Risk factors of supraventricular arrhythmia in adults with congenital heart disease

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Abstract

Background: Supraventricular arrhythmia (SVA) is a frequent clinical complication in adult patients with congenital heart disease (CHD). The aim of this study is to perform a prognostic evaluation of congenital heart defect complexity, performed cardiac surgery, initial functional impairment of the heart — NYHA > I, cyanosis, age and sex of the adult patients with CHD, presenting for the first time to an outpatient clinic, on SVA occurrence during long-term observation.

Methods: We looked at 1,304 patients (586 men), aged 18–72 years (mean 29.4 ± 10.6 years), and followed-up from 1995 to 2004. The mean observation period was 3.52 ± 1.83 years. SVA in the form of atrial flutter/fibrillation (AF/FLA) and supraventricular tachycardia was observed in 133 patients, 10.3% of the study population. Ten-year follow-up showed that the likelihood of SVA occurrence in the whole studied population after two years was 5.2%, and 14.4% after ten years.

Results: Univariate analysis proved that the incidence of SVA is greater in patients with complex heart defects (p = 0.0001), those not previously operated upon (p = 0.0001), those with baseline impairment of cardiac function (NYHA > I; p = 0.0001) and those with cyanosis (0.0001). The patient’s sex seems to have little significance. Cox regression analysis showed that baseline heart failure is the strongest risk factor for SVA (HR = 4.66). Congenital heart defect complexity (HR = 2.31) and the patient’s age are also significant prognostic factors of this arrhythmia (HR = 1.32). Cardiac surgery, cyanosis and patient sex are not significant in prognosis.

Conclusions: Baseline impairment of heart function, heart defect complexity and patient’s age all increase the risk of SVA in the population of adults with congenital heart disease. Cyanosis and the lack of cardiac surgery in the past led to a higher incidence of the analyzed arrhythmia but are not risk factors for its occurrence. Gender has no prognostic significance for SVA. (Cardiol J 2009; 16, 3: 218–226)

Key words: adult patients with congenital heart disease, supraventricular arrhythmia
Introduction

Supraventricular arrhythmias (SVA) are a frequent clinical complication seen in adult patients with congenital heart disease (CHD). They often lead to hospitalization, serious deterioration of heart function and death [1, 2]. The pathogenesis of this arrhythmia in adults is complex and it stems from: a) primary anomalies in the conduction pathways, b) atrial enlargement, followed by its dilation/distension, fibrosis and increased wall tension leading to inhomogeneity of electric stimulation, c) presence of postoperative scarring, aiding in slowed impulse transduction 'incisional reentry', d) deterioration of ventricular function: SVA result from hemodynamic dysfunction but can at the same time lead to progression of dysfunction, e) impairment of sinus function, facilitating recurrent arrhythmia [3–9].

As a result, optimal management of complex patients should involve the specialist cardiologist in adults with congenital heart disease, as well as an electrophysiologist or surgeon with a particular interest and experience in this area. Rational treatment of this scarce but constantly growing population requires sound knowledge of risk factors related to the discussed arrhythmia. The presented pathomechanisms of SVA indicate that its occurrence is influenced by anatomical complexity of the defect, past cardiac surgery and initial impairment of cardiac function. Blood desaturation and the age of the patient seem to play some role as well. The available studies usually relate to patients affected by particular defects [3–6, 10, 11]. There are no risk factor analyses available for SVA in the long-term observation of the adult population with congenital heart disease carried out by a single specialized clinical facility.

This study aims at the prognostic evaluation of selected parameters defining adult patients with CHD who presented to an outpatient clinic for the first time, in the context of SVA incidence in long-term follow-up. The considered variables included: congenital heart disease complexity, previous cardiac surgery, initial impairment of cardiac function — NYHA class > I, presence of cyanosis, patients' age and sex.

