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Research Article

Prognostic index to assess the risk of systemic right ventricular failure after atrial switch operation for transposition of the great arteries

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Abstract

The introduction of atrial switch operation allowed to prolong the life expectancy of those born with transposition of the great arteries. This operation involves extensive surgery in the atria and leaves the right ventricle as the systemic ventricle that develops dysfunction because its anatomy is not intended to handle systemic pressure over a lifetime. We hypothesized that certain echocardiographic variables contribute to the identification of systemic right ventricular failure and accurately predict prognosis in follow-up of these patients. The objective was to desing and validate a prognostic index for the estimation of risk of systemic right ventricular failure after atrial switch operation for transposition of the great arteries. An observational, prospective, cross-sectional study was conducted in 90 patients of the Pediatric Cardio Center "William Soler" from 2011 to 2017. Early systolic dysfunction of the systemic right ventricle was observed, dependent on the increase in afterload. There are no alterations in early diastolic function. The variables that make up the prognostic index are: end-diastolic diameter and parietal thickness of the right ventricle, Right Ventricle Ejection Fraction (RVEF), Tei index, the derivative of pressure over time (dp/dt) and tricuspid regurgitation. The index shows good discriminatory capacity and adequate calibration in prediction of ventricular dysfunction. End-diastolic diameter and parietal thickness of the right ventricle, the derivative of pressure over time and tricuspid regurgitation, demonstrate clinical relevance. The prognostic index shows validity and allows its introduction into clinical practice.

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Introduction

The Transposition of the Great Arteries (d-TGA) is the most frequent cyanotic congenital heart disease in the neonatal period. It represents 5 to 8% of the total cardiovascular malformations. In these children, there is atrioventricular agreement and ventricle-arterial discordance, that is, the aorta originates in the morphological right ventricle and the pulmonary artery in the morphological left ventricle. In the normal heart, the systemic and pulmonary circulations occur in series driven by the corresponding ventricles. In d-TGA, both circulations are arranged in parallel [1,2].

Atrial Switch Operation (ASO)

The Mustard or Senning procedures, involves extensive surgery in the atria and leaves the right ventricle as the systemic ventricle. Although ASO is no longer the gold standard for management of d-TGA, having been superseded by the arterial switch operation in the late 1980s, most adult survivors with d-TGA will have undergone the older procedure [3]. With this surgery it is possible to correct the circulation of blood in parallel, but the right ventricle is still connected to the aorta artery and faces systemic afterload, so the tricuspid valve also assumes systemic function [4,5].

In these patients, the right ventricle undergoes changes to adapt for several decades to the systemic position and function. Systemic Right ventricular Failure (SRvF) evolves in progressive stages. At the beginning, hypertrophy occurs but in the long term there is dilation and gradual deterioration of its function with the appearance of tricuspid insufficiency secondary to ring dilation in a high percentage of patients [4-6].

It is known that the afore mentioned surgical technique produce long-term complications such as rhythm disturbances, intraatrial patches obstructions or residual shunt, SRvF , failure of the tricuspid systemic valve and sudden death [3,5-7].

At present, the arterial switch operation proposed by Jatene is the surgical procedure of choice when the patient's anatomy is favorable. This anatomical correction has the advantage of maintaining the left morphological ventricle as a systemic ventricle and avoids atrial incisions and suture lines that predispose to atrial arrhythmias. However, complications are also identified in the short and medium term, such as right ventricle outflow tract obstruction (supravalvular pulmonary stenosis that can affect the bifurcation of the pulmonary branches), dilation of the new aortic root with secondary aortic insufficiency and obstructive coronary lesions [8,9].

The introduction of these surgical techniques meant the possibility of prolonging the life expectancy of those born with d-TGA. Over the years, SRvF was demonstrated from the subclinical stage through transthoracic echocardiography. Therapeutics, empirically, begins when patients show symptoms and is based on the principles of treatment of left ventricular dysfunction with a generally ischemic cause. It is therefore necessary to carefully consider new diagnostic and therapeutic approaches in order to improve the morbidity, survival and quality of life of this group of patients [4,10,11].

The medical literature consulted did not document any tool with specific predictive capacity for right ventricular dysfunction in patients such as those studied in the present investigation [2,12,13]. Most of the studies consulted are designed for evaluating diagnostic modalities that compare the diagnostic accuracy of echocardiography and nuclear magnetic resonance as evaluators of right ventricular function [14,15].

