Fontan Procedure in Patients with Preoperative Mean Pulmonary Artery Pressure Over 15 mmHg

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Abstract

Background: Several factors affect the long-term outcome of Fontan procedure, but a high pulmonary artery pressure is still one of the most important limitation for proceeding to a Fontan circulation. Herein, we present our experience in Fontan patients with high preoperative pulmonary artery pressures. Methods: A retrospective analysis was performed in order to evaluate Fontan patients with a preoperative pulmonary artery pressure $>$ 15 mmHg between 2009 and 2020. Sixteen patients were operated on with a mean preoperative pulmonary artery pressure of 17.5 $\pm$ 2.1 mmHg. Results: Mean age at the time of Fontan procedure was 7.8 $\pm$ 5.6 years. All of the patients had stage II cavopulmonary anastomosis prior to Fontan completion, with a mean interstage period of 4 $\pm$ 2.6 years. Fontan completion was achieved with a polytetrafluorethylene (PTFE) tubular conduit, two of which were intra-extracardiac. Fenestration was performed in 4 (25%) cases. Postoperative pulmonary artery pressures and arterial oxygen saturation levels were 11.2 $\pm$ 2.8 mmHg and 97.8 $\pm$ 2, respectively. Mean duration of pleural drainage was 3.9 $\pm$ 5.3 days. Any morbidity and mortality were not encountered during a mean follow up period of 4.8 $\pm$ 7.7 years. Conclusions: The mid-term results of stage III Fontan completion in patients with pulmonary artery $>$15 mmHg are encouraging. Pulmonary vascular resistance, not only pulmonary artery pressure may help to identify high risk patients before Fontan completion.

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ABSTRACT

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Methods : A retrospective analysis was performed in order to evaluate Fontan patients with a preoperative pulmonary artery pressure $>$ 15 mmHg between 2009 and 2020. Sixteen patients were operated on with a mean preoperative pulmonary artery pressure of 17.5 $\pm$ 2.1 mmHg.

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Conclusions: The mid-term results of stage III Fontan completion in patients with pulmonary artery $>$15 mmHg are encouraging. Pulmonary vascular resistance, not only pulmonary artery pressure may help to identify high risk patients before Fontan completion.

INTRODUCTION

Fontan Procedure (FP) had been a hope for many patients with congenital heart diseases (CHD) when Dr. Francis Fontan (July 2nd, 1929 – January 14th, 2018) reported this technique for the first time in 1971 [1]. In this original report, the FP was carried out in three patients with the diagnosis of tricuspid atresia (TA). The right side of the heart was bypassed with the combination of a classical cavopulmonary anastomosis between the superior vena cavae and right pulmonary artery and channeling the inferior venae cavae to left pulmonary artery with interposing a homograft [2]. In his original paper, Dr. Fontan emphasized the importance of well-developed pulmonary arteries with a low pressure for the success of this operation.

In the following decades, the technique was further developed and modified and on the other hand, the indications were hugely extended to a variety of CHD with various morphologies. Probably the most important evolutions in FP were the total cavopulmonary connection either with a lateral tunnel or an extracardiac conduit and the idea of fenestration [3-5]. In the current era of cardiac surgery, the potential candidates for a Fontan procedure include a variety of CHD with one well-developed ventricle or not [6].

Early after describing FP, Dr. Fontan and his colleague Dr. Choussat reported the criteria for an 'ideal' Fontan candidate (table-1) [7]. These guidelines, or namely *'the 10 commandments'* were revised and modified during the following decades, since all the criteria were not necessarily portending excellent long-term survival when statistical analysis were concerned [8,9]. Today, mean pulmonary artery pressure (MPAP) and ventricular function are probably the most prevailing criteria for selecting a patient before constituting a Fontan circulation.

Herein, we aimed to present our experience in 16 patients with a MPAP over 15 mmHg who underwent Fontan operation. We also discussed some aspects of mandatory criteria for a satisfactory outcome after FP with regard to the data reported in literature.

MATERIALS and METHODS

A total of 232 Fontan procedures performed in our cardiac surgery center between 2009 and 2020 were retrospectively analyzed following the approval of institutional review board. Sixteen patients who underwent a Fontan procedure with a preoperative catheterization-based measurement of MPAP over 15 mmHg were identified. Afterwards; preoperative, intraoperative and postoperative records were reviewed.

