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Epicardial pacing in growing children: pacemaker performance and positional evolution

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To close, I wish you all a pleasant read. Hopefully this work offers you supplementary information concerning this subject.

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1. Abstract

Introduction

Small body size and future somatic growth presents difficulties in epicardial pacing therapy for infants and children. Lead failure as well as battery failure occurs more in children, compared to adults. Not only the higher heart rate, but also lead stretching, compression of leads, and so on, contribute to the susceptibility of failure of epicardial pacing systems. During implantation, pacemaker position and lead length have to be adjusted to expected growth. Research has been done concerning endovenous pacemakers and the needed length of excess lead in the atria has been calculated. In contrary, in epicardial pacemakers, the required lead length is determined by the positional evolution of pacemaker against the heart. No research has been done to evaluate this distance. This study will describe the evolution of the distance between heart and epicardial pacemakers. The results may have serious impact on the excess of lead required at implantation.

Methods

This study investigates 59 infants and children who recieved a permanent epicardial pacing system, and were followed at the University Hospital of Gent since 1991. Patient charts and electronic database were reviewed and data was collected. In the first part of this study, descriptive and comparative statistical analysis was performed on this data. In the second part, the positional evolution of the epicardial pacemaker was examined through posteroanterior chest roentgenograms made at implantation as well as at the latest follow-up.

Results

Patient follow-up had a mean duration of 7,4 years (SD ± 5,3 years). No correlation was found between age at first epicardial pacemaker implant and pacemaker modus (p= 0,431), number of leads (p= 0,422), number of batteries (p=0,422), occurrence of lead failure (p= 0,431) and type of lead failure (p= 0,422). The age of patients at the first implantation was also unrelated to the progression in distance between the chest X-rays taken at first pacemaker implantation and chest X-rays taken at the latest follow-up (p= 0,346).

Replacement was necessary in 21 leads after a mean period of 7,4 years (SD ± 4,1 years). Lead failure occurred after a mean of 8,9 years, elective substitution occurred after a mean of 4,5 years. The leads which were not substituted, had a mean follow-up period of 5,0 years (SD ± 4,1 years). Replacement was also necessary for 53 batteries. Replacement for battery end of life occurred after a mean of 6,2 years (SD ± 2,4 years). Batteries which were not replaced had a mean follow-up period of 2,6 years (SD ± 2,2 years).

The mean increase in distance between the bottom edge of the heart and the upper edge of the pacemaker, shown on the chest X-rays taken at first pacemaker implantation and the chest X-rays taken at the last follow-up, is 35,8 cm (SD ±28,8 cm). In addition, the mean increase in patient height during this period is 40,8 cm (SD ± 28,5 cm). The correlation between increase in distance and patient height was significant (p= 0,003). In contrast, no significant correlation was found between lead failure and the increase in distance (p= 0,181).

Conclusion

In this patient cohort of 59 children, epicardial pacing was associated with acceptable long-term results. During somatic growth of the children, the increase in distance between generator and heart is proportionate to the increase in patient length. Measuring the excess length of lead necessary in epicardial pacing in infants remains challenging, although in this study lead failure was not correlated to the increase in distance between heart and pacemaker.

2. Introduction

2.1 Question and purpose

Pacing systems have saved thousands of lives over the last decades. They are now so common that it is almost difficult to imagine a time where there was no treatment [1]. Not only are they indispensable for adults suffering from cardiac problems, they are also crucial to a small group of children and neonates who cannot live without pacing systems.

Pacemakers help starting a life that otherwise wouldn't be possible. Unlike in adults, a permanent pacing system for children has to deal with peculiar problems, such as the complex cardiovascular anatomy, the hemodynamic instability, the electrophysiological abnormalities and the limited access to the heart chambers [2,3]. Moreover, the small body size of children makes a specific approach necessary for implantation and evaluation of the pacemaker [2]. Due to the small caliber of the venous system, an endovascular approach is often not possible, therefore epicardial pacemaker systems need to be applied. Cardiac surgeons have to take into account the somatic growth a child will go through. This may cause problems such as fracture or stretching of the leads, which consequently will lead to re-operation [4]. For this purpose, excess lead is inserted in the infant in order to let somatic growth take place without lead-stretching or need for surgery later in life. However a too long lead can also cause problems such as cardiac strangulation [5,6].

There is need for research, investigating the spatial evolution of pacemakers and their leads. This thesis investigates a cohort of infants and children that recieved a permanent epicardial pacing system, and was followed at the University Hospital of Gent since 1991.

The thesis comprises 2 parts:

- First the patient and pacemaker characteristics were investigated, at implantation and during follow-up. Risk factors for reinterventions on the pacemaker were sought for, and the type of reinterventions described.
- Secondly, the spatial relationship of the pacemaker battery and the heart were investigated during growth of the patient, using simple chest x-rays and anthropometric data at implantation and during follow-up. Consequently, we will try to infer guidelines for leaving excess length at implantation.

2.2. General information on pacemakers

2.2.1. What is a pacemaker?

A pacemaker is an electronic device basically consisting of an electrode connecting the heart muscle at one end to a generator, the pacemaker battery, at the other end. The pacing lead is fully insulated, except at the ends. It is implanted in the human body to regulate the heart rate [7]. The system creates an electrical impulse, generated by the battery, that is then transmitted to the patient's heart through a single or multiple electrodes attached to the cardiac muscle [8].

The pacemaker senses and paces. 'Pacing' means sending an electric impulse directly to the heart when the heart rate is disturbed or too low. This electric impulse induces a cardiac contraction. 'Sensing' implies that the pacemaker can detect the natural electrical activity of the heart. When there is a normal heart rate, the system will not deliver an impulse.

In 1958 the first battery controlled pacemaker was introduced by C.W. Lillehei and Earl Bakken [8]. This pacemaker could only stimulate one heart chamber with a steady heartbeat. Since then the original design was repeatedly adjusted and improved [9].

The standard antibradycardial use of the pacemaker was extended with sophisticated possibilities in the course of time, such as rate-responsiveness, exercise-triggered, .. [10]. The modern pacemaker has different assets such as augmented safety, improved durability and cost effectiveness [11].

2.2.2. Epicardial and transvenous approach

The implantation of a pacemaker can be done by two basic anatomical approaches. Historically, the first is the epicardial approach where direct application of the pacemaker electrodes on the heart takes place. This requires general anesthesia to perform a surgical incision down to the exterior surface of the heart. The second approach is the transvenous approach. This is usually performed under local anesthesia or intravenous sedation. Currently, 95% of all implantations is performed through the transvenous approach [12]. After eliminating the problems of exit block and dislodgement, modern transvenous leads have proven more reliable than the epicardial ones with various benefits such as minimal invasiveness, lower pacing threshold (see infra) and longer generator longevity [12,13].

Besides that, the abdominal location of the epicardial pacemaker can cause more discomfort than the prepectoral location of the transvenous pacemaker [12]. Epicardial pacemakers appear to be less durable than transvenous systems [14]. Therefore the epicardial approach is reserved for patients in whom the implantation of a transvenous pacemaker cannot be accomplished safely or effectively. In adults, only unusual circumstances dictate an epicardial implantation such as recurrent dislodgement of the transvenous lead, patients with mechanical tricuspid valves, some congenital anomalies obviating a normal access to the cardiac chambers, or in some cases of pacemaker infections [12]. In infants and small children, transvenous systems are often technically not possible, due to the size discrepancy between the small caval veins and the caliber of the leads, introducing a risk for venous obstruction. [12].

2.2.3. Epicardial lead placement and pocket position

Several surgical techniques can be used for epicardial lead placement. The most common is the median sternotomy, performed at the time of other cardiac surgery. Here, both the atria and the ventricles are exposed and the electrodes are attached directly to the epicardium. The electrode is then tunneled to a subcutaneous pocket in the upper abdomen. Other techniques are the subxiphoid technique, the left subcostal technique and the left anterolateral thoracotomy. The first two access the epicardium through a small supradiaphragmatic abdominal incision. While the subxiphoid technique mainly exposes the right ventricle, the left subcostal technique exposes more of the left ventricle [12]. Both techniques are associated with minimal surgical trauma and can be considered less invasive methods [15]. In the left anterolateral thoracotomy, an incision is made in the fifth intercostal space, facilitating access to the left ventricle and left appendage [12]. The generator is placed using a second incision in the upper abdomen, while the subxiphoid and the left subcostal approach may require one single incision [15].

Epicardial lead placement has also been accomplished by minimally invasive techniques. For left ventricular lead placement thoracoscopic and robotic surgical techniques are now more frequently used. In addition, techniques for percutaneous access to the pericardium are under development [12]. When epicardial atrial leads are necessary, a median sternotomy or left thoracotomy is obligatory, as atrial lead placement is not possible through a small subxiphoid

incision. When only ventricular leads are needed, all previously described access routes can be applied [13,16].

The pacemaker pockets in which the generator is inserted, can also have diverse positions. Historically, the pocket is created in the musculus rectus sheath of the abdominal wall above the level of the umbilicus. This is called the subrectus location. Furthermore the pacemaker can be inserted closer to the heart in a subxiphoid pocket location or a retrocostal pocket location in the thorax [2].

2.2.4. Pacing modes

Pacemaker leads can be inserted in the ventricles or the atria or both chambers [17]. This leads to a categorization of pacemakers according to the NASPE coding system, that usually consists of 3-5 letters [16].

Position I: chamber(s) paced	Position II: chamber(s) sensed	Position III: response to sensing	Position IV: Programmability	Position V: Multisite pacing
O = None	O = None	O = None	O = None	O = None
A = Atrium	A = Atrium	T = Triggered	R = Rate modulation	A = Atrium
V = Ventricle	V = Ventricle	I = Inhibited		V = Ventricle
D = Dual (A+V)	D = Dual (A+V)	D = Dual (T+I)		D = Dual (A+V)

Table 1. The revised NASPE/BPEG generic code for antibradycardia pacing [16].

Frequently used codes are:

- AAI: The atrium is stimulated, when the intrinsic atrial rhythm falls below the pacemaker's threshold [13,16].

- VVI: The ventricle is stimulated, when the intrinsic ventricular rhythm falls below the pacemaker's threshold. This is useful in atrial fibrillation or for backup pacing [16,18].

- VDD: The pacemaker senses atrial and ventricular events, but can solely pace the ventricle. This type of pacemaker is useful in patients with a reliable sinus node, but an existing AV-block [16].

- DDD: This is the most common pacing mode for dual-chamber pacemakers and is useful in AV node and/or sinus node dysfunction. The pacemaker senses both atrial and ventricular rates and can pace either chamber when needed [16,18].

- DDDR: As above, but the pacemaker senses a demand for higher cardiac output and can adjust the heart rate accordingly [16].

