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RESEARCH

Hemodynamics in Adults with Systemic Right Ventricles: Differences Between Congenitally Corrected and Complete Transposition of the Great Arteries

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Abstract

Despite their anatomical differences, congenitally corrected (ccTGA) and complete transposition of the great arteries (d-TGA) post-atrial switch are frequently studied together and managed similarly from a medical standpoint due to the shared systemic right ventricle (sRV). The aim was to assess differences in their underlying hemodynamics. The study is a retrospective review of 138 adults with ccTGA or d-TGA post-atrial switch undergoing cardiac catheterization at Mayo Clinic, MN between 2000 and 2021. ccTGA was categorized into isolated or complex ccTGA depending on concomitant ventricular septal defect and/or left ventricular outflow obstruction. There were 53 patients with d-TGA (91% post-Mustard procedure), 51 with complex and 34 with isolated ccTGA. Isolated ccTGA patients were older (51.8 ± 13.1 years) than those with d-TGA (37.5 ± 8.3 years) or complex ccTGA (40.8 ± 13.4 years). There were no differences in sRV or left ventricular size and function across groups. The ccTGA group more commonly had ≥ moderate tricuspid regurgitation than those with d-TGA; ≥ moderate mitral and ≥ moderate pulmonary regurgitation were most prevalent in complex ccTGA. There were no differences in sRV end-diastolic pressure (sRVEDP) or PAWP between groups. However, the ratio of PAWP:sRVEDP was higher in those with d-TGA compared to those with ccTGA. Cardiac index was higher in the d-TGA group than both groups of ccTGA patients with the latter showing higher indices of ventricular afterload. In conclusion, despite sharing a sRV, adults with d-TGA and ccTGA have substantial differences in hemodynamics and structural/valvular abnormalities. Further investigation regarding disease-specific responses to heart failure therapy in those with d-TGA and ccTGA is warranted.

Keywords Complete transposition of the great arteries · Atrial switch procedure · Congenitally corrected transposition of the great arteries · Hemodynamics

Abbreviations

ccTGA	Congenitally corrected transposition of the great arteries
d-TGA	Complete transposition of the great arteries
PAWP	Pulmonary artery wedge pressure
PVR	Pulmonary vascular resistance
sRV	Systemic right ventricle
SVR	Systemic vascular resistance
TGA	Transposition of the great arteries
TR	Tricuspid regurgitation

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Introduction

The presence of a systemic right ventricle (sRV) is a shared anatomical feature of patients born with complete and congenitally corrected (ccTGA) transposition of the great arteries (TGA). Individuals with a sRV are at risk for progressive sRV enlargement and dysfunction, worsening tricuspid (systemic atrioventricular valve) regurgitation (TR), and atrial and ventricular arrhythmias [1]. Given these long-term sequelae and the inherent complications associated with surgically created atrial baffles, the arterial switch procedure is now the operation of choice in patients born

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with complete TGA. However, a substantial population of patients post-atrial switch operation are still followed and, as they approach the fourth and fifth decades of life, the number of individuals with complete TGA and a sRV presenting with heart failure is expected to rise [2].

Overwhelming data are now available demonstrating the efficacy of medical therapy in improving ventricular function, rates of hospitalization and death in individuals with systemic left ventricular systolic dysfunction [3, 4]. In contrast, these medications have not been proven to be beneficial in those with a sRV [5]. Given the obvious structural differences, it is possible that failing systemic right and left ventricles behave differently from a hemodynamic standpoint. Moreover, it would be intuitive to expect that not all patients with a sRV (given their heterogeneity) would have similar hemodynamic phenotypes, possibly responding differently to medical and interventional/surgical therapy. Accordingly, the aim of this study is to assess differences in underlying hemodynamics between adults with TGA post-atrial switch and ccTGA undergoing catheterization at our institution.

Methods

This retrospective cohort included 138 consecutive patients with ccTGA or complete TGA post-atrial switch procedure undergoing invasive hemodynamic evaluation at Mayo Clinic, Rochester, MN between January of 2000 and February 2021. Individuals undergoing palliative atrial switch procedure or Fontan operation were excluded. Patients with ccTGA were further categorized into *complex* ccTGA if repaired or unrepaired ventricular septal defect, left ventricular outflow obstruction, or pulmonary atresia was present; individuals were otherwise categorized as *isolated* ccTGA. Acknowledging that complete TGA and dextroposition of the aorta are not synonyms, complete TGA will henceforth be referred to as d-TGA to improve readership and avoid confusion. The Institutional Review Board approved the study and only patients previously providing research authorization for the use of medical records were selected.

