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Evaluation of the Adequacy of Blood Mixing by Echocardiographic Parameters in Neonates with the Transposition of Great Arteries

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What is known on this subject?

Transposition of the great arteries is hemodynamically one of the most significant congenital heart diseases. Echocardiography is the most important non-invasive diagnostic tool to evaluate the transposition of great arteries.

What this study adds?

Balloon atrial septostomy requirements of patients with transposition of large arteries can be predicted by evaluating new echocardiographic parameters.

ABSTRACT

Objective: Transposition of the great arteries (TGA) is one of the major causes of cyanotic heart disease in neonates and should be treated surgically in the early stages of life. In these patients, adequate blood mixing between systemic and pulmonary blood flow is required until surgery, and interatrial communication plays a major role during this period. This study aimed to evaluate the echocardiographic factors used to predict adequate interatrial communication with echocardiographic data.

Material and Methods: This study included newborn patients (who were) followed up in the pediatric cardiac intensive care unit with the diagnosis of simple TGA between August 1, 2020, and February 1, 2021. Patients were classified into those who underwent balloon atrial septostomy (BAS) (group I) and those who did not undergo BAS (group II). The atrial septal defect (ASD) size, interatrial septum (IAS) length, peak/mean interatrial pressure gradient, transverse diameter of the left atrium (LA), transverse diameter of the right atrium (RA), and the following ratios; ASD/IAS, LA/RA, mitral/tricuspid valve annulus, peak gradient of ASD/ASD diameter and ASD diameter/(LA: RA ratio) were calculated echocardiographically. The results were evaluated statistically.

Results: Eighteen patients were included (6 patients in group I and 12 patients in group II) during the study period. The median age was 3 days (interquartile range 2 days-7 days). 50% of the cases were male, and 50% were female. ASD peak gradient, ASD mean gradient, ASD peak gradient/ASD diameter, and LA: RA ratios were significantly higher, and ASD size, ASD diameter/(LA: RA ratio) were significantly lower in the group I compared in group II ($p<0.05$). ASD diameter/(LA: RA ratio) was found to independently predict the need for BAS with a cut-off value of 2.7 by multivariate analysis.

Conclusion: The echocardiographic measurement of ASD diameter/(LA: RA ratio) in TGA patients may be helpful in the prediction of BAS requirement.

Keywords: Newborn, transposition of great arteries, echocardiography, balloon atrial septostomy

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Introduction

Transposition of the great arteries (TGA) is one of the most common cyanotic congenital heart diseases in newborns. Today, the treatment of choice is an arterial switch operation in the newborn period (1).

There is a parallel circulation in fetal life, and the transition to a serial circulation occurs after birth. In cases with a diagnosis of TGA, this transition may have adverse effects on the baby. If mixing at the atrial, ventricular, or ductal levels is inadequate, hypoxia and metabolic acidosis that will occur until the operation is performed will lead to the death of these babies (2,3).

Prostaglandin E1 (PGE1) is widely used in many centers to increase this mandatory mixing. However, this treatment may not be enough for a sufficient increase in cerebral oxygen saturation values, especially in patients with restrictive interatrial communication.

Balloon atrial septostomy (BAS) is one of the preferred methods for reducing hypoxemia and mortality. However, some studies have reported that the procedure increases the risk of stroke (3).

In patients with TGA, inadequate mixing should be evaluated with various clinical and laboratory methods until the arterial switch operation. A profound cyanosis is a sign of poor mixing. Therefore, blood oxygen saturation is a helpful parameter for showing the septostomy requirement in these patients (3,4,5,6).

Echocardiography is a widely available, simple, affordable, non-invasive diagnostic tool for managing congenital heart diseases. It provides data about blood mixing in different levels of the heart and vessels, especially in patients with TGA. Interatrial communication plays a key role in this regard (6,7).

This study evaluates the factors that predict adequate interatrial communication by using echocardiographic data.

