PAEDIATRIC CARDIAC DYSRHYTHMIAS

DIAGNOSTIC AND THERAPEUTIC ASPECTS

J.A.E. KAMMERAAD

The studies described in this thesis were performed at the departments of Paediatric Cardiology of the Wilhelmina Children's Hospital, University Medical Center, Utrecht, The Netherlands; Oregon Health & Science University, Portland, Oregon, USA; Guy's Hospital, London, Great Britain; University Hospital Groningen, The Netherlands; Center for Anomalies of the Heart (CAHAL), Leiden and Amsterdam, The Netherlands; Erasmus Medical Center- Sophia Children's Hospital, Rotterdam, The Netherlands; University Medical Center St. Radboud, Nijmegen, The Netherlands.

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diagnostic and therapeutic aspects

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Aan mijn ouders

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Chapter 1

General Introduction

General Introduction

Cardiac dys- or arrhythmias are abnormalities of cardiac rhythm, reflecting disturbances of either impulse initiation or impulse propagation, and frequently resulting in a heart frequency either below or above the normal heart rate for the patient's age.
Frequency and clinical significance of arrhythmias are different in adults and children.
Although cardiac arrhythmias are relatively infrequent in infants and children, it is very important to recognise and manage basic arrhythmias, since symptoms and complications of arrhythmias can be serious. With the continuing advances in the surgical correction of congenital heart defects, the number of children with complex arrhythmias continues to increase.
It is hard to say what the prevalence of cardiac arrhythmias in the paediatric population is. Few large series exist and the incidence reported varies greatly. Supraventricular tachycardia is the most common arrhythmia seen in children and its occurrence is estimated at between 1 per 250 to 1 per 1000 children [1-4]. In children with congenital heart disease, especially when they have undergone heart surgery, the incidence of arrhythmia increases with time.
In this thesis we will discuss different aspects of treatment of diverse arrhythmias. In this regard, catheter therapy of some uncommon arrhythmias will also be discussed. All studies in this thesis were approved by the institutional review boards of the participating centers.

Normal heart rate varies with age: the younger the child the faster the heart rate. Therefore the definitions of bradycardia (<60 beats/min) and tachycardia (>100 beats/min) used for adults, do not apply to infants and children. For children tachycardia is defined as a heart rate beyond the upper limit of normal for patient's age and bradycardia is defined as a heart rate slower than the lower limit of normal (Table).

Tachy-arrhythmias

The mechanism of tachy-arrhythmias is based on either the existence of a re-entry circuit, abnormal automaticity or triggered activity. The most common mechanism in children is re-entry. To obtain a re-entry circuit, two major conditions are necessary: the presence of a unidirectional block and an area of

Table

Normal ranges of resting heart rate.

Age	Beats/minute
New-born	110 - 150
2 year	85 - 125
4 year	75 - 115
Over 6 year	60 - 100

slow conduction, which delays the impulse long enough to allow the circuit ahead to become excitable. Such a re-entry circuit may occur around an anatomical obstacle like the AV node together with an accessory pathway between the atria and ventricles, or with dual AV node physiology. A re-entry circuit may also be due to changes in the conduction properties of cardiac tissue (figure).
Tachycardias caused by rapid firing of one or more foci due to abnormal automaticity are relatively rare. The cellular mechanism that is involved is similar to that which underlies the automaticity of pacemaker cells. In abnormal automaticity, a non-automatic cell acquires diastolic depolarisation. These foci can be situated in the atrial tissue or in the ventricles.
Arrhythmias arising from triggered activity are difficult to distinguish from those induced by re-entry. Triggered activity is always coupled to the preceding action potential and is caused by afterdepolarisations; early afterdepolarisations or late afterdepolarisations.
Clinical arrhythmias however depend on multiple mechanisms. It must be taken into account that apart from the arrhythmogenic substrate, also modulating factors, particularly changes in the automatic nervous system, and the occurrence of triggers are required to initiate and maintain arrhythmia (figure).

The commonest mode of presentation of arrhythmia in early infancy is with heart failure. Many infants will tolerate a supraventricular tachycardia well for about 12 to 24 hours. If the tachycardia is sustained for a longer period, some infants may develop signs of cardiomyopathy and congestive heart failure. This is not surprising, given the very rapid ventricular rate, the immaturity of the myocardium at this age and the fact that tachycardia is usually not noticed unless the baby is under observation for another reason.

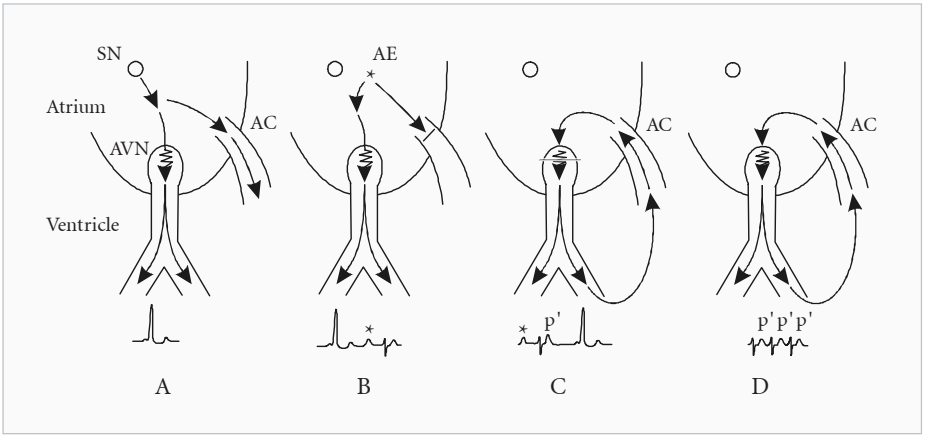

Figure. Drawing summarising the mechanism of tachy-arrhythmia caused by re-entry. In **A** sinus rhythm is shown; the stimulus is generated from the sinus node (SN) and conducted to the ventricle utilising the AV node (AVN) and an accessory connection (AC). In **B** a stimulus is generated from an atrial extrasystole (AE) and is conducted to the ventricle using solitarily the AVN. The AC is blocked antegradely (**B**), which permits the occurrence of retrograde conduction of the same stimulus over the AC from the ventricle back to the atrium in **C**. This beat is limited to one single echo beat by the occurrence of antegrade block in the AVN (**C**). When this block in the AVN is not present, re-entrant tachycardia occurs as shown in **D**. These four drawings also show the relation between the several factors needed for occurrence of tachy-arrhythmia; an arrhythmogenic substrate -the AC-, an initiating trigger -the AE- and modulating factors -antegrade block in the AC in **B** and antegrade block in the AVN in **C-**.

The majority of older children with tachycardia present with palpitations and sometimes with an observed irregularity of the pulse. Hemodynamic compromise will result in symptoms like dizziness, near syncope or even syncope. A severe tachycardia might cause sudden cardiac death, as sometimes occurs in patients with long QT syndrome or in patients having undergone previous cardiac surgery for congenital heart disease. Occasionally tachycardia presents with heart failure and dilated cardiomyopathy in this older paediatric patient group.

Management of tachyarrhythmia

In children presenting with a tachyarrhythmia episode for the first time, vagal stimulation techniques like carotid sinus massage, eyeball compression, or application of an icepack to the face (also termed the diving reflex) are tried to terminate the arrhythmia. If vagal manoeuvres fail, the next step is to try an anti-arrhythmic drug like adenosine (administered intravenously to acutely terminate re-entrant arrhythmias involving participation of the AV node). In some cases atrial overdrive pacing with a catheter in the oesophagus or right atrium might be effective in discontinuing arrhythmia. Electrical cardioversion sometimes is required for patients with sustained atrial flutter, ventricular tachycardia or ventricular fibrillation.
As soon as the arrhythmia episode is over, recurrence of tachycardia is prevented with a maintenance dose of anti-arrhythmic medication. It should be taken into account that only limited knowledge exists regarding pharmacokinetics and pharmacodynamics of the various anti-arrhythmic agents in newborns, infants and children. To date, no antiarrhythmic agent has been specifically developed or tested for use in infants and children. Relatively uniform guidelines for dosing in paediatric practice, to ensure both efficacy and safety have been brought about by the large volume of experience in children over the past years.

Spontaneous resolution of conduction through accessory pathways occurs in nearly one-third of the affected children within 12 months of birth [5,6] and there also seems to be a high rate of spontaneous disappearance for automatic atrial tachycardia [7]. It is well recognised that tachyarrhythmias in young children show a bimodal age distribution. There is an initial peak of incidence in the first year of life, followed by a relatively symptom-free interval between 1 and 5 years of age. Thereafter, these arrhythmias tend to recur, with a second peak progressing into adult life [6,8]. This is also borne out by the numerous published series on catheter ablation, the majority of the procedures having been undertaken in young adults.

Radiofrequency catheter ablation

The basic concept of radiofrequency catheter ablation is the application of unmodulated sinusoidal waveforms at a relatively high frequency (300-750 kHz) via an intracardiac electrode catheter to achieve tissue heating, creating a thermal injury. During an electrophysiology study, the exact mechanism of the

tachyarrhythmia is determined and the arrhythmogenic substrate localised. The delivery of well circumscribed lesions to a specific target results in tissue destruction and loss of electrical conduction. This specific target can be an accessory pathway, or the critical isthmus of an intra-atrial re-entry circuit. In the latter, a number of consecutive radiofrequency energy lesions are applied to create a line of bi-directional block between two natural anatomic barriers, bordering the critical isthmus for the re-entry circuit. This line is unable to conduct electrical pulses and will therefore eliminate the re-entry circuit, rendering the tachycardia non-inducible. The first one to describe the use of radiofrequency catheter ablation in an infant was van Hare in 1990 [9]. At the current time, indications for ablation include failure of medical therapy, unacceptable side effects of medical therapy, complications like tachycardia induced cardiomyopathy, life threatening arrhythmias, or as an elective procedure depending on patient and/or parental choice. Currently, general agreement on indications for the performance of radiofrequency catheter ablation in children exists in a NASPE position statement [8].

Usually the position of intracardiac catheter electrodes during electrophysiological procedures is estimated from biplane fluoroscopic images. With the current advanced techniques applied to ablate complex arrhythmia substrates, the estimation of electrode positions allowed by this method is imprecise and new mapping systems were developed.

LocaLisa mapping system

This mapping system (LocaLisa, Medtronic, Inc.) has the ability to determine accurate three-dimensional localisation of intracardiac electrodes [10]. The localisation technique of LocaLisa uses three skin electrode pairs to send three small currents through the chest in three orthogonal directions. A slightly different frequency is used for each direction. In this way a constant voltage gradient is created across the heart, which standard intracardiac catheter electrodes can measure. The voltage at any given point is measured with reference to a fixed intracardiac electrode. Automatically the 3 electrical field strengths are calculated and by dividing each amplitude (V) by the corresponding electrical field strength (V/cm) the position of any standard electrode can be determined in 3 directions. The LocaLisa mapping system has contributed significantly to catheter ablation procedures for an extensive scala of arrhythmia in children. The

mapping system allows a more aggressive approach for catheter ablation in this particular patient group with small hearts, by enabling the location of the ablation catheters to be more precisely monitored and the distance from the vital conduction structures of the heart (like the His bundle) to be measured.

Electro-anatomical mapping system

This mapping technique (CARTO, Biosense Webster, Diamond Bar, CA) uses three distinct low frequency electromagnetic fields, encompassing the volume of the heart. Specially designed catheters are able to sense these calibrated magnetic fields. By triangulation the exact catheter position can be accurately determined in relation to the locations of the electromagnetic point sources [11]. If a second mapping catheter is inserted into a stable intracardiac position, this can be used as a reference point, creating the ability to measure chamber volumes and absolute and relative catheter tip locations in relation to this reference catheter. By correlation of spatial coordinates and activation timing determined in reference to a fixed cardiac electrical event, activation sequence maps can be reconstructed. A visual representation of the mapped endocardial points is reconstructed and onto this estimated endocardial surface continuous defined isochronal maps can be displayed.

Post-ablation care

Although catheter manipulation in small hearts might be associated with greater technical difficulty of the procedure when compared with adults, current reports show low complication rates [12,13]. Besides creation of complete heart block, complications can include penetration of the myocardium, pericardial effusion, valve damage and coronary arterial complications. In paediatric patients who undergo catheter ablation, many centers often perform echocardiography before and after the ablation procedure to assess these immediate potential subclinical complications. The clinical value of this routinely performed echocardiography is discussed in this thesis.

There also remain concerns about the long-term problems associated with radiofrequency catheter ablation technique in the paediatric age group. Recurrence of arrhythmia has been reported [12,13] and little data exist on the follow up behaviour of radiofrequency ablation lesions in immature myocardium. For these reasons it is critically important to continue performing long-term follow up in this patient group.

BRADY-ARRHYTHMIAS

Brady-arrrhythmia can be caused by sinus bradycardia, sinus pause, sinus arrest and AV block.
In the sick sinus syndrome the sinus node fails to function as the dominant pacemaker of the heart, resulting in the occurrence of a variety of arrhythmias, bradycardic but also tachycardic. In occasional cases, sick sinus syndrome is idiopathic, but for the majority this syndrome occurs after extensive cardiac surgery, particularly if the atria are involved. An example of surgery, often complicated by sick sinus syndrome is the Mustard or Senning procedure for transposition of the great arteries, which is dealt with in chapter 8 of this thesis.

Another rare, and poorly understood condition is idiopathic silent atrium. In this condition, there is electrical, and sometimes associated mechanical, atrial standstill, as diagnosed by the absence of P-waves on the ECG. Although the cause of silent atrium is often unknown, a familial form has been described, as well as forms associated with systemic muscular dystrophy, myocardial amyloidosis and myocarditis. Transient atrial standstill is often seen after cardiac surgery or in reaction to anti-arrhythmic medication. While generally thought to be progressive, some cases of spontaneous recovery of atrial function have been documented. We report two children with idiopathic silent atrium, both of whom developed intra-atrial re-entrant tachycardia, and required catheter ablation. These patients are described in chapter 4 of this thesis.

When the atrioventricular (AV) node is non-functional, the normal sinus impulse cannot be conducted to generate a ventricular response, which may cause bradycardia. High degree AV block can be congenital or acquired. Congenital AV block is strongly associated with maternal connective tissue disease such as systemic lupus erythematosus and Sjögren's syndrome. It can also be associated with structural heart disease. Cardiac surgery is the most common cause of acquired complete heart block in children.

Complications that may occur from bradycardia are symptoms of hemodynamic disturbance, like exercise intolerance, dizziness or syncope. Whether symptoms occur, depends on the frequency of the nodal or ventricular escape rhythm. Patients with congenital complete AV block are also described to be at long-term risk to develop cardiomyopathy, resulting in congestive heart failure [14-17].

Management of bradycardia

Permanent pacemaker therapy is indicated for symptomatic bradycardia and complete heart block with low escape rhythms. A task force of the American Heart Association, the American College of Cardiology and the North American Society for Pacing and Electrophysiology has established guidelines for the implantation of permanent pacemakers [18,19].
Over the past 20 years, remarkable technological advances have been made in pacemaker design and function. The size of the pulse generator and leads have decreased, allowing endocardial pacing, as it already was in adults, to be the preferred route in children also. In contrast with adults, children are subjected to somatic growth, with possible lead tension and the need for lead replacements and lead extractions. Greater technical difficulty associated with the patient's size, the risk of venous occlusion and skin erosion at the generator site are other concerns that make most paediatric centers still advocate the epicardial approach in children.

Dysrhythmias post-surgery

Although the prognosis for patients with congenital heart defects has improved by surgical treatment, they remain at a well-recognized risk for late complications. As discussed previously in this introduction, arrhythmias are likely to occur after cardiac surgery. In addition, the hemodynamic consequences of arrhythmia associated with structural heart disease may be more profound in these patients, than in those with a normal heart.
Besides early post-operative arrhythmias like complete heart block or direct damage to the sinus node, arrhythmia can also arise as a late complication of surgery. Particularly if surgery involves parts of the atria, patients are prone to develop late arrhythmia and many will lose sinus rhythm in follow up. Patients who have lost sinus rhythm are also prone to develop other arrhythmia like the previously described dangerous bradycardia-tachycardia (sick sinus) syndrome. Apart from damage to the sinus node, these patients also usually have numerous sutures and sometimes prosthetic material in the atria. These surgical scars form areas of slow conduction, creating a substrate for scar related re-entry, the mechanism responsible for incisional atrial tachycardia. A good success rate for radiofrequency catheter ablation of incisional atrial tachycardia is described [20,21]. Lines of block were created by radiofrequency current application between scars and natural anatomic barriers, or between two scars, closing the isthmuses that

were demonstrated to be critical for the re-entrant circuit. The use of a mapping system like LocaLisa or Carto has been of great use in facilitating these procedures [20-22].

Unfortunately, also sudden cardiac death remains a worrisome complication of surgery for congenital heart defects [23,24]. Silka described in 1998 that the risk of late sudden death for patients surviving an operation for a common congenital cardiac defect is 25 to 100 times greater than in an age-matched control population [23]. The majority of these sudden deaths occurred in patients with aortic stenosis, coarctation, tetralogy of Fallot or transposition of the great arteries. Most but not all sudden cardiac deaths were presumably due to arrhythmogenic causes.
The incidence of sudden cardiac death in patients having undergone a Mustard or Senning procedure for transposition of the great arteries is reported to be between 2 and 15%. The final chapter of this thesis discusses whether there are any identifiable predictors for sudden cardiac death in patients with transposition of the great arteries, who have survived a Mustard or Senning operation.

Aim of the thesis

The studies in this thesis describe the follow-up of paediatric patients having undergone treatment for different types of arrhythmia. In this respect we concentrated on radiofrequency catheter ablation and transvenous pacemaker implantation. We investigated safety, efficacy and outcome of these treatment options for several different arrhythmias. Special attention is being paid to the advances of new developed mapping systems on radiofrequency catheter ablation of the more challenging arrhythmia substrates.
In addition we have attempted to identify predictors of sudden cardiac death in patients who have survived Mustard's or Senning's operation for transposition of the great arteries.

Outline of the thesis

In chapter 2 the efficacy and safety of radiofrequency catheter ablation in children 18 years or less are described. The clinical outcome, complication- and recurrence rate for different types of arrhythmias were evaluated for sixty-four patients having undergone radiofrequency catheter ablation in a Dutch university

hospital. After each ablation procedure, routine echocardiography was performed in each patient to assess eventual asymptomatic complications of the ablation procedure. In chapter 3 we evaluated the clinical importance of echocardiography performed routinely in all paediatric patients at two institutions after radiofrequency ablation for supraventricular tachycardia.
Chapter 4 deals with idiopathic silent atrium, which is a poorly understood condition. Management and outcome of intra-atrial re-entrant tachycardia occurring in two patients with a co-existing silent atrium are described.
Another rare form of arrhythmia is non-automatic focal atrial tachycardia, an arrhythmia diagnosed when a patient had focal atrial tachycardia, which was inducible with pacing manoeuvres in the electrophysiology laboratory. We investigated the arrhythmia characteristics of non-automatic focal atrial tachycardia in chapter 5. In addition the ablation results for this arrhythmia with fluoroscopy guided catheter manipulation were compared to those with the use of electro-anatomical mapping (Carto) in an American university hospital.
The contribution of the LocaLisa mapping system to the safety and efficacy of radiofrequency catheter ablation of atrioventricular nodal re-entrant tachycardia in children is described in chapter 6.
In chapter 7 is dealt with treatment for bradycardia in the form of pacemaker implantation. The outcome of transvenous pacemaker implantation in children with low bodyweights is studied, since problems of endocardial pacing are expected to occur in this patient group. To obtain a larger study population, the experience with endocardial permanent pacing was combined for two institutions.
Patients, who underwent an atrial switch for transposition of the great arteries in childhood, are known to be prone to several late complications. Besides right ventricular failure and the occurrence of late arrhythmia, sudden cardiac death is one of the most worrisome late complications of physiologic repair. In chapter 8 we have attempted to identify predictors for sudden cardiac death after the Mustard or Senning operation for transposition of the great arteries.

The thesis concludes with a general summary and discussion in English and Dutch.

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Chapter 2

Catheter Ablation Of Tachyarrhythmia Substrates In Children

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Abstract

Background

In adults, radiofrequency (RF) catheter ablation has already been established to be safe and effective fro a variety of arrhythmia substrates. The procedure has also been shown to be effective in infants and children.

Methods/results

Radiofrequency catheter ablation was performed in 64 patients, aged 18 years or less. Out of 38 patients with one or more accessory pathways, ablation was successful during a single session in 34 patients, while 4 patients required additional sessions. Atrioventricular reentrant tachycardia (AVNRT) was found in 14 patients and ablation was successful in 13 of these. No conduction disturbances were observed. Five patients had ventricular tachycardia (VT), one right-sided and four left-sided. In one patient, VT could not be induced. In the remaining four patients, VT was abolished. Finally seven patients had atrial tachyarrhythmia, which was focal in two and reentrant in five. Ablation was successful in six out of seven patients; in one patient the tachyarrhythmia could not be induced.

Conclusion

Catheter ablation in children is a highly successful definitive therapy for most forms of tachyarrhythmia

Introduction

In adults radiofrequency (RF) catheter ablation has already been established to be safe and effective for a variety of tachyarrhythmia substrates. The procedure has also been shown to be effective in infants and children [1-5]. However, the technical difficulties associated with manipulating catheters in small hearts, concerns about an increased risk of complications and about potential growth of the RF lesion with somatic growth have all contributed to the limited use of this approach in paediatric practice. We report our experience with RF catheter ablation treatment of different tachyarrhythmias in children under 18 years of age.

Patients and Methods

In the period from January 1996 to March 2000, 64 patients, aged 18 years or less, underwent 76 RF ablation procedures for different tachyarrhythmia substrates. There were 31 male and 33 female patients with a median age of 15 years (range 3 weeks – 18 years). In 57% of patients the indication for RF ablation was failure of medical therapy using up to two antiarrhythmic drugs. Failure was defined as documented recurrence of the clinical tachyarrhythmia within a six-month period after commencement of medical therapy, despite an adequate drug dosage adjusted for body weight. In 12% pharmacological therapy was associated with unacceptable side effects. In 25% of patients, elective RF catheter ablation was undertaken instead of commencing antiarrhythmic medications. Finally, in 6% of patients, the indication for RF ablation was severe tachycardia-induced cardiomyopathy (one patient) or life-threatening tachyarrhythmias (three patients).

Technique

Electrophysiological studies were performed under general anaesthesia in the majority of patients. Electrode catheters were introduced via the femoral or internal jugular venous approach to the following positions: right atrial appendage, His' bundle area, right ventricle and coronary sinus. In selected patients with intra-atrial reentrant tachycardias, a 20 polar halo catheter was used. For left sided accessory pathways, the transseptal approach was preferred. Standard stimulation and mapping techniques were used to identify the mechanism of the tachyarrhythmia, and the location of accessory pathways. In

patients without manifest preexcitation, tachyarrhythmia induction was performed by various pacing techniques, with intravenous isoprenaline infusion if required. After the diagnosis was established, ablation was performed. Catheter manipulation was guided by fluoroscopy, and since January 1997 by the Localisa system, a novel mapping system developed at our institution which allows precise 3-dimensional localization of standard intracardiac electrodes [6].

Treatment success

Success was defined for each arrhythmia substrate as follows:
- accessory pathways: absence of accessory pathway conduction in both directions, antegrade and retrograde, using pacing and extrastimulus techniques;
- AV nodal reentrant tachycardia: absence of dual AV node physiology following slow pathway ablation;
- Intra atrial re-entry tachycardia (IART) and incisional tachycardia: confirmation of bi-directional block across the line of block created between two natural anatomic barriers or scars.
- Ventricular tachycardia (VT) and ectopic atrial tachycardia (EAT): absence of spontaneous ectopy, and non-inducibility of the clinical tachyarrhythmia.

Results

Arrhythmia substrates

Thirty-eight patients had atrioventricular reentrant tachycardia mediated by one (31 patients) or multiple (seven patients) accessory pathways. Fourteen patients had atrioventricular nodal reentrant tachycardia (AVNRT), five patients had ventricular tachycardia (VT), two patients had ectopic atrial tachycardia, and five patients had intra-atrial reentrant tachycardia. Table 1 summarizes the patient data.

