Review Article

Fontan Operation

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During the past 4 decades, the Fontan operation has been carried out as a surgical treatment in patients with tricuspid atresia. Over the years, it has become established as a revolutionary therapy in patients with univentricular heart physiology. Many experimental and clinical studies have been performed with a view to understanding the Fontan circulation; in consequence, the operation has undergone several modifications and the prognosis of these patients has improved. However, Fontan circulation attrition still remains a problem; elevations in systemic venous pressure and pulmonary artery resistance, decreased preload and increased afterload, are factors that concern researchers in their efforts to improve the circulation. In this review, we focus on the problems of the operation and the questions arising from the study of Fontan circulation.

Fontan operation evolution

The Fontan operation was first used in 1968 for the repair of the tricuspid atresia valve and was described by Fontan and Baudet in 1971. It included the insertion of an aortic or pulmonary homograft valve, at both the inflow and outflow of the right atrium.[1] Some time later, Kreutzer and colleagues described in a simplified way the use of the pulmonary valve of a patient with tricuspid atresia for the connection of the right atrium to the pulmonary artery.[2]

The above operations and many variations that followed were based on the principle that the right atrium can act as the pump for the pulmonary circulation. Subsequently, this role was questioned,[3] and in the contemporary design of the Fontan operation the superior *vena cava* is anastomosed directly to the pulmonary artery and, using a conduit that is created inside the baffle, the inferior *vena cava* is also drained to the pulmonary artery (lateral tunnel technique) (Figure 1a). The advantages of this technique are the decreased risk of thrombosis, because of less blood stasis, as well as the exposure of only a limited portion of the right atrium to high venous pressures, thus lessening the risk of arrhythmias. In addition, the coronary sinus remains in the low-pressure atrium so that no problems are caused to the myocardial venous drainage.[3] The most recent modification of the Fontan operation technique includes the use of an extracardiac interposition graft between the transected inferior *vena cava* and pulmonary artery (Figure 1b).[4]

Nowadays, the two aforementioned techniques of total cavopulmonary anastomosis have been established as operations of choice, and the technique of anastomosis between the atrium and the pulmonary artery (atriopulmonary connection) has been abandoned. Because of the complications that arose, many patients who had undergone operation with the atriopul-

monary anastomosis technique were led to conversion operations for total cavopulmonary anastomosis.[5,6]

Fontan circulation paradox

In a normal circulation, a good hemodynamic state is characterized by low pressures, especially in the inferior *vena cava* (<10 mmHg), with the mean pulmonary artery pressure being at least 15 mmHg in order for the pulmonary vascular network to be patent according to the West zones. The paradox in the Fontan circulation is the existence of systemic venous hypertension and coexisting hypotension in the pulmonary artery.[7] It should be emphasized that the driving force of the circulating blood volume between systemic and pulmonary veins is the pressure gradient between central venous pressure and the left atrium, assisted mechanically by the thoracic muscles and the respiratory function.

Fontan operation criteria

Patients who are potential candidates for the Fontan operation are those who only have one ventricle, with an atrioventricular connection, and with sufficient size and power to provide the driving force when the pulmonary and systemic venous circulation are connected in series. In most patients with a univentricular heart the underlying cause is tricuspid valve atresia. The Fontan operation might have an indication in some patients with normal or abnormal atrioventricular connections, in which the right ventricle is of a very small size or is dysplastic and cannot contribute effectively to the systemic and pulmonary circulation.[8]

Evidential data show that when the size of the hypoplastic right ventricle is less than 30% of normal, the hypoplastic ventricle cannot contribute adequately to the circulation and in these specific cases the Fontan operation should be applied.[9]

The initial criteria for the Fontan operation, set by Choussat and his colleagues for patients with tricuspid atresia, were particularly strict (Table 1).[10] With increasing experience the criteria have become more flexible. However, because of the special physiology accompanying the Fontan circulation, the correct choice of patients remains crucial. The ideal age for the Fontan operation remains contradictory, but the best and earliest result can be achieved when the anatomy and the hemodynamic parameters are suitable for the Fontan circulation to occur. The pulmonary vascular tree develops during the first few months of life,[11] but successful Fontan operations may be performed from the age of 7 months and on, when clinically increased cyanosis and the appropriate hemodynamic parameters render the operation necessary.[12]

