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Physiopathological Approach of the Fontan Patient for Noncardiac Surgery for the Anesthesiologist

Yamile Muñoz, María José Sáenz and Renzo Cifuentes

Abstract

Since 1971, when Dr. Francis Fontan and collaborators described a surgical technique that restored pulmonary flow in patients with tricuspid atresia and despite the fact that it has had modifications over time, the impact on the survival of these patients has been notable. It is currently known as the Fontan procedure and is indicated to treat single ventricle congenital heart defects. Thanks to the great advances in the field of congenital heart surgery, as well as better pediatric cardiology and intensive care management, the survival of patients with congenital heart defects has increased significantly, among whom are patients with univentricular or single ventricle physiology. The objective of this chapter is to provide the anesthesiologist with useful and applicable concepts in the evaluation and perioperative management of patients with a Fontan repair, especially for noncardiac surgeries.

Keywords: congenital heart disease (CHD), chronic heart failure (CHF), single ventricle (SV), Fontan procedure, Fontan physiology, Fontan failure, pulmonary vascular resistance (PVR), systemic vascular resistance (SVR), total cavopulmonary connection (TCPC), cardiac output (CO), cardiac index (CI), preoperative evaluation, intraoperative management

1. Introduction

Univentricular patients in the stage of Fontan palliation have a higher perioperative risk than their counterparts with normal hearts.

The diagnosis and treatment of children with congenital heart disease (CHD) has improved significantly over the last decades. The incidence of CHD has remained stable; the natural history of the lesions and overall survival rate have also changed notably. Advances made in surgical procedures and techniques, in concert with improvements in diagnosis, anesthesia practices, intensive care, and medical treatments, have transformed many of these fatal lesions into manageable chronic conditions [1].

Many more of these patients are surviving with this physiology than could have been contemplated 30 years ago and nowadays they seek medical attention for other causes different from their cardiovascular conditions that require surgical noncardiac procedures.

A normal biventricular cardiovascular system consists of a double circuit, pulmonary and systemic, connected in series and powered by a double pump. Many complex cardiac malformations are characterized by the existence of only one functional

ventricle. This single ventricle (SV) has to maintain both the systemic and the pulmonary circulations, which at birth are not connected in series but in parallel [2].

Regardless of the exact nature of the connections, the completed circulation is often described as one having a single energy source, the systemic ventricle [3].

The survival improvement of patients with univentricular physiology is due to the development of the staged palliation approach for complex congenital heart lesions not suitable for biventricular repair. The final Fontan stage results in the conversion of a parallel circulation, to a pulmonary and systemic circulation that is in series regardless of the underlying cardiac anatomy [2, 4]. Such lesions include hypoplastic left-heart syndrome (HLHS), tricuspid atresia, unbalanced atrioventricular septal defects, double-inlet left ventricle, double-outlet right ventricle, and some forms of heterotaxy syndrome [5].

The objective of this chapter is to provide anesthesiologists the conceptual aspects applicable to the preoperative evaluation and perioperative management of patients with the unique Fontan physiology.

2. The Fontan patient

2.1 Staged palliation

First stage: The goals of initial palliation are to provide unobstructed systemic blood flow, well-balanced pulmonary and systemic circulations with controlled pulmonary blood flow, and unobstructed pulmonary and systemic venous return (including unrestricted atrial level mixing of venous returns). The elevated pulmonary vascular resistance (PVR) characteristic of the newborn period requires a staged approach to achieve these long-term goals that include normalization of the ventricular volume load and provision of normal systemic oxygen delivery. The success of a shunt is evaluated based on the relief of cyanosis, without a significant volume overload of the ventricle, and the induction of pulmonary growth without causing major changes to PVR. The systemic to pulmonary shunt is designed to last 4–6 months, sufficient time for the PVR to drop, allowing a partial cavopulmonary connection to be created safely (**Figure 1**).

Second stage: The superior cavopulmonary connection (SCPC, bidirectional Glenn or hemi-Fontan) is the surgical anastomosis of the superior vena cava (SVC) to the pulmonary artery (PA) and has a significant benefit on cardiac function. The second-stage procedure diminishes the volume load on the SV while maintaining systemic oxygen delivery. Therefore, the ventricular work-load approximates that of the systemic ventricle in a biventricular circulation. One of the critical features of the second-stage procedure is the opportunity for the ventricle to have enough time for remodeling following the removal of the volume load prior to Fontan completion (**Figure 2**). In addition, this stage provides the opportunity to address other anatomic and physiologic abnormalities (including atrioventricular valve regurgitation, PA distortion) in the same surgery, optimizing the chances of a successful Fontan completion later on [4].

Third stage: In 1971, Francis Fontan and colleagues described a surgical technique for successful palliation of patients with tricuspid atresia [3]. Subsequently, this technique has been applied to treat most forms of functional SV. Typically, 1–3 years after the second stage, the inferior vena cava (IVC) is connected surgically to the PA to complete the Fontan procedure [5].

There are three different types of Fontan palliation:

- The atriopulmonary connection (APC) consists of the right atrium connected directly to the PA. Although this surgical reconstruction is not performed

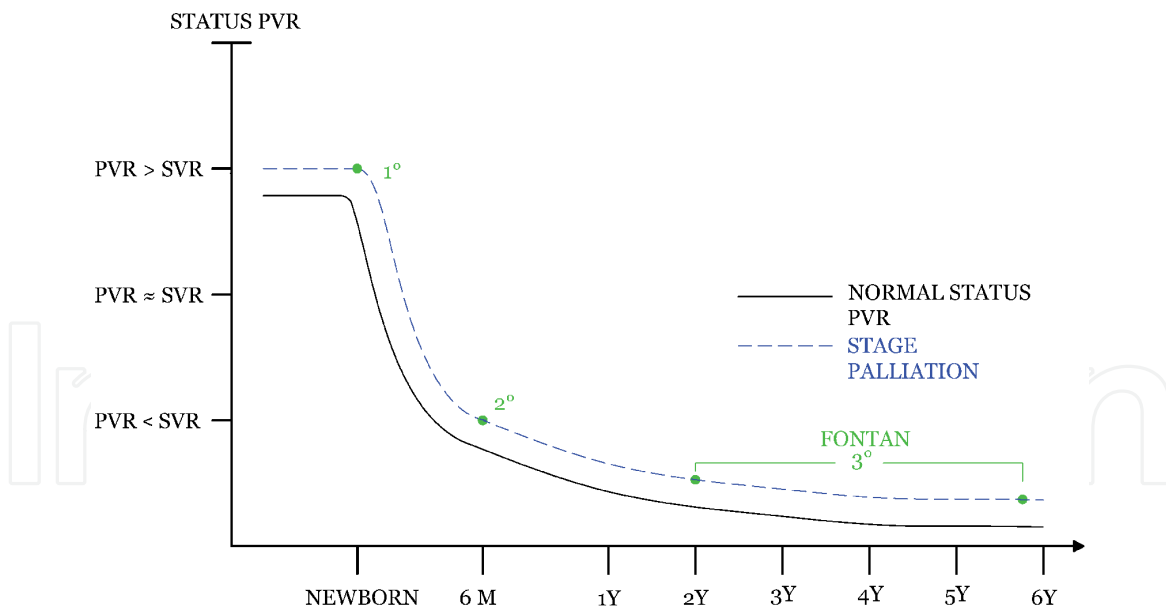


Figure 1. Changes in PVR according to time and the appropriate age for performing stage palliation until completing the Fontan procedure for complex congenital heart disease that does not qualify for biventricular repair (PVR, pulmonary vascular resistance; SVR, systemic vascular resistance).

