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ORIGINAL ARTICLE

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Impaired atrioventricular transport in patients with transposition of the great arteries palliated by atrial switch and preserved systolic right ventricular function: A magnetic resonance imaging study

Magalie Ladouceur, MD[1,2,3] | Nadjia Kachenoura, PhD[4] | Gilles Soulat, MD[1,3] | Emilie Bollache, PhD[4] | Alban Redheuil, MD, PhD[4] | Michel Azizi, MD, PhD[3] | Christophe Delclaux, MD, PhD[3] | Gilles Chatellier, MD, PhD[3] | Pierre Boutouyrie, MD, PhD[1,3] | Laurence Iserin, MD[3] | Damien Bonnet, MD, PhD[2,3] | Elie Mousseaux, MD, PhD[1,3]

[1]INSERM U970, PARCC, Paris Descartes University, Paris, France

[2]Department of Pediatric Cardiology, Complex Congenital Heart Disease Reference Center, M3C, Hôpital Necker Enfants malades, Assistance Publique—Hôpitaux de Paris, Paris Descartes University, Paris, France

[3]Georges Pompidou European Hospital, AP-HP, Assistance Publique—Hôpitaux de Paris, Paris Descartes University, Paris, France

[4]Sorbonne Universités, UPMC Univ Paris 06, UMR 7371, UMR_S 1146, LIB, INSERM, UMR_S 1146, CNRS, UMR 7371, Paris, 75013, France

Correspondence
Magalie Ladouceur, INSERM U970, PARCC, Paris Descartes University, 20 rue Leblanc, Paris 75015, France.
Email: magalie.ladouceur@aphp.fr

Abstract

Objectives: We aimed (1) determine if systemic right ventricle filling parameters influence systemic right ventricle stroke volume in adult patients with D-transposition of the great arteries (D-TGA) palliated by atrial switch, using cardiac magnetic resonance imaging and echocardiography, and (2) to study relationship of these diastolic parameters with exercise performance and BNP, in patients with preserved systolic systemic right ventricle function.

Design: Single-center, cross-sectional, prospective study.

Setting: In patients with D-TGA palliated by atrial switch, diastolic dysfunction of the systemic right ventricle may precede systolic dysfunction.

Methods: Forty-five patients with D-TGA and atrial switch and 45 age and sex-matched healthy subjects underwent cardiac magnetic resonance imaging and echocardiography. Filling flow-rates measured by phase-contrast cardiac magnetic resonance imaging were analyzed using customized software to estimate diastolic parameters and compared with exercise performance.

Results: In D-TGA, early filling of systemic right ventricle was impaired with a lower peak filling rate normalized by filling volume (Ef/FV measured by cardiac magnetic resonance imaging) and a higher early filling peak velocity normalized by early peak myocardial velocity (E_{US}/Ea measured by echocardiography) compared with controls ($P \leq .04$). Stroke volume of systemic right ventricle showed a direct and significant association with pulmonary venous pathway size (respectively $r = 0.50$, $P < .01$). Systemic right atrial area and systemic right ventricle mass/volume index measured by cardiac magnetic resonance imaging, as well as Ef/FV were significantly correlated with exercise performances and BNP ($P < .01$). All correlations were independent of age, gender, body mass index and blood pressure.

Conclusions: Systemic right ventricle pre-load and stroke volume depend mainly on intraatrial pathway function. Moreover, systemic right ventricle remodeling and right atrial dysfunction impair systemic right ventricle filling, leading to BNP increase and exercise limitation. Cardiac magnetic resonance imaging should assess systemic right ventricle filling abnormalities in D-TGA patients.

KEYWORDS

atrial function, cardiac magnetic resonance imaging, diastolic function, filling flow, transposition of the great arteries

1 | INTRODUCTION

The morphological right ventricle functions as the systemic ventricle (sRV) in patients with surgical correction of transposition of the great arteries (D-TGA) using the Mustard or Senning procedure. The poor stroke volume response to exercise during provocative testing in these patients is often attributed to poor sRV function. However, the reduction of stroke volume (SV) response to exercise stress was also found to be related to failure in increasing right ventricular filling rates during tachycardia.[1] This result was presumably due to an impaired atrio-ventricular transport, consequent to the abnormal intraatrial pathways restricting a rise in SV under stress.[1] Similarly, two other studies showed that D-TGA patients failed to increase their SV during exercise or dobutamine stress, supporting the same hypothesis.[2,3] Finally, using conventional echocardiography and speckle tracking, other studies showed that abnormal sRV diastolic function was related to reduced relaxation reserve of sRV,[4–6] but no one established direct relationship with sRV SV.

We recently developed a fast and reproducible technique for both the acquisition and analysis of left ventricle (LV) diastolic function by using velocity encoded data in cardiovascular magnetic resonance (CMR). This method was successfully applied in healthy volunteers to define reference values related to aging[7] and to patients with severe aortic valve stenosis,[8] validating the performance of flow-rate related indices against echocardiography to distinguish patient from elderly controls.

