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# Long-term follow-up in adult patients after Fontan operation

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## Abstract

**Aim of the study:** The aim of the retrospective study was to determine the prevalence of late complications in adult patients after the Fontan operation (FO).

**Material and methods:** Forty-eight Caucasians patients after staged FO (26 men, 22 women) aged between 18 and 40 years (mean 23 ±5 uears) were included in the study. The evaluation included echocardiograms, electrocardiograms, cardiopulmonary exercise tests (CPX), oxygen saturation and medical history and laboratory tests. Based on the postoperative time, the patients were divided into three groups: up to 15 years, between 16 and 20 years and above 20 years after surgery.

**Results:** Thromboembolism was present in 10 patients (21%). Supraventricular tachycardias were noted in 10% of subjects, ventricular tachycardia in 4% of patients. Mean oxygen saturation was 89%, cyanosis was seen in 25% of patients. Protein-losing enteropathy appeared in 4%. While analyzing parameter values in patients belonging to various postoperative time groups, highly significant differences were noted in $VO_{2peak}$, $VO_2$%N, $SaO_2$ (oxygen saturation), and HCT. Along with an increased postoperative period, the SV function deteriorated ($\chi^2$ $p$ = 0.001, Fisher $p$ = 0.001) and a higher degree of systemic atrioventricular valve regurgitation was detected ($\chi^2$ $p$ < 0.001, Fisher $p$ < 0.001).

**Conclusions:** In adults after the Fontan operation, the systolic function of a single ventricle deteriorates with time, atrioventricular valve regurgitation increases and exercise tolerance is reduced. Cyanosis is increased and hematocrit levels are elevated. Such patients require regular assessment in specialist centers for adult patients with congenital heart defects.

**Key words:** Fontan operation, long-term follow-up.

## Streszczenie

**Cel:** Celem pracy była retrospektywna ocena częstości występowania powikłań oraz wpływu czasu pooperacyjnego na ich występowanie u dorosłych chorych po operacji Fontana w odległym okresie obserwacji.

**Materiał i metody:** Do badania włączono kolejnych 48 chorych po operacji Fontana (26 M, 22 K) w wieku od 18 do 40 lat, średnio 23 ±5 lat. U wszystkich chorych wykonano badanie kliniczne, echokardiograficzne, laboratoryjne, EKG, wysiłkowy test spiroergometryczny oraz oceniono saturację krwi tętniczej. W zależności od czasu, który minął od operacji, chorzy zostali podzieleni na trzy grupy: do 15 lat, 16–20 lat i powyżej 20 lat.

**Wyniki:** Powikłania zakrzepowo-zatorowe występowały u 10 chorych (21%). Nadkomorowe zaburzenia rytmu zarejestrowano u 10% chorych, podczas gdy komorowe zaburzenia rytmu u 4%. Saturacja krwi tętniczej w badanej grupie wynosiła 89%, sinice stwierdzono u 25% chorych. Objawy enteropatii wysiękowej występowały u 4% badanych. Analizując wartości parametrów u pacjentów w zależności od czasu pooperacyjnego, stwierdzono wysoce istotne różnice w $VO_{2peak}$, $VO_2$%N, saturacji krwi tętniczej i w wartości hematokrytu dla wszystkich grup. Wraz z upływem czasu od operacji obserwowano upośledzenie funkcji skurczowej komory systemowej ($\chi^2$ $p$ = 0,001; Fisher $p$ = 0,001) oraz zwiększanie się stopnia niedomykalności zastawki przedsionkowo-komorowej ($\chi^2$ $p$ < 0,001; Fisher $p$ < 0,001).

**Wnioski:** U dorosłych chorych po operacji Fontana z czasem obserwuje się upośledzenie funkcji skurczowej pojedynczej komory, zwiększenie stopnia niedomykalności zastawki przedsionkowo-komorowej oraz obniżenie tolerancji wysiłku. Nasila się sinica oraz zwiększa poziom hematokrytu. Chorzy ci wymagają systematycznej oceny w specjalistycznych centrach zajmujących się leczeniem dorosłych z wrodzonymi wadami serca w celu wczesnego rozpoznania i odpowiedniego leczenia w przypadku stwierdzonych powikłań.

