

Echocardiographic predictors of subclinical systemic right ventricular dysfunction

Giselle Serrano Ricardo^a✉, MD, MSc; Adel E. González Morejón^a, MD, MSc; Luis E. Marcano Sanz^b, PhD; Michel Cabrera Ortega^c, MD, MSc; Alfredo M. Naranjo Ugalde^b, MD, MSc; and Jesús F. Carballés García^d, MD, MSc

Department of Echocardiography^a, Cardiovascular Surgery^b, Arrhythmia and Pacemaker^c, and Cardiovascular Rehabilitation, from William Soler Pediatric Cardiology Hospital. Havana, Cuba.

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Acronyms

RV: right ventricle

RVEF: RV ejection fraction

TAPSE: tricuspid annular plane systolic excursion

TGA: transposition of the great arteries

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✉ G Serrano Ricardo.

Cardiocentro Pediátrico William Soler
Ave. 100 y Perla, Altahabana

Boyerros, CP 10800. La Habana, Cuba.

E-mail address:

giselleserrano@infomed.sld.cu

ABSTRACT

Introduction: Transposition of the great arteries with physiological surgical correction predisposes to dysfunction of systemic right ventricle. It is believed that asymptomatic patients have a subclinical dysfunction of this ventricle. Transthoracic echocardiography is sensitive to assess right ventricular function. To date, medical treatment is started when the patient begins with symptoms suggestive of ventricular dysfunction.

Objective: To estimate echocardiographic predictors of subclinical dysfunction of systemic right ventricle.

Method: Observational prospective study from May 2011 to December 2012. The sample (n = 65) was divided into two groups: asymptomatic (n = 33) and symptomatic (n = 32), according to the absence or presence of clinical symptoms suggestive of right ventricular dysfunction..

Results: The two groups were homogeneous in terms of age and surgical time. In both hypertrophy of the right ventricle anterior wall was showed, although lower in the asymptomatic group (p < 0.001). Subclinical systolic dysfunction in the asymptomatic group was evident. There were no differences in diastolic function between the two groups. There were correlations between the tricuspid annular plane systolic excursion and the right ventricular ejection fraction, both in the asymptomatic (r = 0.68, CI 95 % 0.44 to 0.83, p < 0.0001) and symptomatic groups (r = 0.77, CI 95 % 0.59 to 0.88, p < 0.0001). Echocardiographic predictors of subclinical systemic right ventricular dysfunction were identified.

Conclusions: Age, right ventricle anterior wall thickness, surgical time, and diastolic and systolic diameters of the right ventricle are echocardiographic predictors of subclinical systemic right ventricular dysfunction, useful for the timely initiation of medical treatment.

Key words: Transposition of the great arteries, Ventricular performance, Systemic right ventricle, Echocardiography

Predictores ecocardiográficos de disfunción subclínica de ventrículo derecho sistémico

RESUMEN

Introducción: La transposición de grandes arterias con corrección quirúrgica fisiológica predispone a la disfunción del ventrículo derecho sistémico. Se considera que los pacientes asintomáticos tienen una disfunción subclínica de este ventrículo. La ecocardiografía transtorácica se muestra sensible para evaluar la función ventricular derecha. Hasta la fecha, el tratamiento médico se inicia cuando el paciente comienza con síntomas sugestivos de disfunción ventricular.

Objetivo: Estimar predictores ecocardiográficos de disfunción subclínica de ventrículo derecho sistémico.

Método: Estudio observacional y prospectivo desde mayo 2011 hasta diciembre 2012. La muestra (n=65) se dividió en dos grupos: asintomáticos (n=33) y sintomáticos (n=32), según la ausencia o presencia de síntomas sugestivos de disfunción clínica del ventrículo derecho.