2.2.5 Complications

1) Infections due to pacemaker implantation occur in 0,8-5,7% of implants. Early infections are commonly related to Staphylococcus aureus and can be aggressive. Late infections are mostly caused by Staphylococcus epidermidis and may have a more indolent course. Signs of infection such as local inflammation, abscess, erosion of the pocket and fever with sepsis should be detected [8,18]. To avoid pacemaker pocket infections, a routine prophylaxis with antistaphylococcal antibiotics is recommended during placement. The use of these antibiotics at the time of implantation or revision surgery has decreased the rates of short-term pocket infection [8]. When pacemaker infection or endocarditis occurs, removal of the pacemaker leads and generator is usually required in order to eradicate the infection [8,19].

2) The insulation of the lead can break or the lead can fracture, causing problems of oversensing (because of electrical noise) or undersensing. This problem is difficult to detect because of the intermittent manifestation of the problem. The patient may complain of muscle stimulation around the pocket due to a leak around the rupture [18].

3) Failure to capture occurs when a stimulus output, delivered outside the refractory period, is not followed by a P wave or a QRS complex. This may be caused by elevation of stimulation threshold, anti-arrythmic drugs, acute myocardial infarction, lead defect or maturation, dislodgement or perforation, incorrectly low programmed output or battery end of life. Failure of output can be due to battery depletion or component failure and is manifested by the absence of pacing artifacts [8].

4) The pacemaker syndrome is an adverse reaction to VVI pacing or DDD pacing with very long AV intervals. The basis is a loss of AV synchrony. The atrial complex follows rather than precedes the ventricular complex. Symptoms as orthostatic hypotension, near syncope, fatigue, exercise intolerance, malaise chest pain and other nonspecific symptoms occur. When the AV synchrony is restored, the symptoms disappear [18].

5) More a side effect rather than a complication, is the electromagnetic interference with the pacemaker function. Magnetic resonance imaging (MRI) is contraindicated in most patients with pacemakers. However, recent progress is made on safe MRI scanning in patients with cardiac monitoring. Likewise, cellular phones can rarely affect pacemaker function. Therefore patients should keep their phones at least 20 cm away from their pacemaker [18].

2.2.6. Evolution in time

2.2.6.1. Battery performance and longevity

A typical pacemaker diagram is shown in Figure 1. This illustrates that the battery occupies a major portion of the pulse generator in terms of weight, volume and size [20].
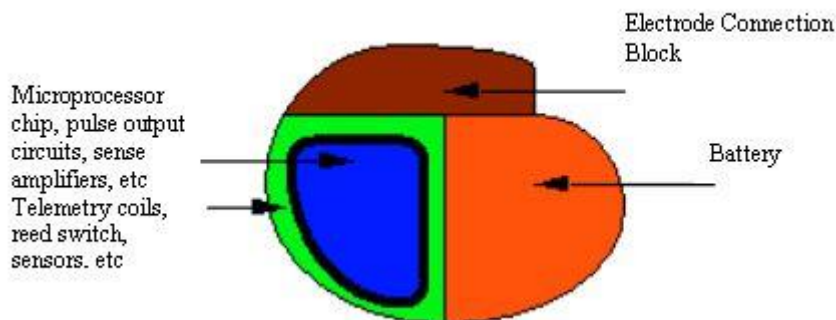
Figure 1. A Typical pacemaker diagram [20].

The battery is a hermetically sealed part of the pacemaker [20]. A battery is conceptually different from the other components, which are designed to last indefinitely. In contrast, the available chemical energy of the battery is consumed during use. Over time, the output of the battery becomes insufficient and needs to be replaced. As batteries are part of the device, the entire pulse generator must be replaced to renew the battery [22]. This is not only a cost for healthcare, it brings also a risk of infection and other complications [21]. Therefore the most

important factor for a cardiac pacemaker battery is its reliability and prolonging the time between generator changes remains an important goal [20,21].

Through time, cardiac pacemaker batteries evolved regarding various characteristics. Rechargeable nickel-cadmium batteries were used in the early era of pacemaker implants. They were recharged by transmitting energy to the implanted receiver. Two problems emerged: the very short life time and the responsibility for recharging placed in the hands of patients. It was known that non-rechargeable batteries would give longer lifetime compared to rechargeable batteries. This type is no longer sold [20].

Later on, different types of batteries were produced and tested. Mercury-zinc, biological and nuclear batteries were tested with variable results. They were repressed by the introduction of the lithium iodine battery in 1975. This type has the highest specific energy of all and extended the pacemaker battery life [20]. Lithium batteries usually last 5-10 years [17]. Some models even have a battery life of more than 10 years [20]. Moreover, lithium batteries meet the requirements of low drain current and voltage characteristics. They demonstrate a stable voltage throughout much of the battery life and then decline in a gradual and predictable manner. The terminal voltage decays slowly enough for battery end-of-life to be anticipated in routine follow up. Because of the low self-discharge rate and high energy density, the lithium battery has exhibited excellent reliability. Therefore this system has become the power source of choice for cardiac pacemakers [20].

2.2.6.2.   Pacemaker lead performance and longevity

The pacemaker lead is the critical interface allowing transfer of electrical signals between the pulse generator and the myocardium. Leads can be divided into two groups: unipolar and bipolar leads. First there only existed one type: the unipolar lead. Such a lead with only one conductor and electrode, is called a unipolar lead, because only one electrode is in contact with the heart. The positively charged pulse generator (anode) connects via one conductor to a negatively charged tip electrode (cathode) [23].

Although once the only option, unipolar leads have largely been replaced by bipolar leads which consist of a lead body containing two conductors, separated and surrounded by insulation. These conductors connect to a cathode tip-electrode and an anode ring-electrode

located a few millimeters more proximally. In this system the pulse generator is not an active electrode [23].

Both systems have strenghts and weaknesses. Unipolar systems have a large interelectrode distance from the tip of the intracardiac lead to the pulse generator. This makes them vulnerable to the oversensing of myocardial signals from another chamber or nonmyocardial signals such as skeletal myopotential or electrical noise. Significant consequences on pacing behavior can be the result. The superior sensing properties of bipolar leads are therefore their great advantage. Although bipolar leads have similar but slightly higher thresholds to unipolar leads, the only disadvantage of bipolar leads worth noting is that reliability is lower than with the less complicated unipolar lead. However some studies have not confirmed this assertion. All these factors have led to the near–universal adoption of the bipolar lead as the configuration of choice for cardiac pacemaker leads [23].

The electrode of a unipolar as well as a bipolar lead has to be attached to the myocardium. Initial pacemaker leads had no fixation mechanisms, consequently lead dislodgement rates were high [23]. Lead fixation of current pacemakers can be active or passive (figure 2) [24]. Passive fixation endocardial leads usually include tines at the tip that become ensnared in trabeculated tissue, providing lead stability. Active fixation leads introduce an electrically active screw into the myocardium [24].
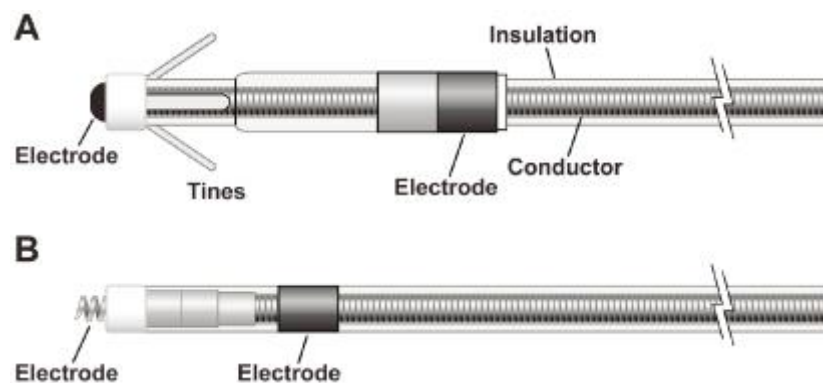
Figure 2. (A) Basic components of a passive fixation pacing lead with tines. (B) Active fixation lead in which the helix serves as the distal electrode [24].

Passive fixation leads are easy to deploy but difficult to extract, owing to the encasement of the tines by fibrous tissue. Active fixation leads are often preferable in patients with distorted anatomy, such as congenital cardiac defects, or when alternative pacing (outside the right atrial appendage and right ventricular apex) is needed. Screw-in leads have the ability to be

stabilized in nontraditional locations. They may have higher initial pacing thresholds at implantation, but thresholds decline significantly within the first 5-30 minutes after placement. This effect has been attributed to hyperacute injury due to positioning of the screw into the myocardium at implantation [24].

One of the most important lead design changes to alter pacing threshold evolution, is the incorporation of steroid elution at the lead tip, to blunt the local inflammatory response. Steroid-eluting leads minimize fibrous capsule formation and result in long-term reduction in energy consumption [24]. A lower pacing threshold and less drain on batteries, means a longer battery life and less need for subsequent surgical interventions [25]. Therefore the use of these steroid-eluting leads shows good longterm outcomes concerning pacing performance and lead survival [25, 26].

After implantation of earlier generations of endocardial leads, the stimulation threshold would usually rise in the first 24 hours and then gradually increase to a peak at 1 week. Over the following weeks, the stimulation threshold would typically decline to a level somewhat higher than that at implantation, but less than the peak threshold. This stabilizes at approximately 4 weeks [24]. After the implantation of a steroid-eluting lead on the other hand, the threshold remains relatively stable, without significant change from short-term threshold measurements (Figure 3) [24].
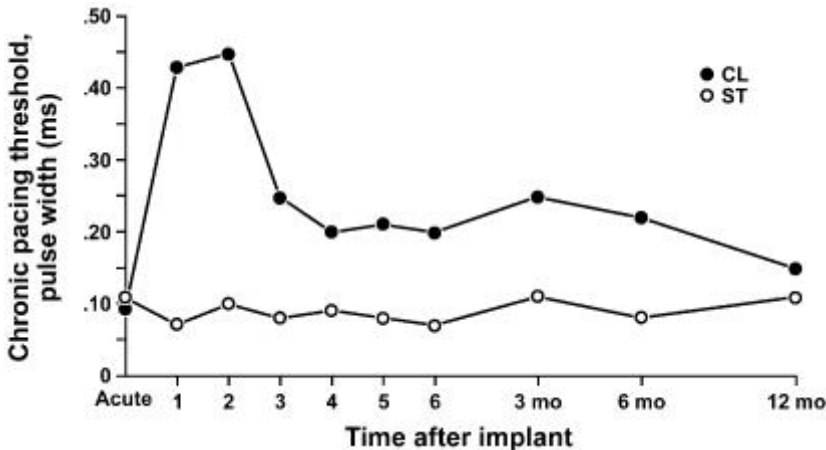
Figure 3. Long-term pacing thresholds from a conventional lead (no steroid elution) (CL) and a steroid-eluting lead (ST) [24].

