Arch Bronconeumol. 2017;xxx(xx):xxx–xxx

Sociedad Española de Neumología y Cirugía Torácica SEPAR

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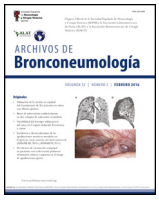

Special article

Guidelines on the Diagnosis and Treatment of Pulmonary Hypertension: Summary of Recommendations☆

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ARTICLE INFO

Article history:
Received 22 October 2017
Accepted 27 November 2017
Available online xxx

Keywords:
Pulmonary hypertension
Pulmonary arterial hypertension
Chronic thromboembolic pulmonary hypertension
Pulmonary circulation
Clinical guidelines

ABSTRACT

Pulmonary hypertension is a hemodynamic disorder defined by abnormally high pulmonary artery pressure that can occur in numerous diseases and clinical situations. The causes of pulmonary hypertension are classified into 5 major groups: arterial, due to left heart disease, due to lung disease and/or hypoxemia, chronic thromboembolic, with unclear and/or multifactorial mechanisms. This is a brief summary of the Guidelines on the Diagnostic and Treatment of Pulmonary Hypertension of the Spanish Society of Pulmonology and Thoracic Surgery. These guidelines describe the current recommendations for the diagnosis and treatment of the different pulmonary hypertension groups.

Guía de diagnóstico y tratamiento de la hipertensión pulmonar: resumen de recomendaciones

Palabras clave:
Hipertensión pulmonar
Hipertensión arterial pulmonar
Hipertensión pulmonar tromboembólica crónica
Circulación pulmonar
Guía clínica

RESUMEN

La hipertensión pulmonar es un trastorno hemodinámico definido por el aumento anómalo de la presión arterial pulmonar, que puede presentarse en numerosas enfermedades y situaciones clínicas. Las causas de hipertensión pulmonar se clasifican en 5 grandes grupos: arterial, debida a cardiopatía izquierda, debida a enfermedad pulmonar y/o hipoxemia, tromboembólica crónica y de mecanismo no establecido y/o multifactorial. El presente documento expone de forma resumida las recomendaciones de la Guía de Diagnóstico y Tratamiento de la Hipertensión Pulmonar de la Sociedad Española de Neumología y Cirugía Torácica. En dicha guía se presentan las pautas actuales de diagnóstico y tratamiento de los distintos grupos de hipertensión pulmonar.

☆ Please cite this article as: Barberà JA, Román A, Gómez-Sánchez MÁ, Blanco I, Otero R, López-Reyes R, et al. Guía de diagnóstico y tratamiento de la hipertensión pulmonar: resumen de recomendaciones. Arch Bronconeumol. 2018. https://doi.org/10.1016/j.arbres.2017.11.014

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1579-2129/

Table 1
Levels of Evidence and Class of Recommendation Used in the Guidelines.

Levels of evidence	
A	Data derived from multiple randomized clinical trials or meta-analysis
B	Data derived from a single randomized or large non-randomized studies
C	Consensus of expert opinion, small or retrospective studies, or patient registries
Classes of recommendation	
I	Evidence and/or general agreement that a particular treatment or procedure is beneficial, useful, or effective
II	Conflicting evidence and/or diverging opinions about the usefulness/effectiveness of a given treatment or procedure
IIa	Evidence/opinion tends toward usefulness/effectiveness
IIb	Usefulness/effectiveness is less supported by evidence/opinion
III	Evidence or general agreement that a particular treatment or procedure is not useful/effective and, in some cases, may be harmful

Introduction

This document is a summary of the recommendations of the Guidelines on the Diagnosis and Treatment of Pulmonary Hypertension prepared by the Spanish Society of Pulmonology and Thoracic Surgery,[1] that was drawn from the clinical practice guidelines of the European Society of Cardiology and the European Respiratory Society.[2] For more details, please refer to the original guidelines,[1] included as an annex to this article. The levels of evidence and class of recommendation used are set out in Table 1.

Definition and Classification

Pulmonary hypertension (PH) is a hemodynamic, pathophysiological disorder defined by elevated mean pulmonary arterial pressure (mPAP) ≥25 mmHg, measured by right heart catheterization (RHC).[2] PH can occur in various clinical processes, that can be classified into 5 groups (Table 2).