**Słowa kluczowe:** operacja Fontana, powikłania odległe.

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## Introduction

Recent progress in cardiac surgery and pediatric cardiology has resulted in large numbers of adult patients who have surgically corrected complex congenital heart defects. The Fontan operation (FO) has become the treatment of choice in patients with a univentricular heart (single ventricle – SV); the anomaly accounts for about 8% of all congenital heart defects. The lack of a chamber that pumps blood to the pulmonary vascular bed results in restricted pulmonary venous return, which in turn decreases preload in the SV. In the Fontan-type circulation, cardiac output is approximately 70% lower as compared to the biventricular heart [1]. The most significant factor affecting the cardiac output is believed to be systemic ventricle preload, which depends on the volume of blood flowing through the heart and the presence of fenestrations. Blood flow through the pulmonary vascular bed depends on pulmonary resistance and a pressure gradient between the central venous pressure and left atrial pressure; after the classic FO, it also depends on right atrial contraction [1, 2]. Despite the improvements in surgical techniques that reduce perioperative mortality, late deterioration in functional status can be observed with longer duration of follow-up [3]. Khairy *et al.* [4] described a 20-year survival rate of 83%, and found no differences among patients operated on by various methods. Masamichi *et al.* [3] reported a 20-year survival rate of 87%; in their study patients with fenestrated total cavopulmonary connection (TCPC) had better cardiac output and lower incidence of arrhythmias.

Previous studies demonstrated evidence of numerous complications such as increase of pulmonary resistance, arrhythmia, thromboembolic complications, cyanosis and heart failure after FO [2, 3, 5, 6].

The aim of this retrospective study was to determine the prevalence of late complications in adult patients late after the Fontan operation.

## Material and methods

Forty-eight Caucasian Fontan patients (26 men, 22 women) aged between 18 and 40 years (mean 23 ±5 years) were included in the study, as previously described in detail [7]. This was a multicenter study. Clinical, demographic and anatomical features, previous interventions and complications were studied by a retrospective analysis of all the clinical records. The patients underwent clinical assessment including physical examination, functional status (NYHA class), the presence of arrhythmias and medical therapy. Oxygen saturation ($SaO_2$) was measured by pulse oximetry in the room air.

Echocardiograms were interpreted by two readers and included the assessment of SV morphology and function and atrioventricular and semilunar valve function. The SV function was assessed semi-quantitatively using the following scale: 1, good; 2, fair; 3, decreased, and 4, poor [8]. Semi-quantitative assessment was also employed in evaluating valvular competence, the scale being 0, none; 1, trivial; 2, moderate; 3, severe [9]. The diagnosis of deep-vein thrombosis was established by a positive finding of color duplex sonography (visualization of an intraluminal thrombus in the calf, popliteal, femoral, or iliac veins). The diagnosis of pulmonary embolism was based on the presence of typical symptoms and positive results of high-resolution spiral computed tomography. In Fontan patients with previous thromboembolic events, thrombophilia screening was performed [10]. The cardiopulmonary exercise test (CPX) was performed to evaluate exercise tolerance. The peak oxygen uptake was determined at peak exercise as $VO_{2peak}$ (ml/kg/min) and as a percentage of a normal value calculated for the age and sex ($VO_2$%N). Fasting blood samples were collected from the antecubital vein on the same day that clinical data were recorded. Red blood cells (RBC), platelet count, hematocrit (HCT), hemoglobin (HGB), total protein, alanine aminotransferase (ALT), creatinine, C-reactive protein (CRP) and international normalized ratio (INR) were assayed by routine laboratory techniques.

Based on the postoperative time, the patients were divided into three groups: up to 15 years, between 16 and 20 years, and above 20 years after surgery.

The University Ethical Committee approved the study and patients provided written informed consent.

### *Statistical analysis*

Descriptive statistics was employed to describe the data. The associations between the groups with various post-operative durations and qualitative changes were analyzed using two-way tables, the $\chi^2$ test and the Fisher exact test; additionally, the $\chi^2$ test for a trend was employed.

