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Original Article

Timely Detection of Subclinical Heart Failure Among Children with D-Transposition of Great Arteries after Senning Operation: A Single Center Experience

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Abstract:
Background*:* Atrial switch operation, was introduced by Ake Senning in 1958 for patients with D-transposition of great arteries (D-TGA). The major disadvantage of the atrial switch procedure is right ventricle (RV) failure in up to 7% to 10% of patients per 10 years.
Aims of the work: To detect subclinical RV failure in children with D-TGA after atrial switch repair using conventional and nonconventional echocardiography.
Subjects and Methods: We studied 25 children with D-TGA who underwent atrial switch operation following in the Postoperative Cardiology Clinic at Cairo University Specialized Pediatric Hospital. They did not have symptoms of heart failure. They underwent conventional echocardiography, tissue Doppler and speckle tracking imaging including RV global longitudinal strain (RV GLS) to detect subclinical heart failure according to New York Heart Association (NYHA) classification. The results were compared to a matched control group.
Results: Mean age ± standard deviation of the studied group was 6.8 ± 4.3 years while mean age at time of operation ranged 14.2 ± 12.7 months (p=0.001). Mean RV global longitudinal strain (GLS) of cases (-14.5± 1.5%) was significantly impaired compared to RV GLS of controls (-20.2 ± 1.4%) (p <0.001). Tricuspid annular plane systolic excursion (TAPSE) of cases (12.7 ± 3.1 mm) was lower than TAPSE of controls (15.5 ± 2.3 mm) (p= 0.001). While RV myocardial performance index (MPI) of cases (0.47 ± 0.10) was higher than RV MPI of controls (0.34 ± 0.03) (p <0.001). There was a negative correlation between age at the time of surgery and RV GLS (r = -0.435) (p = 0.030). Non-conventional echocardiographic parameters RV MPI and RV GLS detected subclinical heart failure among all studied cases post- atrial switch.
Conclusions: Non-conventional echocardiographic parameters RV MPI and RV GLS had higher sensitivity for detection of RV dysfunction and timely diagnosis of subclinical heart failure in patients of D-TGA after Senning atrial switch operation that was not detected by conventional echocardiography.
Level of Evidence of Study: IV (*1*)**.**
Keywords: D-TGA; RV dysfunction; Senning atrial switch operation; RV GLS; global longitudinal strain; myocardial performance index; echocardiography.
Abbreviations: AUC: area under curve; GLS: global longitudinal strain; MPI; myocardial performance index; RV; right ventricle; TAPSE: Tricuspid annular plane systolic excursion; SD: standard deviation; tricuspid A': tricuspid late diastolic velocity; tricuspid E': tricuspid early diastolic velocity.

Introduction

Dextro-transposition of the great arteries (D-TGA) is a common congenital cyanotic heart disease that is associated with shorter life expectancy (*2*). It accounts for 5–7% of congenital heart disease that affects 0.2 of 1000 live births (*3*). The arterial switch operation has been the standard surgical management for children with D-TGA since the early to mid-1980s. It was introduced by Ake Senning in 1958 and since then, there was a dramatic change in the prognosis of TGA patients (*4*). The Senning procedure directs the venous return to the contra-lateral atrioventricular valve and contra-lateral ventricle, using an atrial baffle derived from the septal

tissue of the patient. In 1963, Mustard introduced usage of a synthetic or a pericardial baffle for venous return direction (*5*).

The complications of the right ventricle (RV) being the systemic ventricle include RV dilatation, RV dysfunction, cardiac arrhythmias, sinus node dysfunction, baffle leaks and obstruction to the pulmonary and/or systemic pathways, heart failure and premature/sudden death (*6*). Early and prompt detection of heart failure is crucial for instituting proper timely anti-failure measures among children with D-TGA who underwent atrial switch operation(*7*). Assessment of ventricular function is a major component of the long-term follow-up of patients after atrial repair for (D-TGA) patients. Tissue Doppler echocardiography and speckle tracking are proposed for evaluation of ventricular function in D-TGA patients, and severity of impairment of myocardial function (*8*, *9*). We aimed to detect subclinical RV failure in children with D-TGA after atrial switch repair using conventional and nonconventional echocardiography.