Cardiac catheterization data were abstracted from the procedural reports. The procedure was carried out in a fasting state, without discontinuation of chronic medications, and under mild sedation except for 8 patients (5.7%) whose procedures were performed under general anesthesia. Reported pressure measurements represent a mean of ≥ 5 consecutive beats under spontaneous breathing. Cardiac output was calculated by the Fick principle. In patients with bilateral pulmonary artery and/or pulmonary artery wedge (PAWP) pressure measurements, the right one was arbitrarily chosen since it was more commonly recorded. Pulmonary vascular resistance (PVR) was calculated as the difference between ipsilateral pulmonary artery mean pressure and PAWP divided by pulmonary flow (Qp). Systemic vascular resistance (SVR) was calculated as the difference between the arterial mean pressure and right atrial/systemic venous atrial pressure divided by systemic flow (Qs); effective arterial elastance (Ea) was calculated as (systolic arterial pressure $\times 0.9$)/stroke volume [6]. For patients with d-TGA, the presence of baffle obstruction at cardiac catheterization was based on the operator's interpretation of hemodynamic, angiographic and/or intraprocedural echocardiographic data.

Clinical, echocardiography, and surgical data were obtained from the medical records. The model for end-stage liver disease score excluding international normalized ratio (INR) (MELD-XI), a marker of hepatic disease that has been used in other cohorts of cardiac patients [7], was calculated using creatinine and bilirubin. Given its clinical relevance, if sRV ejection fraction, sRV size, or degree of atrioventricular valve regurgitation were not reported at the time of clinical study, images were reviewed offline by an experienced congenital echocardiographer (H.M.C.). Reflecting the practice of our laboratory, the assessment of RV size and systolic function was performed qualitatively; sRV ejection fraction data reported herein represent visually estimated values.

Statistical Analysis

Nominal data are presented as counts (%) and continuous data as mean ($\pm$ standard deviation) or median (25–75th percentile), whichever appropriate. Comparisons between all 3 groups were performed using one-way ANOVA or the Kruskal–Wallis test for continuous variables and the chi-square test for nominal variables. Individual comparisons were performed using the chi-square for nominal and unpaired t-test or rank sum for continuous variables. Due to sample size, comparisons between nominal and continuous variables within the ccTGA group were done using the rank sum or Fisher's exact test, respectively. Regression analyses were used to assess the association between hemodynamics and transposition type while adjusting for age, with respective results presented as β coefficients $\pm$ standard error. Statistical analysis was performed using JMP 14.1 for SAS (Cary, NC); a p-value < 0.05 was considered statistically significant.

Results

The d-TGA group included 53 individuals. Venous catheterization was performed in all patients and systemic ventricular catheterization in 46. Median age at the time of atrial switch operation was 17 months (9; 32.3 months). Most patients underwent the Mustard procedure (48 individuals, 90.5%) with 3 patients undergoing the Shumacker modification [8]

and 2 undergoing the Senning procedure. A history of systemic or pulmonary venous baffle obstruction was present in 21 (39.6%) and 13 (24.5%) patients, respectively; at the time of catheterization, evidence of residual or de novo systemic and pulmonary venous obstruction was diagnosed in 29 (54.7%) and 9 individuals (16.9%), respectively.

There were 85 patients with ccTGA (51 complex and 34 isolated); cardiac catheterization was ordered as part of pre-operative evaluation in 33 of them (38.6%). Venous catheterization was performed in 74 patients and systemic ventricular catheterization in 75. Among those with complex ccTGA, a history of ventricular septal defect was present in 45 (88.2%) and left ventricular outflow tract obstruction/pulmonary atresia in 38 (74.5%). Forty patients (75.5%) had undergone cardiac operations, including ventricular septal defect closure in 31 (60.8%), implantation of pulmonary valve prosthesis/conduit in 21 (40.1%), tricuspid valve intervention in 12 (23.5%, including 2 prior tricuspid repairs), and relief of subpulmonary/pulmonary stenosis in 11 (22.0%). In contrast, among those with isolated ccTGA, only 5 patients (14.7%) had undergone cardiac surgery (concomitant tricuspid valve surgery/atrial septal defect closure in 2; isolated tricuspid valve replacement, patent ductus arteriosus and coarctation of the aorta repair in one each).