We sought to: (1) determine which sRV filling parameters influence sRV SV at rest, by using CMR and echocardiography, and (2) evaluate these diastolic parameters, by studying their relationship with BNP and exercise performance.

2 | METHODS

2.1 | Study protocol and population

We conducted a single-center, cross-sectional, prospective study that included patients with sRV after atrial switch for D-TGA. An equal number of age and sex matched healthy volunteers were also studied as controls. The study was performed in accordance with the principles set out in the declaration of Helsinki and was approved by the Ethics Review Board of our institution. All patients and healthy volunteers provided written informed consent to participate in the study.

From December 2011 to February 2012, 48 patients with D-TGA after atrial switch (32 ± 4 years old, 11 women) were studied. This population was previously studied.[9] Patients with contraindication for CMR or gadolinium injection, residual ventricular septal defect, and prosthetic systemic atrioventricular valve, as well as pregnant women and patients with atrial arrhythmia were not included in the study. Three patients were excluded because of artifacts on velocity-encoded acquisitions due to arrhythmia or difficulties to hold their breath during the CMR protocol (see below). Forty-five healthy subjects were included. Each volunteer provided their medical history and underwent a complete physical examination, including an electrocardiogram. All patients and healthy subjects underwent CMR and echocardiography the same day. Moreover, patients had a cardiopulmonary exercise test (CPET) within 24 h after CMR.

2.2 | Echocardiography Doppler

Transthoracic echocardiography was performed using a GE-Vingmed Vivid 7 system (Horten, Norway). Echocardiograms were examined by one of the investigators (M.L.), who was blinded to CMR and CPET data. Complete two-dimensional, Doppler color-flow, spectral 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.[10] Doppler method was used to measure peak velocity of early (E_{US}) and late (A_{US}) systemic ventricle filling flow. Early peak myocardial velocity (Ea) and isovolumic relaxation time (IVR-T_{US}) was measured using pulsed Doppler Tissue Imaging, with Doppler sample volume placed in the tricuspid annulus of the sRV free wall in D-TGA and in the mitral annulus of lateral LV free wall in controls.

2.3 | CMR data acquisition and analysis

All CMR examinations were performed on a 1.5 T magnet (SignaHDx, GEMS, Waukesha, WI) using a dedicated 8-channel phased array surface cardiac coil. For volumetric and functional imaging, breath hold standard cine steady-state free-precession (SSFP) sequence was applied in axial, short-axis, 2-, 4-, 3-chamber and RV vertical long-axis views. Short-axis images covering the whole heart without inter-slice gap from apex to base were acquired using the following scan parameters: acquisition matrix = 260 × 192 interpolated to 512 × 512, repetition time = 3.7 ms, echo time = 1.5 ms, flip angle = 50°, pixel size = 0.74 mm × 0.74 mm, slice thickness = 8 mm, views per segment = 12, temporal resolution = 15 ms after applying view sharing. A 3D non ECG-gated coronal contrast enhanced angiography was also acquired during the intravenous injection of 0.1 mmol/kg gadolinium dimeglumine (Dotarem, Villepinte, France) and followed by a second 3D axial angiography to evaluate both caval venous baffle and pulmonary veins pathways in two orthogonal views. Late gadolinium enhancement (LGE) images were finally acquired using both 3D and 2D segmented inversion-recovery CMR sequences. For 3D LGE data, 12 to 16 contiguous 6 mm-thick slices were acquired per breath-hold

