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Arrhythmias in adult congenital heart disease

Paul Khairy†, Annie Dore, Mario Talajic, Marc Dubuc, Nancy Poirier, Denis Roy and Lise-Andrée Mercier

Recent advances in pediatric cardiology and cardiac surgery have allowed a rapidly expanding population of patients with congenital heart disease to thrive well into their adult years. Often after prolonged uneventful clinical courses as children and adolescents, arrhythmias may surface later in life. These arrhythmias are a major source of morbidity. In addition, sudden death is the leading cause of mortality in adult patients with congenital heart disease. This review highlights the various types of brady- and tachyarrhythmias encountered in the more common forms of adult congenital heart disease and explores prognostic implications and therapeutic options.

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CONTENTS

Atrial septal defect
Ventricular septal defect
Atrioventricular septal defect
Single-ventricle physiology
Fontan procedure
Tetralogy of Fallot
D-transposition of the great arteries
Expert commentary & five-year view
Key issues
References
Affiliations

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Adult congenital heart disease (ACHD) is a rapidly expanding subspecialty of cardiology with an exponentially growing patient population [1–3]. Approximately 75 out of every 1000 live births are complicated by some form of cardiovascular malformation, 25% of which are considered to be moderate or severe [4]. Previously, over 50% of children born with congenital defects died before reaching adulthood [5]. With current care, however, over 85% of such infants are expected to survive into their adult years [1,3,5]. In North America, the clinical load in ACHD outpatient visits increased by 400% in 1999, and continues to rise [3].

This extraordinary achievement is, however, tempered by the realization that these early surgical interventions were 'reparative' and not 'curative'. After sometimes lengthy quiescent clinical courses, complications may surface many years later. Arrhythmias figure prominently among the issues encountered by young adults with congenital heart disease [6]. These arrhythmias may result from hemodynamic or hypoxic stress imposed by the original cardiac malformation and/or postoperative sequelae from reparative surgery [7]. In addition to being a major source of morbidity, arrhythmias may be life threatening [8–11]. Indeed, sudden cardiac death is the most common cause of death in ACHD, with up to 100-fold increased risk compared with age-matched controls, often occurring in the third and fourth decades of life [12,13].

Arrhythmias in ACHD are to be distinguished from congenitally inherited forms of arrhythmias of established genetic etiology [14,15]. Many patients with ACHD have structural defects that support re-entrant wavefronts [16–18], while triggered or automatic foci account for a smaller subset of observed arrhythmias [19–21]. Intra-atrial re-entrant tachycardias (IART), and atrial macroreentrant circuits are among the most common and challenging atrial arrhythmias encountered. Ventricular arrhythmias occur in a smaller subset of patients with ACHD, most notably those with left-sided obstructive lesions, tetralogy of Fallot and severe ventricular dysfunction. This review provides an overview of the types of arrhythmias encountered in the more common forms of ACHD.

In the absence of specific evidence-based data, pharmacologic therapy with atrioventricular (AV) nodal blocking agents and anti-arrhythmic drugs is extrapolated from guiding principles established in other forms of heart disease. Thus, considerations include the degree of systemic ventricular dysfunction, sinus node disease, impaired AV node conduction, negative inotropic effects and potential proarrhythmic consequences. While medical

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therapy has traditionally faced limited success, transcatheter ablation is emerging as a promising alternative in many patients. Complexities in underlying anatomy, associated extracardiac malformations and underdeveloped or obstructed vascular access can pose unique challenges to catheter-based interventions and implantation of pacemakers or cardioverter defibrillators [22–24]. In certain circumstances, surgical therapy may complement available nonpharmacologic options.

Atrial septal defect

In adults with unoperated atrial septal defects (ASDs), the estimated incidence of atrial fibrillation and/or flutter is approximately 20% and increases with age [10,25]. In the absence of prior surgical repair, the most common arrhythmia subtype is typical isthmus-dependent atrial flutter, which is amenable to catheter ablation.

Surgical or percutaneous closure of an ASD is generally warranted when associated with symptoms, right-sided volume overload and/or a left-to-right shunt ratio of more than 1.5:1. In the presence of surgical incisions, isthmus-dependent flutter and/or nonisthmus-dependent IART may occur and sometimes coexist. Common substrates include macrore-entry along the lateral right atrial wall, around atriotomy incisions and complex double-loop circuits [26–28].

Surgical ASD closure may decrease the overall occurrence of atrial arrhythmias, but appears to be less effective in older individuals [10,25,29–31]. Gatzoulis and colleagues retrospectively reviewed 218 adults with surgical closure of an isolated ASD and found sustained atrial arrhythmias in 19% prior to surgery: atrial flutter alone in 5%, atrial flutter and fibrillation in 2.8%, and atrial fibrillation alone in 11% [10]. Over a mean postoperative follow-up of 3.8 years, 60% of patients with preoperative atrial flutter or fibrillation continued to have arrhythmias and 2.3% developed new-onset arrhythmias. All of the patients with persistent and new arrhythmias were over 40 years of age at the time of repair. Attie and colleagues randomized 521 adults over 40 years of age with a secundum or sinus venosus ASD, shunt ratio of greater than 1.7:1 and pulmonary systolic pressure less than 70 mmHg to surgical closure versus medical therapy [25]. Over a median of 7.3 years, new-onset atrial flutter or fibrillation occurred in a similar proportion of patients with surgical versus medical therapy (i.e., 7.4 vs 8.7%).

