



**HAL**  
open science

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

Magalie Ladouceur, Alban Redheuil, Gilles Soulat, Christophe Delclaux, Michel Azizi, Mehul Patel, Gilles Chatellier, Antoine Legendre, Laurence Iserin, Younes Boudjemline, et al.

### ► To cite this version:

Magalie Ladouceur, Alban Redheuil, Gilles Soulat, Christophe Delclaux, Michel Azizi, et al.. Longitudinal strain of systemic right ventricle correlates with exercise capacity in adult with transposition of the great arteries after atrial switch. *International Journal of Cardiology*, 2016, 10.1016/j.ijcard.2016.04.166 . hal-01312323

**HAL Id: hal-01312323**

**<https://hal.science/hal-01312323>**

Submitted on 5 May 2016

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

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

Magalie Ladouceur (1, 2, 3), Alban Redheuil (4), Gilles Soulat (1, 4), Christophe Delclaux (5), Michel Azizi (6), Mehul Patel (7), Gilles Chatellier (8), Antoine Legendre (2,3), Laurence Iserin (2,3), Younes Boudjemline (2,3), Damien Bonnet (2), Elie Mousseaux (1,4): STARS Investigators.

(1)INSERM U970, PARCC, Université Paris-Descartes.

(2) Department of PaediatricCardiology, Centre de référence des Malformations Cardiaques Congénitales Complexes, M3C, Hôpital Necker Enfants malades,Assistance Publique—Hôpitaux de Paris, Université Paris-Descartes, Paris, France.

(3) AdultCongenitalHeartDisease Unit, CardiologyDepartment, Hôpital Européen Georges Pompidou, Assistance Publique—Hôpitaux de Paris, Université Paris-Descartes.

(4) Department of CardiovascularRadiology, HôpitalEuropéen Georges Pompidou, Assistance Publique—Hôpitaux de Paris, Université Paris-Descartes.

(5) Service de Physiologie - Clinique de la Dyspnée, Hôpital Européen Georges Pompidou, Assistance Publique—Hôpitaux de Paris, Université Paris-Descartes.

(6) Assistance Publique—Hôpitaux de Paris, Hôpital Européen Georges Pompidou, Centre d'Investigation Clinique, Assistance Publique—Hôpitaux de Paris, Université Paris-Descartes, F-75015 Paris, France.

(7)Baylor College of Medicine, Houston, TX, USA.

(8)ClinicalResearch Unit, Hôpital Européen Georges Pompidou, Assistance Publique—Hôpitaux de Paris, Université Paris-Descartes.

All the authors listed take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

**Corresponding author:**

Dr MagalieLadouceur

INSERM 970 &Adult Congenital Heart Disease Unit

Department of Cardiology

HôpitalEuropéen Georges Pompidou

20 rue Leblanc

75015 Paris

Tel: +33156093043

Fax:+33156092664

Mail:[magalie.ladouceur@egp.aphp.fr](mailto:magalie.ladouceur@egp.aphp.fr)

**Abstract:**

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  $31.6 \pm 4.2$  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 ( $n=23$ ) 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 ( $-10.9 \pm 2.9\%$  vs  $-13.1 \pm 2.3\%$ ,  $p < 0.05$ ), mostly due to significant decrease of interventricular septum longitudinal strain. Other echocardiographic systolic parameters were not significantly different between group 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.

**Keywords:** Transposition of the great arteries; **systemic** right ventricle; magnetic resonance imaging; strain.

## **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<sup>1,2</sup>. 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<sup>3</sup>. The 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, make the longitudinal shortening of the RV greater than the radial<sup>4</sup>. 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 are controversial<sup>5,6</sup>. 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.

## **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<sub>2</sub> value, which was found to be 64.5%. Patients with predicted peak VO<sub>2</sub> > 64.5% formed the group A, and patients with predicted peak VO<sub>2</sub> ≤ 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 function dysfunction, group A was compared to group B. Group A, with the highest VO<sub>2</sub> 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<sub>2</sub>, 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 hours.