Sixteen patients (9 males, 7 females) with a preoperative MPAP $>$15 mmHg were operated by a single surgeon and FP was performed. Mean age was 7.8 $\pm$ 5.6 years (range: 2 to 26 years) and body weight was 22.5 $\pm$ 8.3 kg (range: 15 to 46 kg) at the time of FP. The mean period between the Glenn and Fontan operations

was 4 ± 6.6 years (range: 1.5 to 10 years).The demographic and operative properties of the patients are demonstrated in table-2.

RESULTS

Thirteen patients (81%) had situs solitus and 3 (19%) patients had situs inversus. We encountered double inlet ventricles in 6 of the cases (37%). Three patients had tricuspid and two patients had mitral atresia. In thirteen out of 16 patients (81%), one of the ventricles were hypoplastic, right ventricle in 7 and left ventricle in 6 cases. In 3 cases, both of the ventricles were developed and the indication for Fontan palliation were congenitally corrected transposition of the great arteries (c-TGA) (pt. no 5 and 9) and a criss-cross atrioventricular (AV) connection in the setting of double outlet right ventricle (DORV) and a large ventricular septal defect (VSD) (pt. no 6).

Stage-1 palliation was deemed necessary in 8 of the cases (50%). These interventions included balloon atrial septostomy or surgical atrial septectomy in order to increase mixing at the atrial level, pulmonary banding in order to control pulmonary arterial pressure and flow and modified Blalock-Taussig shunt (MBTS). Patient no. 6 had a history of supramitral membrane resection along with pulmonary artery banding and atrial septectomy. All of the surgical atrial septectomy procedures were performed as concomitant interventions, none of the patients were operated on for surgical atrial septectomy alone. Five patients (31%) had a history of systemic to pulmonary shunt surgery as stage I palliation (pt. no 4,5,8,13 and 14). In patient no.13, early postoperative shunt occlusion was encountered and primary surgical thrombectomy was performed. In all other cases, MBTS grafts were primarily patent until surgical closure at the following stages.

Stage-2 palliation was performed in all cases which included superior cavopulmonary anastomosis and concomitant procedures, which included atrial septectomy, pulmonary banding, pulmonary artery patch augmentation and atrioventricular valve repair. The bidirectional Glenn procedure was bilateral in patients 10, 14 and 15. Prior shunts were clipped or divided at stage II, except for two cases. In patient no.8, MBTS was still functional as an additional pulmonary blood flow source and in pt. no 5, there was an unintentional residual shunt flow at the time of stage III. Both of these cases were operated on at other cardiac surgery centers at stage II palliation and these shunts were closed at stage III.

Stage III Fontan completion was achieved with a*polytetrafluorethylene* (PTFE) tubular conduit (GORE-TEX?, W.L. Gore and Associates Ltd., Livingston, Scotland) at sizes between 16 mm and 22 mm. Extracardiac Fontan procedure was performed in all cases, except for pt. no 11 and 14 where an intra-extra cardiac conduit was interposed. Concomitant procedures at stage III included DeVega tricuspid annuloplasty, pulmonary artery reconstruction, atrial re-septectomy and shunt closure. Fenestration was performed in 4 cases (25%) (pt. no 1,4,11 and 12). At the time of stage III, all of the patients underwent preoperative cardiac catheterization under local anesthesia and sedation. In pt. no7, a major aortopulmonary collateral artery was occluded via femoral route before stage III completion. We did not encounter any inferior vena cava interruption and azygos vein continuity. The mean pulmonary artery (Nakata) index was calculated as 293 +- 72 mm^2/m^2 (range 171 to 456 mm^2/m^2). Interstage period, i.e. the time between stage II and stage III operations were 4 +- 2.6 years (range 1 to 10 years). The stages of Fontan circulation and concomitant procedures are summarized in table-3.

The mean preoperative MPAP measured at the catheterization lab and at the operation room were 17.5 +- 2.1 mmHg and 16.5 +- 1.8 mmHg, respectively. The central venous pressure (measured via internal jugular vein catheter) that was recorded at the initiation of Fontan completion in the operation room represented the MPAP, since all the patients had a prior cavopulmonary anastomosis. All of the patients had antegrade pulmonary blood flow except for the patients no. 4 and 5 who had atresia of the pulmonary valve. The antegrade pulmonary blood flow was diminished either by native valvular or subvalvular pulmonary stenosis and/or a pulmonary band placed at the time of bidirectional Glenn procedure in 13 of the cases, except patient no. 10, who had a double inlet left ventricle with restrictive VSD. The mean pulmonary arterial gradient (except pt. no 4, 5 and 10) was 73.5 +- 10.2 mmHg (range 50 to 86 mmHg) at the time of Fontan operation. Postoperative MPAP and arterial oxygen saturation levels were 11.2 +- 2.8 mmHg (range 4 to

15 mmHg) and 97.8 +- 2 (range 93 to 100), respectively. The preoperative and postoperative MPAP values of the patients following the Fontan completion are presented in figure-1.