This research focuses on the identification of echocardiographic variables useful for the design of the prognostic tool that will avoid intuitive clinical conclusions and will enable an aid to the doctor's decision making assistance, to the strict surveillance of these patients and to the projection of new therapeutic strategies. Identifying subclinical systemic right failure is thus imperative in long-term management after ASO for d-TGA.

We hypothesized that certain echocardiographic variables contribute to the identification of systemic right ventricular failure and accurately predict prognosis in follow-up of patients who underwent atrial switch operation for d-TGA.

The aim of this study was to design and validate a prognostic index for the estimation of risk of systemic right ventricular failure after atrial switch operation for d-TGA.

Patient and method

This was an observational, prospective and cross-sectional study at a single tertiary care center.

We included all consecutive patients who underwent atrial switch operation for d-TGA, who attended in the annual postoperative echocardiographic monitoring in the Pediatric Cardio Center "William Soler", in the period comprised from January 2011 to December 2017.

An overview of the patient participation for the current study is presented in Figure 1.

The study protocol was approved by the local ethics committee. Written informed consent was obtaines for all patients.

Population. Masking the investigation

The hospital where the research was developed is a national reference center for the diagnosis, treatment and monitoring of patients with congenital heart disease, which justifies the possibility of studying all subjects. We worked with a finite population consisting of 90 patients who met the inclusion criteria.

To contrast the working hypothesis, the population was divided into two groups according to the presence or absence of at least one clinical symptoms such as: symptoms of right heart failure, atrial arrhythmias and syncope. Group I (NYHA CLASS I) and Group II (NYHA CLASS II - III or IV).

As a single experienced cardiologist performed echocardiographic examinations of all patients, a third-party blinded study was performed to avoid bias.

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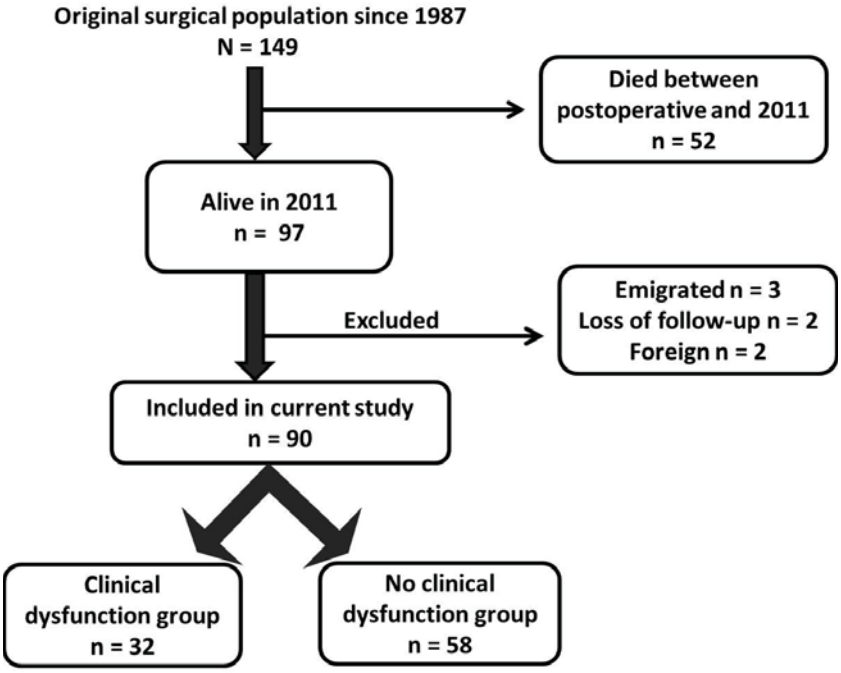

Figure 1: Flowchart of the study population.

Collection of information

Data collected included demographic details such as age, time at operation, clinical characteristics and the results of the transthoracic echocardiograms. The information collected was recorded and organized in the primary data collection model. All stadistical analyses were conducted with MedCalc ® programs in its version 12 and SPSS in its version 15.

Definition of variables

Dependent or response variable: Clinical systemic right ventricle dysfunction.

