

# Can fetal echocardiograms reliably predict the need for urgent balloon atrial septostomy in transposition of the great arteries?

Stockley, Elizabeth L; Singh, Anju; Desai, Tarak; Ewer, Andrew

DOI:

[10.1136/archdischild-2019-317867](https://doi.org/10.1136/archdischild-2019-317867)

License:

Creative Commons: Attribution-NonCommercial (CC BY-NC)

*Document Version*

Peer reviewed version

*Citation for published version (Harvard):*

Stockley, EL, Singh, A, Desai, T & Ewer, A 2019, 'Can fetal echocardiograms reliably predict the need for urgent balloon atrial septostomy in transposition of the great arteries?', *Archives of Disease in Childhood*, vol. 104, no. 11, pp. 1114-1116. <https://doi.org/10.1136/archdischild-2019-317867>

[Link to publication on Research at Birmingham portal](#)

## **Publisher Rights Statement:**

This article has been accepted for publication in Archives of Disease in Childhood, 2019 following peer review, and the Version of Record can be accessed online at <http://dx.doi.org/10.1136/archdischild-2019-317867>.

© Authors (or their employer(s)) 2019 Reuse of this manuscript version (excluding any databases, tables, diagrams, photographs and other images or illustrative material included where a another copyright owner is identified) is permitted strictly pursuant to the terms of the Creative Commons Attribution-Non Commercial 4.0 International (CC-BY-NC 4.0) <http://creativecommons.org>

## **General rights**

Unless a licence is specified above, all rights (including copyright and moral rights) in this document are retained by the authors and/or the copyright holders. The express permission of the copyright holder must be obtained for any use of this material other than for purposes permitted by law.

- Users may freely distribute the URL that is used to identify this publication.
- Users may download and/or print one copy of the publication from the University of Birmingham research portal for the purpose of private study or non-commercial research.
- User may use extracts from the document in line with the concept of 'fair dealing' under the Copyright, Designs and Patents Act 1988 (?)
- Users may not further distribute the material nor use it for the purposes of commercial gain.

Where a licence is displayed above, please note the terms and conditions of the licence govern your use of this document.

When citing, please reference the published version.

## **Take down policy**

While the University of Birmingham exercises care and attention in making items available there are rare occasions when an item has been uploaded in error or has been deemed to be commercially or otherwise sensitive.

If you believe that this is the case for this document, please contact [UBIRA@lists.bham.ac.uk](mailto:UBIRA@lists.bham.ac.uk) providing details and we will remove access to the work immediately and investigate.

Archimedes: Can fetal echocardiograms reliably predict the need for urgent Balloon Atrial Septostomy in Transposition of the Great Arteries?

Corresponding Author:

Dr Elizabeth L Stockley, Neonatal Unit, Birmingham Women's and Children's NHS Foundation Trust, Edgbaston, Birmingham, B15 2TG

Phone: 01213358198

Fax: 01216272749

Co-Authors:

Dr Anju Singh, Neonatal Unit, Birmingham Women's and Children's NHS Foundation Trust, Edgbaston, Birmingham, B15 2TG

Dr Tarak Desai, Department of Cardiology, Birmingham Women's and Children's NHS Foundation Trust, Steelhouse Lane, Birmingham

Professor Andrew K Ewer, Institute of Metabolism and Systems Research, University of Birmingham, Birmingham UK and Birmingham Women's and Children's NHS Foundation Trust, Edgbaston, Birmingham, B15 2TG

Key Words: Transposition of Great Arteries, Balloon Atrial Septostomy

Word Count: 824

## **Clinical scenario**

A term neonate is admitted to the neonatal unit with an antenatal diagnosis of transposition of the great arteries with intact ventricular septum (TGA/IVS) and a 6mm patent foramen ovale, identified by fetal echocardiogram at 34 weeks gestational age. The pre and post-ductal oxygen saturations (SpO<sub>2</sub>) are 45% and 55% in 100% oxygen. Prostaglandin therapy is commenced at 5 ng/kg/min. In view of unresponsive hypoxaemia, the baby is intubated, mechanically ventilated, and prostaglandin dose is escalated to 50 ng/kg/min. However, little improvement in oxygen saturations is noted. You then question the need for urgent Balloon Atrial Septotomy (BAS) although fetal echocardiogram suggested adequate mixing at the atrial connection.