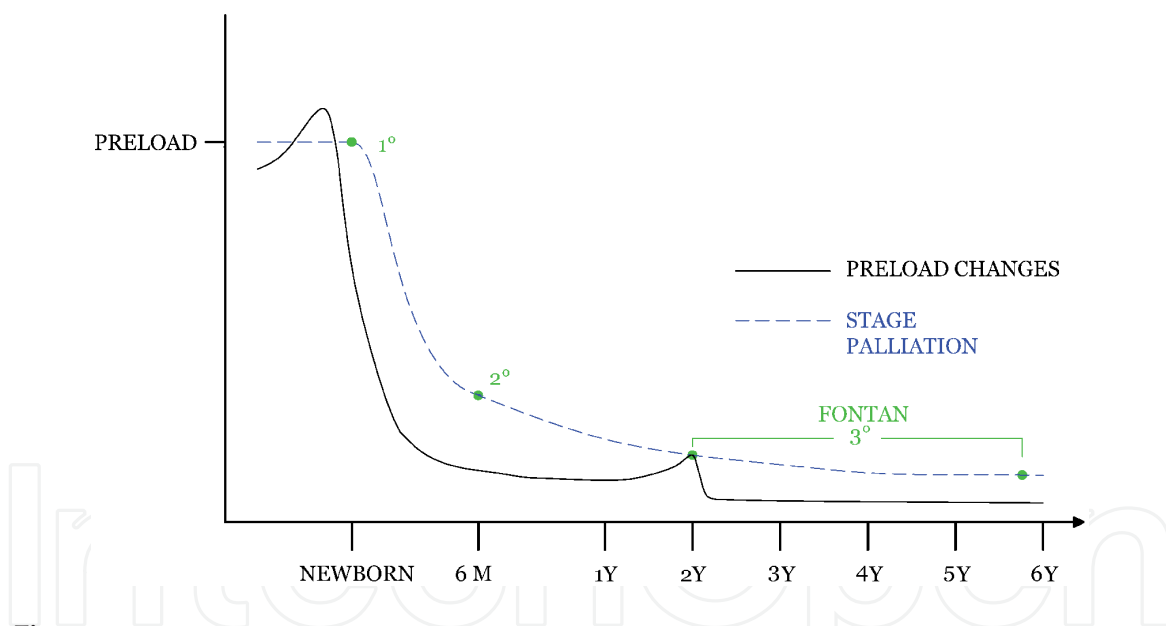


Figure 2. Changes in the preload according to time and the appropriate age for performing stage palliation until completing the Fontan procedure for complex congenital heart disease that does not qualify for biventricular repair.

in modern practice, patients with APCs are presenting to the perioperative setting as adults. The Fontan procedure has been considerably modified since the description of a direct APC by Fontan. Several modifications were subsequently proposed in an effort to improve hemodynamic function and counteract progressive atrial dilation [6].

- The intracardiac total cavopulmonary connection, or lateral tunnel, consists of a SVC surgically connected directly to the right PA. IVC traverses through the atrium via a baffle directly to the PA.

- The extracardiac cavopulmonary connection also consists of a direct anastomosis of the SVC to the PA. However, an extracardiac conduit is used to route IVC blood directly to the PA without traversing the right atrium [5, 7].

Initially, adult survivors were mainly APC Fontan patients, but increasing numbers of both forms of TCPC Fontan patients now survive to adult life [7]. The extracardiac cavopulmonary connection is the main method employed currently in surgical centers.

2.2 Fontan anatomy

The systemic venous blood passively entering the pulmonary circulation through a total cavopulmonary anastomosis (TCPA). Blood bypasses the right atrium via a baffle or a conduit. Blood is oxygenated in the lungs and enters the pulmonary venous system reaching the left atrium. The right and left atrium now function as a common pulmonary venous atrium (CPVA). A single functional ventricle actively drives blood flow through the systemic arteries and capillaries, with systemic venous return passively entering the pulmonary circulation. The final Fontan stage results in the conversion of a parallel circulation to a pulmonary and systemic circulation that is in series [2, 5] (**Figure 3**).

2.3 Fontan physiology

By creating a TCPC, a new portal system is made. A portal system occurs when one capillary bed pools blood into another capillary bed through veins without passing through the heart.

The Fontan morphophysiology has two essential components. First, the presence of a SV pumping oxygenated blood to the systemic circulation, this ventricle can be either, a morphologic right or left depending on the type of CHD. The second

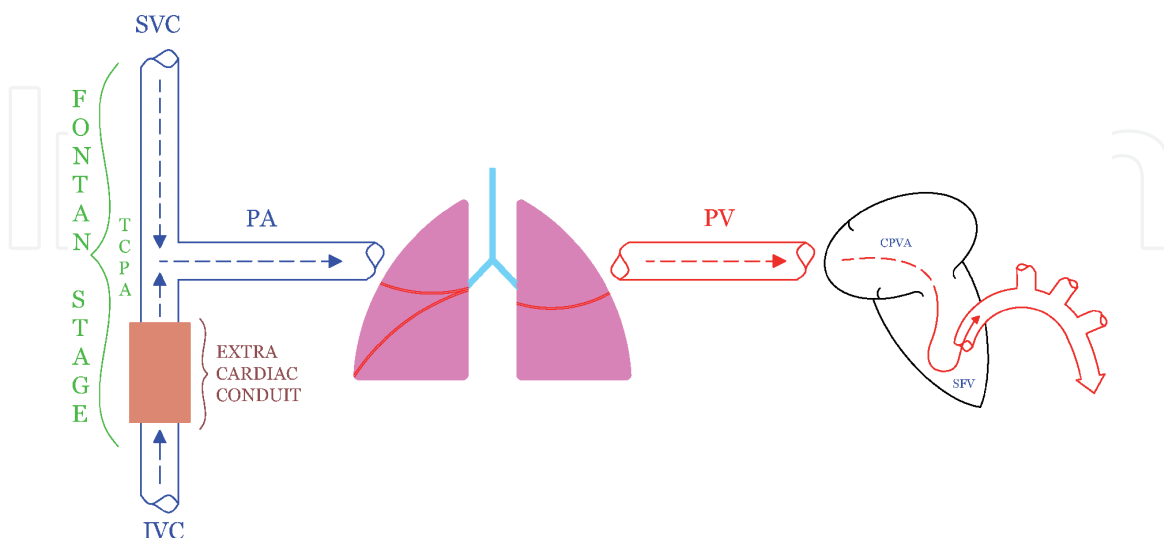


Figure 3.

Fontan anatomy. Shows how systemic venous blood passively enters the pulmonary artery (PA) circulation through a total cavopulmonary anastomosis (TCPA). Blood prevents the right atrium through a baffle or conduit. Blood is oxygenated in the lungs and enters the pulmonary venous (PV) system reaching the left atrium. The right and left atrium now function as a common pulmonary venous atrium (CPVA). A single functional ventricle (SFV) actively drives blood flow through the systemic arteries and capillaries, with a systemic venous return that passively enters the pulmonary circulation. The final stage of Fontan results in the conversion of a parallel circulation to a pulmonary and systemic circulation that is in series.

component is that the systemic venous return will reach the pulmonary arterial system without direct influence of a pumping chamber [2, 5].

The driving force that maintains adequate blood flow and therefore cardiac output (CO), is the pressure difference between the central venous pressure (CVP) and the common atrial pressure (CAP), that is also known as the transpulmonary gradient, for it to be adequate requires a well-functioning SV, decrease afterload and sufficient preload [5] (**Figure 4**).

The Fontan operation produces a state of chronic low CO [8] and relies on nonpulsatile, passive flow of caval blood to the PAs. Because there is not a sub-pulmonary ventricle, the circulation relies on low pulmonary pressures and low PVR. Forward flow through the pulmonary vasculature depends on a differential between the CVP and CAP [5]. Systemic venous hypertension is necessary to drive blood flow through the pulmonary vasculature with systemic venous pressure typically 5 mmHg higher than the pulmonary venous-atrial pressure [7].

2.4 Fenestration

An important feature of Fontan procedures, particularly lateral tunnel TCPC, is the fenestration or a surgically created small opening between the Fontan baffle pathway and the atrium. This 4-mm hole serves as a “pop-off” during times of high PVR and in essence maintains CO at the expense of a right-to-left shunt [5, 9] (**Figure 4**).

There is evidence including a prospective randomized trial that fenestration decreases the incidence of prolonged post-operative effusions, reduce post-operative lengths of hospital stay, and lessen the need for early reinterventions [4].

