

Does the right ventricle size influence the left ventricle size and function in children with Ebstein anomaly?

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Abstract

Purpose: Patients with Ebstein anomaly (EA) have a variety of clinical manifestation. The assessment of structural and geometric characteristics of the heart is important for optimal management.

Methods: We retrospectively analyzed echocardiography database from 2009 to 2020. We evaluate patients in two groups: patients with EA were in Group 1 and children without cardiovascular pathology were in Group 2. All children in both groups underwent echocardiography according to American Society of Echocardiography recommendations. The shape of the heart chambers and their function were studied in both groups.

Results: There were 153 in Group 1 and 2000 children without cardiovascular disease in Group 2. It was shown that in children with EA, the shape of the ventricle became less spherical, which was accompanied by a decrease in myocardial mass, and the ejection fraction was reduced 34% of patients. The functional volume (non-atrialized part) of the right ventricle in patients with EA was reduced, and its contractility was preserved in 62% of cases. Preservation of the contractile properties of the right ventricle in most cases was associated with higher systolic pressure in its cavity.

Conclusion: TAPSE, TESV, and the velocity of the annulus fibrous ring movement according to tissue dopplerography in patients with EA do not allow us to assess the contractility of the right ventricle. The myocardial performance index (MPI) characterizes a decrease in the functional volume of the right ventricle.

KEYWORDS

Ebstein anomaly, tricuspid valve

1 | INTRODUCTION

Ebstein anomaly (EA) is a right ventricular (RV) myopathy with a structural tricuspid valve (TV) pathology variable morphology, this usually leads to severe tricuspid regurgitation (TR). EA has a variety of clinical manifestations from a highly symptomatic newborn to an asymptomatic adult.¹

The hallmark of the EA is “arrested development” of leaflet delimitation from endocardial cushion. Thus, the anterior leaflet is incompletely

delaminated and not apically displaced. The septal leaflet also has apical-anterior displacement and rotation into the right ventricle out-flow tract. And the inferior leaflet is usually most rudimentary and sometime nearly absent.²

The assessment of structural and geometric properties of the heart is important for optimal management, and impact the results of surgical reconstruction of the TV.^{3,4}

The aim of our study is assessment of structural and geometric characteristics of heart function in patients with EA.

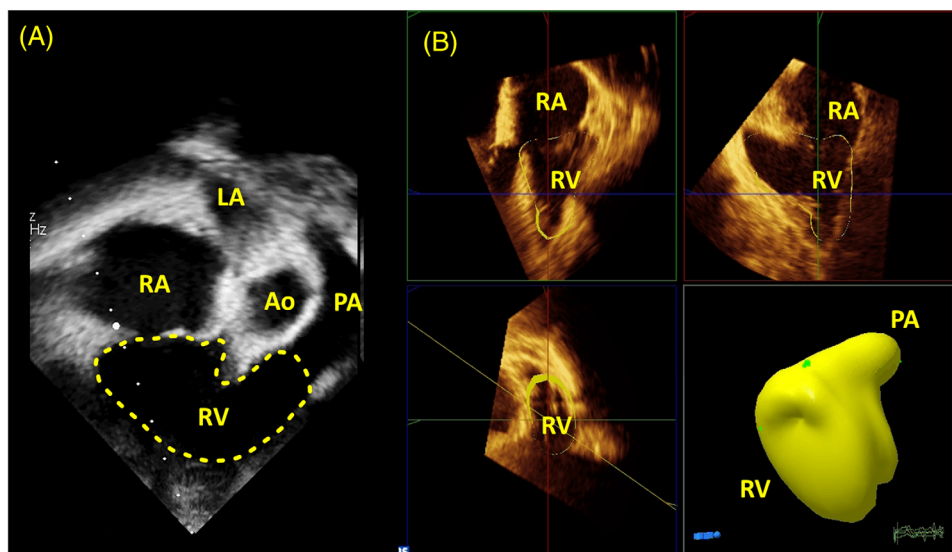


FIGURE 1 (A) Transthoracic echocardiography showing a non-atrialized part of the right ventricle (dash line). (B) Three-dimensional echocardiographic reconstruction of the right ventricle. Ao, aorta; LA, left atrium; PA, pulmonary artery; RA, right atrium; RV, right ventricle.

