CHEST

Original Research

PULMONARY VASCULAR DISEASE

Echocardiography of the Pulmonary Circulation and Right Ventricular Function

Exploring the Physiologic Spectrum in 1,480 Normal Subjects

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Background: **Although transthoracic echocardiography (TTE) is an excellent noninvasive screening test for pulmonary hypertension, the physiologic range of Doppler echocardiography-derived pulmonary pressures remains not completely investigated. The aim of the present study was, therefore, to explore the full spectrum of pulmonary pressures and right ventricular (RV) functional indexes by TTE in healthy subjects and to investigate clinical and echocardiographic correlates.**

Methods: **A random sample of 1,480 healthy individuals (mean age, 36.1 ± 15.5 years; range, 20-80 years; 905 men) underwent a comprehensive TTE. Pulmonary artery systolic pressure (PASP), mean pressure, and pulmonary vascular resistance were estimated by standard Doppler echocardiography formulas. In addition, RV diastolic (Doppler transtricuspid inflow measurements) and systolic indexes (RV fractional area change, RV tissue Doppler peak systolic velocity, tricuspid annular plane systolic excursion) were calculated.**

Results: **PASP and mean pulmonary artery pressure values were significantly higher in subjects aged > 50 years and in those with a BMI > 30 kg/m². In particular, a PASP > 40 mm Hg was found in 118 subjects (8%) of those aged > 50 years and in 103 (7%) of those with a BMI > 30 kg/m². No differences by age were registered in RV systolic indexes and in pulmonary vascular resistances. On multivariate analysis, in the overall study population, age, BMI, mitral E/e′ ratio, and left ventricular stroke volume were the only independent predictors of PASP.**

Conclusions: **This study delineates an estimate of pulmonary hemodynamics in a wide age range cohort of healthy subjects. Pulmonary pressures increased with age and BMI, as expected.**

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Abbreviations: LV = left ventricular; PASP = pulmonary artery systolic pressure; PH = pulmonary hypertension; RAP = right atrial pressure; RV = right ventricular; RVOTTVI = right ventricular outflow tract time-velocity integral; TAPSE = tricuspid annular plane systolic excursion; TD = tissue Doppler; TRV = tricuspid regurgitation velocity; TTE = transthoracic Doppler echocardiography

Pulmonary hypertension (PH) and related right-sided heart function represent key prognostic determinants of several cardiorespiratory conditions, such as left-sided heart disease.[1] Given the nonspecific symptoms and subtle physical signs, particularly in early stages, a high clinical index of suspicion is necessary to detect the disease before irreversible pathophysiologic changes occur.[2] In this regard, transthoracic Doppler echocardiography (TTE), by providing direct and/or indirect signs of elevated pulmonary pressures, is an excellent noninvasive screening test for patients with symptoms, risk factors, or both for PH.[3-5]

However, the physiologic range of Doppler echocardiography-derived pulmonary pressures and right ventricular (RV) functional parameters remains not completely investigated. The aim of this study is to explore the full spectrum of pulmonary pressures and RV functional indexes by TTE in healthy subjects and to investigate clinical and echocardiographic correlates.

Materials and Methods

Study Population

From April 2009 to July 2011 a sample of 1,587 consecutive healthy individuals was enrolled and referred to our echocardiographic laboratory of Monaldi Hospital in Naples (Italy) for the purpose of the present study. Volunteer control subjects were all recruited in Naples (Italy), selected from our department of cardiology among subjects investigated for work eligibility. Fifty of the initial subjects investigated refused to be included in the echocardiographic protocol. None of the selected control subjects included into the study had cardiovascular structural or functional abnormalities or received any medication.

All subjects underwent a detailed history, physical examination, ECG, chest radiography, and comprehensive TTE, including Doppler studies. Exclusion criteria were coronary artery disease, arterial hypertension, valvular or congenital heart disease, bicuspid aortic valve, congestive heart failure, cardiomyopathies, diabetes mellitus, sinus tachycardia, use of illicit drugs, and inadequate echocardiographic image quality. According to these criteria, 57 subjects were excluded: eight for coronary artery disease, 12 for arterial hypertension, 19 for significant valvular insufficiency (nine for mitral and 10 for tricuspid valve regurgitation more than mild), four for bicuspid aortic valve, two for hypertrophic cardiomyopathy, two for dilated cardiomyopathy, five for use of illicit drugs, and five for inadequate echocardiographic image quality.