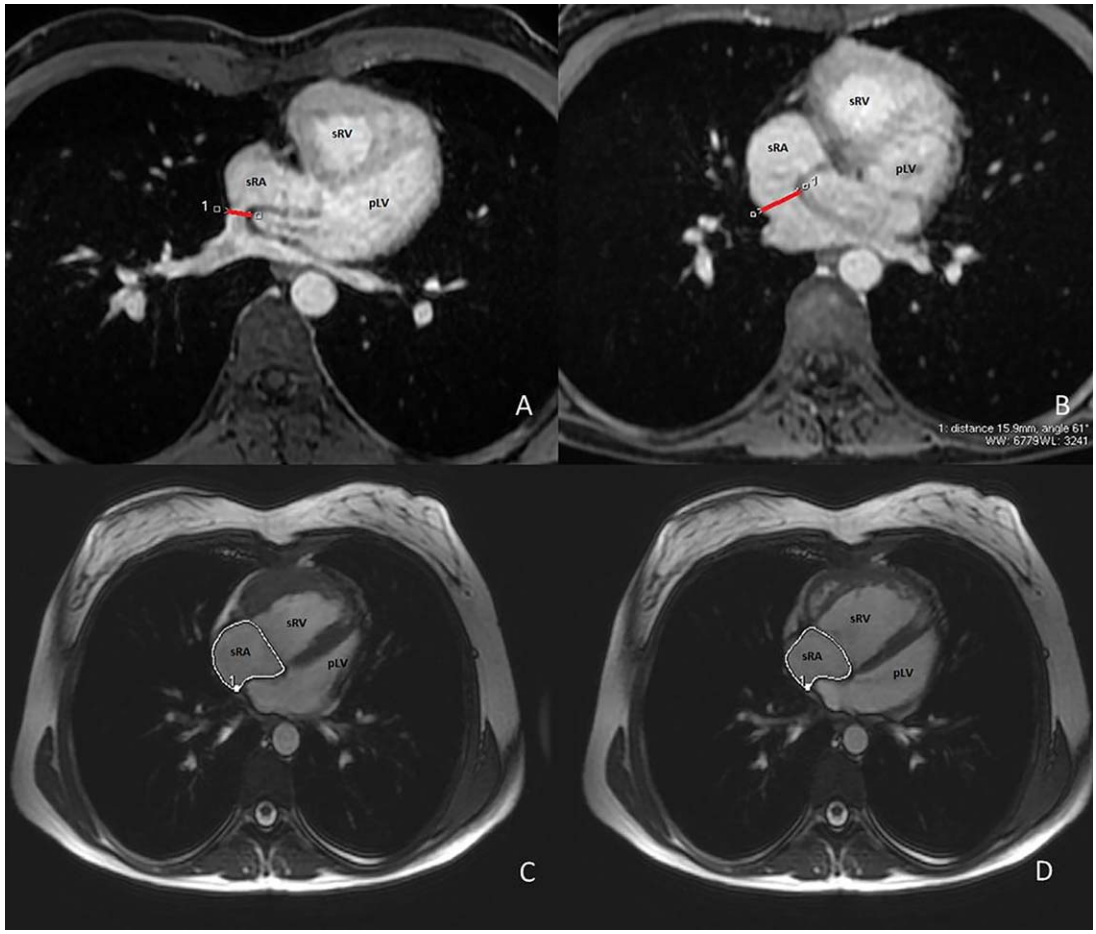

FIGURE 1 Measurements of pulmonary venous pathway diameter (A) and systemic right atrium area (C and D). Systemic right atrium size was measured in 4 chambers view on SSFP images in a D-TGA patient. The pulmonary venous pathway diameter was measured in axial angiography 7 mm in (A) and 15.9 mm in the panel (B, red line) in two different patients. The maximal systemic right atrium area was 12.9 cm^2 (C) and the minimal systemic right atrium area was 9.7 cm^2 (D), in the same patients. pLV, sub-pulmonary left ventricle; sRA, systemic right atrium; sRV, systemic right ventricle

in 3-chamber view and twice in short-axis view, between 8 and 11 min after the gadolinium injection. Such acquisitions were followed by the 2D acquisition of 8 short-axis slices in 4 to 8 successive breath-holds, between 10 and 16 min, after the injection. For each individual patient, the inversion time was optimized to null viable myocardium. LGE 3D and 2D data of each D-TGA patient were visually analyzed by an experienced operator (E.M.) blinded to patients clinical data and the presence or absence of LGE was noted.

As previously described,[8] velocity encoded data were acquired using a retrospectively ECG-gated phase contrast (PC) pulse sequence in a plane perpendicular to the inflow of the systemic ventricle and located below the tricuspid or the mitral annulus at the level of the tips of the opened valve leaflets, and positioned on the aforementioned SSFP data. At this location, two dynamic through-plane velocities, corresponding to a cardiac cycle, were acquired during breath hold. Acquisition parameters were encoding velocity Venc = 130 to 180 cm/s, echo time = 3.1 ms, repetition time = 5 ms, views per segment = 2, acquisition matrix 256 × 128 with 50% of rectangular field of view. View sharing was used with a number of cardiac phases equal to the ratio of the RR interval over 2TR, resulting in an effective temporal resolution of 10 ms. In case of low heart rate, 70% of the rectangular field of view was used but, in association with an accelerating factor, was adapted to have the breath-hold duration compatible with the subject capability.