Accessory pathway ablation

In 38 patients 47 accessory pathways were identified. All pathways were successfully ablated. One patient with a right free wall pathway and two patients with a septal pathway required two ablation sessions. One patient with two Mahaim pathways, one concealed bypass and AVNRT required four sessions. In all other patients successful ablation was accomplished in a single session.

Table 1.

Ablation Results

Substrate	patients (n)	age (median [range], years)	procedures (n)	success (n)	follow-up (median [range], years)
Accessory Pathway	38	13.9 (0.1-17.1)	44	38(100%)#	1.9 (0.2-3.8)
Single	31		34	31	
- left free wall	20		20	20	
- right free wall	4		5	4	
- septal	5		7	6	
- PJRT	2		2	2	
Multiple	7		10 *	7	
AVNRT	14	15.6 (6.4-17.6)	14	13 (93%)	2.1 (0.1-4.0)
VT	5	14.2 (8.8-16.7)	7	3 (60%)	1.7(0.3-3.3)
- LV	4		5	2	
- ARVD	1		2	1	
Atrial tachycardia					
- focal	2	14.8 & 15.3	2	1 (50%)	0.8 & 1.4
- macro-reentrant	5	9.5 (2.9-17.9)	6	5 (100%)	1.3(0.5 –3.3)

PJRT=permanent junctional reciprocating tachycardia; AVNRT=atrioventricular nodal reentrant tachycardia; VT=ventricular tachycardia; LV=left ventricular; ARVD=arrhythmogenic right ventricular dysplasia. Age and follow-up are expressed as median and range. # One patient had a late recurrence (2 years post-ablation) of conduction via a posteroseptal accessory pathway (see text). * One patient with multiple pathways required 4 sessions, the remaining six underwent a single session.

Two patients had permanent junctional reciprocating tachycardia (PJRT). Both developed tachycardia-induced cardiomyopathy in early infancy, despite treatment with several antiarrhythmic medications. Ablation of a slowly conducting right sided posteroseptal pathway with decremental properties was successfully performed at three weeks and five months respectively. Successful ablation was associated with rapid recovery of myocardial function. Both patients were symptom-free and without antiarrhythmic medications at a follow-up of three years and six months respectively.

AV node modification for AV node reentrant tachycardia

Four-teen patients diagnosed as having AV node reentrant tachycardia underwent slow pathway ablation. An anatomical approach was used to target the slow pathway. The end-point for the procedure in 13/14 patients was absence of dual AV physiology. In one six year old girl, the end-point for the procedure was non-inducibility of AV nodal reentrant tachycardia, but with dual AV physiology still

being present. She has since had a recurrence of her clinical tachyarrhythmia two weeks after the RF ablation procedure, and is awaiting a second procedure. For the entire group, the median follow-up is 2.1 years (range 0.1 to 3.8 years); 13 patients remained free of tachycardia without antiarrhythmic medication. No patient developed conduction disturbances after the ablation.

Ablation of ventricular tachycardia

Five patients were diagnosed to have ventricular tachycardia (VT). One patient with arrhythmogenic right ventricular dysplasia underwent successful ablation of two tachycardia circuits during two separate procedures. The other four patients had a fascicular left ventricular tachycardia. Ablation was successful in two patients. In one patient, ablation could not be performed as the tachyarrhythmia was not inducible despite an aggressive extrastimulus protocol with isoprenaline infusion. The remaining patient, a 13 year old girl had been admitted to her local hospital with a short history of palpitations and syncope. A fascicular left ventricular tachycardia was diagnosed. Echocardiography showed a dilated left ventricle with impaired function, and the clinical picture was interpreted as tachycardia-induced cardiomyopathy. She had required cardiopulmonary resuscitation on three occasions prior to transfer to our hospital. The tachyarrhythmia was transiently responsive to verapamil. In view of the life-threatening presentation, emergency ablation of the tachyarrhythmia was undertaken over two sessions, each lasting six hours. The fascicular tachycardia was rendered non-inducible. The low cardiac output state was managed with intravenous inotropic medications including dopamine, milrinone and norardenaline. Following recurrent episodes of polymorphic ventricular tachycardia, for which DC cardioversion was required, she was treated with a continuous infusion of intravenous amiodarone. Finally two days post-ablation she developed intractable polymorphic ventricular tachycardia and could not be resuscitated. Autopsy demonstrated severe dilated cardiomyopathy with global myocardial necrosis, suggesting a pre-existent viral myocarditis.

Ablation of ectopic atrial tachycardia

In two patients ectopic atrial tachycardia was diagnosed. Ablation was successful in one patient. In the second patient, the tachyarrhythmia was not inducible under general anaesthesia. A second ablation procedure under local anaesthesia was undertaken, but the tachyarrhythmia could not be induced during the electrophysiology study. The procedure was therefore abandoned.

Ablation of intra-atrial reentrant tachycardia

Five patients were diagnosed to have intra-atrial reentrant tachycardia (IART). The first two had previously undergone repair of a congenital heart defect (closure of secundum atrial septal defect, and an atriopulmonary Fontan connection for tricuspid atresia). Reentrant circuits related to the surgical scars were identified during the electrophysiology study in these patients. Lines of block were created by application of RF energy between the scars and natural anatomic barriers to abolish the tachycardia circuit.

The third patient presented with congenital complete AV block, and underwent transvenous dual chamber pacemaker implantation at six years of age. At routine follow-up she was noted to have IART. At electrophysiology, common atrial flutter was inducible. Isthmus block was created between the tricuspid annulus and inferior vena cava. However, IART remained inducible at the end of the procedure, and clinical recurrences were documented at follow-up. During a second procedure, a macro reentrant circuit was mapped on the right atrial free wall, within areas of atrial electrical silence. She underwent successful ablation of this circuit, by creation of a line of block to the inferior vena cava.

The fourth patient with IART presented at 14 months with atrial flutter. Following antiarrhythmic therapy she developed progressive sinus node dysfunction and AV block, for which a dual chamber epicardial pacemaker was implanted elsewhere. At serial follow-up she developed silent atrium and had a cerebrovascular accident. Thereafter, she was referred to our institution. On discontinuing the antiarrhythmic medications, atrial electrical activity was restored, and common atrial flutter recurred. This was successfully ablated.

The fifth patient had previously undergone surgical closure of a secundum atrial septal defect. At electrophysiological study, she had typical atrial flutter. In addition, she had a scar-related IART and uncommon AV nodal reentrant tachycardia. All tachyarrhythmia substrates were successfully ablated during a single session.

Fluoroscopy and procedure times

The average fluroscopy time was 16.5 ± 12 minutes. The procedure time was on average two hours, for a single accessory pathway or for modification of AV nodal reentrant tachycardia. For complicated arrhythmia substrates, such as intraatrial reentrant tachycardia, the mean fluroscopy time was 28.4± 13.8 minutes.

Complications

Procedure-related complications occurred in two patients. One patient had a posteroseptal and a para-Hisian pathway. He had incessant orthodromic reciprocating tachycardia and interruption of the posteroseptal pathway did not abolish the tachyarrhythmia. Therefore, a decision was made to ablate the para-Hisian pathway as well. This was complicated by complete AV block. A transvenous dual chamber pacemaker was implanted prior to discharge from hospital. Two years later, at routine follow-up, the patient was noted to have 1:1 AV conduction via the posteroseptal pathway. He did not, however, have tachyarrhythmia. The second complication occurred in a 13-year-old girl, who died two days following ablation of a fascicular ventricular tachycardia, as previously described.

Follow-up

All patients have been followed up serially in the outpatient clinic. Routine investigations at follow-up included physical examination, 12 lead ECG and echocardiography to document normalization of ventricular function. In patients with persistent symptoms such as palpitations, 24 hour Holter recordings and ambulatory patient-operated Holter recordings were performed to confirm that there was no recurrence of the tachyarrhythmia.

Discussion

The first reported application of RF catheter ablation in a child was in 1990 in a 10-month-old baby with junctional ectopic tachycardia [7]. Since then other reports on RF catheter ablation in children have been published, describing its effectiveness in the non-pharmacological therapy of tachyarrhythmias. Concerns about RF ablation in children have also been reported. Lower patient weight (and thus younger patient age) were associated with a higher incidence of procedure-related complications in the earlier series [3]. These technical limitations have largely been overcome with improved catheter technology and better algorithms for diagnosing the location of accessory pathways from the surface ECG. These have contributed to shortening of the procedure time and improved safety. In our own series, there was one episode of complete AV block following ablation of a para-Hisian pathway. Despite good results at short-term follow-up, data for the long-term are not yet available. Consequently little can be said about the possible

deleterious effects of scars on the myocardium in the pediatric age group. RF lesions in lambs appear to grow with time and infiltrate into the normal adjacent myocardium [8]. Conversely this does not occur with RF lesions in adult canine myocardium [9] or in young pigs [10]. The only study performed in children did not report any increase in lesion size at follow-up [11]. We are aware that our follow-up time is indeed short. This limitation is a reflection of the fact that RF ablation therapy has been applied to children very recently. The theoretical risk indeed exists that these RF lesions could grow and may themselves become arrhythmogenic in future. Careful long-term follow-up is therefore indicated.

Growing experience seems to be associated with higher success rates, shorter fluoroscopy time and a lower complication rate [3]. At our center, adult and pediatric ablation procedures are performed by the same team, resulting in a large patient volume. In addition, a non-fluoroscopic mapping system LocaLisa is used to precisely determine the position of intracardiac electrodes. This allows for accurate mapping and measurement of distances to critical structures such as the His' Bundle.

Many different opinions about indications for RF catheter ablation in children exist among paediatric cardiologists. Some recommend the procedure as the treatment of choice even in children with infrequent self-terminating arrhythmias. Others will not recommend the procedure until life-threatening symptoms due to the tachyarrhythmia develop [12]. In general, drug failure or life-threatening arrhythmias are accepted indications for ablation.

Perry et al. described 60 patients with WPW syndrome whose tachycardia occurred for the first time at between zero and two months after birth. In 93% of these patients supraventricular tachycardia did not recur by eight months of age. However, 31% of patients had a recurrence of tachyarrhythmia at an average age of eight years. Additionally, if tachycardia was present above five years of age, it was persistent in 78% of these patients at a mean follow up interval of seven years [13]. This suggests that there is a bimodal age distribution in the occurrence of symptomatic episodes of supraventricular tachycardia, with many children remaining symptom-free between the ages of one and five years. Since RF ablation therapy has become accepted, the majority of arrhythmias that have been cured in the large series reported in the adult literature, are reentrant supraventricular tachycardia due to a manifest or concealed accessory pathways.

This suggests that the congenital accessory connections remain potentially active for the rest of the patient's life, and account for symptoms in adult life requiring ablation therapy.

The frequency of symptoms with medication and life-threatening symptoms, i.e. tachyarrhythmia induced cardiomyopathy, are two important considerations to ablate tachyarrhythmia substrates in children. Increasingly, the good results with this approach means that ablation therapy can also be offered electively to older children, with minimal risks. The low complication rate combined with the high success rate make catheter ablation an attractive alternative to long-term drug treatment. The majority of paediatric series on RF ablation therapy (including our own) deal with older children. This in turn reflects the fact that RF ablation therapy in children is a relatively recent development. In infants, RF ablation should be reserved for patients with life-threatening arrhythmias with myocardial dysfunction.

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Chapter 3

Is Routine Echocardiography Valuable After Uncomplicated Catheter Ablation In Children?

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Abstract

Aims

Although the complication rate of radiofrequency catheter ablation (RFCA) procedures in children is low, clinically asymptomatic complications do occur. We determined the clinical value of routine transthoracic echocardiography (TTE) performed after catheter ablation of supraventricular tachycardia (SVT) in children.

Methods and Results

Between April 1996 and September 2001, 138 children (75M, 63F), (mean age 13 years; range 0-19 years), underwent 160 uncomplicated radiofrequency catheter ablation (RFCA) procedures for SVT at our two institutions. In every child a TTE with Doppler was performed before and after the procedure. The pre-ablation TTEs in all cases were normal. Post ablation, in 4 clinically asymptomatic patients the TTE showed a disorder: one patient with focal atrial tachycardia, ablated via a retrograde aortic approach, had mild aortic valve insufficiency. This had resolved 6 months later. Three other children developed an asymptomatic pericardial effusion. In 2 patients this resolved spontaneously; one patient required pericardiocentesis. This same patient also developed a clinically asymptomatic mild aortic insufficiency, which resolved spontaneously within 6 months.

Conclusion

TTE after uncomplicated RFCA procedures in children is probably not indicated children with structurally normal hearts, but has a role after ablation procedures where the retrograde aortic approach has been used.

Introduction

Radiofrequency catheter ablation (RFCA) has been performed in children for about 10 years with good success rates and low overall complication rates [1,2]. Potential complications of RFCA include pericardial effusion and valve damage which may be asymptomatic and can be detected by echocardiography. However the likelihood of such complications is low [1,2]. In a prior study in adults, Pires et al noted a low value for a routine post-procedure cardiac echo [3]. There is no report on the role of routine echocardiography after RFCA in children.

Patients and methods

Between April 1996 and September 2001, 138 children (75 male, 63 female) with a structurally normal heart who had undergone 160 RFCA procedures for supraventricular tachycardia were retrospectively studied. Their mean age was 13 years (range 0 to 19). In every child a transthoracic 2-D echocardiogram (TTE) with Doppler was performed before and after the procedure. The following echocardiographic indices were documented in all patients: whether the heart was structurally normal, inflow and outflow velocities through all the cardiac valves, the presence or absence of valvar insufficiency, global ventricular function assessed by M-mode measurement of left ventricular fractional shortening, the presence or absence of regional wall motion abnormalities assessed in short and long axis views, and the presence or absence of pericardial effusion. Included in this study were children who had undergone an uncomplicated RFCA procedure for supraventricular tachycardia such as atrioventricular reentrant tachycardia due to an accessory pathway (including Wolff-Parkinson-White syndrome and persistent junctional reciprocating tachycardia) and atrio-ventricular nodal reentrant tachycardia. We excluded children with congenital heart disease and complex arrhythmias such as scar-related reentry and atrial flutter. The arrhythmia substrates are shown in table 1. Except for one, none of the patients had any clinically documented complications during the ablation procedure itself. This single patient was found to have two accessory pathways, one postero-septal and one para-Hisian. Since ablation of the postero-septal bypass tract did not eliminate the arrhythmia, it was decided to also ablate the para-Hisian pathway. This was complicated by complete AV block and the patient underwent implantation of a transvenous pacemaker.

Table 1.

Arrhythmia substrates.

Diagnosis	n
AVNRT	42
Wolff-Parkinson-White syndrome	48
Concealed accessory pathway	41
Non-automatic focal atrial tachycardia	3
PJRT	2
Sinus node reentry	1
Junctional tachycardia	1

Abbreviations: AVNRT: atrio-ventricular nodal reentrant tachycardia; PJRT: persistent junctional reciprocating tachycardia.

Results

Pre-ablation

All children had a structurally normal heart. No single TTE performed before the ablation procedure showed abnormalities.

Post-ablation

The echocardiograms following 156 out of 160 RFCA procedures were considered to be normal. In four asymptomatic cases the TTE did show a disorder as follows:
One 15 year old patient showed mild aortic valve insufficiency after an ablation procedure for focal left atrial tachycardia. In this patient a retrograde catheter approach via the femoral artery was used. The insufficiency had resolved spontaneously 6 months later. Three other children had developed an asymptomatic pericardial effusion. In two of those, (an 11 year old, who had undergone successful ablation of a concealed left sided accessory bypass via a trans-septal approach and a 16 year old, who had had a successful slow pathway AV node modification) the pericardial effusion resolved spontaneously. The third patient, 9 years of age, had a concealed left lateral

bypass ablated via a retrograde approach. TTE showed a moderate sized hemorraghic pericardial effusion requiring pericardiocentesis. This same nine-year-old also developed a clinically asymptomatic mild aortic insufficiency, which resolved spontaneously by 6 months.

Discussion

Our study shows that routine TTE may occasionally detect problems in otherwise asymptomatic patients. Although limited by the retrospective nature of our study, we did not find abnormalities in either left ventricular function or wall motion. We showed one patient with mild aortic valve insufficiency and three patients with pericardial effusion. The mechanisms of postablation pericardial effusion are unclear. However tissue trauma that results from catheter manipulation and transmural lesions could induce a pericardial effusion by inflammation of the visceral pericardium. Secondly, due to the small size of catheters used in electrophysiologic studies, perforation may go potentially unrecognized during the procedure, which also results in pericardial effusion.

Damage to the valvular apparatus secondary to catheter trauma has been well recognized [3-5]. Injury to the aortic as well as the mitral and tricuspid valves have been previously reported [3-5]. We only noted injury to the aortic valve. Previous reports suggest this complication occurs in about 1.1 % of patients having ablation on the left side of the heart using retrograde approach [4]. However for the same catheter aproach, this incidence might rise to values up to 30% in children and adolescents [5]. Manipulation as well as prolonged placement of a catheter across the valve leaflets may stretch and compress the leaflets and subsequently damage them. However, Pires et al. could not find a clear relationship between the valvular injury and technique of ablation. In their study, 9 patients had new onset aortic regurgitation post ablation when in fact 8 of the 9 did not have transaortic valve catheter manipulation performed during their procedure [3]. This raises important questions about the cause of aortic regurgitation observed after catheter ablation procedures, and suggests that trauma to the aortic valve may not be the only explanation.

A limitation of this study was that data were obtained retrospectively. Also TTE's were performed and interpreted by different echocardiographers at two different laboratories. However, the TTEs were done in a standard fashion.

An important aspect of current management is that in most patients, catheter ablation is now performed as a same day procedure. Several institutions allow uncomplicated patients to go home on the same day after the procedure. In view of this we have utilized routine TTE as a tool to assess potential complications prior to discharge of the patient. Our above experience demonstrates that routine TTE is probably not indicated in children with structurally normal hearts undergoing catheter ablation for reentrant atrioventricular tachyarrhythmias. The exception to this may be patients undergoing retrograde ablation via the aortic valve, in whom it may be advisable to assess aortic valve function, especially the presence of aortic insufficiency, prior to discharge from hospital.

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Chapter 4

Ablation Of Atrial Reentrant Tachycardia In Children With Silent Atrium

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Summary

Two children with silent atrium and recurrent intraatrial reentrant tachycardia (IART) are described. Patient 1 developed silent atrium following antiarrhythmic medical therapy. On stopping medications, spontaneous electrical activity returned as did the tachyarrhythmia. At electrophysiological study, areas of both atria were electrically silent despite presence of P waves on the surface ECG. A common atrial flutter circuit was successfully ablated. Patient 2 presented with congenital atrioventricular block, and a transvenous dual chamber pacemaker was implanted at 6 years of age. Thereafter she developed recurrent IART. At 2 separate electrophysiologic studies, common atrial flutter and a microreentrant circuit in the right atrium were ablated. During both electrophysiological studies, silent areas were recorded in the right atrium. The natural history of silent atrium presenting in childhood is unknown. The possibility of spontaneous recovery of atrial function argues for conservative treatment, such as ablation of the tachyarrhythmia rather than His bundle ablation.

Silent atrium (SA) is a syndrome characterised by quiescent atria which cannot be activated by external electrical stimulation.[1] This rare arrhythmia usually presents with junctional bradycardia without any P-wave on the surface electrocardiogram. The cause of SA is often unknown; permanent forms are reported in patients with systemic muscular dystrophy, myocardial amyloidosis and myocarditis.[2] A transient form of SA is seen in reaction to antiarrhythmic medication or after cardiac surgery. A familial form has also been described.[3] Besides bradycardia, atrial flutter can coexist in a partially silent atrium.[4] We here describe 2 children with SA and a coexistent intraatrial reentrant tachycardia (IART) leading to symptoms of heart failure. Both underwent successful ablation of their IART circuit.

Case Reports

Patient 1

The first patient presented at 14 months with IART. She was treated with sotalol (upto 8 mg/kg/day) and thereafter propafenone (upto 10mg/kg/day), without adequate control of the tachyarrhythmia. The IART was successfully converted to sinus rhythm by DC cardioversion. The subsequent ECGs however showed frequent sinus arrest and ventricular standstill for three seconds, for which a dual chamber epicardial pacemaker was implanted. Four months later, IART recurred, and was not controlled with increased dosages of sotalol. Electrical and mechanical silence of the atrium developed, necessitating reprogramming of the pacemaker to VVI-R mode. She had a cerebral infarction probably resulting from a thrombo-embolism arising from the left atrium, leading to a left-sided hemiparesis. Thereafter, she was referred to our institution. Treatment was commenced with oral anticoagulants. On discontinuing the antiarrhythmic medications, atrial electrical activity on the surface ECG was restored two months later, associated with recurrence of IART. Echocardiography showed a dilated left ventricle with a fractional shortening of 24%.

At electrophysiological study, although P waves seen on the surface ECG, areas of electrical silence were recorded in both atria, despite having stopped medications three months previously. A broad QRS complex tachycardia

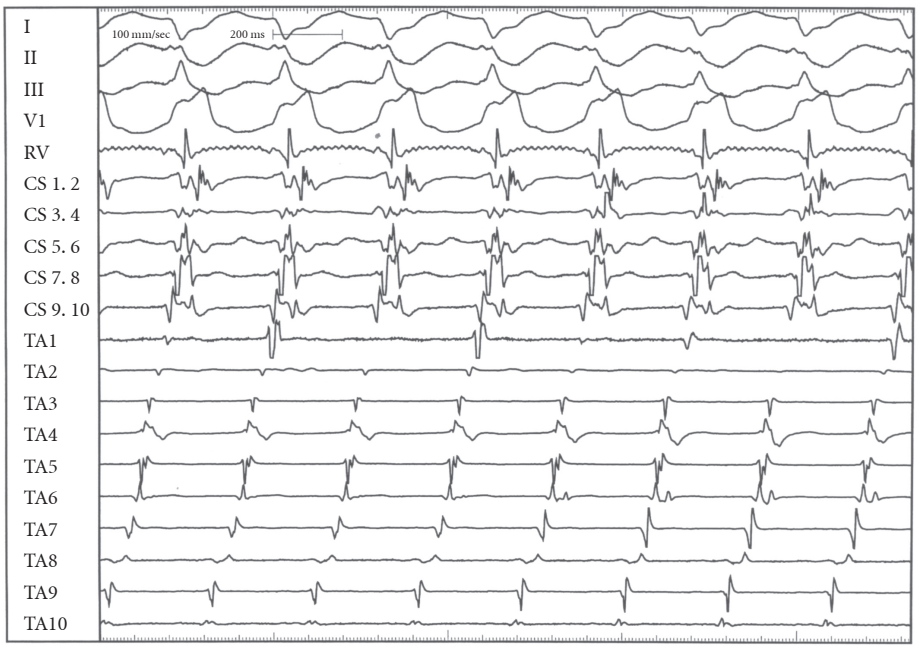

Figure 1. Spontaneous IART in patient 1, with a right bundle branch block morphology of the QRS complexes. A classical flutter circuit with anticlockwise activation of the atrium is seen from the endocardial recordings in the 20 polar halo catheter (TA1 to TA10).

(fig.1) was initiated (rate 240/min). The entire tricuspid valve annulus was mapped using a 20 polar halo catheter introduced from the inferior vena cava and a 10 polar catheter introduced from the superior vena cava (fig.2). The endocardial activation sequence confirmed an isthmus-dependent IART circuit. A line of block was created by a series of radiofrequency current applications, between the tricuspid annulus and inferior vena cava, terminating the IART (fig.2). Bi-directional conduction block was confirmed by pacing on either side of the line of block. One week post-ablation the ventricular function had improved, with a left ventricular fractional shortening of 35%. At follow-up three months later, she remained without symptoms, and with a predominantly paced atrial rhythm.