2 | METHODS

We retrospectively analyzed the echocardiography database of Cardiology Research Medical Center, Tomsk, Russia from 2009 to 2020 and created two groups. Patients with EA were in Group 1. Group 2 consisted of 2000 children without cardiovascular disease.

The inclusion criteria for Group 1 were an atrialization of the RV and the displacement the coaptation point of the TV leaflets to the apex of the RV more than 8 mm/m².⁴ All patients in Group 1 had TR of 2°–3° and 67% of patients had an atrial septal defect (ASD) or patent foramen ovale (PFO).

Written informed consent was obtained from all patients' parents, and the study was approved by the institutional clinical research and ethics committee (IRB – №139, November 18, 2015).

All children in both groups underwent echocardiography according to American Society of Echocardiography recommendations.⁵

1. The *displacement index* as described by Seward et al.⁶ to the coaptation point of the TV leaflets to the top was measured in millimeters per square meter of the body surface was used as one verification criterion.⁷
2. The *volume of the heart chambers, including the atria*, was determined using standard algorithms of two-dimensional echocardiography.⁸ The volume of the RV was measured using three-dimensional echocardiography.⁹ We estimated the “functional” (non-atrialized) part of the RV (Figure 1).
3. The *atrial index* was defined as the ratio of the volume of the right atrium (RA) to the volume of the left atrium (LA).
4. The *left atrial shape index (LASI)* was calculated using the formula

$$LASI = (W1 + W2)/2 \cdot H \cdot 100.$$
 W1 = anteroposterior size measured in parasternal short axis, W2 = width measured in apical

4-chamber projection, and H = height of the LA measured from the posterior LA wall to the mitral annulus in the apical 4-chamber view.

5. The *force of the LA contraction* was calculated using the Simone method.¹⁰
6. The *sphericity index of the left ventricle (LV)* was defined as the ratio of the length of the ventricle in the diastole in the four-chamber position to diameter in the parasternal position.¹¹
7. *LV eccentricity* was estimated as the ratio of the end diastolic LV size to the antero-posterior LV size along the short axis.¹²
8. The *myocardial performance index (MPI)* was determined for both the left and right ventricles using tissue Doppler imaging.^{13–16}
9. *VTI* (the integral of blood flow in the RV outflow tract) was used as a surrogate indicator of the pumping function of the RV.¹⁷

All measurements were performed using Philips iE-33 and IE-33 X-matrix ultrasound systems with sector and matrix probes (frequencies 1–5 and 3–8 MHz).

2.1 | Statistical analysis

All analyses were performed using Statistica base, version 10 (StatSoft, Inc., Tulsa, USA). Continuous variables are expressed as mean or median with interquartile range depending on their normality. Kolmogorov–Smirnov test was used to determine if the variable had a normal distribution. Continuous variables were analyzed using Student's *t*-test or Mann–Whitney *U* test as applicable. The correlation was carried out using the Pearson correlation coefficient. All *p*-values < .05 were considered to be statistically significant.

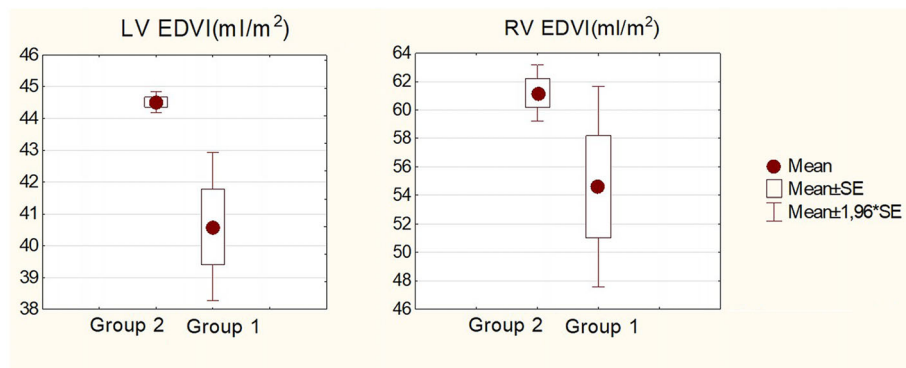


FIGURE 2 Indexed end-diastolic volumes of the left (A) and right (B) ventricles in patients with EA and in the control group. Group 1: patients with Ebstein anomaly; Group 2: control group. LV EDVI, end-diastolic volume index of the left ventricle; RV EDVI, end-diastolic volume index of the right ventricle.

