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Longitudinal strain of systemic right ventricle correlates with exercise capacity in adult with transposition of the great arteries after atrial switch☆

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A B S T R A C T

Background: Systemic right ventricle (sRV) dysfunction in d-transposition of the great arteries following atrial switch (d-TGA) is associated with increased mortality. We aimed to characterize maladaptive sRV mechanisms in d-TGA patients, analyzing relation of echocardiographic parameters of sRV systolic function to objective measurements of exercise capacity.

Methods: Forty-seven adult patients with d-TGA and atrial switch (mean age 31.6 ± 4.2 years) underwent conventional echocardiography, bidimensional strain (2D-strain), cardiac magnetic resonance (CMR) imaging and cardiopulmonary exercise evaluation on the same day. Those with median peak oxygen uptake (VO_2) >64.5% (n = 23) constituted group A, those with $VO_2 \leq 64.5\%$ (n = 24) constituted group B and 23 healthy age and gender matched subjects constituted the control group.

Results: In group A, global longitudinal peak systolic 2D-strain (GLS) of sRV was significantly reduced compared to GLS of normal RV and LV in the healthy control group ($p < 0.01$), however peak longitudinal 2D strain was similar at basal and mid-segment of sRV free wall than normal LV. In group B, GLS was significantly reduced compared to group A (−10.9 ± 2.9% vs −13.1 ± 2.3%, $p < 0.05$), mostly due to significant decrease of interventricular septum longitudinal strain. Other echocardiographic systolic parameters were not significantly different between groups A and B. Only sRV GLS showed significant correlation with functional capacity as measured by VO_2 (r = 0.42, $p < 0.01$), while CMR RVEF did not.

Conclusion: GLS of sRV predicts functional capacity and may be more sensitive than CMR RVEF in detecting early myocardial damage of sRV in patients with d-TGA and atrial switch.

1. Introduction

In patients with transposition of the great arteries (d-TGA) with a Mustard or Senning procedure, the morphological right ventricle (RV) serves as the systemic ventricle (sRV). The native trabeculated RV myocardium undergoes extensive trabecular hypertrophy as an adaptive mechanism to enable pumping in the systemic circuit. However over time maladaptation ensues and long-term follow-up of these patients shows that reduced function of the sRV is associated with increased cardiovascular events and mortality [1,2]. The evaluation of the sRV systolic function by using conventional ejection fraction indices continues to pose major challenges.

Cardiac magnetic resonance (CMR) is now considered the gold standard for the assessment and follow-up of sRV volumes and ejection fraction in d-TGA patients after atrial switch operation [3]. The

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complexity of the shape and dynamic physiology of the sRV raise the need for validation of additional echo derived sensitive parameters to obtain periodic quantitative estimates of RV function. The longitudinal arrangement of the deep RV myocardial fibers from the tricuspid valve annulus to the apex, makes the longitudinal shortening of the RV greater than the radial [4]. Therefore, measurement of the RV longitudinal shortening could be a valuable adjunct to estimate sRV systolic function in patients after atrial switch. We hypothesized that sRV longitudinal 2D-strain could be more sensitive in detecting early myocardial dysfunction compared to conventional measures such as ejection fraction in this specific population.

Subjective functional assessment of patients with congenital heart disease is often flawed because these patients present themselves as being asymptomatic while objective measurements show strong limitations at exercise. Moreover, correlation between peak oxygen consumption and sRV ejection fraction is controversial [5,6]. Considering the potential usefulness of 2D-strain in evaluating sRV function in this setting, we planned to correlate 2D-strain of sRV with exercise capacity, in a population of adult patients after atrial switch for transposition of the great arteries.

2. Methods

We conducted a single-center, prospective, case–control study that included patients with d-TGA following atrial switch, and age- and sex-matched healthy volunteers. The study was performed in accordance with the principles set out in the declaration of Helsinki and was approved by the local ERB (Comité de Protection des Personnes, Paris, Ile de France). All patients and healthy volunteers provided written, informed consent to participate in the study.

From February 2011 to March 2012, 49 patients with d-TGA after atrial switch (32 ± 4 years old, 12 women) were studied. Patients with contraindication for CMR, gadolinium injection, and cardiopulmonary exercise test (CPET), patients with residual ventricular septal defect, prosthetic systemic atrioventricular valve, and pregnant women were not included in the study. All eligible patients were further divided in 2 groups according to the median percent predicted peak VO_2 value, which was found to be 64.5%. Patients with predicted peak $VO_2 > 64.5\%$ formed the group A, and patients with predicted peak $VO_2 \leq 64.5\%$ formed the group B. To characterize adaptive mechanisms of sRV function we compared group A to 23 healthy subjects matched for age and sex (control group), and to determine sensitive echocardiographic parameters of sRV dysfunction, group A was compared to group B. Group A, with the highest VO_2 values, was considered as the patients group with the best adaptive mechanisms of sRV to systemic afterload, and the group B, with the lowest VO_2, was considered as the patients group with maladaptive mechanisms of sRV function to systemic afterload. Healthy subjects were recruited at the Clinical Investigation Center of the institution via a press release after d-TGA patient inclusion. Each subject provided their medical history and underwent a complete physical examination and routine laboratory evaluation, including an electrocardiogram. All patients and healthy subjects had echocardiography, CMR and CPET all within 24 h.

