Fetal Predictors of Urgent Balloon Atrial Septostomy in Neonates with Complete Transposition

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Background: In complete transposition of the great vessels, a restrictive patent foramen ovale leads to inadequate circulatory mixing and severe cyanosis. Urgent balloon atrial septostomy (BAS) improves mixing and bridges neonates to surgery. Several studies have determined risk factors in utero for poor postnatal outcomes in complete transposition of the great vessels, particularly a restrictive patent foramen ovale and ductus arteriosus. In addition to these risk factors, we studied two new features, a hypermobile septum and reverse diastolic patent ductus arteriosus shunt, to determine which patients will require an urgent BAS.

Methods: We reviewed all 26 fetuses from 2001 to 2010 with complete transposition of the great vessels and closely examined the patent foramen ovale and septum primum for hypermobility, restriction, flat appearance, or redundancy. We defined hypermobility as a septum primum flap that oscillates between both atria. We also examined the ductus size and shunting pattern to evaluate whether these features contributed to urgent BAS.

Results: In total, 14 of 26 fetuses required urgent BAS with improved cyanosis. Nine fetuses had an urgent BAS and a hypermobile septum, and 12 fetuses had no urgent BAS or hypermobile septum. Eight fetuses had an urgent BAS and a reverse diastolic patent ductus arteriosus, and 11 fetuses had no urgent BAS or reverse diastolic patent ductus arteriosus. A hypermobile septum and reverse diastolic patent ductus arteriosus had a significant association with urgent BAS ($P < .01$, sensitivity = 0.64 and 0.57, specificity = 1.0 and 0.92, positive predictive value = 1.0 and 0.89, negative predictive value = 0.71 and 0.65). No fetus had a restrictive patent foramen ovale/ductus arteriosus.

Conclusion: A hypermobile septum and reverse diastolic patent ductus arteriosus are new prenatal findings to help predict the need for an urgent BAS postnatally in patients with complete transposition of the great vessels. (J Am Soc Echocardiogr 2011;24:425-30.)

Keywords: Echocardiography, Fetus, Transposition of great vessels

In neonates with complete transposition of the great arteries, a balloon atrial septostomy (BAS) is the accepted standard for improving cyanosis by allowing atrial level shunting.[1] Given that this population of patients can have significant hypoxemia after birth, multiple studies have stressed the importance of prenatal diagnosis to improve neonatal outcomes.[2-6] Only a few studies have looked at fetal predictors of inadequate circulatory mixing in patients with complete transposition.[7-9] A technique that can reliably identify the need for an urgent BAS would be valuable. Maeno *et al.*[7] demonstrated that a restrictive ductus and foramen ovale in a fetus with complete transposition may predict early postnatal mortality. The objective of our series is to examine these previously noted predictors and introduce two new findings, a hypermobile atrial septum, where the septum primum oscillates between the left and the right atrium, described by Allan *et al.*[10] (Figure 1), and a ductus left-right diastolic shunt.

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Conflicts of Interest: None.

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MATERIALS AND METHODS

Demographic Data Collection

We collected all fetal and neonatal patients with complete transposition from our reference database using the *syngo* Dynamics workstation (Siemens Medical Solutions USA, Inc., Ann Arbor, MI). We reviewed all data from January 1, 2001, to June 30, 2010. All newborns with a prenatal diagnosis of complete transposition of the great vessels and postnatal confirmatory echocardiograms were included in the study. Patients with a ventricular septal defect, double outlet right ventricle, or coarctation of the aorta were excluded from the study. Demographic data included gestational age at the time of fetal evaluation and date of birth. Neonatal records were examined for urgent need of BAS within a few hours of birth and decreased or increased oxygen saturation. At our institution, BAS is performed if a neonate has severe hypoxemia caused by inadequate circulatory mixing. Typically, our patients are intubated, mechanically ventilated, and placed on prostaglandin therapy before BAS. For the purpose of

Abbreviations

BAS = Balloon atrial septostomy

NPV = Negative predictive value

PPV = Positive predictive value

this study, neonates who required an urgent BAS were defined as having evidence of significant hypoxemia and a restrictive interatrial communication despite these interventions. The need for an urgent BAS was confirmed by reviewing the oxygen saturation data and carefully examining the interatrial septum for restriction on the initial postnatal study. Therefore, the urgent BAS subgroup in our series had *both* of the following: (1) oxygen saturation in the right upper arm ≤60% despite prostaglandin therapy and (2) an inadequate interatrial communication for circulatory mixing.