Independent or explanatory variables: Right ventricular end-diastolic diameter, right ventricular end-systolic diameter, right ventricular wall thickness, Tricuspid Annulus Plane Systolic Excursion (TAPSE), Right Ventricle Ejection Fraction (RVEF), myocardial function index (Tei), the derivative of pressure over time (dP/dT), S wave, Ea wave, Aa wave and Ea/Aa ratio, tricuspid regurgitation.

Control variables: Age and time of operation.

Echocardiography

A detailed two-dimensional transthoracic echocardiogram were performed by a single laboratory, using Aloka α 10 Prosound® and Philips IE33 and stored in DICOM for offline analysis. Echocardiographic systems were equipped with multiple frequency transducers. All measurement were made in a standard parasternal large-axis view and apical four and five – chambers view were used. Cardiac dimensions and function were measured according to the current guidelines [2,12,13].

Right Ventricle Ejection Fraction (RVEF), S of the tricuspid annulus, and Tricuspid Annulus Plane Systolic Excursion (TAPSE), myocardial function index (Tei), derivative of pressure over time (dP/dT) were used to quantify systolic RV function. Ea, Aa waves and Ea/Aa ratio were used to quantify diastolic RV function. Additionally, more objective measures including tricuspid regurgitation was graded as mildly, moderately or severely impaired.

A single experienced cardiologist blind to the clinical data performed echocardiographic measurements. An average of two measurements for each variable was taken for analysis.

Statistical analysis

Normality of continuos variables was assessed using Kolgomorow-Smirnov test. Variables were expressed as mean ± standard deviation for normally distributed data or median and interquartile range for non-normally distributed data. Paired Mann Whitney U test or Student t test were used to analysed differences in continuos variables between independent groups.

The qualitative variable, characterization of tricuspid regurgitation, was summarized according to absolute and relative frequency. Pearson's non parametric Chi Square test was used for this categorical variable. Statistical significance was set at a p value of <0.05.

Bivariate analysis was performed to determine the correlation of each independent variable with the dependent variable (clinical systemic right ventricle dysfunction). With the results of multivariate analysis (logistic regression), we assessed which variables contributed to a significant independent risk of dysfunction ($p<0.05$), while designing a prognostic index, using the estimated coefficients of the regression model. With the results obtained through logistic regression, we aimed

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to identify the structure of the relationships between these variables, with the purpose of finding the mathematical model of better fit that had a predictive purpose, capable of predicting the early evolution of patients, taking into account independent variables included in the study. Once the prognostic index was obtained, it was validated by demonstrating discrimination and calibration in the population studied. Power of discrimination of the prognostic index for the prediction of systemic right ventricular dysfunction was evaluated using the Receiver Operating Characteristic (ROC) curve analysis.

The analysis of the calibration of the prognostic index was verified by goodness-of-fit test of the model to the data through the Chi Square statistic of Hosmer and Lemeshow. Calibration was also evaluated by calculating the standardized ratio of dysfunction.

Clinical relevance

An effectiveness study was carried out which included the analysis of the incidence and prevalence of the event (clinical systemic right ventricular dysfunction), in each echocardiographic measurement. Relative Risk (RR), a limit value of minimum importance (LIM) and prevalence Odds Ratio (OR) were determinated. To validate their results, a level of significance lower than 5% ($p<0.05$) was adopted for the degrees of freedom previously established, similar to the rest of the statistical processing carried out.