The above described characteristics are valid for both the transvenous and epicardial pacing systems. This study will only consider epicardial pacemaker leads with their own specific problems such as a possible short-term durability, because of an increase in stimulation threshold resulting in an exit block [25]. High pacing thresholds and exit block, but also lead fracture and lead failure tend to occur more frequently with epicardial than with endocardial leads [27].

2.3. Technical specifications

Stimulation threshold and lead impedance are two pacing characteristics used for monitoring the pacemaker system activity.

2.3.1. Threshold

The atrial or ventricular stimulation threshold is the minimum pulse energy required to stimulate the muscle cells of the atria or ventricles to depolarize and so to contract [28]. This is expressed as pulse amplitude measured in volts [24]. Pacing thresholds must be determined when the pacemaker is first implanted in the patient to ensure that reliable "capture" is obtained while expending minimum energy. During subsequent follow-up examinations the pacing threshold is monitored to detect battery depletion or other pacemaker and lead problems [28].

2.3.2. Impedance of the lead

Impedance is a measure of the signal transduction in pacemaker leads and applies to the resistance to current flow [26,29]. The lower the impedance, the greater the flow and vice versa [26]. Not only permanent lead abnormalities, such as insulation breakdown and lead fractures, can be detected but also temporary lead impedance anomalies as well as significant but gradual variations which may be symptomatic of impending lead failure [29].

2.4. Children and pacemakers

2.4.1. Indications for pacemakers in children

Indications for permanent pacing in pediatric patients have been difficult to define due to the lack of data from controlled studies and trials [30]. However, the 2008 guidelines of the American College of Cardiology/ American Heart Association/ Heart Rhythm Society (ACC/ AHA/ HRS) include indications for implantation of pacemakers in children (see addendum 1) [13, 31, 32]. The main indication for pacing in childhood is symptomatic bradycardia, most commonly due to complete heart block [3]. Heart block may occur in children with structurally normal hearts (isolated heart block) as well as in children with congenital heart disease. Although heart block may occur spontaneously in some congenital heart conditions, the most common cause of heart block in congenital heart disease is damage to the conducting system resulting from cardiac surgery [13, 31]. The incidence of postoperative heart block is around 1-2% but it is often transient and most patients who are going to recover will do so within 10 days [13, 31]. If unpaced, postoperative heart block is associated with a risk of sudden cardiac death and common practice is to implant a permanent pacemaker if the heart block has not recovered within 10 days. Even after pacemaker implant, heart block may recover, sometimes years later [13, 31].

Sinus node dysfunction with or without atrioventricular conduction disturbances, specifically when related to congenital heart disease, is a less frequent indication to implant a pacemaker system. Usually a AAI or DDD pacemaker mode is applied in these patients.

2.4.2. Type of pacing leads

Although increasing in frequency, pacemaker implantation in children remains a relatively rare procedure. This makes it difficult to achieve and enhance experience. Most children will be pacemaker dependent for the rest of their lives [33]. As a consequence, the decision regarding the type of pacemaker and lead is important and depends not only on patient size but also on cardiac and venous anatomy [31]. Important factors include the small body size, the venous diameter, presence of a intracardiac shunt and risk of thrombosis [13]. Endovenous pacemaker implantations in children may be complicated by thrombus formation in small vessels, the possibility of pulmonary embolism, limited accessibility through complex

intracardiac structures, and potential difficulty in removing a previous transvenous lead to make room for a new lead [34].

Endocardial lead implantation can result in venous obstruction in small children whose veins have small calibers because of the lead-endothelial interaction and neointimal proliferation, with an inherent risk of stenosis or thrombosis [3, 34]. This occurs in approximately 20% of pediatric cases [13]. Besides the risk of venous thrombosis and vascular obstruction, endocardial pacemakers may damage the atrioventricular valve. If children have relative or absolute contraindications to the transvenous approach because of small body size, presence of a right-to-left shunt, or absence of venous access caused by congenital anomalies or surgical interventions, an epicardial pacemaker has to be implanted [25].

In general, the epicardial pacemaker needs more complex surgery and has a shorter lifetime than the endocardial pacemaker (because of the higher stimulation threshold caused by fibrosis after surgery) [4, 34]. However, due to age-specific characteristics, in most pediatric patients requiring pacemaker implantation it is impossible to implant an endocardial pacemaker [34]. Epicardial leads are commonly used in children with a small body size (weighing less than 20 kg). Nonetheless, there is an increasing trend towards lowering the age and weight limits for endocardial leads in younger children. Some institutes actively implant transvenous leads in children weighing less than 15 kg and even implantation of an endocardial pacemaker in infants weighing less than 10 kg has been reported [13].

A summary of the advantages and disadvantages of epicardial and endocardial leads [35]:

- Advantages of epicardial leads: applicable in every child, the possibility to combine the implantation of the leads with a corrective or palliative operation, fewer problems with the growth of the child, and the absence of the need for anticoagulation in children with a right-to-left shunt.
- Disadvantages of epicardial leads: usually higher thresholds, more extensive surgical procedure and the damage to the epicardial wall, which may result in difficulty in finding epicardium without scars for implantation of another epicardial lead.
- Advantage of endocardial leads: less extensive surgical procedure.
- Disadvantages of endocardial leads: the small size of the veins, the risk of venous obstruction, and the need for the accommodation of the lead to the child's growth.

2.4.3. Pacing mode

In pediatric patients, both endocardial and epicardial pacing systems induce problems. DDD endocardial pacemakers are not always ideal in children, due to the small venous diameter and subsequent venous obstruction [13]. DDD endocardial pacing can be used in children from the age of 3 years and 12,8 kg body weight without problems [36]. This is not always ideal in younger children, due to the small venous diameter and subsequent venous obstruction. Then, a VDD endocardial pacemaker is an excellent alternative choice, because it requires only a single lead [13]. Transvenous ventricular pacing (VVI) can be established in newborns of 2.8 kg body weight [36].

DDD epicardial leads also cause difficulties. Atrial leads cannot be implanted using a subxiphoid approach and either an invasive median sternotomy or a left thoracotomy must be performed. Single-chamber ventricular pacing (VVI or VVIR) should be selected in infants with a small body size and a high-grade atrioventricular block [13]. The pacing site of this ventricular lead is a critical issue. Right ventricular apical leads can worsen cardiac function for both endocardial and epicardial pacing [13]. In contrary, left ventricular apical pacing or lateral wall pacing lead positioning may be a better way for epicardial pacing in children and infants to ensure optimal preservation of ventricular synchrony and function [5, 13, 37].

2.4.4. Long term results and survival

In pediatric patients, compared to adults, more frequent pacemaker generator or lead changes are usually needed [34]. For the child undergoing an initial implantation at age 1 year, a minimum of nine electrode changes and 17 generator changes (at 100% pacing) can be expected during its lifetime [38]. These repeated operations for the changing of generators or leads in young children or infants cannot be avoided [34]. There is a small but finite risk of infection each time a generator change is performed. If patients have less generator changes during their lifetime, the relative risk of complications is reduced [13].

The average longevity of the currently available pulse generators in children is only 5 years. However, when these children are divided into two groups based on age at generator implantation, longevity is much different. The generator half-life is 5 years for children younger than 4 years of age at implantation and increases to 7 years for children older than 4 at implantation. This is mainly the result of the higher heart rates needed in young children,

and the subsequently higher programmed lower pacing rates [38]. Thus the pacemaker generators are often exhausted earlier in younger patients because they need to sustain a more rapid heart rate than pacemakers in older patients [34, 36]. At the same time, the use of a dual-chamber mode to track the atrial rate leads to more energy consumption and earlier exhaustion of the pacemaker generator, compared to single chamber pacing [38].

Nevertheless, pacemaker lead failure is the major source of failure for epicardial systems in children, inducing reoperations [2]. In pediatric pacing patients the incidence of lead problems is high [13]. The average epicardial electrode lasts 7 years [38]. Lead failure is defined as lead fracture, insulation break, displacement, and abnormalities in sensing or pacing [13, 33]. Lead fracture occurs more in children than in adults. Many factors contribute to lead fracture susceptibility, such as lead stretching due to somatic growth, compression of epicardial leads caused by the small space between ribs, direct impact forces during daily activities... [13].

When applying pacing therapy in infants an adequate length of electrode to allow for somatic growth will be required [6]. Increasing patient size and height during growth could result in lead fracture, due to insufficient residual lead length. Lead revisions due to growth of the children remains a considerable problem until puberty [39]. Some growth allowance can be provided by leaving a redundant loop of pacing lead. Generally, the loop of an endocardial lead is located in the atrium and inferior vena cava [13]. Likewise, when an epicardial pacemaker is implanted in pediatric patients, surgeons usually leave a loop in the anterior epicardium or the inferior diaphragmatic surface, allowing patients to grow (Figure 4) [6]. The excess lead is then fixated at the electrode bifurcation to avoid displacement [5].
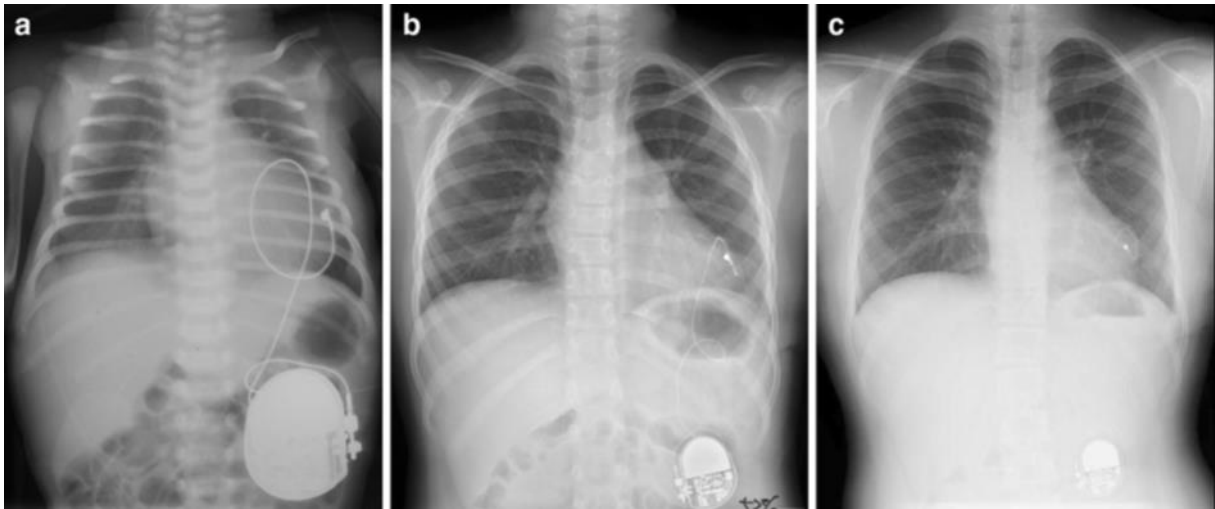
Figure 4. Changes in a loop of the epicardial lead as the child grows. A 16-dayold newborn with congenital atrioventricular block underwent implantation of an epicardial pacemaker and lead. Note the changes in the loop on the radiographs at 16 days of age (a), 7 years later (b), and 12 years later (c) [13].