Clinical and echocardiography data are presented in Table 1. Patients with isolated ccTGA were older than those with complex ccTGA and d-TGA. As expected, the number of prior cardiac operations was higher in those with d-TGA and complex ccTGA than in individuals with isolated ccTGA. Similarly, prior pulmonary valve replacement/conduit implantation was most commonly seen in those with complex ccTGA. Prior tricuspid valve surgery was more prevalent in complex ccTGA but no differences were present between d-TGA and isolated ccTGA. Otherwise, there were no differences in comorbidities, functional capacity, medications, or symptoms. Regarding laboratory values, those with complex ccTGA demonstrated higher MELD-XI scores than both d-TGA and isolated ccTGA groups.

There were no differences in sRV ejection fraction, left ventricular size, and function across groups. Complex ccTGA patients less commonly had ≥ moderate RV enlargement when compared to d-TGA patients. The presence of ≥ moderate pulmonary regurgitation was much more common in complex ccTGA than in the other two groups. Similarly, ≥ moderate mitral (subpulmonary) regurgitation was more commonly seen in patients with complex ccTGA ($p = 0.007$ and $p = 0.03$ when compared to d-TGA and isolated ccTGA, respectively).

Patients with ccTGA more frequently had ≥ moderate tricuspid regurgitation than those with d-TGA, but the prevalence was similar between isolated and complex ccTGA. The median tricuspid valve/prosthesis gradient was 5 mmHg (3; 6.2) for patients with complex ccTGA; all 3 patients in isolated ccTGA who had tricuspid valve intervention had gradients ≤ 6 mmHg, whereas the transtricuspid gradient was 9 mmHg for the single d-TGA patient with a tricuspid prosthesis.

Cardiac Catheterization

Cardiac catheterization findings are presented in Table 2 and summarized in Figs. 1 and 2. There were no differences in sRV end-diastolic pressure (sRVEDP) or PAWP between all groups. However, the ratio of PAWP:sRVEDP was significantly higher in those with d-TGA compared to patients with complex or isolated ccTGA. When adjusting for age, the association between higher PAWP:sRVEDP and d-TGA remained ($\beta = 0.18 \pm 0.04$, $p < 0.0001$), while no association between d-TGA and sRVEDP ($\beta = -1.0 \pm 0.6$, $p = 0.09$) or PAWP ($\beta = 1.2 \pm 0.7$, $p = 0.09$) was seen.

Systemic venous atrium/right atrial pressures were lower in individuals with isolated ccTGA compared to those with d-TGA or complex ccTGA. As anticipated given the anatomic substrate, left ventricle systolic pressure was highest among patients with complex ccTGA. No differences were seen with regards to mean pulmonary artery pressure or PVR. A mean pulmonary artery pressure > 25 mmHg was seen in 45.1% of patients in the d-TGA group, 45.6% in the complex ccTGA group, and 50% in the isolated ccTGA group.

Cardiac index was significantly higher in the d-TGA group compared to both groups of ccTGA patients. Noteworthy, there were no differences in heart rate or body mass index across the 3 groups. Both complex and isolated ccTGA had higher SVR than those with d-TGA; similarly, Ea was lower in the d-TGA group compared to complex ccTGA patients, but no differences were seen between the latter and patients with isolated ccTGA. The associations between d-TGA and higher cardiac index ($\beta = 0.15 \pm 0.06$, $p = 0.02$), as well as higher SVR and ccTGA ($\beta = 122.2 \pm 46.3$, $p = 0.001$) remained present after adjustment for age.

Due to the potential influences of TR on underlying hemodynamics, ccTGA patients with and without ≥ moderate TR were compared (Supplemental Table 1). Among those with complex ccTGA, ≥ moderate TR was associated with higher PAWP:RVEDP ratios and lower right atrial pressure:PAWP indices. The sample size did not allow for intragroup comparisons among those with isolated ccTGA.

Given the inherent impact on PAWP, hemodynamic findings across the 3 groups were also compared after excluding patients with pulmonary venous baffle obstruction (Supplemental Table 2). Even after excluding the 9 patients found to have pulmonary venous obstruction at catheterization, findings were similar to those presented in Table 2.

