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Behavior of Ebstein's Anomaly: Single-Center Experience and Midterm Follow-Up

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Key Words
Ebstein's anomaly · Adult congenital heart disease

Abstract
Objectives: Ebstein's anomaly, characterized by an apical displacement of the tricuspid valve into the right ventricle, occurs in approximately 1/200,000 live births. Because long-term follow-up data of adults with Ebstein's anomaly are scarce, we evaluated the outcome of our Ebstein's anomaly patients. ***Methods:*** All patients >16 years and registered in the congenital heart disease database of our hospital with isolated Ebstein's anomaly were selected for the study. Records were reviewed for outcome. ***Results:*** Forty-nine patients (21 males, mean age at diagnosis 29.1 ± 20.7 years) were followed for a mean time of 11.4 years (range 1.1–32.4). Twenty-five patients (51%) underwent tricuspid valve surgery (16 valvuloplasty and 9 valve replacement). Eight patients (32%) required redo tricuspid valve surgery. Twenty-six patients (52.1%) exhibited supraventricular arrhythmia, and the typical Wolff-Parkinson-White syndrome occurred in 15 patients (31.2%). Seventeen patients (34.7%) underwent ablation therapy and 5 patients (10.4%) required pacemaker implantation. ***Conclusions:*** Half of the patients with Ebstein's anomaly needed tricuspid valve surgery and redo surgery was not uncommon. Supraventricular arrhythmia occurred frequently and ablation therapy was often indicated. Careful follow-up is obligate, as some complications occur for the first time in adulthood.

Introduction

Ebstein's anomaly is a rare congenital heart defect that occurs in approximately 1 per 200,000 live births and accounts for <1% of all congenital heart diseases [1]. It is characterized by a malformation of the tricuspid valve, ranging from mild to severe [2]. The most important morphological feature of Ebstein's anomaly is the apical displacement of the tricuspid valve into the right ventricle. Other characteristics are adhesion of the septal and posterior leaflets to the underlying myocardium; redundancy, tethering and fenestrations of the anterior leaflet; dilatation of the atrialized portion of the inlet part of the right ventricle; and dilatation of the right-sided atrioventricular junction [1, 2]. In addition, Ebstein's anomaly is often associated with a patent foramen ovale (PFO) or an atrial septal defect (ASD; prevalence 80–94%) [3]. This structural anomaly often leads to tricuspid valve regur-

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gitation and elevated right atrial pressure. Therefore, the clinical presentation is mainly characterized by right-sided heart failure, atrial arrhythmias and cyanosis (secondary to a right-to-left shunt or low cardiac output) [1, 3]. However, mild forms might remain asymptomatic lifelong [3]. Finally, pre-excitation and Wolff-Parkinson-White (WPW) syndromes are not uncommon in patients with Ebstein's anomaly (prevalence 10–29%) [4]. To improve the outcome, structural repair (valvuloplasty, valve replacement) and/or ablation therapy are often indicated [1]. Because long-term follow-up data of adults with Ebstein's anomaly are scarce, we wanted to evaluate the outcome of our Ebstein's anomaly patients.

Methodology

Patient Selection

Patients were selected from the pediatric and adult congenital heart disease database of our hospital, which contains the medical records of 30,000 patients. We included patients >16 years, as the cutoff age for pediatrics in most European countries is 16 years. Out of these 30,000 patients we included 49 patients who have been followed for Ebstein's anomaly between 1976 and 2009. We included patients with an associated ASD or a PFO. Patients with associated more complex congenital cardiac diseases, such as double discordance, univentricular heart physiology, severe pulmonary valve stenosis, (multiple) ventricular septal defect(s) or associated cardiomyopathy, were excluded. Approval of the ethics committee of our hospital was obtained.

Review of the Medical Records

We reviewed the medical records on demographic features such as age at diagnosis, gender and follow-up time. The classification of Ebstein's disease was based on echocardiographic findings. We evaluated the morphology of the tricuspid valve according to the classification of Dearani et al. [2] proposed in 2000. Tricuspid regurgitation (TR) was graded from 0/4 to 4/4. Other echocardiographic features included measurements of the apical displacement of the tricuspid valve (in mm), the presence of tricuspid stenosis (TS) and the presence of an interatrial communication (PFO and ASD). Electrocardiographic data at the time of diagnosis and at latest follow-up were evaluated. We looked for existing pre-excitation and the presence of delta waves on the electrocardiogram (ECG, indicating WPW syndrome). Episodes of arrhythmias such as supraventricular tachycardia (SVT), ventricular tachycardia (VT) and atrioventricular (AV) block throughout follow-up were noted. We obtained data on the need for reconstructive valve surgery or valve replacement and the need for redo surgery during follow-up. Interventions such as pacemaker implantation and ablation of accessory pathways were evaluated as well. Cardiac medication at the time of latest follow-up was also a point of interest.

