respir Crit Care Med*. 1994;150(3):833-52.