3 | RESULTS

3.1 | Patients population

A total of 153 patients with EA between the ages of 1 and 17 years (median = 5.0 range, 2.03–9.0 years) underwent transthoracic echocardiography in the study period. There were 57 (37%) males and 96 (63%) females. Median body weight was 19.5 kg (range, 3.0–85.0). 55% (85) patients had grades 2 and 45% (68) patients had grades 3 according to the Celermajer index.^{18,19} Sixty-seven percent of patients had ASD or PFO with left-right, mixed or right-left shunt. 19.5% of patients had SpO₂ below 96%. There were 61 (40%) patients in this group had documented WPW.

The Group 2 consisted of 2000 children without cardiovascular diseases, aged from 1 to 18 years, with median age 5 years (range, 2.1–10.0), and median body weight 19.2 kg (range, 7.9–90.0).

3.2 | Chamber volumes

The most important and easily determined indicator of preload is the end-diastolic volume of the LV, which in patients with EA was significantly lower than in the control group. The end-diastolic volume of the right ventricle (without atrialized part of the RV) in patients was also lower (Figure 2).

3.3 | Left atrium

The volume of the LA did not differ between groups, but changes in LA shape were revealed. The LA was increased in vertical size and decreased in transverse size in Group 1.

3.4 | Left ventricle

The LV also had a more elongated shape in Group 1, as evidenced by an increase in the LV sphericity index (Table 1). The change in the shape of

TABLE 1 Echocardiographic parameters of children with EA and persons in the control group ($M \pm \Delta$)

Variables	Group 1 (n = 152)	Group 2 (n = 2000)	p-value
LA volume (ml/m ²)	19.9 ± 6.3	19.0 ± 5.2	.33
RA volume (ml/m ²)	90.5 ± 15.5	19.9 ± 5.3	.0001
Atrial index	4.4 ± 2.2	1.1 ± .2	.0001
LASI	1.6 ± .1	1.2 ± .09	.03
LA force (Kdin)	8.9 ± 5.1	6.9 ± 4.1	.04
LV sphericity index	2.1 ± .3	1.6 ± .1	.001
LV eccentricity	.9 ± .02	1.0 ± .01	.03
MPIlv (Tei)	.7 ± .02	.3 ± .01	.0001
MPIlv (Tei)	.6 ± .1	.3 ± .08	.001
IVS (mm)	6.3 ± 1.3	7.2 ± 1.0	.001
PW (mm)	5.9 ± 1.3	6.2 ± 1.6	.05
LVmi (g/m ²)	54.7 ± 13.0	66.9 ± 12.1	.001
LVef (%)	69 ± 7	70 ± 5	.21
RVef (%)	52 ± 10	59 ± 10	.06
RVSP (mmHg)	29.2 ± 8.2	22.2 ± 2.7	.002
CI (L/min/m ²)	2.6 ± .6	2.9 ± .5	.03
TAPSE (mm)	23.5 ± 7.2	22.0 ± 3.0	.06
TASV (mm/s)	9.3 ± 3.3	8.8 ± 2.0	.11

CI, cardiac index; EA, Ebstein anomaly; IVS, interventricular septum; LA, left atrium; LASI, left atrial shape index; LV, left ventricle; LVef, the left ventricular ejection fraction; LVmi, the left ventricle mass index; MPI, myocardial performance index; PW, posterior wall of the left ventricle; RA, right atrium; RV, right ventricle; RVef, the right ventricular ejection fraction; RVSP, systolic pressure in the right ventricle; TAPSE, tricuspid annular plane systolic excursion; TASV, tricuspid annular systolic velocity.

the LV was associated with an increase in the RA due to the atrialization of the RV (Figure 3).