Material and Methods

This study was conducted retrospectively on newborns diagnosed with simple TGA and hospitalized in our hospital's pediatric cardiac intensive care unit between August 1, 2020, and January 31, 2021. Premature, patients older than one month old, and patients with complex TGA (presence of hemodynamically significant ventricular septal defect, pulmonary stenosis, aortic arch hypoplasia, or aortic coarctation) were excluded from the study. The study was conducted in accordance with the Declaration of Helsinki and was approved by the University of Health Sciences Turkey, Basaksehir Cam and Sakura City Hospital Local Ethics Committee (2022.04.143).

The patients were grouped into two categories: Those who underwent BAS (group I) and those who did not (group II). Each group was evaluated regarding demographic characteristics, oxygen saturation, blood lactate levels and echocardiographic measurements.

Echocardiographic evaluations were performed using the Philips Affiniti 50 cardiac ultrasound system (Philips Affiniti 50 Cardiac Ultrasound, Bothell, WA, USA) with a 9-MHz probe. In patients who required BAS, the last echocardiographic acquisition just before the BAS was reviewed.

A standard pediatric transthoracic echocardiographic imaging study with a segmental approach was conducted, including parasternal, apical, subcostal and suprasternal windows. Atrial situs, systemic and pulmonary venous returns, atrioventricular concordance, ventricles, ventriculoarterial concordance, the spatial position of great arteries, septal defects and extracardiac vascular anomalies were reviewed, respectively. Following echocardiographic parameters were measured for study: Atrial septal defect (ASD), interatrial septal (IAS) length, peak/mean interatrial pressure gradient, transverse diameter of the left atrium (LA) and right atrium (RA), diameter of mitral and tricuspid annulus, ductus arteriosus (DA). All measurements were performed in subcostal bicaval view for ASD and IAS, apical four chamber view for LA, RA, mitral and tricuspid annulus, and suprasternal view for DA. Additionally, ASD/IAS, LA/RA, mitral/tricuspid annulus ratios, the ASD peak gradient/ASD diameter and ASD diameter/(LA: RA ratio) were calculated (Figure 1a, b).

Statistical Analysis

The distribution of variables was analyzed in a computer environment. Descriptive values were obtained using the SPSS (Statistical Package for the Social Sciences for Windows) software package and expressed as median [interquartile range (IQR)] and percentage-percentile values. Pearson's chi-squared and Mann-Whitney U tests were used to compare the variables between groups. Multivariate analysis was carried out using logistic regressions. The BAS requirement is used as the dependent variable. The covariates were the mean interatrial pressure gradient, ASD diameter/(LA: RA ratio) and ASD peak gradient/ASD diameter. Receiver-operating characteristic curves were constructed, and areas under the curve were calculated. Sensitivities and specificities were determined to identify patients requiring BAS. A p value of <0.05 was considered statistically significant.