Transthoracic echocardiography was performed using a GE-VingmedVivid 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<sup>7, 8, 9</sup>. Systolic RV function indices were measured according to recent American Society of Echocardiography guidelines<sup>8</sup>. 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 P/dT as the time required for the systemic auriculo-ventricular valve regurgitation jet to increase velocity from 1 to 3m/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<sup>10</sup> 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 analysed. 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 (Figure 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 analysing 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 1.5 T system (Signa HDx, 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 ( $\text{VO}_2$ ). After a 2 min warm-up period the workload was increased by 10–20 Watts/minute (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  $>250$  mmHg, 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<sub>2</sub>), oxygen pulse (VO<sub>2</sub>/heart rate), and the minute ventilation-carbon dioxide production relationship (VE/VCO<sub>2</sub> slope) were assessed from gas exchange measurements. Maximal exercise and peak circulatory power were assessed to estimate the level of maximal exercise capacity.

#### *Statistical Analysis:*

Data were presented as mean value  $\pm$  SD when variables were normally distributed, and median value with 95% of confidence interval when they were not. The group A and B of 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 regression. If the r-value  $< 0.4$ , the correlation was considered weak;  $0.4 < r < 0.5$ : moderate and if  $r > 0.5$ , then the correlation is strong. A 2-tailed p value  $\leq 0.05$  was considered to be statistically significant. The repeatability (intraobserver variability) and reproducibility (interobserver variability) of the CMR and echocardiographic parameters were observed by calculating the variability coefficient as the difference between the two observations divided by the means of the observations, expressed as percentage, and analyzed using intraclass correlation coefficients. For the interobserver study, the mean of the two measures by the first observer was used. All data were analysed using MedCalc Statistical Software version 12.7.7 (MedCalc Software bvba, Ostend, Belgium; <http://www.medcalc.org>; 2013).

## Results:

### *Study population*

Patient and control characteristics are summarized in Table 1. Two patients were excluded because sRV free wall could not be adequately visualized during standard echocardiography. Of the remaining 47 patients ( $32 \pm 4$  years old, range 22-39 years, 12 women), 13 were operated on using Mustard procedure and 34 using Senning procedure, combined with ventricular septal defect closure in 2 patients, at a median age of 6.6 months of age, 95% CI [3.8 – 12.2]. The average length of time between the initial surgery and the study was  $31.4 \pm 7$  years. Two patients were in junctional rhythm during the study. Only one patient had undergone additional cardiac surgery after the initial operation to treat a pulmonary venous pathway stenosis. Five patients were in NYHA functional class II, one in class III and the remaining in class I. Only 2 patients had moderate to severe tricuspid regurgitation, and one patient had severe pulmonary stenosis. Twenty three d-TGA patients with peak  $VO_2 > 64.5\%$  formed group A, and 24 with peak  $VO_2 \leq 64.5\%$  formed group B. **No difference in age and sex was found between group A, B and controls. Blood pressure and heart rate were not different between the 3 groups.**

### *Relation between parameters of sRV function and NYHA functional class*

There was no significant difference of peak oxygen uptake between patients with NYHA=1 (n=41, predicted peak oxygen uptake= $62.3 \pm 10.1\%$ ) and patients with NYHA>1 (n=6, predicted peak oxygen uptake= $58.7 \pm 10.8\%$ , p=0.2). Among standard echocardiographic parameters of systemic RV function, only peak S wave and IVA were significantly lower in patients with NYHA>1 compared to patients with NYHA=1 (respectively, p=0.02 and p=0.03). Speckle tracking measures were not related to NYHA functional class, except GLS of

systemic RV which was significantly lower in patients NYHA>1 ( $-12.6\pm 2.7\%$  vs  $-9.5\pm 3.8\%$ ,  $p=0.01$ ). CMR RVEF was also significantly lower in d-TGA patients with NYHA>1 ( $42\pm 17.8$  vs  $50.3\pm 8.3\%$ ,  $p=0.03$ ), with RVEF  $\leq 30\%$  in half of these patients.

*Echocardiography parameters of sRV function:*

Echocardiography and exercise test outcomes of group A and B compared to controls are summarized in Table 2 and 3.

