International Journal of Cardiology 154S (2011) S1–S2

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Preamble

Cologne Consensus Conference on pulmonary hypertension☆

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1. Guidelines for the diagnosis and treatment of pulmonary hypertension

The updated European Guidelines on the diagnosis and treatment of pulmonary hypertension that were jointly developed by the *European Society of Cardiology* (ESC) and the *European Respiratory Society* (ERS) have recently been published [1,2]. Based on board decisions of the German Society of Cardiology (*Deutsche Gesellschaft für Kardiologie, DGK)* and the German Society of Respiratory Medicine (*Deutsche Gesellschaft für Pneumologie, DGP)*, no new national guidelines have been issued so that the European Guidelines were adopted for Germany. A short version of the ESC/ERS guidelines has recently been published in German [3]. However, with regard to the practical implementation of the European Guidelines in Germany, several country-specific issues as well as relevant novel developments could not be sufficiently addressed in the European Guidelines.

The ESC/ERS Guidelines focus in detail on the diagnosis and treatment of pulmonary arterial hypertension (PAH), representing group 1 of the Dana Point Classification [4] (Table 1), but also address other forms of pulmonary hypertension (PH), particularly PH associated with left heart disease and chronic lung disease as well as chronic thromboembolic pulmonary hypertension (CTEPH).

2. Challenge P(A)H

Experts and representatives of professional associations are concerned that the increasing complexity regarding the diagnosis and treatment of various types of PH is not always taken into account in clinical practice. While many cases of PAH are still diagnosed too late, frequent misclassification of PH remains a problem, as the "diagnosis" of P(A)H is often made on the basis of echocardiographic findings alone without an adequate diagnostic workup. A typical example is CTEPH, which is often overlooked or inadequately treated. The treatment of choice for CTEPH remains surgery, i.e. pulmonary endarterectomy (PEA). The failure to refer patients with CTEPH to specialised expert centers means to deny them the possibility of a potentially curative treatment option.

Table 1
Updated clinical classification of pulmonary hypertension (Dana Point, 2008).

1. **Pulmonary arterial hypertension (PAH)**
   - 1.1. Idiopathic PAH
   - 1.2. Heritable PAH
     - 1.2.1. BMPR2 mutations
     - 1.2.2. ALK1, endoglin mutations (with and without hereditary hemorrhagic telangiectasia)
     - 1.2.3. Unknown mutations
   - 1.3. Drugs or toxins induced
   - 1.4. Associated with:
     - 1.4.1. Connective tissue diseases
     - 1.4.2. HIV infection
     - 1.4.3. Portal hypertension
     - 1.4.4. Congenital heart disease
     - 1.4.5. Schistosomiasis
     - 1.4.6. Chronic hemolytic anemia
   - 1.5. Persistent pulmonary hypertension of the newborn

1'. **Pulmonary veno-occlusive disease (PVOD) and/or pulmonary capillary hemangiomatosis (PCH)**

2. **Pulmonary hypertension due to left heart disease**
   - 2.1. Systolic dysfunction
   - 2.2. Diastolic dysfunction
   - 2.3. Valvular disease

3. **Pulmonary hypertension due to lung diseases and/or hypoxemia**
   - 3.1. Chronic obstructive pulmonary disease
   - 3.2. Interstitial lung disease
   - 3.3. Other pulmonary diseases with mixed restrictive/obstructive pattern
   - 3.4. Sleep-disordered breathing
   - 3.5. Alveolar hypoventilation syndrome
   - 3.6. Chronic exposure to high altitude
   - 3.7. Developmental abnormalities

4. **Chronic thromboembolic pulmonary hypertension (CTEPH)**

5. **Pulmonary hypertension with unclear or multifactorial mechanisms**
   - 5.1. Hematological disorders: myeloproliferative disorders, splenectomy
   - 5.2. Systemic disorders, sarcoidosis, pulmonary Langerhans cell histiocytosis, lymphangioleiomyomatosis, neurofibromatosis, vasculitis
   - 5.3. Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders
   - 5.4. Others: tumoral obstruction, fibrosing mediastinitis, chronic renal failure on hemodialysis

BMPR-2, bone morphogenetic protein receptor type-2; ALK-1, activin receptor-like kinase 1 gene.

☆ Source: Rosenkranz S, Ghofrani HA, Grünig E, Hoeper MM. Cologne consensus conference on pulmonary hypertension 2010 – Preamble. Dtsch Med Wochenschr 2010;135(Suppl 3):S64–66.