Resultados: Los dos grupos resultaron homogéneos en relación con la edad y el tiempo de operación. En ambos se mostró hipertrofia de la pared anterior del ventrículo derecho, aunque menor en el grupo asintomático ($p < 0.001$). Se evidenció disfunción sistólica subclínica en el grupo asintomático. No existieron diferencias en la función diastólica entre ambos grupos. Existieron correlaciones entre la recorrida sistólica del anillo lateral tricuspídeo y la fracción de eyección del ventrículo derecho, tanto en el grupo asintomático ($r=0,68$; IC 95 % 0,44 a 0,83; $p < 0.0001$) como en el sintomático ($r=0,77$; IC 95 % 0,59 a 0,88; $p < 0.0001$). Se identificaron predictores ecocardiográficos de disfunción subclínica de ventrículo derecho sistémico.

Conclusiones: La edad, el grosor de la pared anterior del ventrículo derecho, el tiempo de operación, y los diámetros diastólico y sistólico del ventrículo derecho constituyen predictores ecocardiográficos de disfunción subclínica de ventrículo derecho sistémico, útiles para el inicio oportuno del tratamiento médico.

Palabras clave: Transposición de grandes arterias, Función ventricular, Ventrículo derecho sistémico, Ecocardiografía

INTRODUCTION

The transposition of the great arteries (TGA) is the cyanotic congenital heart disease with atrioventricular concordance and ventricular-arterial discordance, most frequent in the neonatal period¹. One of the surgical options is the physiological correction, according to the techniques of Mustard² or Senning³, which is an atrial surgery to redirect venous flows coming from the cava veins into the left ventricle from where the pulmonary artery emerges, while the return from the pulmonary veins reaches the right ventricle (RV) which connects to the aorta, so that the RV holds the systemic circulation. This situation is called systemic RV.

Surgery corrects hemodynamics, but in the long term, predisposes to developing arrhythmias, obstruction of atrial tunnels, tricuspid valve regurgitation and systemic RV dysfunction⁴⁻⁷. Although currently this surgical technique is not the first choice, there are a significant number of surgical patients who have symptoms and others who start to present them.

Often the ventricular deterioration progresses, in an unnoticed manner, before having clinical expression. It is believed that asymptomatic patients have subclinical systemic right ventricular dysfunction. Although there are limitations due to the complex geometry of the RV and its retrosternal position, transthoracic echocardiography is sensitive to assess right ventricular function in these patients⁸⁻¹⁰. To date, medical treatment is started when the patient begins with symptoms suggestive of ventricular dysfunction. There are probably subclinical echocardiographic predictors of systemic RV dysfunction, useful for the timely initiation of medical treatment.

METHOD

Patients

An observational, prospective study was conducted from May 2011 to December 2012. 65 patients with TGA and physiological surgical correction were studied. They were members of the National Pediatric Cardiovascular Rehabilitation Program, to whom a

transthoracic echocardiographic study was performed in an annual postoperative monitoring, at the Echocardiography Department of William Soler Pediatric Cardiology Hospital. All participants in the research were asked to sign their informed consent. The sample was divided into two groups: asymptomatic (n = 33) and symptomatic (n = 32), according to the absence or presence of clinical symptoms suggestive of RV dysfunction.

Echocardiogram

Each patient underwent a transthoracic echocardiogram by an experienced specialist (Level III of the American Society of Echocardiography), with α -10 Aloka or Aloka 5500 equipment, 2.5 and 5.0 Mhz transducers, and built-in software to perform spectral tissue Doppler.

With the patient in supine or left lateral position, with slow breathing and in a suitable environment, conventional views (parasternal, longitudinal and transverse axes), apical of long-axis (four, two and five cameras) and traditional subcostal and with inverted sector (coronal and sagittal axes, and oblique lines) were performed.

Variables

The following quantitative variables were studied: age, surgical time, diameters (right atrial, diastolic RV, systolic RV), thickness of the RV anterior wall, RV ejection fraction (RVEF), tricuspid annular plane systolic excursion (TAPSE), S-wave of tissue Doppler, Ea and Aa waves and the Ea/Aa ratio (early diastolic and late diastolic waves ratio).