To assess whether transcatheter ASD device closure prevents subsequent atrial arrhythmias, the incidence and predictors of symptomatic atrial tachyarrhythmias were reviewed retrospectively [30]. Prior to transcatheter device closure, 15% of 132 patients had atrial tachyarrhythmias. All patients with persistent arrhythmias remained in atrial fibrillation or flutter after closure. Of those with prior paroxysmal atrial tachyarrhythmias in sinus rhythm at the time of procedure, two-thirds remained free of symptomatic recurrence at a mean of 17 months. Symptomatic paroxysmal atrial arrhythmias occurred in 17% per year and persistent atrial fibrillation or flutter in 11% per year. Older age (≥55 years) was predictive of atrial tachyarrhythmias.

Ventricular septal defect

Ventricular septal defects (VSDs) are the most common form of congenital heart malformations. By adulthood, however, most VSDs have either closed spontaneously or caused symptoms of congestive heart failure that prompted surgical closure [32]. While a VSD can occur anywhere along the interventricular septum, effects on the conduction system and arrhythmias in unoperated patients relate to hemodynamic consequences, not specific location [33].

In patients with unoperated VSDs, a higher prevalence of isolated premature ventricular contractions (PVC), couplets and multiform PVCs was noted [33]. Nonsustained or sustained ventricular tachycardia occurred in 5.7% of cases. The most powerful independent predictor for high-grade ectopy was higher mean pulmonary artery pressure. Despite these ventricular arrhythmias, sudden cardiac death is reportedly uncommon, but has been described in the setting of cardiac hypertrophy and progressive fibrosis of the conduction system [34–37].

In the absence of contraindications, VSD closure is recommended in patients with significant shunts (as defined by symptoms, Qp:Qs > 2:1 and pulmonary artery systolic pressure > 50 mmHg), deteriorating ventricular function, right ventricular outflow obstruction or more than mild aortic insufficiency [32]. Late sudden death occurs in approximately 4% of patients with surgically repaired VSD [38,39]. Of the 296 patients with surgical VSD closure between 1954 and 1960, death occurred in 59 patients (20%) at 30 years of follow-up [39]. Risk factors for mortality included surgery after 5 years of age, pulmonary vascular resistance greater than 7 Woods units and complete heart block. Transcatheter VSD closure may be feasible in selected patients. Complete heart block is a recognized complication [40–42]. Long-term follow-up is required to determine whether it is a safe less-morbid alternative to surgery.

Atrioventricular septal defect

Atrioventricular septal defects (AVSDs) are associated with displacement of the AV conduction system, as the compact AV node occupies an inferior position outside of Koch's triangle, anterior to the mouth of the coronary sinus and adjacent to where posterior rims of atrial and ventricular septae unite [43–45]. The common bundle extends along the lower rim of the ventricular septum. This inferior course and relative hypoplasia of the left anterior hemifascicle gives rise to the superior QRS axis typical of AVSD [46,47].

In 18 patients with AVSDs, preoperative electrophysiologic studies revealed sinus node dysfunction in only one, supra-Hisian first degree AV block in five, and intraatrial conduction delay in the majority [38]. Following surgical repair, atrial fibrillation or flutter may develop in 5% of patients [48,49]. Persistent complete AV block occurs in 1–7% of patients during the immediate postoperative period and approximately 2% thereafter [49–52]. Prolonged infra-Hisian conduction time may be a marker for increased risk of late AV block, even in the presence of a normal PR interval [53]. Although increased ventricular

ectopy has been described in up to 30% of patients, complex ventricular arrhythmias occur most commonly in the setting of left-ventricular dysfunction [49].

Left-ventricular outflow tract obstruction

Congenital heart defects with left-ventricular outflow tract obstruction include subvalvar, valvar and supravalvar aortic stenosis. Increased wall stress with secondary left-ventricular hypertrophy is related to the severity of obstruction and is thought to predispose the patient to ventricular arrhythmias [54–56]. In adults with unoperated aortic stenosis, 34% of patients compared with 6% of controls were found to have high grade ventricular ectopy on Holter monitoring [54]. Correlations with lower left-ventricular ejection fraction and higher wall stress were later demonstrated [55,56].

The risk of sudden death persists after surgical repair, warranting careful follow-up. Indeed, in a population-based study of sudden death after surgery for congenital heart disease, the subgroup at highest risk had aortic stenosis, with an incidence of 3% and 20% at 10 and 30 years respectively [12]. Aortic coarctation was also among the highest risk congenital subtypes [12].

L-transposition of the great arteries

In 'congenitally corrected' transposition of the great arteries (L-TGA), atrioventricular and ventriculoarterial discordance coexist, such that the right ventricle is systemically positioned. L-TGA is associated with marked displacement of the AV conduction system. The AV node is located outside Koch's triangle, and is displaced anteriorly and slightly more laterally [57,58]. An elongated common bundle of His runs medially towards the septum to the site of fibrous continuity between the right-sided mitral valve and pulmonary artery. The common bundle then courses along the anterior rim of the pulmonary valve and, if a VSD is present, continues along its upper rim [57,58].

In a study of 107 patients with L-TGA, with a mean of age 22 years, complete AV block occurred in 22% of cases [59]. The risk of AV block was estimated to be 2% per year, irrespective of associated anomalies. Following electrophysiologic testing, the site of AV block was found to be above or within the area that generated His-like electrograms [60–62]. This finding is consistent with clinical and pathologic observations: a stable narrow QRS escape rhythm often accompanies complete AV block [59] and fibrosis of the common bundle is noted histologically [61,63,64]. As the AV node and elongated bundle appear particularly susceptible to catheter or surgical trauma, caution should be exercised with manipulation to these areas. Complete AV block follows surgical repair of an associated VSD in more than 25% of patients [59,65–67].

