Unbalanced Atrioventricular Septal Defect: Definition and Decision Making

David M. Overman, MD,[1] Jeanne M. Baffa, MD,[2]
Meryl S. Cohen, MD,[3] Luc Mertens, MD, PhD,[4]
David B. Gremmels, MD,[5] Anusha Jegatheeswaram, MD,[6]
Brian W. McCrindle, MD, MPH,[4] Eugene H. Blackstone, MD,[7]
Victor O. Morell, MD,[8] Christopher Caldarone, MD,[6]
William G. Williams, MD,[6] and Christian Pizarro, MD[9]

Abstract

Unbalanced atrioventricular septal defect is an uncommon lesion with widely varying anatomic manifestations. When unbalance is severe, diagnosis and treatment is straightforward, directed toward single-ventricle palliation. Milder forms, however, pose a challenge to current diagnostic and therapeutic approaches. The transition from anatomies that are capable of sustaining biventricular physiology to those that cannot is obscure, resulting in uneven application of surgical strategy and excess mortality. Imprecise assessments of ventricular competence have dominated clinical decision making in this regard. Malalignment of the atrioventricular junction and its attendant derangement of inflow physiology is a critical factor in determining the feasibility of biventricular repair in the setting of unbalanced atrioventricular septal defect. The atrioventricular valve index accurately identifies unbalanced atrioventricular septal defect and also brings into focus a zone of transition from anatomies that can support a biventricular end state and those that cannot.

Introduction

Atrioventricular septal defect (AVSD) occurs in approximately 7% of children born with congenital heart disease, and of these, 7% to 10% are unbalanced.[1-4] Identification and surgical treatment of balanced AVSD is straightforward with excellent outcomes.[5-8] Unbalanced atrioventricular septal defect (uAVSD), however, encompasses a broad array of complex anatomies that present significant diagnostic and therapeutic challenges. Indeed, the very definition of what constitutes unbalance in AVSD is not established. In addition, several surgical approaches are available to address the various anatomic substrates of uAVSD. Finally, there is scant literature documenting outcomes associated with these approaches, and currently these outcomes are suboptimal.[4,9-11] Still fewer reports directly address surgical decision making.[12] To achieve significant improvement in the treatment of uAVSD, clearer anatomic understanding and diagnostic criteria are needed. Once diagnostic clarity is achieved, more impactful analysis of presently employed therapeutic strategies may be undertaken.

[1] Division of Pediatric Cardiac Surgery, The Children's Heart Clinic, Children's Hospitals and Clinics of Minnesota, MN, USA
[2] Department of Pediatric Cardiology, The Nemours Cardiac Center, Alfred I Dupont Hospital for Children, Wilmington, DE, USA
[3] Department of Pediatric Cardiology, The Cardiac Center at Children's Hospital of Philadelphia, Philadelphia, PA, USA
[4] Department of Pediatric Cardiology, The Labatt Family Heart Center, Hospital for Sick Children, Toronto, ON, Canada
[5] Division of Pediatric Cardiology, The Children's Heart Clinic, Children's Hospitals and Clinics of Minnesota, MN, USA
[6] The Labatt Family Heart Center, the Hospital for Sick Children, Toronto, ON, Canada
[7] Department of Thoracic and Cardiovascular Surgery, Sydell and Arnold Miller Family Heart and Vascular Institute, the Cleveland Clinic, Cleveland, OH, USA
[8] Division of Pediatric Cardiac Surgery, The Children's Hospital of Pittsburgh of UPMC, Pittsburgh, PA, USA
[9] Department of Pediatric Cardiac Surgery, The Nemours Cardiac Center, Wilmington, DE, USA

Corresponding Author:
David M. Overman, MD, The Children's Heart Clinic at Children's Hospitals and Clinics of Minnesota, 2530 Chicago Avenue South, Suite 500, Minneapolis, MN 55404, USA.
Email: doverman@chc-pa.org

Abbreviations and Acronyms	
AV	atrioventricular
AVSD	atrioventricular septal defect
AVVI	atrioventricular valve index
LAR	long axis left ventricular/right ventricular ratio
LAVV	left atrioventricular valve
RAVV	right atrioventricular valve
uAVSD	unbalanced atrioventricular septal defect

Anatomy of uAVSD

Unbalanced in uAVSD references two distinct but related anatomic features: (1) ventricular hypoplasia and (2) malalignment of the atrioventricular (AV) junction. Malalignment of the AV junction causing inadequate inflow may affect ventricular size developmentally, but this is not a uniform correlation.

