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Development of arrhythmia after Fontan Operation – Lateral tunnel vs extracardiac conduit

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1 Introduction

The heart is the center and the driving force of the circulation of human blood. In a healthy body, it supplies all organs with blood by contracting in a regular rhythm. The human heart is divided into two parts. The left side, providing the oxygenated blood to the body, and the right side, pumping the venous body blood to the lungs for oxygenation. The systemic circulation driven by the left heart and the pulmonary circulation by the right heart, are normally connected in series. Thus, both circulations have their own muscular pump to push the blood through the vessels. Many malformations result in just one single proper working ventricle that supplies both circulations with a mixture of arterial and venous blood. In these cases, one ventricle has to work for both sides, providing the blood for both circulations, which are now placed in parallel. This leads to an overloading of the single ventricle. If no obstruction is present in the outflow tracts to the two circulations, and because of the low pulmonary vascular resistance, this leads to an increasing blood flow through the lungs, which causes symptoms of heart failure and later on of pulmonary hypertension. In patients with pulmonary outflow obstruction, the main problem is cyanosis, which results from the pulmonary blood flow being low and from the mixture of arterial and venous blood having low oxygen saturation. In patients with single ventricle and obstruction in the systemic outflow tract, the dominant symptoms are associated with low cardiac output in the systemic circulation and is manifest usually very early in life.

In order to protect patients from these damages, researchers have attempted to separate the two circulations and to place them back in series.

1.1 History

1.1.1 Development of the “Fontan-circulation” idea

In the beginning of the 1950s, the idea of a cavo-pulmonary shunt arose when researchers tried to find a means of creating a proper functioning circulation without the presence of the right ventricle. The aim was to bypass the right ventricle by taking advantage of the natural changes of the intrathoracic pressure with respiration. Although Glenn and Patino gave their names to the cavo-pulmonary bypass operation, “William Glenn was not the first to introduce the concept of cavo-pulmonary anastomosis. He reported neither the first experimental study, nor the first clinically successful operation” [1]. Carlo A. Carlon and colleagues first described their experimental study of cavo-pulmonary shunt in dogs in 1950 [2]. The initial attempts were carried out in animal experiments and later on in humans. The strategy was to connect the proximal end of the divided azygos vein to the right pulmonary artery end to end and to make a preatrial ligation of the superior caval vein. Carlon's group soon realized that this passive mechanism was totally sufficient to carry deoxygenated blood through the lungs. Nevertheless, more than ten years passed before Carlon reported their first clinical experiences in 1964. Unfortunately, his first clinical reports appeared in journals rarely read by surgeons in those days, and so Carlo Carlon was quickly forgotten [1, 3].

Several other surgeons tried to connect systemic venous vessels directly to the pulmonary arteries and to bypass the right ventricle, but without knowing about each other's work. In the early 1950s, many experimental studies of the vena cava-to-

pulmonary artery anastomoses took place in various countries. In the USA, in 1954, William Glenn and Jose Patino reported their study on dogs who had undergone a superior vena cava-to-right pulmonary artery shunt by using the azygos vein in a similar technique to that of Carlon and colleagues [4]. In the same year, Francis Robicsek et al. reported their first experimental results of a direct vena cava-to-pulmonary artery shunt in Budapest [5]. Harris B. Shumacker also performed experimental direct cavo-pulmonary shunts in the USA [6]. In Russia, Nikolai K. Galankin and Tigran M. Darbinian first brought up the idea of a direct cavo-pulmonary anastomosis [7]. Shumacker performed the first clinical attempts in 1954 [6]. Even though unsuccessful, this was the courageous first step. Some years later, Evgenii N. Meshalkin reported the first clinical success of a direct cavo-pulmonary anastomosis (superior caval vein to right pulmonary artery "end-to-end") [8]. In 1958, this achievement was followed by Glenn [9] and later on by Rasmusen [10] and Robicsek [11].

The person who actually deserves to be called the first surgeon who successfully undertook an anastomosis of the superior caval vein to the pulmonary artery is difficult to determine. Even if retrospectively William Glenn was not the very first, it was this “extensive study undertaken by the Yale University Group and Glenn’s publications in the most-read surgical journals that finally convinced the world” [1]. Subsequently, several surgeons tried to connect the inferior caval blood flow in addition to the superior caval blood flow to the pulmonary circulation. In 1954, John Rose et al. anastomosed both caval veins at the same time to the main pulmonary artery [12], as did Jose Patino et al. in the same year. However, all these attempts were abortive. The researchers concluded that an inferior caval to pulmonary artery

anastomosis unavoidably leads to venous congestion in the splanchic system and consequently to death [13]. This assumption was only disproved after some time had passed and once the surgeons had understood that it was a problem with the adaptation of the circulation and the single ventricle.
In 1960, Francis Robicsek et al. preformed a series of experiments in which they totally bypassed the right heart with success [14-16]. However, the inferior caval blood was not directed to the lung but to the left atrium, and no real clinical application was suitable for this operation. Nevertheless, retrospectively, this experience was hugely valuable to Francis Fontan and the idea that he had had with regard to this problem.

1.1.2 The original Fontan operation

The first time that a so-called “Fontan operation” was performed was in 1968; this was described in 1971 by Francis Fontan and Eugene Baudet [17].
Their surgical method included a classic Glenn anastomosis (superior caval vein to the right pulmonary artery "end-to-end") followed by an anastomosis of the right atrial appendage to the proximal left pulmonary artery and closure of any interatrial communication. In addition, valved homografts were placed in the entry of the inferior vena cava to the right atrium and at the connection of the right atrial appendage to the left pulmonary artery (Figure 1).

Initially, the Fontan operation (FO) was meant to cure only patients with tricuspid atresia. However, later on, it was used as a surgical repair for nearly all forms of single ventricle.

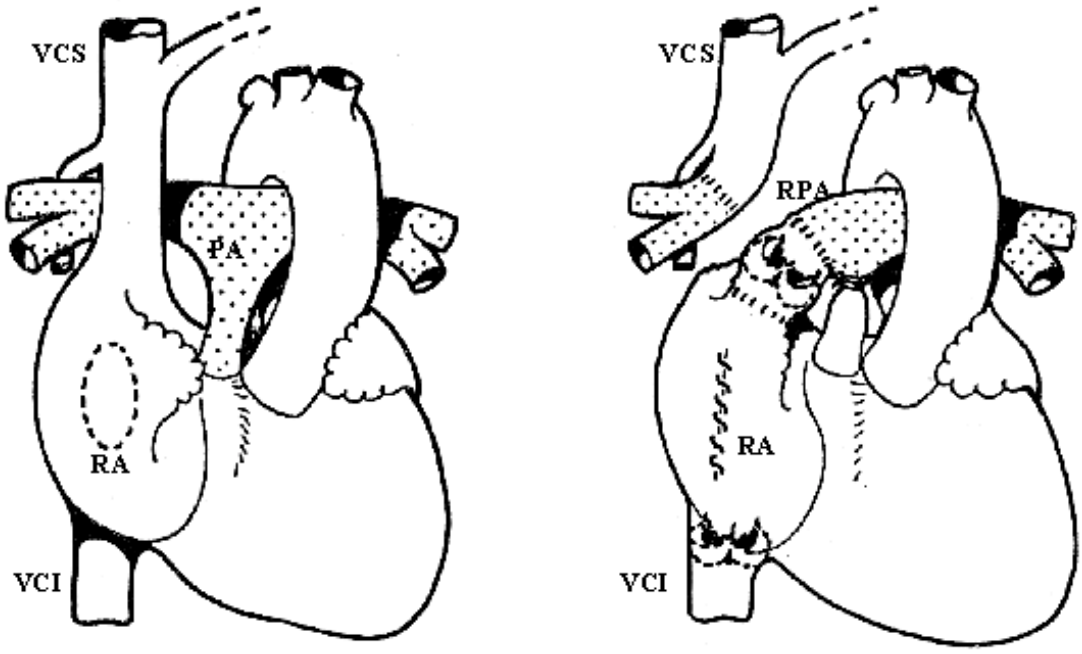

Figure 1: Atriopulmonary connection described by Francis Fontan and Eugene Baudet: connection of the right atrial appendage to the left pulmonary artery after a classic Glenn's anastomosis (superior caval vein to right pulmonary artery "end-to-end"). [17] (PA – pulmonary artery, RA – right atrium, RPA – right pulmonary artery, VCI – vena cava inferior, VCS – vena cava superior).

In 1973, Guillermo Kreutzer et al. published a simplified operation technique, which was undertaken for the first time in 1970. Kreutzer connected the right atrium to the pulmonary artery by using an autologous pulmonary valve as a conduit. Neither a Glenn's anastomosis with a transection of the right pulmonary artery, nor an interposition of a valve in the VCI was required in this operation [18] (Figure 2).

Other modifications followed. V.O. Björk et al. described a direct anastomosis of the right atrium to the right ventricular outflow tract in 1979 [19], whereas R.F. Lins et al. performed a direct atriopulmonary anastomosis [20].

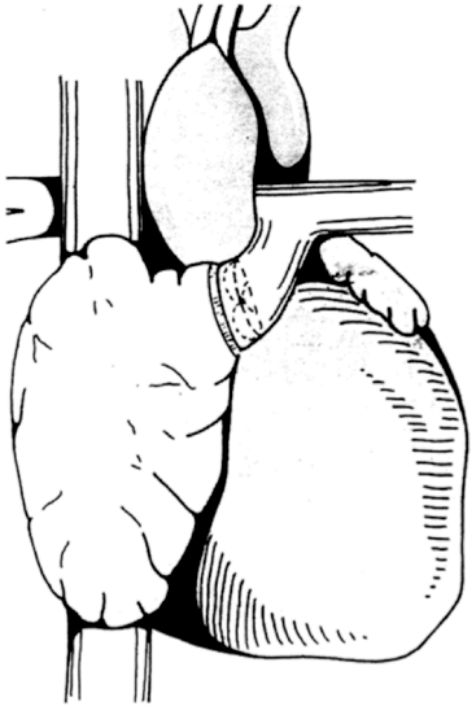

Figure 2: Atriopulmonary connection described by Guillermo Kreutzer: the pulmonary valve as an autologous connection between the right atrium and the pulmonary artery [18].

1.1.3 Modifications of the Fontan operation

1.1.3.1 Total cavopulmonary connections – TCPC

The earliest types of FO, the so-called atriopulmonary connections (APC), involved the use of the right atrium and its pumping function as the driving force for the pulmonary circulation. However, the question was soon raised as to whether the atrial pumping function is really effective for this circuit, and the idea of a total cavopulmonary connection emerged. The exclusion of the right atrium was expected to have a beneficial effect on the outcome after the Fontan procedure, especially with regard to the incidence of atrial arrhythmias. Various authors who compared the original APC to the TCPC provided evidence for this assumption [21].

1.1.3.1.1 Lateral tunnel - LT

In 1987, Mark R. de Leval carried out the first total cavopulmonary connection (TCPC) [22]. Following the Glenn anastomosis, a TCPC was performed by connecting the inferior vena cava to the pulmonary artery by a tunnel in the lateral part of the right atrium.

The benefit of this operation technique is that most of the right atrial chamber remains a low pressure system and is not distended thereby reducing the risk of early or late arrhythmias. Moreover, the turbulent flow in the atrium is minimized, which reduces energy losses and the risk of atrial thrombosis.

1.1.3.1.2 Extracardiac conduit – EC

Even though superior to the original APC, the LT Fontan repair still has potential risk factors influencing the outcome. Aortic cross-clamping and cardioplegic cardiac arrest are still required. Atriotomy with long sutures lines remains necessary and causes extensive scar tissue with proarrhythmogenic potential. Therefore, a new method of total cavopulmonary anastomosis was suggested. The first attempts remained without success, but in 1990, Carlo Marcelletti et al. reported their first effective EC FO [23]. This modification of the Fontan procedure is today the method of choice in most of centers.

Following the bidirectional Glenn anastomosis, the vena cava inferior is connected to the confluent pulmonary artery system by an EC, usually made of polytetrafluorethylen (PTFE, Gore-Tex). Because of the reduced manipulation and shorter atrial suture lines, this method is assumed to cause fewer sinus node dysfunctions and atrial tachyarrhythmias. By keeping a constant low pressure to the right atrium, no dilation occurs, which also minimizes the risk for arrhythmia.

1.1.3.2 Fenestration

In both palliation types, a so-called fenestration can be created. Nancy Bridges advocated this modification of the Fontan procedure; it involves a connection between the pulmonary and systemic circulations [24]. If the resistance of the pulmonary circulation is elevated or the compliance of the single ventricle is reduced, a small amount of venous blood can directly leak into the systemic

circulation thereby increasing the cardiac output at the expense of mild systemic desaturation [25, 26].

To create a fenestration, a 3- to 4-mm large hole is cut out of the LT or an anastomosis between the EC and the atrium is built.

In high-risk patients, this technique effectively increases the rate of survival. Because of the risk of a paradoxical embolism after the adaptation phase, the fenestration can be closed, operatively or interventionally, during cardiac catheterization.

1.2 Selection criteria and indications for Fontan operation

1.2.1 Selection criteria

The initial criteria for patients with tricuspid atresia being selected for FO were set by Choussat and his colleagues in 1977 and were extremely strict.

The original selection criteria were as follows:

1. Minimum age of 4 years
2. Sinus rhythm
3. Normal caval drainage
4. Right atrium of normal volume
5. Mean pulmonary artery pressure ≤ 15 mmHg
6. Pulmonary arterial resistance < 4U/m^2
7. Pulmonary artery to aorta diameter ratio ≥ 0.75

8. Normal ventricular function (ejection fraction > 0.6)
9. Competent atrioventricular valve
10. Absence of pulmonary artery distortion

During the course of the constant modification of the operation technique over the last few decades, the selection criteria have also been refined. The question of age is more open, preoperative sinus rhythm is not imperative, and caval drainage and the volume of the right atrium are disregarded.

However, even if more open today, certain guidelines remain. Cardiac requirements include unobstructed ventricular inflow without significant regurgitation, an adequate single ventricular function, and unobstructed outflow to the systemic circulation (no subaortic stenosis, no arterial hypertension, no aortic coarctation). These aspects are important as ventricular dysfunction and insufficiency of the atrioventricular valve may increase pulmonary pressure and impair prognosis. The conditions of the pulmonary part itself are: a non-restrictive connection between the superior caval vein and pulmonary arteries, good sized pulmonary arteries without distortion, a well developed pulmonary vascular bed, normal pulmonary vascular resistance, and unobstructed pulmonary venous return [27]. Nowadays, many of the cardiac requirements can be achieved by additional surgical or cardiological interventions.

A regular rhythm is also extremely important for a functioning Fontan circulation. Continuous blood flow driven by a regularly contracting muscle is necessary to keep a stable hemodynamic in the circulation.

1.2.2 Indications

The first FO were performed to cure patients with tricuspid atresia. Not only has the original operation been modified, but also the indications have greatly changed. Today, Fontan reconstruction is applied in all forms of functional single ventricle malformation and in complex congenital malformations for which no biventricular correction is possible.

1.2.3 Single ventricle anatomy

Single ventricle malformation is caused by the deficient embryological development of the one of the ventricles. The looping of the primitive cardiac tube is followed by septation of the primitive ventricle and the formation of a common AV canal from endocardial cushion tissue. The poor alignment of this common AV valve with the ventricles may be one of the main reasons for single ventricle anatomy. Another source for functional single ventricle is an incomplete septation of the ventricular chambers and primary pulmonary or aortic valve disease.
Depending on the morphological aspects of the dominant ventricle, two main forms of single ventricle are distinguished: single right ventricle and single left ventricle.

1.2.4 Subtypes of single ventricle

1.2.4.1 SV of the left ventricular morphology

1.2.4.1.1 Hypoplastic right heart syndrome (HRHS)

The structures of the right heart, including the right ventricle, tricuspid valve, pulmonary valve, and pulmonary artery, are hypoplastic or even undeveloped. As a result, the neonate suffers from severe cyanosis because of inadequate pulmonary blood flow. Sometimes, perfusion of the coronary arteries, because of coronary fistulas is also a problem and causes ischemic damage of the heart muscle. In the form with pulmonary atresia, the pulmonary circulation is totally dependent on a ductus arteriosus Botalli or major aortopulmonary collateral arteries (MAPCAs).

1.2.4.1.2 Tricuspid atresia

This involves complete failure of the development of the tricuspid valve. Instead of the valve, an impermeable membrane or muscular tissue closes the inflow to the right ventricle. In most of the cases, a ventricular septal defect (VSD) exists. An atrial septal defect or patent foramen ovale is present, which guides the caval blood from the right atrium to the left one, where venous and arterial blood is mixed. Therefore, patients suffer from cyanosis. In addition, a pulmonary stenosis or even atresia might exist, which limits the pulmonary flow. If not, the high pumping pressure of the left ventricle may cause pulmonary hypertension.

1.2.4.1.3 Double inlet left ventricle (DILV)

Both atria communicate with the single left ventricle by two atrioventricular valves. If no additional pulmonary stenosis is present, an enormous left-to-right shunt leads to a quick development of pulmonary hypertension. The double inlet type of single ventricle is more frequent associated with left ventricle morphology.

1.2.4.1.4 Double outlet left ventricle (DOLV)

DOLV is a very rare cardiac malformation in which both the aorta and the pulmonary artery arise, either exclusively or predominantly, from the left ventricle.

1.2.4.2 SV of the right ventricular morphology

1.2.4.2.1 Hypoplastic left heart syndrome (HLHS)

This malformation is characterized by a hypoplastic or even absent left ventricle and stenosis or atresia of the aortic valve and of the mitral valve. The aorta ascendens and aortic arch is usually also hypoplastic. This leads to severe pulmonary overcirculation and inadequate systemic perfusion. The systemic circulation is totally dependent on a ductus arteriosus Botalli.

1.2.4.2.2 Double outlet right ventricle (DORV)

The pulmonary artery and the aorta arise entirely or predominantly from the right ventricle. The VSD is almost always present and is the only exit from the left ventricle. The double outlet right ventricle with a hypoplastic left ventricle or with a ventricular septal defect that is remote from the great arteries is not suitable for

biventricular repair and is one of the common forms of the functionally single ventricle.

1.3 Arrhythmia as one of the complications after Fontan operation

Even though nowadays, the early and late survival rates are as high as 95-97% [28], many early-, mid-, and long-term problems occur in patients with Fontan circulation. One of the most important problems is arrhythmia with the possible risk of low cardiac output, stroke, or pulmonary embolism, ultimately leading to “failing Fontan”. Arrhythmias can occur during or directly after the operation, but also a long time after the surgical intervention. A proper rhythm of the heart is necessary for a hemodynamically efficient circulation.

Generally, in patients with congenital heart defects (CHD), rhythm irregularity increases morbidity [29] and mortality [30]. Long-lasting volume overload and high atrial pressure are the common reasons for the development of abnormal heart rhythm in this group of patients [17, 31, 32]. In addition to the surgical suture lines, the anatomic conduction barriers may generate arrhythmias [33]. However, the myocardium itself in patients with congenital heart defects may also be a substrate of rhythm problems [34].

1.3.1 Risk factors for arrhythmias after Fontan operation

Surgical manipulations in the atrial myocardium are one of the main reasons for the development of arrhythmias. The substrate for arrhythmia can be the scar tissue in

the suture lines of a cavopulmonary anastomosis or a LT. The anatomic conduction barriers, i.e., the orifices of the inferior and superior vena cavae, the ostium of the coronary sinus, and the atrial septal defect, can also slow atrial conduction, possibly resulting in re-entry phenomena. The next risk factor is abnormal hemodynamics, which leads to dilation with fibrosis of the right atrium and may cause sinus node dysfunction. All these factors cause irregular atrial rhythm and are triggers for the onset of tachycardia [35].

Electron-microscopic analysis has revealed that, in patients with tricuspid atresia, a congenitally abnormal atrial fiber array exists [34] that may cause tachycardia by slowing conduction. Almost 40% of patients with tricuspid atresia who have never undergone any surgery develop tachycardia by the forth decade of life [36, 37].

By totally bypassing the heart and thus reducing the length of the atrial suture lines, the EC FO is theoretically considered to be superior to the other forms of Fontan completion with regard to the development of arrhythmias.

Other factors increasing the risk for the development of rhythm disturbances are an “older age at the time of initial repair, early postoperative arrhythmias, sinus node dysfunction, and double-inlet left ventricle” [21, 35, 38-40].

1.3.2 Forms of arrhythmia

Arrhythmia includes all forms of heart rhythm that are abnormal in terms of frequency, regularity, and impulse generation. Whereas the normal impulse generator is the sinus node, adequate frequency is age-dependent.

The most common way to define the different forms of arrhythmia is by frequency: bradycardia and tachycardia.

1.3.2.1 Tachycardia

Tachycardia refers to an abnormally fast resting heart rate and can be subdivided in supraventricular (SVT) and ventricular (VT) tachycardia.