Results

A total of 90 patients underwent screening echocardiography during the study period. The population was divided into two groups according to the presence or absence of clinical symptoms. The study group consisting of 58 asymptomatic subjects, representing 64.44% of the total patients (Group I - NYHA CLASS I)) and the reference group consisted of 32 patients with symptoms suggestive of right ventricle dysfunction representing 35.56% (Group II - NYHA CLASS II, III or IV). Baseline characteristic are presented in Tabla 1. Both groups were homogeneous, which allows them to be comparable to obtain the results of the present investigation. It was remarkable to obtain lower measurements of right ventricular diastolic and systolic diameters and parietal thickness of right ventricle in the asymptomatic group of patients with respect to the reference group. For the study of systolic function, five echocardiographic parameters were evaluated, as shown in Tabla 1, and only the Tei index showed no differences between the two groups ($p= 0.089$). The measurement of the systolic excursion of the tricuspid lateral ring showed a notable increase ($p= 0.003$) in the population of patients without clinical dysfunction of the right ventricle in relation to the values obtained from the reference set. Higher S-wave values were evaluated by pulsed wave spectral Doppler applied to the tricuspid annulus, significantly ($p= 0.011$), in the study group compared to the reference. Similarly, the ejection fraction of the right ventricle documented a significant increase in this indicator in the study population (mean 54.70%, SD±7.30), ($p= 0.025$). Such expectations were fulfilled when assessing the derivative of pressure over time (dP/dT); an increase in this indicator was documented in the subjects studied if their figures were compared with those reported in the conglomerate with clinical ventricular dysfunction. The difference between both groups showed considerable value ($p= 0.003$). The interval estimation (95% CI) of the variables with normal distribution did not include the unit. Three echocardiographic measurements were considered for the evaluation of diastolic function in this patients. There were no significant differences between both groups under study; Ea wave ($p= 0.49$), Aa wave ($p= 0.40$) and Ea / Aa ratio ($p= 0.11$) Table 1. The results of the grading of tricuspid regurgitation and clinical systemic right ventricle dysfunction showed a considerable difference ($p= 0.0010$) between the study population and the reference group. Moderate tricuspid regurgitation prevailed (30 patients, 63.8%) and mild stratification (22 patients, 84.6%) in the group without clinical dysfunction of the right ventricle.

Multivariate analysis

From the 14 variables of the univariate analysis, the nine most significant variables were selected to enter the logistic regression model shown in Table 2. Tei index showed no significant association with ventricular dysfunction, although it was considered to maintain this variable as part of the model, due to the clinical importance conferred on the prognosis of patients with congenital heart disease.

Three variables were obtained with no significant results ($p>0.05$). These variables were: right ventricular end-systolic diameter, tricuspid annular plane systolic excursion (TAPSE) and the S wave of the pulsed wave spectral Doppler applied to the tricuspid annulus.

The probability of right ventricular dysfunction in the population investigated is significantly influenced by: right ventricular end-diastolic diameter, right ventricular parietal thickness, Right Ventricular Ejection Fraction (RVEF), Tei index, derivative of pressure over time (dP/dT) and tricuspid regurgitation.

As can be seen, the confidence intervals (95% CI) of right ventricular end-diastolic diameter, right ventricular ejection fraction, Tei index, the derivative of pressure over time (dP/dT) and tricuspid regurgitation do not contain the value one, a sign of the importance they have as prognostic factors.

The parietal thickness of the right ventricle had the greatest effect among all the studied factors and showed the highest OR with 6.523, which represents that it is approximately 6 times greater the possibility of presenting right ventricular dysfunction in patients who have a higher degree of hypertrophy right ventricular, with respect to those that do not.

The coefficients for the six variables chosen in the context of the logistic model constitute the new index and can be used to calculate the risk prediction of clinical dysfunction of the systemic right ventricle in patients with ASO with d-TGA.

The probability of dysfunction is calculated by the following formula [16]:

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Table 1: Assessment of baseline characteristic, structure, function and tricuspid regurgitation of the systemic right ventricle.

Variables		Group I (N = 58)	Group II (N=32)	p	95% CI
Baseline characteristic	Age (years)	16.48±6.27	17.25±6.74	0.59*	(-2.05 a .58)
	Time of operation (years)	14.71±6.0	15.31±6.14	0.66*	(-3.25 a .07)
Structure	Right ventricle end-diastolic diameter (mm)	34(30-37)	36(34-41)	0.009§	
	Right ventricle end-sistolic diameter (mm)	27(24-30)	32(30-34)	0.0001§	
	Right ventricular parietal thickness (mm)	7(6-8)	8(7-9)	0.0001§	
Systolic Function	Tricuspid lateral annular plane systolic excursion (mm)	13.91±3.15	11.75±3.42	0.003*	(-3.58a -.73)
	Right ventricle ejection fraction (%)	54.7±7.3	52.1±8.7	0.025*	(-8.6a -0.5)
	S wave of tissue doppler (cm/s)	10.6(9.1a 12)	9.1(8.0a 10.7)	0.011§	
	Tei index	0.39±0.10	0.36±0.05	0.089*	(-0.00a 0.07)
	Derivative of pressure over time (dP/dT) (mmHg/s)	405.8±170.3	312.4±56.9	0.003*	(-155.2a 31.6)
Diastolic Function	Ea wave (cm/s)	93.3±18.2	95.9±16.5	0.49*	(-5.0a 10.3)
	Aa wave (cm/s	74.9±15.1	71.9±17.6	0.40*	(-10.4a 4.0)
	Ea/Aa	1.2±0.3	1.4±0.4	0.11*	(-0.03a0.31)
				TOTAL	
Tricuspid regurgitation	Severe	6(35.3%)	11(64.7%)	17	TOTAL (N= 90)
	Moderate	30 (63.8%)	17(36.2%)	47	
	mild	22(84.6%)	4(15.4%)	26	