Ventricular hypoplasia may be severe, most often manifesting as a variant of hypoplastic left heart syndrome. Such patients are uniformly treated using single-ventricle palliation algorithms, and outcomes in this subset of uAVSD are well documented.[13-15] As it is more readily appreciated echocardiographically, ventricular hypoplasia dominates the diagnostic milieu of uAVSD. Even so, methodologies to assess ventricular volume are inconsistent and imprecise. Furthermore, assessment of ventricular size is confounded by the fact that right ventricular volume is normally greater than left ventricular volume in balanced AVSD.[16-18] Cross-sectional area, end-diastolic dimension, the presence or absence of an apex-forming cavity, and ratios of ventricular length have all been employed to assess ventricular size.[10,12,19-21] None of these or other measures of ventricular volume have been proven to be reliable predictors of a successful biventricular end state.[22,23]

Malalignment of the AV junction results from unequal distribution of the common AV valve over the ventricular septum. Recognition of this malalignment may require more diagnostic vigilance than that needed to identify ventricular hypoplasia. Despite its potential subtlety, however, its presence can lead to significant derangement of inflow physiology and preclude biventricular repair irrespective of ventricular size. Malalignment may be toward either the left or the right with resultant right- or left-sided dominance, respectively. In the extreme, malalignment of the AV junction results in double-outlet atrium.[2]

Abnormalities of the AV valve apparatus in the setting of uAVSD are not well characterized but undoubtedly occur and include parachute leftward AV valve deformity, deficient leaflet geometry, and anomalous chordal insertion.[2,24,25] Right-dominant uAVSD is commonly associated with left ventricular outflow tract obstruction comprising variously subaortic stenosis, aortic valve stenosis or hypoplasia, and/or aortic arch obstruction.[26] Morphology of the ventricular septal defect is likewise variable, both in size and location within the inlet septum, and may include extension into the perimembranous or
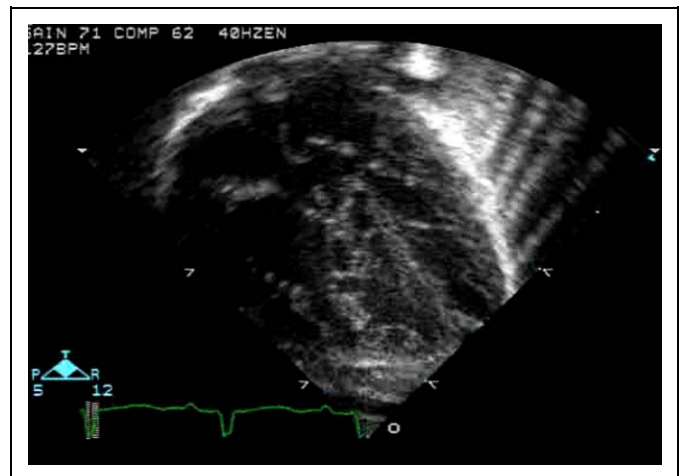

Figure 1. Right-dominant atrioventricular septal defect. In this example, the smaller left ventricle is apex forming. Attempted biventricular repair failed because of severe mitral stenosis.

outlet portions of the ventricular septum.[2,27] Finally, uAVSD is frequently associated with heterotaxy syndrome and its attendant abnormalities of situs, pulmonary and systemic venous drainage, and ventriculo-arterial connections (discordance, stenosis, or atresia).