1.3.2.1.1 Supraventricular tachycardia (SVT)

In SVT, the trigger originates from a point above the bundle of His and leads to a rhythm higher than the age norm. An SVT of duration longer than 30s is called sustained SVT, whereas an SVT lasting less than 30s is a non-sustained SVT.

The ECG shows a narrow QRS complex. Various forms of SVT have been observed.

Generally the most frequent SVT is a sinus nodal tachycardia, which is usually physiological. A higher than age norm heart frequency with a normal sinus rhythm, caused by an appropriate stimulus is termed physiological.

The sinoatrial node re-entrant tachycardia (SANTR) is caused by a re-entrant pathway localized within the sinoatrial (SA) node and perinodal tissue resulting in normal P-waves followed by an also normally configured QRS complex and is therefore difficult to distinguish from a sinus nodal tachycardia. Only the abrupt onset and termination of the arrhythmia aids clinically in differentiating these two types.

Another form of supraventricular tachycardia is an atrial ectopic tachycardia (AET) in which a single focus generates an abnormal P-wave followed by a regular narrow QRS complex, but the PR interval may be inappropriately long relative to the atrial rate. AET occurs because of an area of enhanced automaticity in the atrium, has a variable rate, and is influenced by the autonomic nervous system.

In multifocal atrial tachycardia, at least 3 different foci in the atria are involved that cause 3 different configured P-waves followed by irregular narrow QRS complexes.
Special forms of atrial tachycardia are atrial fibrillation (AF) caused by multiple simultaneous atrial re-entry loops (with rapid ventricular response, fibrillatory P-waves that sometimes lead to a ventricular response with irregular narrow QRS complexes) and atrial flutter (AFL) (with rapid ventricular response, caused by an intra-atrial re-entry with atrial beats around 300bpm, which are conducted to the ventricle 4:1 – 2:1, rarely 1:1).
Junctional ectopic tachycardia (JET) is caused by increased atrioventricular (AV) node automaticity leading to abnormal configured P-waves, which occur anywhere without relation to the regular narrow QRS complexes. Special forms of JET are the atrioventricular nodal re-entrant tachycardia (AVNRT) and atrioventricular reciprocating tachycardia (AVRT).
AVNRT is generated by a re-entry circuit within or just next to the AV node and often consists of two small pathways, one faster than the other. With the AV node directly between the atrium and the ventricle, it often stimulates in both directions and leads to a retrogradely conducted P-wave buried under or just occurring behind the regular narrow QRS complex.

Atrioventricular reciprocating tachycardia results from a re-entry circuit and is larger than in AVNRT. AVRT is caused by an accessory pathway in the conduction system between the atria and ventricles (often a muscular structure). A common syndrome caused by an accessory pathway (bundle of Kent) crossing the AV valvular ring is the Wolff-Parkinson-White syndrome. The re-entry mechanism might be orthodromic (the AV node conducts down to the ventricle, and the accessory pathway leads to a retrogradly conducted P-wave just after the regular narrow QRS complex) or antidromic (the accessory pathway conducts down to the ventricle and the impulse re-enters the atrium via the AV node). Because initially not passing the bundle of His on the way to the ventricle, the QRS complex is often wider than usual, with a delta wave).

In patients with SVT, the pulse is sometimes very fast, and as a hemodynamic result, patients might suffer from dizziness, syncope, dyspnea, angina pectoris, or even a cardiac shock. However, most of the time, SVT is self-limiting and patients do not even realize it. When present for a longer period, SVT might cause cardiomyopathy and therefore needs to be treated. Adenosine can acutely stop the tachycardia as it transiently blocks the AV node. If SVT persists, prophylactic medication, e.g., beta-blockers or even catheter ablation might be required.

1.3.2.1.2 Ventricular tachycardia

Ventricular tachycardia however is life threatening. The morphology of the QRS complexes distinguishes monomorphic VT (all QRS complexes appear to be uniform and originate from the same impulse generator in the ventricle) from polymorphic VT (differently shaped QRS complexes generated by different points in

the ventricle). Furthermore, VT may be continuous (>30s) or non-continuous (<30s). The symptoms of VT depend on the presence of an adequate cardiac output. If this is still possible, VT might even be asymptomatic, however only for a short time. Sooner or later, VT results in pulseless electrical activity or ventricular fibrillation. Ventricular tachycardia always requires treatment. In low frequency VT, cardioversion is the method of choice, and the electric shock application should be ECG controlled and performed during the non-vulnerable phase. If the patient is already unconscious or the ECG shows ventricular fibrillation, non-ECG controlled defibrillation is absolutely vital. If defibrillation is not available or fails, anti-arrhythmic medication, e.g., lidocaine or amiodarone is the second choice. If symptoms recur, a cardioverter-defibrillator has to be implanted.

1.3.2.2 Bradycardia

Bradycardia is an abnormally slow resting heart rate. One reason for bradycardia is a reduced sinus node frequency caused either physiologically (e.g., in athletes) or by hypothyroidism, hypothermia, elevated vagal tone, or sick-sinus syndrome. Another reason can be a dysfunction of the conduction system, e.g., atrioventricular block or bradyarrhythmia absoluta caused by atrial fibrillation.

Atrioventricular block is slowed or non-existing conduction from the atrium to the ventricle. There are three subtypes:

- first degree AV block: delayed atrioventricular conduction with a prolonged PQ time
- second degree AV block: Type 1 (Mobitz 1, Wenckebach) – continuously prolonged conduction with finally one total AV Block and Type 2 (Mobitz 2, Hay) –

intermittently non-conducted P waves not preceded by PR prolongation and not followed by PR shortening, usually with a fixed number of non-conducted P waves for every successfully conducted QRS complex.

- third degree AV block (total AV block): no atrioventricular conduction, no connection between P-wave and QRS complex.

Sick-sinus syndrome (sinus node disease, sinus node dysfunction) is the name for a group of arrhythmias in which the sinus node does not work properly. It is a rare syndrome occurring mainly in patients after congenital heart surgery. The term includes many different arrhythmias, e.g., sinus arrest, sinus node exit block, sinus bradycardia, or even a mixture of all of them. Moreover, episodes of tachycardia might occur in the form of so-called tachycardia-bradycardia syndrome.

Severe bradycardia can be hemodynamically relevant and cause hypoperfusion of the organs resulting in dizziness and syncope. If there is no underlining disease that can be cured, the treatment is either medication or the implantation of a cardiac pacemaker.

1.4 Goal of the study

Arrhythmia is still one of the main complications after FO. The aim of this study has been to evaluate the incidence, forms, and clinical consequences of arrhythmia and its relationship to the surgical technique in the early postoperative period after Fontan repair.

2 Patients and methods

2.1 Collective of patients

From March 2004 until June 2012, 171 patients underwent the Fontan procedure at a single institution (Pediatric Cardiac Surgery, Klinikum Großhadern, Ludwig Maximilian University, Munich).

All medical records, including clinical parameters, medication, echocardiography results, electrocardiograms, cardiac catheterization results, and operative reports, were retrospectively reviewed.

2.1.1 Demographic data

Fifty-six (32.7%) children underwent the LT Fontan procedure and 113 (66.1%) the EC FO. Two children (1.2%) were treated with the semi intra- semi EC Fontan type procedure and were therefore excluded from the study. The remaining 169 children constitute the study population.

Preoperative available data were analyzed retrospectively from birth until the day of FO.

Of the children, 100 (59.2%) were male and 69 (40.8%) female. At the time of FO, the mean age was 3.7 ± 2.9 years, mean weight 14.6 ± 7.3 kg, and mean height

97.1 ± 16.9 cm (median: age (y) 2.8 (1.3-21.1), weight (kg) 12.6 (7.7-64.7), height (cm) 92 (74-176)).

2.1.2 Malformations

The type of cardiac malformation was assessed by echocardiography and cardiac catheterization. The most common malformations were: hypoplastic left heart syndrome (HLHS) - 86 (50.9%), HLHS Variants – 23 (13.6%), hypoplastic right heart syndrome (HRHS) - 22 (13.0%), HRHS Variants - 13 (7.7%), and double inlet left ventricle (DILV) - 14 (8.3%) (Figure 3). The HLHS Variants group included malformations such as unbalanced atrioventricular canal with hypoplastic left ventricle or double outlet right ventricle with hypoplastic left ventricle. The HRHS Variants group included malformations such as unbalanced atrioventricular canal with hypoplastic right ventricle or tricuspid atresia with transposition of the great arteries. In some patients, additional malformations were present, e.g., dextrocardia in 3 cases (1.8%), heterotaxy syndrome in 15 (8.9%).

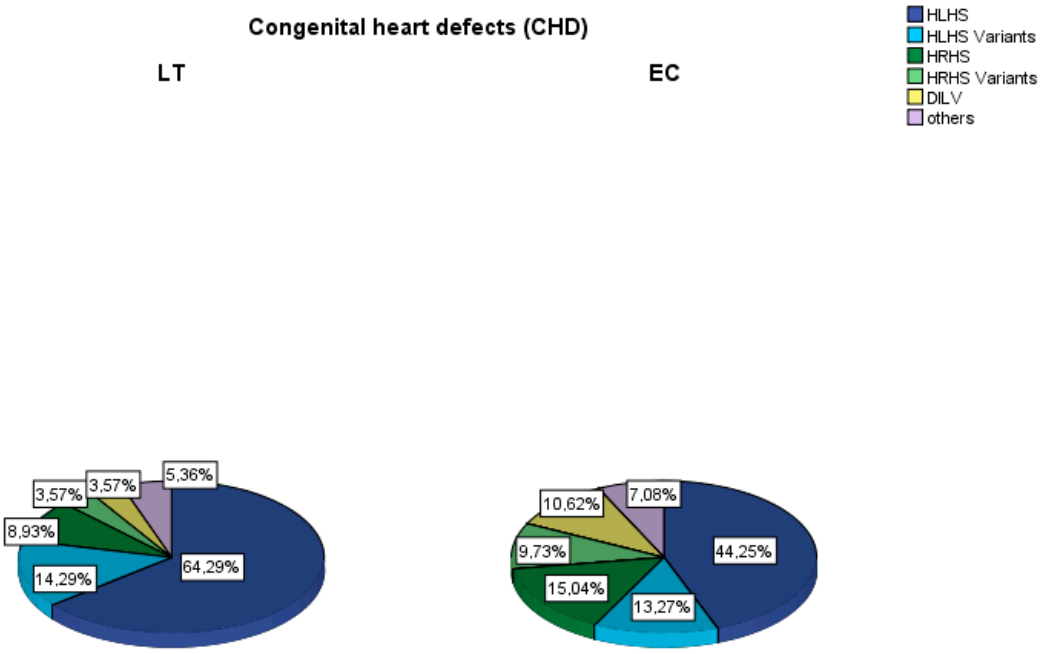

Figure 3: Congenital heart defects in all patients.

With regard to the anatomy of the single ventricle, single left ventricle (SL), single right ventricle (SR), and common ventricle (CV) were distinguished in the patients (SL 48 (28.4%), SR 112 (66.3%), CV 9 (5.3%)).

2.1.3 Hemodynamic type of heart malformations

The hemodynamic type of the single ventricle was analyzed, and four types were distinguished: before surgical treatment, 32 (18.9%) of the children had reduced lung perfusion, 101 (59.8%) had reduced systemic perfusion, 22 (13.0%) had no

reduced perfusion in both circulations with pulmonary overcirculation, and 14 (8.3%) had balanced systemic and pulmonary circulations.

2.1.4 Clinical status before Fontan operation

More than one third of the patients had a reduced exercise capacity (67 (39.6%)) and about half of the patients presented signs of cyanosis (88 (52.1%)) with a mean oxygen saturation of 80.1 ± 6.1%. Fifty (29.6%) children presented cyanotic deformed fingers (clubbed fingers). Dyspnea at rest was nearly absent (5 (3.0%)). Most of the patients had undergone anticoagulant therapy before FO: 111 (65.7%) with acetylsalicylic acid (ASA), 7(4.1%) with phenprocoumon (Marcumar), and 2 (1.2%) with enoxaparin (Clexane). Some of them received medication affecting the heart rhythm, for example, with arrhythmogenic side effects (31 (18.3%)), e.g., digoxin, L-thyroxin, antiepileptics.

2.2 Data analysis

All medical records were retrospectively reviewed. Data analyses included clinical parameters, medication, echocardiography reports, electrocardiograms, cardiac catheterization results, and surgical intervention reports.

With respect to the FO, the time of cardiopulmonary bypass (CPB), aortic cross-clamping, intubation (mechanical ventilation), intensive care unit, and hospital stay were evaluated.

After FO, mortality, the necessity of re-operation, medication, the clinical status of the patients including complications, electrocardiograms, and echocardiography reports were analyzed.

Development of arrhythmia was detected. Arrhythmia was defined as all forms of rhythm other than normofrequent sinus rhythm (NFSR). Hence, the term arrhythmia in the following analyses includes bradycardiac or tachycardiac sinus rhythm, junctional ectopic rhythm (normofrequent, bradycardic, tachycardic), and atrial ectopic rhythm (normofrequent, bradycardic, tachycardic). Parameters that might influence the incidence of arrhythmia were of special interest (e.g., age at Fontan repair, incidence of arrhythmia before Fontan repair, medication, types of cardiac malformations, and the type of Fontan procedure). The analysis also encompassed several parameters that might be influenced by the occurrence of arrhythmia, e.g., duration of hospitalization, intubation time, need of anti-arrhythmic medication, incidence of thromboembolism, and other complications.

With regard to the complications, the following definitions were used:

- prolonged effusion: need for a draining system for longer than 10 days or/and total amount of effusion in at least one system (left pleural, right pleural, or pericardial drainage) of more than 1000 ml.
- infection: secondary increase of infection parameters.
- renal failure: acute renal failure with need of dialysis.
- thromboembolism: thromboembolic event that caused organ ischemia diagnosed clinically or by imaging diagnostics.
- convulsion: clinical convulsion / seizure symptoms.
- stroke: clinical stroke or stroke-like symptoms confirmed by imaging diagnostics.
- bleeding: bleeding that required re-operation/surgical revision.

2.3 Palliative operations before Fontan operation

2.3.1 First stage operation

In the neonatal period, 98 (58.0%) of the patients underwent the Norwood procedure (atrial septectomy, pulmonary artery to ascending aorta association with pulmonary artery homograft reconstruction of the aortic arch). Of these patients, 19 children (19.4%) had a combination of the Norwood procedure with a 3.5- or 4-mm Blalock-Taussig (BT) shunt (expanded polytetrafluoroethylene (ePTFE) tube, IMPRA® ePTFE Vascular Graft, BARD, Tempe, USA; Gore-Tex Vascular Graft, W.L. Gore&Associates, Dundee, Scotland, UK). In 79 newborns (80.6%), the

Norwood procedure was combined with a right ventricle-to-pulmonary artery (RV-PA) shunt with a 5-mm ePTFE tube graft.

Thirty-three (19.5%) patients underwent an aortopulmonary shunt, 23 (13.6%) children required pulmonary artery banding, and in 9 (5.3%) children, an atrial septectomy was carried out. Aortic arch reconstruction was needed in 9 (5.3%) of the patients, and coarctation of the aorta repair in 4 (2.4%). Fourteen (8.3%) patients had no first stage operation, but directly underwent the second stage procedure.

2.3.2 Second stage operation

All patients underwent a partial cavo-pulmonary anastomosis before Fontan repair (hemi-FO or bidirectional Glenn operation).

2.3.2.1 Hemi-Fontan operation

Fifty-four (31.9%) patients underwent a hemi-Fontan procedure. The mean age at this operation was 10.428±11.28 months (median age (m): 7.88 (3.24-82.44)). The surgical technique included division of the systemic-to-pulmonary artery shunt, association of the superior vena cava with the right pulmonary artery followed by the augmentation of pulmonary arteries by using a homograft patch, revision of interatrial communication (if necessary, it was enlarged), and separation of the atrium from the cavopulmonary anastomosis by using a PTFE patch. Of these

patients, 53 children underwent the LT FO as a third stage operation; a single patient underwent an EC FO.

2.3.2.2 Bidirectional Glenn operation

The other 115 patients underwent a Glenn anastomosis. The mean age for this operation was 13.44 ± 25.2 months (median age (m): 6.888 (2.56-196.8)). The technique involved the dividing of the superior caval vein at its junction with the right atrium, over-sewing the atrial end, and creating an end-to-side anastomosis between the SVC and the right pulmonary artery.

Thirteen patients had bilateral bidirectional Glenn operation.

Of the patients after the Glenn anastomosis, 112 underwent the EC FO later on, but only 3 a LT FO.

2.3.2.3 Interstage interventions

In children with aortic re-coarctation, dilation (27 (16.0%)) or stent-implantation (2 (1.2%)) was required. Three (1.8%) of the children needed a pacemaker insertion even before Fontan; in one of the cases, the surgical implantation of the pacemaker was carried out before Fontan, in the second child, this treatment was performed after the second stage operation, and in the third child, the timing of the implantation was unknown.

Three (1.8%) children underwent the Rashkind procedure. RPA/LPA dilation or stent implantation was necessary in 36 (21.3%) cases.

2.4 Fontan operation

2.4.1 Intracardiac Fontan operation – lateral atrial tunnel (LT)

Fifty-six patients underwent a LT FO. All operations were performed by the same surgical team through a median re-sternotomy. The ascending aorta / neoaorta and the inferior and superior caval vein were cannulated, and a hypothermic CPB was established. All operations were performed without circulatory arrest. The body temperature during the operation was around 30°C. Myocardial protection was achieved with crystalloid Bretschneider cardioplegic solution (4°C, 30 ml/kg).
The patch that separated the atrium from the cavopulmonary anastomosis was completely excised. A new patch was cut from a portion of a 10-mm ePTFE tube. In 53 (94.6%) patients, this patch was fenestrated (fenestration about 3 mm in diameter). The patch was then sutured into the right atrium, creating a lateral atrial tunnel. The atriotomy was closed by using the sandwich technique (Figure 4).

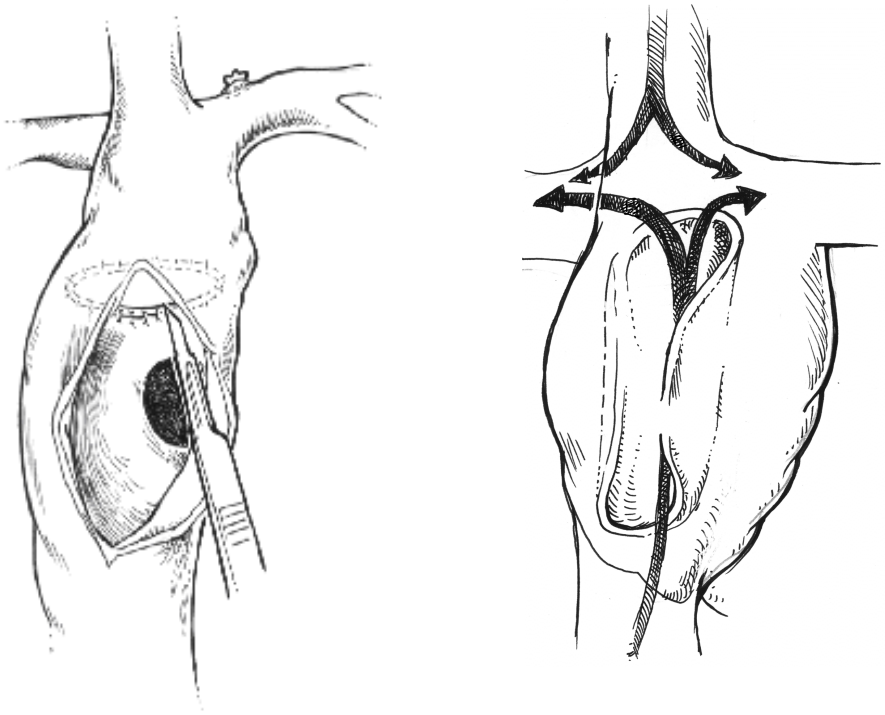

Figure 4: Lateral atrial tunnel after the hemi-Fontan operation.

2.4.2 Extracardiac Fontan operation – extracardiac conduit (EC)

One hundred and thirteen patients underwent an EC FO. The procedure was performed on the beating heart without aortic cross-clamping in nearly all of the patients (100 (88.5%)). After cannulation of the aorta and both caval veins, a normothermic CPB was commenced. The inferior caval vein was divided from the right atrium and then anastomosed with an ePTFE (Gore-Tex Vascular Graft, W.L. Gore&Associates, Dundee, Scotland, UK) conduit (18 or 20 mm in diameter).