The length of this loop, needed for growth from infancy to adult life, is not defined [40]. Although a too short lead can cause traction to the lead if the child grows and result in lead failure, a lead that is too long can equally cause problems. The pacing lead can migrate and encircle the heart, causing progressive entrapment of the myocardium and coronary artery compression [6]. Cardiac strangulation from epicardial pacemaker is a rare event in children. Nevertheless, it can cause serious complications such as progressive compression of cardiac structures and cardiac failure. To minimize the risks of strangulation surgeons should be careful of lead placement, and these should not be routed anteriorly or around the cardiac chambers [5]. Large loops of pacemaker electrodes should be avoided in the pericardial cavity [6].

Concerning a transvenous pacemaker, Gheissari et al. [40] have calculated that a 80 millimeter lead loop in the atrium allows children to grow for 6 to 12 years, with a mean of 8 years, without necessitating a reintervention for lead adjustements. So every year approximately 10 millimeter of lead length is needed to allow body growth of the child [40]. On the other hand, by using the epicardial approach, only the increase in distance between the electrodes attached to the bottom edge of the heart and the pacemaker generator located in the abdomen, has to be considered. Few studies have been conducted to examine this distance.

Does this length increase proportionate to the growth of the child? Or remains this length relatively short and is the excess of lead surgeons leave in the anterior epicardium unnecessary and only causing problems?

3. Methods

3.1. Design and data collection

This study is a retrospective review of all patients that had epicardial pacemaker systems implanted and were followed at Ghent University Hospital between September 1991 and March 2015. The hospital Ethical Committee approval was obtained before data collection (see addendum 2). Belgian registration number: B670201318348. Patient charts and electronic database were reviewed and the following data were collected:

- Demographic and clinical variables at the time of implantation of the first epicardial pacemaker: date of birth, gender, indication for pacemaker implantation and number of previous operations.
- Implantation procedure-related variables: date of implantation, pocket location, incision, type of lead and pacemaker modus.
- Lead-specific follow up: implant and latest follow-up threshold and impedance, lead failure and reason, date of lead replacement.
- Battery-specific follow up: implant and latest follow-up percentage pacing and pacing frequency, battery failure and reason, date of battery replacement.

In an additional part of this study, the positional evolution of the epicardial pacemaker was examined through posteroanterior chest roentgenograms made regularly for follow up. The distance between the bottom edge of the heart and the upper edge of the pacemaker at last follow-up was compared to the same measurement right after implantation.

3.2. Patient characteristics

The group consisted of 59 children of which 31 were male and 28 female. There were various indications for pacemaker implantation: 19 children had a congenital or established atrioventricular block, in 35 children an iatrogenic cause, mostly due to a cardiac intervention, resulted in pacemaker implantation and 5 children had an atrial arrhytmia or a sinus node dysfunction. Fourteen children had no operations prior to the implantation of the pacemaker. 30 children had 1 previous operation, 11 children had 2 previous operations, 3 children had 3 previous operations and 1 child went through 4 previous operations.

Median age of the patients at first epicardial pacemaker implantation was 1,4 years (range 5 days – 29,5 years). As one can see, the observed group is not homogeneous and although most patients were young at implantation, also older children were present in this study (figure 5). The oldest patient had the age of 29,5 years when first pacemaker implantation was conducted. Four patients older than 10,7 years at first pacemaker implantation were included in the first part of the study but excluded from the second part where progression of distance between heart and pacemaker was observed. Since these patients already went through a growing period, it is clear that they were not representative for the increase in distance and height that could be expected.
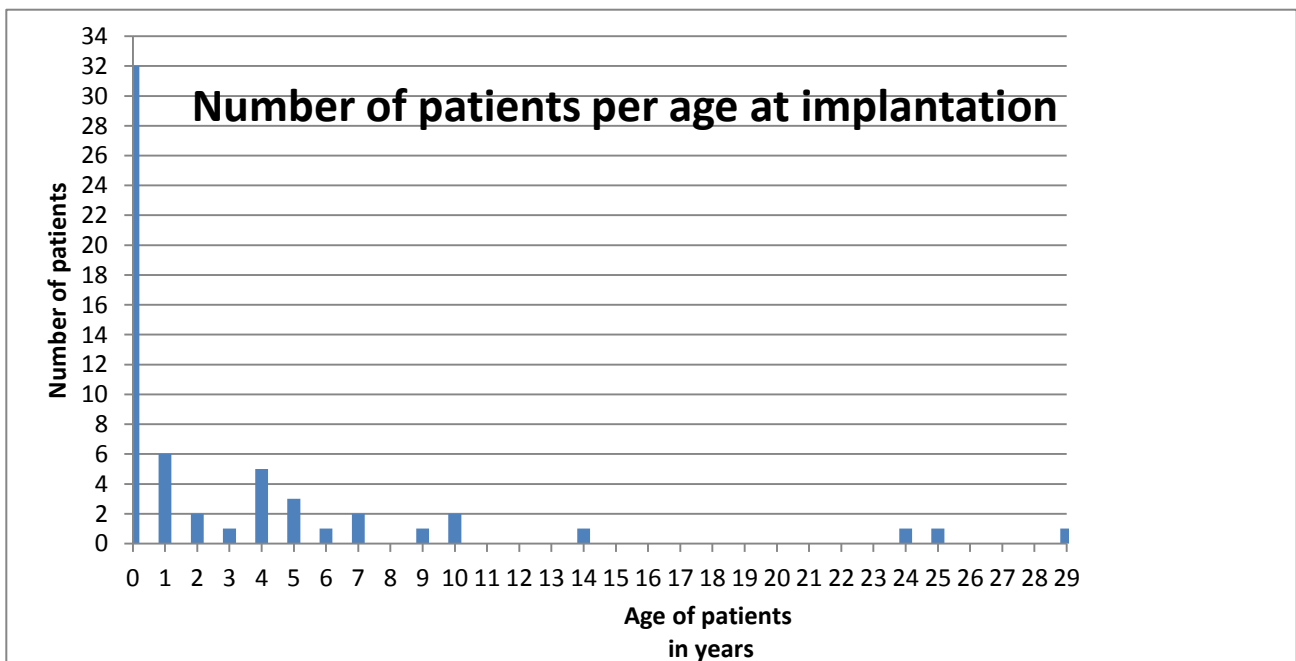

Figure 5. Number of patients per age at implantation. Mind the great disproportion in age. The 4 oldest patients were excluded from the second part of the study.

3.3. Pacing characteristics

At the first pacemaker implantation, access for epicardial pacing lead insertion was sternotomy in 9, thoracotomy in 6, and through a subxyfoidal incision in 44 patients respectively. Pacing leads were connected to various pulse generators, located in a left rectus muscle sheath in 47 children or in a right rectus muscle sheath in 12 children. At the other end

of the lead, electrodes were sutured to the atria (3), the ventricles (45) or both (10). 1 child had an electrode screwed in the ventricle. The pacing mode was purely atrial (AAI) in 3 children, ventricular without atrial synchronization (VVI) in 47 children and atrioventricular in a synchronized mode (DDD) in 9 children.

3.4. Statistical analysis

All statistical analyses were performed using the Statistical Package for Social Sciences (SPSS 22.0). Descriptive statistics were applied and, where appropriate, data were expressed as mean ± standard deviation or median with range. The Paired samples t-tests was needed to examine the evolution of groups over time. Categorical variables were expressed as proportions and Chi-square test was employed to explore group differences. The Mann-Whitney U test was used for analyzing group differences in continuous variables. The pacemaker and lead survival curve were calculated by the Kaplan-Meier method. A value of p < 0,05 was considered statistically significant.

Characteristics	n = 59	%
Male/Female	31/28	53/47
Age at implantation median (range), years	1,4 (5days – 29,5years)	
Indications for pacing		
- Congenital /established AV block	19	32
- Iatrogenic	35	59
- Atrial arrhythmia / sinus node dysfunction	5	8
Previous cardiac operations		
- 0	14	24
- 1	30	51
- 2	11	19
- 3	3	5
- 4	1	2
Surgical access		
- Sternotomy	9	15
- Thoracotomy	6	10
- Subxyfoid	44	75
Pacemaker battery position		
- Left rectus muscle sheath	47	80
- Right rectus muscle sheath	12	20
Electrodes at first implantation		
- Atrial epicardial	3	5
- Ventricular epicardial	45	76
- Atrial + ventricular epicardial	10	17
- Ventricular screw	1	2
Pacing modus		
- VVI	47	80
- AAI	3	5
- DDD	9	15

Table 2. Baseline characteristics of 59 children at first epicardial pacing system implant.

4. Results

4.1. Patient characteristics

In this retrospective study, patient follow-up had a mean duration of 7,4 years (SD ± 5,3 years), although 5 out of 59 patients were lost to follow-up (completeness of follow-up 92%). Primary endpoints were considered mortality or replacement of the epicardial pacemaker by an endovenous pacing system. Among the population, 5 deaths were registered (4 of them had an iatrogenic cause for pacemaker implantation). Deaths were unrelated to the pacemaker surgery or functioning. In 4 other children an endovenous pacing system replaced the epicardial pacemaker at the last follow-up. This occurred on the occasion of a re-intervention for end of life of the epicardial pacemaker, lead fracture or diaphragmatic pacing. Endovenous systems were implanted at a median age of 15,5 years (range 11-38 years).

Consequently, at the end of the follow-up period 45 patients (76%) still had an epicardial pacing system implanted: 2 children in AAI mode, 23 children in VVI mode and 20 children in DDD mode.

No correlation was found between age at first epicardial pacemaker implant and pacemaker modus (p= 0,431), number of leads (p= 0,422), number of batteries (p=0,422), occurrence of lead failure (p= 0,431) and type of lead failure (p= 0,422). The age of patients at the first implantation was also unrelated to the progression in distance between the chest X-rays taken at first pacemaker implantation and chest X-rays taken at the latest follow-up (p= 0,346).