Ebstein's anomaly

In Ebstein's anomaly, the tricuspid valve is displaced apically, creating an 'atrialized' portion of the right ventricle that is morphologically and electrically right ventricle but functionally right atrium [68]. Mechanical stimulation of the 'atrialized' ventricle may provoke ventricular arrhythmias, but spontaneous ventricular tachycardia is otherwise uncommon in the absence of associated malformations [69].

In patients with Ebstein's anomaly, accessory AV and atriofascicular pathways are found in 25% of pateints, and are more often right-sided and multiple than accessory pathways in structurally normal hearts [68,70,71]. In addition to AV reciprocating tachycardia, ectopic atrial tachycardia and atrial fibrillation or flutter can occur. Tolerance to tachyarrhythmias is dependent on the severity of Ebstein's malformation that can range from mild and asymptomatic to severe, with associated tricuspid regurgitation, large ASD, cyanosis and hemodynamic compromize. Sudden death may occur as a result of severe cyanosis or rapid conduction of atrial fibrillation or flutter to the ventricles via high-risk or multiple pathways [71].

In general, the complexity of mapping and ablation procedures is increased by associated malformations, multiple pathways, catheter stability and sometimes misleading signals within the 'atrialized' ventricle [72]. The latter limitation may be addressed by identifying the true AV groove along which accessory pathways are found, using techniques such as right coronary angiography (FIGURE 1) or insertion of very thin multielectrode catheters inside the right coronary artery. Of 65 patients with Ebstein's anomaly and accessory pathways, short-term success rates ranged from 75 to 89%, depending on pathway location (septal vs free wall), with late recurrences in up to 32% of patients [73].

If surgical correction is warranted, arrhythmia management should be coordinated with the surgical team [74]. This may include a preoperative electrophysiologic evaluation and catheter ablation, as perioperative arrhythmias may lead to hemodynamic instability in the presence of accessory pathways [75]. In selected patients, surgical division of accessory pathways may be considered.

Heterotaxy syndromes

Heterotaxy syndromes refer to disorders of lateralization, whereby the arrangement of abdominal and thoracic viscera differ from normal (situs solitus) and mirror image of normal (situs inversus). These syndromes are estimated to occur in 1–2 infants per 10,000 births and are frequently associated with severe congenital cardiac malformations [4]. Although there is tremendous variability, heterotaxy syndromes are generally characterized as either right atrial isomerism (asplenia syndrome) or left atrial isomerism (polysplenia syndrome).

Patients with right atrial isomerism often have two separate sinus nodes, at the junctions of right- and left-sided superior vena cavae with atrial chambers [76,77]. This is often reflected electrocardiographically as a P-wave axis that fluctuates as the prevailing pacemaker shifts from one sinus node to the other [78]. By contrast, the majority of hearts with left atrial isomerism do not have a histologically recognizable sinus node. When present, it is hypoplastic and located posteroinferiorly, far from the orifice of the superior vena cava [77,79]. As a result, slow atrial rates and junctional escape rhythms are common [79].