Statistical Analysis

Continuous variables were reported as the mean ± standard deviation, except when the data set was not normally distributed; in that case, the median and range (minimum and maximum) were used. Proportions were reported as percentages. Descriptive statistics were applied where possible. Kaplan-Meier curves were plotted for the different outcome variables. The log-rank test and bivariate analysis were done where applicable. All statistical tests were 2-sided. $p < 0.05$ was considered to be statistically significant. Analysis was done by SPSS (version 16.0) for Windows.

Table 1. Classification of Ebstein's anomaly at the time of diagnosis

Classification of Ebstein	Patients, n	Patients, %
Type I	17	34.7
Type II	19	38.8
Type III	9	18.4
Type IV	3	6.1

Table 2. Grade of TR at the time of diagnosis

Grade	Patients, n	Patients, %
0/4	3	6.1
1/4	5	10.2
2/4	15	30.6
3/4	18	36.7
4/4	8	16.3

Results

Patient Characteristics

We were able to select 49 patients from our database. The mean age at diagnosis was 29.1 ± 20.7 years and at latest follow-up 39.7 ± 17.4 years. Twenty-one out of 49 patients (42.9%) were men. Patients with associated complex congenital heart defects were excluded, except for those with an associated interatrial communication: 57.1% of our patients had an ASD or a PFO.

Ebstein's Anomaly Characteristics at Diagnosis

We used the morphological classification of Ebstein's anomaly according to Dearani et al. [2] in 2000. We were able to obtain the echocardiographic data at the time of diagnosis of 48 patients. Seventeen patients were classified as Ebstein's anomaly type I, 19 patients as type II, 9 patients as type III, and 3 patients as type IV (table 1). The apical displacement of the tricuspid valve was measured in 33 patients, with a mean apical displacement of 31.9 ± 14.8 mm. Three out of 49 patients presented with TS at

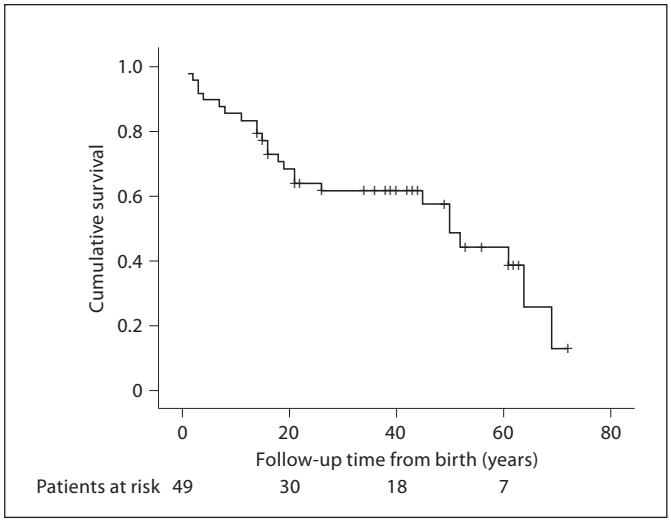

Fig. 1. Kaplan survival curve: freedom of surgery.

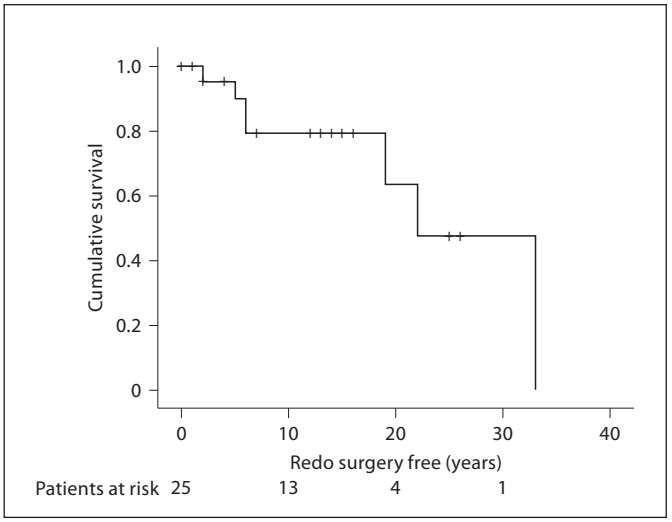

Fig. 2. Kaplan survival curve: freedom of redo surgery.

the time of diagnosis. TR was graded from 1/4 to 4/4. The prevalence at diagnosis is summarized in table 2. Three patients (6.1%) had no TR at the time of diagnosis.

