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Review

Atrioventricular septal defect: From embryonic development to long-term follow-up

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ABSTRACT

Atrioventricular septal defect (AVSD) covers a spectrum of heart anomalies with a common atrioventricular connection and has an incidence of 4–5.3 per 10.000 live births. About half of the AVSDs occur in patient with Down syndrome. This review provides a bench to bedside overview of AVSD. Developmental aspects, nomenclature, anatomy, and classification of AVSD are discussed. Furthermore an overview of genetic and maternal risk factors for AVSD is provided, and available literature on (fetal) diagnosis, surgical techniques and follow-up is presented. Special attention is given to differences in developmental, anatomical and prognostic factors of AVSD between non-syndromic and Down syndrome patients.

The term atrioventricular septal defect (AVSD) covers a spectrum of heart anomalies with a common atrioventricular (AV) junction [1]. With an incidence of 4–5.3 per 10.000 live births, AVSD comprises 7% of all congenital heart diseases (CHD) and is often associated with Down syndrome [2–5]. Despite intensive investigation, the morphogenesis of AVSD is still not fully understood. Furthermore controversy remains in nomenclature and long-term follow-up data are scarce. Recent developments in knowledge on heart development provide new insights in (epi)genetic factors in AVSD development.

The aim of the current review is to give a complete bench to bedside overview, from embryonic development to clinical aspects of AVSD. Special attention is given to the difference between non-syndromic and syndromic, in particular Down syndrome, patients.

1. Nomenclature and types of AVSD

An overview of nomenclature is presented in Fig. 1. Controversies exist on nomenclature and subdivision of the varying morphology of AVSDs, and several different descriptions are currently used. The terms 'atrioventricular canal defect' and 'endocardial cushion defect' are used as synonyms for AVSD.

In this review we will use the classification as agreed upon by the International Paediatric and Congenital Cardiac Code (www.IPCCC.net) [6,7]. *Complete AVSD* according to the IPCCC includes an ostium primum defect of the atrial septum and a non-restrictive defect in the inlet portion of the ventricular septum, with one AV annulus and a common AV valve. The common AV valve classically is composed of two (a superior and an inferior) leaflets bridging across the ventricular septum, as well as a left lateral (mural) leaflet, a right antero-superior and a right inferior leaflet (Fig. 1). In complete AVSD shunting takes place at both the atrial and ventricular level. In an AVSD with an *isolated atrial component* (also known as *ASD primum*, *ostium primum defect* or *partial AVSD*) the bridging leaflets are attached to the ventricular septum. Although there is one annulus, the attachment of the bridging leaflets to the ventricular septum results in two orifices and shunting can take place only above this level, at the atrial level (Fig. 1). Less common is an AVSD with

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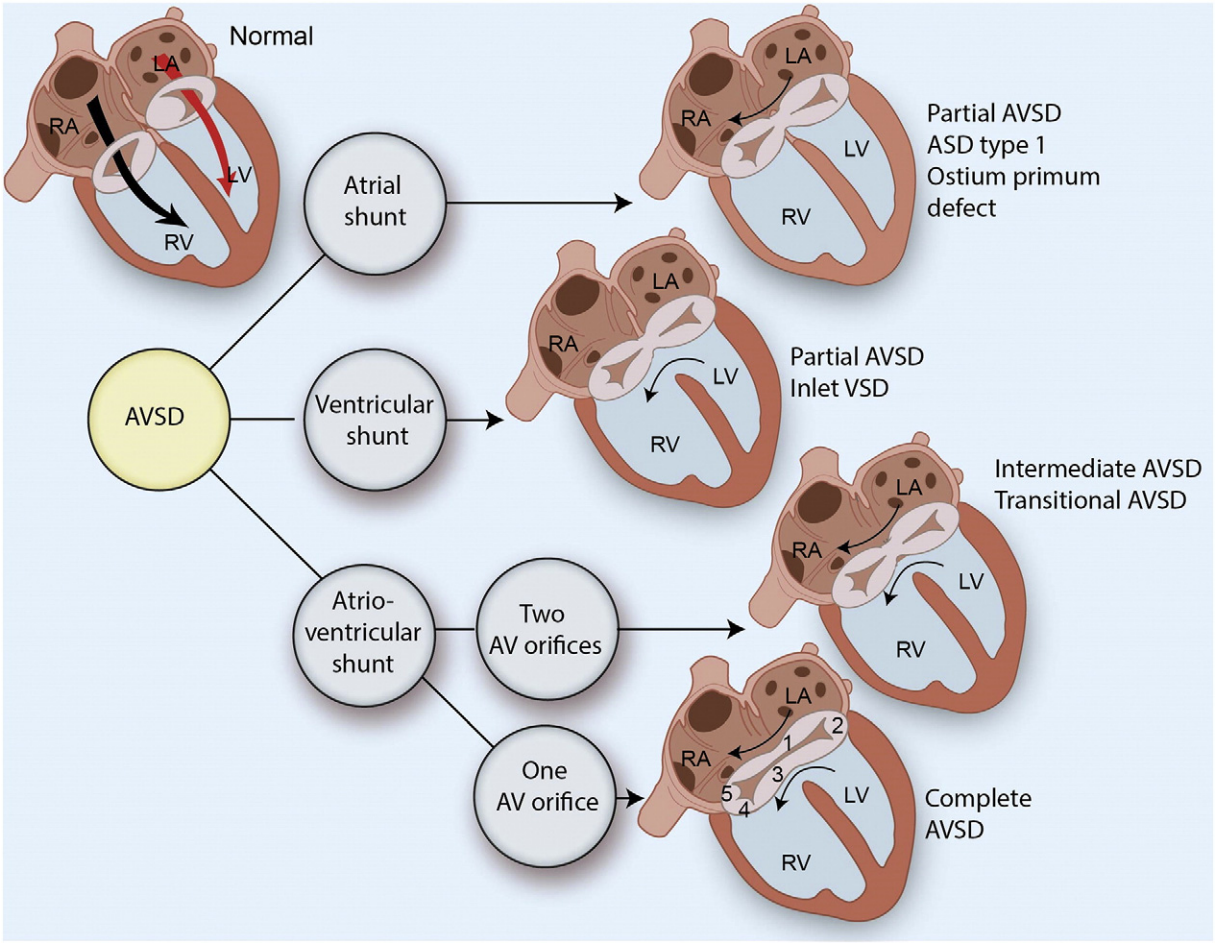

