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Original article

The impact of age and gender on right ventricular diastolic function among healthy adults

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ABSTRACT

Background: Doppler echocardiography is ideally suited for assessment of diastolic function, being widely available, non-invasive, and less expensive than other techniques. However, data regarding age- and gender-matched reference values of right ventricular diastolic function are limited. This study aims to explore the physiologic variations of right ventricle (RV) diastolic function in a large cohort of healthy adults, and to investigate clinical and echocardiographic correlates.

Methods: From June 2007 to February 2014, 1168 healthy Caucasian subjects [mean age 45.1 ± 15.6 years, range 16–92; 555 (47.5%) men] underwent comprehensive transthoracic echocardiography (TTE) following current guidelines. The following RV main diastolic measurements were measured: peak early inflow velocity (*E*), annular both early (e′) and atrial (a′) velocities, *E*/e′ ratio.

Results: RV *E*/e′ constantly increases with age in females, but do not change substantially in males. RV *E*/*A* constantly decreases with age in both genders. Stepwise multiple linear regression analysis underlined a close significant association of RV diastolic function with both right and left heart morphologic measurements (right atrial area, RV diameters, left atrial volume) and functional indexes (TAPSE, RV tissue Doppler peak systolic velocity, left ventricular *E*/*Ee*′), as well as with indexes of increased pulmonary resistance.

Conclusion: Our data highlight the potential usefulness of different normal reference values according to the age and gender to correctly evaluate RV diastolic function. Differences in terms of demographic and anthropometric parameters could be useful to avoid potential misclassification of RV diastolic function when based on dichotomously suggested normal cut-off values.

Introduction

Right ventricular (RV) diastolic dysfunction is observed in several conditions, including both pressure and volume overload pathologies [1], primary and secondary lung disease [2,3], pulmonary arterial hypertension [4], ischemic heart disease [5], congenital heart disease [6], cardiomyopathies [7], and the physiologic aging process [8,9].

Several changes occur in the RV and in the pulmonary vascular system with aging. The pulmonary artery pressure and vascular resistance mildly increase with normal aging, most probably secondary to an increase in arterial stiffness of the pulmonary vasculature [10,11]. RV diastolic function changes with time: Doppler indices, reflective of flow pattern, demonstrate a reduced early RV diastolic filling, increased late filling, and reduced myocardial diastolic velocities [12]. These changes are analogous to change in left ventricular (LV) diastolic filling profile [13].

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The parameters used to assess RV diastolic function are essentially the same as those used to assess left filling pressure [14,15]. Early diastolic velocity of lateral tricuspid annulus (e′) assessed with tissue Doppler imaging (DTI) and the ratio of the trans-tricuspid early peak velocity (E) determined by conventional Doppler imaging over e′, represent two important parameters of RV diastolic dysfunction and E/e′ ratio can estimate with reasonable accuracy the mean right atrium pressure (RAP) [16], that is needed for the echocardiographic estimation of the pulmonary artery systolic pressure (PASP) [17,18]. Several publications on DTI of the LV exist, whereas the application of DTI on the RV is limited. In addition, limited data on the age and gender dependency of these new modalities are available.

This study aims to explore the relation between age and gender with standard and pulsed DTI-derived measurements of RV diastolic function in a large cohort of healthy adults and to suggest reference values for different age groups.