Subjects and Methods

This cross-sectional case control study included children with D-transposition of great arteries aged 1- 14 years who underwent Senning operation and did not have clinical heart failure. They were following up at the Postoperative Cardiology Clinic, Cairo University Specialized Pediatric Hospital. The study included a control group of 25 healthy sex and age matched children. The study was approved by the Research Ethics Committee, Faculty of Medicine, Cairo University, Egypt. Care takers consented to the trial. The study complied to the Declaration of Helsinki for trials (*10*).

Methods

The studied group of children were surgically operated during 2008-2019. All patients in the study underwent full history taking including time of surgery and manifestations of heart failure and palpitations, and thorough clinical examination. All the cases underwent echocardiographic examination in a supine or left lateral position using General Electric Vivid 5 or 7 series system (General Electric Health Care company, USA) with 3 or 5MHz probe (multifrequency transducer) according to age and weight of the patient. The ECG cable was connected to the ultrasound machine to define the beginning of cardiac cycle.

The following parameters were measured and compared to a matched control group in number, age and sex :

- Conventional Parameters of Right Ventricular Systolic Function: Tricuspid annular plane systolic Excursion (TAPSE) and RV dimensions.
- RV tissue Doppler parameters: Systolic, early diastolic and late diastolic myocardial velocities at tricuspid annulus and the septal wall and RV Myocardial performance index (MPI).
- Speckled Tracking Imaging: Assessment of the RV Global Longitudinal Strain (RV GLS). It is to be noted that RV GLS absolute value reflects the intensity of shortening and hence the lower the absolute value, the lower the RV systolic function while negativity reflects the shortening nature of longitudinal function (*11*).

Children were screened for subclinical (asymptomatic cases despite RV dysfunction evidenced with echocardiography) and clinical heart failure according to the modified Ross heart failure classification for children younger than 6 years and the New York Heart Association (NYHA) classification for children older than 6 years. Modified Ross classification of heart failure definitions are: class I: asymptomatic, class II: mild tachypnea or diaphoresis with feeding or exertion, class III :marked tachypnea or diaphoresis, class IV : tachypnea, retractions or grunting at rest. NYHA classification definitions are: class I: asymptomatic, class II: slight limitations of activity, class III: marked limitation of activity and class IV: symptoms at rest (*12*).

Statistical Analysis

Data were analyzed using IBM, SPSS Statistics version 23 (IBM Corp., Armonk, NY). Continuous numerical variables were presented as mean and standard deviation (SD). Inter-group differences were compared using the unpaired t-test. Categorical variables were presented as ratio or number and percentage and differences were compared using Fisher's exact test. Charts and graphs were prepared using SPSS programs. The discriminative value of echocardiographic measures between cases and control group was examined using receiver-operating characteristic (ROC) curve analysis. The area under ROC curve (AUC) was interpreted

as follows: AUC 0.9-1 was considered excellent indicator, AUC 0.8-0.89 was considered good indicator, AUC 0.7-0.79 was considered fair indicator, AUC 0.6-0.69 was considered poor indicator and finally AUC <0.6 was considered failed indicator. P-value <0.05 was considered statistically significant.

Results

- Demographic and clinical data of the cases and control groups: Among 118 children with D-TGA who underwent Senning operation during 2008-2019, only 25 were clinically free of heart failure. These 25 were included in our study. None of them had other surgical complications. Age of the studied group at the time of the study ranged between 1- 14 years (mean ± SD age 6.8 ± 4.3 years). Their ages at time of operation ranged from 5-24 months (mean= 14.2 ± 12.7 months) (p=0.000). Duration between operation and the study ranged from 1-160 months with mean ± SD duration= 67.8 ± 48 months. Of them 18 (72%) were females and 7 (28%) were males. The weight of the studied group was plotted against the Egyptian percentiles for age; 6 were on <3rd percentile, 12 between 3rd and 50th percentile and 6 were on the 50th-95th percentile compared to the control group where 4 were on <3rd percentile, 7 between 3rd and 50th percentile and 14 were on the 50th-95th percentile (p=0.067). Mean ± SD body surface area (BSA) of the cases was 0.88 ± 0.34. All of our cases had normal oxygen saturation and none had cyanosis or clubbing. Clinical manifestations of heart failure were not present among all our studied cases post- atrial switch. No cases were found to have class II, III or IV heart failure. (Table 1).