Table 1 Clinical and echocardiographic data

	d-TGA ($n=53$)	Complex ccTGA ($n=51$)	Isolated ccTGA ($n=34$)	p-value
Age, years	37.5 ± 8.3	40.8 ± 13.4	51.8 ± 13.1	< 0.0001[b,c]
Male sex	32 (61.5%)	30 (58.8%)	22 (64.7%)	0.86
Body mass index, kg/m^2	25.9 (23.2; 31.0)	24.2 (22.1; 28.8)	26.8 (24.1; 31.9)	0.15
Number of cardiac operations	1.8 ± 0.9	2 (0; 3)	0 (0; 0)	< 0.0001[b,c]
New York Heart Association class ≥ 3	16 (44.2%)	19 (37.3%)	10 (29.4%)	0.38
Hypertension	5 (9.4%)	2 (3.9%)	5 (14.7%)	0.22
Diabetes	2 (3.7%)	4 (7.8%)	2 (5.9%)	0.67
Obstructive sleep apnea	8 (15.0%)	6 (11.8%)	4 (11.8%)	0.85
History of atrial arrhythmias	24 (45.2%)	29 (56.9%)	13 (42.4%)	0.35
Atrial arrhythmia at cardiac catheterization	7 (14%)	13 (25.4%)	5 (14.7%)	0.26
Pacemaker	23 (43.4%)	24 (47.1%)	15 (44.1%)	0.92
Tricuspid valve prosthesis/repair	1 (1.8%)	12 (23.5%)	3 (8.8%)	0.002[a]
Pulmonary valve prosthesis/conduit	0	21 (41.2%)	0	< 0.001[a,c]
Symptoms				
Exertional dyspnea	33 (63.4%)	34 (66.7%)	25 (73.5%)	0.62
Fatigue	24 (46.1%)	29(56.7%)	18 (52.9%)	0.55
Leg edema	18 (34.6%)	13 (26.0%)	7 (20.6%)	0.34
Medications				
Digitalis	21 (39.6%)	20 (39.2%)	12 (36.3%)	0.96
Loop diuretic	24 (45.2%)	31 (60.8%)	15 (44.4%)	0.19
Beta blocker	23 (43.3%)	23 (45.1%)	16 (47.1%)	0.94
ACEi/ARB	32 (69.6%)	34 (66.7%)	25 (73.5%)	0.76
Aldosterone antagonist	10 (18.9%)	12 (23.5%)	8 (23.5%)	0.81
Pulmonary vasomodulator therapy	1 (1.9%)	3 (5.8%)	0	0.24
Antiarrhythmic drug	12 (22.6%)	16 (31.3%)	4 (11.7%)	0.11
Laboratory				
Hemoglobin, g/dL	14.2 ± 1.8	13.9 ± 1.8	13.8 ± 1.8	0.49
Creatinine, mg/dL	1.0 (0.8; 1.1)	1.2 ± 0.4	1.1 (0.9; 1.3)	0.05
Bilirubin, mg/dL	0.6 (0.4; 0.9)	0.9 (0.6; 1.2)	0.8 ± 0.4	0.07
MELD-XI	10 (9.4; 11.6)	11.9 (9.4; 15.6)	10.6 (9.4; 12.5)	0.04[a,c]
Echocardiography				
Estimated RV ejection fraction, %	38.9 ± 10.7	35.1 ± 11.9	34.3 ± 9.8	0.85
≥ moderate RV enlargement	45 (86.5%)	30 (66.7%)	27 (84.3%)	0.04[a]
≥ moderate LV enlargement	7 (13.2%)	10 (23.4%)	2 (5.8%)	0.08
≥ moderate LV systolic dysfunction	6 (11.3%)	7 (15.2%)	4 (11.7%)	0.76
≥ moderate systemic tricuspid regurgitation	17 (32.6%)	27 (55.1%)	24 (70.6%)	0.002[a,b]
≥ moderate subpulmonary mitral regurgitation	4 (7.7%)	14 (28%)	3 (8.9%)	0.008[a,c]
≥ moderate pulmonary regurgitation	5 (9.8%)	13 (32.5%)	0	0.0002[a,c]
≥ moderate aortic regurgitation	0	2 (4.2%)	1 (2.9%)	0.39

ACEi/ARB angiotensin-converting enzyme inhibitor/angiotensin receptor blocker, *MELD-XI* model for end-stage liver disease excluding international normalized ratio

[a] $p < 0.05$ when comparing d-TGA and complex ccTGA

[b] $p < 0.05$ when comparing d-TGA and isolated ccTGA

[c] $p < 0.05$ when comparing complex ccTGA and isolated ccTGA

Discussion

We present herein clinical and cardiac catheterization findings in a large cohort of predominantly symptomatic adults with d-TGA and ccTGA. Our results demonstrate that despite sharing a sRV, these patients markedly differ both structurally and hemodynamically. The main findings of our study are as follows: (1) cardiac index was significantly