Methods

Study population

From June 2007 to February 2014, 1270 consecutive adults without known cardiovascular risk factors and/or overt cardiovascular disease were referred to echocardiographic laboratories of the Division of Cardiology, "Cava de' Tirreni-Amalfi Coast", Heart Department, University Hospital of Salerno and of the Department of Cardiology and Emergency Medicine of San Antonio Hospital, San Daniele del Friuli, Udine, Italy for this study. The subjects underwent voluntary (or for work ability assessment) full screening for cardiovascular disease including a questionnaire about medical history, use of medications, cardiovascular risk factors, and lifestyle habits (alcohol intake, smoking, and physical activity) [19]. Physical examination [height, weight, heart rate, and blood pressure (BP)] and clinical assessment were conducted according to standardized protocols by trained and certified staff members. Body surface area (BSA) was calculated according to the DuBois formula [0.20247 × height (m) 0.725 × weight (kg) 0.425]. Three BP measurements were obtained from the right arm with a mercury manometer, and the results were averaged to determine systolic and diastolic BP. Exclusion criteria were: coronary artery disease, systemic arterial hypertension, diabetes mellitus, valvular or congenital heart disease, bicuspid aortic valve, congestive heart failure, cardiomyopathies, sinus tachycardia, use of illicit drugs, elite athletes, and inadequate echocardiographic image quality. According to these criteria, 79 subjects were excluded: 2 coronary artery disease, 11 systemic arterial hypertension, 4 diabetes mellitus, 9 body mass index >30 kg/m^2, 7 more than mild valvular insufficiency (3 mitral, 2 aortic, and 2 tricuspid), 2 aortic stenosis, 4 bicuspid aortic valve, 1 hypertrophic cardiomyopathy, 1 aortic root dilation, 1 dilated cardiomyopathy, 8 use of pharmacological treatment (hyperlipidemia, breast cancer, thyroid, gotta, and prostate disease), 20 elite athletes, and 9 inadequate echocardiographic image quality. In addition 23 of the initial subjects investigated refused to be included in the echocardiographic protocol. Our final study population therefore consisted of 1168 healthy subjects [mean age 45.1 ± 15.6 years, range 16–92; 555 (47.5%) men] [19]. The study was approved by the institution's ethics board and informed consent was obtained from the participants.

Imaging protocol

Standardized transthoracic echocardiography and Doppler examinations were performed with market available equipment (Aloka α10 – Aloka, Tokyo, Japan; Vivid 7 or Vivid E9 – GE Healthcare, Milwaukee, WI, USA). 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, subcostal views and RV-focused apical 4-chamber views. Pulsed and continuous wave Doppler interrogation was performed on all 4 cardiac valves. All studies were reviewed and analyzed off line by two independent observers and specific measurements were made by the average of 3–5 cardiac cycles.

M- and B-mode measurements

M-mode measurements (LV diastolic and systolic diameters, interventricular septum, and posterior wall thickness) were performed in parasternal long-axis view with the patient in the left lateral position. LV mass was calculated by the Penn convention [20] and indexed for height (LVMI) (Cornell adjustment) [21].

Relative diastolic wall thickness was determined as the ratio between twice the posterior wall thickness and LV end-diastolic diameter [15]. LV ejection fraction was calculated by the biplane Simpson's rule in the apical four- and two-chamber views. Left atrial volume index (LAVi) was measured in four- and two-chambers apical view, tracing of the blood-tissue interface and defining LA length as the shortest. Volumes can be computed by using the area-length approximation [15]. Left ventricular outflow tract (LVOT) is measured from the inner edge to inner edge of the septal endocardium, and the anterior mitral leaflet in mid-systole in zoom mode [15].

RV end-diastolic chamber sizes were assessed using basal (RVD_1), mid-cavity (RVD_2), and longitudinal (RVD_3) diameter from the RV-focused apical four-chamber views. Proximal RV outflow diameter (RVOT prox) was measured from the anterior RV wall to the interventricular septal–aortic junction (in parasternal long-axis view) or to the aortic valve (in parasternal short-axis) at end-diastole. Distal RV outflow diameter (RVOT distal) was measured just proximal to the pulmonary valve at end-diastole [15]. Right atrium (RA) area was measured in the apical four-chamber view at end-systole, by tracing the RA blood-tissue interface [15]. Tricuspid annular plane systolic excursion (TAPSE) was calculated as index of RV longitudinal systolic function by placing an 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) [22,23].

Color Doppler analysis

Doppler-derived RV diastolic inflow was recorded in RV-focused apical four-chamber view by placing the sample volume at the tips level. The following RV diastolic measurements were measured: peak early inflow velocity (E), peak atrial velocity (A), and peak velocity E/A ratio [24]. Also pulsed tissue Doppler (TD) was performed in apical four-chamber view, by placing the sample volume at the level of lateral corner of the tricuspid annulus, adjusting the spectral pulsed Doppler signal filters until a Nyquist limit of 15–20 cm/s, and using the minimal optimal gain. By TD, annular systolic velocity (s′) and both early (e′) and atrial (a′) velocities were measured [25]. E/e′ ratio was used to estimate RV filling pressure [14]. Peak tricuspid regurgitant 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. Pulmonary artery systolic pressure (PASP) was then calculated by adding a value of right atrial pressure (RAP) as measured by IVC respiratory index to the systolic trans-tricuspid gradient ($PASP = 4V^2 + RAP$, where V = maximal velocity of tricuspid

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