Electrocardiographic characteristics at diagnosis were found for 48 patients. Sinus rhythm at the time of diagnosis was present in 89.6% of patients. Delta waves, that indicate the presence of WPW syndrome, were found in 18.8%.

Long-Term Follow-Up

The mean time of follow-up was 11.4 years (range 1.1–32.4). During the time of follow-up, 25 out of 49 patients (51.0%) required valve surgery. Severe TR (grade 3/4–4/4) was the major indication for surgery (18 patients). In 4 patients, surgery was performed because of existing cyanosis. Data are lacking for 3 patients. The mean time between diagnosis of Ebstein's anomaly and surgery was 4.5 years within a range of 1 month and 16.1 years. The mean age at time of surgery was 24.8 years, within a range of 1.0–70.0 years and a median age of 16 years. Sixteen of the 25 operated patients underwent primary tricuspid valve repair and 9 patients underwent tricuspid valve replacement. Kaplan-Meier for freedom of surgery is plotted in figure 1. Redo tricuspid valve surgery was necessary in 8 of 25 patients (32%) (fig. 2). The mean time between initial surgery and redo was 13.4 $\pm$ 10.6 years.

In the available dataset, it was found that primary valvuloplasty according to Chauvaud [5] was performed in 30% of the patients and a Carpentier repair was done in 40%. In 30% of the cases, the type of repair was not described in the surgical protocol and not otherwise specified in 3 patients. Glenn surgery was performed in 2 patients. Two patients required tricuspid valve replacement by a mechanical valve after primary valvuloplasty because of severe TR and hepatic congestion, after 2 and 33 years, respectively.

Primary tricuspid valve replacement was necessary in 9 patients: 4 of them received a bioprosthesis and 5 a mechanical valve. The decision for valve replacement was mainly made during surgery, when primary valvuloplasty appeared to have unsatisfactory results. In only 1 patient, decision for valve replacement was made beforehand, because of older age (61 years) and complete valve destruction. Patients who received a mechanical valve required lifelong anticoagulation with warfarin or coumarin, aiming at a therapeutic international normalized ratio between 2.5 and 3.5. In our study population, there were no thrombotic events noted. Endocarditis prophylaxis was indicated as well. Redo valve replacement occurred in 3 patients because of degeneration of the bioprosthesis and in 3 patients because of dysfunction of the mechanical valve. All 6 patients received a new mechanical valve. The mean time between initial surgery and reoperation was 13.4 years. Considering additional mortality and morbidity because of reoperation, we noted 1 episode of postoperative endocarditis of the mechanical tricuspid prosthesis after its implantation. The endocarditis originated from an infected wound in the left groin.

Therapy consisted of surgical debridement of the left groin and of high doses of antibiotics. Redo valve surgery was not required.

During follow-up, 25 out of 48 patients exhibited SVT, of whom 11 patients had undergone reconstructive valve surgery. Sixty percent of all events of SVT were anatomically based on a Kent bundle, seen in WPW syndrome. Electrophysiological ablation of an accessory pathway was performed in 17 patients. In 3 cases, surgery was combined with ablation. Freedom of ablation at 10, 20 and 30 years is 97.8, 85.1 and 76.5%, respectively. Eighty-nine percent of our patients exhibited sinus rhythm on ECG at the latest follow-up. VT was noted in 1 patient. AV block (first, second or third degree) occurred in 13 patients. Mean age at appearance of AV block was 38.5 ± 19.5 years. Pacemaker implantation was necessary in 5 patients (4 for complete AV block, 1 for sinus node dysfunction); all of them had undergone tricuspid valve surgery. One patient had undergone primary tricuspid valve repair, 2 had received a bioprosthesis and 2 a mechanical valve. Four patients received an epicardial pacemaker. In 1 patient, with a mechanical valve, an endocardial pacemaker was implanted. The lead was placed in the right atrium because of sinus node dysfunction. The mean time between the occurrence of clinical bradyarrhythmia and pacemaker implantation was 0.99 years. Only 1 patient exhibited AV block immediately after the operation, with subsequent pacemaker implantation. The mean age at pacemaker implantation was 31.8 ± 11.5 years (fig. 3).