Percent predicted peak oxygen uptake value was significantly lower in group A than in controls ( $74\%$  vs  $96\%$ ,  $p<0.01$ , table 2). CMR RVEF was similar in d-TGA patients of group A and of healthy subjects ( $50\pm 8\%$  vs  $50\pm 11\%$ ,  $p=0.9$ ), and was lower than CMR LVEF of healthy subjects ( $59\pm 5\%$ ,  $p<0.01$ ). All standard echocardiography indices of sRV longitudinal function (IVA, TAPSE, peak S wave and Tei index) were decreased in d-TGA patients of group A, compared to RV and LV controls. Only outflow tract VTI and  $dP/dT$  of systemic ventricle were not different. Longitudinal peak systolic 2D strains of each sRV segment of d-TGA patients in group A were significantly reduced compared to corresponding strains estimated in normal RV. Global longitudinal peak systolic 2D strain of sRV was lower than those of normal LV, however peak systolic 2D strain of the basal and mid segments of sRV free wall in d-TGA were not different than basal and mid segment of LV lateral wall in controls. Global longitudinal peak systolic 2D strain of the pulmonary LV was not different than those of the RV in controls. Global transverse peak systolic 2D strain of sRV in group A was not different to normal RV, but was significantly reduced compared to normal LV. This reduction mainly touched interventricular septum. Transverse peak systolic 2D strain values of RV free wall were higher in sRV than in normal RV, reaching values of the LV lateral wall from the controls. This increase mainly concerned the basal sRV free wall.

When we compared group A and B, systemic RVEF was not different (group A= $50\pm 8\%$  vs group B= $45\pm 10\%$ ,  $p=0.5$ ). Patients with lower exercise performance (group B) had a

significant reduction of global peak systolic 2D strain and of septal longitudinal peak systolic 2D strain compared to d-TGA patients of group A. There was no difference in global longitudinal peak systolic 2D strain of the pulmonary LV, global transverse peak systolic 2D strain of sRV and longitudinal strain rate of sRV between the 2 groups.

*Relation between parameters of sRV function and peak oxygen uptake:*

In univariate analysis, only GLS ( $r=0.42$ ,  $p<0.01$ ) and basal longitudinal peak systolic 2D strain ( $r=0.40$ ,  $p=0.02$ ) correlated moderately with peak oxygen uptake expressed as a percentage of predicted values (table 4, Figure 2). This correlation was not observed in the healthy subjects ( $r=0.12$ ,  $p=0.6$ , Figure 2). None of the volumetric **CMR parameters** of sRV (indexed ED RV volume, indexed ES RV volume, indexed mass, and RVEF) correlated with exercise capacity, in d-TGA. Furthermore, no association was found between peak oxygen uptake and either tricuspid regurgitation grade, sRV standard echocardiographic parameters, pulmonary LV global longitudinal peak systolic 2D strain or systemic RV **transverse strain** derived from speckle imaging parameters (table 4). GLS remained significantly correlated with peak oxygen uptake as percentage of predicted value, after adjusting for systolic BP, age, sex, complexity of d-TGA, and treatment of cardiac failure ( $r=0.41$ ,  $p=0.01$ ). Systemic RVEF **as well as** GLS and GTS were not correlated with anaerobic threshold, oxygen pulse, VE/VCO<sub>2</sub> slope and peak circulatory power. No correlation was found between GLS and systemic RVEF.

*Reproducibility:*

Intra-class correlation coefficient for intra observer and inter observer reproducibility of GLS were respectively 0.95, 95%CI [0.82-0.98] and 0.93 [0.75-0.98], and the coefficient of variation was 6.7% and 8.6% respectively for GLS. Feasibility of this measurement was 93%. The reproducibility for GTS was lower with: intra-class correlation coefficient for intra

observer=0.73 [0.52-0.86] and inter observer reproducibility=0.65[0.49-0.80], and coefficients of variation were 23.1% and 26.4% respectively.

Intra-class correlation coefficient for intra and inter observer reproducibility of CMR sRVEF were respectively 0.96, 95%CI [0.90-0.98] and 0.94, 95%CI [0.85-0.98], and the coefficient of variation was 2.8% and 3.4% respectively.

