Supplement

6 minute walk test

The 6-minute walk testing (6MWT) with Borg scores was performed according to the American Thoracic Society guidelines.[1] In brief, the 6MWT was performed indoors, along a long, flat, straight, enclosed corridor (30 m in length) with a hard surface that is seldom traveled. The patients were instructed precisely before the test. For example, the patient was instructed to wear comfortable clothing and shoes. The patients were not allowed to talk to anyone during the walk. Only the standardized phrases for encouragement were allowed to be used during the test. The tester was not allowed to walk with the patient during the test. The 6MWT was performed more than one hour after eating on the morning of each study day. The test was performed at approximately the same time of day at each visit.

The Borg score for dyspnea was recorded at the beginning and end of each test.

The Borg scale was as follows:

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0 Nothing at all

0.5 Very, very slight (just noticeable)

1 Very slight

2 Slight (light)

3 Moderate

4 Somewhat severe

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5 Severe (heavy)

6

7 Very severe

8

9 Very, very severe (almost maximal)

10 Very, very severe (maximal)

WHO functional class was assessed using the standard definition[2] by experienced PAH clinician-investigators.

WHO functional classification was as follows:

I Patients with PH in whom there is no limitation of usual physical activity; ordinary physical activity does not cause increased dyspnea, fatigue, chest pain, or presyncope.

II Patients with PH who have mild limitation of physical activity. There is no discomfort at rest, but normal physical activity causes increased dyspnea, fatigue, chest pain, or presyncope.

III Patients with PH who have a marked limitation of physical activity. There is no discomfort at rest, but less than ordinary activity causes increased dyspnea, fatigue, chest pain, or presyncope.

IV Patients with PH who are unable to perform any physical activity at rest and who may have signs of right ventricular failure. Dyspnea and/or fatigue may be present at rest, and symptoms are increased by almost any physical activity.

Hemodynamic parameters were measured as described previously.[3] An introducer sheet was placed in the right internal jugular vein, and a quadric-lumen Swan-Ganz catheter (Edwards Lifesciences World Trade Co., Ltd, USA) was advanced into the pulmonary artery. Correct positioning of the catheter was verified by chest fluoroscopy. Transducers were positioned at the mid-axillary line and zeroed at atmospheric pressure. Hemodynamic evaluations were carried out with the patient in the supine position. Patients breathed room air. Oxygen saturations (inferior vena cava; pulmonary artery; right atrium; right ventricle; systemic artery; and superior vena cava) and selected intracardiac pressures (at end-expiration) were measured. Cardiac output was determined using the thermodilution technique or calculated according to the Fick method as appropriate.

Hemodynamic parameters measured during RHC:

☐ Heart rate

☐ Cardiac output

☐ Pulmonary artery pressure (sPAP, dPAP, mPAP)

☐ Mean right atrial pressure

☐Mean pulmonary capillary wedge pressure

☐Noninvasive systolic and diastolic systemic arterial pressure

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Reference

1. ATS statement: guidelines for the six-minute walk test. *Am J Respir Crit Care Med* 2002; 166: 111-117.

2. McGoon M, Gutterman D, Steen V, et al. Screening, early detection, and diagnosis of pulmonary arterial hypertension: ACCP evidence-based clinical practice guidelines. *Chest* 2004; 126: 14S-34S.

3. Jing ZC, Jiang X, Han ZY, et al. Iloprost for pulmonary vasodilator testing in idiopathic pulmonary arterial hypertension. *Eur Respir J* 2009; 33: 1354-1360.