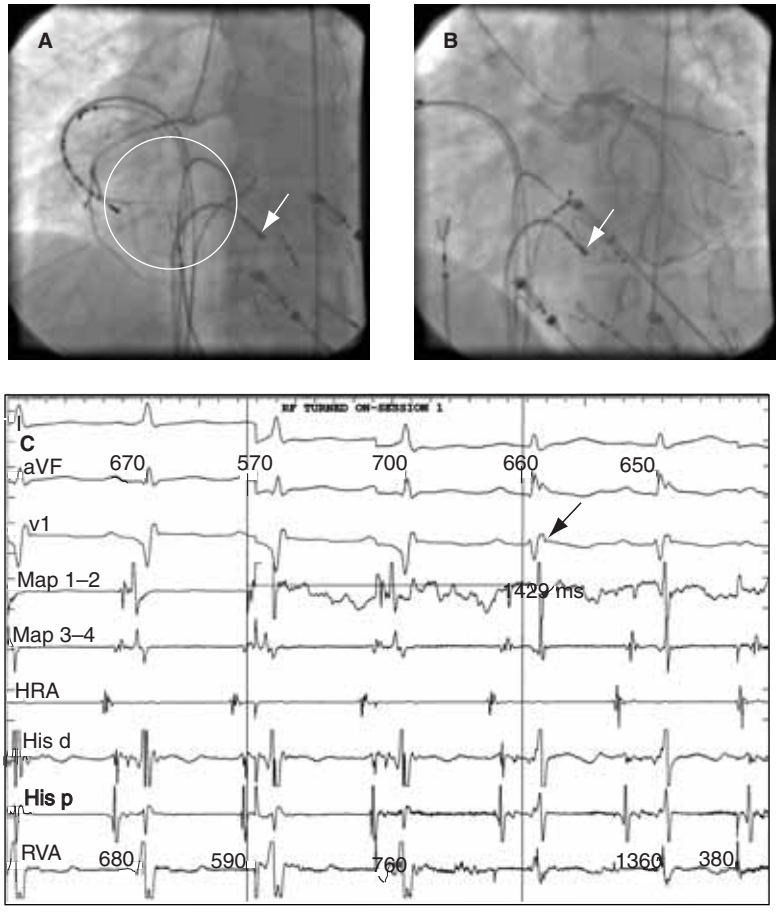


Figure 1. Ebstein's anomaly and catheter ablation of an accessory pathway. Panel A depicts right coronary angiography in a LAO view that displays the tricuspid annulus (indicated by the white circle) in a 'clock face' orientation. The white arrow shows the position of the ablation catheter in a right inferior paraseptal position. Note the absence of a posterior descending artery from the right coronary artery. Panel B depicts angiography of the dominant left coronary artery in an LAO view demonstrating the relationship between the artery and ablation catheter (white arrow). In Panel C, I, aVF and V1 indicate respective surface leads. Maps 1–2 and 3–4 record intracardiac signals at the distal and proximal electrode pairs of the ablation catheter, positioned as shown in panels A and B. His d, His p, HRA and RVA indicate intracardiac electrogram recordings from the distal and proximal His catheter, high right atrium, and right ventricular apex. RF energy is applied. The black arrow signals the first non-preexcited beat, less than 1.5 s into the RF application, as conduction via the right inferior paraseptal accessory pathway, was eliminated successfully.
HRA: High right atrium; LAO: Left anterio oblique; RF: Radiofrequency; RVA: Right-ventricular apex.

In patients with left atrial isomerism, complete AV block presents either at birth or occurring in later life is noted in approximately 15% of cases [78,80]. AV block appears to be less common in right atrial isomerism, but case reports have described congenital AV block [76] and sudden death [81]. In a detailed account of the histopathology of the AV conduction system in 13 patients with isomerism, all four patients with right atrial isomerism had anterior and posterior AV nodes and penetrating bundles [77]. In only one patient was there a discontinuity between the anterior AV node and corresponding bundle. However, of the nine patients with left atrial isomerism, two had anterior and posterior nodes not connected to AV bundles. Both had L-looped and/or single ventricles. All three patients with D-looping and two ventricles had a single posterior AV node connected to an AV bundle. A connecting sling of tissue, known as Monckeberg's sling [82], between the parallel conduction systems was identified in all patients with twin nodes.

In patients with heterotaxy syndromes, clinical tachyarrhythmias are less frequent than bradyarrhythmias. Twin AV node reciprocating tachycardia (FIGURE 2), IART and Wolff-Parkinson–White have been described [78,82,83]. When brady- or tachyarrhythmias do arise, appropriate pharmacologic, device and/or transcatheter therapy should be considered promptly, as underlying structural abnormalities may predispose to hemodynamic instability.

Single ventricle physiology

By definition, patients with tricuspid atresia have no right-sided AV connection. The septal leaflet of the tricuspid valve that normally forms one border of Koch's triangle is absent. Therefore, the usual anatomic landmarks demarcating the location of the AV node cannot be applied. Pathologic studies in tricuspid atresia have suggested that the compact AV node is typically situated on the floor of the right atrium, adjacent to an abnormally formed central fibrous body [84,85]. A small 'dimple' lined with endocardium is found just anterior to the os of the coronary sinus and has been considered to indicate the theoretic site of the absent tricuspid valve [84]. The AV node is found within the confines of the coronary sinus, tendon of Todaro and right atrial 'dimple'. It pierces the central fibrous body to become the penetrating His-bundle, along the left side of the septum. The remaining course of the His–Purkinje system is, to some extent, dependent on the presence and location of associated VSDs. In general, the His-bundle is further leftward and away from more anterior septal defects [85].

Atrial fibrillation, IART and catheter-induced ventricular fibrillation and asystole have been described in tricuspid atresia [86]. The authors reported a case of successful slow pathway ablation in a patient with AV node re-entrant tachycardia [87]. The fast pathway region was mapped electroanatomically during tachycardia and with constant rate ventricular