Surgical Technique

Re-sternotomy was performed in all cases. Femoral cannulation and initiation of cardiopulmonary bypass before sternal re-entrance was not deemed mandatory in any of the cases. Following aortic and bicaval (or tricaval in cases with a persistent superior venae cavae) cannulation aorta was cross clamped except pt. no 12. Cold antegrade blood cardioplegia was administered where intermittent doses were applied at every 15 minutes. Pulmonary artery was divided above the level of pulmonary valve, except for the cases with pulmonary atresia where there was no antegrade pulmonary blood flow. Pulmonary cusps were excised or squeezed between the double row matress suture lines closing the pulmonary outflow of the ventricle. Inferior venae cavae (IVC) was transected at the level of atrial entrance and a PTFE tubular conduit was anastomosed to IVC with an end to end fashion. End to side anastomosis was performed between the pulmonary artery and the conduit and care was taken in order not to compress the pulmonary venous return throughout the course of the conduit from IVC to pulmonary artery in the pericardial cavity. In cases where an intra-extracardiac technique was implemented, the anastomosis was performed within the atrium encircling the ostium of the IVC. Then the conduit was passed from the atrium to outside into the pericardial cavity. Total circulatory arrest was not used in any case. When fenestration was needed, in cases with an extracardiac technique, a side to side anastomosis was performed between the conduit and the atrium. In intra-extracardiac Fontan cases, a punch was used to make a fenestration and leave it inside the atrium. Temporary inotropic agents were infused in pt. no 3,4 and 7 where dobutamine was the first line choice. In patient no. 14, pulmonary reconstruction was performed following transection of the ascending aorta in order to provide better exposure of the pulmonary arteries. Permanent pace maker was not necessary in any case. The mean cardiopulmonary bypass and aortic cross clamp times were 69.7 +- 27.1 and 51.6 +- 25.3 minutes, respectively. All of the patients were hemodynamically stable with the sternum closed when they leaved the operating room. Any postoperative revision for bleeding or any other reason was not encountered in the early postoperative period.

The mean duration of intubation and intensive care unit stay were 7.8 +- 3.5 hours and 2.3 +- 3.5 days, respectively. The chest drainage tubes were in place until the daily drainage was less than 2cc/kg. Mean duration of drainage was 3.9 +- 5.3 days. Oral warfarin, aspirin, sildenafil citrate and bosentan were routinely administered in all of the patients after FP. The target INR was 2 to 2.5. Steroids were administered when the daily drainage exceeded 5cc/kg. Following removal of the chest tubes, daily consecutive chest x-rays were obtained in order to detect pleural effusion. Any chest tube re-insertion was not needed for re-accumulation of the pleural fluid. We did not encounter any phrenic nerve paralysis in this patient population. Mean duration of discharge was recorded as 10 +- 1.8 days.

Mean follow up period was 4.8 +- 7.7 years (range: 1 to 11 years). All of the patients are on lifelong Aspirin (5mgr/kg) therapy. Oral warfarin and sildenafil citrate (3mgr/kg in 3 divided doses) are administered at least for one year, and afterwards individual decision is given primarily according to a presence of fenestration. Oral endothelin receptor antagonist, bosentan is administered at least for one month. All of the patients were discharged with diuretics and angiotensin converting enzyme inhibitors in order to achieve a normal blood pressure.

Early or mid-term Fontan failure and mortality was not encountered. In pt. no 14, fenestration was closed via femoral access one year after the FP. We have not encountered any case with significant arrhythmia, plastic bronchitis or protein losing enteropathy in our patient population. In cases with AV valve repair, trace to mild regurgitations are encountered. All of the patients in our population are followed up with ejection fractions above 50% with NYHA class I-II symptoms at annual outpatient visits.