## **Structured Clinical question**

In neonates, with an antenatal diagnosis of TGA with IVS or small VSD (patient), can fetal echocardiogram (intervention) predict the need for urgent BAS (outcome)?

## **Search**

Cochrane, Medline, Embase, Cinahl and Maternity and infant care databases were searched on 6 March 2019. The following terms were used: exp "INFANT, NEWBORN"/ OR (newborn \* OR neonates\*) AND exp "HEART DETECTS, CONGENITAL"/ OR (congenital heart AND (defect\* OR malformation\*)) AND exp "ULTRASONOGRAPHY, PRENATAL"/ OR ((prenatal OR antenatal) AND (ultrasonography OR ultrasound OR scan)) OR (echocardiogram OR echocardiograph\*, OR "cardiac echo") AND exp FETUS/OR exp "FETAL RESEARCH"/ OR ((fetal OR foetal OR fetus OR foetus OR prenatal OR antenatal) AND echocardiog\*) AND ("Balloon atrial septostomy " OR atrial septostomy), OR Balloon atrial septostomy OR atrioseptostomy). In total, 31 publications were identified, in which 4 studies were relevant on further review<sup>1-4</sup>. All four studies included newborns with an antenatal diagnosis of TGA.

## **Commentary**

Congenital heart defects (CHD) are the most common congenital anomaly affecting approximately 8 per 1,000 livebirths<sup>5</sup>. Data from the National Institute for Cardiovascular Outcomes Research (NICOR-Congenital) shows improving antenatal CHD detection rates across England, with an increase in antenatal diagnoses of TGA/IVS from 27.2% in 2007 to 66.7% in 2016<sup>6</sup>. This correlates with the introduction of routine screening of outflow tracts to the NHS Fetal Anomaly Screening Programme recommended by the National Institute of Health and Clinical Excellence<sup>7</sup>.

TGA accounts for 5-7% of all CHD<sup>8</sup>. The survival of neonates with TGA has improved following adoption of new cardiac surgical techniques and enhanced postoperative management<sup>9</sup>. Antenatal detection, allowing for planned delivery in experienced tertiary centres and improved early neonatal management has also

improved outcomes<sup>10, 11</sup>. Despite these advances, some neonates with known TGA will show profound hypoxaemia after birth, secondary to inadequate circulatory mixing, which can lead to preoperative mortality and morbidity<sup>12</sup>. BAS is an accepted standard treatment. It creates an adequate inter-atrial communication allowing satisfactory oxygenation of the systemic blood, thereby stabilising patients prior to surgery<sup>13</sup>. However predicting which patients will need an urgent BAS on fetal echocardiogram is challenging. BAS is performed in presence of significant hypoxaemia (pre-ductal saturations  $\leq 70\%$ ), despite prostaglandin therapy and invasive ventilatory support, with echocardiographic demonstration of restrictive inter-atrial communication preventing circulatory mixing<sup>1-4</sup>.

From our literature search, only one retrospective cohort study<sup>1</sup> was identified which compared fetal echocardiographic markers in isolated TGA and gestation-matched fetuses to predict the need for urgent BAS. This was a single-centre study with an appropriate control population, although the study cohort was small (n=80). The study found the ratio of Foramen Ovale (FO) to Total Septal length was significantly smaller in those who required an urgent BAS. Other parameters including arterial duct, pulmonary valve or branch pulmonary artery diameters were not significantly different in study groups. A hypermobile and/or aneurysmal atrial septum were also noted in normal fetuses and those with TGA and did not predict need for urgent BAS.