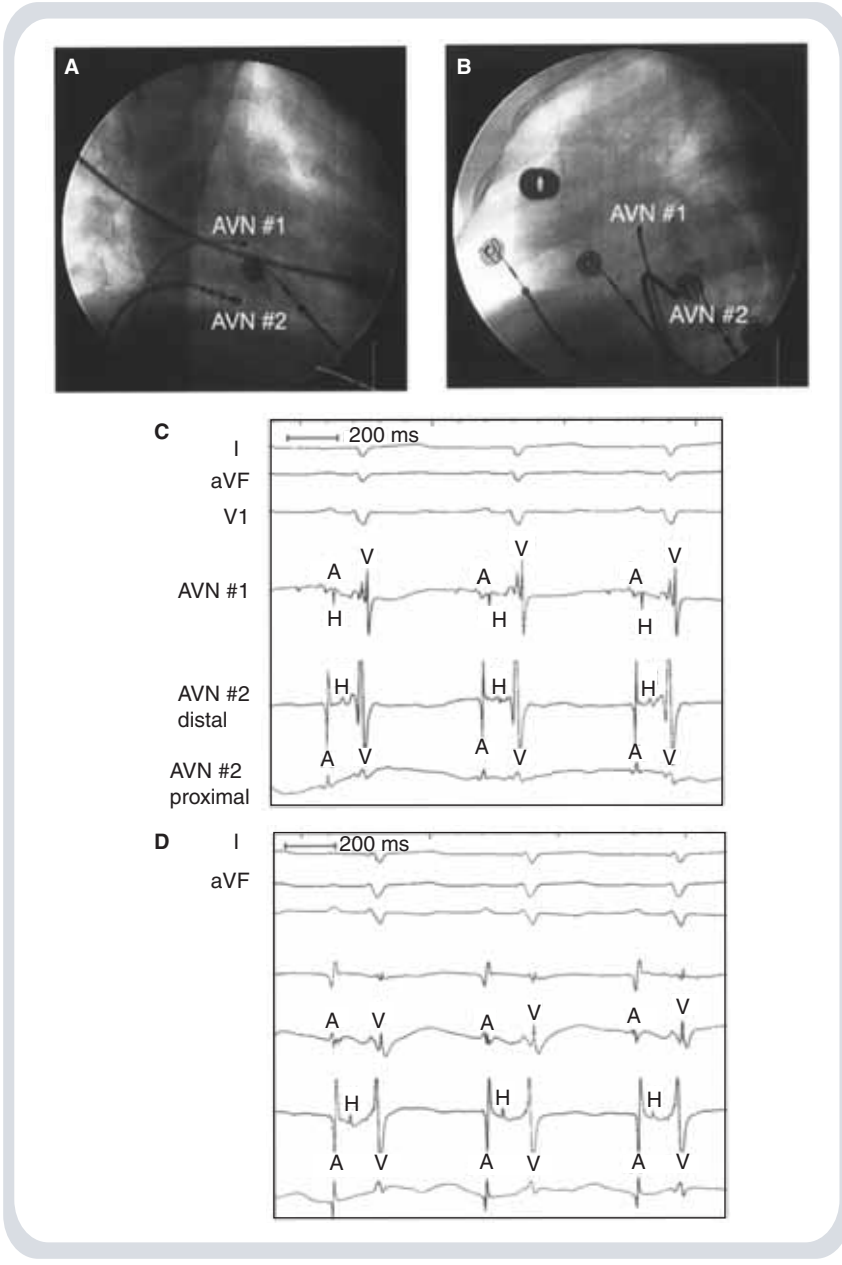


Figure 2. Mönckeberg's sling. In a patient with a double outlet right ventricle, pulmonary atresia and AVSD, electrode catheter tips in the AVN #1 and inferior (AVN #2) AV nodes in (A) anteroposterior and (B) left anterior oblique views. Supraventricular reciprocating tachycardia through a circuit involving both AV nodes was induced by atrial pacing and one premature impulse. (C) Surface leads I, aVF and V1 and intracardiac electrograms at both nodal sites are depicted before ablation. Note the distinct His-bundle deflection at each AV node. (D) Radiofrequency ablation of the superior node resulted in elimination of the His bundle deflection at AVN #1 and an increased HV interval from 57 to 90 ms at AVN #2. Prolongation of the HV interval in one node following ablation of the second node suggests that conduction tissue connects the two as pre-excitation across this 'sling' is eliminated. The arrhythmia was not inducible after ablation and has not recurred since. Reproduced with permission [82].
A: Atrial signal; AV: Atrioventricular; AVN #1: right atrium indicate location of superior; AVSD: Atrioventricular septal defects; H: His-bundle signal; V: Ventricular signal.

pacing. Successful radiofrequency ablation was achieved by placement of lesions in an area adjacent and inferior to the His-bundle electrogram on the left side of the septum.

In considering the course of the conduction system and potential for AV block in other forms of single ventricle physiology, it is important to note the type of ventricular looping and whether the dominant ventricle is right or left. The most conspicuous abnormalities in the location of the AV conduction system occur in single ventricles with AV discordance and AVSD. In the case of an L-looped single left ventricle, in the presence of two AV nodes, the posterior one does not usually make contact with the ventricular septum [45]. The elongated course of the common bundle renders it susceptible to fibrous degeneration and complete AV block [88]. With ventricular D-looping and a dominant right ventricle, the AV node is positioned within its usual landmarks and the common bundle enters the ventricular septum directly [89].

Fontan procedure

Developed in 1971 as surgical palliation for tricuspid atresia [90], the Fontan procedure has undergone multiple modifications to become the procedure of choice for various forms of single ventricle physiology. Atrial arrhythmias after the Fontan procedure are challenging problems in the field of adult congenital electrophysiology. These arrhythmias occur in the context of single functional ventricles and may be associated with substantial morbidity and mortality. Rapid hemodynamic deterioration and heart failure may ensue. Moreover, these arrhythmias are notoriously resistant to anti-arrhythmic pharmacologic therapy.

Depending on the particular type of repair, IART or atrial fibrillation may occur in up to 57% of patients [91]. Tachycardia circuits may be complex and/or multiple [26,92–95]. Using such tools as three-dimensional mapping systems and irrigated-tip ablation electrodes, acute success rates in dedicated experienced centers now exceed 80% [96–98]. Recurrences, however, occur in 30–45% of patients with a median time of less than 6 months, and infrequently after 12 months [96,99,100]. A prospective, randomized, nonblinded study compared irrigated-tip to standard radiofrequency catheter ablation in 26 patients (47 atrial tachyarrhythmias) with congenital heart disease [101]. The operator was limited to use of the assigned therapy for the first 6 min of

ablation. Although no difference in success rates was noted within the 6-min randomization period, crossover from standard to irrigated ablation was more likely to be successful than vice versa and overall success was greater using irrigated catheters.

Patients with failing Fontans and refractory atrial arrhythmias should be considered for surgical conversion to a lateral tunnel or extracardiac conduit with concomitant arrhythmia surgery. This typically includes debulking the right atrium, removing thrombus, excising right atrial scar tissue, epicardial pacemaker implantation, a modified right atrial Maze procedure and, in patients with prior documented atrial fibrillation, a left-sided Maze procedure as well [102,103]. Left-sided Maze procedures are not recommended on a routine basis and should be guided by the clinical scenario and preoperative electrophysiologic study, given the longer ischemic time required, with possible detriment to the compromized patient coming off bypass [102,103]. Case series with short-to-term follow-up report promising results, with arrhythmia recurrence rates of 13–30% [102–106]. On short to medium-term follow-up, advantages of the extracardiac in comparison with the intracardiac lateral tunnel Fontan include a decreased incidence of sinus node dysfunction [107], although not consistently so [108]. However, in the event of recurrent IART, transbaffle puncture to access the arrhythmia circuit for transcatheter ablation may be higher risk with extracardiac baffles.