*: Student's t-test, 95% confidence interval. Mean±standard deviation; §: Mann Whitney U test. Median and interquartile range
(Tricuspid regurgitation) $X^2 = 10.78$; p= 0.0010

Table 2: Logistic regression for the design of the prognostic index.

Explanatory variables	Coefficient β	p	OR	95% CI for OR	
				lower	upper
Right ventricle end-diastolic diameter	-0.428	0.036	0.651	0.436	0.972
Right ventricle end-sistolic diameter	0.310	0.122	1.363	0.919	2.022
Right ventricle parietal thickness	1.875	0.002	6.523	1.942	21.904
Tricuspid lateral annular plane systolic excursion	0.949	0.058	2.585	0.965	6.919
Right ventricle ejection fraction	-0.577	0.045	0.561	0.318	0.989
S wave of tissue doppler	-0.144	0.286	0.864	0.664	1.128
Tei index	-54.101	0.00	0.00	0.00	0.00
dP /dT	-0.014	0.044	0.985	0.971	0.999
Tricuspid regurgitation	-4.522	0.002	0.010	0.00	0.191

Dysfunction risk = 1 / ($e^{(-z)}$ + 1)

where z= 38.726-(right ventricle end-diastolic diameter*0.428)+(right ventricle wall thickness*1.875)-(right ventricle ejection fraction*0.577)-(Tei index*54.101)-(the derivative of pressure over time*0.014)-(tricuspid regurgitation *4.522).

e: is the Euler constant (approximately equal to 2.71828).

Discrimination of the prognostic index

As illustrated in Figure 2, the discriminant analysis corresponding to the population studied generated an AUC of 0.96 (95% CI: 0.90-0.99).

Calibration of the prognostic index

Table 3 showed that the instrument was able to accurately predict 96.5% of the patients who did not have right ventricular dysfunction and 90.6% of those who did have ventricular failure, for a general percentage of correct answers of 94. 4%. The test fitness of Hosmer and Lemeshow was applied (Table 4). The analysis of the statistic test in the study population had a p associated with the goodness-of-fit test of 0.096. This result expresses concordance between the clinical dysfunction observed and predicted. Table 5 showed the result of the standardized ratio of right ventricular dysfunction which also assesses the degree of calibration of an index, in such a way that it evaluates the concordance between the observed and expected dysfunction in a global manner. The value equal to one indicates that the estimated index can predict with acceptable accuracy the dysfunction.

Clinical relevance

A previous publication of these authors shows the

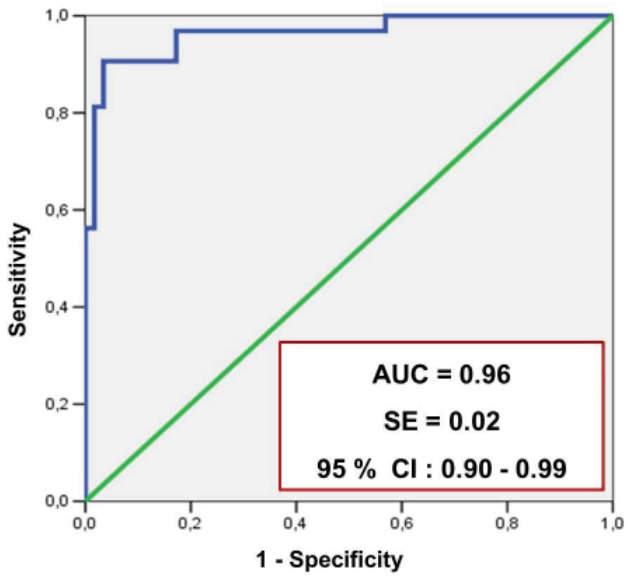

Figure 2: ROC curve for prediction of right ventricle dysfunction with the probability estimated by the logistic regression function in the population studied.