DISCUSSION

Fontan circulation had been evolved to overcome situations in which two distinct ventricular chambers are not readily available to pump blood into pulmonary and systemic circulations in a parallel fashion. In

fact, in early 1940s, it was speculated that pulmonary vascular pressure was lower than systemic venous pressure and this pressure gradient may be sufficient to propel blood to the lungs without a power source (i.e. right ventricle) at least in animal models [10]. Beginning from the initial description of the FP in human in early 1970s, the surgical evolution of the surgical procedures in single ventricle physiology may be classified in 4 generations: i. First generation – atriopulmonary Fontan Kreutzer procedure; ii. Second generation – lateral tunnel Fontan procedure; iii. Third generation – the extracardiac conduit Fontan procedure; Fourth generation – the intra/extracardiac conduit with fenestration [11]. In addition to single ventricle situations, in some cardiac malformations, the biventricular approach is avoided and the patients are treated with construction of a Fontan pathway such as inadequate ventricles (eg. hypoplastic left ventricle in Shone's syndrome) or AV valves (eg. tricuspid stenosis with pulmonary atresia/intact ventricular septum), c-TGA, unbalanced AV canal defect, DORV with non-committed VSD or heterotaxy syndromes with complex ventricular relationships [12]. For the purpose of clarifying the nomenclature, the term *'functionally single ventricle'* is preferred rather than *'single ventricle'* since some abovementioned cardiac anomalies have well developed but non-septatable ventricles [13]. In our current practice, we prefer to perform intra-extracardiac FP in cases with unusual systemic venous and pulmonary artery relationships as well as patients whom a fenestration may be necessary. In our patient population, we operated on three patients with well-developed two ventricles in order to construct a Fontan circulation, two patients with c-TGA and one patient with DORV and criss-cross AV connection.

Inherent to Fontan circulation, chronic elevation of systemic venous pressure and absence of a power source for pumping blood to the pulmonary vascular bed, low pulmonary artery pressure and vascular resistance as well as an optimal systemic ventricular function are essential ingredients of successful long-term results [14]. Beginning from the traditional ten commandments, AV valves have been repaired, subaortic and aortic arch obstructions have been relieved, pulmonary vascular geometry has been optimized, encouraging results have been reported in patients less than 4 years of age and arrhythmias have been taken under control, therefore these 10 factors have been reduced to two in mid 2000s: preoperatively impaired ventricular function and elevated pulmonary artery pressure [7,15]. Moreover, the pulmonary vascular impedance is stated to be the single most important factor limiting cardiac output in some reports [16]. Interestingly, only 15-20% of total pulmonary compliance is determined by the proximal pulmonary arteries [17].

At least five papers in English literature emphasize the elevated MPAP (>15 mmHg) as an important predictor of long-term results in Fontan patients [14,18-21]. On the other hand, in a recent study of Tran and colleagues, elevated pulmonary artery pressure, not pulmonary vascular resistance (PVR) is reported to be associated with short-term morbidity, in patients with bidirectional cavopulmonary connection [22]. In our preoperative evaluation, we did not routinely perform pulmonary vascular resistance calculation. Another parameter with regard to pulmonary artery architecture is emphasized by Itatani and co-workers in which the lower limit for pulmonary artery (Nakata) index is stated to be 110 mm^2/m^2 [23]. In our patient series, the mean pulmonary artery (Nakata) index was 293 +- 72 mm^2/m^2 (range 171 to 456 mm^2/m^2). On the other hand, in the original paper published by Fontan and colleagues, a McGoon ratio of 1.8 and a pulmonary artery index of 200 mm^2/m^2 is defined as a necessary criterion for the indication of a Fontan procedure [24].

Another important concern in patients with Fontan physiology is chronic pulsatile flow deprivation in the pulmonary circulation leading to an impaired endothelial function and nitric oxide release, reduced vascular recruitment and impaired lung growth, all leading to progressive elevation in PVR [25,26]. Nevertheless, tachycardia in a normal circulation may increase pulmonary blood flow by up to 35% without changing the diameter of impedance of the pulmonary vasculature and this mechanism is lacking in Fontan patients [27,28]. At least three exogenously administered pulmonary vasodilators are used to improve exercise capacity and myocardial performance in Fontan patients: iloprost (inhaled form of prostacyclin), sildenafil citrate (phosphodiesterase-5 inhibitor) and bosentan (endothelin receptor antagonist) [28]. In a recent meta-analysis, the oral forms of pulmonary vasodilators significantly and safely improved the hemodynamics of Fontan patients, reduced the NYHA functional class and increased 6-minute walking distance [29]. In our clinical practice, we use iloprost infusion at the early postoperative period in Fontan patients when the central venous

pressure rises over 10 mmHg, especially during the period of extubation at doses between 0.5-2 ng/kg/min. We administered oral sildenafil citrate and bosentan on the postoperative first day routinely in this patient population. We did not have to administer inhaled nitric oxide in our patients in the postoperative period.

