Chapter

Fontan Operation: A Comprehensive Review

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Abstract

Since the first description of the Fontan operation in the early 1970s, a number of modifications have been introduced and currently staged, total cavopulmonary connection with fenestration has become the most commonly used multistage surgery in diverting the vena caval blood flow into the lungs. The existing ventricle, whether it is left or right, is utilized to supply systemic circuit. During Stage I, palliative surgery is performed, usually at presentation in the neonatal period/early infancy, on the basis of pathophysiology of the cardiac defect. During Stage II, a bidirectional Glenn procedure is undertaken in which the superior vena caval flow is diverted into the lungs at an approximate age of 6 months. During Stage IIIA, the blood flow from the inferior vena cava (IVC) is rerouted into the pulmonary arteries, typically by an extra-cardiac conduit along with a fenestration, generally around 2 years of age. During Stage IIIB, the fenestration is closed by transcatheter methodology 6–12 months after Stage IIIA. The evolution of Fontan concepts, the indications for Fontan surgery, and the results of old and current types of Fontan operation form the focus of this review.

Keywords: Fontan operation, bidirectional Glenn procedure, modified Blalock-Taussig shunt, pulmonary artery banding, Norwood procedure, Sano shunt, extra-cardiac conduit, fenestrated Fontan, tricuspid atresia, double-inlet left ventricle, hypoplastic left heart syndrome, unbalanced atrioventricular septal defect

1. Introduction

Following the initial description of the physiologically corrective operation for tricuspid atresia by Fontan and Baudet [1] and Kreutzer and his associates [2] almost simultaneously, such surgery was widely adapted by most pediatric cardiologists and pediatric cardiac surgeons. This concept of bypassing the right ventricle (RV) was further extended to manage other cardiac defects with a functionally single ventricle.

The original surgery as described by Fontan and Baudet [1] consisted of (1) end-to-end anastomosis of superior vena cava (SVC) with the right pulmonary artery (PA) (classical Glenn procedure [3]), (2) connection of the separated right PA to the right atrium (RA) either directly or through an aortic homograft, (3) closure of the defect in the atrial septum, (4) insertion of a pulmonary valve homograft into the orifice of the inferior vena cava (IVC), and (5) ligation of the main PA, to entirely bypass the RV. On the basis of the procedures performed, one must infer that Fontan's concept was to use the right atrium as a pumping chamber;

therefore, he inserted a prosthetic valve into the IVC and right atrial-pulmonary artery junction.

On the contrary, Kreutzer et al. [2] anastomosed the right atrial appendage to the PA directly or by a pulmonary homograft and closed the ASD. Neither a Glenn procedure was performed nor a prosthetic valve was inserted in the IVC. Kreutzer's view appears to be that the RA does not function as a pump and that the left ventricle functions as a suction pump in the system.

The surgical procedure as generally performed appears to shadow Kreutzer's principle, and consequently, I have used the term "Fontan-Kreutzer operation" to describe this procedure [4–8]. However, because of priority of publication and more common usage in the literature, I will use the term "Fontan operation" in this chapter.

In this review, I will discuss the evolution of the Fontan concepts, the indications for Fontan operation, the Fontan procedure as used currently, and the results of old and current types of Fontan.

2. Evolution of the Fontan operation

A number of modifications of the aforementioned surgery were made by these [1, 2] and other groups of investigators [9, 10] in the field. In this section, these concepts/procedures will be reviewed.

2.1 Initial surgical modifications

During the first 20 years after Fontan's [1] and Kruetzer's [2] description of the procedure, a number of modifications of the surgery were undertaken by several surgeons, as extensively reviewed and referenced elsewhere [9, 10]. In general, there was a consensus that there is no need for a classic Glenn anastomosis and that a prosthetic valve is not necessary in the IVC. Detailed review of these papers revealed that four major types of Fontan operations were being performed for physiologic correction of tricuspid atresia. These include (1) RA-PA anastomosis, direct or through a non-valved conduit; (2) RA-PA anastomosis through a valved conduit; (3) RA-RV anastomosis, direct or non-valved anastomosis; and (4) RA-RV anastomosis through a valved conduit.

In order to understand the advantages of one operation over the other, 17 papers published as of December 1990 that have documented adequate information to evaluate mortality and reoperation rates for each of the four types of Fontan surgery were reviewed. Pooled data from these 17 articles and statistical comparisons were presented in Tables I–IV for the interested reader [9]. This analysis revealed that atriopulmonary (RA-PA) connection appears to be better than atrioventricular (RA-RV) anastomosis and direct connection is better than valved or non-valved conduit anastomosis. Nevertheless, atrioventricular valved (homograft) conduit anastomosis appears to have advantages of (1) restoring a four-valved, four-chambered, biventricular heart and (2) lower right atrial pressure than with atriopulmonary connection. Based on these data [9, 10], the following conclusions were drawn: (1) direct atriopulmonary connection for children with tricuspid atresia with normally related great arteries and a small (<30% of normal) right ventricle without trabecular right ventricular component and for patients who had tricuspid atresia with transposition of the great arteries and (2) atrioventricular valved (homograft) conduit anastomosis for patients with tricuspid atresia and normally related great arteries but with a right ventricular size greater than 30% of normal and a trabecular right ventricular component [9, 10].