In the case of quantitative scales, their conformity to a theoretical normal distribution was analyzed by the Shapiro-Wilk test and the uniformity of variances in groups with various post-operative times was analyzed using the Brown-Forsythe test.

The analyses that compared the results of the investigated quantitative scales depending on post-operative time were performed using the analysis of variance (ANOVA) with the Kruskal-Wallis test with the Dunn post hoc test.

Test probability of $p < 0.05$ was deemed significant, while the value of $p < 0.01$ was deemed highly significant. The analysis of the results was performed using the PQStat ver. 1.4.2.324 package and the R software.

## Results

The patient group consisted of 20 (42%) patients with tricuspid atresia, 9 (19%) patients with ventricular septal defect and pulmonary atresia, 9 (19%) patients with double outlet right ventricle with left ventricular hypoplasia, and 10 subjects (21%) with right ventricular hypoplasia. Of this number, 17 (35%) patients underwent direct right atrium-pulmonary artery connection (APC), 2 (4%) underwent modified Fontan surgery, and the remaining 29 (60%) patients underwent TCPC.

The mean age at surgery was 5 ±9.8 (1-17) years. The mean postoperative time was 18 (3-30) years. Ten patients were treated with warfarin (21%), 16 with acetylsali-

cylic acid (33%), 2 took enoxaparin (4%), 3 prednisone (6%), 17 spironolactone (35%), 4 furosemide (8%), 2 sotalol (4%) and 1 sildenafil (2%).

At the last follow-up, the NYHA class was assessed as I in 14 (29%) patients, II in 32 (67%) and III in 2 subjects (4%). There were no significant associations between postoperative time and NYHA class ($\chi^2$ $p$ = 0.3, Fisher $p$ = 0.4).

Upon analyzing parameter values in patients belonging to various postoperative time groups, highly significant differences were noted both in $VO_{2peak}$ and in $VO_2$%N ($p$ < 0.01) in all the groups. Along with increasing postoperative time, $VO_2$ and $VO_2$%N steadily decreased. In the case of HCT, significant differences were observed only for the groups up to 15 years and 16-20 years after surgery (42 ±8.4 vs. 48.8 ±8.3; $p$ < 0.05). There were no inter-group differences in RBC, HGB, platelet count, ALT, creatinine, INR and total protein (Table I).

### Cardiac rhythm

Predominant sinus rhythm was present in 42 (88%) patients. Supraventricular tachyarrhythmias were noted in 5 (10%) patients; in this number, chronic atrial fibrillation was recorded in 4 (8%) and supraventricular tachycardia in 1 (2%) patient. One patient (2%) underwent a pacemaker implant and had a paced rhythm. In 2 (4%) patients, complex ventricular arrhythmias in the form of non-sustained ventricular tachycardia were recorded. All the 4 (8%) patients presenting with arrhythmia leading to cardiac insufficiency were referred for radiofrequency (RF) ablation procedures. There were no significant differences in the frequency of arrhythmia paroxysms between the groups ($\chi^2$ $p$ = 0.8, Fisher $p$ = 0.8).

### Echocardiography

The morphology of SV was left in 39 (81%) and right in 9 (19%) subjects. The SV function was assessed as good in 25 (52%), fair in 16 (33%), decreased in 5 (10%) and poor in 2 (4%) patients. There were significant associations between postoperative time and SV function ($\chi^2$ $p$ = 0.001, Fisher $p$ = 0.001). Along with an increased postoperative period, the SV function deteriorated (Fig. 1). We did not find a correlation between SV morphology and SV function and degree of systemic atrioventricular valve regurgitation.

