Executive Summary: Canadian Cardiovascular Society – Canadian Thoracic Society Position Statement on Pulmonary Hypertension

1. Introduction

Pulmonary hypertension (PH) is a heterogeneous group of conditions, usually classified in 1 of 5 groups. Group 1 is pulmonary arterial hypertension (PAH), group 2 is related to left-sided heart disease, group 3 is related to lung disease and/or hypoxia, group 4 is due to chronic thromboembolic pulmonary hypertension disease (CTEPH), and group 5 is related to unclear or multifactorial causes. The last CCS/CTS joint position statement on PH was published in 2005. Though management of the various clinical forms of PH has changed dramatically over the past 15 years, it remains associated with worse outcomes and there remains an unacceptable delay between symptom onset and diagnosis. This document summarizes current recommendations on the diagnosis and management of PH.

2. Diagnosis

In PH, the presentation is often insidious and nonspecific. Some forms that require specialized therapy are rare but very important, with very poor outcomes, if not treated. The utmost importance of multimodality assessment at an expert center is highlighted. Recommendations focus on echocardiography and catheterization, given that they are essential cardiac tests for the diagnosis and follow up of PH.

We recommend echocardiography for evaluation of any patient with suspected PH or unexplained dyspnea. We outline key features of a complete echocardiographic assessment for screening and evaluation of PH, and key prognostic parameters on follow-up echocardiography for patients already diagnosed with PH. Screening echocardiography is recommended in high-risk populations, such as systemic sclerosis and patients referred for liver transplant. In systemic sclerosis, we recommend annual echocardiographic screening. Right heart catheterization is strongly recommended for the diagnosis of treatable forms of PH (PAH and CTEPH). It is essential for diagnosis and should be performed at an expert center to ensure accurate classification and to avoid duplicate testing. Technical recommendations are provided, including appropriate zeroing of transducers, measurement techniques and vasodilator challenge.

Cardiac MRI is also mentioned as a useful modality in selected patients with PH.

3. Management

The management of PH depends on the clinical classification (WHO Group) in question. This document is focused primarily on the management of WHO Group 1 PH (PAH). General supportive measures are recommended, including education, contraception, supervised exercise and diuretics, and oxygen, as needed. Anticoagulation is recommended in selected patients with idiopathic, heritable and drug- and toxin-associated PAH, so long as the bleeding risk is low. Calcium channel blockers are only helpful in a minority of patients with PAH, and acute vasodilator testing is required to identify those patients. Care for patients with PAH should be carried out in established expert PH centers familiar with treating these complex patients.

Targeted therapies for PAH available in Canada are discussed. These include

agents targeting the prostacyclin pathway (epoprostenol [IV], treprostinil [IV/SC] and selexipag [PO]; the endothelin pathway (bosentan [PO], ambrisentan [PO] and macitentan [PO]; the nitric oxide pathway (sildenafil [PO], tadalafil [PO] and riociguat [PO]). All symptomatic patients with PAH should be treated with targeted medications to reduce symptoms, improve functional capacity, delay progression of PAH and to reduce hospitalization and death. Recent evidence shows that risk stratification using a variety of clinical, echocardiographic and hemodynamic variables improves prognostication. Established risk stratification algorithms should be used to establish risk, and PAH therapies should be chosen with a goal of moving a patient to low-risk status. There is established benefit of upfront combination therapy in PAH. Monotherapy with a single agent is now rarely used. Patients with high-risk features should be considered for parenteral therapy. Ongoing regular follow up is required at PH centers.

Patients with WHO Group 2 PH (PH due to left-sided heart disease) and WHO Group 3 PH (PH due to lung disease and/or hypoxia) have not been shown to derive a benefit from targeted therapy for PAH. In both groups, therapy is directed at the underlying cause, and pulmonary vasodilator therapy can be harmful. The consensus statement recommends against the routine use of such therapies in both groups. Patients with severe PH and right ventricular (RV) dysfunction should be referred to a PH center.

WHO Group 4 PH (PH due to CTEPH) is also discussed thoroughly, as it is an important treatable cause of PH that can be curable with pulmonary endarterectomy (PEA). Dyspnea post-acute pulmonary embolism (PE) should prompt consideration of CTEPH. V/Q scanning should be done in all cases of unexplained PH to exclude CTEPH. The majority of patients have central disease that is accessible surgically, and patients should be referred to a PEA center to determine operability. There is established benefit from PAH therapies (riociguat, macitentan) in CTEPH that is inoperable or that persists

after surgery. Evidence is mounting for a benefit for balloon pulmonary angioplasty, as well.

Finally, aggressive therapies for patients refractory to established therapy are discussed. Eligible patients with persistent severe PH with NYHA III/IV symptoms despite maximal therapy should be referred for consideration of bilateral lung transplantation. Extracorporeal life support (ECLS) can be used as a bridge to transplant, or as a bridge to initiation of PAH therapy with IV epoprostenol.