2.2 Other developments

2.2.1 Bidirectional Glenn procedure (cavopulmonary anastomosis)

Bidirectional cavopulmonary anastomosis is a modified version of classic Glenn procedure in which the upper end of the divided SVC is anastomosed end to side to the right PA without disconnecting the latter from the main PA. Thus, the SVC blood is diverted into both the right and left PAs, justifying the term, "bidirectional."

Experimental bidirectional cavopulmonary anastomosis was first studied by Haller et al. [11] in animal models, and its first clinical use was described by Azzolina et al. [12] in 1972. Other investigators [13–17] later applied this technique to palliate complex heart defects with decreased pulmonary blood flow. Hemodynamic advantages of the bidirectional Glenn procedure are improvement of effective pulmonary blood flow, decrease in total pulmonary blood flow, and reduction of left ventricular volume overloading. In addition, preservation of continuity of the pulmonary artery is an added advantage and may help facilitate a low-risk Fontan procedure. When both right and left SVCs are present, bilateral bidirectional Glenn shunts should be performed, especially if the bridging innominate vein is absent or small. Based on our own experience and that published in the literature [13–17], the author recommended serious consideration in employing bidirectional cavopulmonary anastomosis as an interim palliative procedure for patients who are at an increased risk for the Fontan procedure [9, 10].

2.2.2 Lateral tunnel

Puga et al. [18] positioned a patch inside the right atrium to divert the IVC blood into the PAs; they had good results in the 12 patients that they used this technique. This was later called lateral tunnel and was widely used until extra-cardiac conduits came into vogue.

2.2.3 Total cavopulmonary connection

To better understand the valve-less atriopulmonary anastomosis type of Fontan, de Leval et al. [19] performed hydrodynamic studies and found that (1) the right atrium is not an efficient pump in non-valved atriopulmonary connections, (2) pulsations in a non-valved circulation truly generate turbulence with consequent decrease in net flow, and (3) energy losses occur in the non-pulsatile chambers, corners, and obstructions. In an attempt to address these deficiencies, they developed a procedure which they named "total cavopulmonary connection." In this procedure, they connected the divided SVC, end to side, to the undivided right pulmonary artery (bidirectional Glenn), and the IVC blood is diverted through a composite intra-atrial tunnel (with the use of posterior wall of the right atrium as posterior wall of the tunnel) into the cardiac end of the divided superior vena cava, which in turn was connected to the PA. They felt that technical simplicity, maintenance of low right atrial and coronary sinus pressure, and reduction of risk of atrial thrombus formation are advantages of this type of operation. They performed this procedure on 20 patients and observed two early deaths and one late death. Postoperative hemodynamic studies were performed in 10 of the survivors which indicated good results. They recommended this type of operation for patients with a non-hypertrophied right atrium. While the total cavopulmonary connection was initially devised for patients with complex atrial anatomy and/or systemic venous anomalies, it has since been used extensively for all types of cardiac anatomy with one functioning ventricle and irrespective of venous anomalies.

Subsequent experimental studies by Sharma and his associates [20] indicated that complete or minimal offset between the orifices of the SVC and IVC into the right pulmonary artery decreases energy losses.

2.2.4 Extra-cardiac conduit

Marcelletti et al. [21, 22] used an interposition extra-cardiac conduit from the IVC to the PA in place of lateral tunnel used in total cavopulmonary connection in 1990. Subsequently, most surgeons adopted this modification of total cavopulmonary connection, and currently extra-cardiac conduits are used in most Fontan operations.

2.2.5 Staged Fontan

Since the vast majority of patients requiring Fontan operation present as neonates or in the early infancy, palliative procedures are performed at the time of presentation, and subsequently (at 12–18 months of age) the Fontan operation is undertaken. A considerable mortality (~16%) was seen with primary Fontan surgery, largely related to the impact of rapid changes in ventricular geometry and development of ventricular diastolic dysfunction. The concept of further staging the procedure by performing bidirectional Glenn procedure around 6 months of age followed by final Fontan between 12 and 18 months of age was introduced in early 1990s [23, 24]. Performing the Fontan procedure in stages appears to decrease overall mortality, most likely related to improving the ventricular function by correction of the afterload mismatch that is associated with one-stage Fontan procedure. At the current time, most centers prefer staged Fontan with bidirectional Glenn initially, followed later by extra-cardiac conduit diversion of the inferior vena caval blood into the PA.