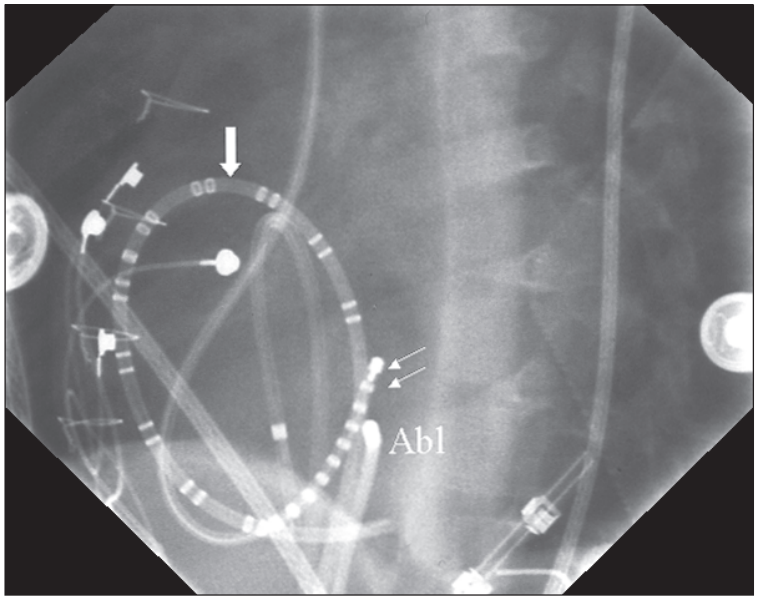

Figure 2. A left anterior oblique radiographic projection showing the location of the 20 polar halo catheter (large arrow) introduced via the femoral vein, and a 10 polar catheter (double arrows) introduced from the internal jugular vein. Together, these catheters enable mapping of the entire tricuspid valve annulus and isthmus. The ablation catheter (Abl) is located in the isthmus.

Patient 2

The second patient presented with congenital complete atrioventricular block (SLE positive mother), and underwent transvenous dual chamber pacemaker at 6 years of age. At routine follow-up, she was noted to have IART. This was initially terminated by overdrive pacing using her own internal pacemaker leads. Due to frequent recurrences (upto 25% of the time), it was decided to undertake ablation of the IART circuit. At electrophysiological study, common atrial flutter was inducible. Areas of electrical silence were recorded within the right atrium. Isthmus block was created between the tricuspid annulus and inferior vena cava, as described for patient 1. Despite this, IART remained inducible. In view of the prolonged duration, it was decided to terminate the procedure.

Four months post-ablation the patient returned with impaired ventricular function (left ventricular fractional shortening of 17%), associated with a recurrence of IART which required DC cardioversion. She underwent a second electrophysiological study. During this procedure, a micro reentrant circuit was mapped on the right atrial free wall. Areas of electrical silence were still recorded from the right atrium. The line of block created during the first electrophysiological study was noted to be complete in both directions. She underwent ablation of this micro reentrant circuit, by creation of a line of block to the inferior vena cava using a series of radiofrequency current applications. Following the procedure, no tachyarrhythmia was inducible. Over a follow-up of three months, she has had no recurrence of tachyarrhythmia, and the ventricular function has improved (left ventricular fractional shortening of 25%).

Discussion

Silent atrium is a poorly understood condition. There is little literature about this in the paediatric population. It may be progressive in adults, with diminution of P wave amplitude followed by complete disappearance of the P wave over several years [5]. In our first patient, silent atrium developed during treatment with high doses of antiarrhythmic medications. On discontinuation of pharmacologic therapy, the surface P wave returned, suggesting an association with antiarrhythmic medical therapy. However, during electrophysiological study, areas of atrial silence were present three months after discontinuing all antiarrhythmic medications. This suggests that there may be an ongoing pathological process in the atria. At follow-up after catheter ablation, her atrial electrical activity is predominantly paced, suggesting persistent sinus node dysfunction.

Patient 2 presented with congenital atrioventricular block. Clinical symptoms arose only after dual chamber pacemaker implantation allowed for 1:1 atrioventricular conduction. She did not receive any antiarrhythmic medications prior to catheter ablation. During the electrophysiological study, areas of electrical silence were recorded in the right atrium, suggesting a diffuse atrial disease process. An autoimmune process, which may also have contributed to the atrioventricular block, cannot be excluded as the cause of the electrical disturbances in the atrium.

Balaji et al have described a patient with SA and coexistent atrial flutter who was treated by His-bundle ablation [4]. There is no literature about long-term follow up of SA in children. Sporadic case reports with recovery of atrial activity seen in infants suggest that SA does not have to be progressive in the paediatric age group [6,7]. In view of this, destructive procedures such as His bundle ablation should probably be avoided. In our two patients the IART circuit, and a separate micro reentrant circuit in the right atrium were successfully ablated. Both patients however still have areas of atrial electrical silence, and it is unknown whether these areas will form the substrate for a new IART circuit in the future.

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Chapter 5

Non-Automatic Focal Atrial Tachycardia: Characterization And Ablation Of A Poorly Understood Arrhythmia In 38 Patients

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Abstract

Non-automatic focal atrial tachycardia (NAFAT) is a rare and poorly understood arrhythmia either due to microreentry or triggered mechanism. NAFAT was defined as a focal atrial tachycardia which was inducible with pacing maneuvers in the electrophysiology (EP) lab. We reviewed the charts and EP study reports of all 38 patients with NAFAT, who underwent an EP study at our center between April 1994 and September 2000. Patients were predominantly female (n=31, 82%), aged 11-78 years (median 46). The mean age at presentation was 31 years (range 7-71 years). None of the patients had structural heart disease or had undergone prior heart surgery. Electroanatomic mapping (EAM) was performed in 22 patients and showed no scars in the atrium. A total of 45 foci were identified (range 1-3 foci / patient). Anatomically NAFAT foci were predominantly right atrial (n=35) rather than left (n=10). The NAFAT cycle length ranged from 270 to 490 (mean±SD; 380±69 ms) and was significantly lower in patients younger than 24 years of age. Ablation, attempted for 42 foci was successful in 33 (79%). The success rate in the EAM group was 20/25 foci (80%) compared to 13/18 (72%) in the non-EAM group. In conclusion, NAFAT is a rare arrhythmia which predominantly affects women with no other associated cardiac disease. It mainly occurs in the right atrium, affects all ages and is amenable to catheter ablation.

Introduction

The term atrial tachycardia continues to be used by many cardiac electrophysiologists [1,2]. However, there is no clearly accepted definition of the term. Most use it to denote a focal atrial tachycardia (FAT), which, by definition excludes macro-reentrant tachycardias such as atrial flutter. Also, it is distinct from atrioventricular reentrant tachycardia via a bypass tract and atrio-ventricular nodal reentrant tachycardia. The term usually excludes atrial fibrillation although recent evidence suggests that atrial fibrillation may be a form of focal atrial tachycardia in some patients [3].

Mechanistically, focal atrial tachycardia may be due to one of 3 etiologies: reentry, automaticity and triggered automaticity. To date the most comprehensive review of this subject is a paper by Chen et al [4]. They analyzed the world medical literature on this subject between 1969 and 1997. They differentiated focal atrial tachycardias into those due to abnormal automaticity and those not due to abnormal automaticity (so-called non-automatic FATs (NAFAT)). FAT due to abnormal automaticity was predominantly a disease of the pediatric population. Indeed, there are papers in the pediatric literature which use the term ectopic atrial tachycardia to denote a FAT which is usually incessant and due to abnormal automaticity [5]. Chen et al. were unable to differentiate between reentry and triggered automaticity despite the use of sophisticated electrophysiological and pharmacological maneuvers [4]. They diagnosed NAFAT when the patient had a focal atrial tachycardia which was inducible by pacing maneuvers in the electrophysiology lab.

There are few reports in the literature about NAFAT. Apart from the two papers from Chen et al. quoted above [1,4], we were able to find only two papers excluding case reports in the Medline database [6,7]. Based on this, we decided to review our clinical experience with this arrhythmia. For the purpose of this paper we utilized Chen et al. definition of NAFAT as a focal atrial tachycardia which could be induced by pacing maneuvers in the electrophysiology lab with or without the use of pharmacologic manipulation using isoproterenol or atropine [4].

Patients and methods

Between April 1994 and September 2000, 1328 catheter ablation procedures were performed at our center. We did a database search on these patients. This identified 96 patients with the terms atrial tachycardia, focal atrial tachycardia or

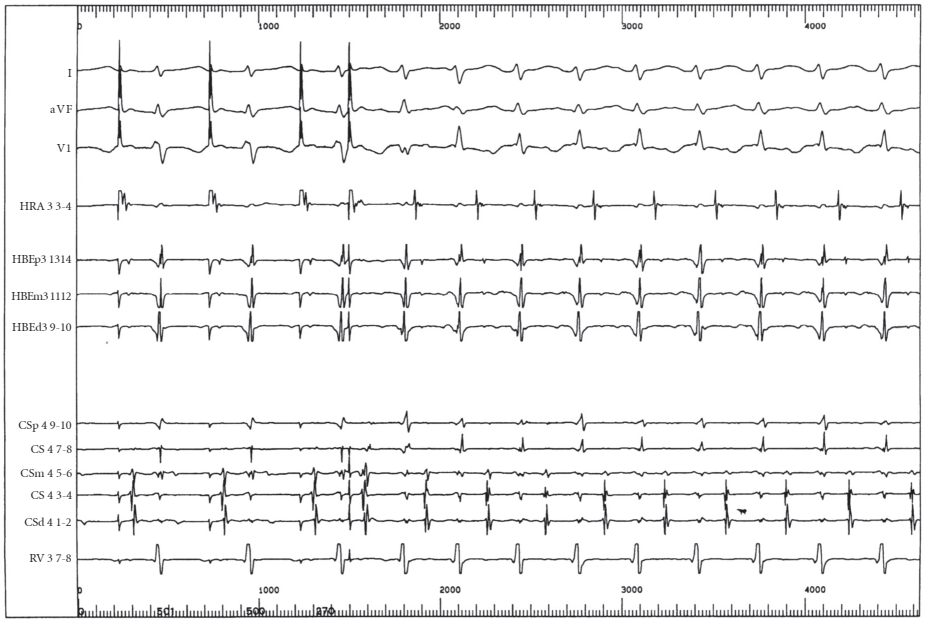

Figure 1. Induction of tachycardia.
Surface leads I, aVF, V1 and intracardiac recordings from the high-right atrium (HRA), His bundle (HBE), coronary sinus (CS) and right ventricle (RV) are shown during induction of tachycardia by pacing the HRA.

ectopic atrial tachycardia. We excluded all patients with AV nodal reentry tachycardia (AVNRT), macro-reentrant tachycardia (i.e. flutters, incisional atrial reentry tachycardia), sinus node reentry tachycardia, atrial fibrillation and concealed accessory pathways. The electrophysiology reports of these 96 patients were further scrutinized and any patient who did not fall into the definition of NAFAT was excluded. We finally found 38 patients who fit the description of NAFAT. We reviewed the charts of all patients with respect to clinical presentation, age at onset of symptoms, antiarrhythmic medication history and history of hypertension, diabetes and other cardiac diseases. The electrophysiology reports of these patients were reviewed in detail.

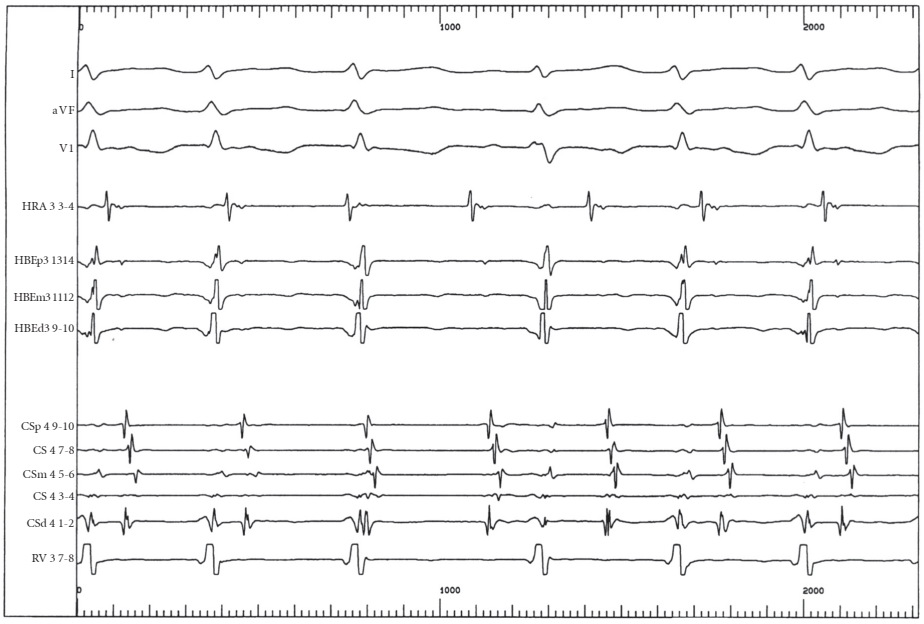

Figure 2. AV dissociation during tachycardia.
Surface leads I, aVF, V1 and intracardiac recordings from the high-right atrium (HRA), His bundle (HBE), coronary sinus (CS) and right ventricle (RV) show AV dissociation during tachycardia, proving it to be atrial tachycardia (Same patient as Fig 1).

Technique

Electrophysiological studies were performed in a standard fashion. Patients received midazolam and fentanyl for sedation and analgesia. Standard catheter placement included a 6 French steerable decapolar catheter in the coronary sinus, a quadripolar catheter in the right ventricle, a quadripolar catheter in the right atrium, a hexapolar catheter in the His bundle area and in selected patients, a 20-polar catheter in the tricuspid valve annulus. Standard pacing and mapping techniques were used to identify the mechanism of tachycardia and to localize the foci (figs.1 and 2). Intravenous isoproterenol infusion (and atropine bolus) was used as necessary. Ablation was performed using standard radiofrequency techniques. Catheter manipulation was guided by fluoroscopy. In October 1997

electroanatomical mapping (Biosense, Diamond Bar, California) became available at our center. All analyses and maps were performed using bipolar electrograms. The propagation maps generated by electroanatomical mapping (EAM) were also examined to help differentiate macro-reentry tachycardia from focal atrial tachycardia. Voltage maps were examined to look for scars (identified as areas of low voltage (<0.1 mV)) in the atrium.

Treatment success

Successful catheter ablation was defined as non-inducibility of the clinical tachycardia with pacing maneuvers performed under the same circumstances as those of the baseline study.

Results

The median age of the 38 patients at time of the procedure was 46 years, range 11-78. There were 31 (82%) females. The mean age at time of presentation was 31 years (range 7-71 years). All but one patient presented with palpitations and 4 had syncope. The one asymptomatic patient was discovered to have an irregular heart beat during a routine pre-military physical exam.

None of the patients had congenital heart disease or had undergone previous cardiac surgery. Seven women (all older than 37 years) had documented hypertension and another two had diabetes.

Antiarrhythmic medications were tried initially in 31 patients. The number of antiarrhythmic medications that had been tried ranged from 1 to 5. The drugs used included beta-blockers (n=19), digoxin (n=7), verapamil (n=6), flecaïnide (n=5) and amiodarone (n=2). Other class 1 agents were used in five patients. Successful control was achieved with drugs in 2/6 patients who took verapamil, 2/5 patients who were on flecaïnide and both patients on amiodarone. All the other drugs were felt to be unsuccessful.

A total of 44 EP studies were performed in 38 patients, identifying 45 different foci (range 1-3 foci per patient). The clinical tachycardia could be induced by pacing maneuvers in all patients. Sixteen patients needed isoproterenol infusion to aid in the initiation of tachycardia and five others needed a combination of isoproterenol and atropine. In 17 patients the tachycardia could be induced without isoproterenol or atropine. Tachycardia foci were predominantly found in the right atrium (n=35, 78%). (Fig. 3).

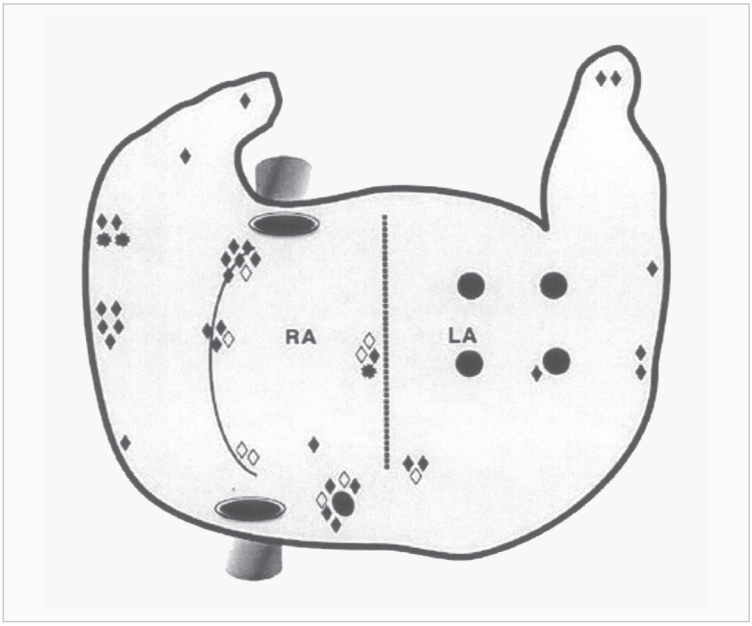

Figure 3. Distribution of the tachycardia foci in the atrium.
A flattened schematic drawing of the right and left atrium (RA and LA) with the appendages turned upwards. Sites of successful ablation are shown by closed diamonds, and open diamonds showing sites of failed ablation. The stars show tachycardia foci for which ablation was not attempted. Note the clustering along the crista terminalis, the right atrial free wall, os of the coronary sinus and Koch's triangle.

Tachycardia cycle length at the EP study ranged from 270 to 490 msec (mean ± SD, 380 ± 69). The cycle length in the patients younger than 24 years was found to be significantly shorter compared to patients older than 37 years (342 ± 50 vs 390 ± 70) ($p < 0.05$).

Radiofrequencey catheter ablation (RFCA)

Catheter ablation was the first choice therapy in 7 patients. Indications for radiofrequency catheter ablation (RFCA) included progressive worsening of symptoms, failure of medical therapy or association of medical therapy with unacceptable side effects.

Thirty-seven of the 38 patients underwent 42 RFCA procedures. In 1 patient, a girl aged 17 years, RFCA was not done because the atrial tachycardia focus was adjacent to the His bundle. There were two other foci (both in the high lateral right atrium) for which catheter ablation was not attempted because the tachycardia could not be sustained during the procedure and therefore could not be mapped successfully (Fig 3). Of the 42 ablation procedures, 23 (in 22 patients) were guided by EAM and 19 (in 17 patients) were done without EAM. One patient had an initial procedure without EAM, followed later by one with EAM. Ablation of tachycardia foci was attempted for 42 atrial tachycardia foci in these 37 patients and was successful in eliminating 33 (79%) foci. Overall, after one or more procedures, RFCA was unsuccessful in 6 patients, partially successful (including successful ablation of at least one of multiple foci) in 3 patients and complete success was achieved in 28 (76%) patients (16 with EAM and 12 without EAM). The success rate in the EAM guided group was 20/25 foci (80%) versus 13/18 (72%) in the non-EAM-guided group (p=ns).

Patients in whom RFCA was unsuccessful did not differ from those where it was successful when examined by sex, age, weight (of the patient) or location of the foci.

Secondary tachyarrhythmia mechanisms were found in 9 patients. These included AVNRT (6 patients), atrial flutter (2 patients) and one patient with AVNRT and flutter. Slow pathway ablation for AVNRT was performed at the same electrophysiological study in 5 patients and was successful in all. Sustained atrial flutter was induced in 2 patients and was not ablated in either. In one other patient AVNRT and sustained atrial flutter were induced. The former was ablated in a separate procedure and no ablation was attempted for the latter.

Fluoroscopy time for the entire group was 21.5 ± 18.5 minutes (mean ± SD) and procedure time was 3.6 ± 1.2 hours (mean ± SD).

The fluoroscopy time was 25 ± 19 minutes (mean ± SD) in the EAM group and 17 ± 16 in the non-EAM group. The procedure time was 3.7 ± 1.2 hours in the EAM group (mean ± SD) versus 3.4 ± 1.1 in the non-EAM group.

The number of RF ablation lesions ranged from 1-33 (mean 8, median 5) for the entire group. The number of lesions in the EAM group was 1-33 (mean 9.4, median 5) and 2-12 (mean 6, median 5) in the non-EAM group.

Complications

No procedure related complications occurred in the EAM group. In the non-EAM group, one patient developed a pericardial effusion with tamponade requiring pericardiocentesis.

Follow up

After a mean follow up period of 29.3 months (range 5 to 81), two of the 28 (7%) successfully ablated patients had recurrence of arrhythmia. Both were documented by event monitoring. In one patient, the atrial tachycardia could not be induced at electrophysiological study despite documentation by event monitoring. This patient was placed on metoprolol with successful symptom control. The other patient was referred to an outside center with special expertise in ablation. However, despite another initially successful ablation procedure, she had further documented recurrence of arrhythmia. She was placed on acebutolol with successful symptom control.

Nine patients had either unsuccessful or partially successful ablation. Of these, two patients had no further symptoms of tachycardia following successful ablation of one of 2 foci. Five other patients were treated with antiarrhythmic medication and 2 patients subsequently underwent complete atrioventricular node ablation in combination with pacemaker therapy.

The patient in whom RFCA was not attempted due to proximity of the focus to the His bundle was placed on a beta-blocker with successful suppression of the arrhythmia.

Discussion

NAFAT is a rare arrhythmia that predominantly affects women with no other associated structural cardiac disease or scars in the atrium. It mainly occurs in the right atrium, affects all ages and is amenable to catheter ablation.

Age

In a reanalysis of the literature on atrial tachycardia, Chen et al. reported that non-automatic atrial tachycardia was predominantly a condition seen in older people [4]. This was in contrast to automatic focus atrial tachycardia, which was predominantly seen in children [4]. Rodriguez et al. studied the gender and age at

presentation for a wide range of supraventricular tachycardias [8]. In their report, patients with focal atrial tachycardia ranged in age from 2-73 years (mean 35 ± 19). They, however, did not differentiate focal atrial tachycardias by mechanism. Our patients, like theirs, came from a wide age range. We also noted that the younger patients in our group had a significantly shorter cycle length when compared to the older patients. The reason for this difference is unclear.

Gender

We found a female preponderance (82%) in our group of NAFAT patients. This has been previously noted, but not emphasised, largely because other authors have studied different arrhythmias. Markowitz et al. reporting on a series of patients with focal atrial tachycardia, had a 71% female dominance in their group of 17 patients [6]. Likewise Rodriguez et al. had a female dominance (67%) in their subset with paroxysmal atrial tachycardia [8]. Both these groups did not specifically look at NAFAT. It is interesting to note that in a re-analysis of atrial tachycardias, Chen et al. did not note a gender difference even after differentiating automatic – from non-automatic atrial tachycardia and paroxysmal from non-paroxysmal atrial tachycardia [4].

Many common arrhythmia mechanisms show gender differences, but the cause of such differences is unclear. For instance Wolff-Parkinson-White syndrome occurs more often in males [9], while AVNRT is more common in women [10]. Recently, Larsen and Kadish reviewed the effect of gender on arrhythmias [11]. They have suggested a variety of influences, chiefly hormonal, which may affect cardiac ion channel expression, autonomic tone, heart rate variability, baroreflex sensitivity and dispersion of repolarization. However definitive proof regarding hormonal influences on these electrophysiologically important factors is, as yet, lacking.

Right atrium versus left atrium

We found that NAFAT is predominantly a right atrial disease. This again fits in with other previous studies. Chen et al. (in their re-analysis paper) found that most non-automatic atrial tachycardias originate in the right atrium [4]. They also found that automatic focus atrial tachycardias are more commonly right atrial in origin. Markowitz et al. also found most focal atrial tachycardias to be right atrial [6]. Indeed 16 of their 17 patients with focal atrial tachycardias were right sided. Marchlinski et al. reported the results of ablation aided by electroanatomical mapping. They reported 6 right atrial and three left atrial foci [7].