Table 2 Invasive hemodynamic data

	d-TGA ($n=53$)	Complex ccTGA ($n=51$)	Isolated ccTGA ($n=34$)	p-value
Catheterization				
Systemic venous atrium/right atrium, mmHg	10 (6.3; 13)	10 (7;15)	7.9 ± 4.9	0.006[b,c]
LV systolic pressure, mmHg	43.5 (36; 59.8)	60 (46; 81.5)	42.5 (36.5; 61.8)	0.002[a,c]
LV end-diastolic pressure, mmHg	12.8 ± 5.7	14.2 ± 5.6	9.5 (8; 12)	0.06
Mean pulmonary artery pressure, mmHg	24 (19; 35)	24 (16; 36.3)	27.2 ± 12.2	0.79
PAWP, mmHg	18.1 ± 6.9	14.5 (10; 21)	17.0 ± 7.6	0.28
PAWP v-wave, mmHg	27.1 ± 11.2	19 (15; 31)	24.7 ± 12.1	0.17
sRV systolic pressure, mmHg	108.5 (98.5; 119)	108.6 (95.5; 115.5)	107.5 (98.3; 117.3)	0.62
sRVEDP, mmHg	12 (9.8; 19)	15 (12; 20)	15.5 (12; 22.5)	0.05
Arterial systolic pressure, mmHg	111.7 ± 13.2	105 (96.8; 118.3)	117.8 ± 19.9	0.04[c]
Arterial diastolic pressure, mmHg	64.7 ± 9.2	64.7 ± 9.1	66.1 ± 9.8	0.80
Arterial mean pressure, mmHg	82.9 ± 10.2	82.6 ± 10.7	85.5 ± 13.0	0.48
Cardiac index, L/min/m^2	2.4 (2; 2.6)	2.0 (1.7; 2.3)	2.1 (1.8; 2.4)	0.003[a,b]
Stroke volume, ml	70.4 ± 23.6	54.9 ± 17.8	60 (52.2; 83.9)	0.0005[a,c]
Heart rate, bpm	69.3 ± 13.7	70.9 ± 11.4	65.5 ± 11.1	0.13
Pulmonary vascular resistance, WU	1.4 (0.8; 2.8)	2.6 (1.1; 4.1)	2.5 (1.2; 3.5)	0.14
Systemic vascular resistance, dynes/s/cm^{-5}	1234 (1018; 1483)	1490 (1215; 1958)	1519 ± 390	0.004[a,b]
Ea, mmHg/ml	1.5 (1.2; 1.9)	1.8 (1.4; 2.3)	1.8 ± 0.7	0.02[a]
PAWP:sRVEDP	1.4 ± 0.4	0.9 (0.7; 1.1)	0.9 ± 0.3	< 0.0001[a,b]
Systemic venous atrium/right atrium:PAWP	0.6 (0.4; 0.8)	0.7 ± 0.2	0.5 ± 0.2	0.0003[a,b,c]

Ea effective arterial elastance, *LV* left ventricle, *PAWP* pulmonary artery wedge pressure, *sRV* systemic right ventricle, *sRVEDP* systemic right ventricular end-diastolic pressure

[a] $p < 0.05$ when comparing d-TGA and complex ccTGA

[b] $p < 0.05$ when comparing d-TGA and isolated ccTGA

[c] $p < 0.05$ when comparing complex ccTGA and isolated ccTGA

lower and afterload higher in those with ccTGA when compared to d-TGA; (2) there were no differences in PAWP but the higher PAWP:sRVEDP suggests a lower contribution of sRV filling pressures and larger role played by the pulmonary venous atrium/baffle in pulmonary venous hypertension among those with d-TGA; (3) venous/right atrial hypertension was more common in d-TGA and complex ccTGA patients; (4) ≥ moderate pulmonary regurgitation and mitral regurgitation were prevalent among complex ccTGA patients.