SSFP images analysis was performed, using QMASS software (version 6, Medis, Leiden, the Netherlands), resulting in the estimation of systemic ventricle indices, such as mass at end-diastole, end-diastolic (ED), end-systolic (ES) volumes and stroke volume (SV) defined as the difference between ED and ES volumes and ejection fraction. Systemic ventricle remodeling was estimated by the ED systemic ventricular mass/ED systemic ventricular volume ratio. In D-TGA patients, pulmonary venous pathway axial oblique diameter was estimated orthogonal to the direction of the pathway, at the narrowest level, by using the axial angiography, on contiguous slices (Figure 1). The atrium draining pulmonary veins in D-TGA patients, defined by the part of atrium just after the pulmonary venous pathway narrowing, was considered as systemic right atrium (RA) in D-TGA group, and was compared with the left atrium (LA) of controls. Maximal area at end-systole and minimal

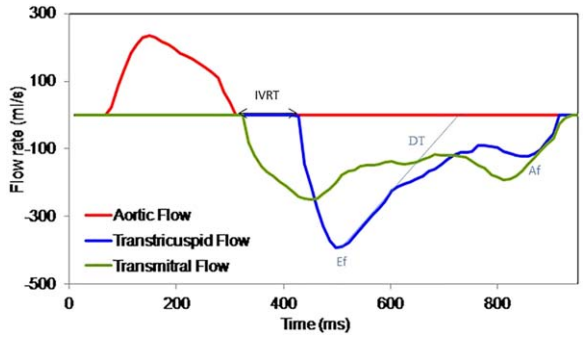

FIGURE 2 Aortic, transtricuspid, and transmitral flow rate curves in D-TGA patient. Flow velocity was estimated from velocity-encoded CMR dataset. Af, late peak filling rate; DT, deceleration time; Ef, early peak filling rate; IVRT, isovolumic relaxation time

area after atrial contraction were measured at the same axial level going through the largest section of the atrium (Figure 1). In D-TGA patients and in healthy subjects, relative atrial area change was calculated as (maximal atrium area-minimal atrium area)/maximal atrium area at the same level.

Velocity encoded images were transferred for off-line analysis using custom software as it was described by Bollache et al.[8] (Figure 2). This custom software allowed a display of velocity images using an adapted color scale designed to distinguish through plane velocities in both directions. After small user interaction to define only one region of interest within inflow area, the software automatically included inflow and outflow areas throughout the all cardiac cycle, based on pixels connectivity in terms of velocity sign. After transtricuspid and transmitral orifice segmentation, curves of maximal and mean velocities (cm/s), as well as flow-rates (mL/s) were automatically derived (Figure 2). The same velocity images were used for simultaneously estimating trans-atrioventricular valve inflow and ejection outflow by superimposing flow-rate curves obtained in the same mean cardiac cycle averaged over the breath hold acquisition. However, because of the important obliquity between the outflow tract and the acquisition plane, such outflow-rate curves were only used for the estimation of temporal parameters and the time period between end of ejection and onset of ventricular filling. Early and late average velocities (E_{CMR} and A_{CMR}) and flow-rates (Ef and Af) of trans-tricuspid and trans-mitral blood flow were automatically extracted from the curves (Figure 2). The Ef/Af ratio, as well as the peak filling rate normalized by the filling volume Ef/FV (in s^{-1}), were further calculated. The filling volume (FV, in mL) was defined as the area under the transtricuspid or the trans-mitral flow-rate curve comprised between the onset and the end of the filling period. Finally, isovolumetric relaxation time ($IVRT_{CMR}$) was estimated as the duration between end of the outflow tract ejection and the onset of the filling period. The deceleration time (DT_{CMR}) was calculated as the duration between the time to peak filling rate Ef and the end of the Ef wave. All temporal indices were calculated using linear interpolations of ascending and descending slopes of flow curves (mL/s), which were automatically performed on the part of the curve comprised between 40% and 70% of its maximal value, as previously presented.[11] Of note, flow-rate curves, being estimated from mean velocities, were preferred to maximal velocity curves for the estimation of temporal parameters because of their expected lower sensitivity to noise.

2.4 | Cardiopulmonary exercise testing

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 progressively increased by 10–20 Watts/min (according to the level of fitness) using a ramp protocol until exhaustion. 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) and oxygen pulse (VO_2/heart rate) were further assessed from gas exchange measurements. Oxygen pulse is related to stroke volume by the formula: oxygen pulse = stroke volume × oxygen arteriovenous difference.

2.5 | Statistical analysis

For both controls and patients groups, diastolic parameters were reported as the mean value ± SD when variables were normally distributed, and median value with 95% of the confidence interval when it was not. A nonparametric Mann-Whitney test or a 2-sample *t* test, when appropriate, was used to evaluate the significance of the differences between controls and patients functional parameters. Associations between continuous variables were tested by linear regression analysis and were adjusted for age, gender, body mass index and mean blood pressure. Pearson's and Spearman's correlation coefficients were provided, when appropriate. Multivariate regression analysis, including significant variables in univariate analysis, was used to determine SV determinant parameters. A *P* value < .05 was considered as significant. All the data was analyzed using MedCalc Statistical Software version 12.7.7 (MedCalc Software bvba, Ostend, Belgium; http://www.medcalc.org; 2013).