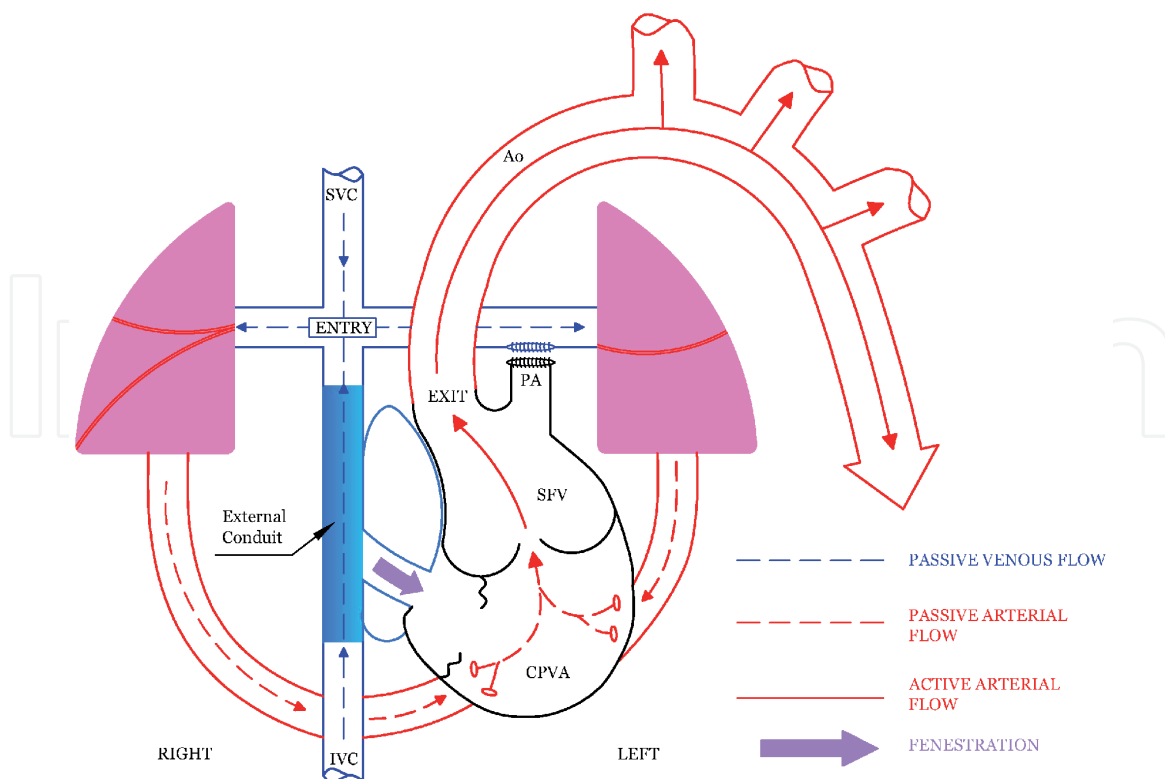


Figure 4.

Fontan physiology. The right-to-left shunt through the fenestration allows the systemic venous blood to bypass the Fontan portal system, thereby increasing the single ventricle preload, increasing cardiac output, and decreasing systemic venous congestion at expense of cyanosis that results from a lower arterial oxygen saturation (SVC, superior vena cava; IVC, inferior vena cava; Ao, aorta; PA, pulmonary artery; SFV, single functional ventricle; CPVA, common pulmonary venous atrium).

The right-to-left shunt through the fenestration allows the systemic venous blood to bypass the Fontan portal system, thereby increasing the SV preload, increasing CO, and decreasing systemic venous congestion at expense of cyanosis that results from a lower arterial oxygen saturation [9, 10].

Theoretically, the fenestration poses a risk for systemic embolic events and persistent cyanosis; however, the improved CO may have beneficial effects on oxygen delivery and will also help to alleviate the congestion felt in upstream organs, particularly the liver [2, 5].

2.5 Fontan failure

Though life-saving, the univentricular Fontan circulation does not reproduce biventricular physiology and although generally well tolerated in childhood, it seems to be less well tolerated over time, affecting organ systems outside the heart. Fontan physiology can best be thought of as a man-made form of chronic heart failure (CHF) [10] and there are a significant number of medical complications associated with the long-term. There is evidence that circulatory failure rather than ventricular failure is most important in the failing Fontan.

Griffiths et al. evaluated the outcomes of failing Fontan patients listed for transplant and observed decreased survival in patients with preserved ventricular function compared with those with impaired ventricular function [11]. The clinical deterioration can occur in the absence of ventricular dysfunction, suggesting that distinct mechanisms are contributive in comparison with heart failure patients from other etiologies.

Depiction of the hemodynamic profile of Fontan failure has been similar to traditional heart failure: elevated CVP, pulmonary capillary wedge pressure and systemic vascular resistance (SVR) with a low cardiac index (CI). Hebson et al. [12] evaluated the hemodynamic profile of a symptomatic adult Fontan (SAF) cohort with significant symptoms such as refractory edema, ascites, protein-losing enteropathy (PLE) or considerable exercise intolerance regardless of ventricular function. In the SAF patients, although CVP and pulmonary capillary wedge pressures were elevated, SVR index was low and CI was preserved even in the context of more severe symptoms. This suggests additional mechanisms influencing the hemodynamics and contributing to the symptoms of Fontan failure.

Fontan patients cannot proportionately augment their CO above a certain threshold, thus potentiating renal hypoperfusion and leading to refractory symptoms [12] and in cases where the systemic ventricle functions poorly, the heart can make an already compromised circulation worse.

In a biventricular system, systolic performance will only affect CO at rest when the ventricular function is severely depressed. In a normal subject, CO is not influenced by an increase of PVR up to 5 Woods Units. In Fontan patients, PVR is the primary modulator of CO. Failing Fontans typically have a high PVR. The loss of pulsatile flow after TCPC affects the usual vasoreactivity of the pulmonary bed. Ideally the lung vessels should be slightly oversized with low resistance. However, more frequently the abnormal development may result in relative hypoplasia of the large vessels coupled with endothelial dysfunction.

In all Fontan patients, an increase in PVR is invariably associated with a decrease in CO. If PVR is low, a reasonable output is achieved in patients with normal or moderately depressed ventricular function. However, severely depressed ventricular function results in low output [2] (**Figure 5**).

Late Fontan failure might present gradually and insidiously over years. The nature of Fontan failure is heterogenous, it is likely that not all patients “fail” in the same way, and each patient should be evaluated individually when looking for underlying causes [12].

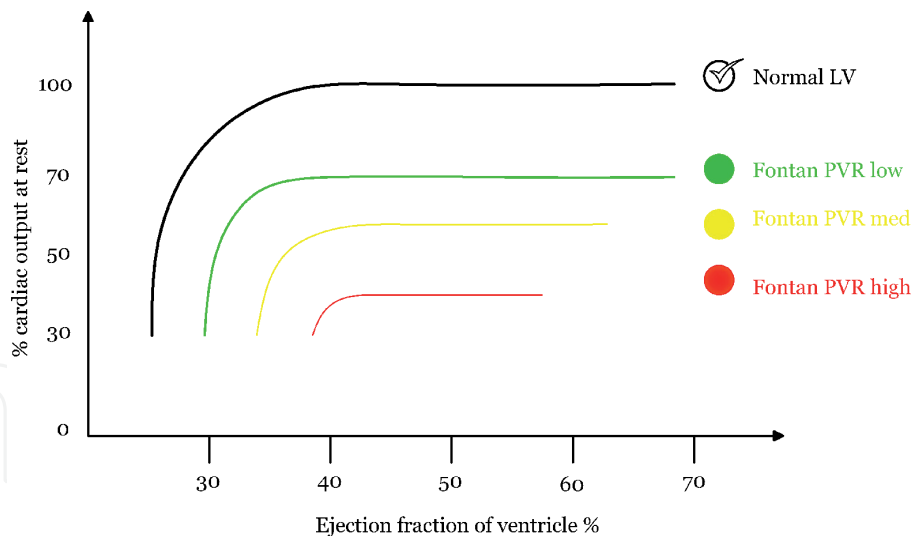


Figure 5. Modulation of CO by PVR in normal and Fontan patients. In Fontan patients, PVR is the primary modulator of CO. If PVR is low, a reasonable CO is achieved in patients with normal or moderately depressed ventricular function. However, severely depressed ventricular function results in low CO (CO, cardiac output; PVR, pulmonary vascular resistance; LV, left ventricle).

The circulatory problem in Fontan is the limit in the preload created primarily by the damming effect of this neoportal system. The strategy is to maximize the efficiency of this system, which could have better outcomes than more traditional heart failure therapies [2].