In patients with a systemic left ventricle, systolic ventricular dysfunction culminates in a reduction in cardiac output. This low-flow state results in an increase in adrenergic tone and neurohormonal activation to maintain systemic perfusion [3, 4]. These physiologic changes are the pillar for the use of intensive medical therapy and provided the foundation for the initial studies assessing the role of beta blockers and angiotensin-converting enzyme inhibitors in heart failure. Systolic dysfunction of the sRV is highly prevalent in adults with d-TGA post-atrial switch and ccTGA [1]. Therefore, it would be intuitive to apply the medical armamentarium proven to be highly effective in dysfunctional left ventricles to individuals with sRV. However, investigations of standard heart failure medical therapy in patients with sRV have been disappointing [5]. The use of sacubitril/valsartan was recently noted to be associated with improvements in cardiac biomarkers and echocardiography parameters in patients with sRV [9–11] but our understanding of its benefits in this population is still incipient. It has been suggested that patients with sRV are unique anatomically but also biochemically, as most have normal catecholamine levels [12, 13]. It is important to note that most studies in patients with a sRV have included patients with d-TGA and ccTGA interchangeably, with d-TGA typically constituting the majority.

Data regarding invasive hemodynamics in patients with sRV are mostly limited to small studies, predominantly including pediatric patients [14–22]. Similar to individuals with a dysfunctional systemic left ventricle, in our cohort, patients with isolated ccTGA were found to have reduced cardiac indices and, notably, higher afterload indices when compared to those with d-TGA. Interestingly, we previously reported systemic hypertension to be a risk factor for progressive sRV dysfunction in ccTGA patients [23]. Given the intrinsic abnormalities of the tricuspid valve, it is not surprising that many patients with ccTGA had significant TR, contributing to the reduction in forward flow and

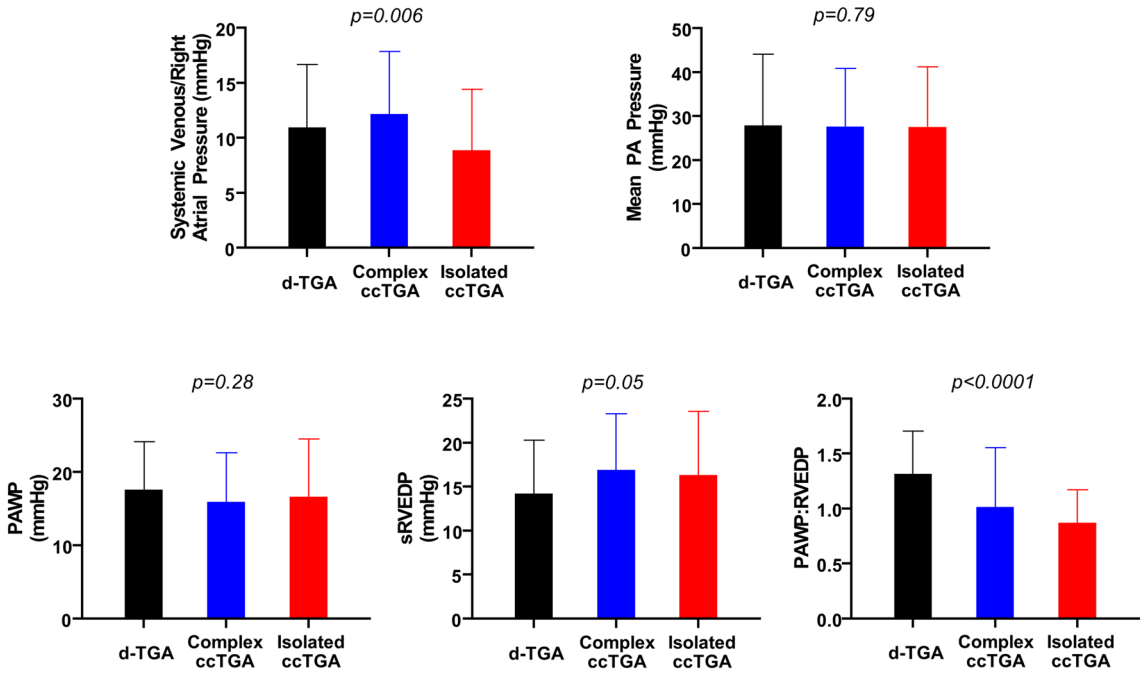
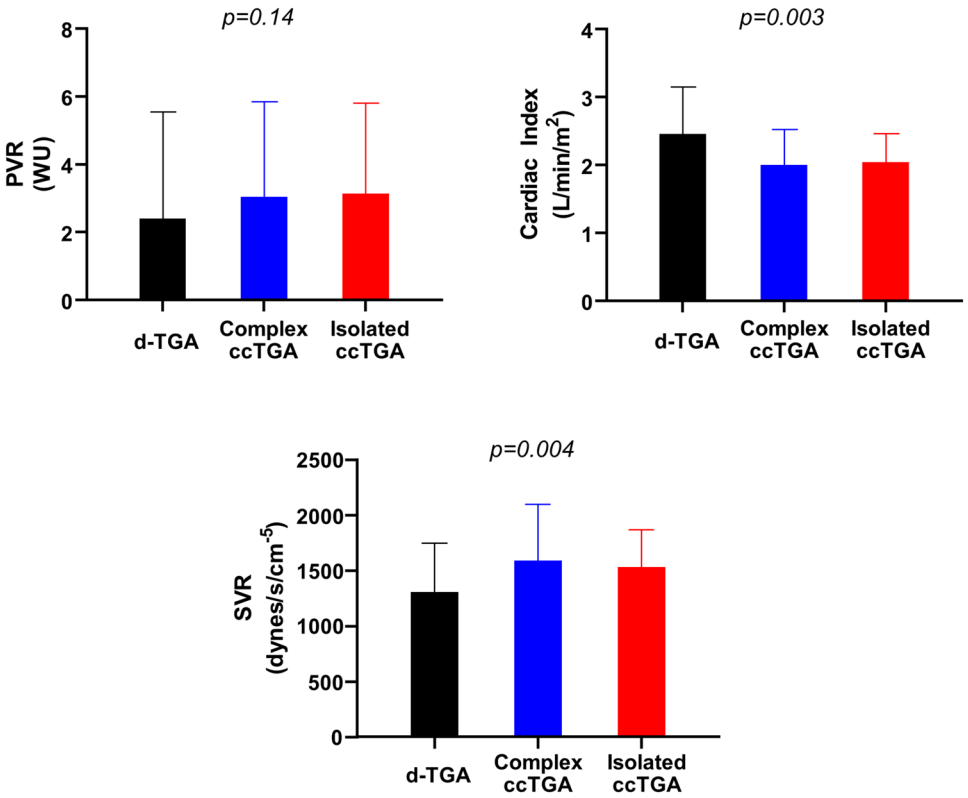