The pulmonary vessels and the functionality of the ventricle remain until today the most important criteria in the choice of patients for a successful Fontan operation.[13]

The size of the pulmonary vessels is also a prognostic factor for the outcome of the Fontan operation and is given by the McGoon ratio: the quotient that is derived from the sum of the diameters of the left and right pulmonary arteries before they split into the ipsilateral branches, divided by the diameter of the descending thoracic aorta just above the diaphragm. A retrospective study by Fontan and colleagues showed that the risk of premature death, such as the danger of attrition of the Fontan circulation, rose steeply when the McGoon ratio was less than 1.8.[14,15] The function of the ventricle is a defining factor of a successful Fontan circulation. However, ventricular dysfunction is not always a contraindication, especially when it is related to volume overload in the case of aortopulmonary shunt. Some of the specific patients can become candidates for a gradual application of the Fontan operation if, before anything else, bidirectional cavopulmonary anastomosis (Glenn procedure) is applied (Figure 1c), for which the indications are more relaxed compared with the Fontan operation,[16] and the aortopulmonary shunt is repaired at the same time. Ventricular hypertrophy has also been recognized as an important risk factor in the Fontan circulation attrition.[17,18]

Most centers in the world use a combination of the above mentioned criteria to decide upon the pa-

Table 1. Primary selection criteria for patients with tricuspid atresia for the Fontan operation.

1. Minimum age 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 left atrioventricular valve
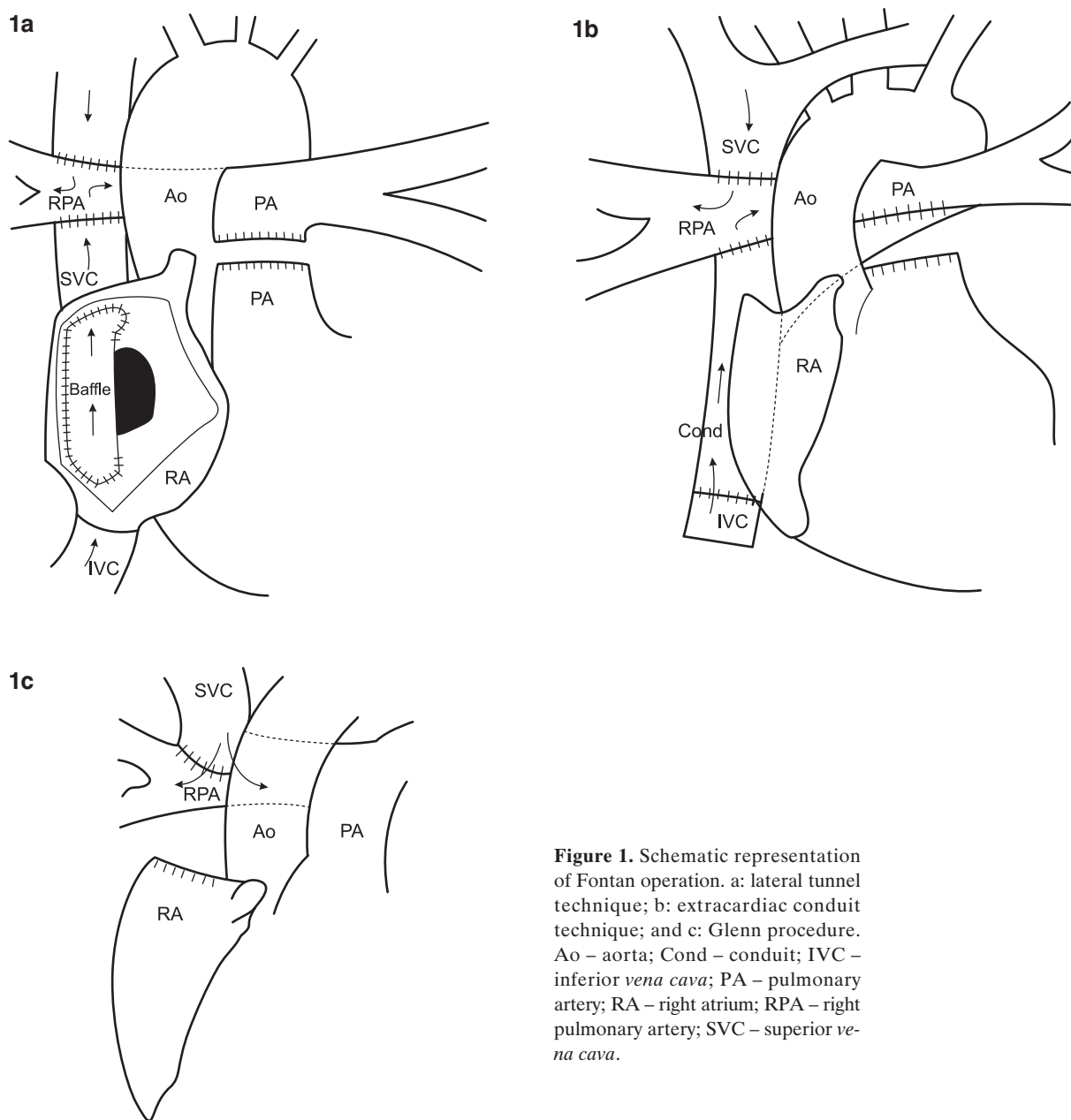10. No impairing effects of previous shunts