Tetralogy of Fallot

Tetralogy of Fallot (ToF) is the most common cyanotic heart disease beyond infancy, accounting for approximately 10% of all congenital heart malformations [109]. Intracardiac repair has been performed for more than 40 years with excellent results [110]. However, atrial incisions are commonly made at the time of repair, predisposing to the late development of IART [111,112]. Moreover, sudden cardiac death has consistently been found to be the single most common cause of mortality late after repair [113,114]. In a cohort study of 793 patients with repaired ToF who were monitored for 35 years, 10% developed atrial flutter, 11.9% experienced sustained ventricular tachycardia and 8.3% died suddenly [112]. Very few arrhythmic events occurred within the first 5–10 years following corrective surgery. Thereafter, there was an appreciable, slow but steady decline in freedom from atrial and ventricular arrhythmias and sudden cardiac death [112,114–116]. In 1997, Nollert and colleagues reported their data on long-term survival of surgically repaired patients with ToF, excluding those who died within the first postoperative year [114]. Of the 490 patients, actuarial survival rates were 97, 94, 89 and 85% at 10, 20, 30 and 36 years, respectively.

Patients with IART may have typical isthmus-dependent flutter and/or incision-related macrore-entrant circuits [26,92,99,117]. Development of IART may herald worsening ventricular function and tricuspid regurgitation [111,112,118,119]. Hemodynamic compromize may be precipitated in some, and acute management is dictated by the level of clinical stability. Reassessment of the repair and consideration for electrophysiologic testing and ablation may be indicated.

Given the small but undeniable risk of ventricular arrhythmias and sudden cardiac death post-ToF repair, considerable efforts have been directed towards identifying predictors allowing stratification of patients into high- and low-risk categories. In the largest cohort study to date with a mean follow-up of 21.1 years, independent risk factors for sustained ventricular tachycardia were QRS interval of 180 ms or more(relative risk [RR] 8.8) and an annual increase in QRS duration (RR 1.1 for each 1 ms increase/year) [112]. Early lengthening of the QRS interval post-ToF repair results from surgical injury to the right bundle branch and myocardium [120], whereas later broadening reflects right ventricular dilation [121,122]. In addition to QRS duration and its rate of change, independent predictors of sudden death include older age at repair (RR 1.1/year of age) and presence of a transannular right ventricular outflow tract patch (RR 11.7). Patients with ventricular

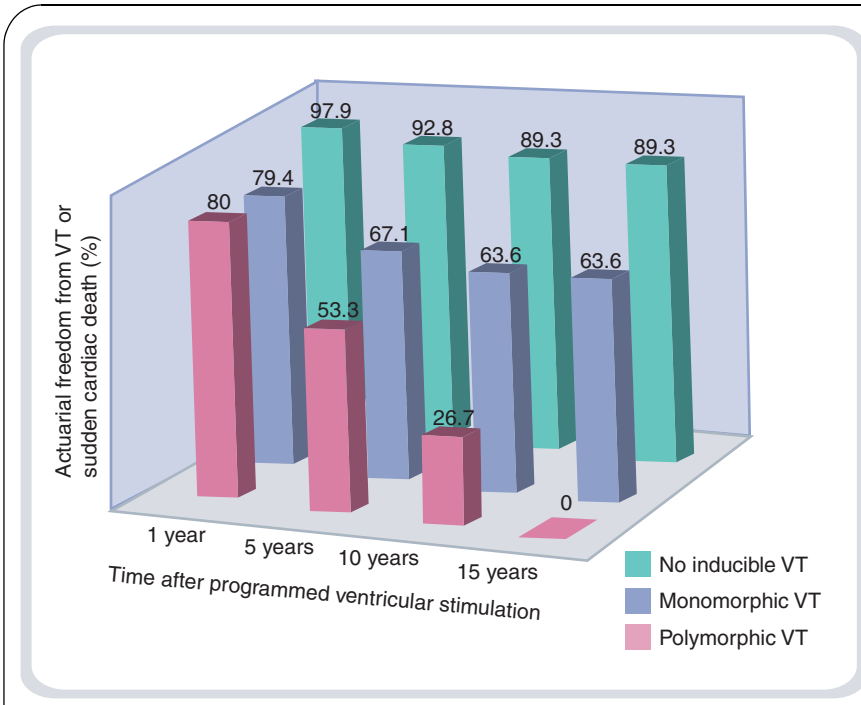


Figure 3. Value of programmed ventricular stimulation in tetralogy of Fallot. Actuarial freedom from VT and sudden cardiac death is depicted in patients with no inducible VT, inducible monomorphic VT and inducible polymorphic VT at 1, 5, 10 and 15 years following programmed ventricular stimulation. Adapted from [8].

VT: Ventricular tachycardia.

tachycardia or sudden cardiac death were more likely to have increased cardiac:thoracic ratios, at least moderate pulmonary and tricuspid regurgitation and peripheral pulmonary stenosis. A higher QT dispersion was also noted, believed to reflect increased heterogeneity in myocardial repolarization. Other reported risk factors include frequent ectopic beats [123], increased right ventricular systolic pressures [115,124,125], complete heart block [115,126] and increased JT dispersion [127,128].