LV contractility in Group 1 did not differ from Group 2 (Table 1), but the pumping function was moderately depressed. The cardiac index (CI) in Group 1 was statistically significantly lower than in the Group 2

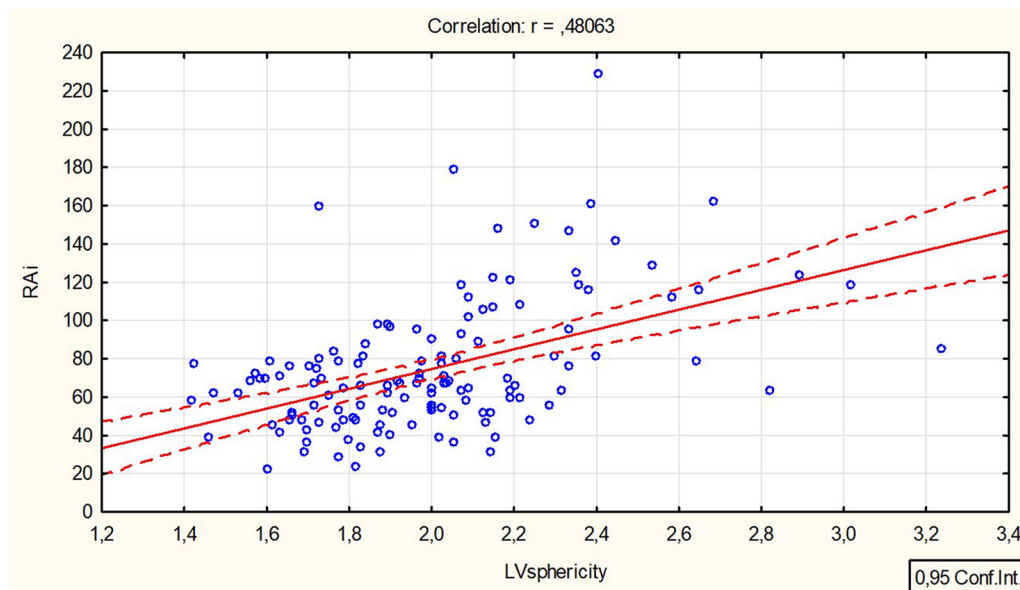


FIGURE 3 Indexed volume of the right atrium and sphericity of the left ventricle.

(Table 1) with an equal heart rate in both groups (96.6 ± 23 in Group 2 and 97.4 ± 23 in Group 1). It was found that the change in the LV shape was not associated with LV contractility ($R = .07$) and had a moderate but significant correlation with the degree of dystopia of the coaptation point of the TV.

The severity of changes in the shape of the LV had an inverse statistically significant correlation with CI, $r = -.43$, $p = .002$. The left ventricular mass index (LVmi) in Group 1 was significantly lower than in the Group 2 (Table 1) and had a statistically significant inverse correlation with the spherication index ($r = -.53$, $p = .001$). In other words, the less spherical the LV, the smaller the myocardial mass. In addition, an inverse statistically significant negative correlation was found between the dystopia of the TV flaps and the LVmi ($r = -.45$; $p = .0001$). There was a positive correlation between the displacement of the TV flaps and the index of sphericity of the LV (Figure 4).

3.5 | Right ventricle

The right ventricular ejection fraction (RVEf) in Group 1 was moderately, but not significantly lower than in Group 2 (Table 1). When evaluating the distribution of RVEf in the Group 1, it turned out that only 38% of patients with EA had an ejection fraction lower than the values of the Group 2 (55%). RV systolic pressure in Group 1 was higher than in the Group 2.

3.6 | Tricuspid valve

It should be noted that the amplitude of the systolic displacement of the fibrous ring (TAPSE) and the speed of its movement (TASV) in patients with EA did not reflect the contractility of the RV.

Correlation coefficients: RVEf TAPSE = .08, TASV = $-.1$. The correlation coefficient between RVEf and the TASV according to tissue Doppler (S wave) amounted to $-.2$. $p = .33$. However, the TASV (M-mode) had a statistically significant positive correlation with the volume index of RA ($r = .39$, $p = .01$).