Methods

We looked at 1,304 patients with CHD (718 women and 586 men), aged 18 to 72 years (mean 29.1 ± 0.6 years), who were treated in the Adult Congenital Outpatient Clinic at the Poznan Medical University between 1995 and 2004. Simple defects occurred in 886 patients (which amounted to 67.9% of the studied population) 418 patients presented with complex defects (32.1%) and 962 (73.7%) patients were operated on at the mean age of 9.8 ± 8.5 years; 78 (5.9%) patients were cyanotic and 108 (8.4%) presented with baseline impairment of cardiac function (NYHA > I).

Baseline clinical analysis

A detailed medical history was taken, including the type and frequency of past cardiac surgery, a thorough physical examination, electrocardiography and echocardiography which allowed for verification of, or arriving at, a clinical diagnosis. Hemodynamic assessment was performed only in cases of inconclusive diagnostic results, in order to evaluate pulmonary pressure and resistance of pulmonary arteries as well as anomalies of the coronary arteries. If patients presented with more than one cardiovascular anomaly, they were put into groups according to the hemodynamically dominant defect. Based on a classification approved by Jane Somerville, the chairman of experts of the British Cardiac Society Working Party [1], the population of patients was divided into a group of patients with simple, and another group with complex, congenital heart anomalies.

Table 1 presents numbers of patients with particular simple and complex congenital heart defects, demographic data, cardiac surgery data, cyanosis and initial impairment of heart function (NYHA > I).

Follow-up clinical analysis

Patients were observed for between one and ten years (mean 3.52 ± 1.83 years). Heart function was presented according to New York Heart Association (NYHA) functional classification. A minimum of class II NYHA was assumed as baseline cardiac functional impairment. Cyanosis was defined as pink coloration of the skin and mucous membranes with oxygen saturation not exceeding 85%, with exclusion of its extracardiac causes. Arrhythmias were recognized when diagnosed with electrocardiography during outpatient clinic observation, local hospital or general practitioner visits or using Holter monitoring (459 24-hour ECGs were performed). Serious SVA included supraventricular tachycardia (SVT) defined as at least five QRS complexes at a rate of > 100 beats/min [7] and atrial flutter/fibrillation (AF/FLA), diagnosed according to generally recognized criteria.

The study was approved by the bioethical committee and all patients gave their informed consent.
Statistical analysis

Continuous variables were presented as mean (standard deviation). Comparisons between the two groups were conducted using Student’s test for normally distributed continuous variables or Mann-Whitney test for those without normal distribution. \( \chi^2 \) or Fisher’s exact test was used for categorical variables. Kaplan-Meier curves were plotted to describe the cumulative probability of arrhythmia-free survival. The long-rank test was used to compare curves according to the patient’s sex, congenital heart disease complexity, presence of cyanosis, baseline impairment of cardiac function (NYHA > I) and by past cardiac surgeries. The aforementioned variables and the patient’s age that were thought to have a possible impact on occurrence of SVA in these patients were included in a multivariate Cox analysis. The results were reported as hazard ratios (HR) and 95% confidence intervals (CI). The statistical significance was assigned at a p value ≤ 0.05.

Results

Supraventricular arrhythmias, atrial flutter/fibrillation and supraventricular tachycardia were observed in 133 patients, 10.3% of the studied...
population. FA/FLA was diagnosed in 48 patients, 3.7% of the total, SVT in 85 patients, 6.6%. Tables 2 and 3 present the incidence of the analyzed arrhythmia for particular simple and complex CHD. Patients diagnosed with SVA were older than those without this arrhythmia: 37.3 ± 14.5 years vs. 28.6 ± 9.8 years (p = 0.0001). SVA incidence was greater in patients with complex lesions: 43 (4.9%) vs. 90 (21.5%); p = 0.00001, in patients without past cardiac surgery: 76 (8.2%) vs. 57 (16.7%); p = 0.00001, in patients with cyanosis: 36 (31.0%) vs. 97 (7.9%); p = 0.00001, and with baseline impairment of heart function (NYHA > I): 52 (47.8%) vs. 81 (6.8%); p = 0.00001, as compared with patients without the above clinical signs. There were no differences between males and females with respect to SVA incidence: 63 (10.7) vs. 70 (9.7%); p = 0.43.