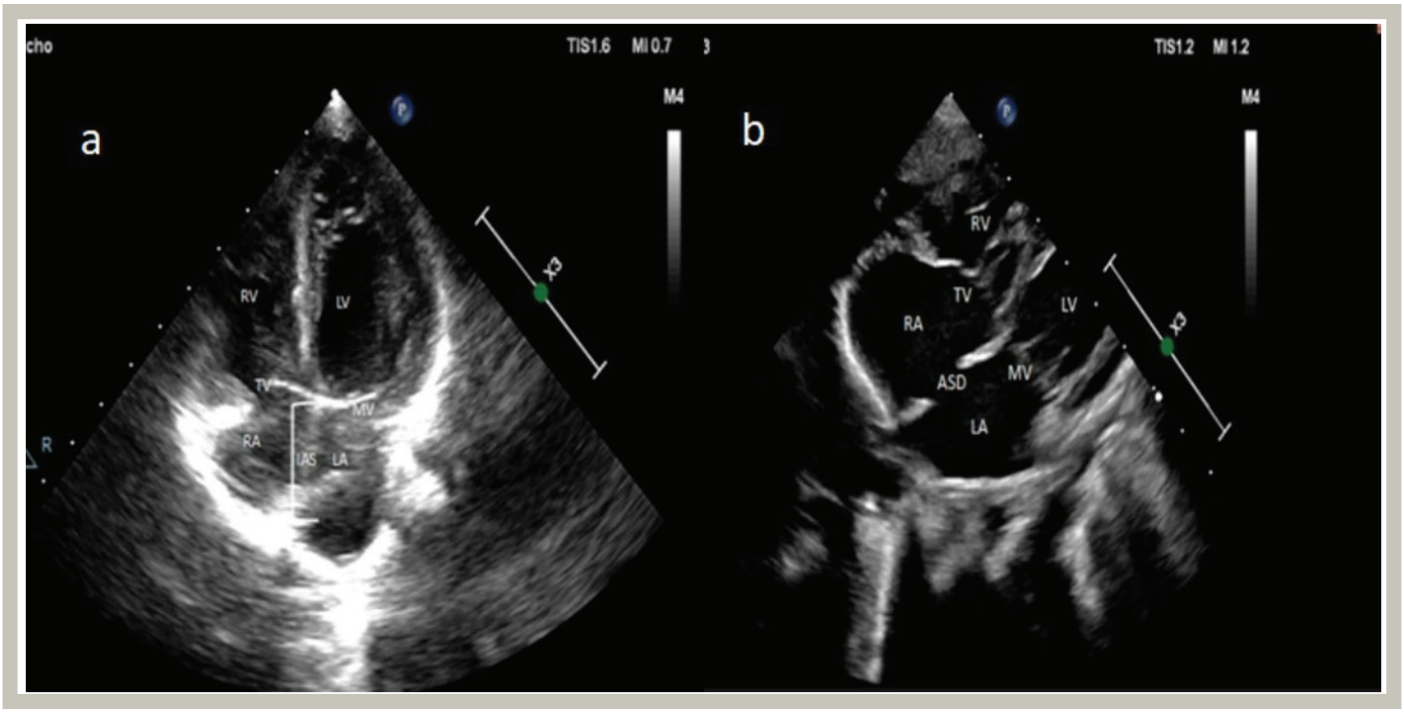

Figure 1a, b). Ten days old male patient with transposition of the great arteries. a) Modified four chamber view on echocardiographic examination, b) modified subcostal chamber view on echocardiographic examination

ASD: Atrial septal defect, IAS: Interatrial septum, LA: Left atrium, LV: Left ventricle, MV: Mitral valve, RA: Right atrium, RV: Right ventricle, TV: Tricuspid valve

Table 1. Demographic features of the patients

	Group I (BAS +) n=6	Group II (BAS -) n=12	p
Gestational week (week)	39 (38-40)	39 (38-40)	NS
Gender (male)	3 (50)	6 (50)	NS
Weight (kg)	3.2 (2.9-3.3)	3.1 (3-3.2)	NS
Prenatal diagnosis (yes)	1 (16)	3 (25)	NS
Saturation (%)	65 (60-72)	81 (78-85)	0.001
Lactate (mmol/liter)	5 (4.5-7)	1.6 (1.2-3)	0.001
Echocardiography time (hours)	8 (6-10)	30 (24-36)	0.030

n (%) or median (IQR). BAS: Balloon atrial septostomy, IQR: Interquartile range, NS: Not significant

Results

There were eighteen patients, six of whom were in group I (underwent BAS) and twelve in group II (without BAS). Fifty percent of the cases were male, and the median weight was 3 kg (IQR 2.8-3.4 kg).

Patients' characteristics are summarized in Table 1. In group I, the oxygen saturation at the time of echocardiography was significantly lower, and the peak blood lactate level was considerably higher than that in group II ($p<0.05$).

Echocardiographic measurements according to group are summarized in Table 2. ASD peak gradient, ASD mean gradient, ASD peak gradient/ASD diameter, and LA: RA ratio were significantly higher, and ASD size, ASD diameter/(LA: RA) ratio was significantly lower in the group I compared to group II ($p<0.05$).