Opposite to the Glenn anastomosis, the right pulmonary artery was longitudinally opened and associated with the ePTFE conduit side-to-end (Figure 5).
If needed, the cardioplegic cardiac arrest was used to correct intracardiac lesions through the right atrial approach. At the same time, the atrial septum was inspected for adequate interatrial communication. The atrial opening was then closed with a running polydioxanon 5-0 suture. The PTFE stretch conduit was pulled down so that it was connected with the inferior caval vein. The length of the conduit was between 5 and 7cm. The anastomosis of the conduit with the inferior caval vein and the right pulmonary artery was performed with a running monofilament polypropylene 5-0 suture.

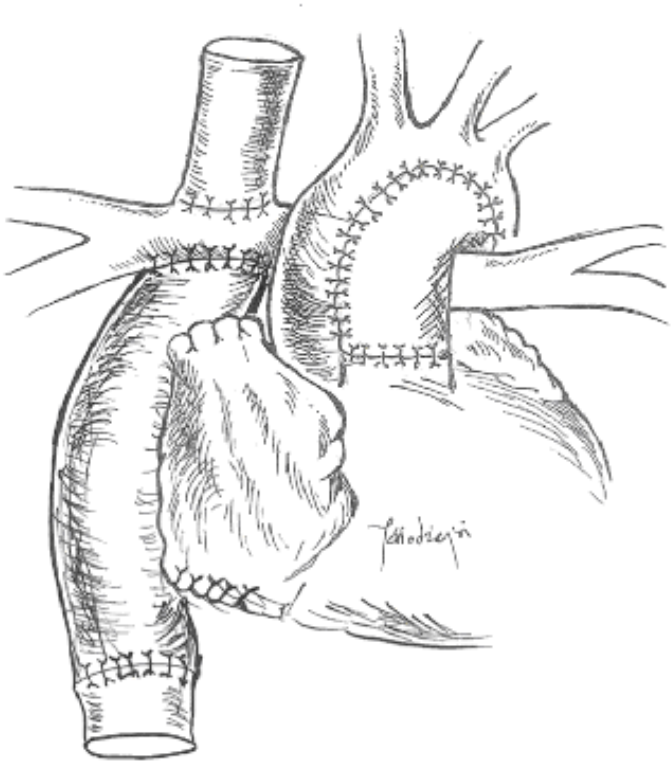

Figure 5: Extracardiac Fontan operation.

2.5 Examinations

All patients underwent the same examinations before FO. For each patient, the following procedures were carried out: clinical examination, measurement of oxygen saturation, electrocardiogram, echocardiography, and cardiac catheterization.

2.5.1 Electrocardiogram

Electrocardiographic examination was performed with a 12-channel ECG and 24h-ECG (Holter). Each patient underwent a 12-channel ECG analysis directly before FO, within 12 hours after FO, and the day before discharge. If any abnormalities were noted, the children also underwent 24h-ECG (Holter) during hospitalization after the Fontan procedure.

Heart frequencies were classified by the age-adjusted norms (if below – bradycardia, if above – tachycardia). Sinus rhythm was defined as a regular p wave followed by a normally shaped narrow QRS complex in a 1:1 ratio. In junctional ectopic rhythm, the AV node provides electrical impulses, and the p wave lies just before or after the QRS complex. Atrial ectopic rhythm was defined as a rhythm with differently shaped p waves coming from different impulse-generating spots in the atrium.

2.5.2 Echocardiography

Each patient underwent a comprehensive preoperative two-dimensional and Doppler echocardiographic examination (ECHO). Atrioventricular valve and aortic

valve insufficiency was graded on a scale from 1 to 3 (mild, moderate, severe). Echocardiography was also used for the qualitative assessment of the ventricular hypertrophy (mild, moderate, severe) and the function of the single ventricle (good, reduced, poor).

2.5.3 Cardiac catheterization

Cardiac catheterization and angiography with the standard technique was performed in 169 (100%) children in the median interval time before FO of 1 day (0–5 d). The main hemodynamic parameters obtained during the procedure were pulmonary venous wedge pressure, pulmonary artery pressure, superior and inferior caval pressures, ventricular pressures, aortic pressures, superior vena cava and aortic saturation, and partial arterial oxygen tension (pO_2). Calculations of the pulmonary-to-systemic blood flow (Qp:Qs) ratio were carried out by using the Fick principle. Data from routine blood tests performed before catheterization (hematocrit value, hemoglobin concentration, red blood cell count) were also collected.

2.5.4 Effusions

The amount and duration of pleural and peritoneal effusions were analyzed. Right pleura drainage was routinely installed during the FO, and left pleura drainage was caarried out postoperatively with local anesthesia if needed (clinically significant amount of fluid). The strategy was to leave the drainage in place until the daily amount of effusion was less than 3 ml/kg.

2.6 Statistical analysis

Nonparametric variables are described as frequencies and percentage. Continuous variables are expressed as means with standard deviation (SD) or medians with range. The two-tailed Student's t-test or Mann-Whitney U-test was performed for comparison of continuous variables between the groups. Pearson's chi-squared test was used to evaluate differences in the frequency distribution of nonparametric variables in two groups. A binary logistic regression was included to re-evaluate the influences on the development of arrhythmia. A p-value (P) of less than 0.05 was considered significant.

Statistical analysis was performed with IBM SPSS Statistical Software Version 21.

3 Results

3.1 Differences between LT and EC patients before Fontan operation

3.1.1 Preoperative demographics and morphologic features

Patient age, weight, and height did not differ significantly between the groups (mean age: LT 3.7 ± 2 vs EC 3.6 ± 2.9 y, P 0.699; mean weight: LT 14.8 ± 8 vs EC 14.1 ± 6 kg, P 0.526; mean height: LT 97.9 ± 15 vs EC 95.7 ± 16 cm, P 0.386) (Table 1).

With regard to gender, more boys were found in the LC group than girls (male:female ratio – LT 76.8:23.2% vs EC 50.4:49.6%, P 0.001).

The most common malformations were: HLHS, HLHS Variants (such as CAVC + hypoplastic left ventricle or DORV + hypoplastic left ventricle), HRHS, HRHS Variants (such as CAVC + hypoplastic right ventricle or TA + TGA), and DILV. In some patients, additional malformations were present, e.g., dextrocardia and heterotaxia (see Table 1 and Figure 6 for detailed numbers).

With respect to the anatomy of the univentricular heart, single left ventricle, single right ventricle, and common ventricle were distinguished (28.4% SL – LT 14.3 vs EC 35.4%, 66.3% SR – LT 82.1 vs EC 58.4%, 5.3% CV – LT 3.6 vs EC 6.2%). The

most frequently seen was the single right ventricle, which was overrepresented especially in the LT group.

Four preoperative hemodynamic types were distinguished: reduced lung perfusion, reduced systemic perfusion, balanced perfusion, and no reduced perfusion: 18.3% (LT 12.5 vs EC 21.2%, P 0.167) of the children had a reduced lung perfusion, 60.4% (LT 73.2 vs EC 54.0%, P 0.016) a reduced systemic perfusion, 13.0% (LT 12.5 vs EC 13.3%, P 0.888) had no reduced perfusion, and 8.3% (LT 1.8 vs EC 11.5%, P 0.031) had balanced circulations.

		LT	EC	P
Sex	male	43 (76.8%)	57 (50.4%)	0.001
	female	13 (23.2%)	56 (49.6%)	
Age (y)		3.7±2	3.6±2.9	0.699
Hight (cm)		97.9±15	95.7±15.9	0.386
Weigth (kg)		14.8±8	14.1±6.1	0.526
Malformation	HLHS	36 (64.3%)	50 (44.3%)	0.014
	HLHS Variants	8 (14.3%)	15 (13.3%)	0.857
	HRHS	5 (8.9%)	17 (15.0%)	0.266
	HRHS Variants	2 (3.6%)	11 (9.7%)	0.157
	DILV	2 (3.6%)	12 (10.6%)	0.118
	others	3 (5.3%)	8 (7.1%)	0.669
	Isomerism/ Heterotaxy syndrome	5 (8.9%)	9 (8%)	0.831
	Dextrocardia	0 (0%)	3 (2.7%)	0.55
Ventricular morphology	Single Left Ventricle	8 (14.3%)	40 (35.4%)	0.004
	Single Right Ventricle	46 (82.1%)	66 (58.4%)	0.002
	Common Ventricle	2 (3.6%)	7 (6.2%)	0.475

Table 1: Preoperative demographics and morphologic features.

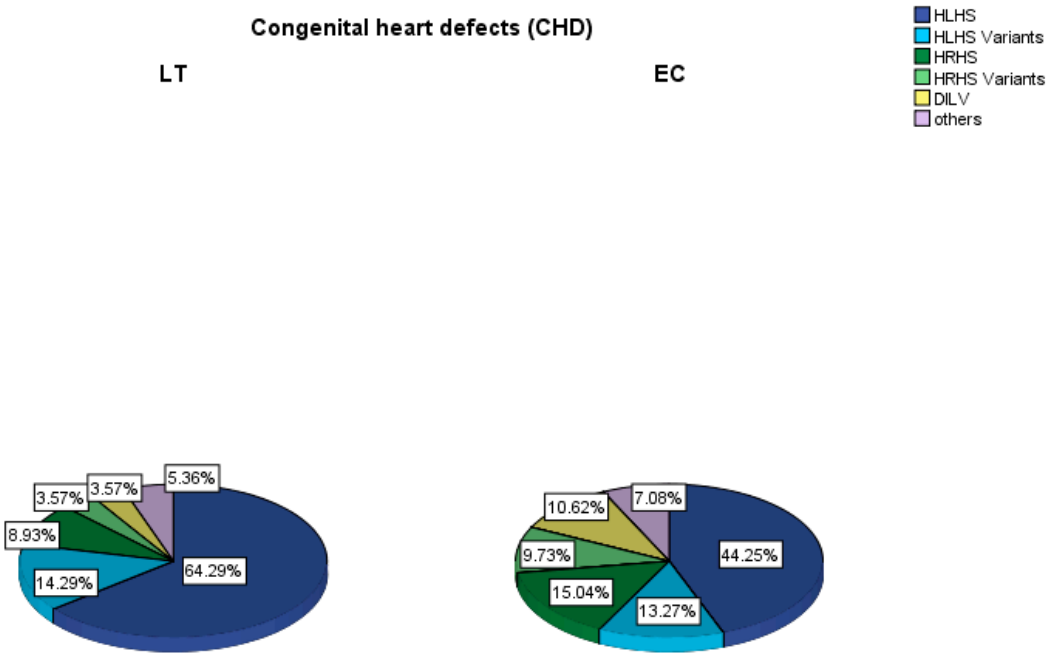

Figure 6: Congenital heart defects in the two study groups.

3.1.2 Operations and other interstage interventions before Fontan procedure

All of the patients received several or at least one palliative operation before the Fontan procedure. The usual sequence after the preliminary stage and depending on the hemodynamic type of the single ventricle was:

bidirectional Glenn operation – EC

or hemi-FO – LC .

Nearly all of the children underwent the operations in the above-mentioned sequence. Only three patients of the LT group had a bidirectional Glenn operation

before the Fontan procedure, and a single patient from the EC group had a hemi-FO.

Regarding the first stage operations, some differences occurred between the two groups of Fontan repair (see Table 2 and 3).

	LT (N = 56)	EC (N = 113)	P
Norwood + RV PA shunt	39 (69.6%)	40 (35.4%)	< 0.001
Norwood + BT shunt	1 (1.8%)	18 (15.9%)	0.006
PA-banding	5 (8.9%)	18 (15.9%)	0.212
Aortopulmonary shunt	8 (14.3%)	24 (21.2%)	0.277
Atrioseptectomy	0	5 (4.4%)	0.117
Pacemaker implantation	1 (1.8%)	2 (1.8%)	0.994

Table 2: Surgical interventions before Fontan operation.

	LT (N = 56)	EC (N = 113)	P
Aortic balloon dilation	10 (17.9%)	13 (11.5%)	0.257
Aortic stent implantation	0	3 (2.7%)	0.219
LPA/RPA stent implantation	6 (10.7%)	6 (5.3%)	0.198
Rashkind procedure	2 (3.6%)	2 (1.8%)	0.468
MAPCA closure	6 (10.7%)	6 (5.3%)	0.198

Table 3: Cardiologic interventions carried out some time (month-years) before Fontan operation.

Some of the children needed a pacemaker implantation even before Fontan repair (LT 1.8% (1) vs EC 1.8% (2), P 0.994): this occurred after the second stage operation in one case from the EC group and in one case from the LT group. One child from the EC group required pacemaker implantation even before the Glenn operation.

The reasons for the need of a permanent pacemaker were sick-sinus-syndrome (1 - EC) and AV block III° (2 – 1 EC and 1 LT).

3.1.3 Clinical status before Fontan procedure

Apart from the reduced exercise capacity (LT 61.9% vs EC 42.9%, P 0.041), no differences were noted between the groups with regard to the clinical status of the children (Table 4). Half of the patients in both groups presented signs of cyanosis (LT 52.9 vs EC 55.1%, P 0.795) with a mean oxygen saturation of 80.1 ± 6.1 (LT 79.4 ± 6.01 vs EC 80.8% ± 5.8 mmHg, P 0.346). 28.4% of the children presented cyanotic deformed fingers (clubbed fingers) (LT 35.7 vs EC 24.8%, P 0.138). Dyspnea at rest was nearly absent (LT 2.1 vs EC 3.8%, P 0.543).

	LT	EC	P
Sat O2 (mean, mmHg)	79.4±6.01	80.8±5.8	0.346
Cyanosis	27 (52.9%)	59 (55.1%)	0.795
Fingers, cyanotic signs	20 (35.7%)	28 (24.8%)	0.138
Reduced exercise capacity	26 (61.9%)	39 (42.9%)	0.041
Dyspnea at rest	1 (2.0%)	4 (3.8%)	0.543

Table 4: Clinical status before Fontan procedure.

3.1.4 Medication before Fontan procedure

Most of the patients received an anticoagulant therapy. Some of them were on medication with arrhythmogenic side effects, e.g., digoxin, L-thyroxin, and antiepileptics (LT 19.6%, EC 17.7%; see Table 5 for all details).

		All	LT	EC	P
Diuretics		54 (32%)	19 (33.9%)	35 (31.0%)	0.698
ACE blockers		83 (49%)	41 (73.2%)	42 (37.2%)	<0.001
ß blockers		2 (1.2%)	1 (1.8%)	1 (0.9%)	1.000
Digoxin		17 (10%)	7 (12.5%)	10 (8.8%)	0.458
Rhythm side effect medication (all)		31 (18.3%)	11 (19.6%)	20 (17.7%)	0.759
Others		9 (5.3%)	3 (5.4%)	6 (5.3%)	0.990
Anticoagulation	ASA		51 (100%)	57 (87.9%)	0.009
	enoxaparin		0 (0.0%)	2 (3.0%)	0.503
	phenprocoumon		0 (0.0%)	6 (9.1%)	0.026

Table 5. Medication before Fontan operation.

3.1.5 Arrhythmias before Fontan procedure

With regard to the ECG findings, the two groups also did not differ from each other (Table 6, Figures 7 and 8). Most of the patients manifested preoperatively sinus rhythm (including normofrequent SR, sinus bradycardia, and sinus tachycardia) (LT 89.3 vs EC 86%). A NFSR was most frequent (LT 64.3 vs EC 68.2%, P 0.612). Only a few children had an atrial ectopic rhythm (LT 5.4 vs EC 11.2%, including atrial

ectopic normofrequent rhythm, LT 5.4 vs EC 8.9%, P 0.548; AET, LT 0 vs EC 2.8%, P 0.552), or junctional ectopic rhythm (all of these junctional ectopic bradycardia, LT 3.6 vs EC 0.9%, P 0.272). Some showed branch blocks or AV blocks. Two children had a regular pacemaker rhythm (LT 1(1.8%) vs EC 1 (0.9%), P 0.994) (one child with a pacemaker underwent no ECG before operation).

	LT (N = 56)	EC (N = 107)	P
Sinus rhythm nfq	36 (64.3%)	73 (68.2%)	0.612
Atrial ectopic nfq	3 (5.4%)	9 (8.4%)	0.548
Junctional ectopic nfq	0	0	
Sinus tachycardia	11 (19.6%)	16 (15.0%)	0.444
Atrial ectopic tachycardia	0	3 (2.8%)	0.552
Junctional ectopic tachycardia	0	0	-
Sinus bradycardia	3 (5.4%)	3 (2.8%)	0.411
Atrial ectopic bradycardia	0	0	-
Junctional ectopic bradycardia	2 (3.6%)	1 (0.9%)	0.272
Bradycardia all	5 (8.9%)	4 (3.7%)	0.277
Tachycardia (without sinus)	0	3 (2.8%)	0.552
AV blocks (degree I°)	4 (7.1%)	3 (2.8%)	0.168
Right bundle branch block	12 (21.4%)	12 (11.1%)	0.076
Right bundle branch block incomplete	16 (28.6%)	17 (15.7%)	0.052
Left bundle branch block	3 (5.4%)	2 (1.9%)	0.216
Left bundle branch block incomplete	0	5 (4.6%)	0.102
VES (ventricular extrasystoles)	0	7 (6.2%)	0.057

Table 6. Rhythm forms and conduction abnormalities before Fontan.

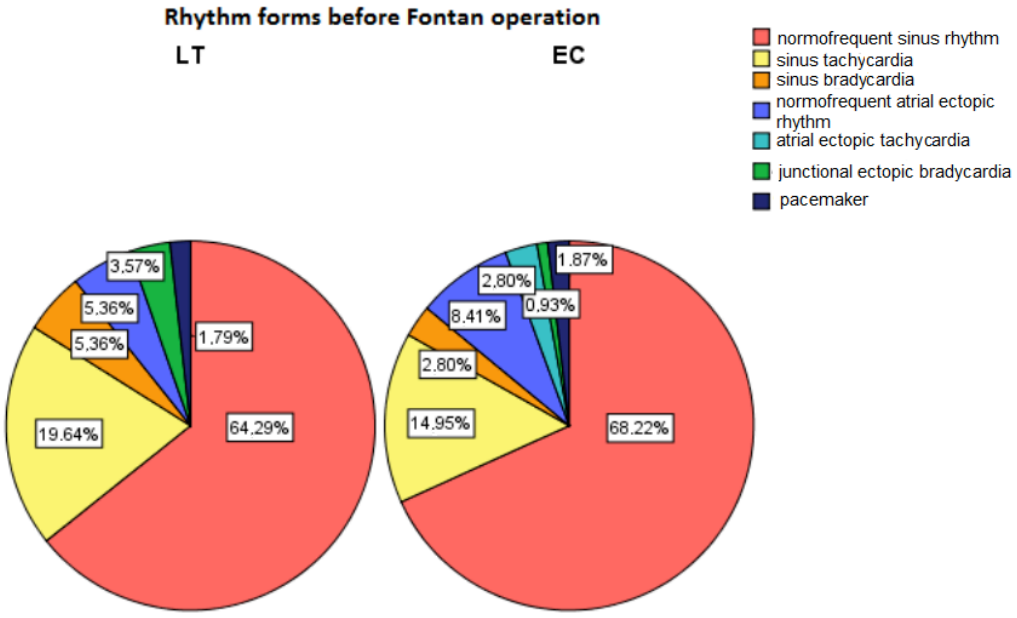

Figure 7. Rhythm forms before Fontan procedure.

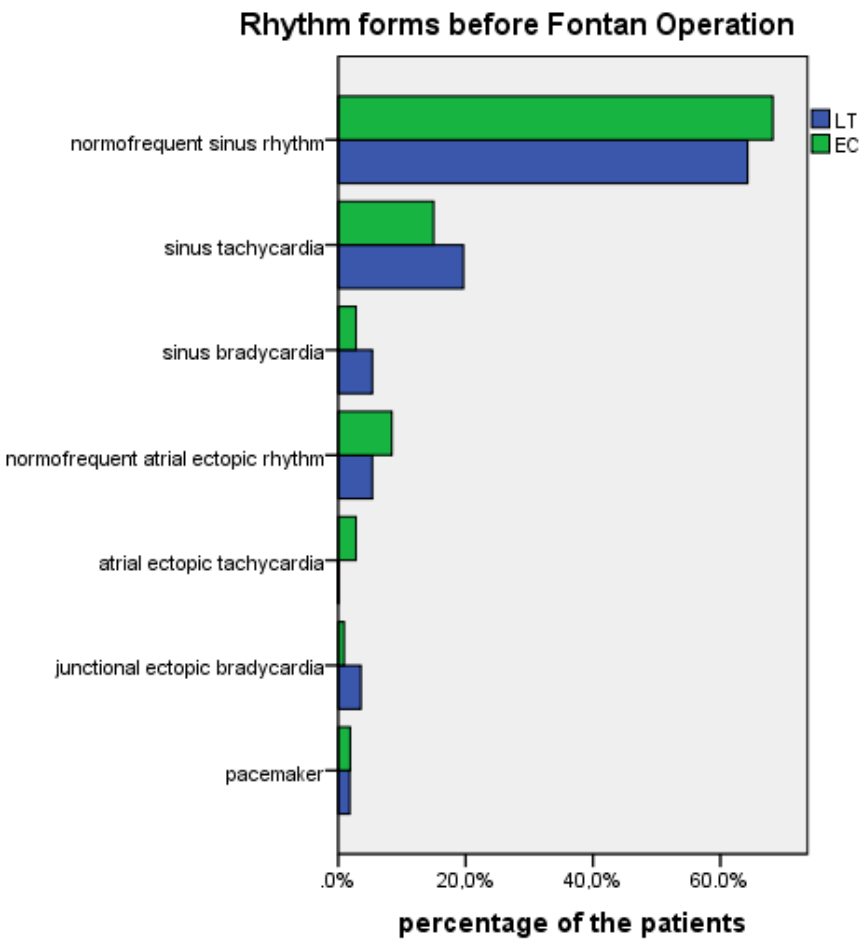

Figure 8. Rhythm forms before Fontan procedure.