Ten-year follow-up revealed that the likelihood of SVA for the whole studied population was after two years 5.2%, after five years 13.7% and after ten years 14.4% (Fig. 1). Univariate analysis proved that the probability of SVA in adults with CHD was also greater in patients with complex lesions (p = 0.00001), without a history of cardiac surgery (p = 0.0001), with baseline impairment of heart function (NYHA > I) (p = 0.0001) and cyanosis (p = 0.0001), as compared to patients without the above clinical signs. Gender does not seem to have much significance (p = 0.32; Fig. 2–6). Cox regression analysis showed that heart function impairment (NYHA > I) is the strongest independent risk factor for SVA (HR = 4.66). Congenital heart disease complexity (HR = 2.31) and patients’ age are also significant prognostic factors for this arrhythmia (HR = 1.32). No prognostic strength was associated with past cardiac surgery, cyanosis presence or gender (Table 4).

### Discussion

SVA were present in 10.3% of the observed adults with CHD. The likelihood of their occurrence equaled 5.2% after two years, 13.7% after five years and 14.4% after ten years. According to Jane Somerville, SVA is the most frequent clinical problem in that population. It occurred in 23% of her treated patients [1], a significantly higher rate than observed in our group. This is probably explained by in the higher number of patients with complex heart defects attending Royal Brompton Hospital presenting with this arrhythmia more frequently.

Our study pointed out the congenital heart defect complexity as an independent risk factor for SVA. It is also known that patients with complex CHD more often require surgery, as surgical
### Figure 1
Estimated survival free from supraventricular arrhythmia (SVA) in the entire studied population of adults with congenital heart disease.

### Figure 2
Estimated survival free from supraventricular arrhythmia (SVA) in the studied population of adults with congenital heart disease with respect to gender.

### Figure 3
Estimated survival free from supraventricular arrhythmias (SVA) in patients with complex and simple congenital heart disease.

### Table 3
Incidence of supraventricular arrhythmia in patients with complex congenital heart disease. Percentage of patients in the individual congenital heart disease subgroups.

<table>
<thead>
<tr>
<th>Heart Disease</th>
<th>Total</th>
<th>CoAo</th>
<th>ToF</th>
<th>ASD</th>
<th>CAVC</th>
<th>Eisen-</th>
<th>Single</th>
<th>Ebstein</th>
<th>DTGA</th>
<th>CCTGA</th>
<th>DORV</th>
<th>Pulmonary</th>
<th>CCA</th>
<th>BWG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Subjects</td>
<td>418</td>
<td>106</td>
<td>101</td>
<td>32</td>
<td>24</td>
<td>3</td>
<td>2</td>
<td>20</td>
<td>19</td>
<td>9</td>
<td>8</td>
<td>5</td>
<td>3</td>
<td>2</td>
</tr>
</tbody>
</table>

| FA+FLA (%) | 34 | 2 | 3 | 2 | 0 | 7 | 2 | 3 | 7 | 1 | 2 | 1 | 1 | 3 | 1 |
| SVT (%) | 56 | 7 | 11 | 4 | 7 | 4 | 2 | 12 | 2 | 2 | 0 | 1 | 0 | 0 | 1 |

### Notes
- FA+FLA+SVT (%) refers to the incidence of supraventricular arrhythmia in patients with complex congenital heart disease.
- Abbreviations as in Table 1.
Correction allows most to reach adulthood. However, the analysis performed showed that despite the reduced probability of SVA following surgical correction it does not predict the risk of this arrhythmia. Cardiac surgery improves hemodynamic parameters in the first place, yet postoperative scarring can turn out to be an additional arrhythmogenic factor and also lead to electrical remodeling. Therefore, adults with complex CHD visiting the outpatient clinic for the first time require particular monitoring for analyzed arrhythmia, regardless of their history of cardiac surgery.