4.2. Lead characteristics

During the study, the observed group of 59 children had a total of 98 epicardial leads implanted. This contained 27 leads sutured to the atrium, 66 leads sutured to the ventricle and 5 leads screwed in the ventricle. Over a period of 24 years, 29 children had 1 lead, 22 children had 2 leads (of which 8 had atrial and ventricular leads implanted at the same procedure), 8 children had 3 leads (of which 5 had atrial and ventricular leads implanted at the same time) and only 1 child had 4 leads.

Replacement was necessary in 21 leads after a mean period of 7,4 years (SD ± 4,1 years). On one hand, 14 leads had to be replaced due to lead failure, which occurred after a mean of 8,9 years. On the other hand, 7 leads were substituted electively at the time of pacemaker

upgrade. Lead replacement as a consequence of an upgrade or for other reasons, was needed after a mean of 4,5 years. The leads which were not substituted, had a mean follow-up period of 5,0 years (SD ± 4,1 years).

Evolution of the thresholds was studied during follow-up. Thresholds of atrial leads (n=22) changed from 0,8 V at implantation or first follow-up to 0,7 V at the last follow-up. This difference was not significant (p= 0,221). The same can be stated concerning the ventricular leads (n=65). These leads had identical thresholds at the last follow-up and at the first implantation: 0,8V. Indeed, this was not considered significant (p= 0,891).

Evolution of the impedance was equally detected. The impedance of the atrial leads (n= 21) decreased from 625 Ohm at the time of implantation to 559 Ohm at the latest follow-up. This was a significant decrease (p=0,007). Again, the same occurred for the ventricular leads (n=60). A significant decrease was seen from 717 Ohm to 445 Ohm (p= 0,0001).
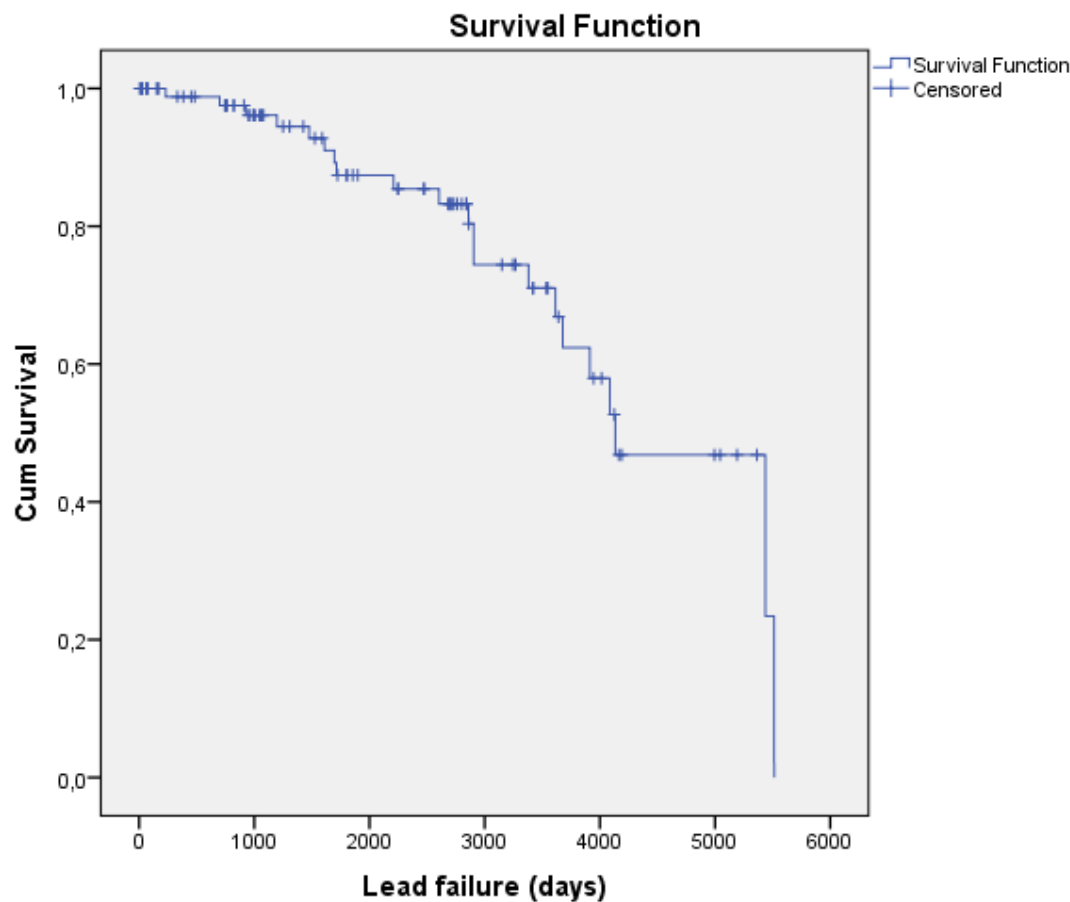

Figure 6: Kaplan-Meyer survival curve for epicardial pacemaker leads. The estimated mean amounts to 4140 days or 11,3 years (range: 3670-4609 days).
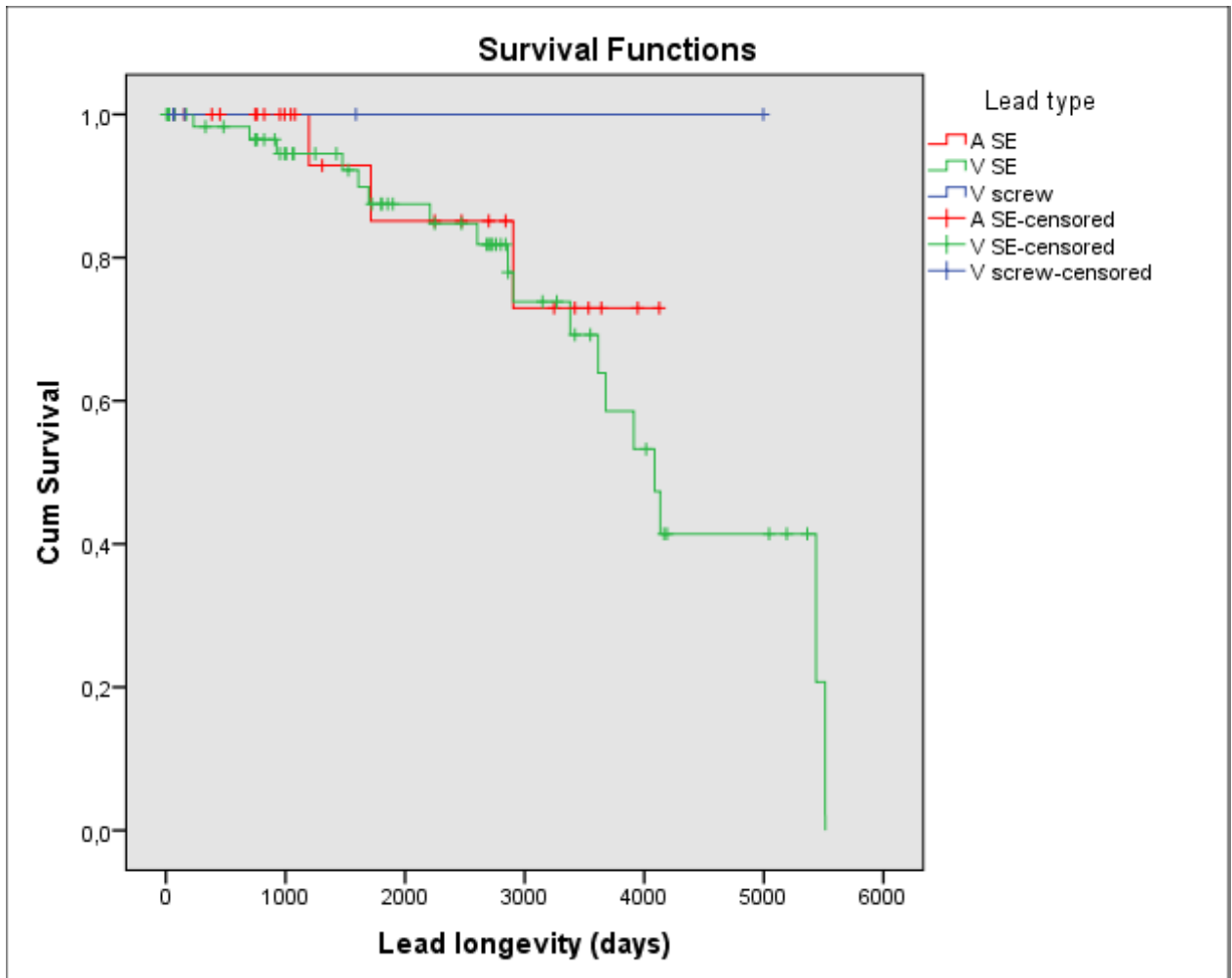
Figure 7: Kaplan-Meyer survival curve for epicardial pacemaker leads by lead position. Cumulative lead longevity does not differ between atrial sutured (A SE), ventricular sutured (V SE) or ventricular screwed lead (V screw) (p=0,527; Mantel-Cox).

4.3. Battery characteristics

In a period of 24 years, 108 batteries were implanted in the total study group. Among the patients, 25 children had only 1 battery, 22 children had 2 batteries, 9 children had 3 batteries and 3 children had 4 batteries implanted during follow-up.