3.1.6 Echocardiography before Fontan procedure

The preoperative echocardiography showed sufficient to excellent ventricular function of the single ventricle in nearly all patients of both groups (LT 50 (89.4%) vs EC 102 (90.3%), P 0.842). Almost none of the patinets had reduced ventricular

function (LT 2 (3.6%) vs EC 0 (0%), P 0.108). Hypertrophy or dilation of the ventricle but with good function affected just a few children (LT 3 (5.4%) vs EC 2 (1.8%), P 0.195). Severe AV valve insufficiency was present in only a few cases (LT 5 (8.9%) vs EC 8 (7.5%), P 0.431) (Table 7).

		LT	EC	P
	none	16 (28.6%)	39 (36.4%)	0.463
AV valve	I°	19 (33.9%)	34 (31.8%)	0.613
insufficiency	II°	16 (28.6%)	26 (24.3%)	0.671
	III°	5 (8.9%)	8 (7.5%)	0.431
Aortic valve	I°	16(28.6%)	32 (28.3%)	0.973
insufficiency	II°	1 (1.8%)	4 (3.5%)	0.526

Table 7. Valve insufficiency before Fontan operation.

3.1.7 Cardiac catheterization before Fontan procedure

The two groups did not differ with respect to the mean pulmonary artery pressure, ventricular end-diastolic pressure or pulmonary resistance. They only differed with regard to the aortic oxygen saturation and Qp:Qs ratio (mean aortic saturation: LT 83.7% vs EC 86%, P 0.019; median Qp:Qs: LT 0.62 vs EC 0.74, P 0.006). All catheterization results before FO are presented in Table 8. MAPCAs, which needed

to be coiled, were present in both groups (LT 30 (53.6%) vs EC 51 (45.1%), P 0.301; Table 9).

The aortic oxygen saturation was the same in patients with MAPCAs (Ao Sat 80.5±5.6%) and those without (Ao Sat 79.7±6.5%) (P 0.418). No statistically significant difference was seen in the aortic oxygen saturation in children with a relevant pulmonary artery stenosis (Ao Sat with RPA or LPA stenosis 83.2±5.7% vs without RPA or LPA stenosis 85.6±5.4%, P 0.061).

	LT	EC	P
PVRIx (RU/m^2)	1.51±0.90	1.56±0.70	0.764
SVRIx (RU/m^2)	13.24 ±4.85	13.86±5.45	0.551
Qp:Qs	0.62* (0.34-1.36)	0.74* (0.2-2.01)	0.006
Sat Ao (%)	83.69±5.5	85.95±5.39	0.019
Sat SVC (%)	66.24±7.2	65.13±7.67	0.427
PA MP (mmHg)	11.39±3.13	11.12±2.49	0.577
RA MP (mmHg)	6.65±2.45	6.59±2.35	0.891
LA MP (mmHg)	7.18±2.39	6.91±2.19	0.503
SV EDP (mmHg)	10.38±3.26	10.53±3.51	0.804
Ao Asc SP (mmHg)	89.19±14.86	87.02±13.27	0.385
Ao Asc DP(mmHg)	45.46±9.07	45.49±8.29	0.931

Table 8: Cardiac catheterization data before Fontan operation presented as means with standard deviation or (*) medians with range (Ao – aorta, AoAsc – aorta ascendens, Ix – indexed for body surface area, DP - diastolic pressure, LA – left atrium, MP – mean pressure, PA – pulmonary artery, PVR – pulmonary vascular resistance, Qp:Qs – pulmonary-to-sytemic-flow ratio, RA – right atrium, RU – resistance unit = Wood unit, Sat – oxygen saturation, SP – systolic pressure, SVC – superior vena cava, SVR – systemic vascular resistance).

	LT (N = 56)	EC (N = 113)	P
MAPCA coil	30 (53.6%)	51 (45.1%)	0.301
Aortic stent implantation	0	3 (3.1%)	0.216
Aortic dilation	1 (1.8%)	1 (0.9%)	0.610
RPA/LPA dilation/stent implantation	12 (21.4%)	12 (10.6%)	0.058

Table 9: Interventions during cardiac catheterization shortly (1-5 days) before Fontan operation.

3.2 Operation

Patients from both groups needed a cardiopulmonary bypass (CPB) with a median time of 56.5(23-214) min (LT 61(36-122) vs EC 49.5(23-214) min, P 0.004). Only 11.5% operations in the EC group were carried out with aortic cross-clamping, whereas in the LT group, all patients needed aortic cross-clamping. The mean time for aortic cross-clamping, if needed, was 35.7 ± 13.4 min (LT 34.9 vs EC 39.4min, P 0.484) (Table 10). In 55 (36.9%) of the children, Fontan repair was performed with fenestration (LT 53 (96.4%) vs EC 2 (2.1%), P < 0.001).

In some of the children, additional operations were performed during FO (Table 11).

	LT	EC	P
CPB time (min)	61* (36-122)	50* (23-214)	0.004
Aortic cross-clamping time (min)	34.85±10.4	39.38±22.1	0.484

Table 10: Cardiopulmonary bypass (CPB) and aortic cross-clamping time during operation presented as means with standard deviation or (*) medians with range.

	All	LT	EC	P
AV valve reconstruction	11 (6.5%)	6 (10.7%)	5 (4.4%)	0.119
Closure of pulmonary valve	5 (3.0%)	0 (0%)	5 (4.4%)	0.110
Atrioseptectomy	7 (4.1%)	4 (7.1%)	3 (2.7%)	0.168
Aortic arch enlargement	2 (1.2%)	0 (0%)	2 (1.8%)	0.317
VSD enlargement	2 (1.2%)	1 (1.8%)	1 (0.9%)	0.610
Pacemaker implantation	3 (1.8%)	2 (3.6%)	1 (0.9%)	0.213
Change of pacemaker	1 (0.6%)	0 (0%)	1 (0.9%)	0.480
Pacemaker electrode placement	2 (1.2%)	0 (0%)	2 (1.8%)	0.317
Closure RV-PA/BT-Shunt	1 (0.6%)	0 (0%)	1 (0.9%)	0.480
Enlargement of Glenn	4 (2.4%)	0 (0%)	4 (3.5%)	0.154
RPA/LPA dilation	5 (3.0%)	2 (3.6%)	3 (2.7%)	0.741
Fenestration	55(32.5%)	53(96.4%)	2 (2.1%)	< 0.001

Table 11: Additional procedures during Fontan operation.

3.3 Postoperative course

The children stayed within the intensive care unit (ICU) for the mean time of 5.3 days (LT 5.5 ± 3 vs EC 5.3 ± 5 d, P 0.760), and the median duration of hospitalization was 15 (6-67) days (LT 13(6-38) vs EC 16(6-67) d, P 0.016). The mean intubation time was 17.73 hours (LT 12.51 ± 20.76 vs EC 20.8 ± 54 h, P 0.163) (Table 12).

	LT	EC	P
ICU time (days)	5.5±3	5.3±5	0.760
Hospitalization (days)	13* (6-38)	16* (6-67)	0.016
Intubation time (hours)	12.5±20	20.8±54	0.163

Table 12: Postoperative course presented as means with standard deviation or (*) medians with range (ICU intensive care unit).

3.4 Postoperative complications

Eighty-two (48.5%) patients showed postoperative complications (LT 24 (42.8%) vs EC 58 (51.3%); P 0.412), including minor (e.g., secondary infection) and severe (e.g., stroke or severe bleeding) complications. Table 13 and Figure 9 show the most frequent complications after the Fontan procedure. Few differences were noted between the two groups (LT, EC) with regard to the chance of developing postoperative complications.

Arrhythmia, which was one of the complications, will be discussed later.

The chance of developing prolonged effusions was higher in EC patients, whereas the LT group was more likely to develop postoperative strokes or bleeding complications.

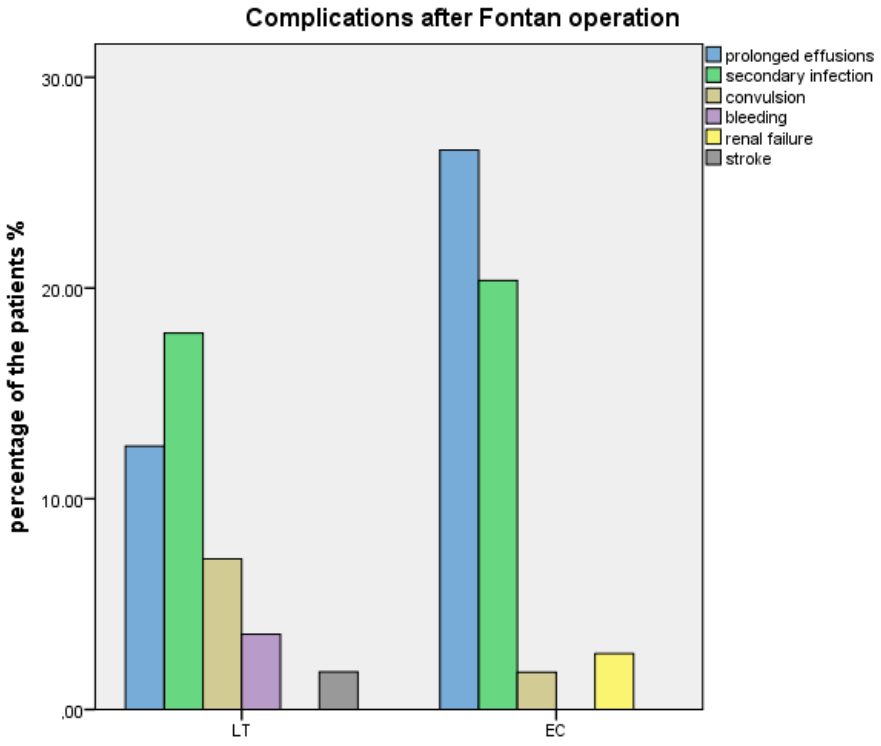

Figure 9: Complications after Fontan repair during hospitalization.

	All	LT	EC	P
Prolonged effusions	37(21.9%)	7 (12.5%)	30 (26.5%)	0.038
Secondary infection	33(19.5%)	10 (17.9%)	23 (20.4%)	0.700
Renal failure	3 (1.8%)	0 (0%)	3 (2.7%)	0.219
Convulsion	6 (3.6%)	4 (7.1%)	2 (1.8%)	0.094
Stroke	1 (0.6%)	1 (1.8%)	0 (0%)	0.154
Bleeding	2 (1.2%)	2 (3.6%)	0 (0%)	0.043

Table 13: Complications after Fontan repair during hospitalization.

3.5 Arrhythmia

3.5.1 Time of onset

Directly (within 12 h) after FO, 40 (25.2 %) of the children presented NFSR. In 24h (Holter) ECG analyzes during hospitalization, 45% had a NSFR, and at the time of discharge from hospital, 50% of the patients showed this rhythm.

Most of the arrhythmia occurred in the first days directly after FO. At the time of discharge, most of the patients had a regular sinus rhythm. Table 14 shows the development of NFSR in the postoperative course.

3.5.2 Forms of arrhythmia

Different forms of arrhythmia were detected at various time points (Table 14).

	Early post OP (N = 159)	24h(Holter)ECG (N = 60)	At discharge (N = 153)
Sinus rhythm nfq	40 (25.2%)	27 (45.0%)	76 (49.7%)
Atrial ectopic nfq	10 (6.3%)	3 (5.0%)	15 (9.8%)
Junctional ectopic nfq	19 (11.9%)	7 (11.7%)	10 (6.5%)
Sinus tachycardia	58 (36.5%)	4 (6.7%)	36 (23.5%)
Atrial ectopic tachycardia	10 (6.3%)	1 (1.7%)	3 (2.0%)
Junctional ectopic tachycardia	10 (6.3%)	0	0
Pacemaker	5 (3.1%)	2 (3.4%)	4 (2.6%)
Sinus bradycardia	2 (1.3%)	3 (5.0%)	5 (3.3%)
Atrial ectopic bradycardia	0	4 (6.7%)	3 (2.0%)
Junctional ectopic bradycardia	5 (3.1%)	9 (15.0%)	1 (0.7%)
Bradycardia all	7 (4.4%)	16 (26.7%)	9 (5.9%)
Tachycardia (without sinus)	20 (12.6%)	1 (1.7%)	3 (2.0%)

Table 14: Rhythm forms postoperatively.

3.5.3 Reasons for arrhythmia

3.5.3.1 Age

Arrhythmia, defined as all rhythm forms other than NFSR, after Fontan repair occurred in all age groups. The group of 2- to 4-year-old children seemed to have

the lowest risk for arrhythmia at any time, even if the variation was not large (Table 15).

	Age	Arrhythmia	No arrhythmia
early	< 2 y	6/11 (54.5%)	5/11 (45.5%)
postoperative	2-4 y	42/119 (35.3%)	77/119 (64.7%)
	4-10 y	12/26 (46.2%)	14/26 (53.8%)
	> 10 y	3/8 (37.5%)	5/8 (62.5%)
at discharge	< 2 y	2/11 (18.2%)	9/11 (81.8%)
	2-4 y	24/113 (21.2%)	89/113 (78.8%)
	4-10 y	9/25 (36.0%)	16/25 (46.0%)
	> 10 y	3/9 (33.3%)	6/9 (66.7%)
before Fontan	< 2 y	2/11 (18.2%)	9/11 (81.8%)
OP	2-4 y	14/120 (11.7%)	106/120 (88.3%)
	4-10y	6/26 (23.1%)	20/26 (76.9%)
	> 10 y	1/8 (12.5%)	7/8 (87.5%)

Table 15: Arrhyhtmia with respect to age at Fontan operation.

3.5.3.2 Type of heart malformation and clinical status

Patients with single left ventricle anatomy were more likely to have NFSR early after operation than single right ventricle anatomy patients (SL 15 (33.3%) vs SR 24 (22%), P 0.142).

Patients who developed sinus bradycardia early postoperatively all had single left anatomy (SL 2 (4.4%) vs SR 0 (0%), P 0.084).

All forms of bradycardia taken together at discharge were more frequent in single left anatomy than in single right (SL 6 (14.6%) vs SR 2 (1.9%), P 0.006).

No correlation was noted between reduced systemic perfusion before FO and the development of sinus tachycardia and other forms of tachycardia early after FO (sinus tachycardia early postoperatively: reduced systemic perfusion 37/99 (37.4%) vs no reduced systemic perfusion 21/62 (33.9%), P 0.652; tachycardia without sinus tachycardia early postoperatively: reduced systemic perfusion 14/99 (14.1%) vs no reduced systemic perfusion 7/62 (11.2%), P 0.601). Patients with reduced lung perfusion were more likely to develop sinus tachycardia (sinus tachycardia early postoperatively: reduced lung perfusion 13/32 (40.6%) vs no reduced lung perfusion 45/84 (34.9%), P 0.545; tachycardia without sinus tachycardia early postoperatively: reduced lung perfusion 4/32 (12.5%) vs no reduced lung perfusion 17/112 (13.2%), P 0.919).

No correlation was observed between the development of early postoperative sinus tachycardia and the ventricle anatomy (SL 15 (33.3%) vs SR 39 (35.9%), P 0.772).

Significant correlation between hypertrophy and variation of heart rhythm could not be seen, either with regard to ECG signs of hypertrophy or in echocardiography (Tables 16 and 17).

		Sinus NFQ	others	P
Early postoperatively	Hypertrophy	24/86 (27.9%)	62/86 (72.1%)	0.336
	No hypertrophy	16/75 (21.3%)	59/75 (78.7%)	
24h-ECG (Holter)	Hypertrophy	16/32 (50.0%)	16/32 (50.0%)	0.405
	No hypertrophy	11/28 (39.3%)	17/28 (60.7%)	
At discharge	Hypertrophy	38/83 (45.8%)	45/83 (54.2%)	0.298
	No hypertrophy	39/72 (54.2%)	33/72 (45.8%)	
Pre Fontan operation	Hypertrophy	60/88 (68.2%)	28/88 (31.8%)	0.659
	No hypertrophy	50/77 (64.9%)	27/77 (35.1%)	

Table 16: Normofrequent sinus rhythm in children with ECG signs of cardiac hypertrophy before Fontan repair.

		Sinus NFQ	others	P
Early postoperatively	Hypertrophy	0/7 (0.0%)	7/7 (100%)	0.120
	No hypertrophy	40/154 (26.0%)	114/154 (74.0%)	
24h-ECG (Holter)	Hypertrophy	1/3 (33.3%)	2/3 (66.7%)	0.677
	No hypertrophy	26/57 (45.6%)	31/57 (54.4%)	
At discharge	Hypertrophy	1/7 (14.3%)	6/7 (85.7%)	0.055
	No hypertrophy	76/148 (51.4%)	72/148 (48.6%)	
Pre Fontan operation	Hypertrophy	5/7 (71.4%)	2/7 (28.6%)	0.785
	No hypertrophy	105/158 (66.5%)	53/158 (33.5%)	

Table 17: Normofrequent sinus rhythm in children with echocardiographic signs of cardiac hypertrophy before Fontan repair.

No significant correlation was detected between the occurrence of heterotaxy diagnosis and the incidence of arrhythmia. Only the prevalence for NFSR before Fontan repair was significantly lower in patients with heterotaxy syndrome (Table 18). Dextrocardia was not a risk factor for the development of arrhythmia (P>0.050). The type of cardiac malformation had no impact on the development of arrhythmia in general.

		Sinus NFQ	others	P
Early postoperatively	Heterotaxy	2/14 (14.3%)	12/14 (85.7%)	0.339
	No heterotaxy	38/147 (25.9%)	109/147 (74.1%)	
24h-ECG (Holter)	Heterotaxy	2/5 (40.0%)	3/5 (60.0%)	0.814
	No heterotaxy	25/55 (45.5%)	30/55 (54.5%)	
At discharge	Heterotaxy	8/14 (57.1%)	6/14 (42.9%)	0.558
	No heterotaxy	69/141 (48.9%)	72/141 (51.1%)	
Pre Fontan operation	Heterotaxy	5/15 (33.3%)	10/15 (66.7%)	0.004
	No heterotaxy	105/150 (70.0%)	45/150 (30.0%)	

Table 18: Normofrequent sinus rhythm in children with heterotaxy syndrome.

Reduced exercise capacity before FO had no significant influence on the development of arrhythmia at any time (Table 19).

		Sinus NFQ	others	P
Early postoperatively	reduced	15/65 (23.1%)	50/65 (76.9%)	0.262
	normal	21/66 (31.8%)	45/66 (68.2%)	
24h-ECG (Holter)	reduced	9/26 (34.6%)	17/26 (65.4%)	0.125
	normal	14/25 (56.0%)	11/25 (44.0%)	
At discharge	reduced	27/64 (42.2%)	37/64 (57.8%)	0.075
	normal	36/62 (58.1%)	26/62 (41.9%)	
Pre Fontan operation	reduced	43/67 (64.2%)	24/67 (35.6%)	0.583
	normal	46/67 (68.7%)	21/67 (31.3%)	

Table 19: Normofrequent sinus rhytm in children with reduced exercise capacity before Fontan operation.

3.5.3.3 Medication

Of all arrhythmogenic medication, e.g., catecholamine, cardiac glycosides, or ß blocker, only catecholamine therapy showed a significant influence on the development of arrhythmia early after FO (Table 20). Other medication had no significant impact (Table 21, Table 22).

	NFQ SR	others	P
Early postoperatively	11/66 (16.7%)	55/66 (83.3%)	0.045
24h(Holter) ECG	11/24 (45.8%)	13/24 (54.2%)	0.916
At discharge	34/63 (54.0%)	29/63 (46.0%)	0.377

Table 20: Arrhythmia in patients with catecholamine therapy.

	NFQ SR	others	P
Early postoperatively	1/7 (14.3%)	6/7 (85.7%)	0.509
24h(Holter) ECG	2/3 (66.7%)	1/3 (33.3%)	0.439
At discharge	4/7 (51.1%)	3/7 (42.9%)	0.686

Table 21: Arrhythmia in patients with cardiac glycoside therapy.