A multivariate logistic regression test was performed on the parameters, which were found to be significant after univariate analysis. The ASD diameter/(LA: RA ratio) result could predict the need for BAS (Odds ratio: 6.1, confidence interval: 2-14.5, $p=0.02$).

In the receiver operating characteristic curve analysis, the ASD diameter/(LA: RA ratio) predicted the need for BAS with a cut-off value of 2.7 (Figure 2).

Table 2. Evaluation of the echocardiographic parameters

	Group I (BAS +) n=6	Group II (BAS -) n =12	p
ASD diameter (mm)	3.0 (2.5-3.5)	5 (4.5-6)	**0.001**
Interatrial septum length (mm)	18 (16-20)	17 (14-19)	NS
ASD diameter/IAS length	0.2 (0.1-0.3)	0.40 (0.3-0.45)	NS
ASD peak gradient (mmHg)	12 (10-14)	4 (2-6)	**0.020**
ASD peak gradient/ASD diameter	3.5 (3-4)	1.3 (1-1.5)	**0.010**
ASD mean gradient (mmHg)	5 (4-6)	2 (1-3)	**0.006**
Presence of IAS aneurysm	2 (34)	5 (40)	NS
LA transverse diameter (mm)	16 (15-17)	15 (14-16)	NS
RA transverse diameter (mm)	14 (13-15)	15 (14-17)	NS
LA/RA ratio	1.1 (0.9-1.2)	1.0 (0.8-1.1)	**0.012**
ASD diameter/LA: RA ratio	2.7 (2.5-3)	6 (5-7)	**0.001**
MV annulus (mm)	10 (9-11)	10 (9-11)	NS
TV annulus (mm)	11 (10-12)	12 (11-14)	NS
MV/TV annulus	0.8 (0.6-1)	0.9 (0.8-1.1)	NS

n (%) or median (IQR). ASD: Atrial septal defect, IAS: Interatrial septum, LA: Left atrium, MV: Mitral valve, NS: Not significant, RA: Right atrium, TV: Tricuspid valve

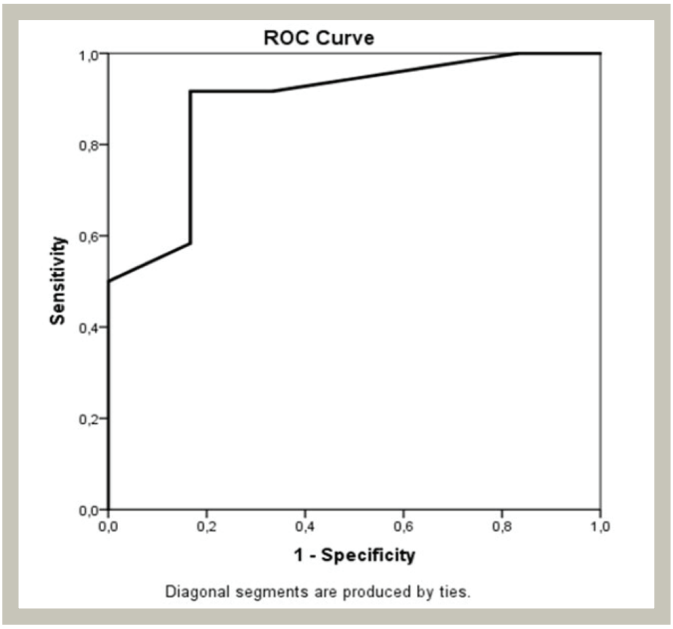

Figure 2. ROC analysis of ASD diameter/(LA: RA), showing an AUC of 0.85 (95% CI 80-92%; p=0.003), with a sensitivity of 92% and a specificity of 88%

ROC: Receiver operating characteristic curve, ASD: Atrial septal defect, LA: Left atrium, RA: Right atrium, AUC: Area under the ROC curve, CI: Confidence interval

Discussion

In this study, we attempted to determine the echocardiographic parameters that predict BAS requirements in newborn patients diagnosed with TGA. In those requiring BAS, peak and mean gradient through ASD, ASD peak gradient/ASD diameter ratio, and LA to RA ratios were significantly higher. In contrast, ASD size and ASD diameter/(LA: RA) ratios were significantly lower. An ASD diameter/(LA: RA) ratio of 2.7 was the optimal cut-off point for predicting the need for septostomy. Our study is one of the limited studies conducted in the literature with these features.