Surgical Treatment Options

When uAVSD is severe, diagnosis is unequivocal, and single-ventricle palliation is consistently employed. When unbalance is milder, however, several surgical options exist (Figures 1 and 2). In the case of right-dominant uAVSD, the therapeutic decision is more or less binary, with a choice of either single-ventricle palliation if left-sided structures are felt to be inadequate to support biventricular physiology or, conversely, biventricular repair if left-sided structures are deemed adequate. Aortic arch obstruction is frequently encountered in the setting of right-dominant uAVSD, and its correction is required for successful biventricular repair. Atrial fenestration is sometimes employed to mitigate left atrial hypertension, but its role and impact are not clear.[12]

In the setting of left-dominant uAVSD, single-ventricle palliation and biventricular repair strategies are similarly employed. In addition, biventricular repair with cavopulmonary shunt (so-called one and a half ventricle repair) may also be applied to facilitate adequate right heart function.[28-30] Atrial fenestration is also sometimes employed, at the expense of some cyanosis, to prevent right atrial hypertension and low cardiac output. Of course, biventricular repair of right- or left-dominant uAVSD may be preceded by interim palliation such as pulmonary artery banding.

These therapeutic strategies, it should be noted, are often colored by the frequent extracardiac abnormalities found in association with uAVSD. Chromosomal anomalies and Trisomy 21, in particular, are known to negatively affect single-ventricle palliation outcomes.[31,32] This, in effect,

Figure 2. Left-dominant atrioventricular septal defect. The hypoplastic right ventricle is non–apex forming. This patient had uneventful one and one-half ventricle repair.

increases the premium placed on achieving a biventricular end state, even when specific anatomic elements are deemed marginal.

Surgical Literature

Data to guide application of these many surgical options to the complex anatomies of uAVSD are sparse. Most often, reference to uAVSD is found within larger series of complete or incomplete AVSD and, in fact, accounts for a measurable proportion of the relatively low mortality in these reports. In the past 5 years, only 3 retrospective single-institution reports addressing surgical management and outcomes of uAVSD have been published. Walter and colleagues[10] reported their experience with 19 right-dominant uAVSD patients over an 18-year period who underwent biventricular repair. Diagnosis was based on a long axis left ventricular/right ventricular ratio (LAR). There were 3 early failures (death or transplant) and 3 late reoperations. Event-free survival at 10 years was 56%. They concluded that although late outcomes may be better after successful biventricular repair, caution should be exercised when the LAR <0.65. De Oliveira and colleagues[12] reported on 38 uAVSD patients treated over a 15-year period, 32 of whom underwent biventricular repair and 6 of whom had single-ventricle palliation. Diagnosis was made using an LV/RV ratio as well as the atrioventricular valve index (AVVI) described by Cohen and coworkers[27] (smaller AVV area/larger AVV area, as discussed in detail later in this manuscript). There were 4 early deaths and 6 early reoperations (all within the biventricular repair group). No late follow-up data were reported. Finally, Lim and colleagues[11] reported their experience with biventricular repair in patients with heterotaxy syndrome. Early outcomes were excellent in this series of 91 patients treated over an 18-year period. There were, however, only 10 patients with uAVSD within this cohort, and uAVSD

was found to be the only significant risk factor for death. Thus, documented experience with uAVSD from even large single institutions is notably small. Diagnostic methodologies are diverse, making comparisons of various reports difficult, and results are suboptimal with early mortality that ranges from 10% to 17% with low event-free survival.