The components that make up the Fontan system are critically important in the overall function of the Fontan circuit. These components include the venoarterial Fontan connection itself, PAs, pulmonary capillary network, pulmonary veins, and the venoatrial connection. Impairment at any level of this portal system will have profound consequences on the output of the Fontan circuit [2] (**Figure 6**). Impairments at any component level include, but are not limited to, stenosis, hypoplasia, distortion, vasoconstriction, pulmonary vascular disease, loss or exclusion

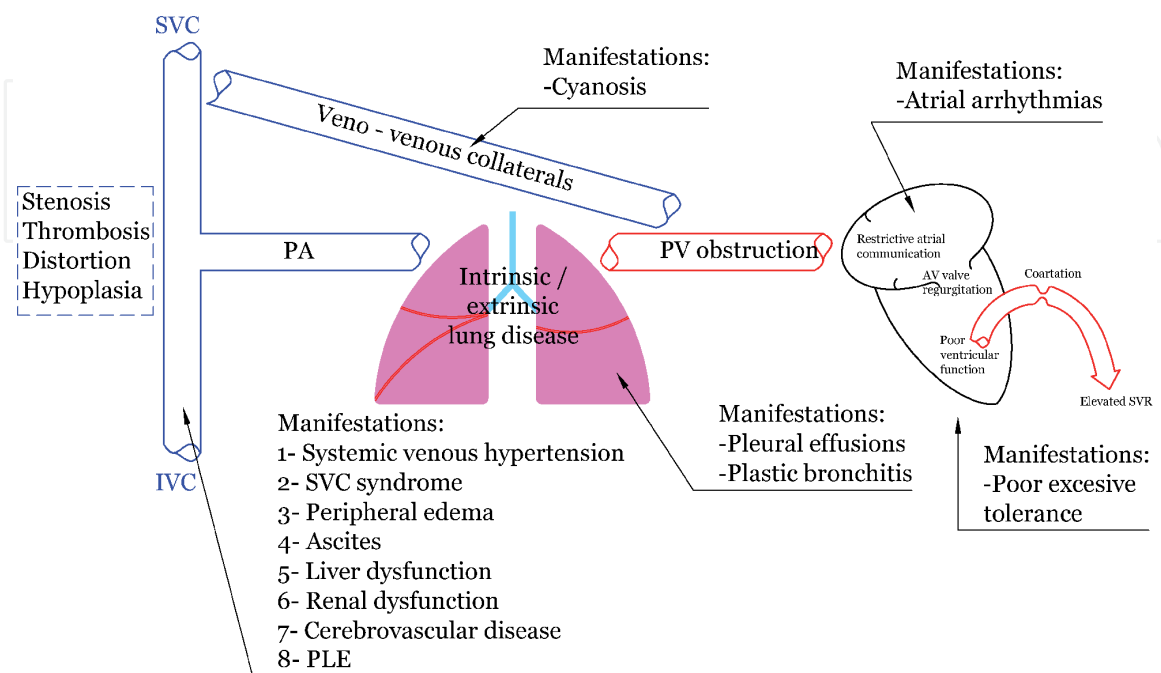


Figure 6. The failing Fontan (PA, pulmonary artery; PV, pulmonary vein; AV, atrioventricular; SVR, systemic vascular resistance; SVC, superior vena cava; IVC, inferior vena cava; PLE, protein-losing enteropathy).

of large vessels or microvessels, turbulence and flow collision, flow mismatch and obstruction by external compression [2].

Bypassing the pulmonary vasculature can partially reverse the restrictions to CO imposed by the neoportal system. A Fontan fenestration allows flow to bypass the neoportal system, which results in venous decongestion and increase in CO.

However, while a fenestration can increase overall output, it does so at the expense of diminished arterial oxygen saturation. Nevertheless, in the setting of a fenestration, the increase in CO can result in an increase in peripheral oxygen delivery even if the saturation is diminished.

The strategy to manage a failing Fontan starts by determining modifiable conditions and intervene if it is deemed necessary. The first step is imaging, using transthoracic echocardiography (TTE) and cardiac magnetic resonance (CMR) to obtain a full image of the Fontan anatomy. Assessment of atrioventricular valve regurgitation could be difficult therefore the use of transesophageal echocardiography (TEE) is needed sometimes. Catheter-based intervention is used if obstruction is identified. Surgical interventions are necessary in certain cases.

The goal of the management of the patient with Fontan physiology is to preserve symptom-free survival for as long as possible.

3. Preoperative evaluation of the Fontan patient

3.1 Perioperative risk stratification

Anesthesiologists outside of referral pediatric cardiovascular hospitals should be familiar with the anatomy, physiology, long-term manifestations and unique perioperative management of patients with Fontan palliation, and in the preoperative anesthesia consultation it is of paramount importance to define if this group of patients have an increased perioperative risk.

Faraoni et al. investigated the post-operative outcomes in children with and without CHD undergoing noncardiac surgery [1]. This study was performed using data from the 2012 pediatric database of the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP Pediatric). They included elective versus emergent surgery, and different surgical types (i.e., thoracic, neurological, orthopedic, general pediatric (including ear, nose, and throat), plastics and urogynecology).

Children with CHD were classified into three groups: minor, major and severe CHD, as defined in the ACS NSQIP database, based on residual lesion burden and cardiovascular functional status (**Table 1**).

This authors evaluated in the cohort of patients if the presence of major or severe CHD is associated with an increased risk of anesthesia and surgery. Of the 51,008 children included in the database, 4520 children with CHD underwent noncardiac surgery. After propensity score matching, they included 2805 children with minor CHD, 1272 with major CHD, and 417 with severe CHD. The overall mortality was significantly higher in children presenting moderate (3.9%) and severe (8.2%) CHD compared with controls (1.2% and 1.7% respectively). No statistical difference was observed in children with minor CHD (1.5%) and their controls (1%).

The conclusions of the authors are children with major and severe CHD undergoing noncardiac surgery have an increased risk of mortality, and a higher incidence of post-operative reintubation compared with matched controls undergoing comparable procedures. In the study, overall mortality in children with CHD was 2.8% compared with 1.2% in children without CHD, corresponding to a 2.3-fold higher mortality rate in children with CHD. In conclusion, children with major or

Minor CHD:
<ul style="list-style-type: none">• Cardiac condition with or without medication and maintenance (e.g., atrial septal defect, small-to-moderate ventricular septal defect with no symptoms)• Repair of congenital heart defect with normal cardiovascular function and no medication
Major CHD:
<ul style="list-style-type: none">• Repair of congenital heart defect with residual hemodynamic abnormality with or without medications (e.g., Tetralogy of Fallot with wide open pulmonary insufficiency, HLHS including stage 1 repair)
Severe CHD:
<ul style="list-style-type: none">• Uncorrected cyanotic heart disease• Patients with any documented pulmonary hypertension• Patients with ventricular dysfunction requiring medication• Listed for heart transplant

CHD, congenital heart disease; HLHS, hypoplastic left-heart syndrome.

Table 1.
Groups of children with CHD.

severe CHD who undergo noncardiac surgery have an increased risk of mortality with a higher incidence of life-threatening postoperative outcomes compared with children without CHD [1].

Then Faraoni et al., developed a validation of a risk stratification score for children with CHD undergoing noncardiac surgery [13]. The objective of this study was to identify the predictors for in-hospital mortality, and to develop a risk stratification score that could be used to help decision making and the development of perioperative management guidelines. This study was performed using data from the 2012, 2013, and 2014 pediatric databases of the ACS NSQIP and included all children with major or severe CHD as previously defined. They were able to identify eight predictors for in-hospital mortality in children with major and severe CHD undergoing noncardiac surgery: four were preoperative markers of critical illness (inotropic support, mechanical ventilation, preoperative cardiopulmonary resuscitation (CPR) and acute or chronic kidney injury), the type of lesion (e.g., single ventricle physiology (SVP)) and the functional severity of heart disease (e.g., severe CHD). All of them were excellent predictors of in-hospital mortality (**Table 2**).

Children with SVP were identified to be at high risk for perioperative complications and at increased risk of in-hospital mortality regardless of their functional status. Although ACS NSQIP Pediatric database allows identification of patients with SVP, does not provide accurate information on their specific stage of palliation [13].

The 2018 ACC/AHA guidelines for the management of adults with CHD (ACHD) stated that patients with ACHD may have greater operative risk than patients without ACHD. The guidelines recommend optimization before and close surveillance after invasive procedures regardless of the complexity of the anatomic defect or type of procedure. In patients with ACHD, especially those with complex disease (ACHD AP classification II and III) and/or whose disease has progressed (stages B, C, D), noncardiac surgical and interventional procedures should be performed in a hospital with or in consultation with experts in ACHD when possible. Because the inability to access resources or urgent conditions may preclude transfer or timely consultation, collaboration with members of the multidisciplinary ACHD team may be helpful [14].

-
1. Critical illness: inotropic support, mechanical ventilation, preoperative CPR, acute or chronic kidney injury
 2. SVP
 3. Functional severity: major CHD and severe CHD
-

CPR, cardiopulmonary resuscitation; SVP, single ventricle physiology; CHD, congenital heart disease.