Some authors have theorized that most right atrial tachycardias originate in the crista terminalis. Indeed Lesh and Kalman preferred to clarify atrial tachycardias by location rather than mechanism and created the concept of cristal tachycardias [12]. The crista terminalis is noted to be an area of electrical inhomogeniety with significant anisotropic conduction [13]. Therefore, it is theorized that arrhythmias can easily arise in this area. Our series showed that roughly a third (13 of 36) of the NAFAT's in the right atrium originated in the crista terminalis. Other important sites were the right atrial lateral free wall (n=10), the mouth of the coronary sinus (n=6) and the region of the AV node (Koch's triangle; n=4)

Structural heart disease

In our study, all patients had structurally normal hearts. No patient had previously undergone cardiac surgery or had evidence of cardiomyopathy. Chen et al. did not notice an association between structural heart disease and focal atrial tachycardia [4]. In the study by Markowitz et al., of the 17 patients with focal atrial tachycardia, 7 had evidence of other cardiac disease ranging from mitral valve disease to myocardial infarct [6]. Also 2 patients had dilated cardiomyopathy. Markowitz et al. did not classify their patients into automatic focus versus non-automatic focus or into paroxysmal versus non-paroxysmal. Incessant atrial tachycardia is a well-known cause of dilated cardiomyopathy. They reported that 1 patient had dilated cardiomyopathy secondary to atrial tachycardia, while the other did not [6]. None of the patients in our study population had dilated cardiomyopathy, which is in line with the fact that none of our patients had incessant atrial tachycardia.

Ablation

Catheter ablation has become the treatment of choice for patients with focal atrial tachycardia. Our results show that successful ablation of NAFAT is possible, but that the success rates are lower than generally seen for other types of supraventricular tachycardias such as AV nodal tachycardia or accessory pathways. We noted an improved success rate with the use of three-dimensional EAM, although the value did not reach statistical significance (presumably due to small numbers). Importantly EAM has not decreased the fluoroscopy time, which was a highly anticipated benefit of this new technology. We feel that the reason for the longer fluoroscopy time in the EAM group is because we were in the learning curve for the use of this new technology in this period. Another potential factor

may be selection bias with the patients having EAM coming from a more difficult arrhythmia subset. Marchlinski et al. [7] gave a detailed description of the method of electroanatomical mapping. They reported low fluoroscopy times although they did not do a comparison between electroanatomical versus conventional mapping.

Another possible cause for failure of ablation may have been the small size of lesions with conventional RFCA. Saline-cooled tip catheters have been shown to increase lesion size and improve success rate of ablation in patients with complex arrhythmia substrates [14]. We did not have this catheter technology available in our institution. One could speculate that this new technology could improve the success rate for ablation in patients with this arrhythmia.

The recurrence rate for patients with successful ablation was high. We did not routinely perform repeat electrophysiological studies in the patients with recurrence. Hence we could not determine whether recurrence was due to reactivation of the same focus or activation of a new focus. One speculation is that these patients have an intrinsically abnormal atrium with many potential foci whose activity may vary from time to time.

Limitations

Our study was a retrospective review of cases seen over a 6.5 year period. We did not use entrainment mapping techniques to differentiate between a reentry versus triggered mechanism. Hence the exact nature of the arrhythmia is unclear. However as pointed out by Chen et al., it is difficult (if not impossible) to differentiate between triggered versus micro-reentry even with the use of time consuming and sophisticated techniques [4]. From a practical standpoint, the most important aspect is the differentiation of automatic from non-automatic, since many automatic tachycardias tend to be incessant and can lead to congestive heart failure. We also did not perform drug studies on our patients. Engelstein et al. suggested that adenosine would be expected to terminate atrial tachycardias secondary to a triggered mechanism and proved their hypothesis in 1 patient [2]. Markowitz et al. showed that focal atrial tachycardia is transiently suppressed or terminated by adenosine [6].

There has been a recent report from the Joint Expert Group from the Working group of arrhythmia of the European society of Cardiology and the North American Society of Pacing and Electrophysiology [15]. This group has proposed a new classification of atrial arrhythmias. They recommend the term focal atrial

tachycardia (FAT) and include all mechanisms (automaticity, triggered and microreentry) where the rhythm originates from a focus and spreads centrifugally within this category. They make no further attempt to subdivide this arrhythmia based on potential mechanisms. Based on their recommendations one would surmise that we have reported a group of patients with focal atrial tachycardia without further subdivision.

Conclusion

We have reported the largest single-center experience with a rare and poorly understood form of supraventricular tachycardia. Further research is needed to clarify some of the intriguing aspects of this arrhythmia including its predilection for women without structural heart disease or scars in the atrium.

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Chapter 6

Radiofrequency Catheter Ablation of Atrioventricular Nodal Reentrant Tachycardia in Children Aided by the LocaLisa Mapping System

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Abstract

Aims

In young patients, slow pathway ablation for treatment of atrioventricular nodal reentrant tachycardia (AVNRT) carries a small but definite risk of permanent AV block. The aim was to assess the efficacy of slow pathway ablation aided by the Localisa mapping system.

Patients and Methods

RF modification of the slow AV nodal pathway was performed in 26 children <19 years of age (median age 9.8 years, range 3 to 18.9). Three measures to limit the risk of AV block were applied: 1) Use of LocaLisa, a non-fluoroscopic mapping system, to determine and mark the location of the AV node/ His bundle axis, and monitor ablation catheter position, 2) continuous atrial stimulation during RF delivery to monitor AV conduction, 3) gradual increase of RF power during RF ablation.

Results

AVNRT was rendered non-inducible in all patients. Dual AV physiology was abolished in 24/26 patients; two patients had single atrial echoes at the end of the procedure. At follow-up, AVNRT recurred in 3 patients (including the above 2), necessitating a second procedure. The median number of RF applications was 4 (3-8); median fluoroscopy time was 16 (7-33) minutes. One patient developed transient second degree AV block, with full recovery within 6 weeks of the procedure.

Conclusion

RF modification of the slow AV nodal pathway in children can be safely accomplished, achieveing the ideal end-point of abolishing dual AV physiology, aided by use of the Localisa mapping system.

Introduction

Atrioventricular nodal reentrant tachycardia (AVNRT) is the most common form of supraventricular tachyarrhythmia in young adults [1]. It accounts for between 11-13% of SVT in infants and 13-23% in the whole pediatric population [2,3]. In AVNRT, there are multiple AV nodal pathways, which are functionally and anatomically distinct, forming the electrophysiologic basis for reentry within the AV node. During the last decade radiofrequency (RF) catheter ablation modification of the slow pathway has become the method of choice for curative therapy of AVNRT in symptomatic patients. Most studies have been performed in adult populations demonstrating success rates in excess of 95% [4]. Of concern in the paediatric population is the risk of inadvertent AV block during AV node modification, with the potential requirement for lifelong pacemaker therapy [5,6]. In this study we present the experience with catheter ablation of AVNRT in children using LocaLisa mapping system [7-9].

Patients and Methods

Patients

Twenty six consecutive patients aged <19 years (17 female, 9 male) with AVNRT underwent RF slow pathway modification at our institution (29 procedures). Their median age was 9.8 years (range 3 to 18.9), and median weight 42 kg (15.0 to 59). All children had a structurally normal heart confirmed on echocardiography. Surface 12 lead electrocardiograms at rest were normal in all. The median duration of symptoms prior to ablation was 14 (11-54) months, and all patients had undergone trial of antiarrhythmic drug therapy (median of 2 drugs/day). Indication for ablation was based on patient or parent preference in all cases. All medical and electrophysiologic (EP) records were reviewed for procedural details, complications, and follow-up.

Electrophysiologic Studies

All but 2 of the procedures were performed under general anesthesia, after written consent was obtained. Antiarrhythmic therapy was discontinued for at least 5 half lives prior to ablation. Electrode catheters were introduced via the femoral vein, and positioned in a standard manner in the right atrium, ventricle, and coronary sinus. The His bundle location was entirely mapped out using a standard temperature controlled mapping/ ablation catheter, and displayed on

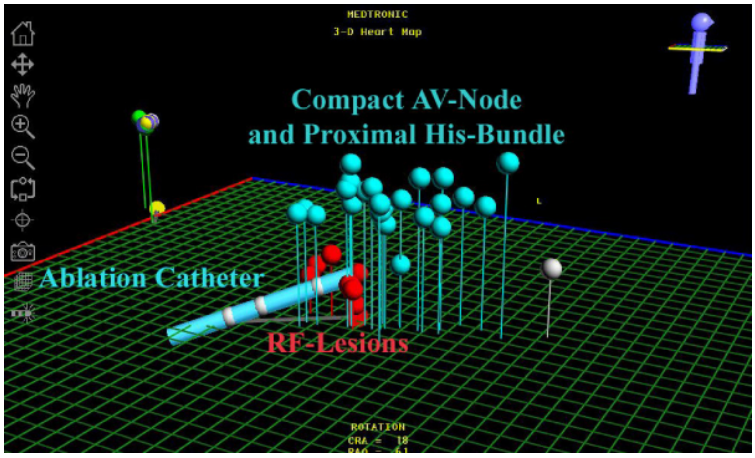

Figure. Localisa map in a right anterior oblique projection, demonstrating the location of the compact AV node and proximal His bundle (blue dots represent sites at which His bundle electrograms were recordable). Individual RF lesions are depicted in red, and the ablation catheter is also shown (with tip electrode depicted in red). The location of the coronary sinus is also shown (yellow/green dots).

the Localisa monitor (figure). The right ventricular catheter was used as the reference catheter for the Localisa mapping system. Using a standard extrastimulus protocol, dual AV physiology (defined as a ≥ 50 ms increase in the A2-H2 interval with a 10-ms decrement in the A1-A2 interval or ≥ 50 ms increase in the A-H interval with a 10-ms decrease in the atrial paced cycle length) was demonstrated in all patients, and sustained AVNRT (defined by the criteria of Ross et al) [10] was induced either at baseline state (17 patients, 19 procedures) or with the use of isoproterenol by infusion (0.02 mcg/kg/min; 9 patients, 10 procedures). The slow pathway was targeted for ablation in all patients.

LocaLisa mapping system

This system, which is commercially available (Medtronic, USA) allows continuous monitoring of intracardiac electrodes. Previous clinical studies have confirmed the efficacy and accuracy of this mapping system [7-9]. All studies described here were performed using the Localisa system.

Ablation

Ablation was commenced approximately 12mm (range 11 to 15) below (inferior to) the location of the proximal His bundle, on the atrial aspect of the tricuspid valve annulus, the latter landmark being based on the appearance of an atrial potential on the distal electrogram of the ablation catheter. This approach was identical to that used in adult patients also during the same time-frame. The localization of the His bundle is based on the steepest bipolar His potential while moving the catheter supero-inferiorly around the His bundle area. By doing so at progressively more posterior sites, one can follow and mark on the Localisa screen the His bundle from its distal to its most proximal extent (antero-posterior extent) (figure). The filter settings for the intracardiac electrograms (Prucka), to eliminate far-field signals were 50-500 Hz bandpass filtering for bipolar electrograms and 0.05-500 Hz for unipolar electrograms. The Localisa system used a 1.5 to 2 second averaging to correct for respiratory variations. Slow pathway potentials were not routinely searched for, but when they were observed (n=7 patients), they were seen as a "slow" hump, usually positive on the bipolar electrogram. Analysis of the location of the slow pathway potential in these 7 patients confirmed that they could be identified between 5-10 mm inferior to the His bundle and 0-5 mm posterior to the tricuspid valve annulus. Sites at which these potentials were seen were definitely targeted for ablation. The compact node could not be identified on the basis of the electrograms, but we take the proximal extent of the His bundle, as marked on the Localisa screen, to be the superior/ anterior margin of the AV node. RF application was performed during continuous atrial pacing, to ensure the presence of AV conduction during each RF application. Pacing was commenced at a cycle length slightly above the resting sinus cycle length (usually at cycle lengths of between 500 to 600 ms).The measured sinus cycle lengths prior to commencing atrial pacing were between 513 and 832 ms. Junctional ectopy during RF delivery, which was used as a marker of proximity to the optimal target area, could be reliably identified. With the occurrence of junctional ectopy the atrial pacing rate was increased to re-enable monitoring of anterograde conduction. Sustained junctional tachycardia during RF application was seen in only 5 patients, at cycle lengths of between 445 – 526 ms, and in all cases pacing at rates higher than the junctional rhythm was possible. Continuous atrial pacing, or changes in pacing rate during RF application did not result in catheter tip instability, or influence the need to terminate lesion application in any patient.

Retrograde conduction of the junctional ectopic beats to monitor retrograde fast pathway conduction was not routinely performed. At sites where junctional ectopy was observed during RF application, the application was continued for upto 60 seconds. The power output of the RF generator was slowly increased, starting at 5W, and increasing gradually to achieve tip electrode temperature in excess of 50^0C. When high grade junctional ectopy, or sustained junctional tachycardia (cycle length >600 ms) was observed at moderate RF power levels (10 to 20 Watts) this was taken as indicating extreme proximity to the AV node, and ablation at these sites was discontinued, and recommenced at a greater distance from the AV node.

After each RF application during which accelerated junctional rhythm was present, the atrial pacing protocol was repeated to either demonstrate dual AV physiology, or reinduction of tachyarrhythmia. If either of these was present, lesions were progressively made closer to the His bundle recording sites, as shown on Localisa (figure). The new site was chosen at between 1 to 4 mm from the previous RF application site, as measured from the Localisa system. The end-point of the procedure was absence of dual AV physiology in 24 of 26 patients. In two patients, both early in our experience (patients 7 and 8 respectively in Table 1) dual AV physiology and single atrial echoes were present at termination of the procedure, but AVNRT was non-inducible. This was accepted as the end-point in these two patients.

Results

RF Catheter Ablation

Catheter modification of the slow pathway resulting in non-inducibility of AVNRT was accomplished in all 26 patients. During each RF application, the distance from the ablation site to the most proximal His bundle electrogram recording was recorded. The median distance of the last RF application site to the His bundle was between 7 (5 to 11) mm. In this patient cohort with a large age range, no differences were observed with regard to the age of the patient and the distance of the successful ablation location from the proximal His bundle electrogram. Two patients had evidence of persisting dual AV physiology and single atrial echo beats. As mentioned previously, early in our experience with children, this was chosen to be the end-point for the procedure in these two cases. None of the other patients had evidence of dual AV physiology at termination of

Table 1.

Patient demographics and follow-up					
No	Age (years)	Weight (kg)	RF pulses (No)	Fluoroscopy (min)	Follow-up (months)
1	16.5	47	8	17	61
2	14	49	5	9	60
3	17.1	47	5	19	56
4	12.3	42	4	12	54
5	16.9	59	4	7	53
6	14.5	48	4	16	51
7	3.1*	15	4.....(4)	14.....(17)	43
8	6.6*	20	4.....(3)	12.....(19)	42
9	14.3	50	7	21	37
10	18.9	56	6	19	33
11	18.7	51	4	16	30
12	4.8	21	6	14	28
13	3	15	3	11	28
14	6	27	4	18	26
15	6.1	26	6	33	26
16	14.7	52	8	29	24
17	14.1	49	4	14	24
18	11	45	7	16	21
19	9	42	5	17	21
20	11.6	36	3	13	19
21	9.9	30	4	21	14
22	10.8*	45	4.....(4)	12.....(20)	14
23	7.2	24	7	19	9
24	4.1	19	3	10	4
25	6.7	27	7	18	3
26	5.3#	22	4	15	3

Symbols: * refers to the 3 patients with documented recurrence of AVNRT, who underwent a second ablation procedure. The fluoroscopy times and number of lesions for re-do procedures are given in parentheses. # refers to the single patient who had transient second degree AV block.
Follow-up refers to the interval at most recent evaluation, after the last ablation procedure.

the procedure. The median number of RF applications was 4 (3 to 8); the median fluoroscopy time was 16 (7 to 33) minutes. The A-H interval remained virtually unchanged (72 ± 12 msec pre-ablation versus 79 ± 21 msec post-ablation). There were one episode of second degree AV block in a 5 year old girl, with fixed 2:1 AV conduction (confirmed at various atrial pacing rates) following slow pathway ablation, and absence of retrograde VA conduction. A total of 4 RF pulses had

been delivered in this patient, at a median distance of 7 (5 to 8) mm from the His bundle. During the last RF application, there had been no evidence for catheter instability. No isoproterenol or atropine was administered to assess AV conduction, and no corticosteroids were administered. The patient was as usual 24 hours post-procedure, on oral aspirin therapy. Overnight telemetry had confirmed ventricular rates of >60/min throughout. At outpatient follow-up 5 weeks later, normal 1:1 AV conduction was documented. Three months post-ablation, transesophageal atrial pacing performed in this patient confirmed a Wenkebach cycle length of 340 ms, which was considered to indicate restoration of functional integrity of the AV node. Apart from this patient, no episodes of AV block occurred during any of the RF applications, and none of the other patients had any procedure-related complications. Patients were discharged on the following day, on oral aspirin therapy (5mg/kg/day) for 6 weeks.

Recurrence Rate

In three patients, AVNRT recurred within 3 months of the initial ablation procedure (Table). This included both patients with evidence of persisting dual AV physiology. The third patient did not demonstrate dual AV physiology at the end of the initial ablation procedure, but had documented AVNRT during a second EP study. All 3 patients underwent a second ablation procedure at 3, 3 and 6 months after the initial procedure. In both patients with dual AV physiology demonstrated at restudy, this was abolished. The third patient showed progressive A-H prolongation during atrial extrastimulus pacing, with induction of AVNRT, but without a classical A-H jump. The slow pathway was again modified, using the techniques described previously. None of these 3 patients has had recurrence of tachyarrhythmia at follow-up of >12 months.

Follow-up

The median follow-up duration was 25 (3 to 61) months after the last ablation procedure. Serial Holter recordings at 6 months (N=19) and at 12 months (N=11) post-ablation did not demonstrate any AV conduction disturbances.

Discussion

Catheter ablation by RF current application is currently the accepted treatment modality for AVNRT in adults. The frequency of this arrhythmia appears to be age-dependent, although it is increasingly diagnosed in childhood [11]. Of

particular concern is the risk of inadvertent AV block during slow pathway modification. In a review of 314 children and adolescents with AVNRT, 5 (1.6%) developed advanced second- or third-degree AV block as a complication of the procedure [5]. This rate did not differ from the 1% risk of AV block reported in adult series of patients with AVNRT. More recent follow-up studies in children reveal a complication rate for AVNRT ablation that appears to be age dependent, varying from 18% in patients <5 years of age to 3% in patients aged between 5 and 21 years [6]. Fluroscopy times and radiation exposure is another important issue when dealing with children. The fluoroscopy times in our series (median 16 minutes, range 7 to 33 min) compare favourably with that reported in the Pediatric Radiofrequency Ablation Registry (29.3 ± 25.7 minutes) [6].

The potential risk of RF lesion growth resulting in late onset AV block should also be considered, during ablation procedures close to the AV node in young patients [12]. In this report we present 26 children with symptomatic AVNRT who underwent RF catheter modification of the slow AV nodal pathway as a curative therapy. The results are comparable to that in adults. Moreover, none of the treated children developed permanent AV conduction disturbances at follow-up.

There are no clear recommendations concerning the end-point AVNRT ablation. The end-point of non-inducibility of AVNRT even in the presence of dual AV physiology and single atrial echo beats is generally accepted, and has been shown to be associated with long-term success in adults. Unlike most previous reports of AV node modification, we attempted to abolish dual AV physiology during the ablation procedure in the majority of patients. This aggressive approach was aided by the use of the Localisa mapping system which enabled the location of the ablation catheter electrodes to be precisely monitored, and the distance from the His bundle to be measured. Ancillary precautions that were taken during RF energy application included incremental AV pacing, and energy delivery starting at low power output, with progressive increase in output to achieve the desired catheter tip temperature. Both patients in whom the desired end-point was not achieved, and where non-inducibility of AVNRT was used as a measure of success, had recurrence of the original tachyarrhythmia within 3 months of the ablation procedure, necessitating a second procedure. The only other patient with a documented recurrence did not have classical dual AV physiology during the second EP procedure, as described above, although the arrhythmia had all the characteristics of AVNRT.

One of the potential limitations of this study is that patients were not randomised to ablation with and without the use of Localisa, so that direct comparisons between the two subgroups from the same institution cannot be made. Recurrence rates following initial ablation (3/26 patients, or 12%) were rather high, although in 2 of the 3 patients non-inducibility of AVNRT with persistent dual AV physiology was the end-point used. The ideal end-point of abolition of dual AV physiology was eventually successfully accomplished in all patients, unlike all previous reports of AVNRT ablation [13]. This end-point was achieved with fluoroscopy times comparable to, or less than that reported for other series [4,5,6,13]. With a relatively small cohort of patients and a modest follow-up interval, it is not possible to make recommendations concerning the ideal end-point for AVNRT ablation in children.

In conclusion, continuous electrode localization, in combination with the ability to measure the distance to the AV node/His bundle axis, improves the safety and efficacy of catheter modification of the AV node in young patients with AVNRT.

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Chapter 7

Endocardial Pacemaker Implantation In Infants ≤ 10 Kg Weight

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Abstract

Background

Background: Epicardial pacemaker implantation is the most common approach for small children requiring pacemaker implantation though is not free from complications. This report reviews the experience with endocardial pacemaker implantation in children ≤ 10 kg at two centres as an alternative approach.

Methods and Results

39 children, median age 3.8 months (2 days-35 months), weight 4.6 (2.3-10) kg underwent endocardial permanent pacing (VVI/R in 38, DDDR in 1). Indications for pacing were complete heart block (CHB) in 34 (congenital in 21, post-surgical in 12, congenitally corrected transposition of the great arteries 1), long QT syndrome in 3 and sinus bradycardia in 2. Two children with post-surgical CHB died 7 days and 3 weeks post-implantation respectively, due to heart failure and septicemia, despite appropriate pacemaker therapy. Over a median follow-up of 4.3 years (9 months-15.3 years) 12 patients underwent 18 generator replacements. Five patients were upgraded to physiological pacing. Ten patients underwent 12 ventricular lead advancements. Ventricular lead extraction was attempted 11 times in 9 patients and succeeded 10 times. Two patients were converted to epicardial dual chamber systems. Two pre-pectorally placed generators required resiting due to threatened skin necrosis. Infective endocarditis on the lead, 9 months post-implant required removal of the system in one patient. The subclavian vein was found to be asymptomatically thrombosed in 4.

Conclusion

Endocardial permanent pacing is feasible and effective in children ≤ 10 kg and an acceptable alternative to epicardial pacing.

Introduction

Many pediatric centers continue to advocate the epicardial approach to permanent pacing in children younger than five years of age or less than 30 kg in weight [1]. The major reason for avoiding the endocardial approach is the perceived risk of venous occlusion, growth related lead problems and the need for future lead extractions and replacements [2]. Skin erosion at the generator site has also been of concern with pectoral placement of the generator. Reduction in lead body and generator size and the use of intravascular loops to cater for future growth has lessened many of these concerns [3-5]. Most of the reports of endocardial pacing in very young children [3-10] have small numbers or have grouped them with older patients so that the total published experience is small and follow up duration is short. The largest report to date has been of 24 patients ≤ 15kg at the time of implantation [4]. An increasing number of centres now prefer endocardial pacing in children older than 1 year and/or weighing more than 8 kg [11]. As problems are to be expected in the smallest children, we present our experience in a large series of children ≤ 10.0 kg at the time of pacemaker implantation.

Patients

Between October 1987 and August 2002, thirty-nine children (20 female, 19 male; 32 at Guy's Hospital, 7 at Wilhelmina Children's Hospital) ≤ 10 kg in weight received an endocardial pacing system. Their weights ranged from 2.3 to 10 kg (median weight 4.6 kg) and their ages from 2 days to 35 months (median age 3.8 months). Indications for permanent pacing are given in Table 1. Congenital complete heart block (CHB) was present in 21 patients (isolated in 19). Five patients underwent pacing within the first 48 hours of life due to heart failure and very low heart rates. In the other 16, a pacemaker was implanted between two weeks and 13 months of age, based on one or more of the following; heart failure, failure to thrive, syncope, increase in heart size, daytime heart rates below 50 beats per minute, runs of more than three ventricular extrasystoles, and QT interval prolongation. In 14 children isolated congenital CHB was associated with maternal anti-Ro antibodies, in 2 the anti-Ro antibody status was unknown and in 3 was negative. One of the mothers, negative for anti-Ro antibodies, had varicella during pregnancy. Eleven children required permanent pacing for (CHB) shortly after surgical

Table 1.