Fig. 1 Filling pressures and mean pulmonary artery pressures in patients with d-TGA and ccTGA. Higher systemic venous pressure/right atrial pressure was seen among patients with complex ccTGA compared to other groups. No differences were seen across groups with regard to mean pulmonary artery (PA) pressures, pulmonary artery wedge pressure (PAWP), or sRV end-diastolic pressures (sRVEDP). However, PAWP:sRVEDP was highest in the d-TGA group, suggesting a larger role played by the pulmonary venous atrium/baffle in pulmonary venous hypertension among these patients.

Fig. 2 Vascular resistance and cardiac index data in patients with d-TGA and ccTGA. No differences in pulmonary vascular resistance (PVR) were seen. The d-TGA group showed lower systemic vascular resistance (SVR) and higher cardiac index than patients with ccTGA.



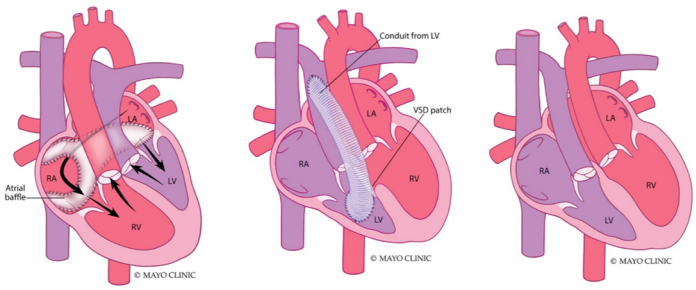
increase in PAWP. Although the small number of individuals with < moderate TR limited our analysis, the hemodynamics in this subset of patients do not appear to markedly differ from those with significant TR, suggesting a significant role played by the sRV itself in these hemodynamic derangements. Importantly, right atrial pressure was lowest in the isolated ccTGA group, underscoring the predominantly systemic/"left-sided" pathology. Therefore, of all 3 groups, patients with isolated ccTGA might be the closest to individuals with myopathic left ventricles. It should also be highlighted that, in contrast to the latter, TR in ccTGA is typically related to a primary pathology of the valve [24] and should be sought and addressed proactively due to negative consequences to the sRV.