Death occurred in 5 patients during follow-up. One patient, who developed associated severe pulmonary disease (bronchiectasis), died because of respiratory failure and right-sided heart failure. Malignancy was the cause of death in 2 patients, who both reached the age of 70 years. Data were lacking for 2 deceased patients.

We reviewed echocardiographic data at the time of the latest follow-up of 47 patients. Forty-three patients had TR. The grade of TR was 1/4, 2/4, 3/4 and 4/4 in 23.4, 31.9, 25.5 and 10.6% of patients, respectively, with a median systolic gradient of 24 mm Hg (range 11–55). Four patients did not exhibit TR. ECG at the time of the latest follow-up was available for 47 patients. The ECG of 42 patients (89.4%) showed a sinus rhythm. There was no presence of delta waves in any ECG at the latest follow-up.

At the time of the latest follow-up, 9 patients required cardiac medication. All of these patients needed β-blockers. Associated medication consisted of diuretics, digitalis, anticoagulation, aspirin, angiotensin-converting enzyme inhibitors and calcium antagonists in various combinations.

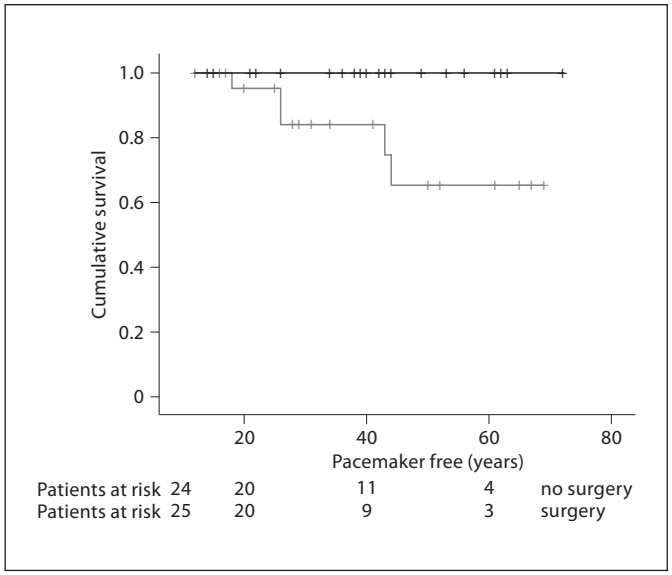

Fig. 3. Kaplan survival curve: freedom of pacemaker implantation, surgery versus no surgery.

Discussion

Valve surgery was necessary in half of our patients with Ebstein's anomaly of the tricuspid valve. Over the past decades, surgical techniques were developed and improved, and an increasing number of patients have been operated [1, 6]. Initially, high early mortality rates were noted [7]. In a study of 505 patients with Ebstein's anomaly, performed by Watson [7] in 1974, 57 patients underwent surgical treatment for Ebstein's anomaly, of whom 31 underwent valve replacement. Twenty-eight patients did not survive surgery (mortality rate 54%). In 2000, Chauvaud [5] examined 142 patients who underwent valve surgery for Ebstein's anomaly. Hospital mortality was 10%. The reoperation rate in this series was 9% [5]. Today, early mortality rates as low as 1.6% have been reported [8]. The majority of patients in our study underwent valve repair. There was no significant difference in survival between the group with valve repair and the group with valve replacement. It is unclear whether tricuspid valve repair or valve replacement is superior in the long-term outcome [3, 8, 9]. However, Chauvaud [5] suggests a superiority of tricuspid valvuloplasty associated with a longitudinal right ventricular plication over valve replacement. Surgery is usually performed during childhood or adolescence [1, 5]. In our series, the mean age at (initial) surgery was 24.8 years (range 1.0–70.0). The ma-