Among adults with complex defects, SVA occurred most frequently in patients with functionally single ventricle. Significantly altered anatomy and Fontan operation led to increased pressure and dilation of the right atrium, as well as so-called ‘incisional tachycardia’ [9, 11, 12]. The analyzed arrhythmia in the transposition of the great arteries (DTGA), resulting from increased atrial pressure and presence of post-operative scarring in its wall after Senning/Mustard procedure, occurs in 35% to 50% of cases after 15 years of follow-up [13, 14]. Long-term observation of patients with DTGA after atrial correction was published by Moons et al. [10], who reported that after 20 years 43% of patients presented with SVA and 65% of them after 25 years. However, other authors say that ten years after surgery, sinus rhythm was retained in 95–98% of these patients [15]. In adults with congenitally corrected transposition of great arteries (CCTGA), discussed arrhythmia is associated with altered conducting fibers pathways observed in 2% to 4% of that group of patients and, resulting from tricuspid insufficiency, left atrial enlargement leading to electrical inhomogeneity [16–18].

The available literature states that patients operated for tetralogy of Fallot (ToF) present with SVA in 2% to 34% of cases [7, 19, 20]. This signifi-
significant discrepancy of data may be due to the fact that most patients with this anatomical defect have right bundle branch block, leading to diagnostic problems differentiating between supraventricular and ventricular arrhythmias [1]. In that group of patients, SVA is associated with increased pressure in the right atrium, secondary to elevated end-systolic pressure in the right ventricle resulting from postoperative pulmonary insufficiency [7, 8, 21]. Pulmonary regurgitation is usually the result of transannular patch use, which was applied to 92% of observed patients. Our population included only seven adults with ToF who had not undergone past surgical correction of this defect; one such person presented with persistent atrial fibrillation. The scope of surgical intervention affects the rate of SVA occurrence in patients with double outlet right ventricle [22]. In Ebstein’s anomaly, the substrate for SVA, observed in 25–40% of those patients is the right atrium, enlarged by the atrialised part of the right ventricle as well as fetal atrioventricular additional conducting pathways seen in 5–25% of them [4, 8, 23].

In patients with partial and common atrioventricular canal (ASDı and CAVC) this arrhythmia is enhanced by additional anatomical substrate of endocardial cushion defects [6, 24]. Subjects with different forms of common atrioventricular canal are also prone to analyzed arrhythmia due to scar formation after closure of septal defect and reconstruction of atrioventricular valves usually leaving significant mitral regurgitation [6, 12, 25]. Probably because of this, SVA was observed more often in the subgroup of patients with atrial septal defect (ASD) primum than in subjects with secundum atrial septal defect. Doubts about the impact of atrial septal defect closure in the adult population are far from being dispelled. Most researchers state that this arrhythmia incidence does not decrease after cardiac surgery but it can be more responsive to pharmacotherapy [26, 27]. Our observations showed that analyzed arrhythmia occurred more often in uno-perated patients (16.6% vs. 4.0%), in keeping with the findings of other investigators [28, 29].