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Furthermore, an uncritical use of PAH treatments (prostanoids, endothelin receptor antagonists, phosphodiesterase type-5 inhibitors) is increasingly observed in patients for whom these drugs are not indicated. This applies especially to patients with PH owing to left heart disease or to chronic lung disease. In many of these cases, the examining physicians or those filling out prescriptions do not seem to be familiar with the difference between PAH and other forms of PH. Targeted PAH treatments may even exert detrimental effects on patients if used outside of their area of indication (e.g. impaired gas exchange in patients with chronic lung disease, pulmonary congestion due to left heart failure). The uncritical use of PAH drugs increases the economic burden on healthcare systems. On the other hand, PAH treatments may be justified in exceptional cases, e.g. when severe PH develops in patients with mild forms of left heart disease or lung disease ("out of proportion PH").

The diagnosis and treatment of PH/PAH remains complex and should therefore be handled at expert centers in order to avoid misdiagnoses, misclassifications and inappropriate therapies. In addition, a center-based management of patients with PH is the prerequisite for clinical research and further improvement in this field which is thoroughly needed.

3. Cologne Consensus Conference

In June 2010, a Consensus Conference organized by the PH working groups of the German Society of Cardiology (DGK), the German Society of Respiratory Medicine (DGP) and the German Society of Pediatric Cardiology (DGPK) was held in Cologne, Germany. The conference aimed to solve practical issues surrounding the implementation of the European Guidelines in Germany, with special emphasis on the critical issues mentioned above. Several working groups had been appointed, which have dealt in detail with the following topics:

- Non-invasive diagnosis
- Invasive diagnosis
- Treatment of pulmonary arterial hypertension (PAH)
- Pulmonary hypertension due to left heart disease
- Pulmonary hypertension due to chronic lung disease
- Chronic thromboembolic pulmonary hypertension (CTEPH).

The results of this conference which reflect general interdisciplinary agreement are summarized in structured publications and were initially published in a supplement of the *Deutsche Medizinische Wochenschrift* [German Weekly Medical Journal]. The results were updated in October 2011, and an English version is now published in this supplement of the *International Journal of Cardiology*. The authors of each publication were members of the corresponding working group, and each article discusses the respective topic in detail. Some sections refer to the recommendations of the *4th World Symposium on Pulmonary Hypertension* (that took place in 2008 in Dana Point, California [4–7]) as well as to novel data and information that were not considered in the European Guidelines because they were not available at the time. All articles contain sections from the European Guidelines that closely reflect the original text [1–3], whereby comments and additions as well as specific recommendations of the Consensus Conference appear in italics. The information on classes of recommendation and levels of evidence corresponds to Tables 2 and 3 listed in this preamble.

Table 2
Classes of recommendations.

Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, and effective
Class II	Conflicting evidence and/or divergence of opinion about the usefulness/efficacy of a given treatment/procedure
Class IIa	Weight of evidence is in favor of the usefulness/efficacy of a given treatment
Class IIb	Efficacy of a given treatment is not well established and there is no general agreement on efficacy
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective and may in some cases even be harmful

Table 3
Level of evidence.

Level of Evidence A	Data derived from >1 randomized clinical trials or meta-analyses
Level of Evidence B	Data derived from a single randomized clinical trial or large non-randomized studies
Level of Evidence C	Consensus of opinion of the experts and/or data from small or retrospective studies and registries

Acknowledgment

The Cologne Consensus Conference was supported by unrestricted grants from Actelion Pharmaceuticals Germany, Bayer Schering Pharma, GlaxoSmithKline, Lilly Germany, and Pfizer Pharma GmbH. United Therapeutics/OMT served as a co-sponsor.

Conflicts of interest

S. Rosenkranz: Remunerations for lectures and/or consultancy for Actelion, BayerSchering, GSK, Lilly, Novartis, Pfizer and United Therapeutics.

H.A. Ghofrani: Honoraria for lectures and/or consultation of Actelion, Bayer, Gilead, GSK, Lilly, LungRx, Novartis, and Pfizer.

E. Grünig: Honoraria for lectures and/or consultancy for Actelion, Bayer, GSK, Lilly, and Pfizer.

M.M. Hoeper: Remunerations for lectures and/or consultancy for Actelion, Bayer, Gilead, GSK, Lilly, LungRx, and Pfizer.

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