jor indication for tricuspid valve surgery was severe TR. We were not able to find echocardiographic features such as classification of Ebstein's disease, TR or TS at the time of diagnosis, or other objective features that could predict the need for surgery. Severe TR was an important reason for surgery; however, not all patients with severe TR were operated. As our study consisted of a relatively low number of patients (n = 49), we presume it is underpowered to detect predictors of surgery. However, other series showed that the need for surgery is an individual matter, primarily based on functional status [5, 8, 9]. There is a benefit from early surgical therapy regarding survival and freedom from redo surgery in the long term [8]. Eight of our patients required redo surgery, given a re-operation rate of 32%. The mean time between initial surgery and redo in our series was 13.4 ± 10.6 years. Re-operation rates of 9 and 20% were reported by Chauvaud [5] and Badiu et al. [8], respectively. Long-term follow-up in operated patients with Ebstein's anomaly is mandatory, as redo surgery in adulthood is not rare.

SVT occurred in half of our study population, and 60% of these patients exhibited WPW syndrome. In 1974, Watson [7] described paroxysmal arrhythmia in 100 of 363 patients undergoing cardiac catheterization. Supraventricular arrhythmia was seen in 80 patients. A recent Asian cohort study of Ebstein's anomaly found SVT in half of the patients [10]. Other series show an incidence of WPW varying from 10 to 29% of patients with Ebstein's anomaly [3, 4, 11]. However, in children, the incidence of arrhythmia is lower than in adults [12]. Delhaas et al. [12] studied children with Ebstein's anomaly, of whom 17% exhibited paroxysmal arrhythmia. SVT was noted in 11 out of 93 patients. In our series, the first episode of SVT occurred in more than half of the patients during adulthood (>18 years). There was no significant difference in prevalence of SVT between operated and non-operated patients. Ablation was performed in 17 patients. In only 3 cases, surgery was combined with ablation. Others underwent percutaneous ablation therapy. Ablation is an effective measure in the treatment of SVT in patients with Ebstein's anomaly in our series. Ninety percent of our patients exhibited sinus rhythm on ECG at latest follow-up. Khositseth et al. [4] favor surgical ablation, as they reported suboptimal success rates for catheter ablation. It is suggested that there is a higher recurrence rate of arrhythmia after catheter ablation in Ebstein's anomaly than in structurally normal hearts [3]. Chang et al. [10] reported a recurrence rate of 41% after the first ablation. The final success rate was 81%. We did not find a correlation between either the classification of Ebstein's anomaly or the degree of apical displacement of the tricuspid valve and the presence of either WPW or SVT. Predictors of SVT or pre-excitation that would identify high-risk patients are yet to be uncovered. Close follow-up of patients with Ebstein's anomaly is necessary, as arrhythmia can occur for the first time in adulthood.

AV block occurred in 13 patients. First-degree AV block has been described in 42% of patients with Ebstein's anomaly [1]. Permanent AV block occurred in 2.2% of patients, studied by Brown et al. [9]. Pacemaker implantation was necessary in 5 of our patients; all of them had undergone tricuspid valve surgery. Attenhofer Jost et al. [1] reported the requirement for pacemaker implantation in 3.7% of patients with Ebstein's anomaly. The relationship with surgery was unclear. Badiu et al. [8] described pacemaker implantation in 10 out of 130 patients, who all underwent reconstructive tricuspid valve surgery. There are few data about the need for antiarrhythmic drugs and other medication in patients with Ebstein's anomaly. The use of β-blockers was noted in 9 of our patients. Most patients with SVT and pre-excitation are treated with ablation therapy, as it is an effective treatment [4, 10, 12].

Five patients died during follow-up, though survival has improved over the past decades. Pillutla et al. [6] reported a 55% reduction in mortality for Ebstein's anomaly between 1979 and 2005 in the USA. Celermajer et al. [13] noted a 10-year survival of 59% of all live-born patients with Ebstein's anomaly. Data about adult survival are scarce.

Limitations

This study was a single-center retrospective study of 49 patients. All limitations of retrospective studies apply. Although we have no evidence for bias, it may have occurred.

Conclusion

Ebstein's anomaly is a rare congenital heart disease. Survival has dramatically improved over the last decades, and surgery has become an important feature in the treatment of Ebstein's anomaly. Half of the study population with Ebstein's anomaly underwent tricuspid valve surgery, and redo surgery was not uncommon. Supraventricular arrhythmia occurred frequently in adult patients and ablation therapy was often indicated. Therefore, careful follow-up is obligate, as some complications seem to occur for the first time in adulthood.

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