Our final study population, therefore, consisted of 1,480 healthy individuals (mean age, 36.1 ± 15.5 years; range, 20-80 years; 905 men). All the subjects enrolled in the study protocol provided a written informed consent.

Imaging Protocol

Standardized transthoracic echocardiography and Doppler examinations were performed with commercially available equipment in all the subjects (Vivid 7 or Vivid E9; General Electric Company). Specific views included the parasternal long- and short-axis views (at the mitral valve and papillary muscle level); apical 4-, 2-, and 3-chamber views; and subcostal views including respiratory motion of the inferior vena cava. Pulsed and continuous-wave Doppler interrogation was performed on all four cardiac valves. All studies were reviewed and analyzed off-line by two independent observers blinded to the clinical characteristics of the study population. Specific measurements were made by the average of three to five cardiac cycles.

M- and B-Mode Measurements: Left ventricular (LV) diastolic and systolic diameters, interventricular septum, and posterior wall thickness measurements were performed in parasternal long-axis view with the patient in the left lateral position. LV mass was calculated by the Penn convention[6] and indexed for height (left ventricular mass index)[2.7] (Cornell adjustment).[7] Relative diastolic wall thickness was determined as the ratio between twice the posterior wall thickness and LV end-diastolic diameter.[8]

LV ejection fraction was calculated by the biplane Simpson's rule in the apical four- and two-chamber views. Left atrial maximal volume was measured at the point of mitral valve opening, using the biplane area-length method and corrected for body surface area.[9] The percentage RV fractional area change was calculated as: (RV end-diastolic area − RV end-systolic area)/RV end-diastolic area × 100. Tricuspid annular plane systolic excursion (TAPSE) was calculated as index of RV longitudinal systolic function, by placing a M-mode cursor through the tricuspid annulus in a standard apical four-chamber window and measuring the difference between end-diastolic and end-systolic amount of longitudinal motion of the annulus (in mm)[10] (Fig 1).

Color Doppler Analysis: Valvular regurgitation was quantified from color Doppler imaging and categorized as absent, minimal (within normal limits), mild, moderate, or severe. Intermediate vena contracta values (3-7 mm) were confirmed by the proximal isovelocity surface area method.[11]

Doppler-derived LV diastolic inflow was recorded in apical four-chamber view by placing the sample volume at the tips level. The following LV diastolic measurements were measured: E and A peak velocities (m/s) and their ratio, E-wave deceleration time (milliseconds), and isovolumic relaxation time (milliseconds, as the time interval occurring between the end of systolic output flow and the transmitral E-wave onset by placing pulsed Doppler sample volume between outflow tract and mitral valve).[8] By tissue Doppler (TD), the early (e′) diastolic velocities were measured at the septal and lateral corner of the mitral annulus, and the mean between the two values was calculated. Mitral E velocity, corrected for the influence of relaxation (ie, the E/mean e′ ratio), was assessed to estimate LV filling pressures.[12] LV stroke volume was calculated as the product of LV outflow tract area and outflow tract time-velocity integral.[13]

Pulsed Doppler evaluation of RV diastolic indexes was performed in the apical four-chamber view by placing the sample volume at the tips of tricuspid valve. The following measurements of global RV filling were obtained: E and A peak velocities (m/s), E/A ratio, and E-wave deceleration time.[9]

To obtain a measure of RV myocardial function by TD, RV peak systolic velocity (RV s′) was assessed from the apical four-chamber view by placing the sample volume at the tricuspid annulus. Because this technique uses Doppler, special care is required to ensure optimal image orientation and avoid underestimation of velocities.[9]

Noninvasive Pulmonary Artery Systolic Pressure and Vascular Resistance: Peak tricuspid regurgitation velocity (TRV) was measured from the spectral profile of the tricuspid regurgitation jet in the RV inflow projection of the parasternal long-axis view, the parasternal short-axis view, or the apical four-chamber view. The highest transvalvular velocity was used for calculation of RV systolic pressure. American Society of Echocardiography-recommended

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