Toward a Diagnosis of uAVSD: The AVVI

In an effort to standardize assessment of the observed degree of malalignment of the AV junction, Cohen and colleagues[27] developed the AVVI. The AVVI was derived by tracing the circumference of the common AV valve orifice during end diastole, averaged over 3 cardiac cycles, using a subcostal 30-degree left anterior oblique 2-dimensional echo view. This circumference was then subtended by a line drawn over the plane of the interventricular septum from the tip of the infundibular septum to the crest of the muscular septum, thus dividing the common AV valve into left and right components (Figure 3). The AVVI was expressed as the smaller AV valve area over the larger AV valve area, so that left-dominant uAVSD was expressed as RAVV area/LAVV area and right-dominant uAVSD the inverse. The authors then applied AVVI to a cohort of 103 patients previously diagnosed with complete AVSD. Of these, 26 were classified as unbalanced by angiography, echocardiography, or surgical inspection. Size of the ventricular septal defect was also assessed and classified as large (unrestrictive), small (restrictive), or absent. Of the 26 uAVSD patients, 11 were ductal dependent and underwent Norwood palliation as neonates, and 15 presented later in infancy and were therefore deemed to have 2 adequate ventricles. These patients all underwent biventricular repair, with 6 early deaths. All patients with balanced AVSD had AVVI >0.67, and no patient with AVVI <0.30 underwent biventricular repair. There was, however, considerable overlap in values of AVVI among
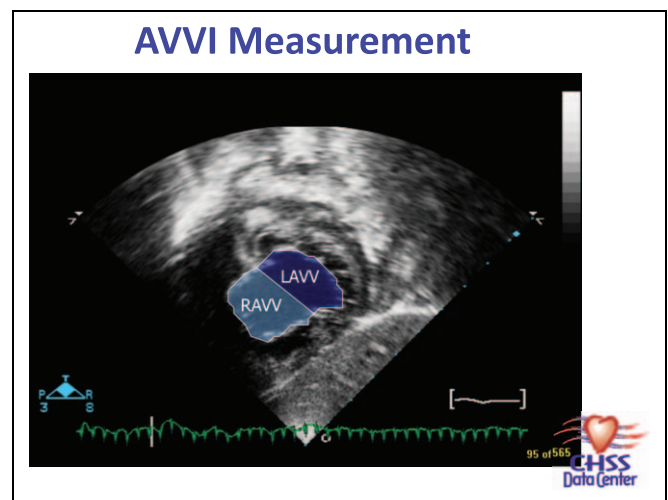

Figure 3. Subcostal left anterior oblique view whereby the common atrioventricular (AV) valve orifice is subtended to delineate left and right AV valve areas.

the uAVSD cohort, and there was no difference in the mean AVVI between survivors and nonsurvivors undergoing biventricular repair of uAVSD. Of note, however, is that 3 of 6 nonsurvivors had marked discrepancy between AVVI and the ventricular cavity ratio employed by the authors (low AVVI and ventricular cavity ratio near mean). Finally, all 6 nonsurvivors of biventricular repair had a large ventricular septal defect, compared with only 4 of 9 survivors. The authors concluded that if AVVI is <0.67 in the presence of a large ventricular septal defect, single-ventricle palliation should be considered.

Ventricular "Competence" vs Inflow Physiology

The introduction of a method to assess degree of malalignment of the AV junction was an important step forward in the understanding of uAVSD. With the AVVI, Cohen and colleagues[27] drew into focus the importance of the atrioventricular connection in the pathophysiology of uAVSD. Historically, the concept of adequacy for biventricular repair has hinged on what might be termed *ventricular competence* (eg, size). This emphasis is reflected in the current Society of Thoracic Surgeons Congenital Heart Surgery Database definition of uAVSD, wherein uAVSD is defined as "an AVC with two ventricles in which one ventricle is inappropriately small but is thought to be a candidate for biventricular repair. AVC lesions with unbalanced ventricles so severe as to preclude biventricular repair should be classified as single ventricles."[33] This is conceptually analogous to anatomic substrates such as Shone syndrome or "hypoplastic left heart complex" and also pulmonary atresia with intact ventricular septum. These anatomies, however, are fundamentally different from uAVSD in that they have normal modes of atrioventricular connection as well as no ventricular level shunt. Therefore, prediction of resulting physiology after biventricular repair is constrained primarily to extant ventricular and valvar dimensions. In uAVSD, however, prediction mechanisms must also account for the impact of surgical division of a common AV valve that may or may not be properly aligned over the interventricular septum. If significant malalignment exists, then inadequate filling of one or the other ventricle will result, irrespective of ventricular size. Thus, the AVVI properly emphasizes the importance of derangements of inflow physiology in uAVSD.