Figure 1. Schematic representation of Fontan operation. a: lateral tunnel technique; b: extracardiac conduit technique; and c: Glenn procedure. Ao – aorta; Cond – conduit; IVC – inferior *vena cava*; PA – pulmonary artery; RA – right atrium; RPA – right pulmonary artery; SVC – superior *vena cava*.

tients who are eligible for the Fontan operation. However, good ventricular function, good hemodynamic performance of the pulmonary vascular bed, and absence of previous surgical procedures may constitute important elements in the success of the Fontan operation.

Results of the Fontan operation

Forty years and on from the first use of the Fontan operation,[1] the perioperative mortality has stabilized at around 5%.[19-21] Early morbidity related to the Fontan operation includes pleural and pericardial effusions, low cardiac output, sinus node injury, and pulmonary and systemic venous obstruction.[22] Table 2 shows the factors that have been associated with long-term morbidity after a Fontan operation.[23,24]

The factors that have led to improvement in the operation's outcome are the more energy-efficient circulation, with the formation of a lateral tunnel into

Table 2. Factors that have been associated with long-term morbidity after a Fontan operation.

- Progressive dysfunction of the atrioventricular connection
- Right atrial distension
- Pulmonary vein bed congestion
- Thromboembolic episodes
- Worsening cyanosis due to:
    existence of surgically created communication (fenestration)
    development of collateral arteriovenous circulation (systemic and pulmonary)
- Decreased exercise tolerance
- Cognitive disorders
- Protein-losing enteropathy
- Progressive liver failure
- Plastic bronchitis

the right atrium using a baffle,[3] and the use of the extracardiac conduit technique.[4] Moreover, a decrease in the use of the aortic clamp, along with a decrease in the use of extracardiac circulation with the extracardiac conduit technique have both contributed to the success of the operation. Additionally, the fenestration technique of the baffle and the application of preliminary operations, such as the anastomosis of the superior *vena cava* to the right pulmonary artery (Glenn double direction operation) (Figure 1c), and the concomitant clamping of any collateral aortopulmonary circulation seem to contribute to the improvement of the results following the Fontan operation.[20,25-32]