One of the important short-term morbidities following the operation of a Fontan patient with high MPAP is prolonged pleural effusions. The necessity for continued chest tube drainage often causes pain and decreases ambulation of the patients. Prolonged pleural effusion is defined as either effusion lasting longer than 14 days or an effusion requiring an intervention for reaccumulated pleural fluid following the removal of the chest tubes [30]. When this definition is considered, we did not encounter any patients with prolonged pleural effusion in our patient population, although elevated preoperative MPAP is reported to be the single most determinant for this situation in some series [30]. Mean duration of drainage was 3.9 +- 5.3 days in our patients. We used the criterion of 2cc/kg/day drainage for chest tube removal as recommended in literature [31]. We agree with the factors reported by Arsdell and colleagues in order to minimize pleural drainage: utilization of the extracardiac conduits, acceptable periods of aortic cross clamping and cardiopulmonary bypass, modified ultrafiltration and institution of inotropes and vasodilators when necessary for an optimal intravascular volume and cardiac output and early postoperative extubation [32]. In our patients, we deliberately used diuretics and angiotensin receptor blockers in the postoperative period. Temporary inotropic support was infused only in 3 of our patients. We think that angiotensin receptor blockers are highly effective in order to control afterload for an optimum cardiac output of the single ventricle as stated in literature [33]. In patients whom the daily chest tube drainage exceeded 5cc/kg, we administered steroids (first three doses through intravenous route followed by oral tablets at a dose of 3 mgr/kg methylprednisolone divided in three doses). The oral form of steroids was gradually weaned and ceased after discharge; we did not administer oral steroids more than one month although Rothman et al. reported a weaning period over 3 – 6 months [34]. At extreme cases of uncontrolled pleural effusion, bleomycin or talc slurry may be used in order to perform pleurodesis [35,36].

Baffle fenestration, initially hypothesized for right-to-left decompression and a smooth postoperative course is an important modification in the history of Fontan physiology [5]. Bridges et al. emphasized the benefits of fenestration including maintenance of optimal cardiac output that may also reduce the incidence and duration of pleural effusions. The authors assigned the patients to a fenestrated or nonfenestrated groups. The fenestrated group had a higher risk profile with regard to MPAP, pulmonary artery distortion and higher ventricular filling pressures. Interestingly, the rate of Fontan failure was equal in both groups but the fenestrated patients significantly had fewer days with pleural effusion. Similar results were reported in a randomized study published by Lemler and colleagues [37]. A recent meta-analysis, a total of 4806 Fontan patients were evaluated in order to analyze the effect of fenestration on Fontan procedure outcomes [38]. The fenestrated group (a total of 2727 patients) had significantly lower need for pleural drainage with a lower MPAP (-0.99 mmHg mean difference) and oxygen saturation (-3.07% mean difference). Importantly, there was no significant difference in stroke occurrence between the fenestrated and nonfenestrated groups. Fenestration (a right-to-left shunt) helps to increase preload, stroke volume and cardiac output for the functioning ventricle at the expense of mild cyanosis. Nevertheless, there's still no general consensus about routine use of fenestration [38]. In our patient population, we did not routinely perform fenestration during the Fontan procedure. The resting room oxygen saturation levels were above 90% in our fenestrated Fontan patients. However, two essential factors should be outlined about this procedure: the fenestration size and postoperative anticoagulation protocol. We perform fenestration with a 4 or 4.5 mm punch on the extracardiac conduit. A larger shunt is known to result in hypoxemia induced acid base disturbance and increased pulmonary vascular resistance with clinically overt cyanosis [39]. This vicious cycle may result in decreased cardiac output. Secondly, although different protocols are available avoiding chronic use of warfarin and administering aspirin alone, we put all the patients on oral anticoagulation and antiaggregant treatment following Fontan procedure at least for one year [40,41]. At the end of the first year, we decide to stop warfarin individually, however patients with fenestration continue to use oral anticoagulants. We did not encounter any stroke or conduit thrombosis in our patient group. Li et al. compared the long-term results of fenestration on systemic oxygen saturation in a meta-analysis including 1929 Fontan patients and

reported that although the early postoperative SaO_2 was lower in fenestrated patients, the late postoperative SaO_2 levels did not differ [42]. Therefore, some centers insist on routine fenestration in all Fontan patients, but we still decide individually depending on the perioperative MPAP value [43].