Diagnosis of Pulmonary Hypertension

Detection

Transthoracic echocardiography (TTE) is the main tool for the early detection and screening of PH. The probability of PH according to TTE findings is shown in Table 3.

TTE screening for PH is recommended in asymptomatic subjects in the following risk groups:

- Patients with systemic sclerosis [I, B].
- First-degree relatives of patients with a diagnosis of hereditary pulmonary arterial hypertension (PAH) [I, C].
- Patients with portal hypertension who are candidates for liver transplantation [I, B].

In other cases, TTE will be performed on the basis of clinical suspicion.

General Approach to Diagnosis

The diagnostic algorithm of PH is shown in Fig. 1. TTE will be performed if PH is suspected. If the probability of PH is intermediate or high, left heart disease (PH group 2) and chronic respiratory disease (PH group 3) will be ruled out. Patients in these PH groups or those with severe right ventricular dysfunction will be referred to an expert in PH[2] [IIa, C]. When PH has been ruled out in groups 2 and 3, ventilation–perfusion lung scintigraphy will be used to rule out thromboembolic disease. If perfusion defects are observed on the ventilation–perfusion scintigraphy, a study for probable chronic thromboembolic pulmonary hypertension will be performed. Hemodynamic diagnosis with RHC will be carried out in an expert PH unit [I, C]. If PAH is confirmed, the subtype should be identified.

Pulmonary Arterial Hypertension

Evaluation

In patients with idiopathic, hereditary, or drug-related PAH, a vasodilator test with inhaled nitric oxide or iv epoprostenol will be performed during the RHC diagnostic procedure [I, C]. The test is positive if mPAP drops ≥10 mmHg to reach a value ≤40 mmHg, with no reduction in cardiac output [I, C]. The subtype will be identified by contrast echocardiography, autoimmunity testing, hepatotropic virus serology, and HIV serology (Fig. 1). If there is a family history of PH, or if it is suspected, a study to identify BMPR2 gene mutations is advisable.[3–5]

The diagnosis of pulmonary veno-occlusive disease (PVOD) or pulmonary capillary hemangiomatosis (PCH) is based on clinical data, very low carbon dioxide diffusing capacity, severe hypoxemia, and consistent findings on high-resolution computed tomography (HRCT).[6] It can also be diagnosed from the presence of EIF2AK4 gene mutations.[6]

A set of variables associated with survival are used for evaluating prognosis[2] (Table 4). For monitoring, clinical parameters and more easily performed tests (functional class [FC], 6-minute walk test, ECG, clinical laboratory tests) should be evaluated every 3–6 months, while the more complex procedures should be performed every 6–12 months,[7] or in case of clinical deterioration [I, C].

Treatment

General Measures and Support

General therapeutic measures for PAH are listed in Table 5. Diuretics are indicated in patients with right ventricular failure and water retention [I, C]. Loop diuretics or aldosterone antagonists should be used.[2] Anticoagulation with vitamin K antagonists is recommended in idiopathic and hereditary PAH, and PAH caused by anorectics [IIb, C]. Oxygen therapy is recommended if PaO_2 is <60 mmHg [I, C]. It may also be considered as an option for correcting desaturation during exercise.[2] Regular monitoring of iron levels is recommended, and supplements should be administered if necessary.

Specific Treatment

Specific drugs for the treatment of PAH include (Table 6):

- Calcium channel blockers: indicated for use in patients with idiopathic PAH and positive vasodilator test [I, C]. High-dose nifedipine, diltiazem and amlodipine are recommended.[8]
- Endothelin receptor antagonists, including ambrisentan, bosentan, and macitentan. Ambrisentan and bosentan can cause liver toxicity, so monthly monitoring of liver enzymes is required. Macitentan carries a risk of anemia, and regular monitoring of hemoglobin levels is recommended.
- Phosphodiesterase type 5 (PDE5) inhibitors and soluble guanylate cyclase (sGC) stimulators: available PDE5 inhibitors are sildenafil and tadalafil, and the only available sGC stimulator is riociguat. The concomitant administration of PDE5 inhibitors and sGC stimulators is contraindicated.
- Prostacyclin analogs and prostacyclin receptor agonists: available prostacyclin analogs include epoprostenol, administered via