Modified AVVI

A modification of the AVVI has been introduced by Baffa and colleagues[34] to simplify the terminology of the AVVI as well as to improve its granulation of unbalance across the spectrum of AVVI. The modified AVVI is derived by dividing left AV valve area/total AV valve area. Thus, all forms of unbalance exist on a continuum from 0.0 to 1.0, with 0.0 having no left AV valve area, 1.0 having all left AV valve area, and 0.5 having exactly equal left and right AV valve areas (Figure 4). The Unbalanced AVSD Working Group of the Congenital Heart
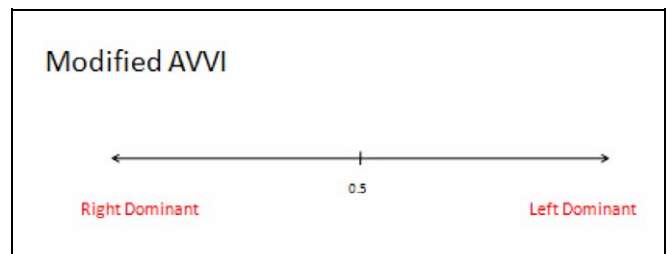
Figure 4. Modified atrioventricular valve index (AVVI) is derived by left atrioventricular (AV) valve/total AV valve area.
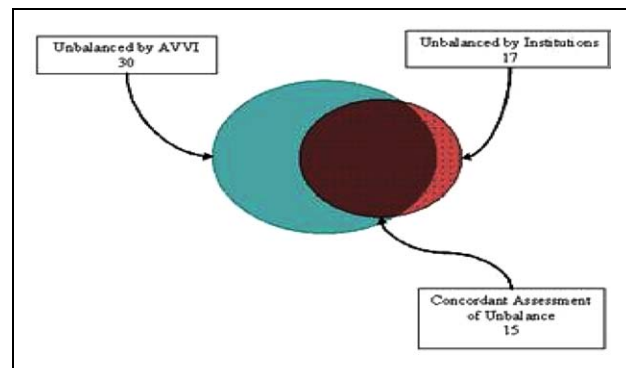
Figure 5. Venn diagram demonstrating significant discrepancy in recognition of unbalanced atrioventricular septal defect (uAVSD) when the atrioventricular valve index (AVVI) is compared with institutional diagnosis.

Surgeons' Society has proposed an inception cohort study to explore the relationship of the modified AVVI and related echocardiographic elements such as color inflow to selected surgical strategy and outcomes. Preliminary data from a retrospective, cross-sectional, multi-institutional study conducted by the group seem to validate AVVI as a diagnostic tool that accurately identifies uAVSD from a cohort of complete AVSD, balanced and unbalanced. AVVI identified more patients as being unbalanced as compared with clinical diagnosis, and some patients classified as unbalanced clinically were not so when assessed by AVVI (Figure 5). More important, within a narrow range of AVVI (0.19-0.39), surgical strategy is varied, and there is a clustering of mortality. It is in this "zone of transition," where sustainability of a biventricular end state becomes tenuous, that clearer predictors of appropriate surgical strategy are needed. It is easy to imagine that such a transitional zone exists within the left-dominant range of AVVI as well, but the low incidence of left-dominant uAVSD would require a much larger study population.

These preliminary data highlight the important role of AV junction malalignment in the pathophysiology of uAVSD. Accurate identification of uAVSD can only be achieved when this aspect of its anatomy is taken into account. This concept should also be reflected in nomenclature and database systems. In a broader sense, what exactly defines uAVSD remains unclear, but an accurate definition clearly must include

assessment of not only ventricular hypoplasia but also AV junction malalignment.