3 | RESULTS

3.1 | Study population

Patient characteristics are summarized in Table 1. All 45 patients were in sinus rhythm during CMR. Mustard operation was performed in 15 patients and Senning operation was performed in 30 patients, at a median age of 8 months, 95% CI.[4–13] Only one patient had an additional cardiac surgery after the initial operation to treat a pulmonary vein pathway stenosis. No significant tricuspid regurgitation (grade >2) was found, and no outflow tract obstruction was detected by Doppler echocardiography. No superior or inferior limb baffle obstruction was noted on CMR images. Systemic RV ejection fraction (sRVEF) was relatively preserved (sRVEF = 50 ± 9%), however sRVEF, as stroke volume,

TABLE 1 Baseline clinical, CPET and CMR characteristics in D-TGA patients and in healthy controls

Baseline characteristics	D-TGA	Controls	*P* value
Age, years	32 ± 4	32 ± 6	NS
Sex ratio (M/F)	34/11	34/11	NS
Heart rate (bpm)	67 ± 11	63 ± 10	.01
Mean BP (mm Hg)	85 ± 9	85 ± 5	NS
History of heart failure, n (%)	3 (6.7%)		–
History of arrhythmia, n (%)	10 (22.2%)		–
BMI, kg/m^2	24 ± 4	24 ± 3	NS
BNP, pg/L	76.7 ± 52.9	12.9 ± 10.9	<.01
CPET			
Maximal heart rate, b/min	161 ± 15		
Peak VO_2, mL/mn/kg	24 ± 4		
Percentage of peak VO_2 predicted value, %	66 ± 12		
Oxygen pulse, mL b min-1	11 ± 3		
Oxygen pulse as percentage of predicted, %	77 ± 14		
CMR	sRV	LV	
SystV ED volume, mL/m^2	65 [60-73]	83 [64-89]	.04
SystV ES volume, mL/m^2 SystV mass indexed to BSA, g/m^2 SystV mass/ volume, g/mL	31 [29-36] 167 ± 49 1.35 ± 0.35	34 [19-37] 114 ± 30 0.84 ± 0.23	NS <.01 <.01
SystV stroke volume, mL	60 [56-72]	84 [75-90]	<.01
SystV EF, %	50 ± 9	62 ± 6	<.01
LGE, n, (%)	17 (38%)	0 (0%)	_
Diameter of pulmonary veins pathway, mm	18 ± 5	_	_
Maximal atrial area, cm^2	13 ± 5	14 ± 4	NS
Minimal atrial area, cm^2	10 ± 4	8 ± 3	<.01
Atrial relative area change, %	23 ± 8	46 ± 11	<.01

Abbreviations: BMI, body mass index; ED, end-diastolic; EF, ejection fraction; ES, end-systolic; LGE, late gadolinium enhancement; SystV, systemic ventricle.

was significantly decreased in D-TGA patients when compared with LV estimates in controls ($P < .01$).

3.2 | Systemic RV filling and stroke volume

Echocardiographic and CMR indices of diastolic function of systemic ventricle in D-TGA and controls are shown in Table 2. Relaxation indices such as deceleration time (DT) and isovolumic relaxation time (IVRT), whether they were measured by echocardiography or CMR, were longer in sRV compared with LV of controls. CMR and echocardiographic parameters of sRV filling (Ef/FV and E_{US}/Ea) also decreased significantly ($P \leq .04$). No significant difference of RV filling parameters (Ef/Af and DT) was observed between sRV in D-TGA and controls RV ($P = .2$). Only tricuspid valve opening area was greater in controls compared with patients ($P < .01$), Table 2.

All of the following correlations were adjusted for age, sex, body mass index and mean blood pressure (Table 3). In D-TGA patients and healthy controls, SV was strongly related to filling volume (FV), Ef/FV, systemic ventricular mass, ED mass/volume ratio and areas of systemic atrium (RA in D-TGA and LA in healthy controls, $P < .01$). In D-TGA, but not in healthy controls, a significant correlation was found between SV, area change of systemic atrium and pulmonary veins pathway diameter (≤ 0.02, Figure 3). There was no correlation between FV and area change of systemic RA as well as pulmonary veins pathway diameter. However, FV was significantly associated with sRV mass/volume ratio in D-TGA patients ($r = -0.41$, $P < .01$) as in controls ($r = -0.34$, $P = .02$). Diastolic echocardiographic parameters (E_{US}, A_{US}, E_{US}/A_{US}, E_{US}/Ea DT_{US}, $IVRT_{US}$) were not correlated with CMR SV.