Indications for pacing		
Arrhythmia	No. of patients	Additional structural heart disease
Congenital CHB	21	
- Isolated	19	Patent arterial duct (4), Atrial septal defect (1)
- Congenital heart disease	2	Tetralogy of Fallot (1), cTGA (1)
Postoperative CHB	11	Coarctation of aorta (3), TGA (2) , Tetralogy of Fallot (1),
- VSD closure	7	Total anomalous pulmonary venous drainage (1),
- AVSD closure	3	Left atrial isomerism (1), Patent arterial duct (1),
- VSD enlargement	1	Atrial septal defect (1), Dysplastic atrioventricular valve (1)
Late Postoperative CHB	1	TGA & VSD
cTGA – postnatal CHB	1	Atrial septal defect, Ventricular septal defect, Patent arterial duct & Ebstein's anomaly
Long QT syndrome	3	
Sinus node disease	2	Atrial septal defect (1)

CHB = complete heart block; cTGA = congenitally corrected transposition of the great arteries; TGA =transposition of the great arteries; VSD = ventricular septal defect; AVSD = atrioventricular septal defect.

repair of a congenital heart defect. They had undergone closure of a ventricular septal defect (VSD) in 7, atrioventricular septal defect in 3 or enlargement of a VSD in 1 at the time of an arterial switch for transposition of the great arteries. A 17-month-old female was paced for late postoperative CHB, after a neonatal arterial switch operation and VSD closure. A 3-month-old child was paced for postnatal onset complete heart block with congenitally corrected transposition. Three patients had a pacemaker implanted as combination therapy with â-blockers for long QT syndrome. Two patients were paced for sinus bradycardias and reflex anoxic seizures.
In two of these children there was a right to left shunt at the time of pacemaker implantation. The first had congenital CHB and Tetralogy of Fallot and had surgical repair 6 months after pacemaker implantation. The second with congenitally corrected transposition, an atrial septal defect, VSD and patent arterial duct had duct ligation after pacemaker implantation which exposed the right to left shunting at atrial level. The VSD is small and he is awaiting transcatheter occlusion of the atrial septal defect when he is older.
All but one of these children received a single chamber endocardial pacemaker. During this period 5 other children ≤ 10.0 kg underwent epicardial

pacing. A child at Guy's Hospital with congenital CHB weighing 1.5 kg had a single chamber pacemaker. At Wilhelmina Children's Hospital, 4 children had dual chamber pacemakers implanted at the time of corrective cardiac surgery as they were considered to need the haemodynamic benefit of atrioventricular synchrony.

Technique

Under general anesthesia, venous access was gained by percutaneous puncture of the left (the majority) or right subclavian vein. Via a 4-7 French introducer, a unipolar (n=13) or bipolar lead (n=27) was introduced and positioned in the right ventricular apex or outflow tract. Leads were steroid-eluting in 25 and were active fixation in 19. In the only patient to receive a dual chamber system, for severe postoperative heart failure, an atrial lead was introduced via an axillary vein cutdown on the same side as the subclavian vein puncture. All the leads were placed with a redundant loop in the atrium, to allow for somatic growth. The generator was placed in a sub-pectoral (n=7) or a pre-pectoral (n=23) pocket or in a pocket in the anterior abdominal wall (n=9), depending on the size of the generator in relation to the patient's size. Abdominal implants were predominantly in the early patients in this study, in those < 2.5 kg and in the infant with a dual chamber pacemaker. In these patients, the extravascular part of the lead was tunnelled subcutaneously to the pacemaker pocket. The lead was secured subcutaneously at its entry point into the subclavian vein, using non-absorbable suture material, usually without the protective sleeve to reduce bulk. During the implantation procedure all patients received antibiotic prophylaxis intravenously, continued intravenously for 48 hours and orally for five days. A variety of different leads (Table 2) and generators (Table 3) were used, reflecting the technological advances over this 15-year period.

Results

At implantation good pacing and sensing thresholds were achieved in all cases. Two children with post-surgical CHB died 7 days and 3 weeks after pacemaker implantation. The former had left atrial isomerism and had undergone repair of an atrioventricular septal defect at 6 weeks of age. The temporary epicardial pacing wires placed at surgery became infected and failed, with a suppurative

Table 2.

Pacemaker leads used at initial implantation						
Lead model	n	Years of implant	Size (French)	Fixation	Polarity	Steroid eluting
Ventricular						
- Biotronic PE60/4DNP	3	'87 – '88	5	P	U	-
- Siemens 424M/60	3	'87 – '88	4.8	P	U	-
- Biotronic TIR-60-BP	1	'92	6.6	P	B	-
- Medtronic 4024	2	'92	5.8	P	B	+
- Siemens EL 1050T	1	'92	6	P	B	-
- Vitatron Slimtine	3	'92 – '01	5	P	U	-
- Vitatron IMD 49B 6546	7	'96 – '98	5.7	P	B	+
- Biotronic Y60-BP	2	'97	6.6	A	B	-
- Medtronic 4023	1	'97	3.6	P	U	+
- Medtronic 5067	1	'99	6.6	A	U	+
- Sulzer/Osypka K467-40	1	'99	4	A	U	-
- Medtronic 5076	6	'99 – '01	6.2	A	B	+
- St. Jude Tendril SDX 1488	8	'00 – '01	6.1	A	B	+
Atrial						
- Sulzer/Osypka K467-40	1	'99	4	A	U	-

P = passive; A = active; U = unipolar; B = bipolar.

pericarditis precluding implantation of an epicardial pacing system. A dual chamber endocardial system was implanted as she was in severe heart failure. Despite effective sequential pacing, she died seven days later from sepsis. The second patient had undergone a hemodynamically suboptimal repair of total anomalous pulmonary venous drainage, VSD and aortic coarctation. Effective endocardial ventricular pacing allowed, the child to go home for palliative care and she succumbed from congestive heart failure and secondary fungal sepsis 3 weeks after pacemaker implantation.

Follow-up

Follow up data were obtained for 36 patients over a median follow up time of 4.3 years after first implantation (range 9 months to 15.3 years). One patient was lost to follow-up after emigrating. During this period 16 (44%) patients continued with their current generator in situ (range 9 to 63 months; mean 28 months), 10 (28%) had the system revised at the end of life of the generator

Figure 1. Outcome of pacemaker implantation in 39 children < 10kg.

(range 48 to 74 months; mean 61 months) and 10 (28%) required an intervention prior to the end of life of the generator (range 2 days to 31 months). Fig. 1 gives an overview of follow up to the major end points and Figs. 2 and 3 give a detailed outcome including subsequent interventions. A total of 30 re-interventions occurred during this follow up period (11 patients having one, 6 patients having two, 1 patient having 3 and 1 patient having 4 re-interventions). Of the 36 patients, 31 (86%) continue with an endocardial pacing system, 2 have an epicardial system and 3 are no longer paced.

Early Re-intervention

In one child the lead was found by echocardiography to have crossed a patent foramen ovale and was successfully repositioned two days after implantation. Three patients, receiving a pre-pectoral pacemaker system at two, three and eight days of age (weights of 3.1 – 3.3 kg), had wound closure or generator pocket problems despite use of some of the smallest generators (Finesse (n=1), Microny (n=2) – Table 3). Two of them underwent repositioning of the generator because of threatening skin necrosis; one (three days old at implantation) from a pre- to a sub-pectoral pocket and the other (eight days old at implantation) from a pre-pectoral to an abdominal pocket, respectively two days and three months post implantation. In the latter patient there was threatened erosion again at 2 years of age and the system was removed and not replaced due to an occluded subclavian vein. At this stage her varicella myocarditis had resolved and she had a good ventricular escape rate despite continued heart block – she remains unpaced 7 years later. The third patient had been given steroids in utero for four months prior to delivery in an attempt to arrest or reverse the progression of AV-block. Following pacemaker implantation the wound would not heal properly and was resutured 2 months after implantation. At 20 months there was a pocket infection and the system was removed and replaced with an epicardial DDD pacemaker. The subclavian vein was noted to be occluded during the lead extraction. One patient with surgically acquired CHB after VSD repair with a residual leak developed infective endocarditis on the tricuspid valve and pacing lead 9 months after pacemaker implantation. The pacing system was removed but not replaced as the patient had recovered sinus rhythm (and remains in sinus rhythm 9 years later). A patient with surgically acquired CHB after an arterial switch operation with VSD enlargement, developed

Table 3.

Generators at initial implantation			
Generator	n	Years of implant	Weights / volumes
Medtronic Spectrax SX 5985	1	'87	45 gr / 20 cm3
Biotronic Mikros 02	2	'87 – '88	26 gr / 10 cm3
Pacesetter Pheonix 251-6	3	'87 – '88	33 gr / 12 cm3
Biotronic Pikos 01	1	'92	27 gr / 8.9 cm3
Biotronic Nanos 01-BP	1	'92	23 gr / 10.8 cm3
Vitatron Ultrafinesse 204	1	'92	18 gr / 7 cm3
Vitatron Ultrafinesse 203	1	'92	18 gr / 7 cm3
Siemens Sensolog III 2034 II	1	'92	26 gr / 14 cm3
Vitatron Finesse 201	1	'95	21 gr / 8.5 cm3
St Jude Microny II SR+ 2425T	9	'96 – '01	12.8 gr / 5.9 cm3
Medtronic Thera SR 8960 I	2	'97 – '99	21.5 gr / 9.7 cm3
St Jude Regency SR+ 2400L	4	'98 – '01	18.5 gr / 8.6 cm3
Vitatron Diamond II *	1	'99	25 gr / 11 cm3
St Jude Microny kSR 2535K	2	'99 – '01	12.8 gr / 5.9 cm3
St Jude Microny II SR+ 2525T	9	'00 – '01	12.8 gr / 5.9 cm3

* Dual chamber pacemaker

progressive mitral and aortic regurgitation and severe heart failure. Four months after implantation of the endocardial pacemaker, she had a mitral valve replacement and aortic valve repair at which time the endocardial pacing system was removed and an epicardial DDD pacemaker was implanted to try improve myocardial performance. In 4 patients (3 with an abdominally sited generator) the redundant atrial loop was inadequate and the lead had to be advanced prior to generator end of life at 3, 10, 13, 31 months after implant. In one of these lead advancement failed and the lead was replaced.

Generator replacement and system removal

Generators were electively replaced 17 times in 12 patients at end of life of the generator. One other patient underwent generator replacement at the time of a necessary lead advancement for lead stretch.
In two patients the endocardial pacing system was replaced by an epicardial DDD system (described in early re-intervention section, Fig. 2). In three patients the entire pacemaker system was removed and not replaced. Two have


Interventions before end of life of generator n = 10
Wound problems n = 3 2 days to 3 months
Lead in LV n = 1 Repositioned following day. System in situ at 36 months
Mitral regurgitation with heart failure 4 months after arterial switch operation n = 1 Mitral valve replacement & Epicardial DDD
Endocarditis n = 1 Surgical removal pacing system at 9 months (sinus rhythm)
Lead length inadequate n = 4 At 3 -10 -13 - 31 months
Wound dehiscence and infection n = 1 Resuture at 2 months
Pocket infection at 20 months Epicardial DDD (Asymptomatic SCV occlusion)
Lead advanced n = 2 System in situ: 31 & 64 months
Threatened skin erosion n = 2 2 days and 3 months Resiting generator pocket
Generator & lead replaced (contralateral due to SCV occlusion) at 110 months Follow up: 117 months
Lead advance with generator replacement n = 1 31 months after implantation

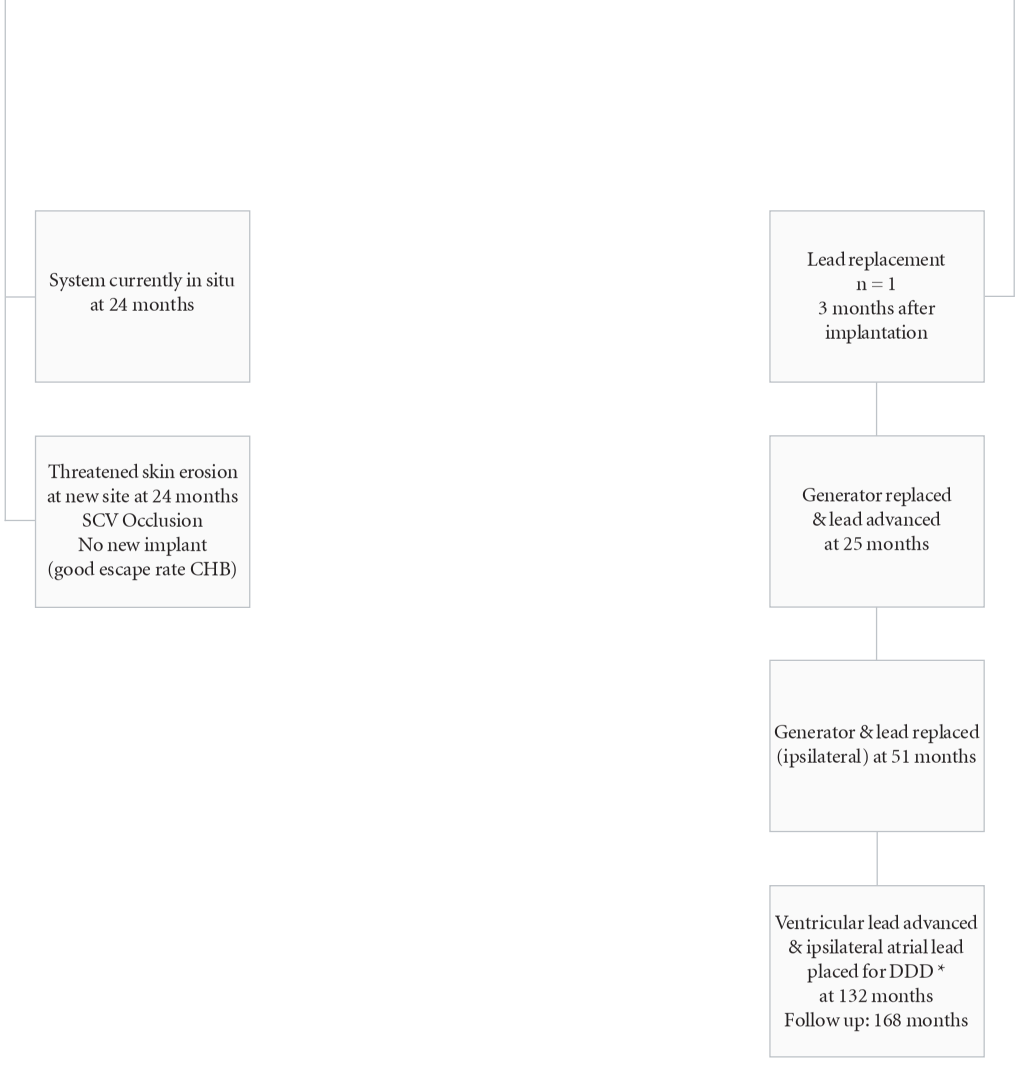


Figure 2. Outcome in 10 children who underwent intervention before end of life of the first generator.
SCV = subclavian vein; * = upgrade to physiological pacing.

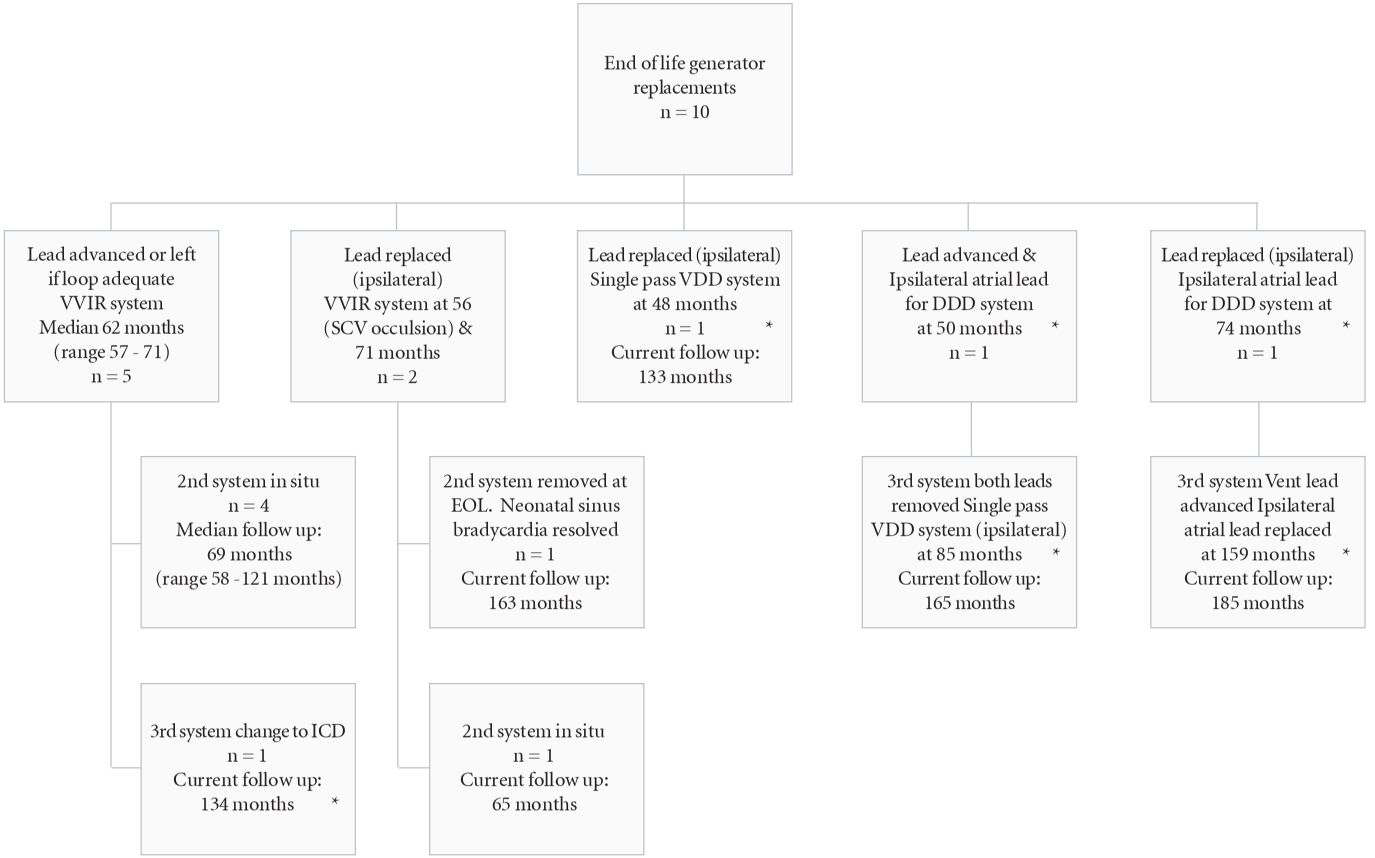


Figure 3. Outcome in 10 children who underwent end of life replacement of the generator.
EOL = End of life; * = upgrade to physiological pacing.

been described in the early re-intervention section (Fig. 2). A third child had received a pacing system at 13 months of age, because of reflex anoxic seizures. Fourteen years later she was found to have normal sinus node function. Her pacing system was completely removed using a diathermy sheath to facilitate lead extraction.
Five patients were upgraded to physiological pacing (* in Figs. 2 and 3) at the time of an elective generator replacement (ipsilateral to the original implant). In an eight-year old, paced for long-QT syndrome, this procedure failed, because of intractable atrial fibrillation and the atrial lead was removed. He was subsequently upgraded to a dual chamber defibrillator at the age of 13 years. In the other four patients, the upgrade procedure was uncomplicated (2 = DDD, 2 = VDD) 4, 4, 6, and 11 years after initial single chamber pacemaker implantation.

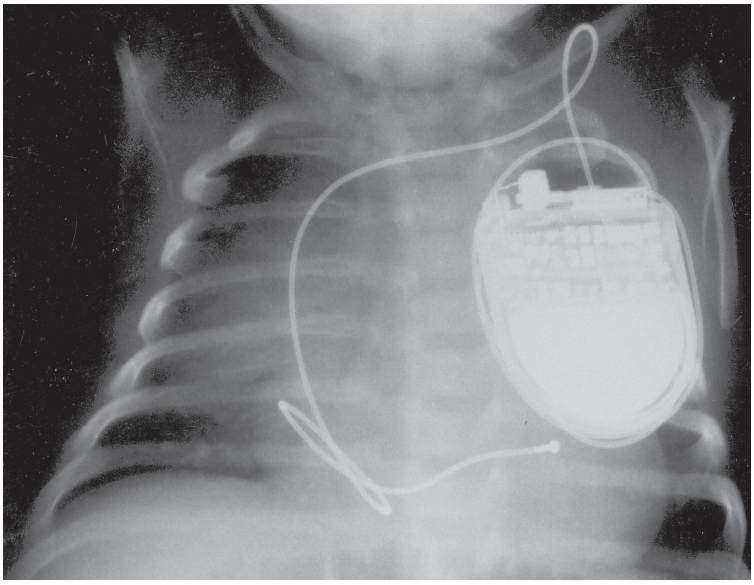
Lead advancement and replacement

Lead advancement

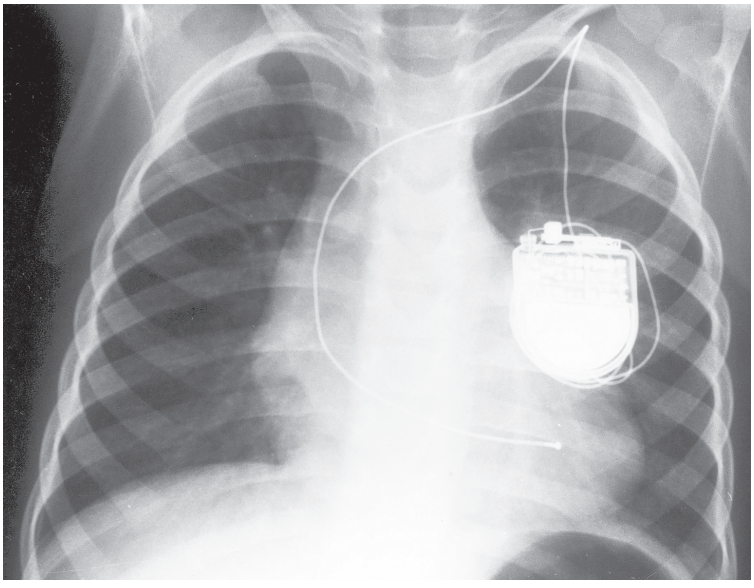
Ventricular lead advancement was attempted 12 times in 10 patients and failed once (Fig. 4). In one child a bipolar lead was damaged during the advancement procedure and was converted to a unipolar lead. In 4 patients, lead advancement was a primary procedure (described in early re-intervention section, Fig.2) but in the remainder lead advancement or replacement was as part of a generator change/upgrade procedure.