2.2.6 Fenestrated Fontan operation

In 1978, Choussat et al. proposed several criteria for performing Fontan operation [25]. Many cardiologists and surgeons have modified these criteria. Patients not meeting these criteria were deemed to be at a higher risk for a poor prognosis following a Fontan operation than patients who are within the limits of the set criteria. For the high-risk group, several investigators have proposed the concept of leaving a small atrial septal defect (ASD) open to facilitate decompression of the right atrium [26–28]. Laks et al. advocated closure of the atrial defect by constricting the preplaced suture in the postoperative period [28], while Bridges et al. [27] used a transcatheter closure method at a later date.

Higher cardiac output and significant decreases in the postoperative pleural effusions and systemic venous congestion were noted after a fenestrated Fontan procedure. In addition, the duration of hospitalization appears to have decreased. Nonetheless, these beneficial effects are at the expense of mild arterial hypoxemia and potential for paradoxical embolism.

While the fenestrated Fontan procedure was initially designed for patients at high risk for Fontan surgery, it has since been used in patients with modest or even low risk. Although rare, reports of cerebrovascular or other systemic arterial embolic events occurring after a fenestrated Fontan operation tend to contraindicate the use of fenestrations in patients with low or usual risk. In following years, fenestrated Fontan have been routinely used at most institutions. Some data indicate that routine fenestration is not necessary [29].

2.2.7 Device closure of Fontan fenestration

Patients who have undergone a fenestrated Fontan operation or patients who have a residual atrial defect, despite correction, may have clinically significant right-to-left shunt causing varying degrees of hypoxemia. These residual defects should be closed not only to address arterial desaturation but also for prevention of paradoxical embolism [30, 31]. Although two types of fenestration closure, namely, constriction of the preplaced suture in the postoperative period [26, 28] and device closure later [27] were described, device closure is opted at most institutions. Closure of such defects can be performed by using transcatheter techniques [32–35]. The procedure is usually performed 6–12 months following fenestrated Fontan procedure. Although a number of devices have been used in the past [32–35], at the present time, Amplatzer septal occluders are the most commonly used devices to accomplish such closures.

3. Indications for Fontan operation

The indications for opting for a Fontan operation are patients who have one functioning ventricle. At first, patients with tricuspid atresia were selected for this procedure [1, 2]. Shortly thereafter, patients with double-inlet left (single) ventricle were added to the indications for Fontan [36]. Following description of surgical palliation of hypoplastic left heart syndrome (HLHS) by Norwood et al. [37, 38] in the early 1980s, HLHS became the major lesion requiring Fontan operation. Subsequently, mitral atresia (with normal aortic root), unbalanced atrioventricular septal defects (AVSDs), pulmonary atresia with intact ventricular septum with markedly hypoplastic right ventricle, and other complex heart defects with one functioning ventricle were selected for Fontan surgery.

Attempts to insert prosthetic ventricular septum for single ventricle patients met with problems, leading to abandoning such procedures. Thereafter, Fontan became a preferred treatment method. With reasonably good results of Fontan, the pendulum swung so that any patient who could not undergo complete repair became a candidate for Fontan.

A middle of the road method, the so-called one-and-one-half ventricle repair was developed for patients with pulmonary atresia with intact ventricular septum with modest-sized right ventricle. In this procedure, a bidirectional Glenn procedure to divert the SVC flow into the PA is performed and allows the small right ventricle to pump the IVC blood into the pulmonary circuit, and the patent foramen ovale is closed. It is generally considered to be a better option than Fontan, although, to my knowledge, there are no comparative studies to assess this issue.

Because of relatively high mortality rates (17.0–31.7%) [39, 40] and low actuarial survival rates (66.5% at 5 years and 64.4% at 15 years) [41] for unbalanced AVSD patients following Fontan, a number of institutions attempted single stage or staged biventricular repair or conversion from single ventricle (Fontan) to biventricular repair [39, 42–47]. Detailed analysis by Nathan et al. [39] suggested that the biventricular repair and conversion from single ventricle (Fontan) to biventricular repair groups had reasonably similar mortality rates and a similar need for cardiac transplantation, but these parameters were lower than those seen in the Fontan palliation cohort.

Cardiac transplantation is a surgical alternative in the management of HLHS [48] and other single ventricle lesions. While heart transplantation was used at several institutions initially for HLHS, because of non-availability of

donor hearts, most institutions have reverted to the Norwood/Fontan route. In addition, following successful cardiac transplantation, multiple medications for the prevention of graft rejection, frequent outpatient visits and periodic endomyocardial biopsy, to recognize rejection very early, are necessary in the management of these children. At the present time, cardiac transplantation is used for patients failing Fontan operation at a limited number of institutions.

4. Current status of Fontan operation

As reviewed above, since the original description in the early 1970s, the Fontan procedure has undergone numerous modifications, and, at the present time it is best described as staged total cavopulmonary connection (TCPC) with an extra-cardiac conduit and fenestration. It is performed in three stages.

4.1 Stage I

The majority, if not all, of patients who require Fontan operation (see Section 3. Indications for Fontan Operation) present during the neonatal and early infancy period, and the Fontan cannot be performed at that time because of naturally high PA pressure and high pulmonary vascular resistance (PVR). Therefore, Fontan, by necessity, becomes a multistage procedure. These babies should receive palliative intervention to allow them to reach the age and size to undergo successful Fontan surgery. The type of palliation is largely dependent upon the hemodynamic disturbance produced by multiple defects associated with a given congenital heart defect (CHD).