Statistical processing

According to the Kolmogorov-Smirnov test, the variables that showed a normal distribution were summarized as mean and standard deviation, while those with non-parametric distributions were expressed as median and interquartile range. For comparison of means, calculated in both study groups, the parametric Student t test was used for quantitative variables with normal distributions and when distributions did not meet this condition; the nonparametric Mann-Whitney test was used substituting the means by the medians. A confidence interval of 95 %

was always taken. Two models of simple linear correlation were constructed, where the Pearson correlation coefficient (r) was identified as an expression of the strength of association between two quantitative variables: RVEF and TAPSE in both study groups. To estimate the echocardiographic predictors of right ventricular subclinical dysfunction a logistic regression was performed, where the Odds Ratio (OR) and the Wald statistic for each variable were identified. To validate the results in terms of significance a confidence level of 95 % was used, and all values of $p \leq 0.05$ for the statistic associated with the test were considered significant. MedCalc statistical software version 12 was used.

RESULTS

Both study groups were homogeneous in terms of age and surgical time (**Table 1**). The mean age was 14.5 in the asymptomatic group and 17.2 in the symptomatic, while the surgical time showed means of 13.5 and 14.7 years in each group, respectively.

Ventricular diameters and systemic RV anterior wall thickness are shown in **Table 2**. Dilation of the right cavities was evidenced: right atrium diameters ($p < 0.001$), diastolic RV ($p < 0.001$) and systolic RV ($p <$

Table 1. Age and surgical time (years).

Variables	Asymptomatic (n=33)	Symptomatic (n=32)	p
Age [±]	14,5 ± 6,0	17,2 ± 6,7	0.09 * (-0,4 a 5,8)
Surgical time [±]	13,5 ± 5,9	14,7 ± 6,0	0.42 * (-1,7 a 4,1)

[±] Mean ± standard deviation

*Student's t test, 95 % confidence interval.

0.001) in the symptomatic group (n = 32), whereas in the asymptomatic group (n = 33) there was no significant dilation of such cavities. In both groups, hypertrophy of RV anterior wall was demonstrated, although it was significantly lower in the asymptomatic group ($p < 0.001$).

Table 3 shows the echocardiographic variables to assess systolic function. The symptomatic group had significantly lower mean values of RVEF (52.1 ± 8.7 %, $P = 0.025$) of TAPSE (11.7 ± 3.4 mm, $p = 0.004$) and S-wave tissue Doppler 9.1 [(8.0 to 10.7 cm/s) ($p =$

Table 2. Ventricular diameters and systemic RV anterior wall thickness (mm).

Variables	Asymptomatic (n=33)	Symptomatic (n=32)	p
RA Diameter [□]	25,6 ± 5,3	32,3 ± 5,3	< 0.001* (4,0 - 9,3)
RVDDiameter [□]	31,9 ± 5,3	38,4 ± 7,5	< 0.001* (3,2 - 9,7) [§]
RVS Diameter ^{□□□}	25 (22 - 28)	32 (30 - 34)	< 0.001 [§]
RV anterior wall thickness ^{□□□}	6 (5,7 - 7,0)	8 (7 - 9)	< 0.001 [§]

□ Mean ± standard deviation

□□ Median and interquartile range

* Student's t test, 95 % confidence interval

§ Mann Whitney U test

RA: right atrium. RVD: right ventricular diastole. RVS: right ventricular systole.

Table 3. Systolic function.

Systolic function	Asymptomatic (n = 33)	Symptomatic (n = 32)	p
RVEF (%) [□]	54,7 ± 7,3	52,1 ± 8,7	0.025* (-8,6 a -0,5)
TAPSE (mm) [□]	14,0 ± 3,0	11,7 ± 3,4	0.004* (-3,9 a -0,7) [§]
S wave (cm/s) ^{□□□}	10,6 (9,1 - 12,1)	9,1 (8,0 - 10,7)	0.011 [§]

□ Mean ± standard deviation

□□ Median and interquartile range

* Student's t test, 95 % confidence interval

§ Mann Whitney U test

Table 4. Diastolic function.