Lead extraction

Ventricular lead extraction was performed 11 times in 9 patients (with additional atrial lead extraction in 2 of these, resulting in a total of 13 lead extractions). Indications for extraction were: high threshold and/or low impedance (4), lead damage during generator replacement or lead advancement procedure (2), stretched leads (2), Siemens 1050T advisory (1), Accufix atrial lead advisory (1), unipolar lead replaced with bipolar for submuscular generator (1), infection (1), sinus rhythm recovery (1).
The technique used for the extraction varied with the time period and weight of the child. In the early years, leads were extracted by mechanical traction on the lead. In later years however, subclavian extraction sheaths (countertraction and radiofrequency sheaths) were used in older children. In a 15.9 kg child in whom the subclavian vein was occluded, a modified extraction technique was used. The lead was snared from the femoral vein and drawn into a femoral



4a



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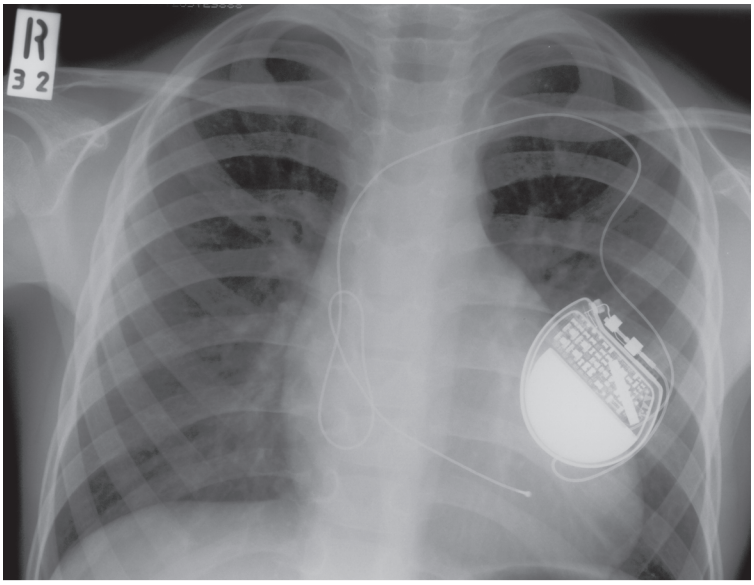

FIGURE 4. Chest radiograph of 3 week-old, 3.7 kg neonate with congenital CHB at prepectoral implant (**4a**) and 4 yrs 9 months later (weight 20 kg) at end of life of Microny generator (**4b**). Lead advanced to increase size of loop with Regency pacemaker placed subpectorally (**4c**).

sheath. Prior to this, an exchange length coronary guidewire was advanced into the stylet channel of the lead, exiting the pectoral implant site. In this way, a subclavian to femoral venous guide wire circuit was created when the lead was pulled out the femoral site. Over this guidewire circuit, a sheath was placed from the subclavian site, creating access to place a new ipsilateral lead. Only one lead could not be removed during an upgrade procedure in a seven year old. The ventricular lead was abandoned when the redundant atrial loop was found to be adherent to the atrial myocardium. A new ventricular lead was inserted through the ipsilateral cephalic vein and an atrial lead was inserted through the ipsilateral subclavian vein. At 14 years, this same patient had the ventricular lead advanced and uncomplicated ipsilateral atrial lead extraction and replacement (Accufix advisory).

Ipsilateral lead or leads were placed via the same subclavian vein during 7 of these procedures. In 3 patients (described in system removal section) the system was not replaced. One patient with a thrombosed subclavian vein received a contralateral lead and generator implant when access could not be maintained.

Subclavian vein occlusion

Four patients (11%) were noticed to have asymptomatic subclavian vein occlusion during a lead extraction procedure as detailed in the preceding sections and Figs. 2 and 3. Implants had been performed at weights of 2.7, 3.1, 3.2 and 4.6 kg with various leads (Vitatron Slimtine, Medtronic 4024, Vitatron IMD 49B 6546, Biotronik Y60-BP – Table 2).

Discussion

The early years of paediatric pacemaker implantation were complicated by the large size of the generators, the short longevity of the generators, lack of fixation methods for endocardial leads and stress on the leads during growth of very small children [12]. Re-operation rates for both endocardial and epicardial pacing in the 1970s were high with a majority of children having a re-operation within 2 years of the initial implant due to early generator battery depletion, lead complications and wound problems. With improvements in epicardial leads and generators sizes, there was a swing towards epicardial pacing, but pocket erosion, infection and electrode problems remained a major cause of morbidity [13-15]. Electrode failure due to acute exit block, thresholds rises and lead fractures were estimated to be as high as 30-40% over 5 years during the 1980s [15-17]. Higher chronic stimulation thresholds resulted in premature battery depletion and consequently the need for repeated operations. The use of steroid eluting epicardial leads in the 1990s contributed to a lowering of the acute and chronic stimulation thresholds compared to epicardial pacing with non steroid-eluting leads [7, 18, 19]. Acute exit block and lead fractures still occurred [20-22]. Beder et al's series of steroid-eluting epicardial leads in 12 patients with a median age of 6 yrs (oldest 49 years) had 3 acute exit blocks and 1 fracture [20]. Cohen et al's large series of 123 "children" < 22 years of age, the majority with congenital heart disease, undergoing epicardial pacing (40% steroid-eluting) reported a 26% lead failure rate by 5 years with a mean time to failure of 2.5 +/- 2.4 years [22].

The progress in epicardial pacing was accompanied by improvements in equipment and implantation techniques for endocardial pacing. The reduction in generator size, the development of endocardial leads with passive and active fixation and the use of redundant loops of intravascular lead, led to an increasing application of endocardial pacing. The reliability of endocardial leads was tempered by concerns for venous obstruction and the potential for venous access problems in the future if the lead had to be replaced [23]. The ability to advance leads with growth and new extraction techniques that maintained vascular access despite occlusion around a redundant lead may lessen these concerns. Figa et al. reported evidence of venous obstruction by echocardiography and/or venography in 21% of 63 children and related this to lead diameter and body surface area at the time of lead implantation [24]. Campbell and colleagues performed serial venographic evaluation in a subset of 10 patients implanted with 4.5 F, bipolar, active fixation leads under the age of 5 years. After 12 months follow-up, all ten patients showed evidence of at least mild asymptomatic subclavian vein stenosis at the lead introduction sites. Five patients also showed signs of collateral vein formation around this stenosis but no thrombus formation or occlusions were observed [25].

There are few studies addressing specifically the challenges of pacing in the < 10 kg infant whether via the epicardial or endocardial route. The only report of epicardial pacing in this group is from Villaine et al in 34 neonates and infants < 10 kg with non-surgical CHB [21]. Of these, 15 received steroid and the remainder non-steroid epicardial leads. There were 4 acute lead failures within the first year of implantation – including 2 steroid lead failures within a month – and one late lead fracture. In addition there were 2 pacemaker system infections and 1 early generator depletion. The majority of these complications of epicardial pacing were managed with an endocardial replacement and the unit's policy is now to electively place an endocardial system at the end of life of the generator in all.

There is a similar paucity of long-term studies of endocardial pacing in very small children. In 1990, Till et al reported on 24 children < 15 kg, of whom 11 < 10 kg, at the time of pacemaker implantation [4]. Of these 6 needed an early re-operation due to lead fracture, generator migration, infection or generator depletion. There were no reports of venous obstruction though this was not specifically sought. Stojanov reported 9 children < 10 kg at pacemaker

implantation using a cephalic vein cut down but there was no follow up or report of complications [26]. There is also an abstract report of 7 children < 4 kg undergoing dual chamber pacemaker implantation with unipolar leads via a subclavian puncture. There was a subclavian vein thrombosis in a 1.2 kg neonate and nearly all required lead advancement prior to generator end of life [27].

In the current study, we have described the outcome of endocardial pacing in 39 children under 10 kg who were followed for up to 15.3 years (median 4.3 years). Ten of them (28%) underwent a lead advancement, nine (25%) lead extraction, and 12 (33%) an end-of-life generator replacement. Four patients (11%) had an asymptomatic venous occlusion found during lead extraction, three patients (8%) had initial wound closure problems and two patients (5%) suffered a wound or lead related infection. Thus the challenges in this group related to generator positioning and venous occlusion.

Despite use of the smallest generators that are currently available, there were 3/39 with a wound closure or erosion complication. None of these occurred with primary abdominal implants where the subcutaneous tissue has more bulk and the generator does not overly the bony thorax or in submuscular pectoral implants where the muscle bulk gives better generator cover. The site of implantation did not achieve statistical significance for wound complications. While a faulty implantation technique may have been responsible, there were confounding factors in 2 of these patients. The mother of the one neonate had been treated with steroids for four months antenatally to try reverse heart block/prevent hydrops and this may have influenced the wound healing process. In the second neonate, the generator was resited in the abdomen but 2 years later began to erode again. While this too may have been due to an occult infection, this case has similarities with the patient reported by Villaine et al who seemed to have an allergy to conventional pacemaker material that required a specially coated pacemaker to prevent a third recurrence – a factor not hitherto considered by us in our patient [21].

The advantage of the larger soft tissue bulk in the abdomen is far outweighed by the effects on lead length during growth if the generator is not sited in the pectoral region. Of the 4 leads that required lead advancement prior to

generator end of life, 3 had been sited in the abdomen. The 4th resulted from the inappropriate choice of a bulky bipolar lead that restricted the ability to form an adequate intra-atrial loop in a 2.7 kg neonate. Encouragingly, the excess intravascular lead that is looped in the atrium – some operators leave a loop in the ventricle [28] – allows growth without distraction of the lead from the ventricular endocardium. In some the lead needs to be advanced at the first generator change but in others an adequate loop remains even after considerable growth. Septal or right ventricular outflow tract placement of the lead tip should theoretically allow more growth than leads placed in the right ventricular apex but it was not possible to assess this in the current study as only a minority of leads were not placed in the apex [2]. It was our impression that the smaller bodied unipolar leads were easier to advance but this too was not rigorously tested in this study.

The most worrying aspect of this study was an incidence of 4/36 subclavian vein occlusions (11%). All these children were < 4.6 kg at the time of pacemaker implantation and had lead body diameters of 5.0 – 6.6 F. In choosing leads for these children we did not always use the smallest lead body diameters available at the time. We were swayed by the advantages of the very small Microny generator, which initially required a bipolar lead (even though pacing was unipolar) and traded off the increased lead body diameter with the smaller generator. The latest version of the Microny allows a unipolar lead that should reduce this problem. While an asymptomatic subclavian vein occlusion around a functional lead in an adult may not affect clinical management, the same cannot be said for a child with a lead that needs replacing. Although extraction techniques are continuing to improve, and often allow lead replacement through an occluded vein, it is not always possible. We have avoided the use of countertraction and radiofrequency sheaths in children < 25 kg preferring a modified technique described ealier. Down sizing of extraction sheaths for smaller leads may allow their safe use even in smaller children. Extrapolation of the data from Figa et al suggests that a 4, 5 and 6 F lead should be accommodated by a 2.5, 5.0 and 8.0 kg child respectively [24]. As there were very few small children in their study this has not been tested but confirms that the leads we chose to use were too big in those < 5.0 kg. Currently smaller bodied leads are available and it is anticipated that leads as small as 2F under development will become available and would be ideal in this population [25].

Endocardial pacemaker implantation is increasingly becoming the approach of choice for children over 1 year of age or above 10 kg in weight. It is in the smallest group – those < 10 kg in weight - that the most controversy exists. The lack of reporting in this group and the absence of any trials has resulted in the choice of the endocardial or epicardial approach being an empirical one. Neither approach is free from complications. The current study demonstrates that endocardial pacing in small children is feasible and effective. The superiority of this approach, however, over epicardial pacemaker implantation has not been demonstrated but it is an acceptable alternative. Use of the smallest available leads and on going developments in this area is likely to make endocardial pacing more widely acceptable. At present, the final choice of an endocardial or epicardial approach in children < 10 kg in weight should be based on the experience and expertise available in the unit treating these patients.

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Chapter 8

Predictors Of Sudden Cardiac Death After Mustard Or Senning Repair For Transposition Of The Great Arteries

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Abstract

Objectives

To identify predictors for sudden death (SD) in patients with transposition of the great arteries (TGA), having undergone atrial inflow repair.

Background

SD is the commonest cause of late death after atrial inflow repair of TGA. Little is known about the predictors of SD.

Methods

A retrospective multi-center, case-controlled study. We identified 47 patients after Mustard or Senning operation who experienced a SD event (34 SD, 13 near miss SD). Each patient was matched with two controls with the same operation, but without a SD event.
Information on numerous variables prior to the event was obtained and compared with controls at the same time frame.

Results

Presence of symptoms of arrhythmia or heart failure at most recent follow-up and history of documented arrhythmia (supraventricular tachycardia (SVT) in particular) were found to increase the risk of SD. ECG, chest Xray, and Holter ECG findings were not predictive of SD. Neither medication nor pacing was found to be protective.

Conclusions

Presence of symptoms and documented SVT are the best predictors of SD in TGA patients.

Introduction

Before the 1980s, most patients with transposition of the great arteries (TGA) were treated by atrial inflow correction using the Mustard's or Senning's operation. Many children who underwent these operations are now adults. While their survival rate has been good [1-7], arrhythmia, RV dysfunction and late death are well recognized complications [1-9]. One cause of late death is sudden death (SD) with an incidence of 2-15% [1-10]. In some studies, SD was the commonest cause of late death [1,2,8]. Little is known about risk factors for SD in this group of patients.
In an attempt to establish predictive factors for SD, we undertook a multi-center, retrospective, case-controlled study.

Methods

We included all patients who had undergone a Mustard or Senning operation, and had suffered either SD or near miss SD from eight institutions. SD was defined as acute unexpected cardiovascular collapse resulting in death or from which the patient never regained consciousness [11]. Near miss SD was defined as acute cardiovascular collapse with successful cardiopulmonary resuscitation or documented appropriate implantable cardioverter defibrillator (ICD) discharge. We excluded patients in severe heart failure who were considered terminal and whose death was expected. With these criteria we identified 47 SD cases (34 SD and 13 near-miss SD). This group of patients will henceforth be referred to as sudden death (SD) cases. For each of the SD patients we matched 2 control patients. Matching criteria were type of operation, operation date within 3 years from corresponding SD case and age at operation as close as possible to that of the corresponding SD case. Controls were obtained from the same center as the corresponding SD case with the operation having been performed by the same surgeon. According to these criteria we were able to identify 93 suitable control patients (we were able to find only one control for one of the SD cases). All medical records were reviewed to obtain clinical data; Data from the last full assessment within 5 years of the event were used for analyses. For controls, data collected pertained to that which had been collected around the time of the event in the corresponding SD case.

All available electrocardiograms (ECG), chest Xrays, Holter 24 hr ECGs, echocardiogram reports, exercise test reports, cardiac catheterisation and electrophysiology study reports were reviewed. Data collection was completed in September 2002. The study was approved by the institutional review boards of the participating centers.

Definitions

TGA was called simple if the ventricular septum was intact or when a small, hemodynamically insignificant ventricular septal defect (VSD) was present. Complex TGA was defined as the presence of a VSD requiring closure or another lesion, such as ventricular outflow tract obstruction requiring surgical intervention. Closed patent ductus arteriosus, aberrant vessels and repaired coarctation of the aorta did not constitute 'complex'.
Heart size measured on roentgenogram was divided into normal (CT ratio ≤ 50%), and enlarged (CT ratio >50 %). RV size on echocardiography, was subjectively assessed as normal or enlarged from the echocardiography reports from each institution. Likewise, RV function, was assessed as satisfactory, moderately impaired or severely impaired. Exercise tolerance during exercise tests was quantified as normal (100%), slightly decreased (80-100%), decreased (60-80%) or poor (<60%), given as the percentage of the normal value expected for age, bodyweight and gender. Sinus node disease (SND) was defined as absence of sinus rhythm with presence of atrial or junctional escape rhythm as dominant rhythm. Sparse sinus beats occurring within a dominant escape rhythm was also considered SND. Patients with paroxysmal episodes of supraventricular tachycardia (SVT), whose underlying rhythm was sinus, were not considered to have lost sinus rhythm. Frequent supraventricular or ventricular extra systoles were noted as arrhythmia if >100 extra beats per hour.

Statistical analysis

Descriptive statistics are reported as frequency, median or mean value and range or standard deviations as appropriate. Data were analysed using SPSS software for Windows.
Risk factors for SD event were identified by univariate conditional logistic regression analyses. Results are reported as Odds ratios (OR) with 95%

Table 1. Baseline characteristics

	SD Cases (n = 47) No. (%)	Controls (n = 93) No. (%)
Male	35 (74,5%)	74 (79,6%)
Female	12 (25,5%)	19 (20,4%)
Simple TGA	36 (76,6%)	75 (80,6%)
Complex TGA	11 (23,4%)	18 (19,4%)
Pre-operative palliation		
None	1 (2,1%)	2 (2,2%)
Rashkind balloon atrioseptostomy	39 (83%)	76 (81,7%)
Blalock Hanlon atrioseptectomy	11 (23.4%)	28 (30%)
Banding Pulmonary artery	2 (4.3%)	1 (1.1%)
Blalock Taussig shunt	0 (0%)	1 (1,1%)
Type of surgery		
Mustard	42 (89.4%)	83 (89.2%)
Senning	5 (10.6%)	10 (10.8%)
Median age at surgery (years (range))	1.1 (0-6.9)	1.2 (0-8.0)
Surgical era	1967-1993	1965-1989
Post-operative (<2 weeks) arrhythmia		
None	17 (36.2%)	44 (47.3%)
Sinus bradycardia	0 (0%)	4 (4.3%)
Nodal rhythm	12 (25.5%)	16 (17.2%)
AV block	4 (8.5%)	4 (4.3%)
Supraventricular tachycardia	9 (19.1%)	4 (4.3%)
Cardiopulmonary arrest	0 (0%)	3 (3.2%)
Re-operations	9 (19.1%)	19 (20.4%)
Baffle repair	4 (8.5%)	13 (14%)
Enlargement Pulmonary venous drainage	3 (6.4%)	4 (4.3%)
Other	3 (6.4%)	8 (8.6%)

Numbers with respect to pre-operative palliation, post-operative arrhythmia and re-operations do not add up, because some patients had more than one intervention or arrhythmia.

confidence intervals (CI) for significant predictors. (Table 3) Since many risk factors were tested within the same data set, we considered a p-value of <0.005 statistically significant.

Table 2. Autopsy findings (n=14).

Autopsy findings	N
Detached pacemaker lead	1
Pulmonary vein stenosis	1
Pulmonary vein stenosis with hypertension	1
One pulmonary vein to left lung	1
Fresh thrombus in little branch coronary artery and irreversible PHTN	1
Fresh thrombus in right coronary artery	1
Bronchopneumonia	2
Fibrosis around patch and conduction system	2
Left ventricular outflow tract obstruction	1
No abnormalities, except signs of right ventricular overload	3

PHTN = pulmonary hypertension.

RESULTS

Baseline characteristics, preoperative palliation, early post-operative arrhythmia and reoperations are shown in table 1.

Events

Thirty-four events (81%) occurred during exercise, 5 (12%) patients died during sleep and 3 (7%) patients had a pre-existing sustained atrial flutter or atrial fibrillation going on during 1 to 2 days prior to event. For 5 of the 34 patients who died, no information was available regarding the circumstances of their death.

Mean age at event was 12.3 years (median 9.7; range 0.3 – 32) and average interval post-surgery 10.6 years (median 7.9; range 0.3 – 28.8) (Fig 1). Thirty of 47 events (64%) occurred <12 years after surgery. No clustering in either age or follow up time was found. Autopsy reports were available for 14 patients (41%) and are listed in table 2. For eight SD cases rhythm documentation was available at time of event and showed ventricular tachycardia (VT) or ventricular fibrillation (VF). Of the 13 patients with a near miss SD, ten had documented VT or VF at time of the event. The other three had loss of consciousness without pulsations felt by onlookers, and, in all, cardiopulmonary resuscitation was successful, without need for defibrillation.

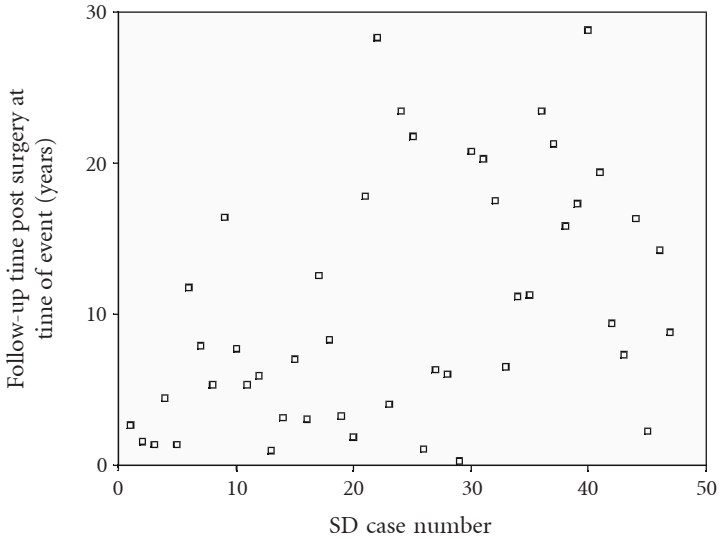

Figure 1. Scattergram of follow-up time post surgery at time of event (vertical axis) for the SD Cases (horizontal axis). No clustering is found, indicating a continuous risk going on.

Seven out of 13 patients with near miss SD received either an ICD (n=4), or a pacemaker (n=3). Of the 3 receiving pacemakers, one had SND and two had poor escape rhythm following medication to suppress arrhythmia.
Four patients, who suffered a near miss SD, died at follow up. Two died from neurologic damage within 24 hours and 2 months respectively despite regaining heart rhythm. One other patient died of VF while awaiting heart transplantation 14 months after the initial event. The fourth patient died six years after the initial event from an unknown cause.

Symptoms

Data regarding symptoms just prior to the event were available for 45 SD patients and 92 controls. Presence of symptoms (combined or analysed separately as arrhythmic (palpitations and syncope) and heart failure (recurrent upper respiratory tract infections, decreased exercise tolerance, tiredness and shortness of breath) symptoms) was a significant risk factor for SD (Table 3).

Table 3. Variables for which conditional logistic regression analysis was performed, noted in mean Odds ratios with 95% confidence intervals.

Symptoms	P-value	OR (95% CI)
Symptomatic *	< 0.0005	6.45 (2.42 – 17.24)
- Arrhythmic symptoms *	0.003	21.60 (2.80 – 166.79)
- Heart failure symptoms *	0.001	4.44 (1.85 – 10.62)
ECG		
- QRS time	0.723	0.32 (0.001 – 175.66)
- QT time	0.668	0.16 (0.000 – 734.27)
- QTc time	0.193	1084.50 (0.029 – 4.1 E+07)
- QRSd > 100 msec	0.251	1.980 (0.618 – 6.324)
- Heart rate	0.054	1.017 (1.000 – 1.035)
- Basal heart rhythm non-sinus	0.790	1.112 (0.509 – 2.427)
Thoracic X-ray		
- Enlarged heart size	0.053	2.227 (0.989 – 5.000)
24-hours Holter		
- Basal heart rhythm non- sinus	0.037	5.260 (1.10 – 25.00)
- Documented episodes of arrhythmia	0.431	1.770 (0.44 – 7.25)
- Mean heart rate	0.527	0.980 (0.919 – 1.044)
- Minimum heart rate	0.952	1.001 (0.956 – 1.050)
- Maximum heart rate	0.803	0.996 (0.965 – 1.028)
History of arrhythmia in follow up		
- Documented arrhythmia *	0.005	3.473 (1.451 – 8.310)
- Documented SND in follow up	0.035	2.405 (1.065 – 5.432)
- Documented SVT in follow up *	0.001	4.866 (1.900 – 12.462)
Arrhythmia treatment		
- Pacemaker implantation	0.550	0.641 (0.149 – 2.758)
- Medication treatment *	0.002	5.159 (1.863 – 14.283)

OR= Odds Ratio, CI = confidence interval, SND = sinus node disease, SVT = supraventricular tachycardia. * Statistically significant risk factor ($p < 0.005$).

Standard 12-lead electrocardiography

ECG's were available for 44 SD cases and 84 controls. Twenty-six SD patients (59%) showed sinus rhythm on ECG, as did 54 controls (64%) (Table 4) (p=ns). Mean QRS duration, QT and QTc intervals and heart rate are listed in table 4 and showed no difference between the two groups (Table 3). A QRS duration of >100 ms was noted in 12 of 39 SD cases (31%) and 15 of 78

Table 4. Basal heart rhythm and mean variables on electrocardiogram and 24-hours Holter recording prior to event.