## **Discussion**

Global longitudinal peak systolic 2D strain of sRV is the only echocardiographic parameter of sRV systolic function which is moderately related to peak oxygen uptake in our study. Systolic RVEF decrease is associated with NYHA functional class impairment. However, NYHA functional class underestimates exercise limitations of patients with d-TGA, and systemic RVEF is not related to peak oxygen uptake. GLS seems to be more sensitive for detecting sRV dysfunction than the gold standard, CMR RVEF, which is not predictive of exercise performance.

### *Echocardiographic parameters of sRV function in patients according functional tolerance:*

All standard echocardiographic parameters of longitudinal sRV function (TAPSE, peak S, IVA and longitudinal strain) in the group of d-TGA patients with the highest VO<sub>2</sub> are significantly reduced, compared to healthy controls with anatomic LV as systemic ventricle. Like in previous studies, we confirm that there is a significant reduction of longitudinal strain in sRV of d-TGA following atrial switch<sup>11, 12, 13</sup>. A decrease in RV longitudinal strain is well described when afterload increases<sup>14</sup>. Longitudinal RV deformation was mainly impaired by increased RV afterload, because RV myocytes arrangement is predominantly longitudinal, to create a peristaltic contraction from the inlet to outlet and a bellows-like motion of the free

wall toward the septum<sup>15</sup>. From our results, 2 adaptive mechanisms of RV chronically and congenitally submitted to systemic afterload may be drawn: 1/ longitudinal strain values at basal and mid segments of sRV free wall are preserved in group A compared to basal and mid segments strain values of normal LV at lateral wall; 2/ transverse 2D strain values at the basal segment of sRV free wall increase compared to values at corresponding segments of normal RV, so that they reach those of normal LV. This shift in the sRV free wall from longitudinal to transverse deformation was already observed in sRV<sup>11, 12</sup>. It mainly concerns basal segment of sRV free wall. We also observe a correlation between longitudinal strain of this segment and peak oxygen uptake, unlike the other segments of sRV free wall. Inward movement of the RV free wall is very important during early phase of RV contraction, inducing the peristalsis like bellows effect. So, deformation of the basal segment of sRV free wall may be preserved or increased to maintain a normal cardiac output. GLS is decreased in patients with lower VO<sub>2</sub> as well as symptomatic patients (NYHA >1), whereas sRVEF is only impaired in patients with NYHA >1, and is not related to VO<sub>2</sub>. GLS seems to be more sensitive than sRVEF to detect myocardial dysfunction in sRV.

#### *Relations between parameters of sRV function and exercise performance.*

A decrease in the functional capacity of d-TGA patients after an atrial switch is above all related to an impairment of longitudinal function with a decrease of TAPSE, peak S wave and longitudinal 2D strain, while RVEF does not change. Interventricular septum longitudinal deformation is more impaired than sRV free wall deformations suggesting the probable role of RV-LV interdependence in exercise limitation of d-TGA patients following atrial switch. RV-LV relationship was also shown in the Diller et al study with a systemic and pulmonary longitudinal 2D strain correlation in patients with TGA<sup>16</sup>.

A decrease in systemic RVEF of group B compared to group A is not statistically significant, whereas all longitudinal function parameters (TAPSE, peak S wave and GLS) are reduced in group B compared to group A. The preservation of transverse deformation (GTS) may explain the absence of sRVEF difference between the 2 groups. Previous data on the relation of RVEF at rest and exercise capacity in patients with sRV have been conflicting. Lack of correlation between exercise capacity and indices of left ventricular performances at rest in acquired heart failure has been previously reported<sup>17</sup>. Here we have shown that longitudinal strain of sRV correlates moderately with peak oxygen uptake, but that systemic RVEF does not correlate with exercise parameters. Similarly, Donal et al.<sup>18</sup> have shown that global longitudinal strain of LV correlated better than LVEF with exercise performances in chronic heart failure. As previously described, no correlation was found between GLS and RVEF, meaning that GLS and RVEF do not definitely provide the same information about systemic RV function<sup>19</sup>, mainly because RV myofiber arrangement is predominantly longitudinal<sup>15,20</sup>.