	NFQ SR	others	P
Early postoperatively	0/3 (0%)	3/3 (100%)	0.315
24h(Holter) ECG	0	0	0
At discharge	1/3 (33.3%)	2/3 (66.7%)	0.567

Table 22: Arrhythmia in patients with ß blocker therapy.

Most children who presented with sinus tachycardia (N 58) or non-sinus tachycardia (N 21) were given postoperative adrenalin therapy (postoperatively ST: adrenalin therapy 30/58 (51.7%) vs no adrenalin therapy 28/58 (48.3%), P 0.038; non-ST: adrenalin therapy 13/21 (61.9%) vs no adrenalin therapy 8/21 (38.1%), P 0.037). Children who received postoperative glycoside therapy experienced sinus tachycardia more frequently, but not non-sinus tachycardia (cardiac glycosides: ST 5/7 (71.4%) vs others 2/7 (28.6%), P 0.046; non-ST 1/7 (14.3%) vs others 6/7 (85.7%), P 0.921). No correlation was seen between other types of medication, e.g., milrinon, noradrenalin, dobutamin, or ß blockers, and the development of postoperative tachycardia (see tables below for all results).

	Therapy -/+	ST -/+	P
Adrenalin	- 95/161	- 67/95 (70.5%)	0.038
		+ 28/95 (29.5%)	
	+ 66/161	- 36/66 (54.5%)	
		+ 30/66 (45.5%)	
Digoxin	- 154/161	- 101/154 (65.6%)	0.046
		+ 53/154 (34.4%)	
	+ 7/161	- 2/7 (28.6%)	
		+ 5/7 (71.4%)	
Milrinon	- 35/161	- 26/35 (74.3%)	0.151
		+ 9/35 (25.7%)	
	+ 126/161	- 77/126 (61.1%)	
		+ 49/126 (38.9%)	
Dobuatmin	- 142/161	- 94/142 (66.2%)	0.108
		+ 48/142 (33.8%)	
	+ 19/161	- 9/19 (47.4%)	
		+ 10/19 (52.6%)	
Noradrenalin	- 160/161	- 103/160 (64.4%)	0.181
		+ 57/160 (35.6%)	
	+ 1/161	- 0/1 (0%)	
		+ 1/1 (100%)	
ß-blockers	- 158/161	- 101/158 (63.9%)	0.922
		+ 57/158 (36.1%)	
	+ 3/161	- 2/3 (66.7%)	
		+ 1/3 (33.3%)	

Table 23: Sinus tachycardia in correlation to postoperative medication after Fontan operation.

	Therapy -/+	non-ST -/+	P
Adrenalin	- 95/161	- 87/95 (91.6%)	0.037
		+ 8/95 (8.4%)	
	+ 66/161	- 53/66 (80.3%)	
		+ 13/66 (19.7%)	
Digoxin	- 154/161	- 134/154 (87.0%)	0.921
		+ 20/154 (13.0%)	
	+ 7/161	- 6/7 (85.7%)	
		+ 1/7 (14.3%)	
Milrinon	- 35/161	- 32/35 (91.4%)	0.375
		+ 3/35 (8.6%)	
	+ 126/161	- 108/126 (85.7%)	
		+ 8/126 (14.3%)	
Dobuatmin	- 142/161	- 124/142 (87.3%)	0.705
		+ 18/142 (12.7%)	
	+ 19/161	- 16/19 (84.2%)	
		+ 3/19 (15.8%)	
Noradrenalin	- 160/161	- 139/160 (86.9%)	0.698
		+ 21/160 (13.1%)	
	+ 1/161	- 1/1 (100%)	
		+ 0/1 (0%)	
ß-blockers	- 158/161	- 138/158 (87.3%)	0.292
		+ 20/158 (12.7%)	
	+ 3/161	- 2/3 (66.7%)	
		+ 1/3 (33.3%)	

Table 24: Non-sinus tachycardia in correlation to postoperative medication after Fontan operation.

3.5.3.4 CPB time and aortic cross-clamping time

Patients without NFSR (no NFSR) in the early postoperative period underwent significantly longer CPB (median CPB: NFSR 45.5(23-214) min vs no NFSR 59(28-433) min; P 0.008) during Fontan repair (Table 26).

Aortal cross-clamping time, if necessary, had no impact on the occurrence of NFSR in the early postoperative period (NFSR 38.3 ±15.9 vs no NFSR 35.9±13.6 min; P 0.625) (Table 26). However, patients who underwent the FO without aortal cross-clamping showed significantly more NFSR at all times (Table 27).

Patients who developed junctional ectopic tachycardia (JET) in the first few days after Fontan repair had longer periods of CPB, but this was statistically not significant (JET mean 95.1±112.9 min vs no JET mean 65.4±35.2 min; P 0.395).

The cases with postoperative sinus tachycardia (ST) had longer but not significant CPB (ST 73.8±38.6 min vs 62.8±47.7 min; P 0.134).

The occurrence of AET at any time was not influenced by CPB or aortal cross-clamping time. This also applied to any form of bradycardia.

	LT	EC	P
CPB (min)	61* (36-122)	50* (23-214)	0.004
Aortic cross-clamping (min)	34.85±10.4	39.38±22.1	0.484

Table 25: Operation parameters: LT vs EC - presented as means with standard deviation or (*) medians with range.

	Sinus NFQ	others	P
CPB (min)*	46* (23-214)	59* (28-433)	0.008
Aortic cross-clamping (min)	38.3±15.9	35.9 ±13.6	0.625

Table 26: Operation parameters: Sinus NFQ vs others early post OP - presented as means with standard deviation or (*) medians with range.

	Aortic cross-clamping (N = 69)	None (N = 102)	P
Sinus rhythm nfq, early post OP	10 (15.6%)	30 (30.9%)	0.028
Sinus rhythm nfq, 24h(Holter) ECG	12 (37.5%)	15 (53.6%)	0.212
Sinus rhythm nfq, at discharge	26 (39.4%)	51 (58.3%)	0.027

Table 27: Normofrequent sinus rhythm in the course of hospitalization in correlation to aortal cross-clamping.

3.5.3.5 First stage operations

Children who underwent the Norwood operation combined with a RV-PA shunt were more likely than those without a combined RV-PA shunt to develop ventricular extrasystoles (VES) during hospitalization after FO (VES after Fontan: RV-PA 3/76 (3.8%), no RV-PA 0/92, P 0.059). However, no correlation was seen between RV-PA combined with the Norwood operation and the incidence of VES before FO (VES before FO: RV-PA 1/79 (1.5%), no RV-PA 6/86 (6.5%), P 0.084).

3.5.3.6 Effect of Fontan type repair on the development of arrhythmia

The main interest of the study was to analyze the impact of the type of Fontan repair on the development of arrhythmia. The two groups were compared regarding all possible forms of arrhythmia at the various points of time.

Directly after Fontan repair, only 23.8% of all patients showed NFSR, whereas 76.2 % had diverse forms of arrhythmia, including sinus tachycardia and normofrequent atrial ectopic rhythm up to JET (for the differences between the two groups LT/EC early postoperatively, see Table 28).

	LT N=53	EC N=106	P
Sinus rhythm nfq	8 (15.1%)	32 (30.2%)	0.039
Atrial ectopic nfq	2 (3.8%)	8 (7.5%)	0.498
Junctional ectopic nfq	11 (20.8%)	8 (7.5%)	0.016
Sinus tachycardia	13 (24.5%)	45 (42.5%)	0.027
Atrial ectopic tachycardia	4 (7.5%)	6 (5.7%)	0.732
Junctional ectopic tachycardia	10 (18.9%)	0	< 0.001
Pacemaker	3 (5.7%)	2 (1.9%)	
Sinus bradycardia	0	2 (1.9%)	0.553
Atrial ectopic bradycardia	0	0	
Junctional ectopic bradycardia	2 (3.8%)	3 (2.8%)	1.000
Bradycardia all	2 (3.8%)	5 (4.7%)	0.785
Tachycardia(without sinus)	14 (26.4%)	6 (5.7%)	< 0.001

Table 28: Rhythm forms early postoperatively – LT vs EC.

Directly after Fontan repair, NFSR occurred more frequently in the EC group (LT 15% vs EC 30.2%, P 0.039). In 24h (Holter) ECG results regarding NFSR, the EC group appeared to be superior (LT 30% vs EC 58%, P 0.030). Moreover, at the time of discharge, the EC group had a higher incidence of NFSR (LT 36.5% vs EC 56%, P 0.020) (Table 31, Figure 10).

	Early post OP (N = 159)		24h(Holter) ECG (N = 60)		At discharge (N = 153)	
	LT(53)	EC (106)	LT (27)	EC (33)	LT (52)	EC (101)
Sinus rhythm nfq	8 (15.1%)	32 (30%)	8 (30%)	19 (58%)	19 (37%)	57 (56%)

Table 29: Normofrequent sinus rhythm in the course of hospitalization.

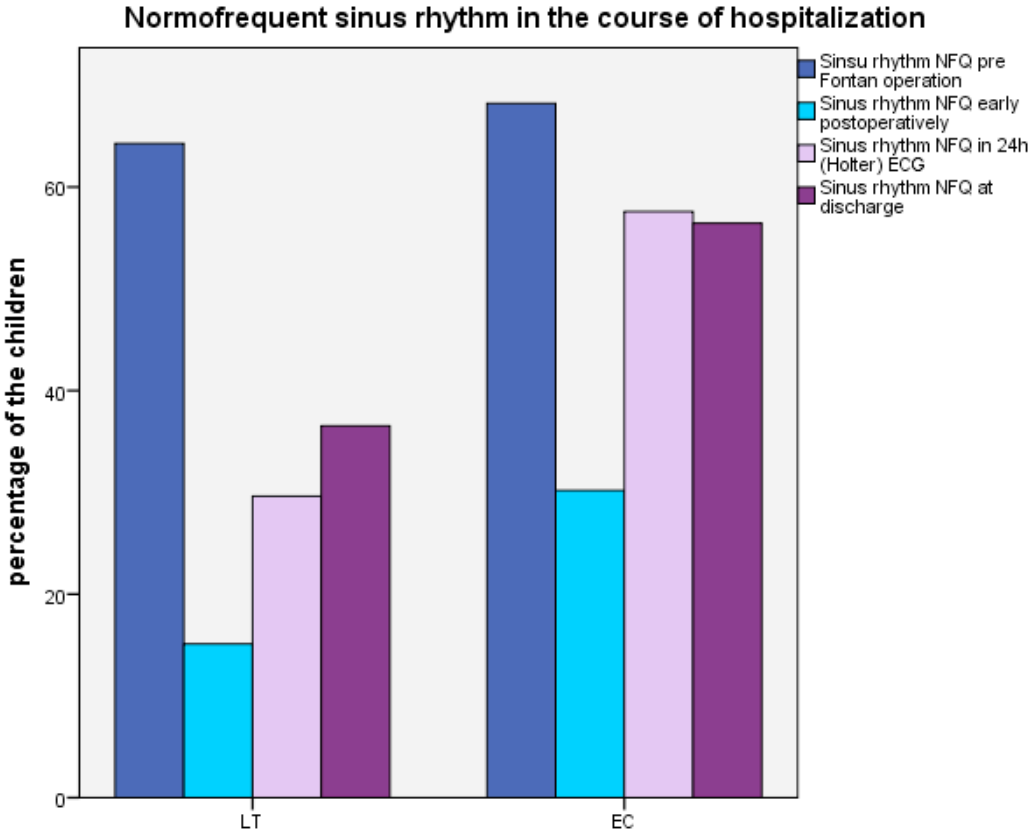

Figure 10: Normofrequent sinus rhythm in the course of hospitalization.

The incidence of normofrequent atrial ectopic rhythm did not differ significantly between the two groups at any time point, even though the EC group seemed to show a slightly higher percentage of normofrequent atrial ectopic rhythm (LT 3.8% vs EC 7.5%; P 0.498) directly after Fontan repair.

Normofrequent junctional ectopic rhythm early postoperatively after Fontan repair was significantly more frequent in the LT group (LT 20.8% vs EC 7.5%, P 0.016). Even more significant results were presented at discharge (LT 17.3% vs 1.0%, P <0,001). A similar trend could be seen in long-term ECG analyses (LT 18.5% vs EC 6%, P 0.135).

JET during the early postoperative period appeared only in LT patients (LT 18.9% vs EC 0%, P < 0.001).

AET occurred in both groups without significant differences (LT 7.5% vs EC 5.7%, P 0.644 early post-operative period; LT 1.9% vs EC 2.0%, P 0.981 at discharge).

Postoperative bradycardia and sinus node dysfunction, excluding the above-mentioned forms, did not differ significantly between the two groups (LT 3.8% vs EC 4.7%, P 0.785 early postoperative period; LT 5.8 vs EC 5.9%, P 1.000 at discharge).

Some patients demonstrated postoperative sinus tachycardia; this was more frequent in the EC group (LT 24.5% vs EC 42.5%, P 0.027). However, at the time of discharge and in long-term ECG analyses, the two groups did not differ from each other with regard to sinus tachycardia (LT 21.2% vs EC 24.8%, P 0.619 at discharge; LT 7.4% vs EC 6.1%, P 0.835 in long-term ECG).

Table 28, 29, 30, and 31 show the rhythm variations between the two groups (LT, EC) at the various points of time. Figures 11 to 15 show the different forms of ectopic rhythm and their development during hospitalization.

	LT N=27	EC N=33	P
Sinus rhythm nfq	8 (29.6%)	19 (57.6%)	0.030
Atrial ectopic nfq	0	3 (9.1%)	0.245
Junctional ectopic nfq	5 (18.5%)	2 (6.1%)	0.135
Sinus tachycardia	2 (7.4%)	2 (6.1%)	0.835
Atrial ectopic tachycardia	1 (3.7%)	0	0.450
Junctional ectopic tachycardia	0	0	
Pacemaker	1 (3.7%)	0	
Sinus bradycardia	0	3 (9.1%)	0.245
Atrial ectopic bradycardia	2 (7.4%)	2 (6.1%)	1.000
Junctional ectopic bradycardia	7 (25.9%)	2 (6.1%)	0.065
Bradycardia all	9 (33.3%)	7 (21.2%)	0.291
Tachycardia(without sinus)	1 (3.7%)	0	0.450

Table 30: Rhythm forms in 24h-Holter ECG – LT vs EC.

	LT N=52	EC N=101	P
Sinus rhythm nfq	19 (36.5%)	57 (56.4%)	0.020
Atrial ectopic nfq	8 (15.4%)	7 (6.9%)	0.096
Junctional ectopic nfq	9 (17.3%)	1 (1%)	< 0.001
Sinus tachycardia	11 (21.2%)	25 (24.8%)	0.619
Atrial ectopic tachycardia	1 (1.9%)	2 (2.0%)	1.000
Junctional ectopic tachycardia	0	0	
Pacemaker	1 (1.9%)	3 (3.0%)	
Sinus bradycardia	1 (1.9%)	4 (4.0%)	0.662
Atrial ectopic bradycardia	1 (1.9%)	2 (2.0%)	1.000
Junctional ectopic bradycardia	1 (1.9%)	0	0.340
Bradycardia all	3 (5.8%)	6 (5.9%)	1.000
Tachycardia(without sinus)	1 (1.9%)	2 (2.0%)	1.000

Table 31: Rhythm forms at discharge – LT vs EC.

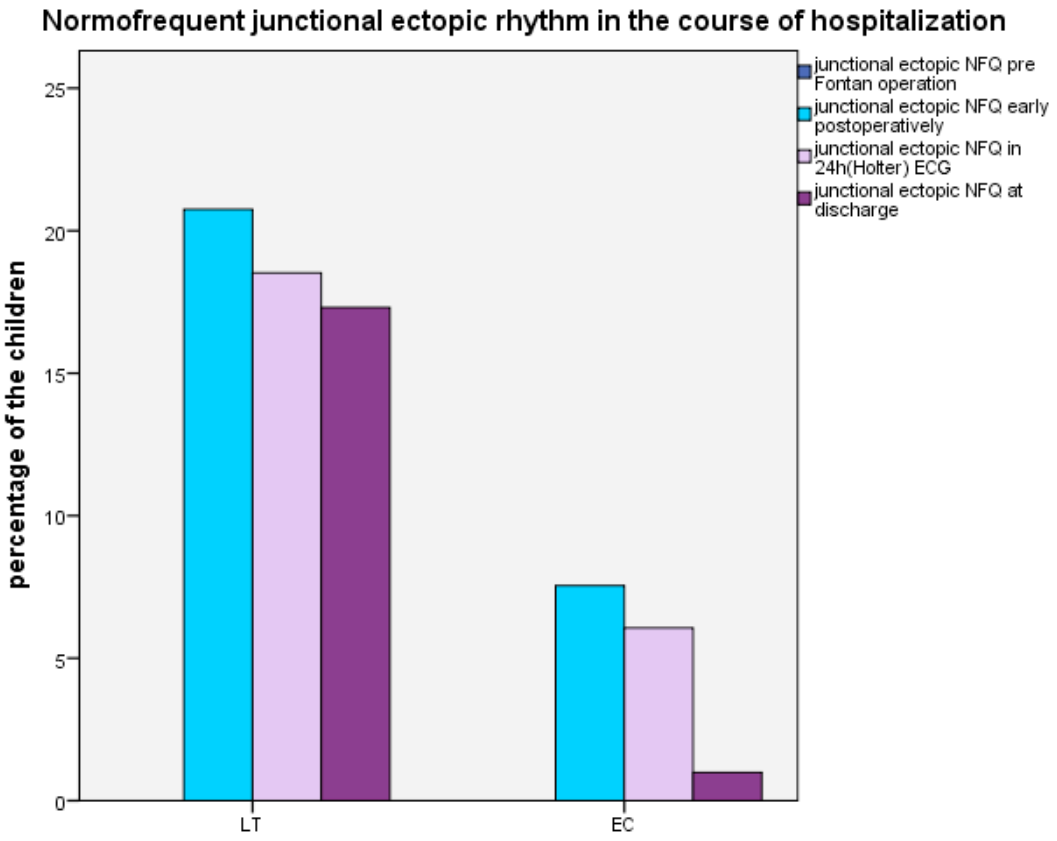

Figure 11: Normofrequent junctional ectopic rhythm in the course of hospitalization – LT vs EC.

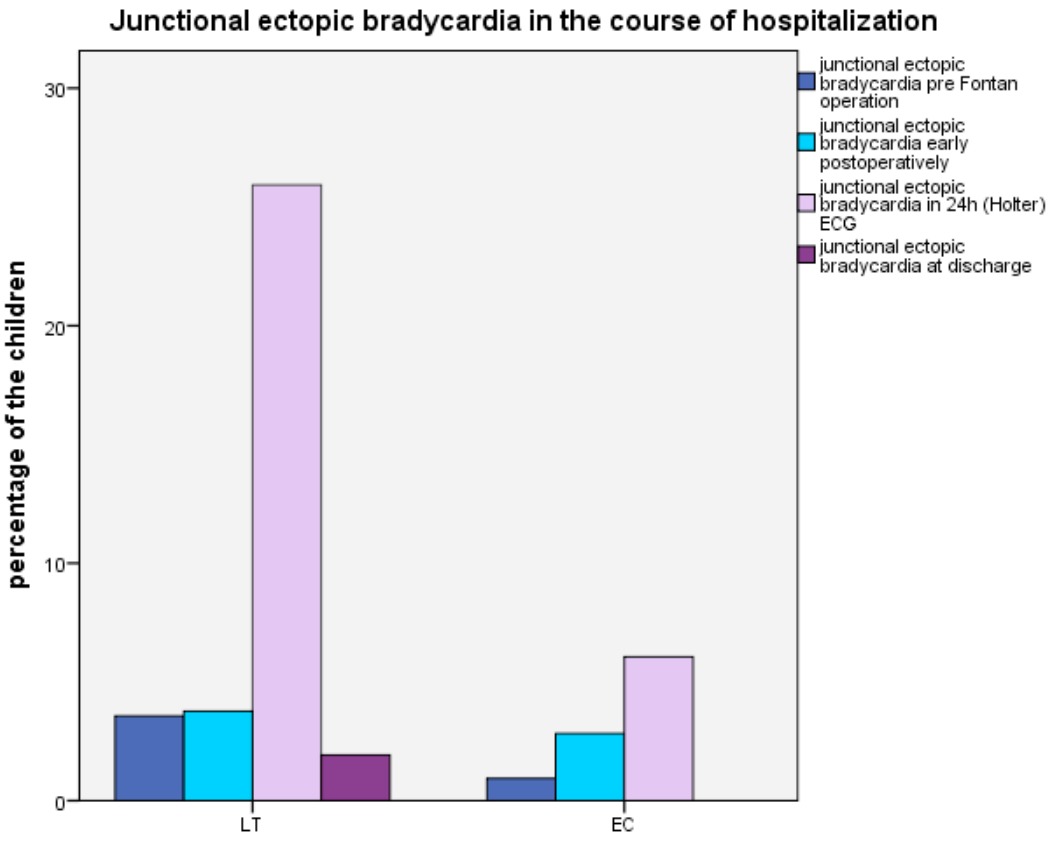

Figure 12: Junctional ectopic bradycardia in the course of hospitalization – LT vs EC.