4.1.1 Decreased pulmonary blood flow

In neonates with decreased pulmonary blood flow, the ductus arteriosus should be kept open by administration of prostaglandin E_1 (PGE_1) intravenously at a dose of 0.05–0.1 mcg/kg/min. Once the O_2 saturation improves, the dosage of PGE_1 is gradually reduced to 0.02–0.025 mcg/kg/min to minimize the side effects of the prostaglandins. Following stabilization and diagnostic studies, as necessary to confirm the diagnosis, a more permanent way of providing pulmonary blood flow should be instituted. A number of methods to augment pulmonary blood flow have been used over the years [49, 50]. These include subclavian artery to ipsilateral PA anastomosis (classic Blalock-Taussig shunt), descending aorta to the left PA anastomosis (Potts shunt), ascending aorta to the right PA anastomosis (Waterston-Cooley shunt), SVC to right PA anastomosis, end-to-end (classic Glenn shunt), enlargement of the ventricular septal defect (VSD), formalin infiltration of the wall of the ductus arteriosus, central aortopulmonary fenestration or expanded polytetrafluoroethylene (Gore-Tex; W. L. Gore and Associates, Inc., Newark, Delaware) shunt, Gore-Tex interposition graft between the subclavian artery and the ipsilateral PA (modified Blalock-Taussig shunt), balloon pulmonary valvuloplasty, and stent implantation into the ductus arteriosus. Currently modified Blalock-Taussig (BT) shunt [51] by insertion of a Gore-Tex graft between the subclavian artery to the ipsilateral PA (**Figure 1a**) is performed by most surgeons to address pulmonary oligemia. More recently connecting the RV outflow tract with the PA via non-valve Gore-Tex graft is being used at several institutions to palliate pulmonary oligemia. Placement of a stent in the ductus arteriosus [52–54] and balloon pulmonary valvuloplasty (if the predominant obstruction is at the pulmonary valve level) [55–57] are other available options to augment the pulmonary blood flow.

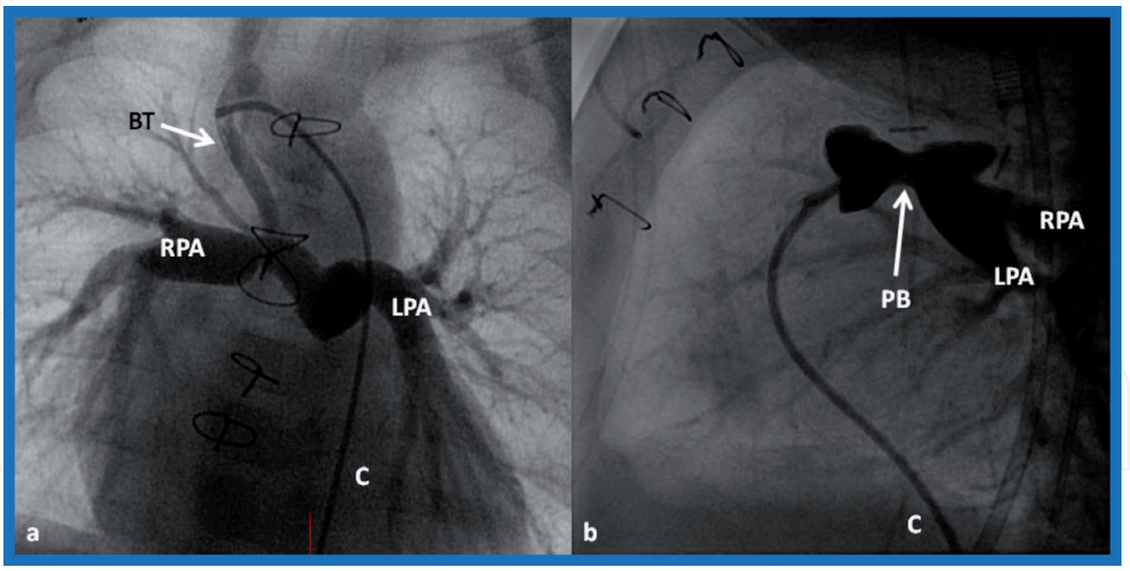

Figure 1.
Stage I Fontan. Selected frames form cineangiograms in two different babies; the first with pulmonary oligemia who received Blalock-Taussig (BT) shunt (a) and the second with pulmonary plethora who had pulmonary artery banding (PB) (b). C, catheter; LPA, left pulmonary artery; RPA, right pulmonary artery (Reproduced from [30]).

4.1.2 Increased pulmonary blood flow

In babies with increased pulmonary blood flow, optimal anti-congestive measures should be started immediately. Once the congestive heart failure (CHF) is adequately addressed, PA banding (**Figure 1b**) is performed [58] irrespective of control of CHF.