Complications of the Fontan operation

Along with the improvement in surgical mortality, recent results of the Fontan operation have also changed. Fontan reported that the patients who have undergone the procedure suffer from an early gradual decrease of the functional state of the applied Fontan circulation, which also affects the survival rate.[33] Even in the cases where the operation was carried out under "ideal" circumstances, there was a progressive regression of the functionality of the circulation, and survival 5, 10 and 15 years after surgery was 86%, 81% and 73%, respectively.[33] The long-term increase in the systemic venous pressure seems to play an important role and is reflected in many complications that may appear, such as distension of the right atrium and coronary sinus, hepatic dysfunction and increased splanchnic venous pressure.[31,32]

Mair and colleagues[33] described the risk factors contributing to long-term complications after the Fontan operation as:

- The age of the patient before the operation
- Existence of previous palliative surgical procedures
- The anatomy of the complex congenital disease (tricuspid atresia alone is not a risk factor)
- Heterotaxy syndromes
- Elevated pulmonary artery pressure before the time of operation
- Failure of the atrioventricular connection
- New York Heart Association class III or IV before the operation

Atrial arrhythmias, collateral circulation development, ventricular attrition, protein-losing enteropathy, thromboembolic episodes, and plastic bronchitis are the most discussed complications after a Fontan operation.

Arrhythmias

The evoked atrial fibrillation and supraventricular tachycardias are difficult to control using conservative treatment and can lead to ventricular failure.[34] The heterotaxy syndromes and the relative anomalies of the atrioventricular valve are followed by high percentages of development of such arrhythmias. The lateral tunnel technique *per se* is a risk factor, leading to the development of arrhythmias due to the suture lines placed inside the atrium.[35] Bradyarrhythmias have also been observed in patients undergoing the extracardiac tunnel technique.[36] Atrial pacing has been suggested in order to avoid moderate degree bradyarrhythmias, which contribute in their turn to the development of atrial tachycardia.[37]

In certain patients, surgical management of the arrhythmias and the Fontan circulation conversion from atriopulmonary to total cavopulmonary anastomosis can relieve the supraventricular arrhythmias. Because of the common incidence of supraventricular arrhythmias there is the possibility of performing a Maze operation in every conversion operation, even if the functionality of the sinus node is preserved. The incidence of atrial arrhythmias can be expected to decrease with the prevalence of the lateral tunnel and extracardiac conduit techniques, and probably also with the application of the fenestration technique. Indeed, in a study where the patients underwent the lateral tunnel technique operation, freedom from supraventricular arrhythmias reached 96% and 91% at 5 and 10 years, respectively.[32] Ventricular arrhythmias are rare in Fontan patients and when present they are related with severe ventricular dysfunction.[38]

Collateral circulation

Communications may develop between the higher pressure superior caval system and the lower pressure inferior caval system, left atrium or pulmonary veins.[39,40] Their etiology remains unclear; however, the exclusion of hepatic venous flow from the pulmonary territory may be a factor.[41,42] Collateral channels can promote significant right-to-left shunt with resultant hypoxemia and cyanosis.

Collateral circulation can also develop between the aorta and its branches towards the pulmonary circulation, due to the existence of previous communications, incomplete ligation of the main pulmonary artery, or failed occlusion of previous shunts.[38] These kinds of communication act as a left-to-right shunt, increasing the volume load of the systemic ventricle.

When patients with the Fontan circulation show progressively developing cyanosis or heart failure, they should be referred for cardiac catheterization to search for the existence of collateral circulation.

Ventricular failure

As in other congenital heart diseases, it is possible for the myocardium to have an endogenous ventricular functional disorder.[43] Additionally, anatomic and structural characteristics of the ventricle may limit the application of the Fontan circulation conditions. At the same time the reduced volume load heart must respond to a higher afterload because the systemic and pulmonary circulations are now in series. The higher energy requirements of the single ventricle in the Fontan circulation, the higher afterload and limited preload that are applied to the ventricle after the Fontan operation, render the single ventricle less efficient.[7,44] This state can be manifested as either an early or a long-term complication, but in most cases it is develops more than 8 years after the initial operation.[31]