Transthoracic echocardiography was performed using a GE-Vingmed Vivid 7 system (Horten, Norway) with high frame rate (60–90 Hz). Echocardiograms were examined by one of the investigator (M.L.), who was blinded to CMR and CPET data. Complete two-dimensional, Doppler color-flow, spectral and Tissue Doppler studies were performed, and tricuspid regurgitation (TR) was graded as mild, moderate, or severe, according to the guideline of the American Society of Echocardiography [7,8,9]. Systolic RV function indices were measured according to recent American Society of Echocardiography guidelines [8]. Right ventricle fractional area change (FAC) and tricuspid annular plane systolic excursion (TAPSE) were measured in the apical 4-chamber view. Doppler method was used to measure dP/dT as the time required for the systemic auriculo-ventricular valve regurgitation jet to increase velocity from 1 to 3 m/s, from the ascending limb of the TR continuous-wave Doppler signal. Velocity time integral (VTI) was measured from pulsed-wave Doppler signal of the right outflow tract. Systolic excursion velocity (S), isovolumic acceleration (IVA) and Tei index [10] were measured using pulsed Doppler Tissue Imaging, with Doppler sample volume placed in the tricuspid annulus of the RV free wall.

Using a dedicated software package designed for LV strain measurement (Echopac PC; GE Healthcare, Waukesha, Wisconsin), 2D strain was measured by using standard bidimensional acquisitions. The RV and the LV, visualized from the apical 4-chamber view, were divided into 6 segments and each segment was individually analyzed. By tracing endocardial contours on end-diastolic frames, the software automatically tracked the contour on subsequent frames. End systole was defined by aortic valve closure. Adequate tracking was verified in real-time and corrected by adjusting the region of interest or by manually correcting the contour to ensure optimal tracking. Two-dimensional longitudinal and transverse peak systolic strains (i.e. radial strain) were assessed in apical 4 chamber view (Fig. 1). Average longitudinal and transverse peak systolic strains were globally calculated for the right and left ventricles, regionally for RV free wall, interventricular septum and lateral left ventricle wall, at basal, mid and apical level. Two-dimensional longitudinal and transverse peak systolic strains were measured on the same consecutive cycles by analyzing offline 2D acquisitions.

Measurements were repeated three months apart by the same observer (ML) and by a second blinded observer (AL). Each observer independently performed the measurements for 13 randomly selected patients, corresponding to 78 segments (78 longitudinal and 78 transverse strains). The reader was allowed to select the best cardiac cycle to perform the measure each time.

All CMR examinations were performed on a 1.5T system (SignaHDx, GEMS, Waukesha, WI, USA) using a dedicated 8-channel phased array surface cardiac coil. For volumetric and functional imaging, breathhold standard cine steady-state free-precession (SSFP) sequences in short-axis, 4- and 3-chamber views and RV vertical long-axis orientation were acquired. CMR image analysis was performed by an investigator (E.M.), using QMASS platform and software (Medis, the Netherlands), resulting in RV end-diastolic (ED) and end-systolic (ES) volumes, and RVEF (%). Measurements were repeated apart by the same observer (EM) and by a second blinded observer (GS) in 23 randomly selected patients.

Each patient had to perform an exercise stress test on a bicycle ergometer (Sensor Medics, Yorba Linda, CA) with measurements of oxygen consumption (VO_2). After a 2 min warm-up period the workload was increased by 10–20 W/min (according to the level of fitness) using a ramp protocol until exhaustion. Patients were encouraged to perform maximal exercise. Testing was terminated after the patient reached the target heart rate (based on age) or because of fatigue, dyspnea, leg discomfort, systolic blood pressure > 250 mm Hg, ventricular tachycardia, or ischemic electrocardiographic changes. Respiratory quotient during exercise testing (target 1.1) was used to indicate whether maximum work had been achieved. Peak oxygen consumption (peak VO_2), oxygen pulse (VO_2/heart rate), and the minute ventilation–carbon dioxide production relationship (VE/VCO_2 slope) were assessed from gas exchange measurements. Maximal exercise and peak circulatory power were assessed to estimate the level of maximal exercise capacity.

2.1. Statistical analysis

Data were presented as mean value ± SD when variables were normally distributed, and median value with 95% of confidence interval when they were not. The groups A and B of d-TGA and the control group of healthy subjects were compared by 2-sample t tests or Mann–Whitney when appropriate. Correlations between echocardiographic parameters, CMR RVEF and CPET measurements were tested by Spearman correlation, and adjustments were made using a multiple