Conclusion

Unbalanced AVSD continues to be a challenging lesion. Its low incidence and widely varying anatomies, coupled with the broad array of available surgical strategies, make clinical decision making difficult. Assignation to an appropriate surgical strategy is straightforward in the setting of severe uAVSD, but the same cannot be said for more moderate degrees of unbalance. Present methods of identifying uAVSD lack sensitivity and specificity, and outcomes are suboptimal. Although ventricular hypoplasia is important in the pathophysiology of uAVSD, derangement of inflow physiology by malalignment of the AV junction is a critical element in determining the feasibility of biventricular repair. AVVI improves discrimination of unbalance in the setting of complete AVSD. Within a narrow range of AVVI, a transition is made from anatomic substrates that are capable of supporting biventricular physiology to those that cannot. Where this transition occurs and what anatomic components are important factors therein are presently obscure. Elucidation of the interaction between AVVI, patient factors, and selected surgical strategy will require a larger, prospective inception cohort study.

Declaration of Conflicting Interests

Funding

References

1. Ferencz C, Loffredo CA, Correa-Villasenor A, Wilson PD. *Genetic and Environmental Risk Factors of Major Cardiovascular Malformations: The Baltimore-Washington Infant Study 1981-1989*. Armonk, NY: Futura; 1997.
2. Freedom RM, Bini M, Rowe RD. Endocardial cushion defect and significant hypoplasia of the left ventricle: a distinct clinical and pathological entity. *Eur J Cardiol*. 1977;7:263-281.
3. Bharati S, Lev M. The spectrum of common atrioventricular orifice (canal). *Am Heart J*. 1973;86:553-561.
4. Corno A, Marino B, Catena G, Marcelletti C. Atrioventricular septal defects with severe left ventricular hypoplasia: staged palliation. *J Thorac Cardiovasc Surg*. 1988;96:249-252.
5. Suzuki T, Bove EL, Devaney EJ, et al. Results of definitive repair of complete atrioventricular septal defect in neonates and infants. *Ann Thor Surg*. 2008;86:596-603.
6. Nunn GR. Atrioventricular canal: modified single patch technique. *Semin Thorac Cardiovasc Surg*. 2007;10:28-31.
7. Crawford FA, Stroud MR. Surgical repair of complete atrioventricular septal defect. *Ann Thorac Surg*. 2001;72:1621-1629.
8. Bando K, Turrentine MW, Sun K, et al. Surgical management of complete atrioventricular septal defect: a twenty year experience. *J Thorac Cardiovasc Surg*. 1995;110:1543-1554.
9. Owens GE, Gomez-Fifer C, Gelehrter S, Owens ST. Outcomes for patients with unbalanced atrioventricular septal defects. *Pediatr Cardiol*. 2009;30:431-435.
10. Walter EMD, Ewert P, Hetzer R, et al. Biventricular repair in children with complete atrioventricular septal defect and a small left ventricle. *Eur J Cardiothorac Surg*. 2008;33:40-47.
11. Lim HG, Bacha EA, Marx GR, et al. Biventricular repair in patients with heterotaxy syndrome. *J Thorac Cardiovasc Surg*. 2009;137:371-377.
12. De Oliveira NC, Sittiwangkul R, McCrindle BW, et al. Biventricular repair in children with atrioventricular septal defect and a small right ventricle: anatomic and surgical considerations. *J Thorac Cardiovasc Surg*. 2005;130:250-257.
13. Jacobs ML, Rychik J, Murphy JD, Nicholson SC, Steven JM, Norwood WI. Results of Norwood's operation for lesions other than hypoplastic left heart syndrome. *J Thorac Cardiovasc Surg*. 1995;110:1555-1561.
14. Daebritz SH, Nollert GD, Zurakowski D, et al. Results of Norwood stage I operation: comparison of hypoplastic left heart syndrome with other malformations. *J Thorac Cardiovasc Surg*. 2000;119:358-367.
15. Stasik CN, Gelehrter S, Goldberg CS, Bove EL, Devaney EJ, Ohye RG. Current outcomes and risk factors for the Norwood procedure. *J Thorac Cardiovasc Surg*. 2006;131:412-417.
16. Thanopoulos BD, Fisher EA, DuBrow IW, Hastreiter AR. Right and left ventricular volume characteristics in common atrioventricular canal. *Circulation*. 1978;57:991-995.
17. Jarmakani JM, George B, Wheller J. Ventricular volume characteristics in infants and children with endocardial cushion defects. *Circulation*. 1978;58:153-157.
18. Graham TP Jr, Jarmakani JM, Atwood GF, Canent RV Jr. Right ventricular volume determinations in children: normal values and observations with volume or pressure overload. *Circulation*. 1973;47:144-153.
19. Latson LA, Cheatham JP, Gutgesell HP. Relation of the echocardiographic estimate of left ventricular size to mortality in infants with severe left ventricular outflow tract obstruction. *Am J Cardiol*. 1981;48:887-891.
20. Hammon JW, Lupinetti FM, Maples MD Jr, et al. Predictors of operative mortality in critical aortic valvar stenosis presenting in infancy. *Ann Thorac Surg*. 1988;45:537-540.
21. Drinkwater DC, Laks HL. Unbalanced atrioventricular septal defects. *Semin Thorac Cardiovasc Surg*. 1997;9:21-25.
22. van Son JA, Phoon CK, Silverman NH, Haas GS. Predicting feasibility of biventricular repair of right-dominant unbalanced atrioventricular canal. *Ann Thorac Surg*. 1997;63:1657-1663.
23. Phoon CK, Silverman NH. Conditions with right ventricular pressure and volume overload, and a small left ventricle: "hypoplastic" left ventricle or simply a squashed ventricle? *J Am Coll Cardiol*. 1997;30:1547-1553.