In multivariate regression analysis, by including significant diastolic variables which could determine SV in D-TGA, that is systemic RA

TABLE 2 Echocardiography CMR parameters of systemic and subpulmonary ventricles filling in D-TGA and controls

	D-TGA(n = 45)	Controls (n = 45)	
Systemic ventricle	**sRV**	**LV**	***P* value**
Echocardiography			
E_{US}/A_{US}	1.58 [1.48-1.74]	1.33 [1.17-1.57]	NS
E_{US}/Ea	10.2 [8.2-15.3]	4 [3.6-5.2]	<.01
DT_{US}, ms	194 [168-206]	165 [156-176]	.01
$IVRT_{us}$, ms	60 [48-70]	41 [26-52]	<.01
PC-CMR			
E_{CMR}/A_{CMR}	1.3 [1.2-1.4]	1.5 [1.3-1.7]	NS
Ef/Af	1.4 [1.3-1.6]	1.6 [1.3-2.0]	NS
Ef/FV, s^{-1}	4.2 [3.9-4.5]	4.7 [4.1-5.0]	.04
DT_{CMR}, ms	228 [210-280]	169 [161-186]	<.01
$IVRT_{CMR}$, ms	96 [90-110]	80 [73-87]	<.01
Systemic AV valve opening area, cm^2	9.0 [8.5-10.8]	9.5 [7.8-11.4]	NS
Filling volume, mL	79 [65-88]	73 [65-81]	NS
Subpulmonary ventricle-PC-CMR			
Ef/Af	1.3 [1.1-1.5]	1.5 [1.1-1.6]	NS
DT, ms	244 [208-298]	298 [213-334]	NS
Pulmonary AV valve opening area, cm^2	8.2 [7-8.9]	13 [12.4-16.7]	<.01
Systemic ventricle-subpulmonary ventricle filling onsets, ms	114 [89-123]	28 [17-41]	<.01

Abbreviations: Af, late peak filling rate; AV, atrio-ventricular; DT, deceleration time; ED, end diastolic; Ef, early peak filling rate; FV, filling volume; IVRT, isovolumic relaxation time; pulm-LV, subpulmonary LV; RA, right atrium; RVEF, right ventricle ejection fraction.

function (area change of systemic atrium), pulmonary veins pathway diameter, sRV diastolic function (Ef/FV) and sRV remodeling (sRV mass/volume), only pulmonary veins pathway diameter (adjusted $R^2 = 0.39$, $P = .04$) remained significantly associated with sRV SV. Although no variables (maximal LA area, LV mass/volume ratio and Ef/FV) were significantly related to systemic SV after multivariate analysis in controls.

3.3 | Relationship between diastolic CMR and US parameters with CPET and BNP measurements in D-TGA

CPET measurements in D-TGA patients are shown in Table 1. Relations between echocardiography and CMR parameters with peak oxygen uptake (peak VO_2), oxygen pulse (VO_2/heart rate) and BNP are shown in Table 4. All relations were adjusted for age, body mass index, sex and mean blood pressure. While peak VO_2 and VO_2/HR were not related to sRV volumes, sRV ejection fraction and to sRV mass, whether indexed to ED sRV volume or not, they were weakly but significantly associated with the sRV filling measurement, Ef/FV ($r = -0.30$ to 0.37, $P \leq .4$). Systemic RA area and systemic RA relative area change were significantly correlated with peak VO_2 and BNP ($P \leq .01$).

4 | DISCUSSION

We have shown here that impaired atrio-ventricular transport in D-TGA is mainly related to restrictive atrial baffle and systemic RA dysfunction. However, concentric sRV hypertrophy also impaired sRV filling. At rest, SV depended much on pulmonary veins pathway diame-

TABLE 3 Determinant values of CMR systemic ventricle filling parameters for systemic stroke volume in D-TGA and controls

	D-TGA (n = 45)		Controls (n = 45)	
	r	***P* value**	***r***	***P* value**
PC-CMR systemic ventricle filling indices				
Ef/Af	0.14	NS	0.18	NS
Ef/FV, s^{-1}	−0.33	.02	0.05	NS
DT, ms	−0.04	NS	0.02	NS
IVRT, ms	0.08	NS	−0.08	NS
Filling volume, mL	0.69	<.01	0.77	<.01
PC-CMR subpulm ventricle filling indices				
Ef/Af	0.03	NS	0.15	NS
DT_{CMR}, ms	0.05	NS	−0.29	NS
SSFP indices				
ED sV mass, g	−0.39	<.01	−0.37	.01
ED sV mass/volume	−0.38	<.01	−0.37	.01
Max SA area, cm^2	0.49	<.01	0.74	<.01
Mini SA area, cm^2	0.55	<.01	0.65	<.01
SA relative area change, %	0.36	.02	0.15	NS
Size of pulmonary veins pathway, mm	0.50	<.01	NA	NA

Correlation was between PC-CMR parameters of diastolic systemic ventricle filling, systemic ventricle function, systemic atrium function and pulmonary veins baffle size (for D-TGA only), with systemic stroke volume. All correlations were adjusted for age, body mass index, sex and mean blood pressure.