It would be natural to focus on the systemic ventricle in all individuals with ccTGA presenting with symptoms. Contrary to these expectations, our findings in the subgroup of patients with complex ccTGA actually share several similarities with observations in adults late after repair of tetralogy of Fallot. Firstly, the prevalence of ≥ pulmonary regurgitation was high, being present in more than 25% of patients. Secondly, one third of patients had significant subpulmonary mitral regurgitation. Subpulmonary atrioventricular valve regurgitation is a well-known late complication in adults with tetralogy of Fallot, particularly in those with dilated subpulmonary ventricles and pulmonary regurgitation. In our experience, the mechanisms of subpulmonary mitral regurgitation in complex ccTGA are due to a combination of annular dilatation, intrinsic mitral valve abnormalities and, in some, device lead-related regurgitation [25]. Although not the focus of the study, this is an important observation given the propensity of this group to develop conduction abnormalities and other arrhythmias which require pacemaker/device implantation. Thirdly, right atrial hypertension was common, perhaps explaining the MELD-XI score seen in this group. Therefore, it is mandatory that adults with complex ccTGA are seen as having biventricular pathology with equal attention paid to the subpulmonary and systemic ventricles and valves.

We have highlighted the role of the atrial baffles in pulmonary venous pressure and pathophysiology of pulmonary hypertension in patients with d-TGA [26]. This contribution went beyond the risk of pulmonary venous baffle obstruction with some patients having clear invasive hemodynamic findings of atrial noncompliance. In the present study, no differences in the degree of pulmonary venous hypertension (i.e., PAWP) were seen between patients with d-TGA and ccTGA. However, the ratio of PAWP:RVEDP was significantly higher in those with d-TGA, supporting a different mechanism in the pathogenesis of pulmonary congestion in the two groups. It is also interesting that despite the presence of atrial baffles, cardiac indices were higher and afterload lower in those with d-TGA than ccTGA. These findings reinforce the differences in underlying hemodynamics between the two transposition groups and might have explained the findings of previous studies focusing on neurohormonal activation and catecholamine release in patients with d-TGA.

Future Implications

Figure 3 summarizes the invasive hemodynamic and structural abnormalities according to subgroups of individuals



	d-TGA	Complex ccTGA	Isolated ccTGA
Systemic venous/right atrium	↑	↑	↔
PAWP	↑	↑	↑
PAWP:RVEDP	↑	↔	↔
Cardiac index	↓	↓↓	↓↓
SVR	↔	↑	↑
Valvular disease	–	MR, TR, PR	TR

Fig. 3 Summary to hemodynamics abnormalities in patients with sRV. *MR* mitral regurgitation, *PAWP* pulmonary artery wedge pressure, *SVR* systemic vascular resistance, *TR* tricuspid regurgitation

with TGA. Neurohormonal activation and biomarker release may differ among those with ccTGA and d-TGA [10] not only due to the presence of atrial baffles, but also due to the differences in filling pressures and intrinsic ventricular/myopathic disease (including the subpulmonary left ventricle). As we investigate the role of additional heart failure therapies such as sodium-glucose cotransporter-2 inhibitors [9] and expand our experience with sacubitril/valsartan in this population, further analyses regarding the disease-specific therapeutic responses (i.e., ccTGA vs d-TGA) are warranted. Lastly, the impact of percutaneous or surgical valvular interventions in adults with sRV (particularly in those with significantly reduced systolic function) is still poorly delineated and requires additional investigation.

Limitations

We acknowledge the limitations of the study, including its retrospective nature. This represents a cohort of patients referred for cardiac catheterization at a quaternary care center, and some of the findings may not be fully applicable to asymptomatic individuals with preserved functional capacity seen in the outpatient practice. Despite the relatively large sample size compared to other studies including patients with a sRV, the number of individuals in some subgroups limited our analyses. Additionally, the sample size might have resulted in type II error. Specifically, the number of individuals with isolated ccTGA and < moderate TR was particularly small. Lastly, cross-sectional data were unavailable and, therefore, might have affected the prevalence of significant ventricular enlargement and dysfunction given the inherent limitations of transthoracic echocardiography in those with sRV.

Conclusion

Despite sharing a sRV, adults with d-TGA and ccTGA have substantial differences in hemodynamics and associated structural/valvular abnormalities (particularly those with complex ccTGA). As we expand our experience and investigate the role of newer heart failure therapeutic agents, further investigation regarding the disease-specific responses in those with d-TGA and ccTGA is warranted.

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Declarations

Competing interests The authors declare no competing interests.

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