24. Kim WH, Lee TY, Kim SC, Lee YT. Unbalanced atrioventricular septal defect with parachute valve. *Ann Thorac Surg*. 2000;70:1711-1712.

25. Piccoli GP, Ho SY, Wilkinson JL, Macartney FJ, Gerlis LM, Anderson RH. Left sided obstructive lesions in atrioventricular septal defects: an anatomic study. *J Thorac Cardiovasc Surg*. 1982;83:453-460.

26. Gow RM, Freedom RM, Williams WG, Trusler GA, Rowe RD. Coarctation of the aorta or subaortic stenosis with atrioventricular septal defect. *Am J Cardiol*. 1984;53:1421-1428.

27. Cohen MS, Jacobs ML, Weinberg PM, Rychik J. Morphometric analysis of unbalanced common atrioventricular canal using two-dimensional echocardiography. *J Am Coll Cardiol*. 1996;28:1017-1023.

28. Van Arsdell GS. One and one half ventricle repairs. *Semin Thorac Cardiovasc Surg*. 2000;3:173-178.

29. Stellin G, Vida VL, Milanesi O, et al. Surgical treatment of complex cardiac anomalies: the one and one half ventricle repair. *Eur J Cardiothorac Surg*. 2002;22:1043-1049.

30. Alvarado O, Sreeram N, McKay R, Boyd IM. Cavopulmonary connection in repair of atrioventricular septal defect with small right ventricle. *Ann Thorac Surg*. 1993;55:729-736.

31. Malec E, Mroczek T, Pajak J, Januszewska K, Zdebska E. Results of surgical treatment of congenital heart defects in children with Down's syndrome. *Pediatr Cardiol*. 1999;20:351-354.

32. Wada N, Takahashi Y, Ando M, Sasaki T. Single ventricle repair in children with Down's syndrome. *Gen Thorac Cardiovasc Surg*. 2008;56:104-108.

33. Jacobs JP, Burke RP, Quintessenza JA, Mavroudis C. Congenital Heart Surgery Nomenclature and Database Project: atrioventricular canal defect. *Ann Thorac Surg*. 2000;69(suppl): S36-S43.

34. Baffa JM, Cohen MC, Gremmels DB, et al. Unbalanced atrioventricular septal defect: diagnosis, surgical decision-making, and associated outcomes. A multi-institutional study. Presented at: Second Joint Meeting of the Congenital Heart Surgeons' Society and the European Congenital Heart Surgeons' Association; September 12-13, 2008; Warsaw, Poland.