There was a negative statistically significant correlation between the surrogate index of RV stroke volume (VTI) and the degree of TV dystopia, $r = -.51$, $p = .001$. The RV end diastolic volume index had an average statistically significant negative correlation with the TV dystopia, $r = -.55$, $p = .001$. There was not significant correlation between the degree of TV dystopia and LVEf ($r = -.02$).

4 | DISCUSSION

4.1 | Ventricles contractility and volume

Atrialization of the RV in patients with EA was the cause of serious changes in the shape and function of the right and left chambers of the heart. Previously, it was reported that three-dimensional magnetic resonance imaging did not find changes in LV volume, but its contractility was reduced in adult patients with EA.²⁰ In the children we examined, on the contrary, LV contractility was normal, but LV volume was reduced. In adult patients, the RV is enlarged and its contractility decreases,²¹ while in the children's EA group analyzed, the RV volume was reduced, and its contractility remained normal (Table 1).

The shape of the LV in the examined patients was more elongated (ellipsoid), which nevertheless did not affect its contractility (Table 1). An increase in eccentricity and a change in the sphericity of the LV were previously detected in adults.

Reduction of left ventricular contractility, found in 34% of patients, was not associated with changes in the shape of the LV. Changes in the

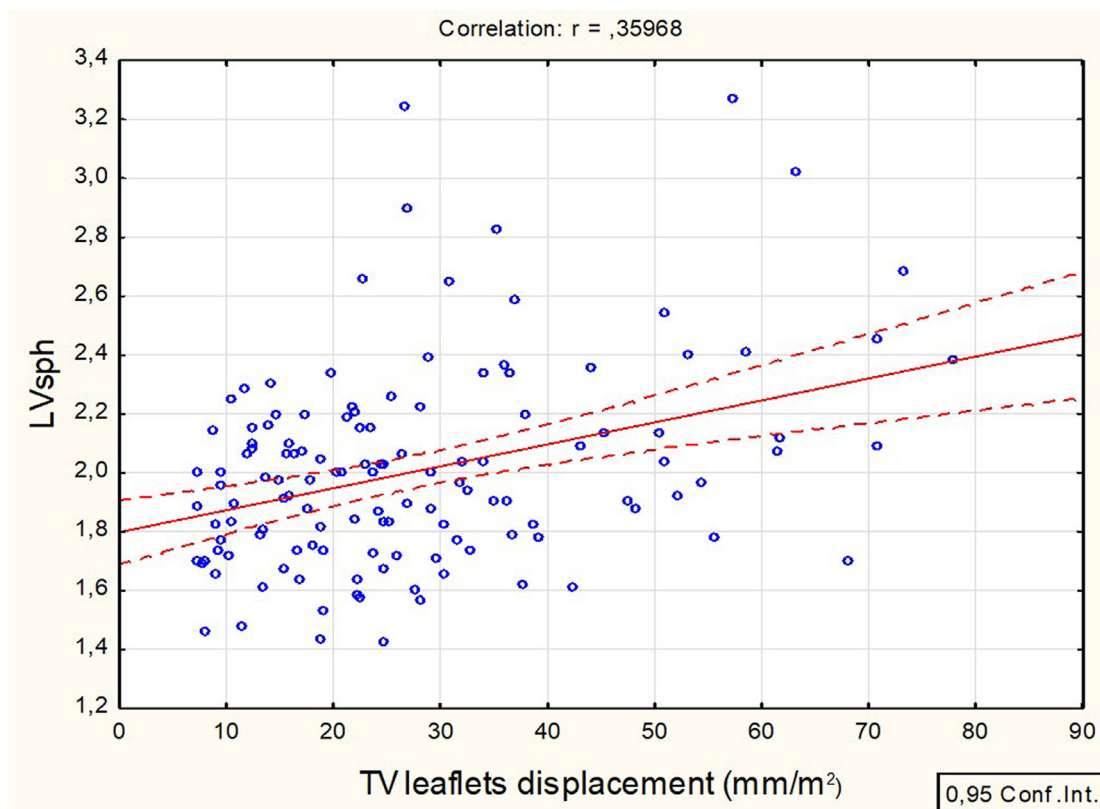


FIGURE 4 Correlation of dystopia of the TV leaflets and LV spherification. LV, left ventricle; TV, tricuspid valve.