Staged approach for achieving a successful Fontan circulation have been advised in early 1980s [44]. Hopkins and associates recommended to perform a bidirectional cavopulmonary anastomosis before a Fontan completion. We adopted this approach in our clinic and all of the patients in our patient population had a stage II Glenn anastomosis before FP. In fact, this algorhythm has some important advantages. Patients with a prior bidirectional cavopulmonary anastomosis tolerate stage III FP better. Secondly, any additional intracardiac interventions and/or optimization of a sufficient pulmonary vascular architecture becomes possible. We performed pulmonary artery patch augmentation, AV valve repair and atrial septectomy as concomitant procedures in stage II. On the other hand, after the stage II palliation, systemic to pulmonary artery shunts that are mandatorily interposed as stage I interventions are closed. Early closure of a systemic to pulmonary artery shunt is important, since the diastolic run off steals blood from coronary circulation which may lead to deprived performance of the future single ventricle. Moreover, bidirectional Glenn procedure is a more effective way of pulmonary gas exchange and provides better hemodynamic performance when compared to MBTS [45] . We uneventfully performed bilateral bidirectional Glenn procedure in three patients as stage II palliation, which is speculated to have a worse outcome tendency in Fontan patients especially in association with pulmonary artery bifurcation stenosis [46].

Kreutzer and co-workers reviewed the reflections on five decades of the Fontan Kreutzer procedure and grouped the factors that jeopardize the late outcome into three categories: i. suboptimal surgical approach, ii. ventricular dysfunction and iii. increases in pulmonary vascular resistance [47]. On the other hand, Vigano and colleagues suggest that in the modern era of congenital cardiac surgery, either the *'ten commandments'* of Choussat [7] or the *'two commandments'* of the Birmingham-UK group [14] are helpful for identifying the 'high risk' candidates for Fontan completion [48]. They report that there is no actual difference in perioperative outcome in a mean of 7 years follow up. Our results are consistent with their findings.

Mean pulmonary artery pressure, transpulmonary gradient and PVR along with ventricular function are still the most important parameters addressing the long-term outcome of Fontan circulation [49]. However, even the cardiac catheterization at increased altitudes may present variability [49]. In fact, determination of the exact MPAP value is not always reliable, since the pressure measurements may differ when the patient is under local anesthesia and sedation at the catheterization lab or under general anesthesia with neuromuscular blockage in the operation room (17.5 +- 2.1 mmHg vs 16.5 +- 1.8 mmHg in our patient population). Therefore, we recommend routine evaluation of the PVR and transpulmonary pressure gradient in these patients. In future, more real time monitorization tools for pulmonary artery pressures may become available on routine basis and provide improved management of pulmonary hemodynamics in Fontan patients [50]. Obviously, the story of seeking for a perfect Fontan candidate and research focusing on stem cells and optimal medical management strategies will not end in the following decades [15].

In our limited patient population, we think that Fontan procedure may be performed with satisfactory mid-term results in patients with a preoperative mean pulmonary artery pressure over 15 mmHg. These patients should be carefully followed up after the operation for the well-known complications in long term course of Fontan physiology.

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None

TABLE and FIGURE LEGENDS

Table – 1: Ten Commandments advised for an ideal Fontan candidate (adopted from reference no.7).

Table – 2: Summary of the patients who underwent Fontan procedure.

Table – 3: Operative details of the patients, concomitant surgical procedures and summary of the stages

of Fontan circulation.

Figure – 1: The preoperative and postoperative mean pulmonary artery values of the patients following the Fontan completion are presented.

AUTHOR CONTRIBUTIONS

Arda Ozyuksel: Drafting the article, data analysis/interpretation, data collection

Baran Şimşek: Data analysis/interpretation, drafting the article, data collection

Ömer Özden: Data analysis/interpretation, data collection

Şener Demiroluk: Concept/design, Critical revision of the article, approval of the article

Murat Saygı: Data analysis/interpretation, statistics, data collection

Mehmet Salih Bilal: Concept/design, Critical revision of the article, approval of the article

REFERENCES

1. Fontan F, Baudet E. Surgical repair of tricuspid atresia. Thorax 1971;26(3):240-248.

2. Giroud JM, Jacobs JP. Fontan's operation: evolution from a procedure to a process. Cardiol Young 2006;16 Suppl 1:67-71.

3. de Leval MT, Kilner P, Gewillig M et al. Total cavopulmonary connection: a logical alternative to atriopulmonary connection for complex Fontan operations. Experimental studies and early clinical experience. J Thorac Cardiovasc Surg 1988;96:682-695.

4. Marceletti C, Corno A, Giannico S et al. Inferior vena cava-pulmonary artery extracardiac conduit. A new form of right heart bypass. J Thorac Cardiovasc Surg 1990:100:228-232.

5. Bridges ND, Lock JE, Castenada AR. Baffle fenestration with subsequent transcatheter closure. Modification of the Fontan operation for patients at increased risk. Circulation 1990;82:1681-1689.