Table 1. Demographic characteristics of the study and control groups.

	Cases (n=25)	Controls (n=25)	P value
Age (yr)	6.8 ± 4.3	6.5 ± 5.4	0.224
Gender (M/F)	7/18	7/18	0.085
BSA (m^2)	0.88 ± 0.34	0.83 ± 0.23	0.079
SpO_2 (%)	98 ± 3	99 ± 1	0.069
Heart rate (bpm)	100 ± 25	93 ± 16	0.216

BSA: Body Surface Area; SpO2: Oxygen Saturation.

- Echocardiographic RV function Findings: Non-conventional echocardiographic parameters RV MPI and RV GLS detected subclinical heart failure among all studied cases post- atrial switch that was not detected by conventional echocardiography. The mean ± SD tricuspid E' of cases (8.6 ± 3.1cm/s) was lower than that of the control group (13.3 ± 4.3 cm/s) (p <0.001). Mean RV GLS of the cases was worse than the mean RV GLS of controls (-14.5± 1.5% and -20.2 ± 1.4 % respectively), (p <0.001). Hence, the absolute value of RV GLS in cases was lower compared to controls, reflecting the impaired RV systolic functions in cases. TAPSE of cases was lower than TAPSE of controls (12.7 ± 3.1 mm and 15.5 ± 2.3 mm respectively (p= 0.001). RV MPI of cases was also higher than MPI of controls (0.47 ± 0.10 and 0.34 ± 0.03 respectively (p= <0.001). There was no significant difference in Tricuspid A' and Tricuspid E'/ A' ratio between cases and controls. (Table 2). RV GLS correlated negatively with the patient age at time of Senning operation (p=0.03). (Table 3).

Table 2. Echocardiographic findings of RV function in cases and control groups.

	Cases (n=25)		Controls (n=25)		P value
	Mean	SD	Mean	SD	
Tricuspid E' (cm/s)	8.6	3.1	13.3	4.3	<0.001
Tricuspid A' (cm/s)	6.7	3.1	7.9	2.9	0.150
Tricuspid E'/ A' ratio	1.49	0.67	1.80	0.61	0.095
RV GLS (%)	-14.5	1.5	-20.2	1.4	<0.001
TAPSE (mm)	12.7	3.1	15	2.3	0.001
MPI	0.47	0.10	0.34	0.03	<0.001

Tricuspid A': tricuspid late diastolic velocity by tissue Doppler; Tricuspid E': tricuspid early diastolic velocity by tissue Doppler; Tricuspid E'/ A' ratio: the ratio of early to late tricuspid diastolic velocity by tissue Doppler; RV GLS: Right ventricular global longitudinal strain; TAPSE: Tricuspid annular plane systolic excursion; MPI: Myocardial performance index.

The receiver-operating characteristic (ROC) curve defined the most sensitive RV echocardiographic parameters of highest diagnostic value for detection of subclinical RV dysfunction after Senning operation. The RV GLS was found to have an excellent diagnostic value (AUC = 1.000, P< 0.001, cut-off criterion -17 with sensitivity 100% and specificity 100%). RV MPI also was found to have an excellent diagnostic value (AUC = 0.921, p < 0.001, cut-off criterion >0.39, sensitivity 84% and specificity 92%). Tricuspid E' was found to have a good diagnostic value (AUC = 0.832, p <0.001, cut-off criterion ≤ 10 with sensitivity 80% and specificity 84%). TAPSE was found to have a fair diagnostic value (AUC = 0.761, p< 0.001, cut-off criterion ≤ 15 with sensitivity 80% and specificity 64%). On the other hand, tricuspid A' was found to have a poor diagnostic value (AUC = 0.667, p= 0.039, cut-off criterion ≤ 6 with sensitivity 60% and specificity 88%). (Table 4) (Figure 1).