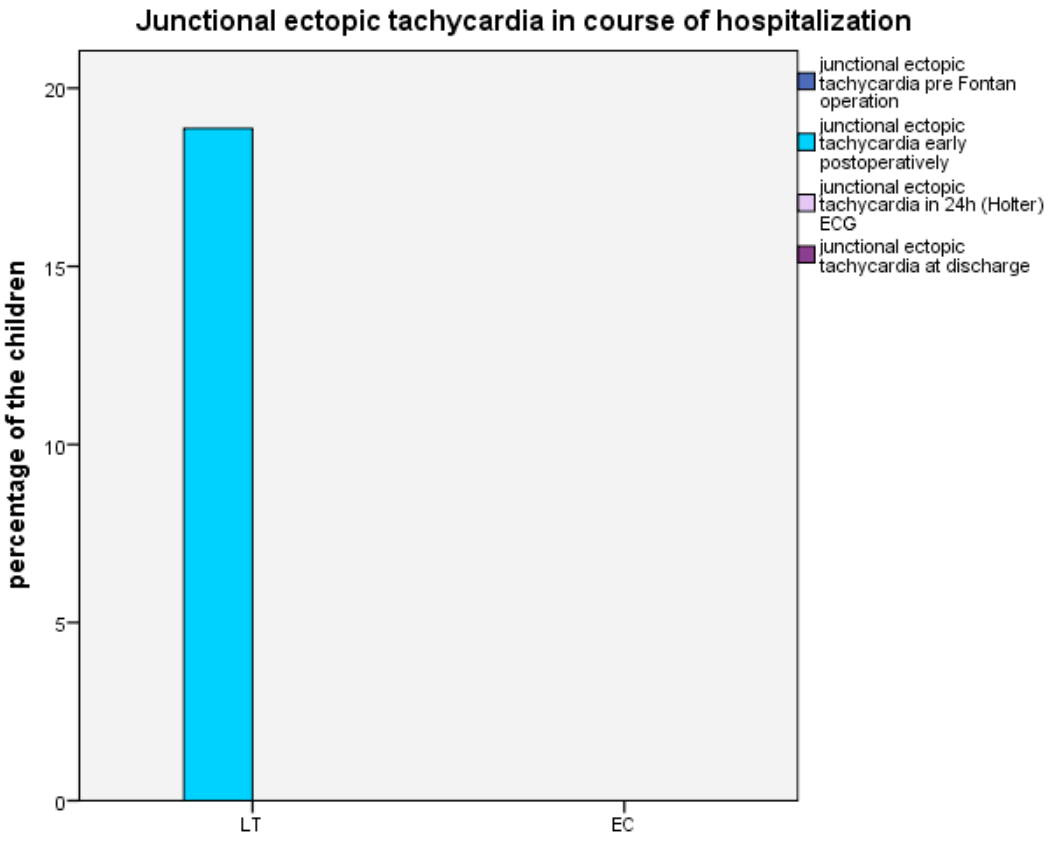

Figure 13: Junctional ectopic tachycardia in the course of hospitalization – LT vs EC.

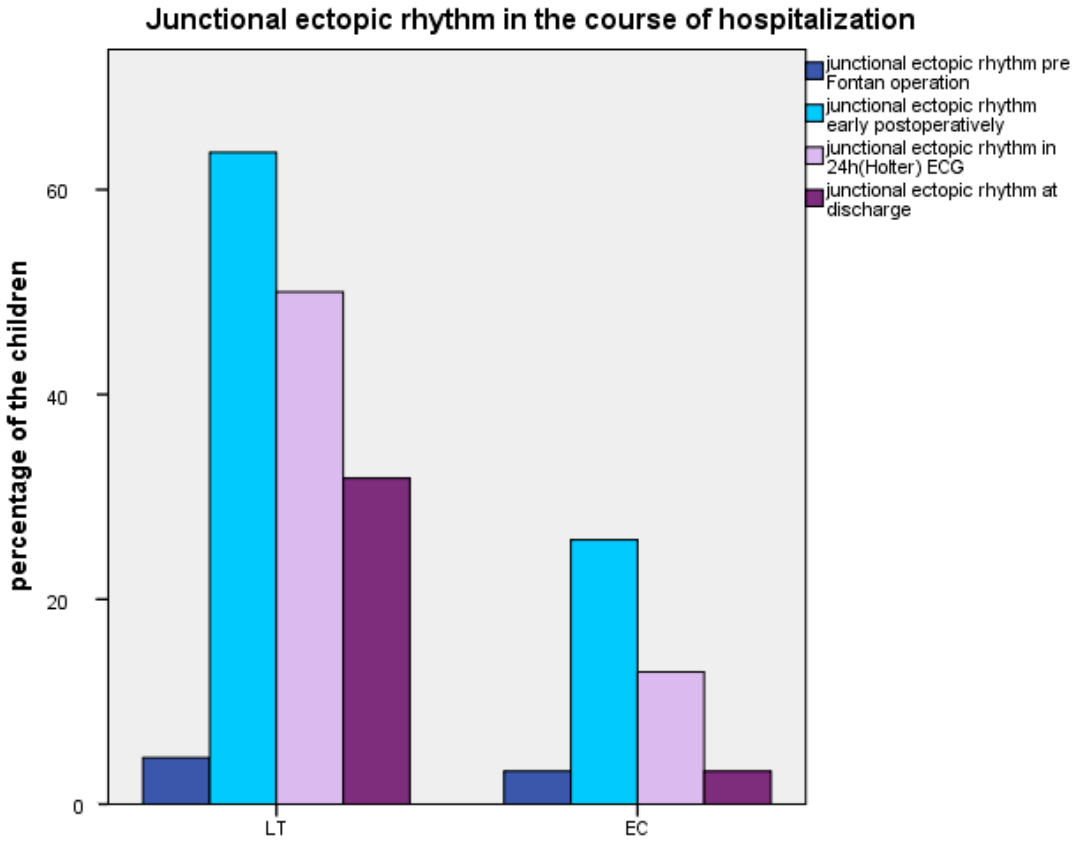

Figure 14: Junctional ectopic rhythm in the course of hospitalization - LT vs EC.

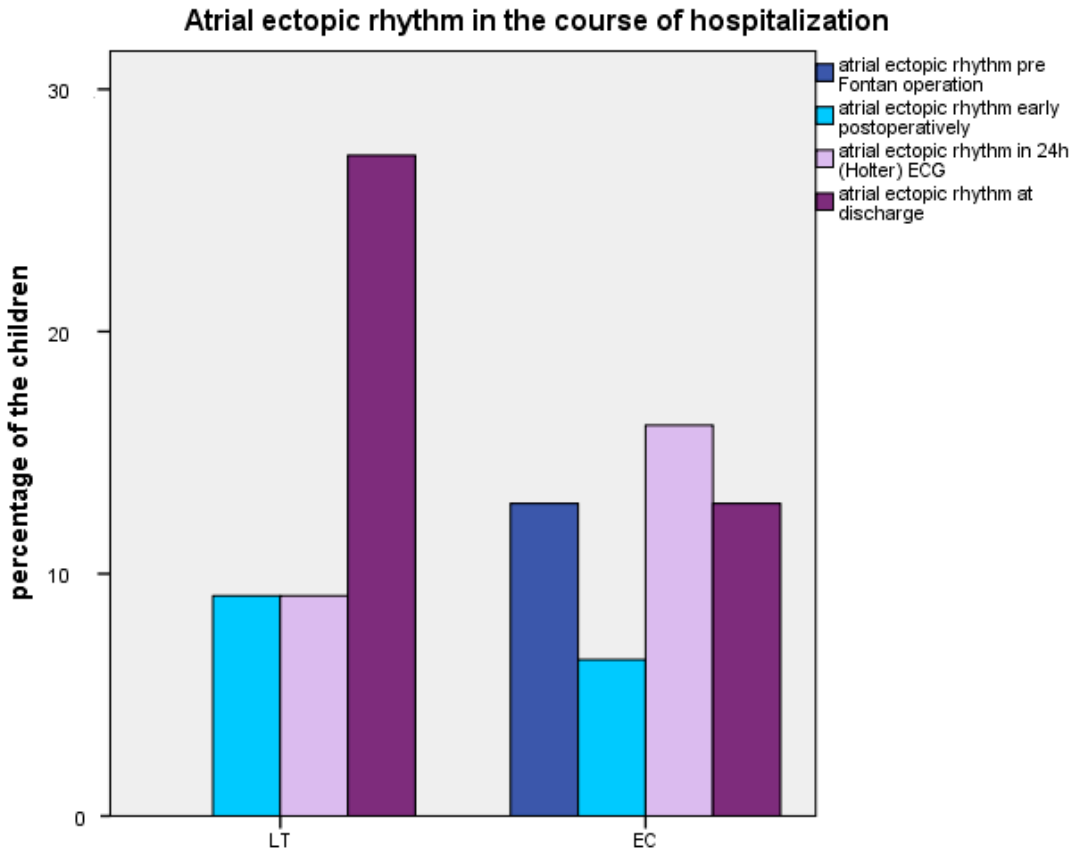

Figure 15: Atrial ectopic rhythm in the course of hospitalization - LT vs EC.

3.5.4 Consequences and complications of arrhythmia

3.5.4.1 Intubation time

Patients without NFSR (no NFSR) in the early postoperative period had a longer intubation time (mean intubation time: NFSR 11.9h vs no NFSR 19.3h, P 0.371) after the Fontan procedure, but the differences did not reach statistical significance. The cases with postoperative sinus tachycardia (ST) experienced a longer intubation time (ST 27.1 h vs no ST 11.8 h, P 0.105). Intubation time was not

influenced by the occurrence of AET at any time. This also applied to all forms of bradycardia (see Table 32).

	Intubation time (h)	P
Sinus NFQ	11.9±18.9	0.371
others	19.3±50.4	
Juncitional ectopic tachycardia	24.5±46.7	0.628
others	17.0±44.7	
Sinus tachycardia	27.1±68.8	0.105
others	11.8±19.0	

Table 32: Infuence of rhythm on the intubation time – presented as means with standard deviation.

3.5.4.2 Time of hospitalization and ICU time

No difference was detected between the mean ICU time or time of hospitalization between the groups with and without NFSR during the early postoperative period (NFSR 4.6 and 17.4 days vs no NFSR 5.4 and 17.3 days, P 0.242 and 0.942, respectively).

The occurrence of JET, AET, or sinus tachycardia had no significant impact on ICU time or time of hospitalization. This was similar for all forms of bradycardia.

3.5.4.3 Medication during hospitalization

Of those patients who presented with early postoperative non-sinus tachycardia (N 21), only 9.5% (2/21) required amiodarone, and only 4.5% (1/21) needed adenosine.

Of the patients who presented with postoperative bradycardia, 42.9% (3/7) had dopamine as their only medication, with other medication having only a frequency of 13.6% (20/154), P 0.027.

3.5.4.4 Medication at discharge

	All	LT	EC	P
ACE	33 (19.3%)	15 (26.8%)	18 (15.9%)	0.094
Digoxine	7 (4.1%)	1 (1.8%)	6 (5.3%)	0.279
ß Blockers	3 (1.8%)	1 (1.8%)	2 (1.8%)	1.000

Table 33: Medication at discharge – LT vs EC.

3.5.4.5 Effusions

Some 22.0% of all children had prolonged effusions. Patients with bradycardia during 24h-Holter ECG analyses, especially atrial ectopic bradycardia, tended to have more prolonged effusions than others (prolonged effusions: bradycardia 7/16 (43.8%) vs no bradycardia 7/37 (15.9%), P 0.024; atrial ectopic bradycardia 4/4 (100%) vs no atrial ectopic bradycardia 10/56 (17.9%), P 0.002). No correlation was detected between other forms of arrhythmia at other times of ECG analysis (early postoperatively, at discharge) and the development of prolonged effusions.

Patients with sinus bradycardia in long-term ECG during hospitalization developed higher amounts of pleural effusion on the right side (22.4 (18.4-23.9) ml/kg/d vs children without sinus bradycardia 12.3 (2.2-38.8) ml/kg/d, p=0.017).

	LT	EC	P
Pericardial drainage (ml/kg/d)	9.98±15.03	8.48±5.7	0.366
LP drainage (ml/kg/d)	11.6±10.1	11.4±7.3	0.929
RP drainage (ml/kg/d)	10.7*(1.2-25)	12.7*(1.3-52)	0.061
Ascites (ml/kg/d)	61.03±27.77	51.81±52.8	0.749

Table 34: Effusions during hospitalization – LT vs EC - presented as means with standard deviation or (*) medians with range (LP – left pleura, RP – right pleura).

	LT	EC	P
Pericardial drainage (d)	2.55±1.77	2.98±3.09	0.338
LP drainage (d)	2.20±4.20	2.96±5.42	0.359
RP drainage (d)	6.16±5.69	8.20±7.62	0.053
Ascites (d)	0.73±3.02	0.62±2.39	0.793

Table 35: Duration of effusions – LT vs EC - presented as means with standard deviation.

Even if not statistically significant, the effusions of the RP drainage were of a higher amount in patients without fenestration (Table 36). The children with fenestration showed lower incidence of prolonged effusions (P 0.030) (Table 37) (12.5 % vs. 27.7%).

	No Fenestration	Fenestration	P
Pericardial drainage (ml/kg/d)	8.45±5.9	9.89±15	0.421
LP drainage (ml/kg/d)	10.66±5.9	11.37±10.4	0.742
RP drainage (ml/kg/d)	12.98±6.8	10.79±5.3	0.050
Aszites (ml/kg/d)	38.04±19.3	61.57±26.9	0.098

Table 36: Effusions during hospitalization (patients with vs without fenestration) - presented as means with standard deviation.

	No Fenestration (N = 94)	Fenestration (N = 56)	P
None	68 (72.3%)	49 (87.5%)	0.030
Prolonged effusions	26 (27.7%)	7 (12.5%)	

Table 37: Prolonged effusions - (patients with vs without fenestration).

Patients with prolonged effusions had a longer duration of hospitalization (P < 0.001). However, effusions had no impact on ICU time (Table 38).

	None	Prolonged effusions	P
ICU time (days)	5.0 ± 3.6	6.6 ± 6.3	0.151
Hospitalization time (days)	13* (5-41)	25* (11-67)	< 0.001

Table 38: Time of ICU or hospitalization in correlation to effusion - presented as means with standard deviation or (*) medians with range.

3.5.4.6 Temporary heart stimulation

Temporary pacemaker stimulation (AAI) was required in 24.3% of the patients after Fontan repair (LT 44.6% vs EC 14.2%, P < 0.001), but in most cases (88.1%, LT 92.3 vs EC 81.3%, P 0.281) for less than 5 days.

The most frequent reason for a temporary pacemaker was a junctional ectopic rhythm (75.6%, LT 76.0 vs EC 75.0%), followed by atrial ectopic rhythm (12.2%, LT 12.0 vs EC 12.5%; Table 39, Figure 16).

	All (N=169)	LT (N=56)	EC (N=113)	P
Need for pacing	41 (24.3%)	25 (44.6%)	16 (14.2%)	< 0.001
Junctional ectopic	31/41 (75.6%)	19/25 (76.0%)	12/16 (75.0%)	0.001
Atrial ectopic	5/41 (12.2%)	3/25 (12.0%)	2/16 (12.5%)	0.334
Bifascicular block	1/41 (2.4%)	0/25 (0.0%)	1/16 (6.3%)	1.0
Sinus bradycardia	1/41 (2.4%)	1/25 (4%)	0/16 (0%)	0.331
Defective pacemaker	1/41 (2.4%)	0/25 (0%)	1/16 (6.3%)	1.0
Ventricular tachycardia	1/41 (2.4%)	1/25 (4%)	0/16 (0%)	0.331
Atrioventricular block	1/41 (2.4%)	1/25 (4.0%)	0/16 (0.0%)	0.331

Table 39: Reasons for postoperative temporary pacemaker stimulation.

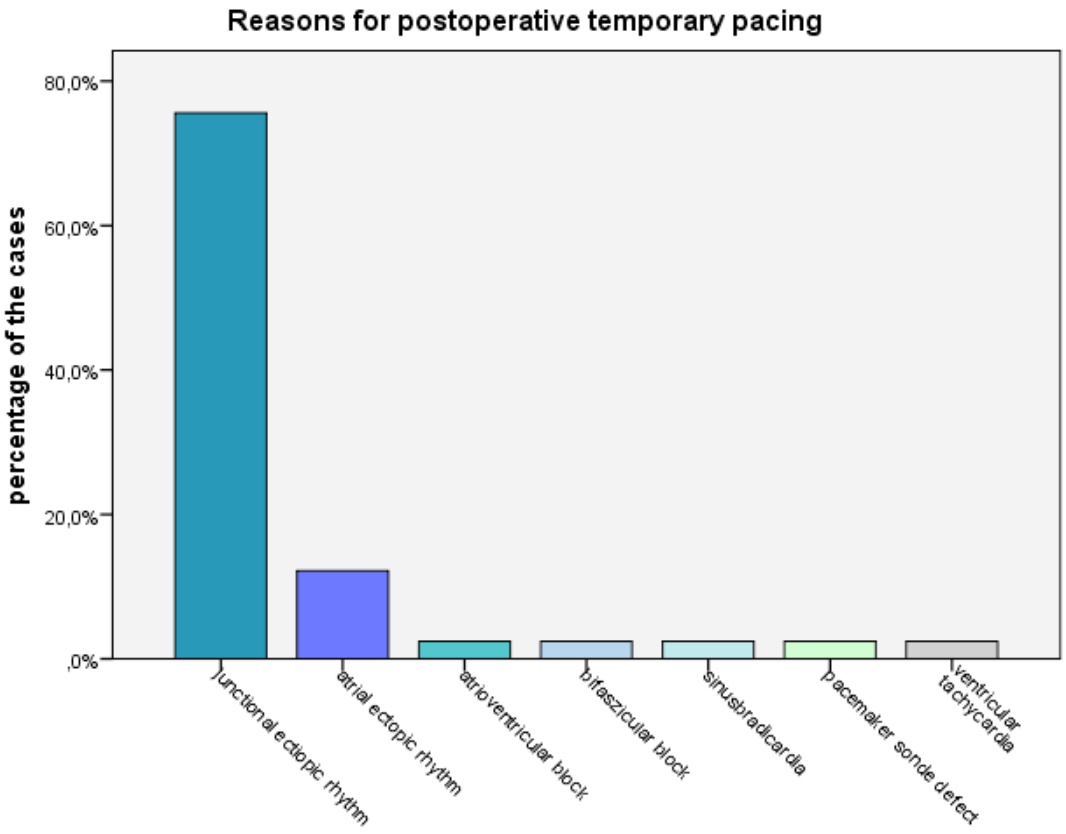

Figure 16: Reasons for use of postoperative temporary pacemaker.

3.5.4.7 Permanent heart stimulation

New implantation of a permanent pacemaker during hospitalization after FO was necessary in two (1.2%) of the children (LT 1/56 (0.9%) vs EC 1/113 (1.8%), P 1.000).

3.6 Binary logistic regression

The OP variant (LT, EC), CPB and age at FO were included as covariates in the model to value their influence on the development of arrhythmias after FO.

For this binary logistic regression model the LT OP variant was the only independent predictor of the development of arrhythmias after FO.

LT was the only independent predictor for no NFSR early postoperatively (OR 1.43 vs EC; P 0.042), in 24h (Holter) ECG (OR 2.22 vs EC; P 0.033) and at discharge (OR 1.25 vs EC; P 0.021).

Besides LT was the only independent predictor for normofrequent junctional ectopic rhythm early postoperatively (OR 2.21 vs EC; P 0.02) and at discharge (OR 19.93 vs EC; P 0.004). In 24h (Holter) ECG no significant influence of the above-mentioned covariates could be detected by binary logistic regression.

For the need of postoperatively temporary pacing independent significant predictors were LT (OR 3.9 vs EC; P < 0.000) as well as CPB (OR 0.01; P 0.042).

Additionally including the need for aortal cross-clamping as covariate to the model, the binary logistic regression showed slightly different results. Early postoperatively the need for aortal cross-clamping is the only independent predictor for no NFSR (OR 1.32 vs no aortal cross-clamping; P 0.039). However, LT is still the only independent predictor for no NFSR in 24h (Holter) ECG (OR 2.22 vs EC; P 0.033) and at discharge (OR 1.25 vs EC; P 0.021).