Three other retrospective case-series studies that examined possible predictors of urgent BAS using different fetal echocardiography markers in neonates with TGA were identified. Tuo *et al.*<sup>2</sup> demonstrated restrictive FO or hypermobile or redundant septum primum was significantly associated with need for urgent BAS. Punn *et al.*<sup>3</sup> also examined the morphology and function of FO, and ductal size and shunting pattern. They found a hypermobile septum and reverse diastolic DA had a significant association with urgent BAS. Jouannic *et al.*<sup>4</sup> examined the size of the FO and DA to determine the specificity and sensitivity for urgent BAS. They concluded that a restricted FO and/or constricted DA had a specificity of 84%, to predict the need for urgent BAS, but a low sensitivity of 31%.

In conclusion, all identified studies were retrospective and single centred with small sample sizes. The individual markers in each study were not universally present in all affected cases, making the interpretation of the results challenging. The findings of each study were variable, with contradictory conclusions. With the lack of evidence to make reliable prediction of need for BAS on fetal echocardiograms, neonates with TGA and IVS or small VSD should be delivered in centres with emergency interventional cardiology support, should there be an urgent need for intervention. For those neonates delivered inadvertently in neonatal units with no interventional cardiology services, there should be an urgency of transferring to a cardiology center, following commencement of prostaglandin therapy.

## Clinical bottom line

- There are no consistent markers on fetal echocardiography that reliably predict need for BAS in TGA (Grade D)

## References

1. Vigneswaran TV, Zidere V, Miller OI, et al. Usefulness of Prenatal Echocardiogram in Fetuses With Isolated Transposition of the Great Arteries to Predict the Need for Balloon Atrial Septostomy. *The American journal of cardiology* 2017; vol. 119 (no. 9); p. 1463-1467
2. Tuo G, Paladini D, Montobbio G, et al. Prenatal Echocardiographic Assessment of Foramen Ovale Appearance in Fetuses with D-Transposition of the Great Arteries and Impact on Neonatal Outcome. *Fetal Diagnosis and Therapy* 2017; 42:48-56
3. Punj R, Silverman NH. Fetal Predictors of Urgent Balloon Atrial Septostomy in Neonates with Complete Transposition. *Journal of the American Society of Echocardiography* Apr 2011; vol. 24 (no. 4); p. 425-430
4. Jouannic J, Gavard L, Fermont L, et al. Sensitivity and Specificity of Prenatal Features of Physiological Shunts to Predict Neonatal Clinical Status in Transposition of the Great Arteries. *Circulation* 2004; 110:1743-1746
5. Dolk H, Loane M, Garne E. Congenital heart defects in Europe: prevalence and perinatal mortality, 2000 to 2005. *Circulation* 2011;123:841–9.
6. <https://www.nicor.org.uk/wp-content/uploads/2018/11/National-Congenital-Heart-Disease-Audit-Summary-Report-2014-17.pdf>
7. <http://www.nice.org.uk/CG062fullguideline> (accessed 17 Sep 2014)
8. Martins P, Castela E. Transposition of the Great Arteries. *Orphanet Journal of Rare Diseases*. 2008; 3:27
9. Villafane J, Lantin-Hermoso MR, Bhatt AB, et al. D-Transposition of the great arteries. The current era of the arterial switch operation. *J Am Coll Cardiol* 2014; 64:498-511
10. Blyth M, Howe D, Gnanapragasam J, et al. The hidden mortality of transposition of the great arteries and survival advantage provided by prenatal diagnosis. *Brit J Obstet Gyn* 2008;115:1096–100
11. Calderon J, Angeard N, Moutier S, et al. Impact of prenatal diagnosis on neurocognitive outcomes in children with transposition of the great arteries. *J Pediatr* 2012;161:94–8
12. Maeno YV, Kamenir SA, Sinclair B, et al. Prenatal features of ductus arteriosus constriction and restrictive foramen ovale in d-transposition of the great arteries. *Circulation*. 1999;99:1209-1214
13. Rashkind WJ, Miller WW. Creation of an atrial septal defect without thoracotomy. A palliative approach to complete transposition of the great arteries. *JAMA* 1996;991-2