4.1.3 Normal pulmonary blood flow

Infants with near normal pulmonary blood flow with O_2 saturations in the low 80s do not need intervention and are clinically followed until Stage II.

4.1.4 Hypoplastic left heart syndrome

Neonates with hypoplastic left heart syndrome usually have Norwood palliation (**Figure 2**) [37, 59] in the neonatal period; in this operation, the following procedures are performed: (1) the main pulmonary artery and the aorta are anastomosed together; additional prosthetic material is used as needed; (2) the pulmonary circulation receives blood supply by connecting the aorta to the PA via a modified BT shunt [51] (**Figure 2b**); (3) atrial septum is excised to allow unhindered blood flow from the left to the atrium; and (4) ductal tissue is removed, and coarctation of the aorta, if present is repaired. Some surgeons use alternative Sano shunt [60], connecting the RV outflow tract to the PA (**Figure 2c**) instead of BT shunt.

4.1.5 Address other defects during Stage I

In patients with inter-atrial obstruction, it should be relieved either by transcatheter methodology or by surgery as deemed appropriate for a given clinical scenario. If there is associated coarctation of the aorta, it should also be relieved. Some patients with double-inlet left ventricle may have significant obstruction at the level of bulboventricular foramen [61]. Similarly some babies with tricuspid

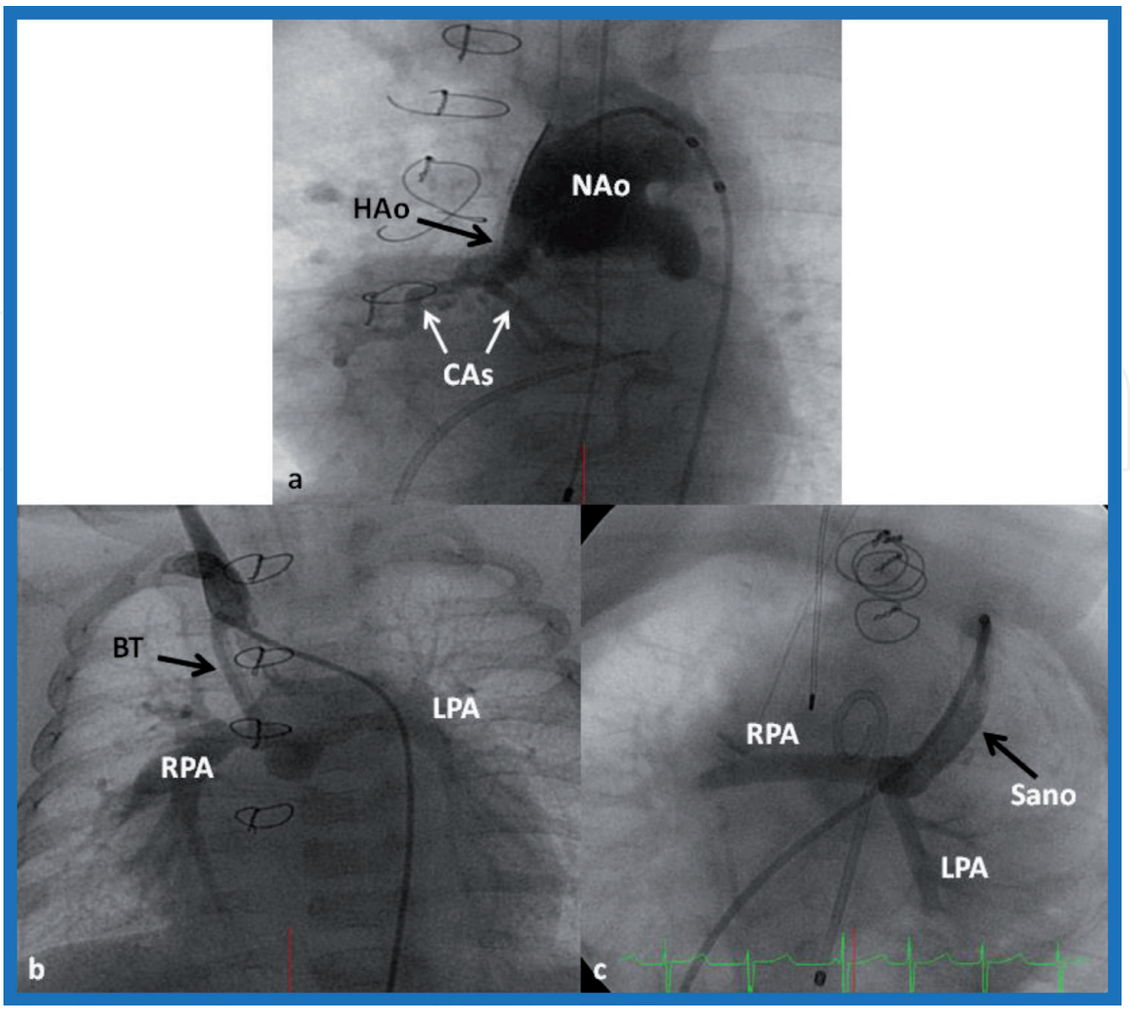

Figure 2.
Stage I Fontan for hypoplastic left heart syndrome. Selected frames from cineangiograms demonstrating Norwood operation in which the neoaorta (NAo) and hypoplastic aorta (HAo) perfuse the coronary arteries (CAs) as shown in (a), Blalock-Taussig (BT) shunt as illustrated in (b) and Sano shunt as depicted in (c). (b) and (c) are from two different babies. LPA, left pulmonary artery; RPA, right pulmonary artery (Reproduced from [30]).