*Limitations:* The group A and B were formed by finding the median VO<sub>2</sub>, a value intrinsic to this specific set of patients, rather than clinically meaningful cut-off as NYHA functional class. This was explained by the limit of subjective functional assessment in patients with congenital heart disease illustrated by patients with low peak oxygen uptake in NYHA 1 (19/24, 79%). We only studied systolic function, but abnormal diastolic function due to restrictive atrial baffles can also restrict a rise in stroke volume at exercise<sup>21</sup>. Transverse strain measured from apical view has got a poor reproducibility. This result could be explained by off-plane radial displacements of sRV tissue in the apical view. Because of the shape of the RV, most of parameters of function could not include the RV outflow tract. The population included here is a selected one for methodology reasons, limiting the number of study patients. However, atrial switch population is likely to contain patients with pacemakers, often with sRV dysfunction<sup>22</sup>.

## **Conclusion**

In patients with d-TGA after atrial switch, longitudinal and transverse deformations are significantly reduced compared to controls, except in basal and mid regions of the systemic ventricular free wall. This adaptive response may allow sRV to support normal cardiac output, even if the systemic RVEF is lower than healthy subjects. Measurement of RV longitudinal 2D strain is better correlated to exercise intolerance **than** RVEF which is the gold standard to evaluate sRV function. RV longitudinal 2D strain should be part in evaluation of sRV function.

**Acknowledgement:** This study was fully supported by Grant CRC P080609 from the French Ministry of Health, Paris, France. **We thank MrNaill Taylor for revising all English of the text.**



## References

1. Cuypers JA, Eindhoven JA, Slager MA, et al. The natural and unnatural history of the Mustard procedure: long-term outcome up to 40 years. *Eur Heart J.* 2014;35(25):1666–74.
2. Schwerzmann M, Salehian O, Harris L, et al. Ventricular arrhythmias and sudden death in adults after a Mustard operation for transposition of the great arteries. *Eur Heart J.* 2009;30(15):1873-9.
3. Baumgartner H, Bonhoeffer P, De Groot NM, et al; Task Force on the Management of Grown-up Congenital Heart Disease of the European Society of Cardiology (ESC); Association for European Paediatric Cardiology (AEPC); ESC Committee for Practice Guidelines (CPG). ESC Guidelines for the management of grown-up congenital heart disease (new version 2010). *Eur Heart J.* 2010;31(23):2915-57.
4. Ho SY, Nihoyannopoulos P. Anatomy, echocardiography, and normal right ventricular dimensions. *Heart.* 2006; 92 (suppl 1): i2–i13.
5. Winter MM1, van der Plas MN, Bouma BJ, Groenink M, Bresser P, Mulder BJ. Mechanisms for cardiac output augmentation in patients with a systemic right ventricle. *Int J Cardiol.* 2010;143(2):141-6.
6. Benson LN, Bonet J, McLaughlin P, et al. Assessment of right ventricular function during supine bicycle exercise after Mustard's operation. *Circulation.* 1982;65(6):1052-9.

7. Douglas PS, DeCara JM, Devereux RB, et al; American Society of Echocardiography Standards; American College of Cardiology Foundation..Echocardiographic imaging in clinical trials: American Society of Echocardiography Standards forechocardiographycorelaboratories: endorsedbythe American College of CardiologyFoundation.J Am SocEchocardiogr. 2009;22(7):755-65.
8. Rudski LG, Lai WW, Afilalo J, et al. Guidelinesfortheechocardiographic assessment of the right heart in adults: a report fromthe American Society of Echocardiographyendorsedbythe European Association of Echocardiography, a registeredbranch of the European Society of Cardiology, andthe Canadian Society of Echocardiography.J Am SocEchocardiogr. 2010;23(7):685-713.
9. Zoghbi WA, Enriquez-Sarano M, Foster E, et al; American Society of Echocardiography. Recommendationsforevaluation of theseverity of native valvularregurgitationwithtwo-dimensionaland Doppler echocardiography. J Am SocEchocardiogr. 2003;16(7):777-802.
10. Salehian O, Schwerzmann M, Merchant N, Webb GD, Siu SC, Therrien J. Assessment of systemic right ventricularfunction in patientswithtransposition of thegreat arteries usingthemyocardial performance index: comparisonwithcardiacmagneticresonanceimaging. Circulation. 2004;110(20):3229-33.
11. Pettersen E, Helle-Valle T, Edvardsen T, et al. Contractionpattern of thesystemic right ventricle shift fromlongitudinaltocircumferentialshorteningand absent globalventriculartorsion. J Am CollCardiol. 2007 Jun 26;49(25):2450-6.