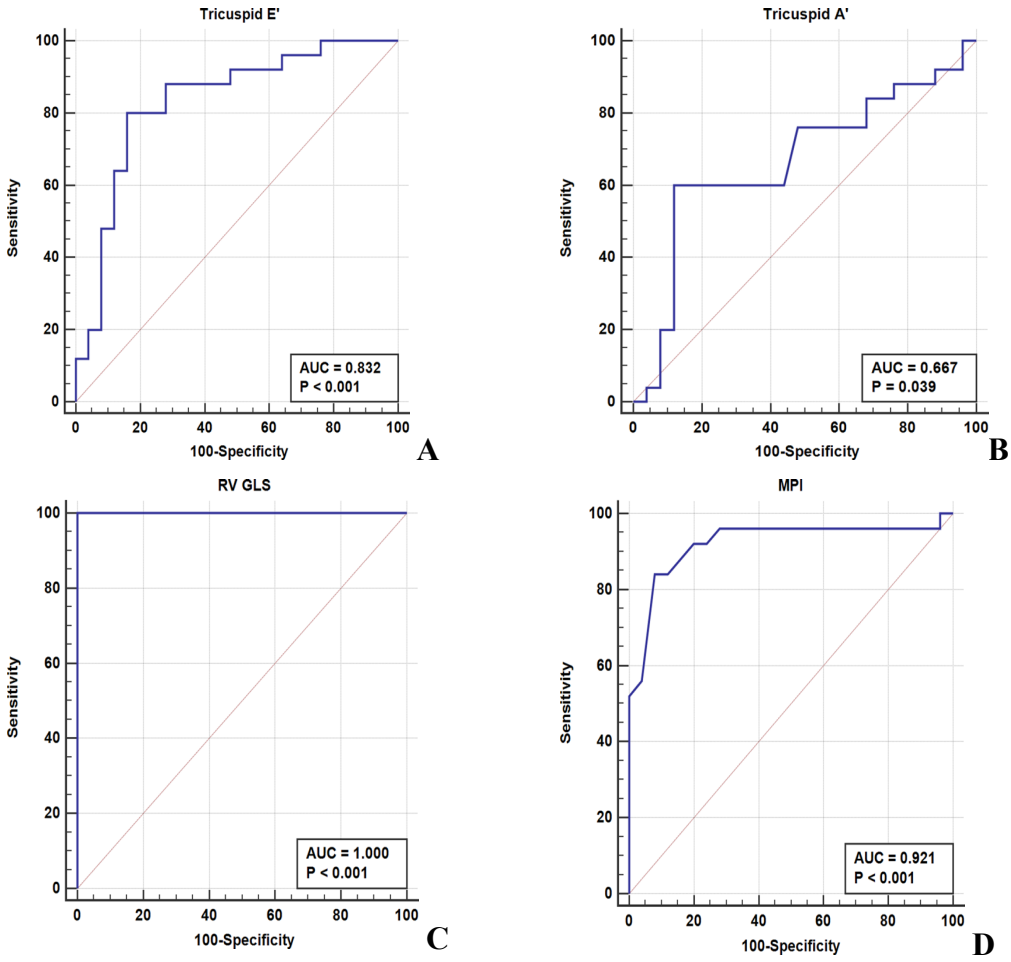

Figure 1. Receiver-operating characteristic (ROC) curve analysis of different RV echocardiographic parameters discriminative diagnostic accuracy between cases and control group. A) Tricuspid E'; tricuspid early diastolic velocity by tissue Doppler. B) Tricuspid late diastolic velocity by tissue Doppler. C) RV GLS: Right ventricular global longitudinal strain. D) MPI: Myocardial performance index.

Table 3. Correlation between right ventricular echocardiographic measures and age at atrial switch.

		Tricuspid E' (cm/s)	Tricuspid A' (cm/s)	Tricuspid E'/A' ratio	RV GLS (%)	TAPSE (cm)	MPI
Age at the time of operation	r	-0.034	-0.181	0.126	-0.435	0.002	0.005
	p	0.871	0.386	0.548	0.030	0.994	0.979

RV GLS: Right ventricular global longitudinal strain; MPI: Myocardial performance index; TAPSE: Tricuspid annular plane systolic excursion; Tricuspid A': Tricuspid late diastolic velocity by tissue Doppler; Tricuspid E'; tricuspid early diastolic velocity by tissue Doppler.

Table 4. Receiver-operating characteristic (ROC) curve analysis for discrimination between cases and controls using different RV echocardiographic parameters.