atresia with transposition of the great arteries may have obstruction at the VSD level, causing obstruction to systemic blood flow [61, 62]. Such babies require Damus-Kaye-Stansel (connection of the aorta to the PA) [63] along with a BT shunt. Inter-atrial obstruction may be present frequently in babies with mitral atresia and single ventricle [64]. In such babies, predictable fall in PVR occurs following balloon or surgical relief of inter-atrial obstruction [64]; consequently, PA banding should be undertaken without hesitation at the time of relieving the atrial septal obstruction, so as to reduce the probability for CHF, lower the PVR and PA pressure, prevent pulmonary vascular obstructive disease (PVOD), and pave the way for Fontan approach [64].

4.2 Stage II

Irrespective of the type of palliative surgery in the neonatal period, bidirectional Glenn procedure [12–14, 17, 23], namely, anastomosis of the SVC to the right PA, end-to-side (**Figure 3**) is performed around the age of 6 months. The previously performed BT or Sano shunt is ligated at the same time. Although performing the procedure at 6 months is generally adopted, it can be performed as early as 3 months provided normalcy of PA pressure and anatomy can be documented.

In patients with persistent left SVC, bilateral bidirectional Glenn (**Figure 4**) is undertaken especially in patients with a small or absent left innominate vein. A bidirectional Glenn procedure may also be performed for patients with infrahepatic interruption of the IVC with azygos or hemiazygos continuation, and such a procedure is called a Kawashima procedure by some authorities.

Prior to the bidirectional Glenn procedure, normal PA pressures and adequate size of the branch PAs should be ensured by cardiac catheterization and

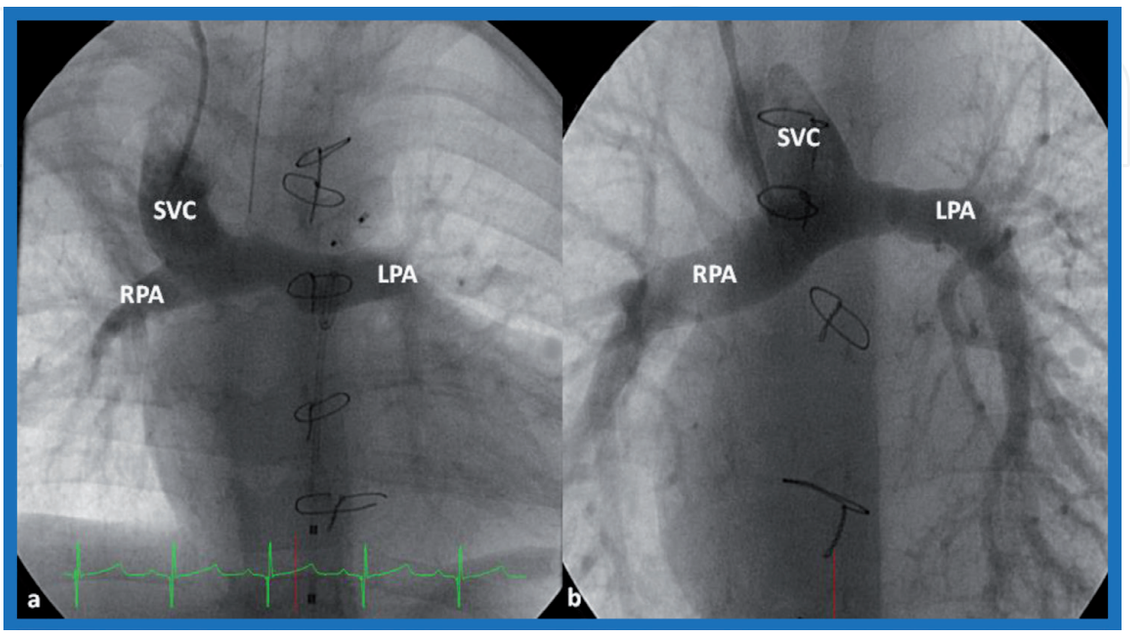

Figure 3.
Stage II of Fontan. Selected frames from cineangiograms in two different children illustrating bidirectional Glenn operation in which the superior vena cava is anastomosed to the right pulmonary artery (RPA). Unobstructed flow from the SVC to the right (RPA) and left (LPA) pulmonary arteries is clearly seen. (Reproduced from [30]).