4 Discussion

The main interest of the study was to determine the effect of Fontan repair on the development of arrhythmia in the early period after FO. Arrhythmia is still one of the most frequent complications that can lead to morbidity and mortality after FO. Therefore, the incidence of arrhythmia needs to be reduced or even avoided.

The aim of our study has been to detect possible risk factors that might influence the occurrence of arrhythmia in Fontan patients. Of special interest has been the influence of the type of FO on the development of arrhythmia. Furthermore, complications caused by arrhythmia have been analyzed, and other differences between the intracardiac (LT) and extracardiac (EC) FO have been detected and analyzed.

All patients included in our study underwent the FO at a single institution. Surgery was performed in two constant operative techniques. During the years from 2004 to 2012, the two modifications of Fontan repair (LT, EC) were performed in parallel. Hence, because of both types of FO occurred within the same institution, patients from the two groups received the same treatment protocol during operation and hospitalization. This is of great value compared with other studies, which often refer to a historical group or compare patients form different centers.

4.1 Arrhythmia in Fontan patients

The results of our study clearly show a significantly higher incidence of arrhythmia in the first weeks after FO in patients who undergo LT Fontan surgery compared with those who had an EC FO. Hence, we wanted to analyze whether the type of Fontan repair primarily caused arrhythmia, or whether other variables influenced these results.

4.1.1 Differences before Fontan operation and their possible impact on the development of arrhythmia after this procedure

4.1.1.1 Demographic and clinical differences

Before FO, most of the patients showed NFSR (109, 66.9%). Furthermore, no significant difference was noted between the groups regarding the incidence of NFSR before FO (LT 36(64.3%) vs EC 73(68.2%), P 0.612).

However the two groups showed other preoperative differences. Thus, our interest was to ascertain whether the various forms of FO, rather than demographic differences, triggered arrhythmia. The groups showed demographic differences regarding gender and type of malformation. In the LT group, boys (P 0.001) and single ventricle of right ventricular morphology (P 0.002) were overrepresented. This is because the incidence for HLHS, which means a right ventricular morphology, is higher in boys. In general, 70% of all children with HLHS are boys. This explains the overrepresentation of boys in the LT group. Nevertheless, neither boys nor patients with single right ventricle morphology tended to develop

arrhythmia any more frequently after FO than the other patients. We could not find any comments in previous studies regarding the influence of sex on the development of arrhythmia after FO. However, patients with single right ventricle morphology are known generally to have a worse outcome than others [41-43]. This is based on a poorer coronary arterial perfusion of the right ventricle [44]. The molecular biology of the right ventricular myocardium and the geometry of the ventricle anatomy and the anatomy of the tricuspid valve also play an important role [42, 45, 46]. Thus, the single right ventricle has a lower cardiac output and a higher atrial pressure [47].

In cardiac catheterization performed before FO, the EC group had a higher aortic saturation (P 0.019) and a higher pulmonary-to-systemic flow ratio (P 0.006). The possible reason for this finding could be that more children in the EC group had an additional pulmonary flow source, i.e., apart from Glenn, additional antegrade flow through the main pulmonary artery, a still open aortopulmonary shunt, or more collateral vessels (MAPCAs). Before FO, fewer of the EC children showed reduced exercise capacity than those from the LT group (P 0.041). In our study, children who had a reduced exercise capacity before FO were more likely not to develop NFSR at discharge after FO (P 0.075).

Moreover, children with signs of cardiac hypertrophy, which can also be a reason for reduced exercise capacity, were more likely not to develop NFSR early postoperatively (P 0.120) and at discharge (P 0.055). Even if these differences are not significant, other studies have described a significantly higher risk for arrhythmia [35] and Fontan failure [48] [41] in children with ventricular hypertrophy.

As well as hypertrophy and single right ventricle morphology, heterotaxy syndrome is known to be a risk factor of arrhythmia, as described by Kim et al. [49].

In a study of Stamm et al. [50], heterotaxy was the only patient-related risk factor for early and late arrhythmias. In patients with heterotaxy, numerous abnormalities in the conduction system are able to activate arrhythmia, irrespective of the type of Fontan repair, e.g., twin atrioventricular node, dual sinus node, and atrioventricular blocks [51].

In our study, patients with heterotaxy syndrome presented with higher numbers of no NFSR before FO, even though we could not show an elevated risk for arrhythmia after Fontan surgery in those patients.

AV valve insufficiency, as described by Durongpistikul [52], exhibited no relationship to arrhythmia after FO in our study.

In our study, the lowest risk for developing arrhythmia, without considering the type of Fontan repair, was for children who underwent FO at the age of 2 to 4 years. This differs from the age that was originally set for the FO selection criteria by Choussat and his colleagues in 1977. In their selection criteria, they suggested a minimum age of 4 years. However, today, these criteria have become less strict [53, 54]. Our study shows better outcomes with regard to arrhythmia at discharge for patients of a younger age (2-4y). Undergoing FO at a younger age means an overall shorter period of time in which the ventricle is exposed to insufficient oxygenated blood. Chronic hypoxemia to the ventricle and, therefore, to the conduction tissue is known to cause fragility to the system and more fibrosis in the atrial wall. These reactions consecutive disturb rhythm conduction and therefore lead to arrhythmia. Another reason could be the insufficient AV valve in the single ventricle circulation before FO. A longer or higher level of insufficiency of the AV valve means more distension of the atria, which in consequence leads to a higher risk for arrhythmia. However, no

relationship between the level of AV insufficiency before FO and the incidence of arrhythmia after FO could be seen in our study. In addition, in general terms, a younger organism has a better regeneration potential.

4.1.1.2 Previous operations

With regard to the influence of operations carried out previously to FO, no difference was noted to the prevalence of arrhythmia if the children had undergone a hemi-Fontan or Glenn operation before FO in our study. Thus, the second stage operation (Glenn, hemi-Fontan) seems to have no impact on the development of arrhythmia. In a study performed by Reichlin et al. [55], children after a bidirectional cardiopulmonary anastomosis demonstrated only mild forms of arrhythmia early postoperatively, most frequently, sinus bradycardia. None of the forms were life-threatening, and all were transient, and so, in most cases, the children had stabilized with a NFSR by the time of discharge. A study by Cohen et al. [56] showed similar results. According to their investigations, children who underwent a hemi-FO had arrhythmia more frequently at the first day after the operation than those who underwent a Glenn operation. However, at discharge, again, there was no difference. The Glenn operation includes a transection of the SVC at 5-10 mm above the right atrial junction with a closure of the cardiac end of the SVC and a connection to the ipsilateral pulmonary artery. In contrast, in the hemi-FO, the incision is performed from the superior part of the atrium, close to the sinus node, until the medial part of the SVC [56]. Hence, the sinus node and the sinus node artery are directly exposed to injury. As the previous hemi-FO facilitates completion

with a LT Fontan, these children are then once again exposed to the manipulation of the atrium and incisions next to the sinoatrial node, possibly increasing the risk for arrhythmia [57].

Whether the type of second stage operation is a predictor for the onset of arrhythmia after FO itself is hard to say, as in our study and in others [56], nearly all of the children from the LT group had a hemi-FO as a second stage operation and those from the EC group experienced a Glenn operation. However, the onset of arrhythmia after FO leads to the assumption that it is the type of FO that provokes the occurrence of arrhythmia.

Furthermore, the type of the first stage operation had no impact on the incidence of arrhythmia before FO. After FO, even if not statistically significant, children who underwent a Norwood operation with an RV-PA shunt had VES more often than the others (P 0.059). However, no increased risk was seen for other forms of arrhythmia. Thus, one can assume a RV-PA shunt to be a risk factor for the development of arrhythmia, especially VES. The RV-PA shunt as a modification of the Norwood operation is known to have hemodynamic advantages, e.g., better coronary perfusion, higher diastolic blood pressure, and more balanced systemic-to-pulmonary flow ratio (Qs:Qp) [58]. Nevertheless, as it is a direct manipulation to the ventricle, concerns remain about ventricular function after ventriculotomy, e.g., arrhythmia, ventricular dysfunction, or aneurysm formation [59]. Our findings can therefore be seen as a consequence of direct ventricular manipulation and ventricular dysfunction. However, most of the other studies describe good early and late outcome after the Norwood operation with an RV-PA shunt, and no comments can be found on the increased risk for arrhythmia [58, 60]. As our results are not

statistically significant, we cannot conclude that the RV-PA shunt is a risk factor for the development of arrhythmia after FO.

4.1.2 The Fontan operation as special risk factor for arrhythmia

4.1.2.1 Type of Fontan repair, the surgical procedure itself – LT vs EC

In our investigations, the differences between the two groups of Fontan repair (LT, EC) regarding the incidence of arrhythmia in the early period after FO are evident. Since the early beginnings of FO, arrhythmia has been one of the feared complications. Several studies have described the high risk for the development of arrhythmia after FO [22]. In particular, the atriopulmonary connection with its direct connection to the atrium was expected to cause arrhythmia difficulties. Gelatt et al. identified the atriopulmonary connection as being an independent risk factor for the development of atrial tachyarrhythmias [21].

These results have inspired the development of further alterations of the original FO and the bypassing of the atrium with a total cavopulmonary connection. This modification was first proposed by de Leval et al. in an in vitro flow modeling study. With their new findings, they performed the LT cavopulmonary connection in their first 20 patients and demonstrated a reduced risk for early and late arrhythmia [22]. The advantage of a total cavopulmonary connection regarding the reduced risk for early and late arrhythmia was established in several other studies, e.g., Gardiner et al. [61].

Although this variation is advantageous compared with the original atriopulmonary FO, it still entails risk factors for arrhythmia. The creation of a LT nevertheless causes new surgical scars to the atrium, which might form the morphological basis for arrhythmia. This has been demonstrated in an animal study by Gandhi et al. [62]. In a canine model, they confirmed that suture lines alone, without atrial hypertension or stretch, are able to produce arrhythmia.

A long suture line, especially next to the crista terminalis, as is necessary in the LT technique, might cause atrial re-entry followed by supraventricular tachycardia. Even though new techniques aim to avoid the crista terminalis, the presence of extensive right atrial trabeculation sometimes makes this impossible. Apart from this, during the LT operation, the sinus node itself or its blood supply might be damaged by an incision in the top of the atrium, a procedure that is often required to enlarge the superior anastomosis. Damage of the sinus node will result in sinus node dysfunction and bradyarrhythmia.

The most recent modification of the FO, namely the EC method, might overcome the deficit of the LT cavopulmonary connection. It totally bypasses the atrium and therefore avoids any form of surgical intervention in the atrium or the creation of an intra-atrial baffle. By totally bypassing the heart and thus reducing the length of the atrial suture lines, the EC FO is considered theoretically to be superior to the other forms of Fontan completion with regard to the development of arrhythmias. This is supported by Amodeo et al. [63] who have demonstrated a 5-year arrhythmia-free rate of 92% in an early follow-up report.

However, the disconnection of the superior or inferior caval vein from the atrium might cause damage to the atrium and therefore the loss of NFSR and development of arrhythmia, despite the EC technique.

The results of our analyses confirm the benefit of an EC Fontain repair technique regarding the reduced risk for arrhythmia. During hospitalization, the EC group presented with significantly higher numbers of NFSR at all time points. Normofrequent junctional ectopic rhythm was significantly more frequent in the LT group. JET was only presented by the LT group. However, the incidence of postoperative bradycardia did not differ significantly between the two groups. The need for a temporary pacemaker after FO was significantly higher in the LT group. However, the implantation of a new permanent pacemaker was only required in two patients (1 LT and 1 EC).

Several other studies have confirmed the benefit of the EC modification. Azakie et al. describe the reduced risk of early postoperative and mid-term arrhythmia in their series of 47 LT vs 60 EC patients [41]. Similar to our results, their LT group had a higher risk for supraventricular tachycardia early postoperatively (LT 33%(16) vs EC 8%(5); $P < 0.001$) and for junctional rhythm (LT 45%(21) vs 15%(9); $P < 0.001$). The need for a temporary pacemaker was also reduced (LT 32%(15) vs EC 12%(7); P 0.01). In mid-term follow-up (LT 2.8 ± 1.9 vs EC 2.5 ± 1.4 years), the EC group showed less arrhythmia, e.g., sinus node dysfunction, supraventricular tachycardia, or need for pacemaking (LT 25% vs EC 7%; P 0.02).

Similar results can be seen in the studies of Nürnberg et al. who compared 29 LT vs 45 EC patients, during an even longer follow-up period (median: LT 7.9 vs EC 4.4) [64]. In their study, an early postoperative sinus rhythm was presented more frequently in the EC group (LT 50%(13) vs EC 86%(37); P < 0.001). The incidence for supraventricular tachyarrhythmia was higher in the LT group (LT 38%(11) vs EC 11%(5); P < 0.001). Moreover, during follow-up, the EC group presented with less arrhythmia than the LT group.

In a study concerning the postoperative outcome of 200 EC patients, Kim et al. describe 85% freedom from arrhythmia after 10 years of follow-up [49].

Lee et al. also report reduced sinus node dysfunction among the EC group in the postoperative period (LT 22.4% vs EC 11.2%; P 0.05) [65].

Although the findings of many investigations support the results of our study, a few have been unable to determine a beneficial effect of the EC modification of Fontan repair or have even described a poorer outcome for EC patients with regard to arrhythmia. Kumar et al. describe a higher incidence of sinus node dysfunction in the EC group early postoperatively (LT 8% vs 27%, P 0.09), at discharge (LT 0% vs EC 10%, P 0.02), and during follow-up (LT 15% vs 28%, P 0.2) [66]. Even though, in the study of Cohen and colleagues, the EC group was not disadvantaged with respect to arrhythmia, they were not able to show a beneficial effect of totally bypassing the atrium [56]. Hakacova et al. have presented similar results for both groups. They have identified rhythm abnormalities early after Fontan repair in 31 (52%) EC and 22 (54%) LT patients. Moreover at the 1-year follow-up, the prevalence of arrhythmia was similar in LT and EC patients [67].

4.1.2.2 Forms of arrhythmia

The forms of arrhythmia presented within the LT group were mainly of the junctional or atrial ectopic rhythm type. Early postoperatively, the LT group had a significantly higher incidence of tachycardia without sinus tachycardia (JET, AET) (P <0.001). This is similar to SVT. Moreover, normofrequent junctional ectopic rhythm was more frequent than in the EC group (P 0.016). Sinus tachycardia and NFSR have significantly lower representation than in the EC group (P 0.027, 0.039, respectively). In 24h (Holter) ECG analyses, the LT group showed mainly normofrequent junctional ectopic rhythm or junctional ectopic bradycardia. At discharge, the main part of the group demonstrated normofrequent atrial or juntional ectopic rhythm. However, the EC group mainly showed NFSR or sinus bradycardia in 24h (Holter) ECG analyses and NFSR or sinus tachycardia at discharge.
Not only does the LT group show a reduced incidence for NFSR compared with the EC group (P 0.039), but also the frequencies for the different forms of arrhythmia differ from each other. The arrhythmia forms demonstrated by the EC group are mainly sinus tachycardia and sinus bradycardia. In contrast, the arrhythmia forms presented within the LT group are mostly junctional ectopic or atrial ectopic rhythms: early postoperatively, mainly tachycardia and, at the time of discharge, normofrequent. The commonest forms presented by the EC group are physiological deviations from NFSR. Sinus tachycardia and sinus bradycardia might be a consequence of the new form of circulation and the not yet fully adapted organism. Moreover, hypovolemia caused by postoperative chest effusions might provoke the incidence of sinus tachycardia. Most cases stabilize during hospitalization so that, at discharge, the main part of the group again presents NFSR. On the contrary, the

most often presented forms of arrhythmia in the LT group are signs of a sinus node dysfunction. This sinus node dysfunction might be explained by a sinus node injury or damage of the sinus nodal artery due to surgery. However, not all of these signs persist as, at the point of discharge, some of these children have returned to a NFSR. Thus, those cases might be explained by a light irritation attributable to manipulation during FO. According to these results, we assume that the forms of arrhythmia presented by the EC group in the early period after FO are mainly physiological and are caused by a missing adaption to the newly achieved Fontan circulation. However, the forms of arrhythmia presented by the LT group are mainly caused by surgical manipulation and are therefore more severe.

Similar to our findings, Azakie et al. report higher incidences of sinus node dysfunction and SVT, including JET and AET, postoperatively in patients who have undergone a LT FO [41]. However, they do not mention a higher frequency of sinus bradycardia, possibly because sinus bradycardia is often seen as a sign for sinus node dysfunction. Nürnberg et al. have also reported SVT and sinus node dysfunction as being the forms of arrhythmia significantly more often represented by the LT group [64]. Even if not with the same significant differences, other studies have demonstrated the same forms of arrhythmia [21, 56, 68].

4.1.2.3 Perioperative differences in LT and EC

The negative influences of CPB, aortal cross-clamping, and cardioplegic cardiac arrest on the postoperative outcome after FO are wide spread [69-72]. CPB is a known risk factor for postoperative ventricular dysfunction and consecutively emerging SVT [73]. Cardioplegia and aortal cross-clamping causing ischemia of the

myocardium are especially dangerous for patients with ventricular hypertrophy. However, in other cases, cardiac ischemia might also lead to postoperatively reduced systolic and diastolic ventricular function with decreased cardiac output and elevated end diastolic pressure and an increased risk for arrhythmia. We can confirm these experiences with our study results, as patients with NFSR early postoperatively had significantly shorter CPB times in our study (P 0.008). In particular, those patients who showed junctional ectopic or sinus tachycardia had longer CPB times. Patients with aortal cross-clamping during Fontan repair had a lower incidence of NFSR at all times (P 0.028).

Generally, EC FO is known to have a shorter CPB time or is sometimes even possible without any CPB at all. In our study, the EC group had significantly shorter CPB times (P 0.008). Even though the time of aortal cross-clamping, if necessary, did not differ between the two different Fontan repair types, nearly 90% of the EC were carried out without aortal cross-clamping. Our findings can significantly confirm the negative influence of CPB and aortal cross-clamping on the development of postoperatively arrhythmia.

A conclusion is therefore difficult to make as to whether only the operation technique itself, with the various suture lines and forms of manipulation, or the reduced need for aortal cross-clamping and the shorter CPB times in the EC group are also responsible factors for the lower incidence of arrhythmia in this group.

4.1.2.4 Time of onset of arrhythmia and its course

In patients with Fontan surgery, two time points for the onset of arrhythmia have to be distinguished: early after FO or later on, even 2 decades after the repair.

Early postoperative tachycardia is seen in a small number of patients directly after the Fontan repair and, in the majority of cases, is associated with the early adaptation to Fontan circulation. The inotropic support used in these situations is an independent risk factor for the development of arrhythmia. In this situation, we must consider the benefits and risks of such medication and whether it can be discontinued (if necessary, a normal rhythm has to be adjusted by pacing). Intravenous amiodarone shows a good effect on rhythm control in cases of ectopic or juncitional tachycardia [35].

Late postoperative tachycardia, e.g., SVT, is mainly presented 6-11 years after FO [74]. After the initial appearance of tachycardia, isolated episodes of tachycardia will occur. With the passage of time, episodes of tachycardia will become more frequent and prolonged with the risk of the development of atrial fibrillation after some years [75].

Symptoms presented by the patients differ with the type of conduction. A 2:1 conduction with a ventricular frequency of 110-130 beats per minute will cause “vague symptoms of unexplained fatigue or respiratory symptoms” [35], whereas a rapid 1:1 conduction will bring syncope or even cardiac arrest.

In both cases, patients with single ventricle physiology are not able to compensate for the persistence of tachycardia and may consequently develop massive congestive heart failure 12-36 hours after the onset of the heart constantly beating faster than 100 bpm.

Tachycardia increases the risk of atrial thrombi, which may lead to cerebral (in the case of the fenestrated Fontan tunnel) or pulmonary emboli. Therefore, the tachycardia must urgently be terminated within 24 hours of onset.

Even though our study does not include long-term follow-up, a point of interest is that the incidence of arrhythmia decreases during the time of hospitalization. Compared with the first ECGs after Fontan repair, the ECG analyses at the time of discharge show less arrhythmia for patients of both groups. However, the incidence of NFSR is still significantly higher in the EC group. The EC group presents with nearly the same numbers of NFSR before FO and at discharge, whereas in the LT group, only half of the patients regain a NFSR at discharge, compared with the number before FO. Similar results have been obtained in other studies [41]. The reason for the decrease of arrhythmia during hospitalization might be the rapid adaption to the Fontan circulation and the regeneration of the myocardial wounds. Because of the inflammatory reaction after operation, the risk for arrhythmia, especially tachyarrhythmia, might be increased. In addition to the myocardium itself, the adjacent conduction system with its connections might be irritated by the surgical procedures in the period directly after FO. However, as they are only irritated and not totally destroyed, they are able to recover and revive NFSR. Nevertheless, a study by Quinton et al. [76] reports a sudden peak of prevalence in arrhythmia at 20-26 years after FO. However, 63% of the study population underwent an atriopulmonary (AP) FO and only 24% EC and 13% LT. Another important remark is that nearly none of the LT or EC group reached the

postoperative span of 20 years in this study. Thus, the peak of sudden arrhythmia after 20-26 years is mainly formed by the patients who underwent an AP Fontan. With increasing follow-up, the incidence of arrhythmia in patients after FO will increase [21, 76], especially in those who manifested early arrhythmia. Hence, they should be regularly monitored.