12. Di Salvo G, Pacileo G, Rea A, et al. Transverse strain predicts exercise capacity in systemic right ventricle patients. *Int J Cardiol.* 2010;145(2):193-6.
13. Grewal J, Crean A, Garceau P, et al. Subaortic right ventricular characteristics and relationship to exercise capacity in congenitally corrected transposition of the great arteries. *J Am Soc Echocardiogr.* 2012;25(11):1215-21.
14. Jamal F, Bergerot C, Argaud L, Loufouat J, Ovize M. Longitudinal strain quantitates regional right ventricular contractile function. *Am J Physiol Heart Circ Physiol.* 2003;285(6):H2842-7.
15. Geva T, Powell AJ, Crawford EC, Chung T, Colan SD. Evaluation of regional differences in right ventricular systolic function by acoustic quantification echocardiography and cine magnetic resonance imaging. *Circulation.* 1998;98:339-345
16. Diller GP, Radojevic J, Kempny A, et al. Systemic right ventricular longitudinal strain is reduced in adults with transposition of the great arteries, relates to subpulmonary ventricular function, and predicts adverse clinical outcome. *Am Heart J.* 2012;163(5):859-66.

17. Franciosa JA, Park M, Levine TB. Lack of correlation between exercise capacity and indexes of resting left ventricular performance in heart failure. *Am J Cardiol.* 1981;47(1):33-9.
18. Donal E, Coquerel N, Bodi S, et al. Importance of ventricular longitudinal function in chronic heart failure. *Eur J Echocardiogr.* 2011;12(8):619-27.
19. Iriart X, Horovitz A, van Geldorp IE, et al. The role of echocardiography in the assessment of right ventricular systolic function in patients with transposition of the great arteries and atrial redirection. *Arch Cardiovasc Dis.* 2012;105(8-9):432-41.
20. Sanchez-Quintana D, Anderson RH, Ho SY. Ventricular myoarchitecture in tetralogy of Fallot. *Heart* 1996;76:280-6.
21. Fratz S, Hager A, Busch R, et al. Patients after atrial switch operation for transposition of the great arteries cannot increase stroke volume under dobutamine stress as opposed to patients with congenitally corrected transposition. *Circ J.* 2008;72(7):1130-5.
22. Vejstrup N, Sørensen K, Mattsson E, et al. Long-Term Outcome of Mustard/Senning Correction for Transposition of the Great Arteries in Sweden and Denmark. *Circulation.* 2015;132(8):633-8

## **Figures legends**

Figure 1: Global longitudinal peak systolic 2D strain (panel A), and transverse peak systolic 2D strain (panel B) of sRV in a d-TGA patient from group A on the left, and of normal sub-pulmonary RV in a healthy subject on the right.

Figure 2: Regression curve between peak oxygen uptake and global longitudinal peak systolic 2D strain (GLS) of sRV in d-TGA and LV in controls

**Tables:**

	<b>Global d-TGA population (n=47)</b>	<b>group A (n=23)</b>	<b>group B (n=24)</b>	<b>controls (n=23)</b>
<b>Age, mean±SD, years</b>	31.6±4.2	33.0 ± 4.9	33.5 ± 6.0	32.6 ± 7.0
<b>Sex ratio (M/F)</b>	12/35	17/6	18/6	17/6
<b>BSA, mean±SD, m<sup>2</sup></b>	1.8±0.2	1.9 ± 0.2	1.8 ± 0.2	1.9 ± 0.2
<b>Systolic BP, mean±SD, mmHg</b>	114.6 ± 12.0	114.7 ± 12.4	114.6 ± 11.8	115.9 ± 7.5
<b>Diastolic BP, mean±SD, mmHg</b>	70.8 ± 11.0	70.1 ± 10.9	71.5 ± 11.2	68.7 ± 6.1
<b>Heart rate, mean±SD, bpm</b>	66.9 ± 11.2	65.8 ± 8.9	66.4 ± 11.8	63.2 ± 10.2
<b>History of heart failure, n (%)</b>	3 (6.2)	1(4)	2 (8)	–
<b>History of arrhythmia, n (%)</b>	10 (21.3)	5 (21.7)	5 (20.8)	–
<b>NYHA I/II/III/IV, n</b>	41/5/1/0	23/0/0/0	19/4/1/0	23/0/0/0
<b>Sinus rythm, n (%)</b>	45 (95.7)	22 (96)	23 (96)	23 (100)
<b>QRS duration, mean±SD, ms</b>	97±25	105±52	97±39	–