The authors conducted a multicenter cohort study to assess the prognostic value of programmed ventricular stimulation [8]. A total of 252 patients with surgically repaired ToF and programmed ventricular stimulation studies were enrolled from eight centers. Mean follow-up after corrective surgery and electrophysiologic testing was 18.5 ± 9.6 and 6.5 ± 4.5 years, respectively. Clinical ventricular tachycardia and/or sudden cardiac death occurred in 24.6% of patients. Independent risk factors for inducibility of sustained ventricular tachycardia were 18 years or older at study (odds ratio [OR] 3.3), palpitations (OR 2.8), prior palliative surgery (OR 3.1), modified Lown's criteria of 2 or more (OR 5.6), and cardiothoracic ratio of 0.6 or more (OR 3.3). As shown in FIGURE 3, event-free survival rates in noninducible and inducible patients at 1, 5, 10 and 15 years were 97.9, 92.8, 89.3 and 89.3% versus 79.4, 62.6, 58.7 and 50.3%, respectively ($p < 0.0001$). Inducible sustained ventricular tachycardia was an independent risk factor for subsequent clinical ventricular tachycardia or sudden death (hazard ratio [HR] 4.7).

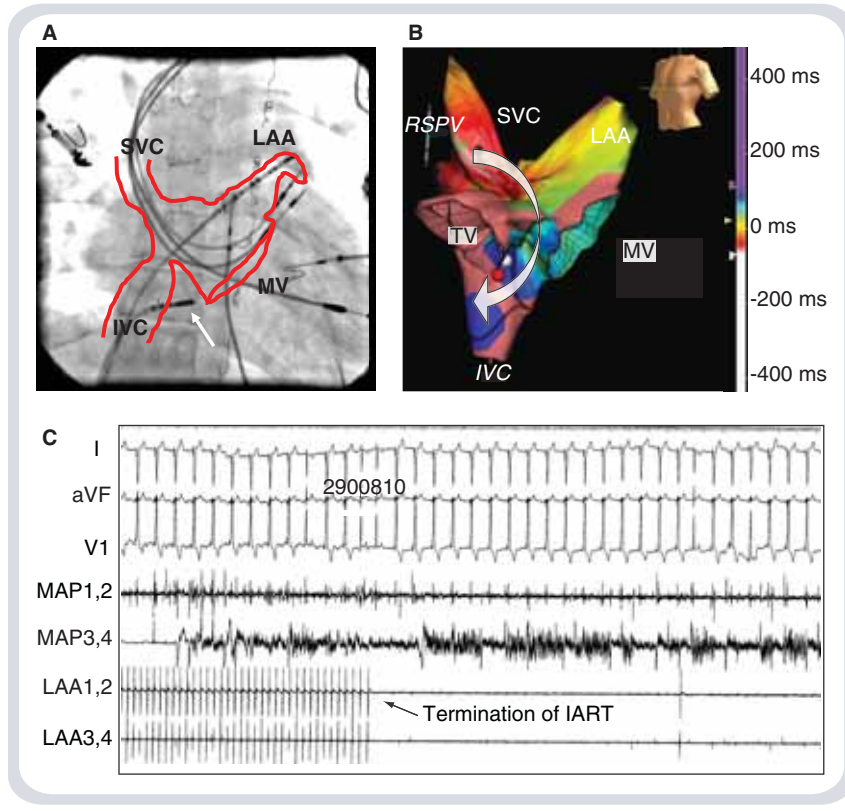


Figure 4. Transcatheter ablation of IART in a patient with a Senning procedure. Panel A depicts angiography of a Senning baffle, outlined in red, in a patient with a dual chamber pacemaker and symptomatic recurrent IART. The white arrow indicates position of an 8-mm tip radiofrequency ablation catheter at the site of successful IART entrainment and ablation. To access the pulmonary venous atrium, the catheter was positioned across a baffle leak. Panel B illustrates a left anterior oblique view of a 3D electroanatomic map. Local activation times in tachycardia are color-coded, using left atrial appendage as a reference. Earliest to latest signals are colored white, red, yellow, green, light blue, dark blue and purple, respectively. The large curved arrow indicates direction of an IART circuit involving the cavotricuspid isthmus. The white dot represents the site of successful entrainment and ablation in the pulmonary venous atrium, corresponding to the arrow in Panel A. Two additional ablation lesions (red dots) completed the line of block. In Panel C, the first three tracings are surface leads I, aVF, and V1 at 10 mm/s. Map 1,2 and 3,4 record endocardial signals from proximal and distal electrode pairs of the ablation catheter during a radiofrequency application. Intracardiac tracings from the left atrial appendage (LAA 1,2 and 3,4) initially display the IART that terminates during ablation, followed by a 16 s sinus pause with a ventricular paced rhythm, indicative of underlying sinus node dysfunction.
IART: Intra-atrial re-entrant tachycardia; IVC: Inferior vena cava; LAA: Left atrial appendage; MV: Mitral valve; RSPV: Right superior pulmoary vein; SVC: Superior vena cava; TV: Tricuspid valve.

Further studies are required to determine the utility of programmed ventricular stimulation in risk stratification algorithms. In addition, while early surgical intervention for residual pulmonary regurgitation with or without concomitant intraoperative ablation appears to halt the progression of right ventricular dilation, protective effects on ventricular arrhythmias and sudden death remain to be defined [119,129,130].

D-transposition of the great arteries

In 'complete' transposition of the great arteries (D-TGA) the atrioventricular relationship is preserved, but ventriculoarterial discordance is present. D-TGA accounts for 5–7% of all congenital cardiac malformations 109]. In the absence of a shunt allowing for mixing between the parallel systemic and pulmonary circulations, D-TGA is incompatible with life. Indeed, if untreated, 90% of infants die within the first year [131].