4.2 Other complications after Fontan repair and their triggers

4.2.1 Adaption to the Fontan circulation

Azakie et al. reported the longer intubation times for children who underwent a LT FO; moreover, the ICU time and hospitalization were longer in this group [41]. For patients undergoing an EC procedure, other studies have described shorter ventilation times in order to reduce CPB times and avoid cardioplegia [69, 73]. In our study, differences with regard to intubation time were not statistically significant. However, patients from the EC group tended to have longer intubation times. This was the same for children without NFSR early postoperatively. The development of arrhythmia after FO had no influence on the ICU time or hospitalization time of the children. However, children from the EC group had a significantly longer time of hospitalization (P 0.016). This was a remarkable result. Arrhythmia could not have been the problem, as it was significantly of lower prevalence in this group. The only complication that was significantly higher in children who underwent an EC FO was prolonged effusions. Even if the duration of drainage of the total amount of effusion

was about the same in both groups, the incidence of developing prolonged effusions was higher for the EC group (P 0.038). Moreover, hospitalization for children with prolonged effusion was significantly longer than for others (P >0.001). Patients with bradycardia in 24h (Holter) ECG had prolonged effusions more often than other patients. Moreover, the amount of RP drainage was significantly higher in children with sinus bradycardia in 24h (Holter) ECG (P 0.017). However, further significant differences in the amount of effusions and bradycardia could not be seen. Other investigations have not led to descriptions of a direct correlation between arrhythmia and the incidence of prolonged effusions. However, increased pulmonary arterial pressure and a reduction of ventricular function are known as risk factors for prolonged pleural effusions [50, 73]. In this context, the correlation between bradycardia and prolonged effusions in our study might be seen as the physiological result of stasis caused by bradycardia and as the limitation of ventricular function caused by a lowered heart beat rate. Other studies have also reported prolonged effusions attributable to longer CPB time [41]. This correlation cannot be seen in our study.

Interestingly, those patients who underwent the FO without fenestration showed more frequent prolonged effusions than those with fenestration (P 0.030). Fenestration is known to reduce the incidence of prolonged effusions by lowering prepulmonal stasis [22, 73]. Fenestration leads to better ventricular filling and maintains cardiac output. Generally, fenestration is propagated to reduce not only effusions, but also the time of hospitalization and mortality [26, 28].

Hence, a possible explanation of the longer hospitalization times in the EC group might be the prolonged adaption to the Fontan circulation in those patients. Nearly

all of the EC FOs were carried out without fenestration, whereas most of the LT FOs included fenestration.

4.2.2 Thromboembolism

Generally, all Fontan circulations have a higher risk for thromboembolism because of the decelerated systemic venous return. In a study of Rosenthal et al., the incidence of thromboembolism was 20%, irrespective of the type of Fontan repair [77]. Many studies suggest a higher risk for thromboembolism in patients who later undergo FO [78, 79]. In these patients, the atrium is exposed to increased pressure, which results from the systemic venous circulation and which leads to turbulences and dilation that might cause intra-atrial thombosis followed by thromboembolism. Other authors however report that the EC Fontan modification is a risk factor for thromboembolism [73, 80]. Limited endothelialization of the artificial material of the EC might provoke pulmonary thromboembolism. In our study population, we could not find such a complication; however, only massive pulmonary embolism can be clinically detected. The LT group shows one case of stroke, which can be a consequence of thromboembolism. In our study, almost all children from the LT group received fenestration, which can be the route of crossed (paradoxical) embolism.

4.2.3 Bleeding

Patients who underwent a LT Fontan repair had more frequent bleeding complications. Damaging erythrocytes and thrombocytes, the long time needed to accomplish the CPB is known to cause bleeding or anemia. Even though all patients

in our study were operated on with the CPB, CPB was significantly shorter in patients who underwent the EC FO. Sometimes the EC Fontan repair is even possible without the use of a CPB [73]. Another important factor can be the hypothermia that is used during the LT FO; this can also have deleterious effect on the coagulation system and was avoided in all children from the EC group without intracardiac procedures.

4.2.4 Medication

Patients who presented with bradycardia early postoperatively received significantly more often dopamine therapy than others. Of those who showed non-sinus tachycardia only a few needed amiodarone or adenosine therapy. Thus, one might assume that patients with bradycardia have a special need for anti-arrhythmic medication. However, other forms of arrhythmia are often treated with temporary pacemaking (see below). Nonetheless, in our study, the need for anti-arrhytmic medication after FO was rare, and no difference was seen regarding the need for anti-arrhythmic medication between the two groups of Fontan repair. Contrary to these findings, Nürnberg et al. described a higher rate of postoperative need for anti-arrhythmic medication in children who underwent the LT FO [64].

A significant correlation was found between the incidence of arrhythmia early postoperatively and catecholamine therapy, especially adrenaline therapy. Children who showed no NFSR early postoperatively after FO received significantly more often catecholamine therapy. In particular, those having adrenaline therapy presented significantly more often with sinus tachycardia or non-sinus tachycardia.

The children who received glycoside therapy showed sinus tachycardia significantly more often than others. Catecholamines, e.g., adrenaline, are used to stabilize the cardiac output in children with low blood pressure. Glycosides are also used in children with low cardiac pump function. Even if not reported by other colleagues, such medication is generally known to cause arrhythmia as a negative side effect. Hence, the high frequencies of tachycardia, especially sinus tachycardia, can also be explained by the need for this medication in the first few days after FO.

4.2.5 Pacemaking

The need for temporary pacemaking after FO was significantly higher in the LT group ($P < 0.001$). The main reason for temporary pacemaking was the junctional ectopic rhythm. Similar results were presented by Azakie et al. [41]. With regard to the new implantation of a permanent pacemaker during hospitalization after FO, no significant difference was found between the two groups (LT, EC). In the patients of the study by Nürnberg et al., the need for temporary pacemaking was significantly higher in the group of children who underwent LT FO. Permanent pacemaker implantation during mid- and long-term follow-up was only necessary in patients from the LT group [64]. In the study of Kumar et al., arrhythmia and the need for new permanent pacemaker implantation during hospitalization after FO was more frequent in the EC group; however, the authors did not mention new pacemaker implantation during follow-up [66]. Cohen et al. report the rare need for pacemaking after FO. New permanent pacemaker implantation was only necessary in one of LT patients.

4.3 Conclusions

Patients who underwent EC FO demonstrated significantly more often NFSR in the early postoperative period. Normofrequent junctional ectopic rhythm and junctional tachycardia was significantly more frequent in the LT FO group (early postoperatively and at discharge). JET was only manifested by the LT group, and the need for temporary pacemaking, above all reasons, was significantly higher in the LT group.

In the long-term follow-up after second stage procedure directly before FO, no significant differences were seen between the children after bidirectional Glenn anastomosis and hemi-FO with regard to the incidence of the various forms of arrhythmia.

Longer CPB time and the use of aortal cross-clamping had a negative effect on the cardiac rhythm postoperatively. Patients without NFSR in the early postoperative period had significantly longer CPB times and were operated upon more often with cardioplegic cardiac arrest.

The presence of fenestration in the Fontan circulation facilitates the early postoperative adaptation to the passive pulmonary blood flow. Children without fenestration stayed longer in the hospital and more often presented prolonged effusions.

Children at the age of 2 to 4 years at the time of FO presented a trend toward lower incidence of all forms of arrhythmia in the early postoperative period.

4.4 Limitations of the study

The design of the study was retrospective. The selection for the type of FO was given by the previous second stage operation. Nearly all LT FO previously underwent a hemi-Fontan operation and nearly all EC FO a Glenn operation. However the final decision to perform either a LT or an EC FO was made by the surgeon himself. This causes a certain bias to the study. A double-blinded study design could give more plausible results.

A single person has retrospectively analyzed the ECG diagnostic. Most of the data have been collected from patient files and have been retrospectively analyzed.

The number of patients (169) included in this study is generally seen as being suitable for statistically significant analyses. However, the two groups (LT, EC) were of different sizes (LT 56, EC 113). Moreover, the spectrum of the cardiac anomalies differed between the two groups. HLHS, which not in our but in other studies forms a risk factor for arrhythmia, was overrepresented in the LT group.

Fenestration, which had a positive influence on the duration of hospitalization, was only performed in the LT group.

5 Lists

5.1 List of references

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5.2 List of abbriviations

AAI	atrium-atrium-inhibition
ACE	angiotensin converting enzyme
AET	atrial ectopic tachycardia
AF	atrial fibrillation
AFL	atrial flutter
Ao	aorta
APC	atriopulmonary connection
ASA	acetylsalicylic acid
Asc	ascendens
AV	atrioventricular
AVNRT	atrioventricular nodal reentrant tachycardia
BT	Blalock-Taussig
bpm	beats per minute
CAVC	common atrioventricular canal
CHD	congenital heart disease
cm	centimeters
CPB	cardiopulmonary bypass
CV	common ventricle
d	days
DILV	double inlet left ventricle
DOLV	double outlet left ventricle

DORV	double outlet right ventricle
DP	diastolic pressure
d-TGA	d-transposition of the great arteries
EC	extracardiac conduit
ECG	electrocardiogram
ECHO	echocardiography
ECMO	extracorporeal membrane oxygenation
EDP	end diastolic pressure
ePTFE	expanded polytetrafluoroethylene
FO	Fontan operation
FU	follow up
h	hours
HLHS	hypoplastic left heart syndrome
HRHS	hypoplastic right heart syndrome
ICU	intensive care unit
Ix	index
JET	junctional ectopic tachycardia
kg	kilogramms
LA	left atrium
LP	left pleura
LPA	left pulmonary artery
LT	lateral tunnel
MAPCA	major aortopulmonary collateral artery

m	months
ml	milliliters
mm	millimeters
MP	mean pressure
MWU	Mann Whitney U test
NFQ	normofrequent
NFSR	normofrequent sinus rhythm
OP	operation
PA	pulmonary artery
pO_2	partial oxygen pressure
PTFE	polytetrafluoroethylene
PVR	pulmonary vascular resistance
Qp:Qs	pulmonary-to-systemic flow ratio
QRS	QRS complex
RA	right atrium
RP	right pleura
RPA	right pulmonary artery
RU	resistance unit = Wood unit
RV-PA	right ventricle-pulmonary artery
SA	sinoatrial
SANTR	sinoatrial node reentrant tachycardia
Sat	saturation
SD	standard deviation

SL	single left
SP	systolic pressure
SR	single right
ST	sinus tachycardia
SV	single ventricle
SVC	superior vena cava
SVT	supraventricular tachycardia
SVR	systemic vascular resistance
TA	tricuspid atresia
TCPC	total cavopulmonary connection
TGA	transposition of the great arteries
VCI	vena cava inferior
VCS	vena cava superior
VES	ventricular extrasystoles
VSD	ventricular septal defect
VT	ventricular tachycardia
y	years

5.3 List of tables

5.4 List of figures

6 Abstract

The Fontan operation (FO) allows to separat the blood circulation in children with a univentricular heart. It thereby establishes two circulations, which are placed in series: a passive pulmonary and an active systemic circulation. This new gained circulation system allows a good survival of the children with a nearly normal upgrowth.

The first so-called FO was performed in 1968 [17], although this had taken a long time to be achived. Many surgeons were involved in the process of establishing this method [2, 4-8]. Today, mainly two modifications of FO are performed: the lateral tunnel (LT FO), which connects the inferior vena cava to the pulmonary artery by a tunnel in the lateral atrium, and the extracardiac conduit (EC FO), which connects the vena cava inferior to the confluent pulmonary artery system. Because of less manipulation, shorter atrial suture lines, and constant low intra-atrial pressure, the EC FO is supposed to cause less arrhythmia.

The aim of our study was to analyze whether the type of Fontan repair has an influence on the incidence of arrhythmia and whether one procedure is superior to the other regarding the postoperative outcome.

169 children constituted the study population. 56 (33.1%) children underwent a LT Fontan procedure and 113 (66.9%) an EC FO. Most of them had single right ventricle anatomy (66.3% SR – LT 82.1 vs EC 58.4%). Depending on the

hemodynamic type, all children had at least one palliative operation before FO. Nearly all of the EC patients had undergone a bidirectional Glenn operation beforehand, and nearly all of the LT patients had had a hemi-FO. The final FO was performed by a single surgical team in a single institute (Pediatric Cardiac Surgery, Klinikum Großhadern, Ludwig Maximilian University, Munich). The patient data was analyzed retrospectively.

In our study, FO had a significant influence on the development of arrhythmia. Patients who underwent EC FO had significantly more NFSR in the early period after FO (early postoperatively - LT 15% vs EC 30.2%, P 0.039, 24h ECG (Holter) during hospitalization - LT 30% vs EC 58%, P 0.030, at discharge - LT 36.5% vs EC 56%, P 0.020). Normofrequent junctional ectopic rhythm was significantly more frequent in the LT group (early postoperatively - LT 20.8% vs EC 7.5%, P 0.016, at discharge - LT 17.3% vs 1.0%, P <0.001). JET was only presented by the LT group (LT 18.9% vs EC 0%, P < 0.001). Moreover, the need for temporary pacemaking was significantly higher in the LT group (P <0.001).
In addition to the type of Fontan repair, CPB time and the use of aortal cross-clamping had a negative effect on the development of arrhythmia postoperatively. Patients without NFSR in the early postoperative period had significantly longer CPB times (P 0.008), and those who were operated upon without aoral cross-clamping showed significantly more NFSR (P 0.027). Patients from the EC group had significantly shorter CPB times (P 0.004) and less need for aortal cross-clamping.

The time of adaption to the total passive pulmonary blood flow and therefore the time of hospitalization (P 0.016) was longer in the EC group. Children who underwent an EC FO had a higher incidence of prolonged effusions (P 0.038). However, we see this as based not on the EC Fontan repair itself, but on the lack of fenestration in this group. LT FO included significantly more often fenestration (P <0.001). Patients who underwent fenestration had a lower incidence of prolonged effusions (P 0.030) and, therefore, shorter times of hospitalization (P <0.001).

According to the results of our study, we assume that EC FO outmatches LT with respect to the postoperative outcome, especially regarding the early development of arrhythmia.

Besides, the fact, that both procedures were performed during the same periode of time by one surgical team in a single institute, provides a special initial situation for analyses.

Nevertheless, we have only observed the early period after FO, and we have to await the passage of time to be able to make statements regarding mid- and long-term follow-ups. However, other studies with similar results of early outcome allow estimations suggesting that the EC group will still show advantages in the near future.

7 Zusammenfassung

Die Fontan Operation ermöglicht die Trennung der Blutkreisläufe bei Kindern mit univentrikulärem Herzen. Hierbei werden zwei separate Kreisläufe geschaffen, die in Serie zueinander geschaltet sind: ein passiver pulmonaler und ein aktiver systemischer Kreislauf. Dank dieser neuen Kreislaufsituation wird den Kindern ein Überleben mit nahezu normaler Entwicklung ermöglicht.
Die erste sogenannte Fontan Operation wurde 1968 durchgeführt [17]. Die Etabilierung dieser Methode dauerte jedoch einige Jahre. Viele verschiedene Chirurgen waren an der Entwicklung dieser OP Technik beteiligt [2, 4-8]. Heute finden hauptsächlich zwei Varianten der Fontan Operation Anwendung. Das Laterale Tunnel (LT), welches die untere Vena cava mit der Pulmonalarterie über einen Tunnel im lateralen Vorhof verbindet, und das Extracardiale Conduit (EC), welches die Vena cava inferior mit dem konfluenten pulmonlarteriellem System zusammenführt. Die extrakardiale Variante soll auf Grund von geringerer Manipulation und kleineren Nähten im Vorhof sowie konstant niedrigen intraatrialen Drücken weniger Arrhythmien verursachen.

Mit unserer Studie wollten wir den Einfluss der Fontan OP auf die Entstehung von Arrhythmien, sowie die mögliche Überlegenheit einer der beiden Varianten auf das postoperative Ergebnis untersuchen.

Die Studiengruppe fasste 169 Kinder. 56 (33.1%) der Kinder erhielten eine laterale Tunnel Operation und 113 (66.9%) eine Operation mittels Extracardialem Conduit. Der Großteil der Kinder hatte eine Rechtsherztyp Anatomie (66.3% SR – LT 82.1 vs EC 58.4%). Abhängig vom hämodynamischen Typ erhielten alle Kinder vorab zumindest eine weitere palliative Operation vor der Fontan Operation. Fast alle der EC Patienten hatten eine bidirektionale Glenn Operation und fast alle der LT Patienten eine hemi-Fontan Operation. Die finale Fontan Operation wurde stets von ein und demselben chirurgischen Team in einem einzigen Krankenhaus durchgeführt (Herzchirurgische Kinderklink, Klinikum Großhadern, Ludwig Maximilians Universität, München). Die Datenanalyse erfolgte retrospektiv.

In unserer Studie hatte die FO einen signifikanten Einfluss auf die Entwicklung von Herzrhythmusstörungen. Patienten, die mittels EC FO versorgt wurden, hatten in der frühen postoperativen Phase nach Fontan OP signifikant häufiger einen normofrequenten Sinusrhythmus (früh postoperativ - LT 15% vs EC 30.2%, P 0.039, 24h EKG während des stationären Aufenthalts - LT 30% vs EC 58%, P 0.030, bei Entlassung - LT 36.5% vs EC 56%, P 0.020). Ein normofrequenter junctionaler ektopischer Rhythmus fand sich signifikant häufiger in der LT Gruppe (früh postoperativ - LT 20.8% vs EC 7.5%, P 0.016, bei Entlassung - LT 17.3% vs 1.0%, P <0.001). Junktionale ektopische Tachykardien zeigten sich lediglich in der LT Gruppe (LT 18.9% vs EC 0%, P < 0.001). Auch ein temporärer Schrittmacher wurde signifikant häufiger in der LT Gruppe benötigt (P <0.001).
Neben der Fontan OP Variante hatte die kardiopulmonale Bypasszeit und die Verwendung eines Aortencrossclampings einen negativen Effekt auf die

Entwicklung postoperativer Rhythmusstörungen. Patienten ohne normofrequenten Sinusrhythmus in der frühen postoperativen Phase hatten signifikant längere kardiopulmonale Bypasszeiten während der OP gehabt (P 0.008). Patienten, die ohne Crossclamping operiert wurden, hatten signifikant häufiger einen normofrequenten Sinusrhythmus (P 0.027). Patienten der EC Gruppe hatten signifikant kürzere CPB Zeiten (P 0.004) und weniger häufig Anwendung eines Crossclampings.

Anzumerken ist, dass die Gewöhnung an den neuen Kreislauf und der damit verbundene stationäre Aufenthalt nach der OP in der EC Gruppe singnifikant länger dauerte (P 0.016). Kinder, bei denen eine extracardiale Fontan Operation durchgeführt wurde, hatten eine höhere Inzidenz an verlängerter Ergussbildung postoperativ (P 0.038). Dennoch sehen wir den Grund hierfür nicht bei dem extracardialen Vorgehen selbst, sondern bei der fehlenden Fenestration. Die LT FO war signifikant häufiger mit einer Fenestrierung kombiniert durchgeführt worden (P <0.001). Patienten die eine Fenestration erhielten, hatten eine niedrigere Inzidenz für verlängerte Ergussbildung (P 0.030) und somit kürzere Hospitationszeiten (P <0.001).

Anhand der Ergebnisse unserer Studie sehen wir die extracardiale Fontan Operation dem lateralen Tunnel gegenüber überlegen was das postoperative Ergebnis und die Entwicklung von Herzrhythmusstörungen angeht.

Die Tatsache, dass beide Operationsvarianten zur gleichen Zeit an ein und dem selben Institut durch ein idenentisches chirurgisches Team praktiziert wurden, stellt eine besondere Ausgangssitutation für die Auswertung dar.
Bislang haben wir nur die frühe postoperative Periode nach der Fontan Operation analysiert und es dauert noch, bis Aussagen bezüglich der Langzeitverläufe gemacht werden können. Jedoch erlauben andere Studien mit ähnlichen Ergebnissen in der frühen postoperativen Phase Vermutungen anzustellen, dass auch im Langzeitverlauf die EC FO die überlegene Operationsvariante darstellt.

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9 Affirmation in lieu of oath – Eidesstattliche Versicherung

Schuh, Anna Maria

_____

Name, Vorname

Ich erkläre hiermit an Eides statt,

dass ich die vorliegende Dissertation mit dem Thema:

“Development of arrhythmia after Fontan Operation – Lateral tunnel vs extracardiac conduit’’

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