Table 2.
Predictors of in-hospital mortality.

3.2 Multisystem approach for Fontan patient evaluation

Even though mortality in patients with SVP who undergo staged palliation has decreased significantly over the past decades, Fontan physiology and its long-term complications (e.g., arrhythmias, circulatory failure, multi-organ compromise, etc.) continue to pose significant challenges in the management of children and adults requiring anesthesia for noncardiac surgical or invasive procedures.

The preoperative evaluation of the patient with Fontan physiology involves a thorough history and physical examination as well as review of recent cardiovascular imaging studies, using a multisystem approach with attention to the unique characteristics of this patient population (**Figure 7**).

In the preoperative evaluation the anesthesiologist must define if the Fontan patient has a normal functioning or a failing Fontan, since it has important implications in the anesthetic management and in the perioperative care.

Medical history should focus on changes in health status, exercise capacity, hospital admissions, current medication and allergies. In addition to clinical examination, medical records, electrocardiography, chest X-ray, echocardiography, most recent catheterization, CMR imaging and laboratory data are invaluable to elucidate cardiac anatomy and the Fontan circuit, oxygen saturation, transpulmonary gradient and to assess ventricular function and valve regurgitation.

The physical exam of a well-functioning Fontan despite the univentricular pathology should be relatively unremarkable. The patient should be acyanotic, warm and well perfused. Precordial auscultation should be devoid of murmurs and peripheral arterial pulses are palpable. The arterial oxygen saturation is typically between 90% and 95% [5].

Failing Fontan physiology involves multiple organ systems: ventricular failure, hepatic dysfunction, long lasting pleural effusions, pulmonary hypertension, PLE, plastic bronchitis. Symptoms indicative of a failing Fontan include dyspnea, fatigue, decline in exercise tolerance, weight gain or volume retention, palpitations, syncopal or pre-syncopal episodes, a new or worsening murmur, hepatomegaly, oxygen saturation below 90% and dyspnea [5]. Cardiomegaly and/or pleural effusions may herald a failing Fontan.

3.2.1 Cardiovascular evaluation

3.2.1.1 Functional status and exercise capacity

At peak exercise, a normal subject with a biventricular circuit can increase his CO by a factor of 5. In a patient with Fontan physiology, there is not physiologic mechanisms to allow for a similar increase in CO because the maximal mean venous pressure rarely reaches 30 mmHg, there is inability to power blood through the pulmonary vasculature and subsequent blood acceleration, and the reactivity of PVR is

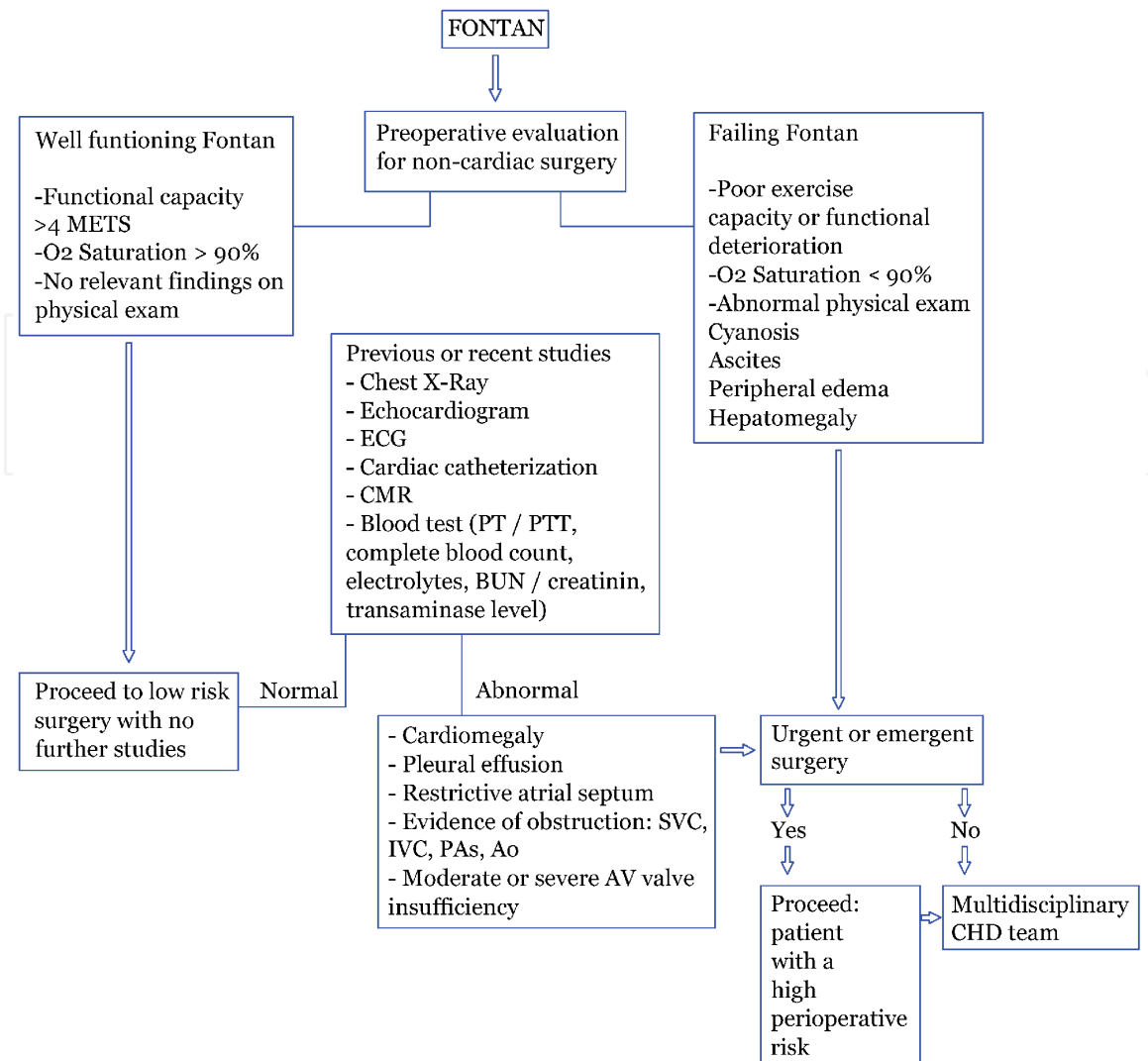


Figure 7.
 Multisystem approach for Fontan patient preoperative evaluation.

attenuated or absent. These limitations combined, result in the diminished ability to augment CO in response to an increase in metabolic demand, therefore limiting the Fontan patient to perform exercise (**Figure 8**).

Under resting conditions, the CO of a Fontan patient is 70–80% of what it would normally be for age and body surface area. During physical activity the limitations of the Fontan circuit are substantially magnified; a small difference of CO at rest can become a much larger difference during activity. At the best Fontan, the output is mildly decreased at rest with moderate capacity to increase flow during moderate exercise. In the failing Fontan patient, the output is severely reduced at rest and barely augments during minimal exercise [2] (**Figure 9**).

Fontan patients have lived with less than ideal CO their entire lives and might not recognize symptoms or demonstrate overt manifestations of progressive decline in functional status until deterioration is quite advanced [6].

The New York Heart Association (NYHA) classification, originally established for patients with CHF, is now widely used in CHD. It represents a simple classification of exercise intolerance based on subjective symptoms. NYHA class does stratify patients, distinguishing patients with mild impairment from those with moderate or severe impairment of objective exercise capacity and the presence and severity of symptoms signify a worse objective exercise capacity. In the study of Diller et al., ACHD patients had exercise capacities as poor as those of patients with acquired

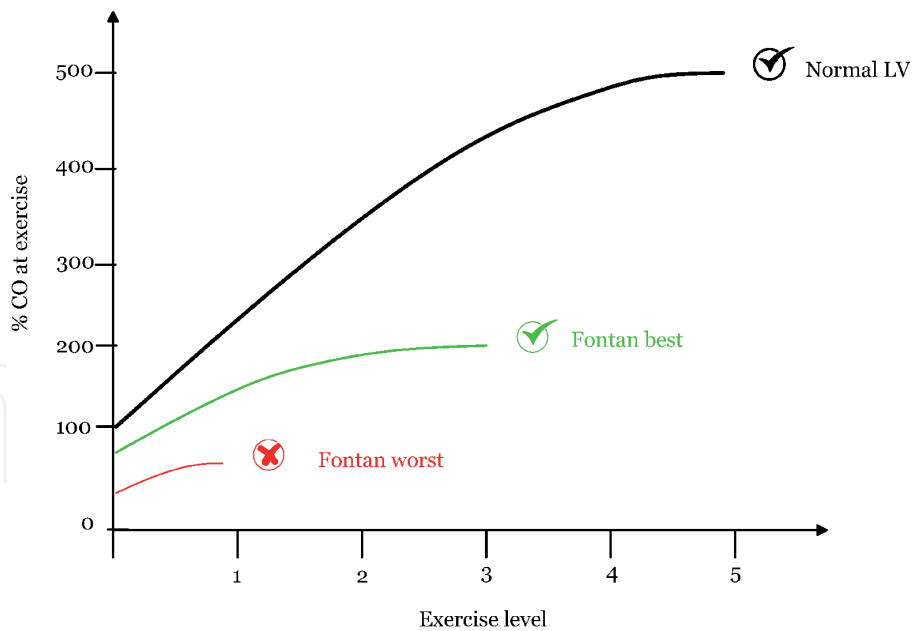


Figure 8.