In 1959, Senning introduced an intra-atrial baffle repair redirecting systemic and pulmonary venous return without the use of grafts or prostheses [132]. In 1964, Mustard described an alternative technique for creating an intra-atrial baffle using a pericardial patch [133]. Although arterial switch surgery [134] has now supplanted atrial correction as the procedure of choice in many centers, the large majority of adults with D-TGA have had intra-atrial baffle repairs. Late complications include sinus node dysfunction, atrial tachyarrhythmias, baffle leaks, obstruction to

systemic and/or pulmonary venous return, systemic right ventricular dysfunction and sudden cardiac death [135]. The most common cause of late mortality after an intraatrial baffle for D-TGA has consistently been reported to be sudden death [11,12,136–140].

Of the 478 patients who survived the perioperative period after Mustard repair, bradyarrhythmias increased steadily over time [137]. The actuarial rate of loss of sinus rhythm was 39 and 60% at 10 and years, respectively. Atrial flutter and ectopic atrial tachycardia occurred in 14 and 1% of patients, respectively. The actuarial rate of atrial flutter 20 years after repair was 24%. Loss of coordinated atrial activity and rapid ventricular rates can result in severe symptoms and hemodynamic compromise. Attempts to maintain sinus rhythm are usually warranted due to poor hemodynamic tolerance. As depicted in FIGURE 4, catheter ablation of IART can be effective but often requires access to the tricuspid valve isthmus on the pulmonary venous side of the circulation via a retrograde or transbaffle approach [99].

Development of atrial arrhythmias is also associated with impaired ventricular function [141,142] and increased risk of sudden death in some, but not all, studies [143]. In a retrospective multicenter case-control study that identified 47 patients with D-TGA and Mustard or Senning surgery who experienced sudden death, risk factors included the presence of symptoms of arrhythmia or heart failure and history of documented atrial fibrillation or flutter [144]. The electrocardiogram, chest x-ray and Holter findings were not predictive of sudden death and medical therapy, and pacemakers were not found to be protective.

Reports have yielded conflicting opinions as to whether the type of atrial reconstruction, such as Mustard or Senning, is associated with different risks regarding specific complications and overall survival. Proponents of the Senning procedure advance that minimal, if any, nonviable tissue or prosthetic material favors future growth and optimizes atrial function, with potential reduction in pathway obstruction and arrhythmias [145–148]. Supporters of the Mustard procedure have claimed lower mortality, reduction in systemic and pulmonary venous obstruction and decreased incidence of arrhythmias [135,149–152]. The authors performed a meta-analysis comparing outcomes in 885 patients from seven studies with Mustard and Senning baffles [153]. Sinus node dysfunction was more commonly observed in patients with Mustard procedures. Data regarding atrial tachyarrhythmias were inconclusive. A trend towards lower mortality favored patients having undergone the Mustard procedure (HR 0.63, p = 0.13), perhaps in part owing to less pulmonary venous obstruction and residual shunting.

Expert commentary & five-year review

A thorough understanding of conduction system variants, arrhythmia mechanisms and underlying anatomy and physiology is imperative to the safe management of arrhythmias in ACHD, be it by pharmacologic, transcatheter, devic, and/or surgical approaches. As such, these complex patients should be referred to national or regional ACHD centers with expertise in electrophysiology and a multidisciplinary team-based approach. For example, surgical methods can assist in areas not amenable to transcatheter interventions and, failing all other options, cardiac transplantation may be considered.

The next 5 years are likely to witness a more thorough appreciation of the incidence, subtype and risk factors for various arrhythmias in ACHD. Risk stratification algorithms will be refined, permitting a more accurate identification of the subgroup of patients at highest risk of ventricular arrhythmias and sudden death. With a clearer notion of high-risk patients, collaborative multicenter randomized studies may begin to assess preventive therapies against sudden death, overcoming some limitations inherent to the heterogeneous nature of the patient population. In parallel, technologic advances in transcatheter arrhythmia ablation may result in improved procedural outcomes. 3D electroanatomic mapping systems are becoming fully integrated with imaging techniques, including computerized tomography and magnetic resonance imaging. Local activation times and voltages will be superimposed on imaged 3D anatomy, providing an unprecedented degree of structural detail. In addition, robotic and stereotactic catheter navigation will facilitate catheter contact and creation of linear lesions for arrhythmia substrates that are currently accessed suboptimally with available technology.

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Key issues

- Patients with adult congenital heart disease represent a heterogeneous population with diverse underlying diagnoses and arrhythmic issues. The past decade has witnessed huge strides in our understanding of arrhythmia mechanisms and therapeutic options in such patients.
- Sudden cardiac death of presumed arrhythmic etiology is the leading cause of mortality in adult congenital heart disease.
- Sinus node dysfunction is common in adults with left atrial isomerism and Mustard, Senning or Fontan surgery.
- Complete atrioventricualar block may complicate the clinical course of patients with L-looped ventricles and/or left atrial isomerism.
- Right atriotomy and atrial surgery is associated with scar-based intra-atrial re-entrant tachycardia circuits, as in surgically repaired atrial septal defects, Mustard and Senning baffles and tetralogy of Fallot.
- Ventricular arrhythmias and sudden death threaten a smaller subset of patients, most notably adults with left-sided obstructive lesions, D-transposition of the great arteries and intraatrial baffles, tetralogy of Fallot and severe ventricular dysfunction.

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