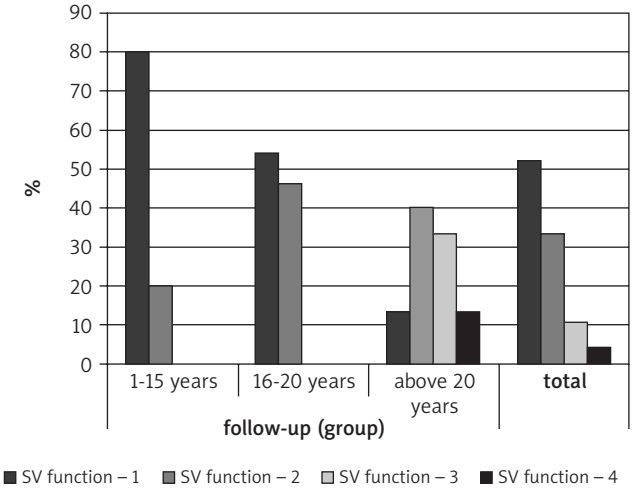
Significant atrioventricular valve regurgitation was present in 2 (4%) patients, moderate in 8 (17%) and mild in 10 (21%) subjects. A highly significant association was also demonstrated between the degree of systemic atrioventricular valve regurgitation and postoperative period duration ($\chi^2$ $p$ < 0.001, Fisher $p$ < 0.001) – Fig. 2. Moderate aortic valve regurgitation was observed in 5 (10%) patients and mild in 9 (19%) patients. No significant associations ($\chi^2$ $p$ = 0.2, Fisher $p$ = 0.3) were noted between postoperative time and prevalence of aortic valve regurgitation. The associations did not reach statistical significance ($p$ = 0.6).

### Thromboembolism

Thromboembolic complications were noted in 10 (21%) patients. Three patients presented with a thrombus in a lateral tunnel, 1 patient had a history of ischemic cerebral stroke, and 6 were diagnosed with chronic venous thrombosis. All the patients with thromboembolic complications were treated with oral anticoagulants.

No significant association ($\chi^2$ $p$ = 0.2, Fisher $p$ = 0.2) was observed between postoperative duration and prevalence of thromboembolic complications. The relation was not statistically significant ($p$ = 0.09), although the percentage of patients presenting with complications increased with increasing postoperative time (Fig. 3).

Symptoms of exudative enteropathy manifesting as low protein levels, ascites and lower extremity edema were observed only in 2 patients (4%) in the group above 20 years after surgery. No significant association ($\chi^2$ $p$ = 0.1, Fisher $p$ = 0.2) was noted between postoperative duration and prevalence of exudative enteropathy symptoms.




*SV – single ventricle*

**Fig. 1.** SV function in patient groups depending on postoperative time

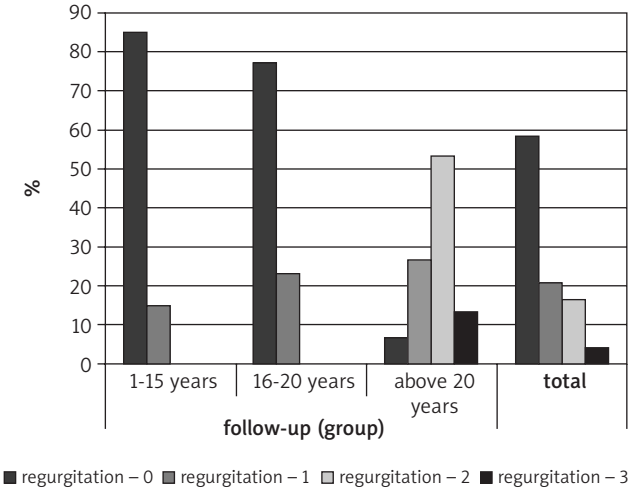



**Fig. 2.** Atrio-ventricular valve regurgitation in patient groups depending on postoperative time

### *Cyanosis*

The mean arterial oxygen saturation was 89 ±7%. Significant differences were observed in $SaO_2$ between groups with various postoperative durations (92.1 ±6 vs. 88.5 ±3.3 vs. 84.9 ±8.7; $p < 0.05$) (Table I, Fig. 4). Cyanosis was noted in 12 (25%) patients. No significant association ($\chi^2$ $p = 0.1$, Fisher $p = 0.09$) was seen between postoperative duration and prevalence of cyanosis. However, the trend was significant ($p = 0.03$); in other words, along with an increasing follow-up time, the number of cyanosis cases steadily increased (Fig. 5).