Diastolic function	Asymptomatic (n = 33)	Symptomatic (n = 32)	p
Ea wave (cm/s) [□]	97,9 ± 21,4	95,9 ± 16,5	0.67* (-11,5 a 7,5)
Aa wave (cm/s) [□]	75,5 ± 15,4	71,9 ± 17,6	0.43* (-11,4 a 5,0) [§]
Ea/Aa ^{□□□}	1,5 (0,8 - 1,5)	1,5 (0,9 - 1,6)	0.34 [§]

□ Mean ± standard deviation

□□ Median and interquartile range

* Student's t test, 95 % confidence interval

§ Mann Whitney U test

0.011)]. Although the asymptomatic group showed higher mean values, these are parameters of subclinical systemic RV dysfunction.

Both groups had similar echocardiographic values of diastolic function (**Table 4**), with no significant difference among each of them: wave Ea [(p = 0.67) (-11.5 to 7.5)], Aa wave [(p = 0.43) (-11.4 to 5.0)] and Ea/Aa ratio (p = 0.34).

Figure 1 shows the simple linear correlation between TAPSE and RVEF in the symptomatic group with a correlation coefficient r = 0.77, 95% CI of 0.59 to 0.88 and p < 0.0001, while in the asymptomatic group (**figure 2**) the correlation coefficient was r = 0.68, 95% CI of 0.44 to 0.83 and p < 0.0001. This situation demonstrates the strength of association between both variables as evaluators of systolic function in the two study groups.

Table 5 presents logistic regression to demonstrate the association of subclinical systemic RV dysfunction regarding probable echocardiographic predictors of dysfunction, where the following variables were identified as significant: age (OR : 53.97 , 95% CI 3.6 to 802.4, p = 0.003) , RV anterior wall thickness (OR: 4.76 , 95% CI 1.2 to 17.5, p = 0.019), surgical time (OR: 0.011, 95% CI 0,0006 to 0.2, p = 0.003), RV diastolic diameter (OR : 0.536, 95% CI 0.3 to 0.8, p = 0.016) and RV systolic diameter (OR: 2.968, 95 % 1 4 to 6.2, p = 0.003).

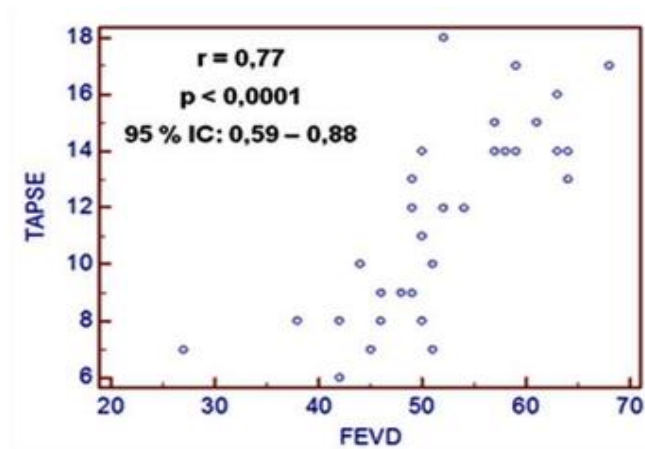
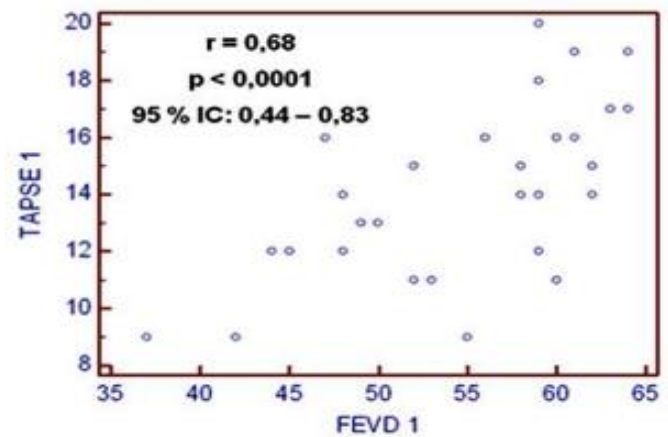
DISCUSSION

Patients with TGA and physiological surgical correction keep the morphologically right ventricle in systemic position, a situation that causes its long-term dysfunction. The incidence with which ventricular failure develops during follow-up is not known with certainty. Roos-Hesselink¹¹ presented figures of 61 % at 25 years, whereas Moons¹² showed lower figures (ventricular dysfunction in 30 % of patients), with up to 85 % survival at 32 years. Ebenroth¹³, in a long term follow up of 45 patients reported that 13% of them died between the second and third decades of

Table 5. Logistic Regression.