geometry of the LV were accompanied by a decrease in its pumping function, as evidenced by a decrease in the CI compared to the control group and a significant correlation between the increase in ellipsoid and a decrease in CI. Changes in the shape of the LV were associated with the severity of TV pathology.²²

4.2 | Left ventricle contractility and tricuspid valve

In our study, a significant direct correlation was also determined between dystopia of the TV and a decrease in the sphericity of the LV (Figure 3). Based on this, the detection of LV dysfunction in adults and the data obtained, we could assume that a decrease in the LV contractility develops with age. Our study included children with EA aged one to 18 years, and we were unable to find any correlation between LV dysfunction and age.

In patients with EA, we found statistically significant differences in the LASI, which was “flattened” in the antero-posterior direction and stretched vertically (Table 1). There was exactly the same tendency to change the shape as the left ventricular deformity, the correlation of the LASI and the sphericity index was positive ($r = .48$, $p = .001$). The change in the shape of the LA was accompanied by an increase in the force of its contraction (Table 1), which was higher than in the control group. The LASI did not correlate with the strength of its contraction ($r = -.14$, $p = .2$), but there was a weak but reliable negative correlation of the LASI with the degree of increase in the RA volume ($r = -.33$,

$p = .001$). Thus, in patients with EA, a change in the LA shape and an increase in its mechanical activity were accompanied with change of the LV shape.

4.3 | Right ventricle volume

The volume of the RV cavity in the EA patients was reduced which was due to its atrialization. However, most well-known publications report an increase in the volume of the RV in patients with EA.^{21,23,24} In the presented cases, we are talking about adult patients with congestive RV failure, in our case – children. The volume of the right ventricle was defined as the functional, active part, without an atrialized component. TR, while maintaining the Starling mechanism of the RV, did not prevent the maintenance of the necessary volume of blood flow to the lungs for circulation. The severity of dystopia of the valve flaps, as well as the reduction of the functional volume of the RV, had an inverse correlation with the pumping function of the ventricle, but had no connection with its contractility.

4.4 | Right ventricle systolic pressure

In most patients with EA, there is an increase in pressure in the right chambers of the heart. As a rule, the systolic pressure in the right ventricle (RVSP) does not exceed 30–35 mmHg with a simultaneous

increase in pressure in the RA.²⁵ In our study, 41 patients (27%) had RVSP above 30 mmHg. Higher RVSP was associated with a more preserved functional RV. The volume of the RV, ejection fraction, and ejection integral (VTI) had a positive reliable correlation with RVSP (from .36 to .50).

It can be assumed that the integral of blood flow in the RV outflow tract will be a very useful indicator for evaluating the pumping function of the RV in patients with EA compared to the more labor-intensive and inaccurate determination of the volume and contractility conventional 2D echo methods. It should be noted that such indicators as TAPSE and TASV did not show their informative value in patients with EA. None of these indicators correlated with contractility and RV ejection, in addition, these indicators did not differ from the values in the control group (Table 1). The velocity of movement of the fibrous ring estimated using M-mode echocardiography had a positive correlation with an increase in the volume of the RA, which in principle can be used for rapid quantitative assessment of RV atrialization and preservation of the Starling mechanism.²⁶

4.5 | The myocardial performance index

The MPI in patients with EA was significantly higher than in healthy patients. The indicator did not correlate with RV contractility, but rather reflected a decrease in the functional volume of the right ventricle. That is, the higher the MPI index, the lower end diastolic index of the right ventricle ($r = -.45, p = .002$).

5 | CONCLUSION

1. In children with EA, the shape of the left heart chambers is changed, which is accompanied by a decrease in myocardial mass, a 34% decrease in LV contractility and depression of pumping function.
2. The preservation of the contractile properties of the RV was found in 62% of cases and was associated with higher systolic pressure in its cavity.
3. Echocardiographic parameters such as TAPSE, TESV, and the velocity of the annulus fibrous ring movement according to tissue dopplerography in patients with EA do not allow us to assess the contractility of the right ventricle.
4. The MPI does not reflect the state of contractility and pumping function of the right ventricle in patients with EA, but rather it characterizes a decrease in the functional volume of the right ventricle.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests.

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