



## Prevalence and Prognostic Value of Left Ventricular Diastolic Dysfunction in Idiopathic and Heritable Pulmonary Arterial Hypertension

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### **e-Appendix 1.**

#### **Methods section supplement:**

Each one of these patients underwent a careful selection process that included a variety of testing including complete blood count, comprehensive metabolic panel, antinuclear antibody, sedimentation rate, thyroid-stimulating hormone, hepatitis panel, human immunodeficiency virus, pulmonary function, six-minute walk, Chest XR and V/Q scan to exclude other etiologies of pulmonary hypertension. We performed further evaluations if any of the previous testing was inconclusive or abnormal.

#### **Echocardiographic measurements and determinations:**

Transthoracic Doppler echocardiography was performed with commercially available equipment, using 2.5 MHz transducers, in the left lateral recumbent position at end-expiration. Images were recorded from the standard views using two-dimensional, M-mode and color, pulsed and continuous wave Doppler modes. Recordings were analyzed with the use of an offline quantification system (syngo® Dynamics, Siemens Medical Solutions, USA).

We determined the areas of all four cardiac chambers in the apical four-chamber view by tracing the endocardial border and using single-plane area-length method. The right and left biplane ventricular areas were measured at end diastole. Right and left atrium areas were determined at end systole. Volumes were calculated and indexed by body surface area. We measured left ventricular eccentricity index, a measure of interventricular septal

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displacement, in the parasternal short axis view at the level of papillary muscles at end-systole, end- and early-diastole. This index was calculated by the method of Ryan et al. as  $D1/D2$ , where  $D1$  is the diameter of the left ventricle parallel to the interventricular septum (anterior to inferior wall) and  $D2$  is the diameter perpendicular to and bisecting the interventricular septum (septum to posterolateral wall). Right ventricular function was graded as normal, mild, moderate, moderately severe and severe impairment by expert clinical echocardiography readers.

Transmitral and pulmonary vein flow velocities were obtained by pulsed Doppler in the apical four-chamber view. The sample volume (1-2 mm) was placed at the mitral valve leaflet tips (position confirmed in all patients) and at > 0.5 cm into right upper pulmonary vein, respectively 6. The angle between the interrogating Doppler beam and apparent mitral inflow was < 20 degrees in all cases. Waves from three consecutive cardiac cycles were averaged. The RR and PR intervals were measured from the ECG that was recorded simultaneously with transmitral flow Doppler. Pulse wave tissue Doppler imaging was performed in the apical 4-chamber view. The sample volume was positioned at or 1 cm within the septal and lateral insertion sites of the mitral leaflets and adjusted to cover the longitudinal excursion of the mitral annulus in both systole and diastole.

### **Right heart catheterization measurements:**

All patients underwent RHC within 2 months of the echocardiographic study. Right heart catheterization was performed in the standard manner in the cardiac catheterization laboratory using a 7 F pulmonary artery catheter. Pressure measurements were obtained from paper recordings at end-expiration. Cardiac output (CO) was obtained by the thermodilution method and transpulmonary gradient (mean PAP – pulmonary artery occlusion pressure) and pulmonary vascular resistance (transpulmonary gradient / CO) were calculated.

### **References:**

- 1 Ryan T, Petrovic O, Dillon JC, et al. An echocardiographic index for separation of right ventricular volume and pressure overload. *J Am Coll Cardiol* 1985; 5:918-927