Despite successful palliation after Fontan procedure, even asymptomatic patients have an abnormal cardiorespiratory response to exercise.[45] There are many studies evaluating the hemodynamic and cardiopulmonary response to exercise and the aerobic capacity in patients with Fontan circulation.[46,47] Inotropic and chronotropic challenge with dobutamine may unmask subtle hemodynamic and arrhythmogenic disturbances.[48] Patients with fenestrated Fontan are desaturated during exercise or tachycardia.[49] Recently, dobutamine stress echocardiography has been employed as a safe method of assessing cardiac reserve in patients who have undergone a Fontan procedure.[48]

Measures taken for the prevention of ventricular failure are the timely and prompt repair of structural abnormalities, such as atrioventricular valve regurgitation/stenosis and ventricular outflow obstruction. Inotropes, vasodilators, b-blockers and afterload reducing agents have no impact on the failing ventricular function in these patients.[38]

Protein-losing enteropathy

Protein-losing enteropathy involves protein loss through the gastrointestinal tract and may appear over a time span of weeks to years after the Fontan operation, with significant mortality rates.[50,51] The exact reasons for its occurrence are not known. The increased venous pressures in the splanchnic territory[7] and the postoperative low cardiac output[51] have been proposed as etiologic factors.

Clinical manifestations are related to the degree of hypoproteinemia and therefore ascites, peripheral edema, pleural effusions, immunodeficiency and coagulation disorders may be present. The increase of a1-antitrypsin in feces confirms enteric protein loss.[28] Fenestration, pacing, or even transplantation may be needed. Pharmaceutical treatment includes the administration of diuretics and dietary supplements. Corticosteroids and heparin have been empirically proved to reduce the protein loss in some patients.[52,53] However, the prognosis of protein-losing enteropathy remains poor. Recently, a case of improvement of the enteropathy symptoms was described after sildenafil administration.[54]

Thromboembolic episodes

Thromboembolic complications may be present in any part of the Fontan circulation. Pulmonary artery thrombosis and stroke can also occur with the analogous clinical symptomatology, but many of these incidents may not be recognized.[55,56] The etiology is multifactorial, including blood flow disorders in the Fontan circulation, arrhythmias, cyanosis, and the presence of foreign material in the Fontan circulation, existing coagulability disorders and hepatic dysfunction.[54] Patients with univentricular hearts are also known to be in a hypercoagulable state, with deficiencies of protein C, protein S, antithrombin III and elevated levels of factor VIII.[57] The clinical incidences of the above-mentioned conditions vary through different

studies from 3% up to 16% for venous thromboses[58,59] and from 3% up to 19% for vascular strokes.[60] Commonly, these complications appear in the first 32 months following the operation, although episodes have also been reported more than 16 years after the operation.[61] However, the effectiveness of the preventive administration of anticoagulant therapy has not been explored in a systematic way. Aspirin, warfarin and heparin are mentioned in the literature in different doses, yet thromboembolic episodes still occur.[62] Additionally, anticoagulant treatment has the danger of hemorrhage, which should be borne seriously in mind, especially in the context of a child with a high level of activity and possible cyanosis or heart failure that may make the anticoagulant treatment control difficult. The daily administration of aspirin (80 mg) is probably a convenient, safe and effective medical regimen.[63]

Plastic bronchitis

Plastic bronchitis leads to airway obstruction by the formation of fibrous and mucosal material inside the trachea and bronchi. It remains a complication whose mechanism has not yet been understood.[64] The symptomatic therapeutic treatment includes a bronchoscopic lavage and respiratory physiotherapy. Regression of the phenomenon has been observed after heart transplantation.[65]

The aforementioned problems were more usual and intense in the early days of the Fontan operation, when atriopulmonary anastomosis was dominant, whereas the results of total cavopulmonary anastomosis seem better.[7,31,44] The conversion of the inadequate atriopulmonary Fontan to total cavopulmonary anastomosis with concomitant antiarrhythmic surgical operation and repair of possible disorders is suggested as an efficient management of the problem.[5,6] In the case where heart failure dominates, heart transplantation is the final therapeutic solution. We have to note that heart transplantation may not solve the problem in the case of protein-losing enteropathy.[51]