6. van Doorn CA, de Leval MR. The Fontan operation in clinical practice: indications and controversies. Nat Clin Pract Cardiovasc Med 2005;2(3):116-117.

7. Choussat A, Fontan F, Besse P. Selection criteria for the Fontan procedure. In: Anderson RH, Shinebourne (editors) Pediatric Cardiology. Churchill Livingstone, Edinburgh, Scotland (1977) pp:559-566.

8. Driscoll DJ. Long term results of the Fontan operation. Pediatr Cardiol 28:438-442.

9. Stern HJ. Fontan 'Ten Commandments' revisited and revised.

Pediatr Cardiol 2010;31(8):1131-1134.

10. Starr I, Jeffers WA, Meade RH Jr. The absence of conspicuous increments of venous pressure after severe damage to the right ventricle of the dog, with a discussion of the relation between clinical congestive failure and heart disease. Am Heart J 1943;26:291-301.

11. Jonas RA. The intra/extracardiac conduit fenestrated Fontan. Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu 2011;14(1):11-18.

12. Jonas RA. Fontan or septation: When I abandon septation in complex lesions with two ventricles. Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu 2009:94-98.

13. Jacobs ML, Mayer JE. Congenital heart surgery nomenclature and database project: single ventricle. Ann Thorac Surg 2000;69(4 Suppl)S197-204.

14. Hosein RBM, Clarke AJB, Mc Guirk SP et al. Factors influencing early and late outcome following the Fontan procedure in the current era. The 'Two Commandments'? Eur J Cardiothorac Surg 2007;31(3):344-352.

15. Burkhart HM. Closing in on the perfect Fontan. J Thorac Cardiovasc Surg 2014;148(6):2525.

16. Gewillig M, Brown SC, Eyskens B et al. The Fontan circulation: who controls cardiac output? Interact Cardiovasc Thorac Surg 2010;10(3):428-433.

17. Saouti N, Westerhof N, Postmus PE, Vonk-Noordegraaf A. The arterial load in pulmonary hypertension. Eur Respir Rev 2010;19(117):197-203.

18. Alsaied T, Bokma JP, Engel ME et al. Predicting long-term mortality after Fontan procedures: A risk score based on 6707 patients from 28 studies. Congenit Heart Dis 2017;12(4):393:398.

19. Kim SJ, Kim WH, Lim HG, Lee JY. Outcome of 200 patients after an extracardiac Fontan procedure. J Thorac Cardiovasc Surg 2008;136(1):108-116.

20. Burkhart HM, Dearani JA, Mair DD, Warnes CA et al. The modified Fontan procedure: early and late results in 132 adult patients. J Thorac Cardiovasc Surg 2003;125(6):1252-1259.

21. Pundi KN, Johnson JN, Dearani JA, Pundi KN et al. 40-Year follow-up after the Fontan operation: Long-term outcomes of 1,052 patients. J Am Coll Cardiol 2015;66(15):1700-1710.

22. Tran S, Sullivan PM, Cleveland J, Kumar SR, Takao C. Elevated Pulmonary artery pressure, not Pulmonary vascular resistance is an independent predictor of short-term morbidity following bidirectional cavopulmonary connection. Pediatr Cardiol. 2018;39(8):1572-1580.

23. Itatani K, Miyaji K, Nakahata Y et al. The lower limit of the pulmonary artery index for the extracardiac Fontan circulation. J Thorac Cardiovasc Surg. 2011;142(1):127-135.

24. Fontan F, Fernandez G, Costa F et al. The size of the pulmonary arteries and the results of the Fontan operation. J Thorac Cardiovasc Surg. 1989;98(5 Pt 1):711-719; discussion 719-724.

25. Henaine R, Vergnat M, Bacha EA et al. Effects of lack of pulsatility on pulmonary endothelial function in the Fontan circulation. J Thorac Cardiovasc Surg 2013;146(3):522-529.

26. Gewillig M, Brown SC, Heying R et al. Volume load paradox while preparing for the Fontan: not too much for the ventricle, not too little for the lungs. Interact Cardiovasc Thorac Surg 2010;10(2):262-265.

27. Milnor WR, Bergel DH, Bargainer JD. Hydraulic power associated with pulmonary blood flow and its relation to heart rate. Circ Res. 1966;19(3):467-480.

28. Jolley M, Colan SD, Rhodes J, DiNardo J. Fontan physiology revisited. J.Anesth Analg. 2015;121(1):172-182.

29. Wang W, Hu X, Liao W et al. The efficacy and safety of pulmonary vasodilators in patients with Fontan circulation: a meta-analysis of randomized controlled trials.