CO and exercise level. At peak exercise, a normal subject with a biventricular circuit can increase his CO by a factor of 5. The Fontan patient has a diminished ability to augment CO in response to increased metabolic demand, and therefore limit the ability of a patient with a Fontan to perform exercise (CO, cardiac output; LV, left ventricle).

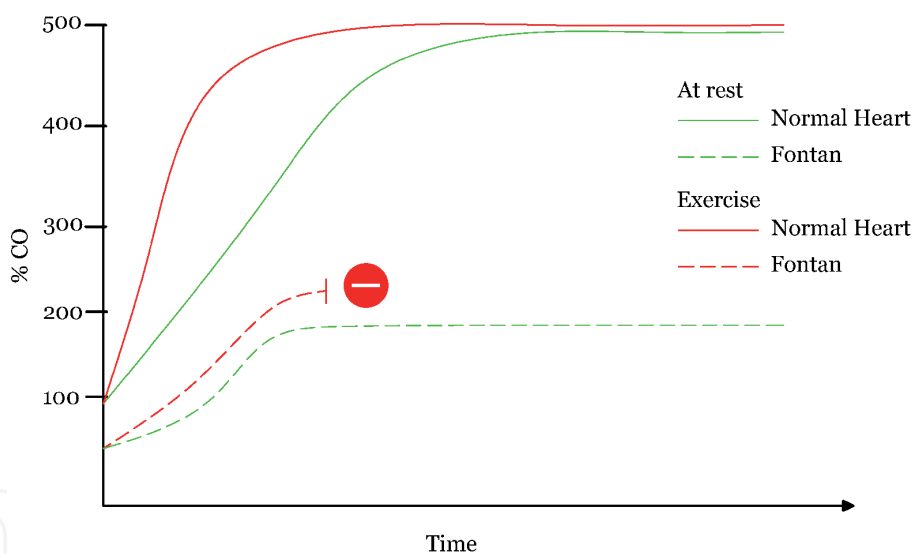


Figure 9.

Cardiac output in normal heart and the Fontan patient, during exercise and at rest. (CO, cardiac output).

CHF, even though the latter were much older [15]. Although NYHA class is used widely, the underlying criteria are subjective and the reproducibility is low.

In contrast to NYHA, cardiopulmonary exercise testing is the best way to assess exercise performance in ACHD patients, because it gives accurate, reproducible and quantifiable data on cardiac and respiratory performance, also allowing the assessment of unexpected deterioration. Most Fontan patients have undergone two or three re-operations, and this can lead to the development of restrictive lung defects in many patients. This finding, in addition to the restrictions in augmentation of the CO on exercise, contribute to a reduction in the measured peak oxygen uptake (peak VO_2), with average Fontan patients achieving a peak VO_2 of 60–70% that of age/sex/size-matched controls [7]. Longitudinal studies of late adolescents and young adults demonstrate this point well; as patients progress to late adolescence

and early adulthood, exercise capacity tends to continue to decline by about 2.6% predicted per year [9, 16]. In many forms of CHD the cutoff for the development of symptoms of heart failure is an exercise capacity of 45–50% of the predicted value. Assuming a starting point of 65% predicted for age and at the onset of puberty in a Fontan patients, and calculating a decline of 2.6% per year thereafter, the cutoff of 45% predicted can be expected to be reached at the end of the second decade of life [2] and as typically occurs in the third decade of life, hospitalization rates and symptoms increase significantly [6, 16, 17]. Cardiopulmonary exercise testing can objectively quantify exercise tolerance and help guided therapy, therefore, peak VO_2 is an essential component of a tailored exercise and activity program [6].

In the Mayo Clinic cohort [10], 80% of the patients after the Fontan operation rated their current health as excellent, and a similar percentage of patients thought that their physical status was improved. This is consistent with previously reported data suggesting that patients tend to perceive themselves as having a higher functional status compared with control populations.

In the preoperative evaluation, it is important to recognize that NYHA class underestimates the true degree of exercise limitation in Fontan patients. It is likely that Fontan patients have made lifelong adaptations to their cardiovascular disease and its slow progression, so they are not aware of the true extent of their exercise intolerance and could consider themselves asymptomatic. The presence and severity of symptoms signify a worse objective exercise capacity in these patients [15].

3.2.1.2 Arrhythmias

Some factors contributing to arrhythmogenicity include systolic and diastolic dysfunction, atrioventricular valvular regurgitation, atrial enlargement, multiple cardiac procedures, myocardial fibrosis, APCs, intra-atrial tunnels and an abnormal array of atrial fibers. The incidence of late atrial tachyarrhythmias approaches 50% in the adult population after Fontan palliation and often results in decreased exercise capacity, fatigue and congestive heart failure [5–7, 10].

In the Mayo Clinic cohort [10], the diagnosis of new clinical arrhythmias during long term follow-up was present in 44% of the patients. Freedom of arrhythmia at 10, 20 and 30 years after the Fontan operation was 71%, 42% and 24% respectively. The majority of this patients had atrial fibrillation or flutter, and a smaller proportion presented, atrial tachycardia, re-entrant supra ventricular tachycardia and ventricular tachycardia.

Sinus node dysfunction is common in all Fontan variants, with prevalence rates as high as 40%. Sinoatrial dysfunction and bradyarrhythmias may necessitate placement of a dual-chamber pacemaker or resynchronization therapy [5].

In general, many strategies have been employed to reduce the arrhythmia burden, including oral antiarrhythmics and catheter ablation. A catheter-based ablation strategy has a considerably lower success rate in Fontan patients compared with other forms of CHD, with recurrences or new arrhythmias in approximately 50% within 4–5 years [6].

In the preoperative evaluation one should recognize the history of such arrhythmias and history electrophysiological procedures.

3.2.2 Pulmonary evaluation

In the preoperative evaluation determine the patient's saturation on room air, which in a well-functioning Fontan should be between 90% and 95%. In the case of desaturation, it is important elucidate the cause of hypoxemia (**Table 3**).

Low pulmonary venous saturation:
<ul style="list-style-type: none"> • Pleural effusions • Pulmonary arteriovenous malformations • Intrinsic lung disease • Plastic bronchitis
Right-to-left shunt:
<ul style="list-style-type: none"> • Veno-venous collateral vessels • Persistent fenestration • Baffle leak

Table 3.
Common sources of hypoxemia in the Fontan patient.

Persistent or recurrent pleural effusions can be a source of hypoxemia in Fontan patients. Systemic oxygen desaturation can also be found because of intrapulmonary shunting due to arteriovenous malformations. The unequal distribution of hepatic blood flow to the pulmonary system is the most accepted etiology. Less hepatic blood flow to the pulmonary vasculature makes it more prone to developing arteriovenous malformations [5].

As pointed before, most Fontan patients have undergone at least two or three open chest procedures and may have undergone a thoracotomy that leads to a restrictive lung defect. Nearly half of all ACHD patients have lung disease with a primarily restrictive pattern, which represents an independent predictor for mortality [18]. The etiology is multifactorial: intrinsic causes of restrictive lung disease range from decrease in the pulmonary blood flow, development of arteriovenous malformations at the level of the lung and the long standing persistent abnormal physiology that contributes to the changes in the pulmonary vascular bed. Extrinsic causes are related to the multiple re-operations, congenital chest wall and spinal deformities, preexisting muscle weakness, all having an effect in the pulmonary mechanics. Other contributing factors as extended mechanical ventilation due to critical illness during childhood, chronic aspiration, acquire muscle weakness, and poor nutrition, can result in impaired pulmonary function [18].