Abbreviations: Af, late peak filling rate; DT, deceleration time; ED, end diastolic; Ef, early peak filling rate; EF, ejection fraction; FV, filling volume; IVRT, isovolumic relaxation time; SA, systemic atrium; sRV, systemic right ventricle.

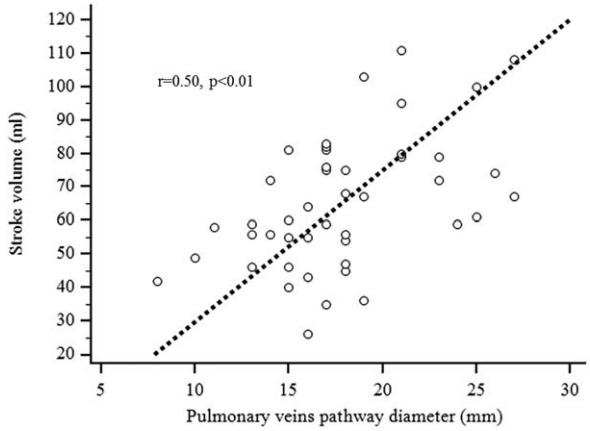

FIGURE 3 Correlation between stroke volume and pulmonary veins pathway diameter

ter, while systemic RA dysfunction and sRV remodeling were more involved in exercise limitation of patients.

D-TGA patients, without significant tricuspid regurgitation and with relative preserved systolic sRV function, had a lower SV at rest compared with controls. Significant relationship between SV and pulmonary vein pathway diameter confirms here that an abnormal conduit function of intraatrial pathways impacts on sRV filling and SV. Moreover, the weak but significant correlations of SV with Ef/FV (positive correlation) and sRV mass/volume ratio (negative correlation) suggest that abnormal systemic RV stiffness due to a concentric sRV hypertrophy may impair sRV filling and then SV in D-TGA patients. This was also confirmed by the stronger association between FV and systemic ventricle remodeling mass/volume index in D-TGA compared with healthy subjects. Like in other studies[1,5,6] we observed the lengthening of the isovolumic relaxation period, and a longer deceleration time of the early filling rate, confirming the abnormal sRV relaxation. By extension, study of diastolic function using CMR could be applied in univentricular heart, specifically in hypoplastic left heart syndrome where systemic ventricle is also a morphological RV. D-TGA patients in our study had a relative preserved sRVEF, so we could study apart diastolic function of sRV. This explained the absence of relationship between BNP and sRVEF.

Systemic atrial function is very impaired in D-TGA with a significant reduction of atrial relative area change compared with controls. This impairment was associated with a decrease in SV and exercise limitation, and is probably due to surgical scars. Not surprisingly, BNP, which is mainly secreted by atrium, was significantly correlated with systemic atrium area and pulmonary veins pathways diameter. For this reason, this biomarker should be interpreted with caution in this population.

Inadequate exercise capacity in patients after atrial repair of D-TGA has been thoroughly addressed in several studies, but its origin is still a matter of debate.[12] Systolic dysfunction of sRV cannot fully explain the problem, since this function is well preserved in patients in our series. Moreover, Derrick et al. found a 'normal' response of the systemic RV to its afterload, confirming little or no direct relationship

TABLE 4 Correlation between CMR and US systemic RV filling parameters with peak oxygen uptake (VO_2), oxygen pulse (VO_2/HR) and BNP

	Peak VO_2		VO_2/HR		BNP	
	r	*P* value	*r*	*P* value	*r*	*P* value
Echocardiography						
E_{US}/A_{US}	0.26	NS	0.29	NS	0.12	NS
DT_{US}, ms	0.34	.02	0.11	NS	−0.18	NS
E/Ea	0.22	NS	−0.04	NS	−0.21	NS
$IVRT_{US}$, ms	0.18	NS	0.06	NS	−0.18	NS
PC-CMR RV filling indices						
Ef/FV, s^{-1}	−0.49	.01	−0.40	.01	0.1	NS
Ef/Af	−0.25	NS	−0.14	NS	0.29	NS
DT_{CMR}, ms	−0.21	NS	0.03	NS	−0.05	NS
$IVRT_{CMR}$, ms	−0.05	NS	0.10	NS	0.28	NS
SSFP indices						
ED sRV volume, mL	−0.16	NS	0.11	NS	0.19	NS
sRV stroke volume, mL	0.00	NS	0.29	.07	0.15	NS
ED sRV mass/volume	0.18	NS	0.39	<.01	0.05	NS
sRVEF, %	0.21	NS	0.17	NS	−0.02	NS
Max SA area, cm^2	−0.43	<.01	0.12	NS	0.40	<.01
Mini SA area, cm^2	−0.46	<.01	0.08	NS	0.48	<.01
SA relative area change, %	0.39	.01	0.07	NS	−0.39	.01
Size of pulmonary veins pathway, mm	−0.24	NS	0.10	NS	0.40	<.01