<b>Treatment</b>				–
<b>ARA2- ACEinhibitors</b>	5	1	4	
<b>B-blockers</b>	7	4	3	
<b>Diuretics</b>	1	0	1	
<b>CMR</b>				
<b>RVEDV, mean <math>\pm</math>SD, ml/m<sup>2</sup></b>	93 $\pm$ 31	89 $\pm$ 12	98 $\pm$ 40	85 $\pm$ 16
<b>RVESV, mean <math>\pm</math>SD, ml/m<sup>2</sup></b>	50 $\pm$ 26	43 $\pm$ 14	57 $\pm$ 34	40 $\pm$ 8
<b>RVEF, mean <math>\pm</math>SD, %</b>	47 $\pm$ 9	50 $\pm$ 9	45 $\pm$ 10	50 $\pm$ 11

**Table 1:** Demographic, clinical and CMR characteristics in d-TGA (global population, group A and B) and controls. ARA2: angiotensin receptor antagonist 2- ACE inhibitors: antagonist conversion enzyme inhibitors, CMR: cardiac magnetic resonance imaging, RVEDV: right ventricle end-diastolic volume, RVESV: right ventricle end-systolic volume, RVEF: RV ejection fraction. No difference was significant between group A and B.

Variable	Healthy subjects (n=23)	Global d-TGA population (n=47)	Group A (n=23)	Group B (n=24)	p-value
Exercise duration (sec)	666 [601-744]	599 [483-672]	551 [480-660]	486 [412-559]	<0.001
Peak systolic BP (mmHg)	176 [158.5-195]	160 [140-179]	153 [140-165]	147 [133-178]	0.02
Peak diastolic BP (mmHg)	86 [78-94]	85 [75-93]	81 [71-93]	83 [75-90]	0.3
Peak heart rate, (bpm)	176 [170-183]	166 [154-176]	166 [157-171]	154 [145-161]	<0.001
Peak VO <sub>2</sub> (%)	96 [79-106]	74 [63-90]	74 [70-79]	60 [52-62]	<0.001
Peak VO <sub>2</sub> , L/min	2.6 [2.1-2.8]	1.9 [1.5-2.5]	1.8 [1.4-2.0]	1.6 [1.2-1.9]	<0.001
Anaerobic threshold (%)	52 [45-62]	41 [34-49]	42 [35-46]	32 [29-36]	<0.001
VE/VCO <sub>2</sub> slope	27 [26-29]	30 [27-35]	31 [30-36]	35 [31-40]	<0.001



**Table 2:** Results of exercise test in group A, B and controls. Values are medians [interquartile range], p values were given for the comparison between global d-TGA population and controls.

BP: blood pressure

	Systolic parameters	d-TGA (n=47)		Control n=23	
		group A (n=23) systemic RV	group B (n=24) systemic RV	RV	LV
Standard parameters	FAC, median 95%CI, %	38 [33 – 42]	36.8 [32-39]	61 [51-66]§	–
	dP/dT, median 95%CI, mmHg/s	868 [723-1111]	1220 [723 – 1263]	273 [186-333]§	947 [735-1114]
	outflow tract TVI, median 95%CI, cm	19 [17-23]	18 [15-20]	21±5	21±4
	IVA, median 95%CI, m/s <sup>2</sup>	0.9 [0.7-1.2]	0.8 [0.7-1.1]	2.0[1.6-2.8]§	3.2 [2.7-3.6]¥
	APSE, mean±SD, mm	12.5 ±2.9	10.3±3.5*	23.2±3.7§	15.3±3.0¥
	Peak S wave, median 95%CI, cm/s	8.0 [7.0-9.0]	6.0 [5.0-7.0]*	13.9±2.2§	12.2±2.5¥
	Tei, mean±SD	0.41±0.12	0.46±0.12	0.40±0.16§	0.26±0.16¥
Speckle tracking parameters	GLS, mean±SD, %	-13.1±2.3	-10.9±2.9*	-19.5[-19.9- -21.1]§	-18.1±2.6 ¥
	Free wall LS, mean±SD, %	-14.6±3.4	-11.7±5.2*	-23.1±9.3§	-17.3±3.6¥
	Basal LS, mean±SD, %	-17.4±6.9	-15.0±7.3	-28.2±10.6§	-19.6±6.5