Fig. 1. Schematic presentation of nomenclature of different types of AVSD. Defect can occur at atrial, ventricular or atrioventricular level. Black arrows indicate the defects, but do not necessarily represent blood flow direction. RA = right atrium, LA = left atrium, RV = right ventricle, LV = left ventricle. In the complete AVSD the five leaflets are shown: superior bridging leaflet (1), left lateral (mural) leaflet (2), inferior bridging leaflet (3), right inferior leaflet (4) and right antero-superior leaflet (5).

an *isolated ventricular component* (*also known as partial AVSD*), where the partially fused bridging leaflets are attached to the atrial septum and shunting is just at the ventricular level. This type of AVSD is in the clinical setting mostly referred to an inlet VSD (Fig. 1). Fourthly, the IPCCC defines *an intermediate* (*or transitional*) AVSD with an ostium primum defect and a (often restrictive) VSD just below the AV valves, but with two remaining separate AV orifices due to fusion of the bridging leaflets (Fig. 1). Of note, some authors distinguish between a transitional AVSD, being an AVSD with two annuli and an inlet VSD and an intermediate AVSD, being an AVSD with 1 annuli and 2 orifices [8]. This difference is not acknowledged by the IPCCC that equally classifies the 2 forms. We support the latter, as we do not consider AVSD to have 2 annuli, but rather a common annulus and a common AV valve that can have 2 orifices in case of attachment of the valve to either the ventricular (most common) or atrial septum. Fifth, the IPCCC describes an AVSD *with ventricular imbalance*, with an unequal position of the common AV valve above the (unbalanced) ventricles with a variable degree of ventricular hypoplasia. The imbalance may occur in the setting of either a complete, partial or intermediate/transitional AVSD.

Another defect at the level of the AV septum is the so-called Gerbode defect. This malformation is on the spectrum between an AVSD and a membranous VSD being a defect in the membranous part of the AV septum allowing shunting between the left ventricle (LV) and right atrium (RA). According to Gerbode [8] shunting can take place either directly (supra-annular) through the membranous septum or indirect (infra-annular) via a perimembranous VSD and a defect in the tricuspid valve. In the IPCCC the Gerbode defect is classified as a subtype of VSD [9], however as the defect is present in the AV septum one could also argue that the anomaly could be designated a form of AVSD.

The Rastelli classification, originally described in 1966 [10], subdivides complete AVSD based on the anatomy of the superior (anterior) common/bridging leaflet. A completely split leaflet (i.e., the superior bridging leaflet is divided), with the superior bridging leaflet almost completely adherent to the left ventricle and firmly attached on the ventricular septum by multiple chordal insertions is designated as Rastelli type A. Type A is the most frequently found [11]. A divided (split) superior leaflet, with the superior bridging leaflet attached over the ventricular septum by an anomalous papillary muscle of the right ventricle is designated Rastelli type B. Rastelli type C indicates a large, non-divided, superior leaflet without chordal attachment to the interventricular septum, also known as the 'free floating'. Type C is often seen in association with other cardiac defects [12]. From classes A to C ventricular shunting increases. The Rastelli classification was originally designed to predict the outcome of surgery. However, due to the lack of correspondence between the classification and surgical outcome and enormous variability in leaflets [13,14], the use of the Rastelli classification is currently largely omitted in literature.

A mitral cleft in an otherwise normal mitral valve (*isolated mitral cleft*) should not be considered the same as the 'cleft' in the left part of the common AV valve in AVSD. An isolated cleft is a cleft in the aortic (anterior) mitral leaflet, whereas a 'cleft' in the setting of AVSD is a gap between the superior and inferior bridging leaflets, clearly distinguishing the anatomy of the left AV valve in AVSD from a normal mitral valve anatomy [15–17]. Although anatomically features are