All correlations were adjusted for age, body mass index, sex and mean blood pressure. Abbreviations: A, late filling velocity; Af, late peak filling rate; DT, deceleration time; E, early filling velocity; ED, end diastolic; Ef, early peak filling rate; EF, ejection fraction; FV, filling volume; IVRT, isovolumic relaxation time; SA, systemic atrium; sRV, systemic right ventricle.

between indexes of sRV systolic function and exercise performance.[1] Negative correlation between Ef/FV and peak VO_2 and VO_2/HR may be explained by a worsening of abnormal myocardial relaxation of sRV, leading to increase in sRV pressure filling during exercise. Poerner et al.[4] showed a severely reduced diastolic exercise reserve, with a decrease in diastolic myocardial velocities during exercise. We further confirmed their hypotheses that diastolic disorders without baffle obstruction were related to impaired myocardial relaxation caused by hypertrophic sRV and play a role in the diastolic dysfunction.

Because sRV is more spherical, its cross-sectional area enlarges, and the interventricular septum flattens, inducing also LV diastolic dysfunction by impairing LV diastolic filling, by reduction of mitral valve opening and increasing filling duration of sub-pulmonary ventricle in D-TGA patients compared with controls. Correlations of trans-mitral early and late peak filling flow rate with sRV SV further suggest that sub-pulmonary LV diastolic dysfunction, with reduced LV filling, reduces sRV SV by reducing sRV preload.

4.1 | Limitations

Noninvasive evaluation of sRV diastolic function is challenging in D-TGA. As Schaefer et al.,[13] we found limitations to evaluate sRV diastolic function by only using echocardiography. Except the E/Ea ratio, all echocardiographic diastolic parameters were not related to SV, exercise performance or BNP. However, for the same reasons, Ef/FV seems the more reliable CMR parameter to assess sRV diastolic function. Moreover, CMR evaluation allows measurements of pulmonary vein pathways, and systemic RA function, which are significant determinants of sRV preloading and SV. The differences in diastolic parameters found between echocardiography and CMR can be explained by the differences in imaging principles of the two techniques, including the difficulties of plane or beam positioning particularly at level of RV inflow tract.

Since only one stack of 8 mm-thick axial image series were achieved in our study, systemic RA function was estimated by using only maximal RA areas and relative change of these areas through time rather than volumes. Even if this method has been used by other groups,[14] better results should be obtained to study systemic atrial function by using thinner axial SSFP images, to decrease the partial volume effect at upper and lower part of the atrium. By using atrial area changes between maximal and minimal areas corresponding to ventricular end-systole and time following atrial contraction, we have only studied the total atrial emptying fraction corresponding to the reservoir function. As previously described,[15] it would be interesting to further study conduit and atrial contraction by using phasic volumes as well as atrial strain in CMR.

Similarly, better than the smallest 2D axial diameter of the pulmonary venous pathway used in the present study, the cross-sectional areas obtained from 3D dataset should be more accurate to estimate the narrowing of the pathway and its relation with SV and exercise performances.

CMR limitations included the limited temporal resolution of PC-CMR imaging as opposed to Doppler echocardiography, and the presence of phase offset errors, which were not corrected in the present study but were minimized using a 50% rectangular field of view centered on the mitral annulus. Despite these technical limitations, by using flow-rate related to diastolic filling instead of velocity filling, we have shown here that PC-CMR parameters better characterized sRV filling by having stronger relationship with haemodynamic biomarkers and exercise performances.

5 | CONCLUSIONS

Function of the systemic right atrium and diastolic function of the sRV are profoundly impaired in D-TGA after atrial switch, which impacts on atrio-ventricular haemodynamic coupling. This diastolic dysfunction is related to maladaptive sRV remodeling, and is associated with decrease in exercise performances. The size of pulmonary vein pathways and the size of the systemic atrium are related to sRV pre-load and then sRV stroke volume. Consequently, exercise capacity and BNP secretion are dependent of sRV compliance, and above all, of systemic atrial function. Evaluation of diastolic function including systemic atrium area change, sRV filling profile, and sRV mass should be part of CMR sRV evaluation since this method only requires one more breath hold PC acquisition.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

AUTHOR CONTRIBUTIONS

Concept and design: Magalie Ladouceur, Nadjia Kachenoura, Emilie Bollache, Elie Mousseaux

Data analysis/interpretation: Magalie Ladouceur, Gilles Soulat, Christophe Delclaux, Laurence Iserin

Drafting article: Magalie Ladouceur, Elie Mousseaux, Nadjia Kachenoura, Pierre Boutouyrie, Pierre Boutouyrie

Critical revision: Gilles Chatellier, Pierre Boutouyrie, Emilie Bollache, Damien Bonnet

Statistics: Gilles Chatellier, Gilles Soulat

Approval of article: all authors

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