The performed analysis showed that impaired cardiac function (NYHA > I) observed during the first visit was the strongest independent risk factor for supraventricular arrhythmias in long term follow-up. The relationship between this arrhythmia and heart failure has been confirmed by other authors. SVA, observed in about 70% of our patients with hearts of the single ventricle physiology is associated with its functional impairment and secondly with increased atrial pressure and, in consequence, atrial remodeling [11, 30]. Fontan repair delays, but does not prevent, hemodynamic deterioration which leads to increased incidence of discussed arrhythmia, appearing in 11% to 57% of those patients after 15 years of observation [11, 30, 31]. Supraventricular arrhythmias occurred in more than half of adults with Eisenmenger syndrome, usually presenting functional impairment [32]. Heart failure in this group of patients results from intracardiac shunts and growing tricuspid insufficiency leading to volume overload as well as right ventricular pressure overload due to increased pulmonary pressure [33, 34]. SVA is likely to be the result of right atrial volume overload, dilatation of its wall leading to ‘electrical remodeling’ [6, 26]. SVAs at the same time as impairment of cardiac function is also seen in patients with DTGA [14, 35, 36]. According to Harrison et al. [20], in patients after ToF total correction, the risk of SVA incidence is associated with a palliative shunt, which facilitates left ventricle failure, and also with pulmonary regurgitation, resulting in right ventricle failure [7]. It has been proved that impairment of cardiac function is a significant contributor of SVA in patients with Ebstein’s anomaly [37]. In adults with CCTGA the incidence of analyzed arrhythmia increases with the worsening of tricuspid regurgitation, influencing the function of the systemic ventricle [16, 18]. In patients after ASDı correction, a similar relationship exists between mitral regurgitation and left ventricle function [24, 25]. Among those with complex defects, SVAs appeared least frequently in patients with coarctation of the aorta, in whom they are likely the result of functional impairment due to hypertension and coronary heart disease [8, 38]. In the subgroup of simple defects, analyzed arrhythmia occurred mostly in patients with ASD. Age-related left-right shunt due to decreased left ventricle compliance and increased systemic pressure can lead to mitral regurgitation and a gradual deterioration of cardiac function. On the other hand, SVA enhances left-right shunt, which further impairs cardiac function [27, 28]. In adults with ventricular septal defect this arrhythmia occurs less frequently, usually in those who underwent cardiac surgery later in life, which entails functional impairment due to chronic left-right shunt [39, 40].

The ten-year observation of adults with congenital heart disease showed that the risk of SVA in all studied groups was higher in patients with cyanosis. Desaturation is always the result of serious anatomical and hemodynamic changes. According to Perloff et al. [41], it leads to significant myocardial changes, similar to chronic ischemia. However,
Cox regression analysis did not yield any prognostic value of this clinical feature. It can be explained by the fact that the majority (92%) of patients with cyanosis and SVAs presented with heart failure and also 89% of cyanotic patients represented complex anomalies. Statistical impact of desaturation was weaker in this analysis and eclipsed by both above-mentioned factors. Except for a single report pertaining to Ebstein’s anomaly, which confirmed the role of cyanosis as one of the risk factors of SVA, there is no known data documenting such a direct relationship [37].

Regression analysis showed that patient age is a significant risk factor for SVA. The results were undoubtedly influenced by the advanced age of the population presenting with this arrhythmia, the large group of patients with ASD and the age of the oldest subgroup of patients with Ebstein’s anomaly who also frequently presented with SVA. Literature data confirms that the incidence of this arrhythmia in patients with ASD and ventricular septal defect increases with age [28, 39, 40]. Other authors also claim that age is a risk factor for SVA in some complex defects, which has been documented in patients with previous Mustard [42], Fontan operation [43], with CCTGA [17] and after ToF correction [7, 20].

The sex of studied patients had no prognostic value in analyzed arrhythmia. The available literature also does not confirm any such relationship.

Conclusions

1. The initial impairment of heart function, congenital heart defect complexity and the patient’s age, all increase the risk of supraventricular arrhythmia in adults with congenital heart disease.
2. Cyanosis and the lack of a past cardiac operation lead to higher incidence of the analyzed arrhythmia, but are not risk factors for its occurrence.
3. A patient’s gender has no prognostic significance for supraventricular arrhythmias.

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References


38. Rosenthal E. Coarctation of the aorta from fetus to adult: Curable condition or the long disease process? Heart, 2005; 91: 1495–1502.