Replacement was necessary for 53 batteries. Substitution took place due to battery failure for 37 batteries and 16 others were replaced electively or because an upgrade was required. Replacement for battery end of life occurred after a mean of 6,2 years (SD ± 2,4 years). Batteries which were not replaced had a mean follow-up period of 2,6 years (SD ± 2,2 years).
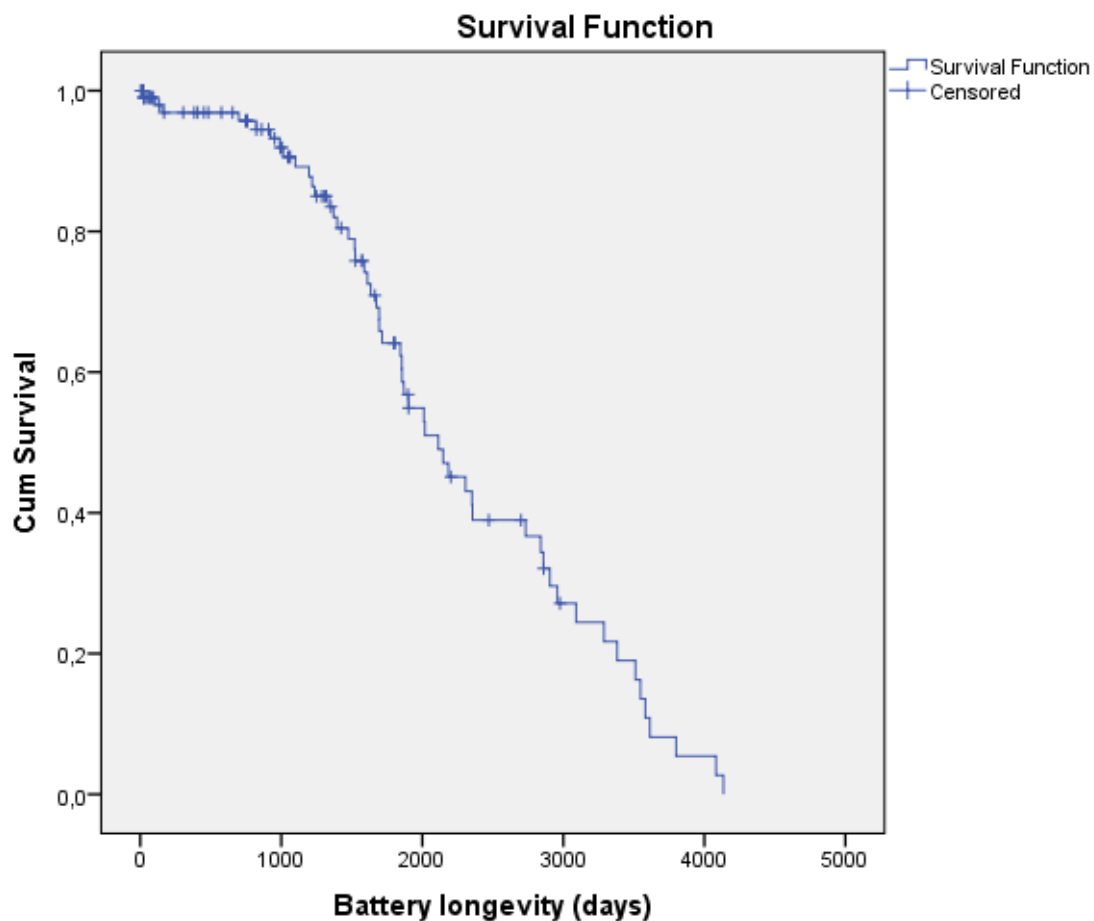

Figure 8: Kaplan-Meyer survival curve for pacemaker batteries. The estimated mean survival time amounts to 2289 days or 6,2 years (range: 2037-2540 days).
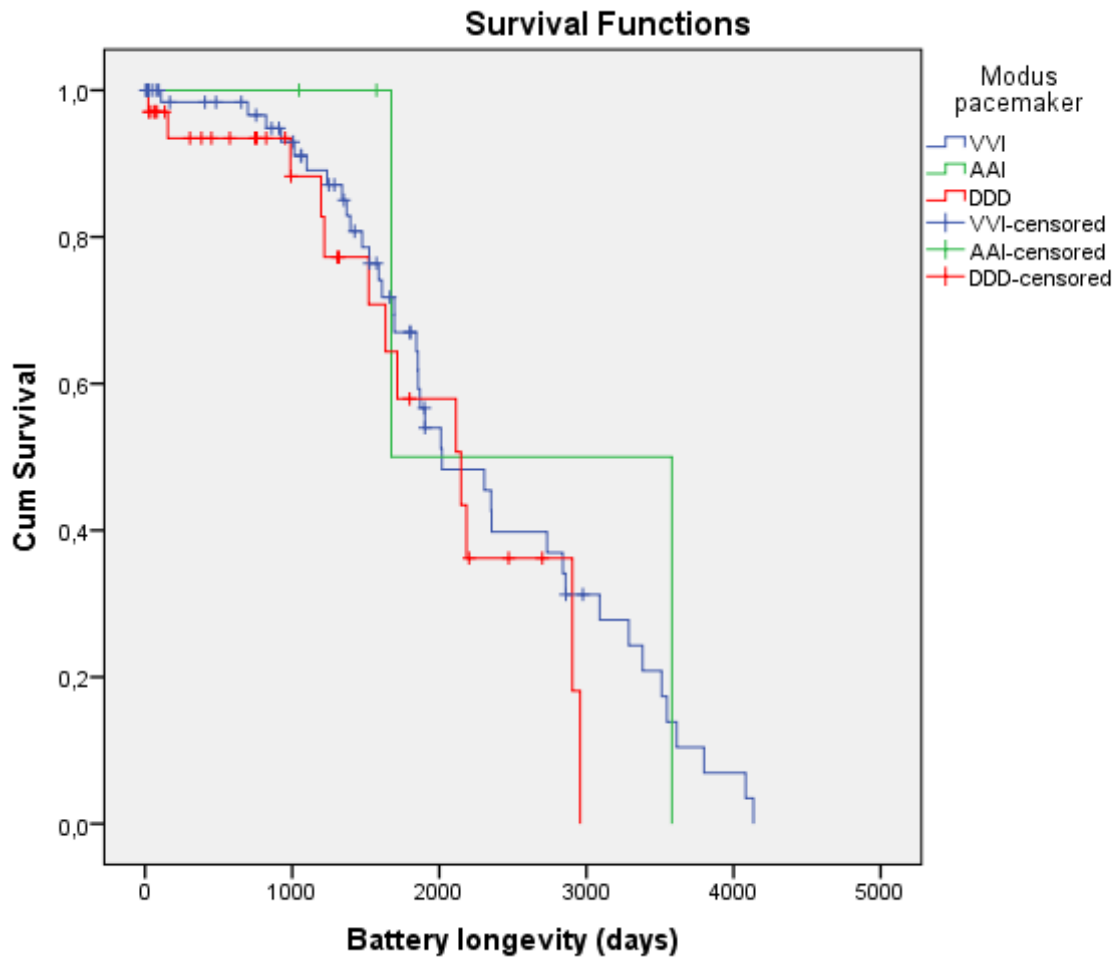
Figure 9: Kaplan-Meyer survival curve for pacemaker battery by modus. Cumulative battery longevity does not differ significantly between AAI, VVI or DDD modus (p=0,513; Mantel-Cox).

4.4. Positional evolution and growth

The mean increase in distance between the bottom edge of the heart and the upper edge of the pacemaker, measured on the chest X-rays taken at first pacemaker implantation and the chest X-rays taken at the last follow-up, is 35,8 mm (SD ±28,8 mm) (see figure 10).
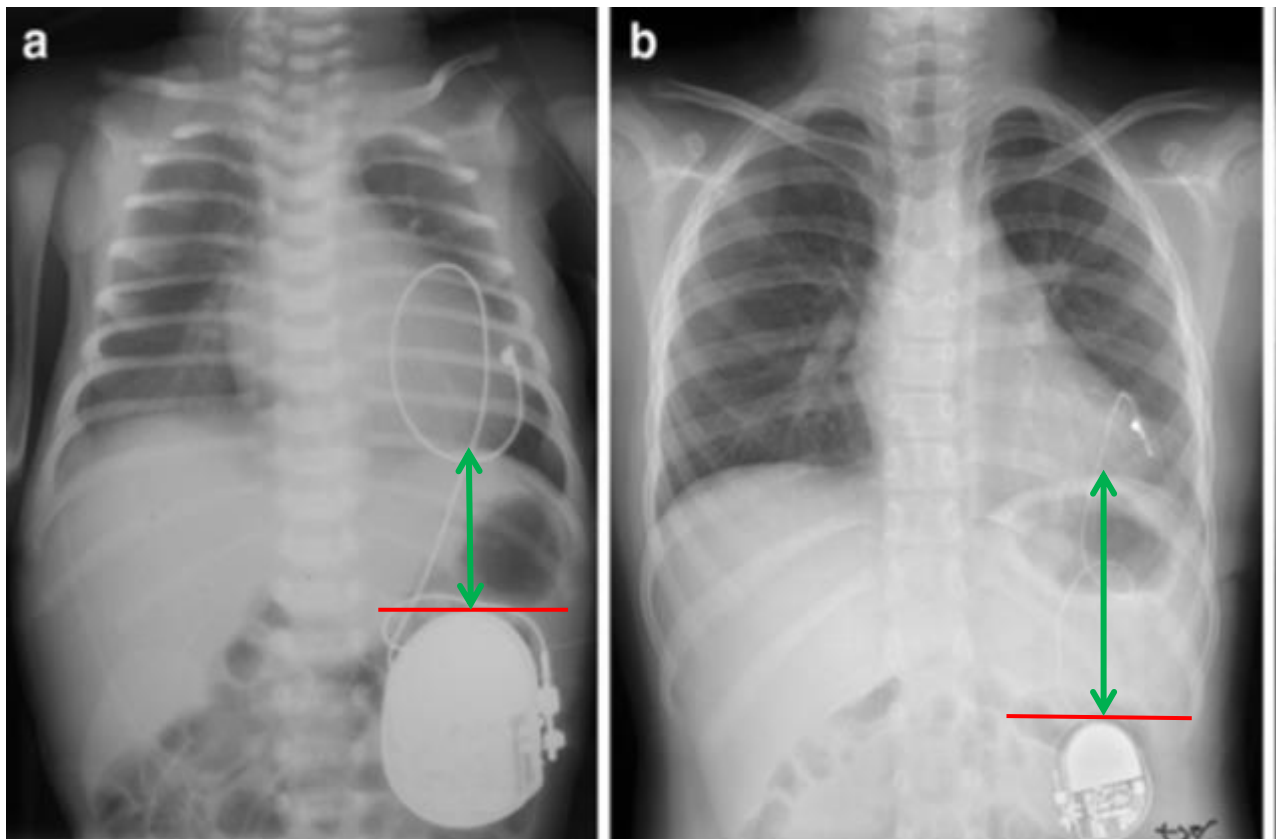
Figure 10. Measuring the perpendicular distance (green arrow) between pacemaker and heart.

In addition, the mean increase in patient height during this period is 40,8 cm (SD ± 28,5 cm). The correlation between increase in distance and patient height was significant (p= 0,003). In contrast, no significant correlation was found between lead failure and the increase in distance (p= 0,181). As stated above, the age of the patients at the first implantation was equally not correlated to the progression in distance between the 2 chest X-rays (p= 0,346).

Figure 11. Increase in patient height compared to the increase in distance between heart and pacemaker. Note the logaritmic correlation.