## Discussion

Single ventricle patients after the Fontan operation are a heterogeneous group with respect to underlying etiology, method of correction and clinical status. We presented a retrospective analysis of the prevalence of late complications in adult Fontan patients who were admitted to specialized centers for adult congenital heart diseases.

In the present study, the most frequent long-term complication in adult patients after the Fontan procedure was cyanosis, which occurred in 25% of the patients. Saturation of arterial blood with oxygen was 89% on average. There was a significant decrease in $SatO_2$ with increasing time elapsed from the operation. Moreover, there was also an increased incidence of cyanosis, significant deterioration of ventricular systolic function, an increased degree of atrioventricular valve regurgitation, and increased RBC and HCT with increasing postoperative time. Some other authors have reported similar findings [11, 12]. Cyanosis might be a result of abnormal communications between the arteries and veins of the lung, polyglobulia, intrahepatic venous communications and intracardiac shunts, for instance fenestrations [2]. Furthermore, impaired ventricular systolic function and atrioventricular valve regurgitation leading to increased ventricular end-systolic pressure increase venous congestion, and formation of abnormal communications in the lung and in the liver, which in turn increases cyanosis [5, 8]. Giardini *et al.* [13] demonstrated that oral administration of sildenafil in Fontan patients was associated with a decrease in pulmonary resistance, an increase in cardiac index and exercise tolerance improvement. In our study, sildenafil was initiated in 2% of patients, in whom clinical improvement was achieved.

In the present study, thromboembolic complications occurred in 21% of patients. There was no significant relationship between postoperative time and the incidence of thromboembolic complications, although the rate of postoperative complications increased with time elapsed from the procedure. In previous investigations, thromboembolic complications have been detected in 3% to 33% of patients, depending on follow-up, study protocol and diagnostic evaluation. Varma *et al.* [14] used CT and ventilation/perfusion lung scintigraphy and detected old asymptomatic pulmonary embolisms in 17% of patients. A pulmonary embolism impairs blood flow in the lung and may aggravate cyanosis. Balling *et al.* [15] found asymptomatic thrombi in