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relationship between echocardiographic parameters and clinical systemic right ventricle dysfunction according to the quantification of risk estimators (incidence) and LIM [17].

Table 6 illustrates the link between echocardiographic parameters and clinical systemic right ventricle dysfunction as an event to be evaluated, according to the indicators of incidence and prevalence analysis and the respective confidence intervals of each echocardiographic modality. The measurements corresponding to the parietal thickness of the right ventricle, the derivative of pressure over time, the right ventricular end-diastolic diameter and the tricuspid regurgitation showed their predominance in decreasing order.

The parietal thickness of the right ventricle, the derivative of pressure over time, the right ventricular end-diastolic diameter and the tricuspid regurgitation presented significance according to the predominant presence of clinical systemic right ventricle dysfunction according to the variations of the intervals of confidence corresponding to each estimated RR. The existence of clinical relevance was verified in the four mentioned measures.

Table 3: Classification table using the population prognostic model.

Leaderboard		Forecasted		Correct Percentage
		No clinical dysfunction	Clinical dysfunction	
Observed	No clinical dysfunction	56	2	96.5
	Clinical dysfunction	3	29	90.6
Overall percentage				94.4

Table 4: Hosmer and Lemeshow test.

Decile of risk of dysfunction	No clinical dysfunction		Clinical dysfunction		Total
	Observed	Predicted	Observed	Predicted	
1	9	9.00	0	0.00	9
2	9	8.99	0	0.00	9
3	8	8.95	1	0.04	9
4	9	8.78	0	0.21	9
5	9	8.19	0	0.80	9
6	7	6.88	2	2.11	9
7	6	4.85	3	4.14	9
8	1	1.99	8	7.00	9
9	0	0.32	9	8.67	9
10	0	0.00	9	8.99	9
Hosmer and Lemeshow test X^2= 14.70, p= 0.09					

Table 5: Observed, predicted right ventricle dysfunction and Standardized Dysfunction Ratio (SDR) and Hosmer and Lemeshow test.

Model	N	Observed Dysfunction	Predicted Dysfunction	SDR	95% CI
Validation	90	32	31.96	1.00	0.68 – 1.41

Discussion

This study analyzes the echocardiographic evaluation of the functionality of the systemic right ventricle after ASO for d-TGA and characterizes potential factors of early right ventricular dysfunction while designing and validating the prognostic echocardiographic index.

Different health centers from all latitudes have published their experiences in the search for factors that may influence long-term results [3,5,6,10,18]. The incidence of right ventricular dysfunction in the systemic position ranges from 10 to 61 % in several series. This wide range can be attributed to the variability of years of evolution after surgery, as well as to the different modalities of images obtained to evaluate right ventricular function according to the technological development of the time. Progressive decline in systemic right ventricle systolic function is confirmed by our study and remains the major concern in Mustard or Senning patients. There is no difference between patients who received the Mustard procedure and those who received the Senning procedures [6,19,20,21]. The two groups of patients studied were homogeneous according to age and time of operation, which makes the comparison between both groups valid. A higher incidence of clinical systemic right ventricle dysfunction was identified in relation to the years elapsed since the surgical intervention.

It was remarkable to obtain lower measurements of the right ventricular diameters, both diastolic and systolic, in the group of patients without SRvF with respect to the reference group, although values compatible with ventricular dilatation are described. In the beginning, the right ventricle hypertrophies well tolerates systemic pressure with normal functioning short and medium term. The SRvF evolves in progressive stages. In the long term there is dilation and gradual deterioration of its function. It is feasible to suppose that, in view of the increase in ventricle dimensions, the myocardium reacts by means of parietal thickening of an appropriate type, thereby maintaining the necessary balance in oxygen consumption [7,11,18,22].

Table 6: Incidence and prevalence analysis.