5. Discussion

An epicardial lead system remains the technique of choice for children and infants who are either too small or possess contraindications to standard tra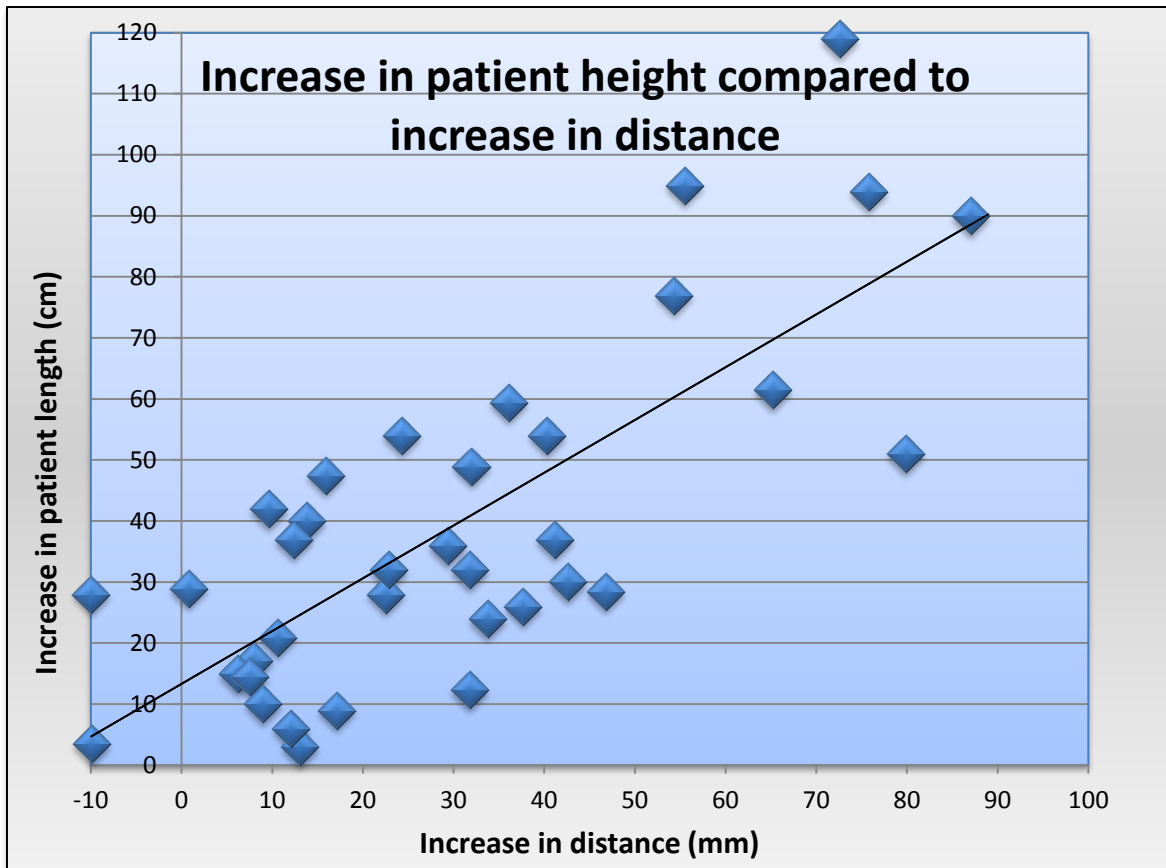nsvenous lead placement [2]. Permanent epicardial pacing is challenging, due to the difficult surgical procedure of implantation on one hand and the limited longevity of epicardial pacemakers compared to transvenous pacing systems on the other hand [41]. Moreover, epicardial leads can cause epicardial fibrosis which results in difficulties in implanting a new epicardial lead [35]. Although epicardial pacing systems have disadvantages, also many advantages may be found. Epicardial leads are applicable in every child, without need for anticoagulation [35]. The risk of thrombosis of the small venous system caused by the leads, is avoided. The implantation can be combined with a corrective or palliative operation and above all there are fewer problems with somatic growth of the child, compared to the transvenous pacing method [35].

Lead revisions due to growth of the children remains a considerable problem until puberty [39]. Increasing patient size could result in lead fracture, if the lead length is not sufficient. Some growth allowance can be provided by leaving a redundant loop of pacing lead [13]. The length of this loop, needed for growth from infancy to adult life, is not defined [40]. Few studies have been conducted to examine the needed lead length, especially concerning epicardial pacemakers in children.

This study aimed to investigate longevity of leads and generators of pacing systems in children. Furthermore, it provides an impulse for investigating the required epicardial lead length in children.

5.1. Lead characteristics

More lead changes could be expected in younger children compared to older children. Yet, in this study no correlation was found between age at implantation and number of leads. The occurrence of lead failure and type of lead failure was also not correlated to age at implantation. The same conclusion has been stated by Kwak et al.: patient age at the time of lead implantation did not significantly affect lead longevity [34]. Thus, it cannot be stated that younger children have more lead failures, in contrast to the study of Paech et al [43], where young age at implantation seemed to be a risk factor for lead dysfunction. This result may be due to the subxyphoid method for lead implantation and generator position in the posterior

rectus sheath, which go for most patients in this study. This technique provides additional protection for the pulse generators in young children who may be active, where a realistic risk of lead trauma and fracture exists [30].

In this study 98 leads were observed, of which 21 were replaced during follow-up. Serwer et al. stated that the average epicardial electrode lasts 7 years [38]. This was exactly what was found in our study. Replacement was necessary after a mean period of 7,4 years. In contrast, Kwak et al. found a mean longevity of leads of 10,8 years. However, when the group of 21 replacements in this study was segmented into leads replaced because of lead failure and leads replaced electively, it becomes clear that lead failure occurred later in follow up, that is after a mean of 8,9 years. Lead replacement was performed earlier when the leads were substituted electively. With the Kaplan-Meyer analysis the estimated mean of survival of all epicardial leads (charging also the leads that did not fail during follow up) amounts to 11,3 years.

The satisfactory follow-up outcome might have resulted from efforts to find a suitable area for lead implantation, extensive tissue dissection, or by using a different incision to approach areas not approached in prior cardiac operations [34]. In addition, the use of steroid-eluting epicardial leads also prevents threshold increase in the long term, reduces lead troubles and improves epicardial lead longevity. This has been shown in infants with excellent long-term outcome [13].

Evolution of threshold and impedance was administered during follow-up. The difference in threshold between implantation and follow-up was not significant, for both atrial and ventricular leads. Low pacing thresholds were also found in a 6-year follow-up study investigating 29 epicardial steroid-eluting leads in 22 patients ranging in age from 2 days to 18,5 years [30]. In contrast, for atrial as well as ventricular leads, the impedance of leads decreased significantly in our study. Small decreases in lead impedance may identify failing leads, yet serial measurement of pacing lead impedance over time is a more useful tool to monitor pacing lead performance [42].

5.2. Battery characteristics

The pacemaker generator is often exhausted earlier in younger patients because younger patients' pacemakers need to sustain a more rapid heart rate than pacemakers in older patients [34, 36]. Even though more battery changes could be expected in younger children compared

to older children, no correlation was found between age at implantation and number of batteries.

In a follow-up of 24 years, 108 batteries were implanted in all patients. Replacement was necessary for 53 batteries. Substitution took place due to battery failure for 37 batteries and 16 others were replaced electively or because an upgrade was required. Replacement for battery end of life occurred after a mean of 6,2 years. With the Kaplan-Meyer analysis the estimated mean survival of all batteries is 6,3 years. This exceeds the data found in literature, where the average longevity of a currently available pulse generator in children was only 5 years [38] or even less than 4 years in a study also containing non-steroid eluting leads [36].

Factors controlling current drain of the generator include pacing rate, per cent pacing, programmed voltage and high lead impedance. Several studies have reported extended battery life with high impedance leads [44]. Furthermore, pacemaker longevity can be prolonged by autocapture controlled devices which minimize pacing voltage. This may be even more important than maximizing lead impedance [44]. In this study, autocapture algorithms were performed on several leads. This can cause the better battery longevity results. As Shepard et al. [44] stated: "Much battery drain is not related to pacing at all, but from static current drain and housekeeping functions."

5.3. Positional evolution and growth

The mean increase in distance between the bottom edge of the heart and the upper edge of the pacemaker was significantly correlated to the mean increase in patient height during this period. This means that the increase in distance between generator and heart is proportionate to the increase in patient length. Stating that no excess of lead would be necessary to allow for growth, would be incorrect. There has to be enough lead to tolerate the anticipated growth of the child. Growth calculators can be useful in estimating the required excess of lead, to reach the battery lifetime of 6,2 years when reintervention is needed. In this study, this already seems successful.

In contrast, no significant correlation was found between lead failure and the increase in distance. The age of patients at the first implantation was equally not correlated to the progression in distance between subsequent chest X-rays. Further research should be

conducted on a larger group of patients getting a pacemaker early in life. This way the impact of growth can be understood.

5.4. Study limitations

This study had a limited amount of patients included. Consequently a limited number of leads and generators was observed. There is need for more research describing a large group of patients of the same age, who were prospectively followed. The mean follow-up in this study was only 7,4 years. A (life)- long follow-up should be performed to detect lead and battery failure and to notice a significant difference in the number of leads and batteries used in younger and older children.

Moreover, more lead characteristics and pacemaker settings should be kept constant to be able to deduct conclusions from the results. Due to the heterogeneous group of patients included in this study, this was not always easy.

The time of follow-up was also too short to see the full somatic growth in all patients. Thus, at the same time, a long prospective study with a large amount of patients is necessary to determine the exact length of lead loop that is needed to allow growth into adulthood, without necessitating a reintervention to adjust lead length. Gheissari et al. [40] have calculated this length for endovenous leads. The same should be done for the epicardial leads.

6. Conclusion

Based on the outcomes of this study, younger children had no need for more lead or generator replacements. Lead replacement for lead failure was necessary after a mean period of 8,9 years. Battery replacement was needed after a mean period of 6,2 years. During somatic growth of the children, the increase in distance between generator and heart is proportionate to the increase in patient length. Lead failure was not correlated to the increase in distance between heart and pacemaker. Life-long follow-up studies of children with epicardial pacing systems is mandatory to increase the current knowledge about late outcomes.

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8. Addenda

Addendum 1: Recommendations for Permanent Pacing in Children, Adolescents, and Patients With Congenital Heart Disease [31].