Circ. 2019;9(1):2045894018790450.

30. Mascio CE, Wayment M, Colaizy TT et al. The modified Fontan procedure and prolonged pleural effusions. Am Surg 2009;75(2):175-177.

31. Yun TJ, Im YM, Jung SH et al. Pulmonary vascular compliance and pleural effusion duration after the Fontan procedure. Int J Cardiol. 2009;133(1):55-61.

32. Van Arsdell GS, McCrindle BW, Einarson KD et al. Interventions associated with minimal Fontan mortality. Ann Thorac Surg 2000;70(2):568-574.

33. François K, Bove T, Groote KD et al. Pleural effusions, water balance mediators and the influence of lisinopril after completion Fontan procedures. Eur J Cardiothorac Surg 2009;36(1):57-62.

34. Rothman A, Mayer JE, Freed MD. Treatment of chronic pleural effusions after the Fontan procedure with prednisone. Am J Cardiol 1987;60(4):408-409.

35. Tansel T, Sayin OA, Ugurlucan M, Dayioglu E, Onursal E. Successful bleomycin pleurodesis in a patient with prolonged pleural effusion after extracardiac Fontan procedure. J Card Surg 2006;21(6):585-586.

36. Kiziltepe U, Eyileten Z, Uysalel A, Akalin H. Prolonged pleural effusion following Fontan operation: effective pleurodesis with talc slurry. Int J Cardiol 2002;85(2-3):297-299.

37. Lemler MS, Scott WA, Leonard SR, Stromberg D, Ramaciotti C. Fenestration improves clinical outcome of the Fontan procedure: a prospective, randomized study. Circulation 2002;105(2):207-212.

38. Bouhout I, Walid BA, Khalaf D, Raboisson MJ, Poirier N. Effect of Fenestration on Fontan Procedure Outcomes: A Meta-Analysis and Review. Ann Thorac Surg 2020;109(5):1467-1474.

39. Cai J, Zhaokang S, Zhenying S et al. Nitric oxide and milrinone: combined effect on pulmonary circulation after Fontan-type procedure: a prospective, randomized study. Ann Thorac Surg 2008;86(3):882-888.

40. Backer CL. An aspirin a day. J Am Coll Cardiol 2013;61(3):354-355.

41. Jacobs ML, Pourmoghadam KK, Geary EM et al. Fontan's operation: is aspirin enough? Is coumadin too much? Ann Thorac Surg 2002;73(1):64-68.

42. Li D, Li M, Zhou X, An Q. Comparison of the fenestrated and non-fenestrated Fontan procedures: A meta-analysis. Medicine (Baltimore) 2019;98(29):e16554.

43. Airan B, Sharma R, Choudhary SK et al. Univentricular repair: is routine fenestration justified? Ann Thorac Surg 2000;69(6):1900-1906.

44. Hopkins RA, Armstrong BE, Serwer GA, Peterson RJ, Oldham HN. Physiological rationale for a bidirectional cavopulmonary shunt. A versatile complement to the Fontan principle. J Thorac Cardiovasc Surg 1985;90(3):391-398.

45. Vallecilla C, Khiabani RH, Trusty P et al. Exercise capacity in the Bidirectional Glenn physiology: Coupling cardiac index, ventricular function and oxygen extraction ratio.

J Biomech 2015;48(10):1997-2004.

46. Keizman E, Yarden ST, Mishali D et al. The bilateral bidirectional Glenn operation as a risk factor prior to Fontan completion in complex congenital heart disease patients. World J Pediatr Congenit Heart Surg 2019;10(2):174-181.

47. Kreutzer C, Kreutzer J, Kreutzer GO. Reflections on five decades of the Fontan-Kreutzer procedure. Front Pediatr. 2013;1:45.

48. Vigano G, McMahon CJ, Walsh K et al. High-risk Fontan completion patients achieve low perioperative risk and benefit from cavopulmonary connection 7 years out. Eur J Cardiothorac Surg 2019;56(4):664-670.

49. Di Maria MV, Mulvahill M, Jaggers J, Ivy DD, Younoszai AK. Predictive value of presuperior cavopulmonary anastomosis cardiac catheterization at increased altitude. Congenit Heart Dis 2018;13(2):311-318.

50. Salavitabar A, Bradley EA, Chisolm JL et al. Implantable pulmonary artery pressure monitoring device in patients with palliated congenital heart disease: Technical considerations and procedural outcomes. Catheter Cardiovasc Interv 2020;95(2):270-279.

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