Variables	OR	95 % CI	Wald	p
Age	53,97	3,6 a 802,4	3,988	0.003
RV anterior wall thickness	4,76	1,2 a 17,5	1,560	0.019
Surgical time	0,011	0,0006 a 0,2	-4,443	0.003
RVD	0,536	0,3 a 0,8	-0,622	0.016
RVS	2,968	1,4 a 6,2	1,088	0.003

RVD: right ventricular diastole. RVS: right ventricular systole.

**Figure 1.** Simple linear correlation, according to RVEF and TAPSE in symptomatic patients.**Figure 2.** Simple linear correlation, according to RVEF and TAPSE in asymptomatic patients.

life. The literature only records one 49 year-old patient treated with physiological surgical correction in the neonatal period, with favorable evolution¹⁴.

The cause of postoperative right ventricular dysfunction is multifactorial. Several factors are set forth: a) RV lack of capacity to accommodate to the pump function of systemic circulation, b) coronary circulation maintained by a right coronary artery that has to supply all the blood flow to the systemic ventricle c) myocardial damage produced by maintained severe hypoxia before surgery d) perioperative damage caused by insufficient myocardial protection¹⁵.

It is known that dysfunction symptoms begin the older the patients and the longer the surgical time^{6,7}. Asymptomatic systemic ventricular dysfunction persists for long periods of time before symptoms appear. Some patients have systemic ventricular dysfunction with a decreased ejection fraction or even dilated cardiac cavities in the absence of symptoms¹⁶.

In systemic position, the RV modifies the archi-

ture of its muscle fibers resembling the interspersed pattern observed in normal left ventricle with an oblique orientation of surface fibers, longitudinal in the endocardium and circumferential in the myocardium. The shortening of the free wall is predominantly circumferential rather than longitudinal^{17,18}. The RV anterior wall usually has a thickness of 3-5 mm, but under pressure overload such thickness can be greater, which sets the ventricular hypertrophy, but it is unknown whether it helps normalize wall tension or leads to contractile dysfunction. Hypertrophy in the systemic RV even in the subclinical stage is demonstrated. These changes allow the RV to adapt, to a great extent and for several decades, to the systemic position and function^{17,19}.

Right ventricular function is a difficult variable to quantify due to the complex geometry of the RV; that is why the two-dimensional transthoracic echocardiography is considered an accurate, accessible and relatively inexpensive method in clinical practice⁷.

The determination of the RVEF is an important tool, although it is difficult to define normal ejection fraction in a systemic ventricle as it depends on the method of determination. Some authors consider that the estimated fraction over 55 % can be considered normal (in the absence of significant tricuspid regurgitation). As qualitative estimation, the two-dimensional method has great value and is correlated with the ejection fraction estimated by cardiac catheterization²⁰. Lower values of RVEF were demonstrated in the asymptomatic group. According to the means of values obtained in TAPSE and S-wave tissue Doppler, a decrease was shown in the group without symptoms, which is consistent with the reports of other authors^{16,21,22}.

Few studies have demonstrated the prognostic significance of diastolic dysfunction, since its study is complex because of its close dependence on preload and filling ratios, which accounts for the lack of differences between the two study groups^{21,23}.

According to the results, a group of prospective echocardiographic predictors in the occurrence of subclinical systemic RV dysfunction was identified. Timely intervention in this asymptomatic stage is crucial to change the prognosis in terms of improving symptoms of heart failure, reduce hospitalization, reduce mortality and improve quality of life. It is important to regularly monitor patients because when the predictive values of subclinical dysfunction are known, therapeutic strategies to preserve ventricular function can be designed.

CONCLUSIONS

Age, RV anterior wall thickness, diameters of right heart chambers and surgical time are echocardiographic predictors of subclinical systemic right ventricular dysfunction.

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