	ECG		24-uurs holter	
	SD Cases (n = 44)	Controls (n = 84)	SD Cases (n=26)	Controls (n=40)
Sinus rhythm	26 (59,1%)	54 (64,3%)	9 (34,6%)	26 (65%)
AV junctional rhythm	10 (22,7%)	19 (22,6%)	3 (11,5%)	1 (2,5%)
Atrial rhythm	2 (4,5%)	3 (3,6%)	12 (46,2%)	13 (32,5%)
SVT	1 (2,3%)	1 (1,2%)	1 (3,8%)	0 (0%)
VT	1 (2,3%)	0 (0%)	0 (0%)	0 (0%)
VVI paced	3 (6,8%)	4 (4,8%)	1 (3,8%)	0 (0%)
AAI paced	1 (2,3%)	3 (3,6%)	0 (0%)	0 (0%)
Mean ECG variables				
QRS time (msec) (range)	98.8 (60-200)	93.8 (50-160)		
QT time (msec) (range)	367 (240-530)	377 (240-490)		
QTc time (msec) (range)	426 (340-550)	413 (210-500)		
Heart rate (bpm) (range)	88 (38-150)	76 (43-150)		
Mean Holter variables				
Mean heart rate (bpm) (range)			73 (40–110)	75 (61-100)
Minimum heart rate (bpm) (range)			48 (26–80)	46 (30-70)
Maximum heart rate (bpm) (range)			149 (100–240)	150 (70-190)

SVT = supraventricular tachycardia; VT = ventricular tachycardia, bpm = beats per minute

control patients (19%) (ventricular paced patients were excluded from this analysis). This was not statistically significant (Table 3).

Holter 24-hours ambulatory ECG monitoring

Holter 24 hour ECG was available in 26 SD cases and 40 controls. The dominant heart rhythm on Holter is shown in table 4. Presence of non-sinus rhythm at just failed to reach statistical significance as risk factor for SD (Table 3).

Forty-two percent (11 of 26) SD cases and 23% (9 of 40) controls showed episodes of arrhythmia on Holter, which are listed in table 5. This difference was not statistically significant (Table 3). The mean of the mean, minimum and maximum heart rates on 24-hours holter recording was similar for the two groups (Table 4).

Table 5. Documented episodes of arrhythmia on 24-hours Holter recording.

	SD Cases (n=26)	Controls (n = 40)
SVT	3 (12%)	1 (3%)
Sinus arrest	1 (4%)	4 (10%)
Sinus rhythm with junctional escape at rest/night	1 (4%)	4 (10%)
Frequent SVES	3 (12%)	0 (0%)
Frequent VES	1 (4%)	0 (0%)
VT	2 8%)	0 (0%)

SVT = supraventricular tachycardia, SVES = supraventricular extra sustolies, VES = ventricular extra systolies, VT = ventricular tachycardia.

Chest XRay

Chest Xrays were available for 42 SD patients and 77 controls. In 31 SD cases (64%) and 40 (52%) of controls, the heart size was enlarged (p=ns, Table 3).

Echocardiography

Echocardiography data are listed in table 6. RV size was similar for SD cases and controls. SD cases, however, tended to have a more impaired RV function and slightly more tricuspid regurgitation than controls. The incidence of baffle obstruction, as identified by echocardiography, was similar for the two groups. The paucity of available echocardiograms prevented us from performing reliable statistical analysis.

Cardiac catheterisation

Data on cardiac catheterisation are listed in table 7. Two of the SD cases and two of the controls with mild systemic venous baffle obstruction and one control patient with pulmonary venous obstruction subsequently underwent baffle repair. Two out of four control patients with a baffle leak underwent repair. Two of the SD patients with an obstruction, were also found to have a baffle leak.

Only 12 electrophysiology studies (two SD cases; ten controls) were performed. Both SD case patients showed SND. Control patients showed

Table 6. Echocardiography results.

	SD Cases No. (%)	Controls No. (%)
Right ventricular size	n=22	n=40
Normal	1 (4.5%)	2 (5%)
Enlarged	21 (95.5%)	38 (95%)
Right ventricular function	n=19	n=31
Satisfactory	5 (26.3%)	16 (51.6%)
Mildly-Moderate impaired	9 (47.4%)	14 (45.2%)
Severely impaired	5 (26.3%)	1 (3.2%)
Tricuspid regurgitation	n=18	n=42
Absent	4 (22.2%)	19 (45.2%)
Mild	8 (44.4%)	18 (42.9%)
Moderate	2 (11.1%)	3 (7.1%)
Severe	4 (22.2%)	2 (4.8%)
Baffle obstruction	n=15	n=38
Absent	13 (86.7%)	31 (81.6%)
Present	2 (13.3%)	7 (18.4%)

SND alone (n=3), AV node dysfunction (n=1), SND plus AV node dysfunction (n=3) and inducible VT (n=1). Two controls had a normal electrophysiology study. No statistical analysis was performed on the catheterisation and electrophysiology data, due to small numbers.

Exercise testing

Data on exercise capacity are listed in table 8. Arrhythmias were induced during exercise in 5 (38%) SD cases and 9 (24%) controls, including atrial flutter degenerating into VF in one SD patient. The others had junctional rhythm (2 SD cases and 7 controls) or ventricular ectopy (2 SD cases and 2 controls) either during exercise or during the recovery phase.
Statistical analyses could not be performed on exercise test data due to small numbers.

Table 7. Cardiac catheterisation.

	SD Cases (n=16) No. (%)	Controls (n = 27) No. (%)
Normal	6 (38%)	10 (37%)
Mild systemic baffle obstruction	4 (25%)	5 (19%)
Mild pulmonary venous obstruction	1 (6%)	2 (7%)
Mild systemic and pulmonary venous obstruction	1 (6%)	0 (0%)
Baffle leak	3 (19%)	4 (15%)
Left ventricular outflow tract obstruction	1 (6%)	5 (19%)
Abnormal lungvein drainage into SVC and collaterals from aorta to right lung	1 (6%)	0 (0%)
Calcification conduit LV to PA	1 (6%)	0 (0%)
Patent ductus arteriosus	0 (0%)	1 (4%)

SVC = superior vena cava, LV = left ventricle, PA = pulmonary artery

Arrhythmia during follow up

Of the 47 SD cases, 34 (72%) had a documented arrhythmia prior to their event, in contrast to only 47 of 93 controls (51%). Presence of arrhythmia was a significant risk factor for SD (Table 3). The different arrhythmias are listed in table 9. SVT constituted atrial flutter or fibrillation. Presence of SND barely approached significance (Table 3), but presence of prior documented SVT was a significant risk factor for a SD event (Table 3).
In 15 SD cases (30%) and nine controls (10%) more than one arrhythmia was diagnosed. Twenty-eight SD cases suffered SND and of these 14 (50%) also had SVT. One SD patient with SND had frequent ventricular extrasystoles. Of the 41 controls with SND, nine (22%) also had documented SVT (Table 9).
The mean interval between surgery and first arrhythmia was 4.0 years (range 0-22.3 years) for SD cases and 3.7 years (range 0-15.6 years) for controls. The mean interval between the first episode of arrhythmia and SD event was 7.2 years (range 0.5 – 27.4 years) in the SD group. No association was found between the occurrence of sudden death and the time of onset of arrhythmia.

Table 8. Exercise testing.

Exercise capacity	SD Cases (n=13) No. (%)	Controls (n = 38) No. (%)
Normal	2 (15%)	8 (21%)
Slightly decreased	5 (39%)	19 (50%)
Decreased	2 (15%)	9 (24%)
Bad	4 (31%)	2 (5%)

Arrhythmia treatment

Pacemaker implantation

Eight SD cases (17%) and fifteen controls (16,1%) had a pacemaker, which was implanted at average follow-up post-surgery of 12.1 years (range 0.1-26.1 years) for SD cases and 8.6 years (range 0-24.3 years) for controls. Although controls tended to get a pacemaker implanted earlier, statistical analysis could not be performed due to small numbers.
Seven of eight SD cases received a pacemaker for SND, as did 14 of 15 controls. The others (one SD and one control) had complete AV block. Pacemaker implantation turned out to have no protective value against SD (Table 3).

Cardiac medication

At time of event, 20 SD patients (43%) and 17 controls (18%) were using cardiac medication. Of the 20 SD patients, 18 were on digoxin (4 also on verapamil and 1 also on betablocker) and 2 were on betablocker. Of the 17 controls, 9 were on digoxin (2 of whom were also on betablocker), 3 on verapamil, 2 on sotalol and 1 on amiodarone. Two (2%) were using an ACE inhibitor. The use of cardiac medication appeared to increase the risk for a SD event (Table 3).

Table 9. Documented arrhythmia in follow up.

Exercise capacity	SD Cases (n=47)	Controls (n = 93)
Sinus node disease	28 (60%)	41 (44%)
SVT	18 (38%)	13 (14%)
Sinus node disease together with SVT	14 (30%)	9 (10%)
Complete AV block	1 (2%)	2 (2%)
Frequent VES	2 (4,3%)	0 (0%)
Sinus node disease together with frequent VES	1 (2%)	0 (0%)

SVT = supraventricular tachycardia, VES = ventricular extra systolies

Discussion

Oechslin and colleagues found that in a large cohort of adult survivors with congenital heart disease, SD was the most common cause of late death [12]. In a population based study, Silka et al. reported a 25-100 fold increase in risk of late SD for patients operated for common congenital heart defects relative to age-matched controls. Together with aortic stenosis, aortic coarctation and tetralogy of Fallot, surgically corrected transposition of the great arteries was one of the congenital heart defects in which the majority of sudden cardiac deaths occurred [11]. In their report there were 7 SD among 172 TGA patients, giving an incidence of 4.9/1000 patient-years.
A number of studies have looked at the long-term problems occurring after Mustard/Senning repair of TGA. The main long-term sequelae are baffle obstruction, arrhythmias (particularly SVT), systemic right ventricular dysfunction, and SD. The incidence of SD reported by various studies has ranged from 2 to 15% [1-9]. Studies have shown SD to be the most important cause of late death [1,2,8].

An adequate surgery database had been maintained in only five of the eight participating centers in our study. In those five centers, a total of 582 Mustard or Senning operations have been performed with a mean SD incidence of 6%. The incidence of SD was different for each of these five centers, ranging between 3% and 11%. Out of the 47 SD cases in our study population, five SD cases had undergone a Senning operation and 42, a Mustard's operation. Although we haven't performed a direct comparison in our study, this finding

probably reflects the superior outcome for the Senning operation when compared to the Mustard operation as reported by several authors [4,5,10].

Not much is known about risk factors for SD in the Mustard and Senning population since few studies have addressed this issue. Our study found presence of symptoms and presence of documented SVT (mainly atrial flutter) to be associated with risk of SD. Interestingly, both arrhythmic and heart failure symptoms were associated with SD. Use of cardiac medications was also a risk factor. It is not possible to say whether this indicates that patients on medications were a sicker group or whether this represents a negative side effect of the drugs themselves.

Arrhythmias

SVT, in particular atrial flutter, has been identified as a predictor of sudden cardiac death by others. Flinn et al. reported 9 SD among 372 survivors and showed a weak association between atrial flutter and SD [3]. Sarkar et al. reported that documented atrial flutter resulted in a 21-fold increase in the risk of late SD [4]. In contrast Gelatt and colleagues could not find a relationship between the incidence of atrial flutter and SD [1]. Janousek et al. studied 359 patients after Mustard/Senning operation [13]. Fifteen patients (4.2%) died suddenly. By multivariate analysis, they found severe tricuspid regurgitation and/or RV dysfunction and medically uncontrolled SVT to be the risk factors for SD. Our findings suggesting that heart failure symptoms and documented supraventricular arrhythmia may be risk factors for SD are somewhat similar to those of Janousek et al. It is difficult to determine whether arrhythmia is the cause or the effect of ventricular dysfunction. To date there is no study (including ours) which has been able to determine which of these factors is primary.

As early as 1972, El-Said remarked on the frequent occurrence of arrhythmias after the Mustard operation [14]. Other reports soon confirmed that both bradyarrhythmias (primarily due to sinus node dysfunction) and tachyarrhythmia (primarily atrial flutter) were significant problems after the Mustard/Senning approach for TGA [15-17]. There is a continued risk of sinus node disease despite modification of surgical techniques [3,5,17-19]. However bradyarrhythmias appeared to be less important than tachyarrhythmias where mortality was concerned [1,3,8,9].

Bink-Boelkens et al. showed that even asymptomatic children after the Mustard operation have significant electrophysiologic abnormalities of the sinus node [18]. In our study 44% of the controls and 60% of the SD cases had documented SND. Of the 28 SD patients with SND, 14 (50%) also had documented SVT, as had nine of the 41 controls with SND (22%). Like others, our study showed no association between SND and risk for SD [5,8,19].

As shown by others, pacemaker implantation had no influence on the risk of sudden cardiac death in our study [3].

Symptoms

We found the presence of symptoms to be a risk factor for SD. Previous studies have not reported this association. Indeed, Gewillig et al. found that functional status or lack of symptoms had no prognostic value for late death (including hospital and non-cardiac deaths) [8]. In our series, only 33% of the SD cases were symptom-free prior to their event, compared to 71% of the controls. Arrhythmic symptoms such as palpitations, dizziness and syncope increased the risk for sudden cardiac death by a factor of 21.6 (95% CI of 2.80 to 166.8). There was a high association between the occurrence of documented arrhythmia (a separate risk factor for SD) and arrhythmic symptoms (Pearson Chi-square = 10.0; p = 0.002). Heart failure symptoms resulted in a 4.4-fold increase in the risk for a SD event.

Right ventricular function

Right ventricular failure has been shown to be a risk factor for late death in Mustard and Senning patients [1,6,8]. Janousek and colleagues have been the only ones who have also demonstrated a relationship between RV failure and SD in this patient group [13]. Whether RV failure causes, or is caused by SVT is unclear. Millane et al. have shown that perfusion and wall motion abnormalities are common in the systemic RV late (10 to 20 years) after Mustard's operation and postulated this to be the cause of systemic RV dysfunction [20]. Poor ventricular function causes RV enlargement and progressive tricuspid regurgitation, resulting in atrial volume and pressure overload. This atrial overload may contribute to the development of arrhythmias [1,21]. In this context, Gatzoulis et al. showed the occurrence of atrial flutter often following right ventricular failure, identifying atrial flutter as surrogate marker for right ventricular failure [21].

We were unable to show an association between right ventricular function and SD because few patients had undergone adequate echocardiography or catheterisation.
QRS dispersion and duration are reported as markers of inhomogeneity of ventricular depolarisation and as predictor of dangerous arrhythmias and sudden cardiac death in patients with tetralogy of Fallot [22,23]. In Mustard patients QT dispersion was identified as predictor of clinical arrhythmia [21]. We were unable to measure QRS and QT dispersions. However, we did not find any differences with respect to QRS, QT- or QTc times between SD cases and controls. Unlike for tetralogy of Fallot, we were unable to demonstrate a relationship between QRS width and the risk for SD although both anomalies have a RV dilatation [23].

Of the seven SD in Silka et al's study, five died during active physical exertion [11]. In our study, of the 47 SD events , 34 (81%) occurred during physical exercise. From a hemodynamic perspective, the atrial inflow repair of TGA suffers from two main drawbacks. Firstly, the systemic RV seems intrinsically suboptimal compared to the LV [24]. Secondly, the absence of an adequate capacitance chamber, (namely the atrium) which has been replaced by a baffle, inherently imposes limits to ventricular filling [25]. Exercise poses specific risks, because these patients may not be able to augment cardiac output in the face of rising demand due to the above-mentioned two factors. Given these limitations, it is possible that occurrence of an arrhythmia during exercise will cause further deterioration leading to death. In addition, this inability to adequately increase cardiac output may be amplified by coexisting baffle obstruction, pulmonary vein stenosis or ventricular disease.
These findings stress the importance of an adequate diagnosis and treatment of the above mentioned complications. Since presence of atrial flutter could function as surrogate marker for these structural problems, hemodynamic assessment is indicated in patients presenting with arrhythmia.
Exercise testing can identify patients with inadequate cardiac output [21]. A review of four studies demonstrated that an average of 61% of the asymptomatic Mustard and Senning patients had abnormal ventricular function when challenged with exercise [26]. In our study, only eight out of 38 controls (21%) and two out of 15 SD cases (13%) were reported to have normal exercise capacity. In one of the SD cases ventricular fibrillation was induced during exercise testing. These numbers were too small to perform

statistical data-analysis. However Meijboom et al indicated exercise capacity to correspond well with the patients health self assessment, increasing the importance of the presence of symptoms [27].

Silka et al. reported that each of the seven SD in their study was due to an arrhythmia [11]. They had ECG documentation during the event in four patients and all showed either polymorphic VT or ventricular fibrillation (VF) as the terminal rhythm [11]. In our group with near-miss SD (n=13), ten had documented VT or VF during their event as had the eight patients who suffered SD (n=34) for whom rhythm documentation at time of event was available. Thus, polymorphic VT or VF seems to be the final rhythm in most cases of SD where rhythm documentation is available. We demonstrated that routine follow-up ECG's or 24-hours Holter recordings showed few rhythm disturbances and were consequently of little help identifying patients at risk. Scagliotti and colleagues postulated that inducible polymorphic VT at electrophysiology study may be a marker for SD and advocated the use of electrophysiology studies as a risk-stratifying test in these patients [28]. No study to date has further explored this hypothesis. An important finding in our study was the fact that the majority of patients in whom the rhythm had been documented during the SD event had either VT or VF. In view of this, we would recommend undertaking EP study for inducible VT/VF in patients presenting with symptoms, in whom no arrhythmia has been documented. Where VT/VF is inducible using moderately aggressive pacing protocols, an ICD should be considered.

Therapy

We identified SVT as a risk factor for sudden cardiac death. Digoxin had no protective value in our study population. This finding argues for an assessment of other therapies for SVT control/cure. There has been recent interest in the use of catheter ablation in critical zones of slow conduction as a means of controlling atrial flutter in these patients [29-32]. Future studies could determine the impact of this strategy on the incidence of arrhythmia and SD. However, since SVT may be secondary to ventricular dysfunction, the role of RF catheter ablation in these patients is questionable.

Study Limitations

This study has limitations inherent to any retrospective study, limiting data collection to variables available from clinical records. Decisions on cardiac testing were based solely on clinical grounds and were not standardised for the different patients. The participation of eight different centers with different approaches to management and follow up made it difficult to obtain uniform data. If a SD case patient developed an arrhythmia after the last clinical visit and before event, this would have been missed and could potentially lead to underestimation of the importance of an arrhythmia.
We have chosen to perform this study in a case-matched control setting. Such a design is open to criticism when data on pertinent variables are not available. In our study this limitation results for certain pieces of data being available in only small subsets of patients with consequently inability to perform statistical comparisons. We have not described data on operation technique. Several studies have shown that the type of operation, the year of birth and era of operation influence late outcome in Mustard and Senning patients [9,10]. To exclude the influence of these factors, we have matched our SD cases and controls for these variables and have in addition constituted our SD case-control sets operated and followed up in the same center.

Conclusions

Presence of symptoms of arrhythmia or heart failure and presence of documented SVT are the best predictors of SD in patients who have survived a Mustard or Senning operation. It is not possible to say whether SVT directly contributes to SD or is merely a marker for it. Further study with larger patient cohorts may help us whether any specific tests, such as an echocardiogram, cardiac catheterisation, and particularly exercise testing or electrophysiology testing can improve the accuracy of identifying patients at risk for SD.

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Chapter 9

General Summary And Discussion

TACHY-ARRHYTHMIAS

Over the past decade, management of tachyarrhythmias in children has evolved remarkably. In particular the introduction of radiofrequency catheter ablation (RFCA) in the pediatric population has been a major contribution to this development. This possibility to cure children of their arrhythmia as an alternative to chronic anti-arrhythmic drug therapy clearly represents an advance in medical management.

In chapter 2 we describe the experience with RFCA in paediatric patients in a university hospital. Sixty-four patients who had undergone catheter ablation for the more common tachy-arrhythmia substrates were enrolled. The majority of these children either had atrioventricular re-entrant tachycardia (n=38) or atrioventricular nodal re-entrant tachycardia (AVNRT) (n=14). In all but one patient with AVNRT, successful abolition of their arrhythmogenic substrate was achieved after RFCA. Twelve other children underwent RFCA for less common tachyarrhythmias, including ventricular tachycardia, ectopic atrial tachycardia and intra-atrial reentrant tachycardia. The ablation procedure was successful in nine of them (75%). Procedure related complications occurred in two patients (3%). We conclude that RFCA is a safe and effective alternative therapy to anti-arrhythmic drugs for the treatment of tachyarrhythmia in children.

The technical difficulties associated with manipulating catheters in small hearts in combination with the application of radiofrequency (RF) lesions raise concerns for potential post-ablation complications in children. The major complications, such as permanent atrioventricular block or cardiac perforation are likely to be recognised immediately. In order to assess potential subclinical complications, echocardiography was routinely performed in children undergoing an ablation procedure. The clinical value of a routine post-procedure cardiac echo in children had not been evaluated and was therefore studied in chapter 3. In this study, 138 patients undergoing ablation had transthoracic echocardiograms before and after ablation. We detected one asymptomatic complication requiring medical intervention and three asymptomatic disorders that resolved spontaneously. Our results suggest that routine transthoracic echocardiograms are not indicated for the majority

of children undergoing a straightforward catheter ablation for atrioventricular tachyarrhythmias. An exception could be made for children in whom the retrograde approach has been used for a left-sided ablation, in order to specifically assess the aortic valve function.

In the next two chapters we concentrate on two rare forms of arrhythmia. Chapter 4 describes two patients with silent atrium, who experienced coexisting episodes of intra-atrial re-entrant tachycardia. Successful catheter ablation of the intra-atrial re-entry circuits led to improvement of cardiac function. Little is known about silent atrium and as long as the natural history is poorly understood, ablation of the His bundle should not be the initial therapeutic option for intraatrial reentrant tachycardia associated with this entity. In one of our patients, atrial electrical and mechanical function recovered during follow-up. Our data suggests that even when the atrium appears electrically to be silent, as seen by absence of a P wave on the ECG, islands of electrically active atrial tissue are present, which may contribute to reentrant circuits within the atrium.
Previous studies suggest that familial inherited forms of the disease may exist. Further research in these areas will help to increase our understanding of this disease and its long-term prognosis.

Another type of atrial arrhythmia is discussed in chapter 5. Although many electrophysiologists continue to use the term atrial tachycardia, it has been shown that this group of arrhythmias can have numerous mechanisms. We describe a form of focal atrial tachycardia, of which the mechanism remains unclear. In general, automatic focal tachycardia cannot be induced in the electrophysiologic laboratory. In this chapter we characterised 38 patients with a non-automatic focal atrial tachycardia, that was inducible in the laboratory. We found that this arrhythmia predominantly affects women in all age-groups, that most of the tachycardia foci were located in the right atrium and that younger patients had shorter tachycardia cycle lengths when compared to the older patient group. Catheter ablation of the foci was possible, though with success rates lower than generally reported for supraventricular tachycardia ablation. We also compared catheter ablation aided by an electroanatomical mapping system versus ablation without this specialised mapping system. While the number of successfully ablated foci tended to increase with the use

of this mapping system, we could not demonstrate either a shortening of procedure time or a decrease in fluoroscopy time. Future studies should determine whether the procedure and fluoroscopy times would decrease with growing experience with the new mapping techniques.

The development of different mapping systems has given a further impulse to the possibilities of catheter ablation. The more advanced mapping technologies make complex arrhythmia substrates amenable for catheter ablation. In chapter 5 we have discussed the use of electroanatomical mapping in catheter ablation of non-automatic focal atrial tachycardia. In chapter 6 we describe the use of another specialised mapping system, LocaLisa, in catheter ablation of AVNRT in children. Twenty-six patients less than 19 years old with structurally normal hearts and symptomatic AVNRT underwent catheter ablation of their arrhythmia. Modification of the AV node slow pathway was performed. Three of the 26 patients in whom AVNRT was not inducible after RF ablation had recurrence of tachycardia and underwent a second successful ablation procedure. In one child a second degree AV block complicated the procedure. This however resolved spontaneously six weeks later.
The LocaLisa mapping system improves the safety and efficacy of slow pathway modification in young patients in two ways. Firstly, by the possibility to measure the distance of each RF ablation site to the proximal His bundle. Secondly, by a continuously displayed relation of the ablation catheter tip-electrode to the AV node and His bundle on the LocaLisa monitor. It is not clear however whether such an aggressive approach of slow pathway modification may have deleterious effects on AV node function in the future. Late PQ prolongation and even AV block have been described in adult patients following modification of the AV node. To date, we have not seen any progressive AV block in our patient population.