A lack of improvement would suggest pulmonary hypertension or an inadequate rupture of the septum primum. Any complications after a BAS were also recorded. Additional data gathered included initial arterial blood, need for intubation, timing of intubation, time of birth, method of delivery, and time of BAS if performed. This study was approved through our institution's review board (Protocol 17194), and all data were made anonymous in accordance with the Health Insurance Portability and Accountability Act.

Echocardiographic Data Collection

Ultrasound equipment included the Siemens Acuson Machine C512, rev 12.0 (Siemens Medical Solutions USA, Inc., Mountain View, CA) and the Philips IE33 (Philips Medical Systems, Bothell, WA). The diagnosis of complete transposition was verified in both the fetal and multiple postnatal studies. Fetal echocardiograms were closely examined by the authors at the atrial and ductal levels. The atrial septum was appropriately profiled with the plane of the atrial septum oriented perpendicular to the ultrasound beam and examined for particular characteristics.

Atrial Septum In Utero

1. Hypermobile atrial septum: The septum primum oscillates between the left and the right atrium (Figure 1).[10] Video 1 (view video clip online) is also available for the image in Figure 1.
2. Redundant atrial septum: The septum primum herniates more than 50% beyond the plane of the septum secundum across the length of the left atrium, as described by Wilson *et al.*[11] (Figure 2).
3. Restrictive atrial septum: A small orifice with color flow aliasing across the atrial septum is noted.[12]
4. Fixed atrial septum: The angle between the septum primum and secundum is less than 30 degrees.[11]
5. Flat atrial septum: No mobility of the atrial septum is noted.[11]

Ductus Arteriosus In Utero

The size of the ductus was measured against reference standards for gestational age, and a *z*-score was determined (Table 1).[7,13,14] Color and spectral Doppler evaluation of the ductus was conducted to determine restriction or diastolic reversal of flow (Figure 3). The first author carefully examined all prenatal and postnatal studies, and all prenatal assessments were made while blinded to the postnatal outcomes. In a subset of study patients, the ductal shunt direction and atrial septum were independently assessed by the senior author, who was also blinded to postnatal outcomes.

Postnatal Echocardiogram

As described, the urgent BAS subgroup in our series had severe cyanosis and an inadequate atrial communication, which is defined as follows:

1. A septum primum flap that abuts the septum secundum resulting in pressure restrictive flow with a mean gradient >2 mm Hg.
2. No flow noted across the atrial septum.

For all neonates in the study, the atrial septum was assessed from the subcostal coronal plane and a mean gradient was established from this view. In addition, the ductal size and direction of shunt were determined for all patients from the suprasternal notch views.

Statistics

Because these predictive variables are nominal with a relatively small sample size, the Fisher's exact test was implemented to determine statistical associations with an urgent BAS. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) analyses were performed for each of the predictors. A Student *t* test was used to compare the fetal ductus arteriosus *z*-score and the mean foramen ovale pressure gradient on postnatal studies between patients who did and did not require an urgent BAS. A *P* value of less than .05 was considered statistically significant. All statistical calculations were performed using SAS Enterprise Guide version 4.2 (SAS Institute Inc., Cary, NC).

RESULTS

Among the 153 patients with complete transposition of the great vessels at our institution from January 1, 2001, to June 30, 2010, 26 (17%) were included in our study with both prenatal and postnatal studies for evaluation (Table 1). Given that our institution is a referral center, not all patients with complete transposition had available fetal studies for evaluation; none of the study patients delivered at the referring hospital. One patient had a persistent left superior vena cava noted prenatally and confirmed postnatally. The only discrepancy between prenatal and postnatal studies was two patients who had a circumflex coronary artery off of the right coronary system. Some 9 of the 26 patients had 2 or more fetal studies, whereas the remaining patients had only 1 fetal study; the findings on each study of the 9 patients were consistent. Nine patients had a hypermobile atrial septum, and 11 patients had a redundant atrial septum. Three patients had a septum that was both hypermobile and redundant. Ten patients had a normal appearance of the atrial septum with the primum flap confined to the left atrium. None of our patients in this series had a restrictive, flat, or fixed atrial septum on fetal echocardiogram. In all of the fetal studies, the atrial septum was adequately profiled to allow for accurate characterization.

All fetuses had a normal-sized ductus arteriosus based on reference standards for gestational age, but none had evidence of ductal restriction.[7,13,14] Nine patients had diastolic flow reversal in the ductus arteriosus by color or spectral Doppler. Given that spectral Doppler was not always available, it is unclear if the flow reversal was holodiastolic or not.

Fourteen patients required an urgent BAS within a few hours after birth in our series secondary to significant hypoxemia ≤60% and a restrictive interatrial communication, as defined in the "Materials and Methods" section (Table 1). All patients were receiving prostaglandin therapy before this intervention. The recorded oxygen saturation was