Mid LS, mean±SD, %	-15.0±5.6	-12.6±6.9	-25.6±7.9§	-16.9±4.6
Apical LS, mean±SD, %	-8.8±5.6	-8.8±4.7	-18.9±9.1§	-15.1±6.8¥
Septum LS, mean±SD, %	-12.1±2.4	-9.2±3.3*	-19.0±3.1§	
GTS, median 95%CI, %	14.5 [11.9-21.6]	14.3 [9.2-19.8]	18.3 [13.8-24.6]	21.8 [18.2-26.7] ¥
Free wall TS, median, 95%CI, %	18.0 [6.5-26.8]	11 [7.8-17.7]	12.5 [8.6-18.5]	18.3 [9.3-21.8]
Basal TS, median 95%CI, %	28 [8.0-38.9]	11;0 [3.2-27.2]	11.5 [7.9-14.0]	9.0 [5.0-20.0]
Mid TS, median 95%CI, %	15.0 [8.8-25.3]	12 [7.2-16]	12.0 [6.0-19.2]	17.0 [7.9-22.0]
Apical TS, median, 95%CI, %	12.5 [7-16.8]	12.0 [4.2-20.8]	15.0 [8.0-26.0]	22.5 [14.9-28] ¥
Septum TS, median 95%CI, %	16.2 [12.9-23.2]	13.7 [4.9-22.0]	27.7 [16.3-36.6] §	
Strain rate, median 95%CI, s <sup>-1</sup>	0.61 [0.49-0.76]	0.60 [0.39-0.65]	–	0.98 [0.93-1.13] ¥

**Table 3:** Comparison of standard echocardiographic parameters and peak systolic 2D strain of systemic ventricle function between d-TGA patients of group A and controls, and between d-TGA patients from group A and B. FAC: fractional area change, GLS: global longitudinal peak

systolic 2D strain, GTS: global transverse peak systolic 2D strain, LS: longitudinal peak systolic 2D strain, TS: transverse peak systolic 2D strain. TVI: time velocity integral, IVA: isovolemic acceleration, APSE: annular plane systolic excursion.\*: significant difference between RV parameters of group A and group B, §: significant difference between RV parameters of group A and controls; ¥: significant difference between RV of group A and LV of controls. All p values were <0.05.

variables	Correlation coefficient r	95% confidence interval for r	p value
GLS	0.424	0.129-0.649	0.0065
GTS	-0.070	-0.970-0.243	0.7
dP/dT	0.047	0.389-0.307	0.8
Peak S wave	0.254	-0.055-0.518	0.3
CMR RVEF	0.214	-0.096-0.487	0.2
FAC	0.092	-0.218-0.385	0.6
Aortic VTI	0.260	-0.052-0.526	0.3
IVA	0.054	-0.254-0.353	0.7
TAPSE	0.264	-0.052-0.532	0.1
Tei	0.025	-0.288-0.334	0.9

**Table 4:**Correlation between standard echocardiographic and speckle tracking measurements of sRV function and percent predictive value of peak oxygen uptake. CMR RVEF: right ventricle ejection fraction by cardiac magnetic resonance imaging. FAC: fractional area change, GLS: global longitudinal peak systolic 2D strain, GTS: global transverse peak systolic 2D strain, VTI: velocity time integral, IVA: isovolumic acceleration, TAPSE: tricuspid annular plane systolic excursion.