Plastic bronchitis is a rare complication reported in less than 1–2% of Fontan patients. It is characterized by bronchial casts, with potential for airway obstruction. Segmental airway obstruction can result in regional atelectasis and hypoxemia. Dyspnea, chronic cough, and recurrent expectoration of rubber airway casts are characteristic of this disorder. Plastic bronchitis can be life-threatening on presentation [6].

Another source of hypoxemia in Fontan patients include persistent right-to-left shunting. Maintaining adequate preload for the SV is challenging in the Fontan patient, and it relies on a number of “auto-regulatory” phenomena, including the development of veno-venous collateral vessels that pass from the systemic veins to the pulmonary venous circulation shunting deoxygenated blood directly into the oxygenated pulmonary venous system or the common atrium. The downside to maintaining an adequate preload and CO is the profound cyanosis that can be worsened by physical exertion (**Figure 6**).

The strategy employed in many centers is a catheter based embolization of these vessels. The impact on the symptoms or survival has not been determined, and further reduction in oxygen saturation post-procedure, suggest a high recurrence rate [5, 7].

Systemic-to-PA collaterals are a frequent finding in cyanotic Fontan patients. Left alone, these collateral vessels may result in pulmonary hypertension and failure of the Fontan circulation.

3.2.3 Hematologic evaluation

Hypercoagulability and hypocoagulability both are more prevalent in patients with Fontan physiology [18].

After the Fontan operation, patients have been reported to have numerous clotting abnormalities including deficiencies of protein C, protein S and antithrombin III. Hypercoagulability combined with decreased CO, a nonpulsatile low flow state to the pulmonary circulation, a high incidence of atrial arrhythmias and the presence of prosthetic material, contribute to a higher risk for thrombus formation in the Fontan patient [9].

Some studies have reported a rate of thrombus formation of up to 20% in patients after a Fontan procedure and they are a source of significant morbidity and mortality [5, 9]. The incidence of thromboemboli after the extracardiac cavopulmonary connection is estimated to be 7.1% at 10 years after Fontan completion. This can result in pulmonary emboli, systemic emboli through a patent fenestration and systemic thrombi in the atria, PA stump or rudimentary ventricle [9].

Approximately 10% of patients within the first 5 years after Fontan palliation, develop thrombotic occlusion of central veins, this can result in pulmonary emboli and in SVC obstruction. Clinicians should not assume patency or availability of venous access for central monitoring of the subclavian, internal jugular or femoral vessels. The anesthesiologist relies on cardiac catheterization reports and Doppler ultrasound to assess vascular patency of the venous and arterial tree [5]. Many patients are on anticoagulants or aspirin, especially those with thrombosis history or with a failing Fontan with any of the following manifestations: ventricular failure, hepatic dysfunction, long lasting pleural effusions, pulmonary hypertension, PLE, and plastic bronchitis.

3.2.4 Neurologic evaluation

The reported incidence of stroke ranges from 3% to 20%. Cerebral vascular accidents have been reported in adult patients with Fontan physiology secondary to atrial arrhythmias, hematologic derangements and systemic embolic events [5].

3.2.5 Hepatic and gastrointestinal evaluation

Fontan physiology, in particular, with the multitude of insults from persistent congestive hepatopathy, hypoxia, and ischemic hepatitis, has a high incidence of liver dysfunction [18].

There is growing recognition of the deleterious effects of systemic venous hypertension on hepatic function and the development of fibrosis, cirrhosis and hepatocellular carcinoma.

PLE is a cardinal sign of failing Fontan palliation. Pleural effusions with associated decreases in oxygen saturation, peripheral edema, ascites, malabsorption and loss of immunoglobulins are consistent findings in patients with PLE. Hypoalbuminemia, decreased total protein and stool positive for alpha 1-antitrypsin confirm the diagnosis [5, 7].

In the Mayo Clinic cohort [10] was found that although the Fontan procedure has improved overall survival in patients with SV, various events impact long-term survival, including diagnosis of PLE. The overall incidence of PLE in this study was 9%. Overall mortality in the PLE cohort was 72% during 7 + - 7.4 years of follow-up. Survival at 5, 10, and 20 years after PLE diagnosis was 50%, 35% and 19%, respectively [10].

3.2.6 Renal evaluation

ACHD patients have a prevalence of renal dysfunction 18 to 35 fold higher compared to the general population. Renal dysfunction is seen in 50% of Fontan patients, including a 15% presenting with severe reduction of glomerular filtration rate [19].

3.2.7 Imaging

Preoperatively the use of recent or previous imaging studies allows the proper assessment of the Fontan cardiac function, pathway and vascular anatomy.

Chest radiography can present with abnormalities consistent with a failing Fontan, including cardiomegaly, pleural effusion and pulmonary edema.

To evaluate systolic and diastolic ventricular function is important to perform a preoperative TTE or TEE, it also evaluates atrioventricular valve function, the presence of an open fenestration and detects intracardiac thrombi.

Cardiac catheterization evaluates the Fontan hemodynamics measuring CAP, CVP, ventricular end-diastolic pressure, sampling blood along the vessels and chambers to determine their saturations and, CI calculation with the Fick Method. A high preoperative CAP suggests poor ventricular function, atrioventricular valve dysfunction or the presence of aortopulmonary collaterals. Isolated high CVP with low CAP reflects increased PVR or an obstruction along the Fontan pathway.

Cardiac catheterization can also allow the measurement of pressure gradients of obstructive lesions in the vena cava, pulmonary vessels and across the atrial septal defect. It is also used to assess the presence of right-to-left shunts causing desaturation as baffle leaks, fenestrations, decompressing veno-venous collateral vessels, pulmonary arteriovenous malformations and systemic to pulmonary collaterals. Catheter-based interventions may be required to alleviate obstruction in the Fontan pathway, for managing profound cyanosis or for stenting of branch PA stenosis or venous pathway obstruction [7].

CMR imaging is increasingly used in assessing anatomy, flow, and function in the Fontan patient without a pacemaker [5, 7]. It is used to assess Fontan pathway flow, it also assess pulmonary venous return to exclude obstruction. In addition it can provide with an accurate assessment of the ventricular function and assessment of the branch PAs, and in the ventricular outflow pathway it can exclude recoarctation or narrowing [7].

Urgent and emergent noncardiac surgeries or invasive procedures should not be delayed for sophisticated imaging in the preoperative evaluation, but the anesthesiologist should be aware of the previous studies and the actual anatomy of the patient.

4. Intraoperative management

Although there are guidelines for the perioperative management of patients with CHD undergoing noncardiac surgery [14, 18, 20–22], these recommendations are based on experience and expert opinion. The diversity of structural malformations in CHD, each with specific physiologic perturbations, hemodynamic consequences, and functional limitations, makes the development of general guidelines for perioperative management challenging [13].

4.1 Hemodynamic monitoring

Standard American Society of Anesthesiologists (ASA) intraoperative monitoring is often adequate for patients with a well-functioning Fontan, particularly for procedures in which minimal hemodynamic derangements or fluid shifts are expected.

For the failing Fontan patient or well-functioning Fontan patient presenting for more complex surgical procedures, intra-arterial blood pressure monitoring is useful for beat-to-beat monitoring of blood pressure and blood sampling to assess sufficient systemic perfusion and adequate balance in oxygen delivery and consumption by measuring laboratory values such as lactate levels and central venous oxygenation [5, 18].

Upper-extremity blood pressure (noninvasive and radial arterial catheters) should be measured in the arm opposite to a previous Blalock-Taussig shunt (subclavian artery-to-PA) to avoid falsely low blood pressure measurements [5].

It should be noted that CVP actually reflects mean PA pressure (MPAP) in Fontan patients.

Intraoperative placement of transcutaneous defibrillator pads is prudent in patients with a history of arrhythmias [5].

4.2 Vascular access

Regarding vascular access, abnormal vascular anatomy of the initial CHD, post-surgical changes, multiple vascular interventions, and prior thrombus formation can pose significant challenges when patients are in need of vascular access [5].

Even though upper central venous access is possible in patients with Fontan circulation, exact knowledge of vascular anatomy is crucial for venous cannulation. Venous mapping can be highly valuable before any intervention, and access obtained by interventional radiologists under direct fluoroscopic guidance may be required. A graph depicting which vascular access is patent in a particular patient should be readily available to the care team in order to avoid difficulty in placing lines in an emergency [18].