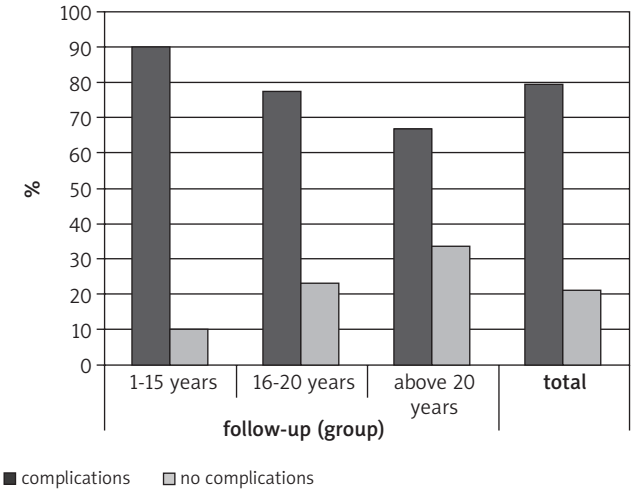



**Fig. 3.** Prevalence of thromboembolic complications in patient groups depending on postoperative time

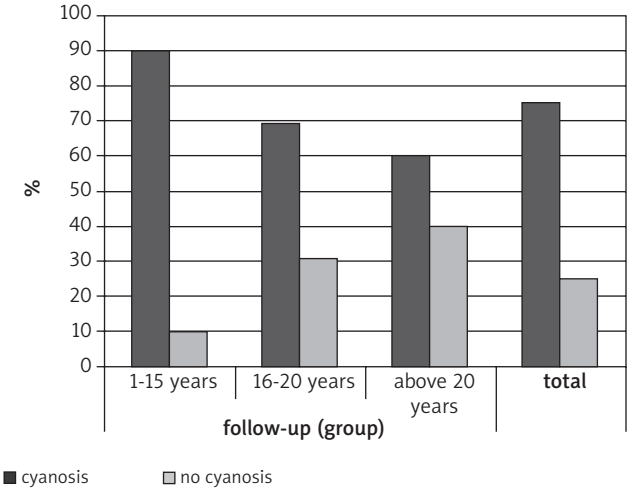



**Fig. 4.** Incidence of cyanosis in patient groups depending on postoperative time

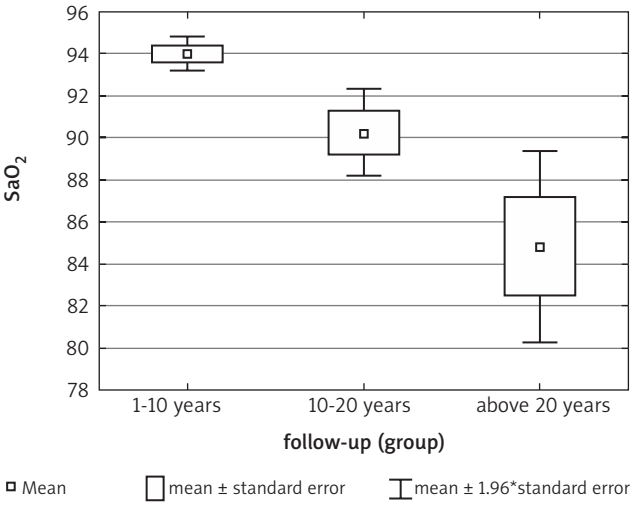



**Fig. 5.** $SaO_2$ in patient groups depending on postoperative time

**Tab. I.** Values of the investigated parameters depending on follow-up duration

| | Follow-up (group) | Descriptive statistics | | | | | ANOVA | Kruskal-Wallis test | Dunn test |
|---|---|---|---|---|---|---|---|---|---|
| | | Mean | Standard deviation | Minimum | Median | Maximum | | | |
| $VO_2$ ml/kg/min | total | 20.44 | 4.86 | 14.00 | 19.50 | 29.00 | | | |
| | 1-15 | 24.15 | 4.26 | 14.00 | 25.50 | 29.00 | | | a |
| | 16-20 | 19.55 | 3.72 | 14.00 | 19.00 | 27.00 | < 0.001 | < 0.001 | ab |
| | > 20 | 16.25 | 1.90 | 14.00 | 16.00 | 20.00 | | | b |
| $VO_2$%N | total | 49.35 | 8.27 | 35.00 | 48.00 | 73.00 | | | |
| | 1-15 | 55.35 | 7.70 | 43.00 | 55.50 | 73.00 | | | a |
| | 16-20 | 47.46 | 5.11 | 40.00 | 46.00 | 55.00 | < 0.001 | < 0.001 | b |
| | > 20 | 43.00 | 5.37 | 35.00 | 40.00 | 54.00 | | | b |
| RBC | total | 5.43 | 0.90 | 3.66 | 5.30 | 9.93 | | | |
| | 1-15 | 5.39 | 1.20 | 3.66 | 5.30 | 9.93 | | | |
| | 16-20 | 5.55 | 0.74 | 4.29 | 5.75 | 6.67 | 0.9 | 0.5 | |
| | > 20 | 5.39 | 0.54 | 4.58 | 5.30 | 6.41 | | | |
| HGB | total | 15.76 | 1.66 | 12.10 | 15.70 | 18.90 | | | |
| | 1-15 | 15.34 | 1.81 | 12.10 | 15.40 | 18.10 | | | |
| | 16-20 | 16.44 | 1.48 | 13.30 | 16.40 | 18.20 | 0.2 | 0.2 | |
| | > 20 | 15.75 | 1.50 | 13.70 | 15.60 | 18.90 | | | |
| HCT | total | 45.14 | 6.96 | 25.17 | 46.50 | 55.30 | | | |
| | 1-15 | 42.00 | 8.42 | 25.17 | 44.70 | 51.90 | | | a |
| | 16-20 | 48.75 | 4.34 | 39.30 | 49.80 | 54.30 | 0.02 | 0.03 | b |
| | > 20 | 46.19 | 4.78 | 33.80 | 46.00 | 55.30 | | | ab |
| PLT | total | 148.77 | 47.85 | 64.00 | 143.00 | 307.00 | | | |
| | 1-15 | 161.55 | 56.91 | 64.00 | 156.00 | 307.00 | | | |
| | 16-20 | 139.08 | 35.05 | 101.00 | 142.00 | 234.00 | 0.3 | 0.3 | |
| | > 20 | 140.13 | 42.86 | 67.00 | 136.00 | 232.00 | | | |
| ALT | total | 29.40 | 11.77 | 4.00 | 29.00 | 60.00 | | | |
| | 1-15 | 31.54 | 10.50 | 16.00 | 29.00 | 60.00 | | | |