Class I

1. Permanent pacemaker implantation is indicated for advanced second- or third-degree AV block associated with symptomatic bradycardia, ventricular dysfunction, or low cardiac output. *(Level of Evidence: C)*

2. Permanent pacemaker implantation is indicated for SND with correlation of symptoms during age-inappropriate bradycardia. The definition of bradycardia varies with the patient's age and expected heart rate. *(Level of Evidence: B)*

3. Permanent pacemaker implantation is indicated for postoperative advanced second- or third-degree AV block that is not expected to resolve or that persists at least 7 days after cardiac surgery. *(Level of Evidence: B)*

4. Permanent pacemaker implantation is indicated for congenital third-degree AV block with a wide QRS escape rhythm, complex ventricular ectopy, or ventricular dysfunction. *(Level of Evidence: B)*

5. Permanent pacemaker implantation is indicated for congenital third-degree AV block in the infant with a ventricular rate less than 55 bpm or with congenital heart disease and a ventricular rate less than 70 bpm. *(Level of Evidence: C)*

Class IIa

1. Permanent pacemaker implantation is reasonable for patients with congenital heart disease and sinus bradycardia for the prevention of recurrent episodes of intra-atrial reentrant tachycardia; SND may be intrinsic or secondary to antiarrhythmic treatment. *(Level of Evidence: C)*

2. Permanent pacemaker implantation is reasonable for congenital third-degree AV block beyond the first year of life with an average heart rate less than 50 bpm, abrupt pauses in ventricular rate that are 2 or 3 times the basic cycle length, or associated with symptoms due to chronotropic incompetence. *(Level of Evidence: B)*

3. Permanent pacemaker implantation is reasonable for sinus bradycardia with complex congenital heart disease with a resting heart rate less than 40 bpm or pauses in ventricular rate longer than 3 seconds. *(Level of Evidence: C)*

4. Permanent pacemaker implantation is reasonable for patients with congenital heart disease and impaired hemodynamics due to sinus bradycardia or loss of AV synchrony. *(Level of Evidence: C)*

5. Permanent pacemaker implantation is reasonable for unexplained syncope in the patient with prior congenital heart surgery complicated by transient complete heart block with residual fascicular block after a careful evaluation to exclude other causes of syncope. *(Level of Evidence: B)*

Class IIb

1. Permanent pacemaker implantation may be considered for transient postoperative third-degree AV block that reverts to sinus rhythm with residual bifascicular block. *(Level of Evidence: C)*
2. Permanent pacemaker implantation may be considered for congenital third-degree AV block in asymptomatic children or adolescents with an acceptable rate, a narrow QRS complex, and normal ventricular function. *(Level of Evidence: B)*
3. Permanent pacemaker implantation may be considered for asymptomatic sinus bradycardia after biventricular repair of congenital heart disease with a resting heart rate less than 40 bpm or pauses in ventricular rate longer than 3 seconds. *(Level of Evidence: C)*

Class III

1. Permanent pacemaker implantation is not indicated for transient postoperative AV block with return of normal AV conduction in the otherwise asymptomatic patient. *(Level of Evidence: B)*
2. Permanent pacemaker implantation is not indicated for asymptomatic bifascicular block with or without first-degree AV block after surgery for congenital heart disease in the absence of prior transient complete AV block. *(Level of Evidence: C)*
3. Permanent pacemaker implantation is not indicated for asymptomatic type I second-degree AV block. *(Level of Evidence: C)*
4. Permanent pacemaker implantation is not indicated for asymptomatic sinus bradycardia with the longest relative risk interval less than 3 seconds and a minimum heart rate more than 40 bpm.*(Level of Evidence: C)*

Addendum 2: Approval Ethical Committee Ghent University Hospital.

UZ Universitair Ziekenhuis Gent

UNIVERSITEIT GENT

Afz: Commissie voor Medische Ethiek

IZ Cardiochirurgie
Kliniekgebouw 12-E - 5de Verdieping
Dr. Katrien FRANCOIS
ALHIER

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UW KENMERK	ONS KENMERK	DATUM	KOPIE
	2013/697	12-sep-13	Zie "CC"

BETREFT

Advies voor monocentrische studie met als titel:

Epicardiale pacing in een opgroeiende pediatrische populatie : performantie en positionele evolutie van pacemakersystemen

Belgisch Registratienummer: B670201318348

Fase (Phase): NVT/NA

* Adviesaanvraagformulier dd. 9/09/2013
   (document B volledig ontvangen dd. 10/9/13)

Advies werd gevraagd door:
   Dr. K. FRANCOIS ; Hoofdonderzoeker

BOVENVERMELDE DOCUMENTEN WERDEN DOOR HET ETHISCH COMITÉ BEOORDEELD.
ER WERD EEN POSITIEF ADVIES GEGEVEN OVER DIT PROTOCOL OP 12/09/2013. INDIEN DE STUDIE NIET WORDT OPGESTART VOOR 12/09/2014, VERVALT HET ADVIES EN MOET HET PROJECT TERUG INGEDIEND WORDEN.

THE ABOVE MENTIONED DOCUMENTS HAVE BEEN REVIEWED BY THE ETHICS COMMITTEE.
A POSITIVE ADVICE WAS GIVEN FOR THIS PROTOCOL ON 12/09/2013. IN CASE THIS STUDY IS NOT STARTED BY 12/09/2014, THIS ADVICE WILL BE NO LONGER VALID AND THE PROJECT MUST BE RESUBMITTED.

DIT ADVIES WORDT OPGENOMEN IN HET VERSLAG VAN DE VERGADERING VAN HET ETHISCH COMITE VAN 17/09/2013
THIS ADVICE WILL APPEAR IN THE PROCEEDINGS OF THE MEETING OF THE ETHICS COMMITTEE OF 17/09/2013

- *Het Ethisch Comité werkt volgens 'ICH Good Clinical Practice' - regels*
- *Het Ethisch Comité beklemtoont dat een gunstig advies niet betekent dat het Comité de verantwoordelijkheid voor het onderzoek op zich neemt. Bovendien dient U er over te waken dat Uw mening als betrokken onderzoeker wordt weergegeven in publicaties, rapporten voor de overheid enz., die het resultaat zijn van dit onderzoek.*
- *In het kader van 'Good Clinical Practice' moet de mogelijkheid bestaan dat het farmaceutisch bedrijf en de autoriteiten inzage krijgen van de originele data. In dit verband dienen de onderzoekers erover te waken dat dit gebeurt zonder schending van de privacy van de proefpersonen.*
- *Het Ethisch Comité benadrukt dat het de promotor is die garant dient te staan voor de conformiteit van de anderstalige informatie- en toestemmingsformulieren met de nederlandstalige documenten.*
- *Geen enkele onderzoeker betrokken bij deze studie is lid van het Ethisch Comité.*
- *Alle leden van het Ethisch Comité hebben dit project beoordeeld. (De ledenlijst is bijgevoegd)*

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Addendum 4. Summary in Dutch.

Inleiding

De toekomstige lichaamsgroei en lichaamslengte van zuigelingen en jonge kinderen vormt een probleem bij de therapie voor hartritmestoornissen. Defecten van zowel pacemakerdraad als batterij komen meer voor bij kinderen dan bij volwassenen. Niet enkel de hogere hartslag, maar ook het uitrekken en de compressie van de pacemakerdraden door groei, dragen bij tot een grotere vatbaarheid voor gebreken bij epicardiale pacemakersystemen. De positie van de pacemaker alsook de lengte van de pacemakerdraden moet dus tijdens de implantatie aangepast worden aan de verwachtte groei van deze patiënten.

Er werd reeds onderzoek uitgevoerd waarbij de nodige overmaat aan pacemakerdraad in de atria bij endoveneuze pacemakers is berekend. Dit in tegenstelling tot epicardiale pacemakers, waarbij er tot nu toe nog geen onderzoek is gebeurd om de nodige overmaat aan draadlengte te evalueren. De nodige draadlengte wordt hier immers bepaald door de veranderende afstand tussen de abdominale pacemaker en de onderboord van het hart.

Deze studie tracht de ontwikkeling van de ruimte tussen hart en epicardiale pacemaker te beschrijven. De resultaten van deze analyse hebben mogelijks een grote impact op de benodigde surplus aan pacemakerdraden tijdens de implantatie van de pacemaker.

Methoden

Er werden 59 zuigelingen en kinderen onderzocht die een permanent epicaridaal pacemakersysteem kregen en gevolgd werden in het universitair ziekenhuis van Gent tussen 1991 en 2015. Patiëntendossiers en gegevens uit elektronische databases werden bestudeerd. Hieruit werd data verzameld.

In het eerste deel van deze studie werden descriptieve en vergelijkende statistische analyses uitgevoerd op de vergaarde data. In het tweede deel werd de evolutie van de afstand tussen hart en pacemaker doorgelicht door vergelijking van posteroanterieure thoracale röntgenopnames die net na de implantatie en tijdens de laatste follow-up genomen werden.

Resultaten

De onderzochte patiënten werden gevolgd over een gemiddelde tijdsduur van 7,4 jaar (SD ± 5,3 jaar). Er werd geen correlatie gevonden tussen leeftijd ten tijde van de eerste implantatie en pacemaker modus (p=0,431), aantal pacemakerdraden (p=0,422), aantal batterijen (p=0,422), draadfalen (p=0,431) en de aard van het defect aan de draden (p=0,422). De leeftijd van de patiënt tijdens de eerste implantatie was eveneens niet gecorreleerd aan de ruimtelijke progressie tussen hart en pacemaker, te zien op de RX-foto's genomen tijdens de implantatie en tijdens de laatste follow-up (p=0,346).

Vervanging van 21 pacemakerdraden was nodig na een gemiddelde periode van 7,4 jaar (SD ± 4,1 jaar). Complicaties aan de draden traden op na een gemiddelde duur van 8,9 jaar; electieve vervangingen gebeurden na een gemiddelde termijn van 4,5 jaar. De pacemakerdraden die niet vervangen werden, hadden een gemiddelde follow-up periode van 5,0 jaar (SD ± 4,1 jaar). Bovendien waren er ook 53 batterijen aan vernieuwing toe na een gemiddelde periode van 6,2 jaar (SD ± 2,4 jaar). Batterijen die niet vervangen werden, hadden een gemiddelde follow-up tijd van 2,6 jaar (SD ±2,2 jaar).

De gemiddelde toegenomen afstand tussen de onderste rand van het hart en de bovenste rand van de pacemaker, gevonden op de RX-foto's van de thorax genomen tijdens de eerste implantatie en de RX-foto's genomen tijdens de laatste controle, is 35,8 cm (SD ± 28,8cm). Daarnaast is de gemiddelde toename van de lichaamslengte gedurende deze periode 40,8cm (SD ± 28,5cm). De correlatie tussen pacemaker-hart afstand en lichaamslengte was significant (p=0,003). De toename in pacemaker-hart afstand was echter niet gecorreleerd aan pacemakerdraadverwikkelingen (p=0,181).

Conclusie

In deze patiëntenpopulatie van 59 kinderen was epicardiale pacemaker therapie geassocieerd aan aanvaardbare resultaten op lange termijn. Tijdens de lichaamsgroei van de patiënten was de uitdijing van de afstand tussen pacemaker en hart in proportie met de toename van de lichaamslengte. Een levenslange follow-up studie betreffende kinderen met epicardiale pacemaker systemen is noodzakelijk om de huidige kennis te vergroten.