Another consideration when obtaining and maintaining vascular access is the risk of paradoxical emboli in the presence of right-to-left or bidirectional shunting through the post-surgical fenestration. Entrained air and dislodged thrombotic or infectious material can lead to paradoxical emboli and to infarction of brain, gut, kidney, and other end organs [18]. Before the administration of intravenous fluids or medications, all air must be evacuated meticulously and filtered to avoid systemic air embolism and use of air filters can mitigate the risk of accidental air entrainment [5, 18].

It is recommended that central venous catheters be removed as soon as possible to avoid thrombotic complications [5].

4.3 Anesthetic goals

There are important anesthetic considerations for the patient with Fontan physiology.

4.3.1 Maintenance an optimal transpulmonary gradient

The mainstay of anesthetic management is to maintain an optimal transpulmonary gradient in order to achieve an adequate pulmonary blood flow and CO. The Fontan (CVP = MPAP) is typically 10 to 15 mmHg with a transpulmonary gradient of 7 mmHg. It is helpful to determine CAP values from the preoperative catheterization because the anesthesiologist will not monitor this value in the operating room.

4.3.2 Differential diagnosis of desaturation

The differential diagnosis of acute oxygen desaturation in the intraoperative period may include factors unique to the Fontan patient.

Right-to-left shunts become important causes of hypoxemia. Acute elevation of PVR may cause right-to-left shunting across a fenestration or a baffle leak with the consequent drop in the saturation of the patient. PVR may be decreased acutely with hyperventilation ($p\text{CO}_2$ 30 mmHg or pH 7.45) and increasing concentrations of oxygen. Usual sources of hypoxemia in the perioperative period such as endo-bronchial intubation, bronchospasm, and atelectasis always should be considered.

4.3.3 Respiratory management

The circulatory arrangement of the Fontan amplifies the effects of respiratory mechanics upon venous return. Negative intra-thoracic pressure augments the antegrade flow from the SVC, IVC, and hepatic venous circulation into the pulmonary arterial tree. The work of breathing is a significant additional energy source to the circulation in these patients. Normal negative pressure inspiration has been shown to increase pulmonary blood flow in patients after the TCPC [3]. Physiologically there is a correlation between total hepatic venous flow and respiration. During inspiration there is marked increase in hepatic venous contribution to the total venous return, due to a dual effect on venous pressure and compression of the liver by diaphragmatic descent. The liver acts as a sump of blood which can be drawn upon during inspiration [3].

Magnetic resonance flow measurements have shown that approximately 30% of the CO can be directly attributed to the work of breathing in patients after the TCPC [3]. In Fontan patients, inspiration resulted in increased ventricular filling at rest and during exercise [23].

The opposite happens with positive pressure ventilation (PPV). It has long been known that increasing levels of positive end-expiratory pressure (PEEP) during PPV are adverse to the Fontan circulation. The available data suggests a linear relationship between mean airway pressure and CI in these patients: the higher the mean airway pressure, the lower CI [3]. This can be explained by the effect of lung volumes on PVR, since both over-distention and collapse of alveoli, result in increases in PVR.

The management of these patients should therefore be directed towards minimizing mean airway pressure when these patients are being ventilated for cardiac and noncardiac procedures. Also, an early postoperative restoration of normal negative pressure ventilation can be beneficial in these patients.

Adjustments to minimize positive intra-thoracic pressure can be made using minimal PEEP, smaller tidal volumes, pressure-regulated ventilatory modes, or spontaneous ventilation with minimal pressure support [18], and avoid prolonged Valsalva maneuvers. One should maintain these patients with the minimum mean airway pressure compatible with normal oxygenation and adequate alveolar ventilation.

A sound strategy when using PPV would be to adjust ventilatory parameters that allows to achieve the lowest mean airway pressure, moderate alkalosis (pH 7.45, $p\text{CO}_2$ 35 mmHg), and one that reduces the risk of atelectasis. Fontan patients have tolerated PPV with minimal hemodynamic effects as long as proper ventilatory settings are used. Furthermore, it has been proposed that monitored anesthesia care without adequate ventilation may be more detrimental than the physiologic effects of PPV per se [5].

4.3.4 Circulatory management

Fontan patients pose a particular clinical challenge for the anesthesiologist due to their abnormal physiology and high risk for adverse events. Pre-existing chronic end-organ dysfunction makes these patients susceptible to acute exacerbation or organ failure [18]. Information of baseline cardiac function and hemodynamics

from prior heart catheterizations can provide reference filling pressures to minimize the risk of over-resuscitation or under-resuscitation.

Fontan physiology patients are very sensitive to changes in preload, and high PPV settings can exacerbate hemodynamic instability as was explained before. Acute hypovolemia or vasodilation during critical illness can result in significant hypotension.

The effect of vasoconstrictors in augmenting preload in Fontan physiology is unclear because the compliance of the venous capacity system is reduced, and also an increase in ventricular afterload, due to arterial vasoconstriction, can decrease forward flow [18]. Hypervolemia due to excessive fluid resuscitation or chronically in the failing Fontan, can result in a reduced CO due to a decreased pressure gradient between systemic arterial and venous capacity system. Global congestion can lead to impaired pulmonary blood flow and right-sided congestion with subsequent pulmonary edema, kidney and hepatic dysfunction.

Finding the optimal volume status that balances adequate preload, venous congestion and organ perfusion could be challenging and requires vigilance and significant experience with these complex pathophysiologic states. Defining the end point of fluid administration (Blood components, Crystalloids) should be a balance of the risks and benefits of resuscitation. It is important to have the baseline pressures, hemoglobin level, signs of inadequate oxygen delivery, and concurrent factors affecting hemodynamics in order to decide how much and which fluid requires a particular patient [18].

Universally important applicable components when managing hemodynamics in these patients include maintaining adequate heart rate and intrinsic sympathetic tone, avoiding increases in PVR, and limiting harm from elevated intra-thoracic or intra-abdominal pressures [18].

Risks associated with medical intervention especially adrenergic agents are exacerbation of arrhythmias.

Low-cardiac-output syndrome will manifest as hypotension, elevated CVP, metabolic and lactic acidosis, and low urine output in the intraoperative period. Pharmacologically improving ventricular compliance lowers the CAP and increases the transpulmonary gradient without raising CVP. Milrinone, with its lusitropic and pulmonary vasodilatory properties, is well suited for the Fontan patient. Because systolic performance is not generally the primary issue in the Fontan circulation, the role of inotropic agents is often limited, and lowering the SVR while maintaining preload can be challenging. Inodilators increase the contractility of the SV, but may not result in clinically significant more CO. There may be a role for inotropes in the Fontan patient with significant ventricular dysfunction but in general the role of these agents is limited [2].

5. Conclusions

- Since prognosis of patients with univentricular heart has improved significantly in recent decades, this has resulted in the general anesthesiologist being able to meet at some point in his professional practice with this type of patients, whether to perform a noncardiovascular diagnostic or therapeutic procedure or noncardiac surgery. Therefore, the anesthesiologist must have an appropriate knowledge of Fontan's anatomy and physiology as well as those patients with failed Fontan in order to provide them with a correct preoperative evaluation and an adequate intraoperative and postoperative management, and to obtain the best results, thus achieving a better survival and quality of life in this population group.

- The differentiation between a patient with Fontan palliation in a compensated state versus the failing Fontan patient is one of the goals of the preoperative evaluation since the latter has a higher perioperative risk.
- Fontan patients may present with a multisystemic compromise and this poses challenges in the intraoperative management of noncardiac surgical or invasive procedures.
- Causes of intraoperative hypoxemia may be different from a patient with biventricular physiology. Situations unique for the Fontan patient include right-to-left shunting through the fenestration and the presence of venovenous collateral vessels.
- There is evidence that circulatory failure rather than ventricular failure is most important in the Fontan patient. In the failing Fontan one should rule out any problem in the Fontan circuit.
- Finally, this chapter covers a series of information with the purpose of facilitating a timely and complete orientation of univentricular patients in the stage of Fontan palliation, since these imply a challenge in professional practice.

Conflict of interest

No conflicts of interest to declare.

Thanks/other declarations

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Author details

Yamile Muñoz^{1*}, María José Sáenz² and Renzo Cifuentes³


¹ Department of Anesthesia, Clínica Cardio VID, Medellín, Colombia

² Department of Anesthesia, National Children Hospital, San José, Costa Rica

³ Department of Surgery, Division of Thoracic Transplantation and MCS, Miller School of Medicine, University of Miami, USA

*Address all correspondence to: yamilemp@yahoo.com

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