| | 16-20 | 25.08 | 11.67 | 4.00 | 21.00 | 45.00 | 0.3 | 0.4 | |
| | > 20 | 30.29 | 13.20 | 7.00 | 32.00 | 58.00 | | | |
| total protein | total | 72.97 | 10.37 | 36.20 | 75.00 | 89.00 | | | |
| | 1-15 | 74.83 | 6.16 | 64.00 | 76.50 | 89.00 | | | |
| | 16-20 | 74.39 | 11.82 | 36.20 | 77.30 | 82.90 | 0.2 | 0.1 | |
| | > 20 | 69.25 | 12.95 | 39.40 | 70.80 | 88.00 | | | |
| creatinine | total | 74.01 | 15.36 | 23.00 | 75.50 | 102.00 | | | |
| | 1-15 | 75.20 | 12.16 | 50.20 | 75.50 | 101.00 | | | |
| | 16-20 | 68.82 | 16.80 | 31.00 | 68.00 | 91.00 | 0.4 | 0.3 | |
| | > 20 | 76.91 | 17.70 | 23.00 | 78.00 | 102.00 | | | |
| PT INR | total | 1.16 | 0.19 | 0.60 | 1.12 | 1.90 | | | |
| | 1-15 | 1.13 | 0.15 | 0.60 | 1.12 | 1.37 | | | |
| | 16-20 | 1.16 | 0.23 | 0.80 | 1.12 | 1.60 | 0.6 | 0.9 | |
| | > 20 | 1.20 | 0.23 | 1.00 | 1.12 | 1.90 | | | |
| $SaO_2$ (%) | total | 88.98 | 6.99 | 70.00 | 92.00 | 97.00 | | | |
| | 1-15 | 92.15 | 5.99 | 70.00 | 93.00 | 97.00 | | | a |
| | 16-20 | 88.54 | 3.36 | 84.00 | 89.00 | 94.00 | 0.02 | 0.03 | ab |
| | > 20 | 84.86 | 8.72 | 70.00 | 87.00 | 96.00 | | | b |

*ALT – alanine aminotransferase; HCT – hematocrit; HGB – hemoglobin; INR – international normalized ratio; PLT – platelets; RBC – red blood cell; $SaO_2$ – oxygen saturation*

the Fontan circulation in 33% of patients. The present study comprised adult patients >18 years of age with a mean follow-up of 18 years. We assessed only the incidence of symptomatic thromboembolic complications. The known risk factors for the development of thromboembolic complications include arrhythmias, slow venous blood flow, cyanosis, liver injury and exudative enteropathy leading to loss of proteins involved in blood clotting [16-19]. Previous studies showed that adult Fontan patients were characterized by enhanced platelet activation and endothelial injury, heightened thrombin formation and impaired fibrinolysis. Patients after thromboembolic events observed late after Fontan surgery display reduced free protein S, increased platelet activation and endothelial damage [7]. There are no clear anticoagulation treatment guidelines for such patients, either. In our group, 33% of participants were on antiplatelet therapy and 21% on anticoagulation therapy, which concurs with results published by others [6, 12].