Variables		Right ventricular clinical dysfunction. Incidence and prevalence analysis			
		RR	Odds no clinical dysfunction	Odds clinical dysfunction	OR
Right ventricle end-diastolic diameter	No.	7.22	0.97	0.72	11.81
	IC 95 %	1.06a 49.25	0.93a 1.00	0.63a 0.82	1.49a 93.86
Right ventricle parietal thickness	No.	14.74	0.97	0.52	28.93
	IC 95 %	2.11a -102.7	0.93a 1.00	0.41a 0.62	3.70a 226
Right ventricle ejection fraction (RVEF)	No.	1.93	0.91	0.79	2.52
	IC 95 %	0.68a 5.53	0.85a 0.97	0.71a 0.88	0.66a 9.71
Tei index	No.	1.28	0.72	0.64	1.45
	IC 95 %	0.68a 2.41	0.63a 0.81	0.54a 0.74	0.57a 3.71
Derivative of pressure over time (dP/dT)	No.	8.30	0.97	0.69	13.95
	IC 95 %	1.21a 56.92	0.93a 1.00	0.59a 0.79	1.76a 110
Tricuspid regurgitation	No.	2.84	0.88	0.62	4.28
	IC 95 %	1.11a 7.30	0.81a 0.94	0.52a 0.72	1.32a 13.84

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The presence of free wall hypertrophy of the right ventricular suggests pressure overload and is considered when its thickness is greater than 5 mm. Less thickening of the anterior wall of the right ventricle was reported in asymptomatic patients, although myocyte hypertrophy is already detected. This situation is evident if takes into account that the right ventricle in a systemic position presents its own adaptation mechanisms and acquires mechanical characteristics similar to those of the left ventricle due to the phenomenon of "left-overs", with the appearance of isovolumetric systolic and diastolic phases and a synchronous contraction pattern in its ejection phase. It is logical to think that according to the right ventricle in the systemic circulatory position adopts the mechanical characteristics and cardiac cycle of the left ventricle, it can assume a similar neurohormonal and geometric ventricular profile [23-26].

Pettersen and colleagues showed that in systemic right ventricle the circumferential shortening of the anterior wall of the right ventricle over longitudinal shortening predominates. This pattern of contraction is similar to that shown by the left ventricle in normal anatomical position and constitutes the adaptive response of the right ventricle to the increase of afterload [27].

The results of the present investigation showed systolic dysfunction from the subclinical stage from the values obtained from systolic excursion of the tricuspid annular plane (TAPSE), S wave, right ventricle ejection fraction (RVEF) and derivative of pressure over time (dP/dT) by two-dimensional echocardiography and pulsed wave spectral Doppler applied to tissues (TDI). The Tei index did not show differences between both groups due to the influence of diastolic function, not early affected in patients with this particular hemodynamic condition.

Several studies agree and consider the TAPSE useful to evaluate the global systolic right ventricular function. Its main limitation is to assume that the displacement of a single segment represents the global function of the right ventricle, so it is not very useful when there are segmental changes in contractility [6,12,28-30].

In a prospective follow-up study, Winter and colleagues reported TAPSE as the only echocardiographic measure that is linked to the clinical condition of patients with ASO for d-TGA [31].

Conversely, De Caro and colleagues found no correlation between TAPSE and end-diastolic and end-systolic volumes by nuclear magnetic resonance and demonstrated that it is not an useful tool to evaluate ventricular function in patients with systemic right ventricle [32].

These controversial valuations on TAPSE justify the lack of significance in the multivariate analysis in the present investigation. Analogously, the S wave did not show significance in the multivariate analysis if we take into account that the measurements were made with the pulsed wave spectral Doppler applied to tissues, which was not very sensitive to load variations and it seems that the studied patients predominated the increase in afterload, a situation that justifies its lack of significance.

Several authors agree that the presence of symptoms is associated with worse degrees of ventricular dysfunction [2,3,6,10,19-21]. Piran and colleagues stated that 82 % of patients who developed right heart failure had RVEF values decreased before the onset of symptoms, suggesting the concept of subclinical ventricular dysfunction in this population of patients [33].

Salehian and colleagues reported a good correlation between the Tei index and RVEF and concluded that Tei index is useful for evaluating the global function of the right ventricle in patients with systemic right ventricle [34].

This situation is corroborated in the study of other authors [3,12,13,31].

The present study showed that diastolic dysfunction is not an early alteration in the follow-up of patients with systemic right ventricle, although the presence of intratrial baffles, rigid and not contractile, generates a certain increase in atrial pressures with inadequate emptying [7,35].

In a prospective study of patients with physiological surgical correction, there was no association between diastolic function of the right ventricle and the presence of clinical symptoms of right ventricular dysfunction. No association was found between diastolic function of right ventricle and left ventricle compared with clinical parameters [31]. These findings confirmed previous published data that describe the absence of a relationship between diastolic function and the clinical conditions of the patients [35]. The right ventricle according to its more complacent nature and its lower anterior wall thickness presents less involvement of its diastolic phase compared with left ventricular hypertrophy [7,22,24,25].