In conclusion, in chapters 2-6, we demonstrate that radiofrequency catheter ablation in children is a safe and effective therapy for tachyarrhythmia treatment with a low complication rate. However, we need to realise well that our follow up time is relatively short. It is not known, for example, whether scars produced in the immature heart by RFCA, may themselves be the focus for new arrhythmia substrates in adult life. Given on the one hand that RF ablation appears to be feasible, safe and effective in young patients, and on the

other hand concerns exist about the long-term effects of RF lesions in the immature heart, it is important to establish guidelines for which child should be considered for catheter ablation as opposed to treatment with anti-arrhythmic agents.
The indications for catheter ablation in children have evolved over the past decade. Responsible for this process are the technological advances in catheter technology, the development and improvements of specialised mapping systems and the increasing experience with RFCA for complex arrhythmia substrates. We have performed one comparative and one descriptive study on specialised mapping systems. To show improvement of RFCA results caused by the use of specialised mapping systems, one should perform a prospective randomised comparative study. This however will be difficult to set up for ethical reasons. An alternative could be to compare fluoroscopy and procedure times in combination with RFCA results for the different arrhythmias in retrospect. However such a study design would exclude the learning curve for any new system. Another confounding factor would be that with the contribution of new mapping systems, more difficult arrhythmia substrates are being treated with catheter ablation, which in the past would not have been considered for this therapy.

Brady-arrhythmias

Also paediatric pacing has evolved over the past decade. Technological advances in the development of smaller leads, steroid eluting leads and smaller generators have clearly improved pacing therapy in children. In adults, endocardial pacing is extensively used, while many children are still epicardially paced. The reason for this is that in children the smaller patient size rises concerns for a high risk of venous occlusion with endocardial pacing. Particularly in this young patient group with potential requirement for life-long pacing, one is in general very cautious in order to safe the veins as access for pacemaker leads in later life. This results in a preference for the epicardial approach in the paediatric population.
In chapter 7 we describe a follow-up study on a large series of transvenous pacemaker implantation in children under 10 kg. Our results suggest that endocardial pacing is effective and feasible in children under 10 kg, though not

free from complications. We enrolled thirty-nine children from two centers who had undergone implantation of a transvenous pacing system over the past 15 years. The majority underwent pacemaker implantation for either congenital complete heart block or surgically acquired complete heart block following repair for congenital heart disease. Good pacing and sensing thresholds at implantation were achieved in all cases. Follow up for 36 of these children ranged from nine months to 15.3 years (median 4.3 years). Sixteen patients (44%) (with a mean follow up of 28 months) did not undergo any re-intervention during this period. Ten others (28%) had a system revision at end of life of the generator at a mean of 61 months post initial implantation. Finally, ten (28%) patients underwent a re-intervention prior to the generator end of life. In three of them, this was because of generator pocket problems and four others required a pacemaker lead advancement, because the lead had stretched out. This latter problem is inherent to putting pacemakers in a very small patients, no matter whether they are endo- or epicardially implanted. The same applies for the generator pocket problems, which might be partly overcome by putting all generator pockets abdominal. These percentages and mean follow up times at time of re-intervention appear very reasonable and suggest transvenous pacemaker implantation in children to be feasible and effective.

However, during re-intervention, four asymptomatic patients (11%) were found to have venous occlusion. Since these occlusions were noticed in asymptomatic patients during four out of 12 lead advancements and 11 lead extractions, this number of occlusions will probably be underestimated. Further research is needed to define the exact occlusion rate, also in asymptomatic patients not undergoing an intervention.

To make transvenous pacing more widely acceptable in small patients, the number of patients with venous occlusion (11%) needs to be reduced. We need to find out which patient groups under ten kilograms are at higher risk to develop venous occlusion. The development of smaller leads could contribute to decrease the occlusion rate. It is also likely that newer catheter based technologies, such as the use of laser sheaths, which have already found application in adult practice, will be extended to the pediatric population, and will thereby enable occluded veins to be recanalised and reutilised.

DYSRHYTHMIAS POST-SURGERY

The improvements in outcome of cardiac surgery for congenital heart disease have resulted in a growing population of surviving adolescents and adults who have undergone cardiac surgery during childhood. This patient group suffers from its own problems and risks. After surgical repair of certain congenital heart defects, a considerable risk for the occurrence of sudden cardiac death has been reported. Chapter 8 describes a study in which we tried to determine risk factors for sudden cardiac death after atrial repair for transposition of the great arteries. In this multi-center study, we enrolled 47 patients who had undergone an atrial switch (Mustard or Senning) operation and had died suddenly or had experienced near-miss sudden death at follow-up. Each of these 47 patients was matched with two control patients each having undergone the same type of repair, but who had not died suddenly. Information on numerous variables recently before event was obtained and compared with the corresponding controls. The presence of symptoms of arrhythmia or heart failure was associated with risk of sudden death. In addition a history of documented arrhythmia and in particular supraventricular tachycardia appeared to increase the risk for sudden death. Neither medication nor pacemaker implantation had a protective effect. This finding argues for assessment of other therapies to control arrhythmias in this patient population. Future studies should evaluate the impact of improved techniques of RFCA in the Mustard/Senning population on the control of arrhythmia and incidence of sudden death. On the other hand the role of catheter ablation might be questionable in these patients since it has been shown that supraventricular tachycardia can cause ventricular dysfunction, but can also be caused by ventricular dysfunction. ECGs, 24-hours Holter recordings and chest X-rays are not of predictive value for sudden death. Further study with larger patient cohorts may help to improve risk stratification in patients with symptoms or a history of arrhythmia.

Chapter 10

Algemene Samenvatting en Discussie

Hartritme stoornissen bij kinderen
Diagnostiche en therapeutische aspecten

TACHY-ARITMIEËN

De afgelopen tien jaar heeft de behandeling van tachy-aritmieën bij kinderen zich aanzienlijk ontwikkeld. Aan deze ontwikkeling heeft met name de introductie van radiofrequentie catheter ablatie (RFCA) bij kinderen een grote bijdrage geleverd. Deze mogelijkheid om kinderen te genezen van hun ritmestoornis als alternatief voor het chronisch gebruik van anti-aritmische medicatie is een grote vooruitgang op het gebied van de behandeling van deze aandoening.

In hoofdstuk 2 beschrijven we de ervaringen met RFCA bij kinderen onder de 18 jaar in een Academisch ziekenhuis. Deze studie beschrijft 64 patiënten die een catheter ablatie procedure voor hoofdzakelijk minder gecompliceerde vormen van tachy-aritmie hadden ondergaan. De meeste van deze kinderen hadden een atrio-ventriculaire re-entry tachycardie (n=38) of een atrio-ventriculaire nodale re-entry tachycardie (AVNRT) (n=14). RFCA was succesvol in het verwijderen van het aritmogene substraat bij 51 van deze patiënten. In één patiënten met een AVNRT faalde de ingreep. De twaalf overige kinderen ondergingen RFCA voor meer complexe tachy-aritmieën, zoals ventriculaire tachycardie, ectopisch atriale tachycardie en intra-atriale re-entry tachycardie. De ablatie procedure was succesvol bij negen van hen (75%). Complicaties gerelateerd aan de ingreep kwamen voor in twee patiënten (3%). Wij concluderen dat RFCA als behandeling voor hartritmestoornissen bij kinderen een veilige en effectieve therapie is als alternatief voor anti-aritmische medicatie.

RFCA bij kinderen heeft een potentieel verhoogd risico op complicaties in vergelijking met volwassenen. Ten eerste vereist het nauwkeurig manipuleren van catheters in een klein hart grote technische vaardigheid en ten tweede worden radiofrequentie (RF) laesies aangebracht in een niet volgroeid hart met onrijp myocard. Grote complicaties, zoals een compleet AV blok of een hartperforatie, zullen naar alle waarschijnlijkheid onmiddellijk ontdekt worden. Met het doel eventuele complicaties die zich klinisch niet uitten op te sporen, werd in alle kinderen die een ablatie ondergingen, routinematig een echocardiogram verricht. De klinische waarde van deze routine-echo na iedere procedure was nog niet eerder geëvalueerd en werd daarom bestudeerd in hoofdstuk 3. In deze studie werd bij 138 patiënten die een ablatie ondergingen, een trans-thoracaal echocardiogram gemaakt vóór en na de ablatie procedure.

De resultaten van deze studie laten zien dat een routinematig uitgevoerd echocardiogram na iedere ablatie, niet geïndiceerd is voor de kinderen, die een ongecompliceerde ablatie procedure hebben ondergaan voor een atrio-ventriculaire ritmestoornis. Een uitzondering hierop, zou gemaakt kunnen worden in het geval de retrograde benadering is gebruikt voor een linkszijdige ablatie, zodat specifiek de aortaklepfunctie beoordeeld kan worden.

In de volgende twee hoofdstukken concentreren we ons op twee zeldzamer vormen van ritmestoornissen.
Hoofdstuk 4 beschrijft twee patiënten met een stilstaand atrium die eveneens perioden van intra-atriale re-entry tachycardie hadden. Succesvolle ablatie van het intra-atriale re-entry circuit leidde in beide patiënten tot een verbetering van de hartfunctie. Er is weinig bekend over stilstaand atrium en zolang het natuurlijk beloop van deze aandoening nog niet volledig bekend is, mag ablatie van de bundel van His als behandeling van een intra-atriale re-entry tachycardie in patiënten met een stilstaand atrium, niet de eerste therapie van keuze zijn. In één van onze patiënten herstelde de atriale elektrische en mechanische functie zich gedurende follow-up. Onze resultaten suggereren dat, hoewel het atrium elektrisch geen activiteit vertoont, -vastgesteld door de afwezigheid van P-toppen op het oppervlakte ECG-, eilandjes van elektrische activiteit nog steeds aanwezig kunnen zijn. Deze eilandjes kunnen bijdragen aan re-entry circuits in het atrium.
Bekend is dat er familiair overervende vormen van deze aandoening bestaan. Er is meer onderzoek nodig naar stilstaand atrium om meer te weten te komen over het ontstaansmechanisme, het beloop en ook de lange termijn prognose.

Een ander type atriale ritmestoornis wordt besproken in hoofdstuk 5. Hoewel veel electrofysiologen de term ‘atriale tachycardie’ gebruiken, blijkt deze groep tachycardieën te berusten op diverse pathofysiologische mechanismen. Wij beschrijven een vorm van atriale tachycardie waarvan het mechanisme nog niet duidelijk is. In het algemeen kan een atriale ‘automatisch focus’ tachycardie niet worden geïnduceerd in het electrofysiologisch laboratorium. In dit hoofdstuk beschrijven wij 38 patiënten met een atriale ‘niet-automatisch focus’ tachycardie, die wel induceerbaar was in het electrofysiologisch laboratorium. De resultaten van deze studie laten zien dat deze vorm van

tachycardie met name voorkomt bij vrouwen van alle leeftijdscategorieën en dat de foci die de tachycardie veroorzaken hoofdzakelijk gelokaliseerd zijn in het rechter atrium. Tevens blijkt dat jongere patiënten een kortere tachycardie cycluslengte hebben dan oudere patiënten. Catheter ablatie van deze foci was mogelijk, echter met een aanzienlijk lager succes percentage dan in het algemeen voor de ablatie van supraventriculaire tachycardieën wordt beschreven. Tevens hebben we catheter ablatie met behulp van een speciaal electroanatomisch mapping systeem vergeleken met conventionele ablatie zonder dit gespecialiseerde mapping systeem. Hoewel het aantal succesvol geableerde foci leek te stijgen met behulp van dit mapping systeem, konden we geen gemiddelde verkorting van de procedure- noch doorlichtingstijden aantonen. Toekomstige studies zullen moeten uitwijzen of de gemiddelde procedure- en doorlichtingstijd zullen afnemen al naar gelang de ervaring met deze nieuwe mapping technieken groeit.

De introductie van nieuwe mapping systemen heeft een verdere impuls gegeven aan de ontwikkeling van nieuwe mogelijkheden voor catheter ablatie. Deze geavanceerde mapping systemen maken ook de meer complexe aritmie substraten geschikt voor ablatie. In hoofdstuk 5 bespraken we het gebruik van een electro-anatomisch mapping systeem in de ablatie van atriale 'niet-automatisch focus' tachycardie. Vervolgens beschrijven we in hoofdstuk 6 het gebruik van een ander gespecialiseerd mapping systeem, de LocaLisa, bij ablatie van AVNRT in kinderen. Zesentwintig patiënten, onder de 19 jaar oud, met een structureel niet afwijkend hart en symptomatische episoden van AVNRT, ondergingen een catheter ablatie procedure. Hierbij werd een modificatie van de 'slow pathway' van de AV knoop uitgevoerd. Bij alle patiënten was de AVNRT na ablatie niet meer induceerbaar. Drie patiënten hadden een recidief en ondergingen een tweede ablatie-procedure. Bij één kind werd de ablatie procedure gecompliceerd door een tweede-graads AV block, welke zes weken later spontaan weer hersteld was.
Het gebruik van het LocaLisa mapping systeem vergroot de veiligheid en effectiviteit van slow-pathway AV knoop modificatie in jonge patiënten op twee manieren. Ten eerste door de mogelijkheid om de afstand van iedere potentiële radiofrequentie laesie tot de proximale bundel van His te meten. Ten tweede doordat op het beeldscherm van de LocaLisa monitor continu de relatie tussen de tip van de ablatie electrode ten opzichte van de AV knoop en de bundel van His weergegeven wordt.

Nog onduidelijk is of deze agressieve methode van 'slow-pathway' ablatie, in de toekomst schadelijke effecten op de AV knoop zou kunnen hebben. Late PQ prolongatie en zelfs AV block zijn beschreven in volwassen patiënten die een 'slow pathway' modificatie van de AV knoop hebben ondergaan. Tot op de dag van vandaag hebben wij nog geen tekenen van progressief AV block in onze patiëntenpopulatie waargenomen.

In conclusie hebben wij in de hoofdstukken 2 tot en met 6 laten zien dat voor de behandeling van ritmestoornissen bij kinderen, RFCA een veilige en effectieve therapie is, die gepaard gaat met een laag complicatie risico. Daarbij moeten we ons echter wel realiseren dat onze follow up tijd relatief kort is. Zo is het bijvoorbeeld onbekend of littekens aangebracht door RFCA in het onrijpe myocard, op latere leeftijd zelf een nieuw aritmogeen substraat zullen vormen. Gezien het feit dat aan de ene kant RFCA mogelijk, veilig en effectief lijkt te zijn in jonge patiënten, maar aan de andere kant zorgen bestaan over de lange termijn effecten van RF lesies in het onrijpe hart, is het belangrijk dat richtlijnen opgesteld worden. In deze richtlijnen zou duidelijk beschreven moeten worden welke kinderen precies in aanmerking komen voor RFCA, als alternatief voor de conventionele behandeling met anti-aritmische medicatie. De afgelopen tien jaar hebben de indicaties voor RFCA bij kinderen zich uitgebreid. Verantwoordelijk voor deze uitbreiding lijken onder andere de ontwikkeling in catheter technologie, de introductie van gespecialiseerde mapping systemen en de toenemende ervaring met RFCA voor complexe ritmestoornis substraten. In dit kader hebben wij één vergelijkende en één beschrijvende studie met betrekking tot gespecialiseerde mapping systemen verricht. Echter om aan te tonen dat deze mapping systemen betere RFCA resultaten tot gevolg hebben, zouden we een prospectief gerandomiseerde studie moeten uitvoeren. Ethisch gezien zal dit erg moeilijk zijn om op te zetten. Als alternatief hiervoor zouden de procedure- en doorlichtingstijden in combinatie met de RFCA resultaten voor de verschillende ritmestoornissen, retrospectief vergeleken kunnen worden. Zo'n onderzoeksopzet houdt echter geen rekening met de leercurve gebonden aan de introductie van ieder nieuw systeem. Tevens wordt hierin niet meegenomen dat bij gebruik van meer geavanceerde mapping systemen, ook de meer complexe aritmie substraten voor RFCA in aanmerking komen, welke dat in het verleden, vanwege hun complexiteit niet hadden gedaan.

BRADY-ARITMIEËN

Ook de pacemaker therapie bij kinderen heeft zich over de afgelopen tien jaar aanzienlijk ontwikkeld. Met name de ontwikkeling van kleinere pacemakerdraden, draden die steroïden afgeven en kleinere pacemakerkastjes, zijn van groot belang geweest voor de vooruitgang van pacemaker therapie bij kinderen. Hoewel bij volwassenen endocardiaal pacen uitgebreid wordt toegepast, worden de meeste kinderen nog steeds epicardiaal gepaced. Dit komt hoofdzakelijk omdat bij een transveneus geplaatste pacemakerdraad, de kleine afmetingen van deze jonge patiënten een vergroot risico op veneuze occlusie met zich meebrengen. Juist in deze patiëntengroep, waar vaak een indicatie bestaat voor levenslange toepassing van pacemaker therapie, is men extra voorzichtig om zodoende de bloedvaten zoveel mogelijk te behouden als toegangsweg voor later. Dit heeft geresulteerd in de voorkeur voor een epicardiale implantatie van pacemakers op de kinderleeftijd.
In hoofdstuk 7 beschrijven we een follow up studie van een grote serie kinderen die een transveneuze pacemaker implantatie hebben ondergaan toen hun lichaamsgewicht nog onder de tien kilogram was. De resultaten van deze studie laten zien dat transveneuze pacemaker implantatie in kinderen onder de tien kilogram mogelijk en effectief is, maar niet geheel zonder complicaties verloopt. Negenendertig kinderen in twee centra kregen de afgelopen 15 jaar een transveneuze pacemaker. Het overgrote deel hiervan had een ventriculaire pacemaker gekregen voor dan wel een aangeboren compleet hartblok of verworven compleet hartblok na chirurgie voor een aangeboren hartafwijking. In alle gevallen werden er bij implantatie goede pacing en sensing drempels gemeten. De follow up voor 36 patiënten van deze groep varieerde tussen de 9 maanden en 15.3 jaar (mediaan 4.3 jaar). Zestien patiënten (44%) hebben gedurende deze hele periode nog geen enkele re-interventie ondergaan (gemiddeld 28 maanden follow up). Tien andere patiënten (28%) ondergingen wel een re-interventie, gemiddeld 61 maanden na implantatie, omdat de batterij op was en de pacemaker dus vervangen moest worden. Tenslotte ondergingen om verschillende redenen tien kinderen (28%) een re-interventie vóórdat de batterij op was. In drie gevallen was dit omdat er problemen met de wond van de pacemaker pocket waren. Bij vier anderen moest de pacemakerdraad wat opgeschoven worden, omdat de patiënt zoveel gegroeid was dat de pacemakerdraad 'te kort' werd. Dit laatste probleem is inherent aan het plaatsen van pacemakers in zeer kleine patiënten, onafhankelijk van het

plaatsen van de pacemaker epi- of endocardiaal. Ditzelfde geldt voor de pacemaker pocket problemen die plaatsvonden in drie patiënten. De pacemaker pocketproblemen zouden mogelijk gedeeltelijk kunnen worden opgelost door alle pacemaker pockets in de buik te plaatsen.
De percentages en gemiddelde follow up tijd ten tijde van re-interventie zijn zeer acceptabel en laten zien dat transveneuze pacemaker implantatie in deze patiëntengroep mogelijk en effectief is.
Wij vonden echter ook dat tijdens re-interventie vier asymptomatische patiënten (11%) een occlusie hadden van het vat waar de pacemakerdraad doorheen liep. Deze vier occlusies werden waargenomen tijdens vier van de 11 pacemakerdraad extracties en 12 pacemakerdraad opschuif procedures, die werden verricht. Het daadwerkelijke aantal veneuze occlusies zal dus waarschijnlijk hoger zijn, aangezien deze vier occlusies bij asymptomatische patiënten werden gevonden, die toevallig een interventie aan de pacemakerdraad ondergingen. Verder onderzoek is nodig naar het exacte occlusie aantal, ook in de asymptomatische patiënten die geen interventie ondergaan.
Om transveneus pacen in (kleine) kinderen wereldwijd meer acceptabel te maken, zal het percentage patiënten dat een occlusie van het bloedvat ontwikkelt, moeten dalen. Onderzocht moet worden welke patiënten in deze gewichtscategorie een groter risico hebben om veneuze occlusie te ontwikkelen. Het ontwikkelen van kleinere pacemakerdraden zou kunnen bijdragen om het percentage veneuze occlusies naar beneden te brengen. Het is ook waarschijnlijk dat nieuwe catheter technologieën, zoals het gebruik van 'laser sheaths', momenteel alleen bij volwassenen, ook bij kinderen in praktijk gebracht gaan worden. Met deze technologie is het mogelijk om geoccludeerde vaten te rekanaliseren en opnieuw te gebruiken.

ARITMIEËN NA HARTCHIRURGIE

De verbetering in uitkomsten na hartchirurgie voor aangeboren hartafwijkingen, hebben gezorgd voor een groeiende populatie adolescenten en volwassenen die hartchirurgie op kinderleeftijd hebben ondergaan. Deze patiëntenpopulatie heeft zijn eigen specifieke problemen en risico's. In de

follow up van chirurgisch ingrijpen voor bepaalde congenitale hartafwijkingen, is een aanzienlijk risico voor plotselinge hartdood beschreven. Hoofdstuk 8 beschrijft een studie waarin we risicofactoren hebben bepaald voor plotselinge hartdood na een atriale switch operatie voor transpositie van de grote vaten. In deze studie hebben we 47 patiënten geïncludeerd die op jonge leeftijd een atriale switch (Mustard of Senning operatie) hebben ondergaan en in follow up plotseling overleden zijn of een 'bijna' plotselinge hartdood hebben doorgemaakt. Elk van deze patiënten werd gematched met twee controle patiënten, die dezelfde operatie hadden ondergaan, maar niet plotseling overleden waren. Verschillende variabelen recent voor overlijden werden verzameld en vergeleken met dezelfde informatie van de corresponderende controles. Uit het onderzoek blijkt dat het bestaan van symptomen van ritmestoornissen of hartfalen geassocieerd is met een verhoogd risico op plotselinge hartdood. Daarnaast vergroot een voorgeschiedenis van gedocumenteerde ritmestoornissen, met name supraventriculaire tachycardie, het risico op plotselinge hartdood. Anti-aritmische medicatie noch pacemaker implantatie hadden een beschermend effect. Deze bevindingen pleiten voor onderzoek naar alternatieve therapieën voor het behandelen van ritmestoornissen in deze patiëntenpopulatie. Toekomstige studies zullen moeten uitwijzen of de verbeterde technieken van RFCA een positief effect hebben op de behandeling van ritmestoornissen en incidentie van plotselinge hartdood in de Mustard/Senning populatie. Aan de andere kant is de rol van RFCA in deze patiëntenpopulatie dubieus, omdat is aangetoond dat supraventriculaire tachycardieën, ventriculaire disfunctie kunnen veroorzaken, maar ook veroorzaakt kunnen worden dóór ventriculaire disfunctie. Uit het onderzoek blijkt tevens dat zowel een thoraxfoto, als een ECG en een 24-uurs Holter registratie geen voorspellende waarde hebben voor plotselinge hartdood. Om risicopatiënten nauwkeuriger te definiëren is verder onderzoek met grotere patiënten cohorten nodig. Uitgezocht moet worden of andere testen, zoals bijvoorbeeld echocardiografie, hartcatheterisatie, inspanningstesten en electrofysiologische testen, toevoegende waarde hebben voor het nauwkeuriger vaststellen van het risico op plotselinge hartdood bij patiënten met symptomen of een voorgeschiedenis van ritmestoornissen.

Dankwoord
Curriculum Vitae
Lijst van publicaties

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De auteur van dit proefschrift werd op 7 maart 1977 geboren in Gouda. De middelbare schooltijd werd doorgebracht op het Coornhert Gymnasium in deze zelfde stad. Na het behalen van het diploma in 1995, startte zij met de studie geneeskunde in Utrecht. Het doctoraal examen werd behaald in augustus 2000. Tijdens haar studententijd was zij naast diverse student-assistentschappen, actief als voorzitter van een gala-commisie en penningmeester van het bestuur van de medische faculteitsvereniging.
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