**Table 1:**

Citation	Study Group	Study Type	Outcomes	Key Results	Comments
Vigneswaran et al <sup>1</sup>	40 neonates with isolated TGA compared to 40 gestation-matched neonates. 12 neonates with TGA had urgent BAS.	Retrospective cohort study	To predict need for urgent BAS with prenatal echocardiographic markers: <ul style="list-style-type: none"> <li>• foramen ovale length(FO)</li> <li>• FO: Total Septal length (TSL) ratio</li> <li>• Arterial valves, branch pulmonary arteries (PA) and arterial duct measurements</li> <li>• Atrial septum (AS) flap valve appearance: aneurysmal, fixed, hypermobile or normal</li> </ul>	<ul style="list-style-type: none"> <li>• FO length and FO:TSL similar in normal fetuses and in TGA group not requiring urgent BAS</li> <li>• Urgent BAS group had smaller FO length (p 0.005) and FO:TSL (p =0.001) (S)</li> <li>• All cases (3) with limited AS movement required BAS</li> <li>• Hypermobile AS not associated with need for urgent BAS</li> <li>• Arterial duct, pulmonary valve, or branch PA diameters not significantly different between urgent BAS and other groups</li> </ul>	Likelihood of an emergency BAS increased by FO:TSL <0.5 and a fixed appearance of the AS flap valve.
Tuo G et al	40 neonates with antenatal d-TGA of which 20 neonates had urgent BAS	Retrospective case series	To evaluate correlation between need for urgent BAS and antenatal appearance of the AS/ foramen ovale (FO), ductus arteriosus (DA) and pulmonary veins (PV)	<ul style="list-style-type: none"> <li>• All neonates with antenatal restrictive FO (=9) required an urgent BAS (p&lt; 0.0001) (S)</li> <li>• 5/8 neonates with antenatal hypermobile FO, and 6/8 fetuses with a redundant FO appearance required an urgent BAS (p= 0.002 and 0.0001 respectively) (S)</li> </ul>	The challenges of the prenatal evaluation of FO morphology for accurate prediction of need for urgent BAS were highlighted.

Punn et al	26 neonates with complete TGA, sub-grouped into urgent (within a few hours after birth) BAS (=14) or non-urgent BAS (=12).	Retrospective case series	To identify foetal predictors for need for an emergency BAS	<ul style="list-style-type: none"> <li>• Antenatal Hypermobility AS was associated with an urgent BAS (P = .0007, specificity and PPV 1) (S), however the sensitivity and NPV were only 0.64 and 0.71 respectively</li> <li>• Antenatal reverse diastolic ductal shunt was associated with an urgent BAS (P = .0145, specificity of 0.92 and PPV of 0.89) (S); however, the sensitivity and NPV were 0.57 and 0.65, respectively</li> </ul>	The hypermobile AS and diastolic reverse ductal shunt are promising predictors for need of urgent BAS.
Jouannic et al.	130 neonates with antenatal diagnosis of TGA. 108 neonates had TGA with an intact ventricular septum (IVS) or small VSD	Retrospective case series	To determine the specificity and sensitivity of a restricted FO and/or constricted DA in predicting need for urgent BAS	<ul style="list-style-type: none"> <li>• Specificity of restricted FO or constricted DA to predict urgent BAS was 84% while sensitivity was 54%</li> <li>• The specificity of both FO and DA restriction to predict urgent BAS was 100% (S), but the sensitivity was 31%</li> <li>• 6/95 neonates who were considered to have a normal foetal prenatal shunts, required urgent BAS</li> </ul>	Presence of restricted FO and DA constriction helps to predict need for urgent BAS but absence of the above does not rule out need for urgent BAS.

NS = Non-significant, S = Significant