	AUC	SE	Z	P value	Youden index J	Cut-off criterion	Sens. (%)	Spec. (%)
Tricuspid E'(cm/s)	0.832	0.061	5.473	<0.0001	0.640	≤10	80	84
Tricuspid A'(cm/s)	0.667	0.081	2.064	0.039	0.480	≤6	60	88
RV GLS (%)	1.000	0.000	NA	<0.0001	1.000	-17	100	100
TAPSE (mm)	0.761	0.067	3.881	<0.001	0.440	≤15	80	64
MPI	0.921	0.044	9.630	<0.0001	0.760	>0.39	84	92

AUC: area under the ROC curve; MPI: Myocardial performance index; RV GLS: Right ventricular global longitudinal strain; SE: Standard error; Sens.: Sensitivity; Spec.: Specificity; TAPSE: Tricuspid annular plane systolic excursion; Tricuspid A': Tricuspid late diastolic velocity by tissue Doppler; Tricuspid E'; tricuspid early diastolic velocity by tissue Doppler; Z : Z-statistic.

Discussion

All our studied 25 children who underwent Senning during 2007-2019 operation were clinically asymptomatic, yet all proved to have subclinical heart failure by non-conventional echocardiography. Throughout the 1970s and 1980s, Senning procedure was the treatment of choice for TGA patients being the first surgical technique that allowed infants with TGA to survive and reach adulthood. Despite not being an anatomical repair, Senning operation results are satisfactory with low reported surgical mortality added to the benefit of correction of hypoxia (*13*), yet the most of the patients develop NYHA class I or asymptomatic heart failure and a minority develop NYHA class II or more (*14*). While arterial switch is the operation of choice for neonates diagnosed with D TGA, yet Senning remains of value for those diagnosed later in beyond the first year of life (*15*).

Prompt timely diagnosis of subclinical RV failure post Senning helps to tailor the medical treatment post-operatively, improve the quality of life and increase the post-operative survival. RV GLS was reported to be an accurate parameter to assess RV function in Senning survivors (*16*, *17*). Our work provides more evidence to support the accuracy of RV GLS in assessment of RV function. RV GLS proved sensitive and specific for RV subclinical heart failure diagnosis among our studied children who were clinically free of heart failure. RV GLS was more sensitive and specific for diagnosis of RV dysfunction and subclinical heart failure compared to other RV echocardiographic parameters including TAPSE, RV MPI and Tricuspid E' and A'. Conventional echocardiography parameters failed to detect subclinical heart failure class 1 NYHA among our studied cases. According to our results the RV GLS -17 % was a cut off value for detection of subclinical RV failure in our studied patients.

It is interesting however, that our studied children post-atrial switch had comparable weight to their age and matched control group (p=0.06) despite having subclinical heart failure. Senning is a good second option for those with D TGA who do not undergo arterial switch early in life. It allows the children to grow and develop.

Our study was a cross-sectional one and not a prospective one, hence we are not aware of the causes of decline in the RV GLS, the rate of decline, or the factors that arrest this decline. We do not have baseline RV GLS of these children before the operation, shortly after the operation or yearly values to compare with our findings at the time of the operation. We are aware that all our studied group of children had RV GLS -17 %, and more studies are needed to deduce evidence based guidelines for initiation of anti-failure therapy. Yet, we find that RV GLS -17 % warrants introduction of an inhibitor of angiotensin-converting enzyme.

There was a significant negative correlation between the age at the time of surgery and RV GLS (r =-0.435, p = 0.030). Hence, it is not advised to delay of the timing of surgical treatment of D-TGA patients because the long standing hypoxia adds to the depletion of the RV global systolic reserve. Senning operation has been recently replaced in the last 3 decades by the arterial switch operation (ASO) that provides prompt anatomical correction for D-TGA patients (*15*). We did not compare our studied group to another group that underwent ASO. Yet, the late diagnosis of D-TGA in some cases and the unavailability of the surgical experience of ASO in all cardiac centers, renders Senning operation a good surgical option for D-TGA patients as it offers adulthood survival with overall satisfactory results.

Conclusion

Non-conventional echocardiographic parameters RV MPI and RV GLS had higher sensitivity for detection of RV dysfunction and timely diagnosis of subclinical heart failure in patients of D-TGA after Senning atrial switch operation that was not detected by conventional echocardiography.

Author Contributions

All authors contributed to the study conception and design. All read and approved the final manuscript.

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CONFLICT OF INTEREST

The authors declare no conflict of interest in connection with the reported study. Authors declare veracity of information.

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