TGA is hemodynamically one of the most significant congenital heart diseases. Both patients with antenatal diagnosis and postnatally diagnosed newborns should be followed up in the intensive care unit to monitor postnatal changes due to the transition from parallel to serial circulation. It is necessary to protect the babies against the adverse effects of hypoxemia until the surgery. PGE1 and/or BAS may be required for this purpose. The most critical passage in considering the blood mixing is through interatrial communication (5,6,7,8). In our study, 22% (n=4) of all patients had antenatal diagnoses, and 33% (n=6) required BAS.

Echocardiography plays an essential role in the management of critical congenital heart diseases. It is a radiation-free, reproducible, repeatable, and reliable diagnostic tool. Algorithms derived from echocardiographic measurements can be used in the management of congenital heart disease. For example, in cases of pulmonary atresia with an intact ventricular septum or borderline left ventricular patients, treatment decisions are usually based on echocardiographic Z score measurements (9,10).

Echocardiographic evaluation of the interatrial septum is crucial in newborns with critical congenital heart disease, such as hypoplastic left heart syndrome, total anomalous pulmonary venous return and TGA. Especially in patients with TGA, adequate interatrial communication provides a much better blood mixing than interventricular or ductal mixing. Restrictive atrial septal communication may quickly impair patients' hemodynamic status and lead to mortality. There is no consensus in the literature regarding which echocardiographic parameter best predicts restrictive interatrial communication. Some authors proposed that the mean gradient through ASD above 8 mmHg is restrictive, between 3 and 8 mmHg acceptable and below 3 mmHg is non-restrictive (11). Also, the largest ASD diameter smaller than 4 mm and peak velocity through ASD above 2 m/sec was considered restriction criteria in some studies (12). Others have suggested that clinical findings are more important than echocardiographic measurements in restriction decisions.

Muntean et al. (13) proposed a new echocardiographic parameter for estimating the need for BAS in the TGA. In their thirty-seven case series (21 patients with BAS), the LA/RA ratio, ASD diameter/(LA: RA ratio) and ASD peak gradient/ASD diameter was significantly elevated in those needing septostomy, whereas PDA size was not significant. The most important predictor of septostomy was ASD diameter/(LA: RA ratio) (cut-off 2.58).

In our study, the patients' clinical condition was the most important parameter for predicting septostomy. Our results are consistent with that of Muntean et al. (13). We found that the PDA diameter was not a significant factor and that ASD diameter/(LA: RA ratio) (cut-off 2.7) was the most important parameter.

Study Limitations

This study was conducted in a single center with a limited number of patients and was retrospective. Another limitation is that the echocardiographic measurements were performed retrospectively through the PACS system.

Conclusion

As a result, the BAS requirement of patients with TGA can be predicted by evaluating echocardiographic parameters such as ASD diameter/(LA: RA). However, multicenter studies involving more patients are required to confirm our findings.

Ethics

Ethics Committee Approval: The study was conducted in accordance with the Declaration of Helsinki and was approved by the University of Health Sciences Turkey, Basaksehir Cam and Sakura City Hospital Local Ethics Committee (2022.04.143).

Informed Consent: Informed consent was obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: İ.C.T., Concept: E.Ö., Design: E.Ö., Data Collection or Processing: E.Ö., Analysis or Interpretation: E.Ö., İ.C.T., Literature Search: İ.C.T., Writing: E.Ö., İ.C.T.

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