Current surgical technique of Fontan operation and perspectives

The Fontan connection can be performed in a number of ways. Currently, the most acceptable methods are the extracardiac conduit and lateral tunnel total cavopulmonary connection (Figures 1a & 1b). The hemodynamic superiority of total cavopulmonary

anastomosis with total right heart bypass over atriopulmonary anastomosis is generally accepted.[7] The lateral tunnel technique (Figure 1a) creates a perfect flow towards the pulmonary artery, preserves low pressure conditions in the coronary atrium and involves a low risk of injury to the atrioventricular node. The extracardiac conduit technique (Figure 1b) offers exactly the same advantages, its design being based on the avoidance of the obstruction of the pulmonary veins in patients with a small right atrium.[4] The extracardiac conduit technique has the extra advantage of not requiring intraatrial access, and therefore can be performed without aortic cross-clamping and in some cases without the use of extracorporeal circulation.[66,67] Our experimental findings (unpublished data) indicate that total cavopulmonary connection may be performed by the beating heart technique without the use of extracorporeal circulation or even the use of a temporary bypass. An additional advantage of the extracardiac conduit technique is that intraatrial suture lines, which are potentially arrhythmogenic,[35] are avoided; however, bradyarrhythmias have also been observed when this technique was used.[36] A disadvantage of the extracardiac conduit technique is the tendency for clot formation inside the conduit and the inability of the conduit to follow the physical development of the child. The creation of an oversized conduit is tempting, but involves the risk of disturbing the patient's hemodynamic status.[68,69]

A recent retrospective study comparing the extracardiac conduit to the lateral tunnel operation at two institutions showed no significant difference in hospital mortality and late survival between the groups.[69] The need for readmission to manage chylous effusions, the preservation of sinus rhythm and the presence of neurologic events at the time of a long-term follow up, were similar in both study groups. Only a trend for greater embolic events was observed in the extracardiac conduit group. In addition, the absence of a fenestration in most patients undergoing the extracardiac conduit technique was associated with increased resource usage.[69] However, this study had methodological flaws, as data were collected from two institutions in a nonrandomized manner and the operations were performed by four surgeons, where the choice of the surgical technique was biased by each surgeon's preference.

Conclusions

The Fontan operation is a revolutionary surgical treatment which clearly improves the outcome of the

operation for patients with a single ventricle. In the last few years, important progress has been made in the evolution of the selection criteria, in the development of surgical techniques and in the design of the Fontan circulation. However, it appears we still have a long way to go as regards a complete understanding of the physiology and the attrition of the Fontan circulation. Clinical experience and experimental studies, in combination with the cooperation of different fields in medicine and positive sciences, are definitely expected to help the evolution even more. The increased systemic venous pressure and pulmonary resistance, the reduced preload of the systemic *cava* and the increased afterload are the parameters that will monopolize the experts' interest. Moreover, the exact condition of the physiology of the pulmonary vascular bed and the effects of the non-pulsatile flow in the pulmonary circulation need to be studied attentively. In a normal two-ventricle circulation, the mean pressure in the *cava* veins is below 10 mmHg and the mean pulmonary pressure must be at least 15 mmHg in order for the pulmonary vascular bed to be patent. The Fontan paradox, as mentioned before, is a systemic venous hypertension (especially in the splanchnic part) with relative pulmonary arterial hypotension. According to the pioneer researcher and surgeon de Leval, the Fontan circulation paradox could be potentially reversed, if a mechanical assisting device was implanted that could lower the pressure in the inferior *vena cava* by 5 mmHg while also producing an increase by 5 mmHg in the pulmonary arteries.[7,44] At this level a number of investigative protocols have already been started.[70-74] For the time being, of course, heart transplantation is the solution for non-reversible attrition of the Fontan circulation.

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