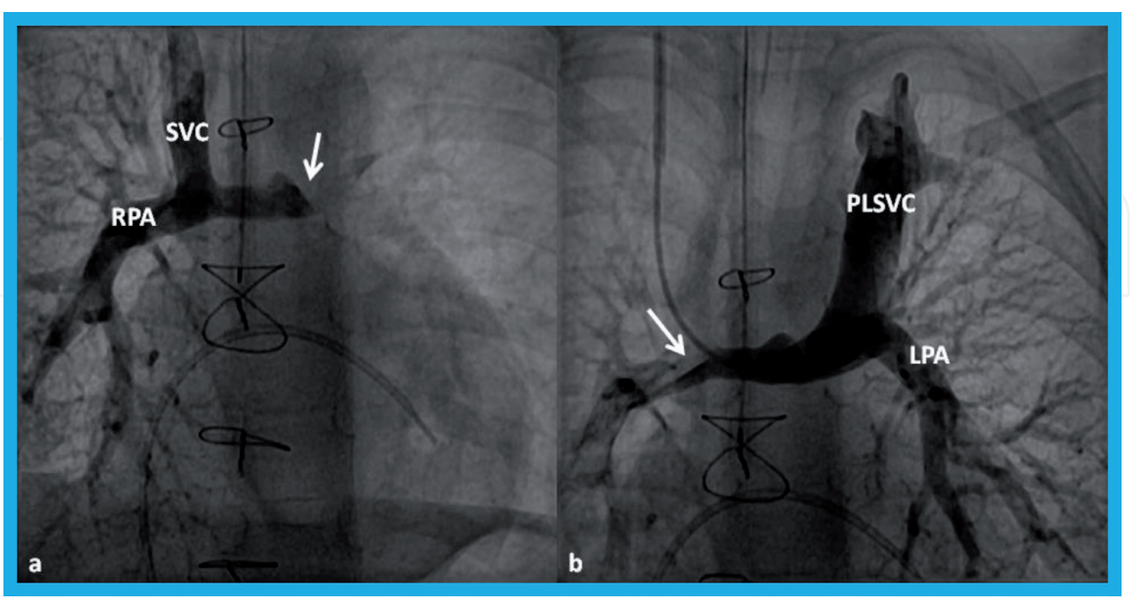

Figure 4.
*Stage II Fontan. Selected frames from cineangiograms in a different child than shown in **Figure 3**, illustrating bilateral bidirectional Glenn operation. (a) Superior vena caval angiogram demonstrates immediate visualization of the right pulmonary artery (RPA). Un-opacified blood flow from persistent left SVC (PLSVC) is indicated by the arrow in (a). (b) PLSVC angiogram illustrates rapid opacification of the left pulmonary artery (LPA). Un-opacified blood from the right SVC is shown by the arrow in (b). Flow from the respective SVCs into the pulmonary arteries is clearly seen (Reproduced from [30]).*

cineangiography. Echo-Doppler or other imaging studies (magnetic resonance imaging [MRI] or computed tomography [CT]) is advocated at some institutions.

If PA stenosis is present, it may be addressed with balloon angioplasty or stent implantation, as deemed appropriate, or it may be addressed during the bidirectional Glenn procedure. Atrioventricular valve regurgitation, aortic coarctation, subaortic obstruction, and other abnormalities should also be repaired/addressed at the time of this operation.

4.3 Stage III

During the final Stage III, the IVC flow is diverted into the PA along with creation of a fenestration. We arbitrarily divided [30] these procedures into Stage IIIA (diversion of IVC into the PA) and Stage IIIB (closure of the fenestration).

4.3.1 Stage IIIA

In the final Stage III, the total cavopulmonary connection is achieved by diverting the IVC flow into the PA either by a lateral tunnel [18, 65] or by an extra-cardiac, non-valved conduit (**Figures 5** and **6**) [21, 22]; the procedure is usually performed between the ages of 1 and 2 years, usually 1 year following the bidirectional Glenn procedure. Most surgeons seem to prefer extra-cardiac conduit to accomplish this final stage of Fontan. The majority of surgeons construct a fenestration, 4–6 mm in size, between the conduit and the atria (**Figures 5** and **6**) [27]. While the creation of fenestration during the Fontan operation was initially proposed for high-risk patients [27, 28], most surgeons now seem to prefer fenestration, since fenestration during the Fontan improves mortality rate and reduces morbidity during the immediate postoperative period [30].