The association between SRvF and tricuspid regurgitation is well established, although it is difficult to determine whether regurgitation is the cause or effect of ventricular dysfunction. In the current investigation, moderate tricuspid regurgitation prevailed in the group without clinical dysfunction of the right ventricle and it can be assumed that valvular regurgitation is initial and secondarily conditions the ventricular failure.

Tricuspid regurgitation increased in line with further deterioration of right ventricle systolic function and dilation of the ventricle. The morphologic right ventricle has not been designed to work as a systemic pumping chamber. It is a one coronary ventricle with only one conduction system radiation and without two well-balanced papillary muscles. The multiple papillary muscles of the tricuspid valve, which partly arise from the septal wall, are pulling the tricuspic valve leaflets apart in the presence of right ventricle dilatation. This applies particularly if the tricuspid orifice becomes circular as it does in the systemic circulation and if the septum is shifted to the left. Concomitant tricuspid regurgitation due to stretching of the originally noncircular tricuspid ring or leaflet coaptation is frequent [5-7,19,20].

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Szymanski and colleagues reported that the presence of characteristic tricuspid regurgitation was a predictor of right ventricular dysfunction and was associated with the time duration of valve exposure to systemic pressures [36]. This situation is consistent with the Roos-Hesselink report and prognosis index [20].

Prognosis index

Discrimination of the prognostic index is evaluated by calculating the Area Under the Curve (AUC), which assesses the ability of the instrument to differentiate between subjects with different results. The ideal test has an area of 1.0, that is, no false positive or false negative. In the validation of the prognostic index, created in this investigation, the area under the ROC curve obtained was considered adequate.

The calibration of the index created in this investigation according to the Ji squared test (X^2) of Hosmer and Lemeshow is considered adequate since it does not differ significantly what was predicted and what was observed in patients with right ventricular dysfunction and those who remain without symptoms.

Another indicator used to assess the degree of calibration of the index is the standardized ratio of dysfunction. The value of this ratio equal to one, as found in this study, indicates that the estimated index has the capacity for the accurate prediction of right ventricular dysfunction in patients operated according to physiological surgical correction.

Clinical relevance

The inclusion of tools from Evidence-Based Medicine in the present investigation led to the study of the functionality of the systemic right ventricle and constituted external validation their results coincide with those obtained from the descriptive or inferential statistics standards. The incidence and prevalence of greater or lesser clinical dysfunction associated with the four echocardiographic quantifications mentioned is significant according to fluctuations in the confidence intervals corresponding to the Relative Risk (RR) or Odds Ratio (OR). In this way, the importance of predicting risk in currently afflicted patients and prospectively in those who will suffer from right and middle-term long-term ventricular dysfunction is highlighted. This gives credit, precision and validity to the criterion proposed that any classic study of effectiveness must be accompanied by its effective counterpart in order to provide the necessary objectivity to the analysis of any event [17,37].

Strengths and limitations

The prognostic index is constructed with proven accuracy. The index was validated and demonstrated clinical utility with the tools of evidence-based medicine, which makes the study notable.

As a limitation in the evaluation of diastolic function, it was not possible to perform a tricuspid flowgram with its corresponding measurements because in the majority of the patients studied, moderate-range tricuspid regurgitation predominated. Right ventricular systolic function was assessed globally without segmental analysis.

Conclusions

In patients with atrial switch operation for transposition of the great arteries, early systolic dysfunction of the systemic right ventricle is observed, dependent on loading conditions due to increased afterload and not due to myocardial disorder. There are no alterations in the early diastolic function. End-diastolic diameter and parietal thickness of the right ventricle, Right Ventricle Ejection Fraction (RVEF), Tei index, derivative of pressure over time (dP/dT) and the tricuspid regurgitation are variables that make up the prognostic index. The results of calibration and validation of the prognostic index show that it is a reliable instrument and can be taken to the care practice to estimate the probability of systemic right ventricle dysfunction. End-diastolic diameter and thickness of the anterior wall of the right ventricle, the derivative of pressure as a function of time (dP/dT) and the tricuspid regurgitation demonstrate clinical relevance.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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