In the present study, 10% of patients developed supraventricular tachyarrhythmias and 4% of patients had complex ventricular arrhythmias with non-sustained ventricular tachycardia. Data regarding the actual incidence of arrhythmias in adults after the Fontan procedure are scarce. In a group of 520 patients, Stephenson *et al*. [20] found supraventricular tachyarrhythmias in 9.4% and ventricular tachycardia in 3.5% of patients at 8.6 years after the Fontan procedure. Idorn *et al*. [21] reported the occurrence of heart rhythm disorders in 32% of Danish patients undergoing the Fontan operation at the age > 20 years. Scarring after atrial incision, site of synthetic fabric sewing and atrial remodeling predispose to intra-atrial reentrant tachycardia (IART) and atypical atrial flutter. Supraventricular arrhythmia is more frequent in patients with right atrial-pulmonary artery anastomosis [22, 23]. In the present study, 60% of the subjects had TCPC; of this number, 23% had patent fenestrations. Supraventricular tachycardia may aggravate hemodynamics in the Fontan circulation and lead to heart failure over a short period of time. RF ablation is performed in drug-refractory disorders. In our study, 8% of patients had rhythm disorders causing cardiac decompensation. RF ablation was successfully performed in 2 cases (50%). Other investigators report the efficacy of ablation in 50-70% of cases, although recurrent arrhythmia is common [24]. In patients with atrial-pulmonary artery anastomosis and refractory arrhythmia, conversion to TCPC with surgical ablation (MAZE) and epicardial lead placement are recommended. Hiramatsu *et al*. [25] demonstrated one- and five-year survival of 80% and 64%, respectively, after conversion. In the present study, the patients did not require reoperation. None of the patients was referred for heart transplantation.

Symptoms of exudative enteropathy including low protein level, low extremity edema and ascites were found in 4% of patients. Feldt *et al*. [26] reported that protein losing enteropathy occurred in up to 10% of Fontan patients. However, none of these patients had a fenestration. In the present group, fenestrations were detected in 23% of patients.

In the present study, the patients who have undergone the Fontan operation have a decreased exercise capacity with low peak oxygen consumption. Along with increasing post-operative time, peak oxygen consumption steadily decreased. Diller *et al*. [27] also found decreased physical activity in a group of 321 adult patients after the Fontan procedure. The spiroergometric exercise test has no prognostic value in this group of patients. Decreased peak oxygen consumption in patients who have undergone the Fontan operation is caused by decreased pulmonary blood flow, increased dead space, altered chemoreceptor function, and impaired systolic function of the single ventricle. In patients with fenestrations, a right-to-left shunt is present, which is increased during exercise [27, 28]. Idorn *et al*. [29] demonstrated that the pulmonary diffusing capacity was reduced in Fontan patients because of a reduced pulmonary capillary blood volume, whereas the alveolar capillary membrane diffusing capacity was preserved. However, spiroergometric exercise tests play a significant role in long-term follow-up of patients with single ventricles. Objective assessment of exercise capacity facilitates prescription of physical activity and is useful in the selection process for invasive treatment.

Pregnancy carries high risks in women after FO. In our presented group there were 22 (46%) women, of whom 3 (14%) were pregnant. Three deliveries were terminated by cesarean section, while the other 3 ended with miscarriage. In Fontan patients pregnancy should be actively discouraged. Pregnant women after FO should be referred to specialist centers and require multidisciplinary care [30].

Several limitations of the study should be acknowledged. First, it was a retrospective study.

Second, the number of patients in the study was small and heterogeneous with respect to cardiac diagnosis and Fontan surgery type. The true incidence of thrombosis may have been underestimated because we analyzed only symptomatic events and imaging studies were not performed in all the patients. Furthermore, we did not perform hemodynamic measurements and determine single ventricular function on magnetic resonance. However, Margossian *et al*. [31] reported similar interobserver reproducibility for echocardiographic and CMR assessment of SV systolic function. Overall, the CMR data were inadequate or incomplete in 30% of patients in whom the test was performed, predominantly due to metallic artifacts [32].

## Conclusions

In adults after the Fontan operation, the systolic function of a single ventricle deteriorates with time, atrioventricular valve regurgitation increases and exercise tolerance is reduced. Cyanosis is increased and hematocrit levels are elevated. Fontan patients require regular assessment in specialist centers for adult patients with congenital heart defects.

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