Cardiac catheterization and selective cineangiography are usually performed shortly prior to Fontan conversion in order to assess the PA anatomy and pressures, trans-pulmonary gradient, PVR, and ventricular end-diastolic pressure and

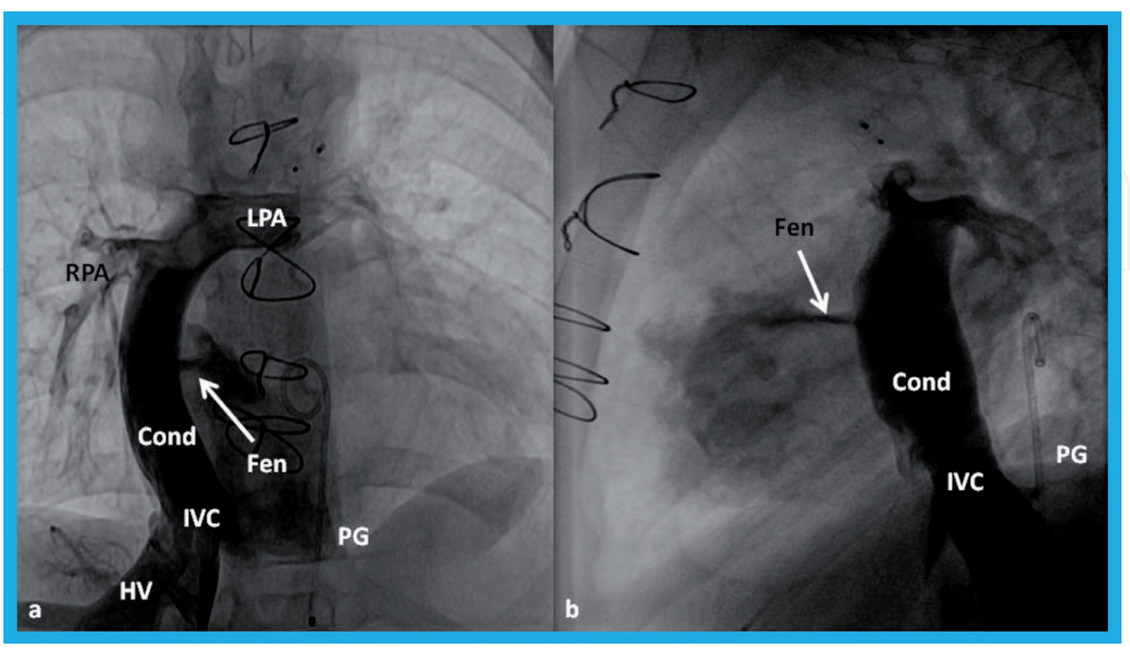

Figure 5.
Selected cine frames in posteroanterior (a) and lateral (b) views, demonstrating Stage IIIA Fontan procedure diverting the inferior vena caval flow into the pulmonary arteries via a non-valve conduit (Cond). Flow across the fenestration (fen) is shown by arrows in (a) and (b). HV, hepatic veins; LPA, left pulmonary artery; PG, pigtail catheter in the descending aorta; RPA, right pulmonary artery.

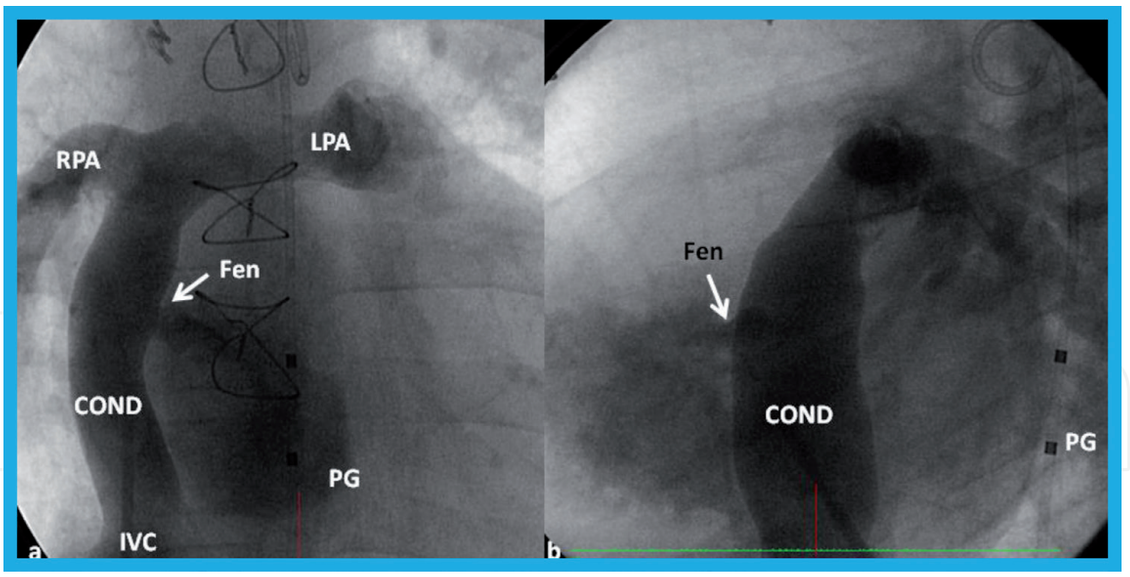

Figure 6.
Selected cine frames in posteroanterior (a) and lateral (b) views in a different patient to the one shown in ***Figure 5****, demonstrating Stage IIIA Fontan procedure diverting the inferior vena caval (IVC) flow into the pulmonary arteries via a non-valve conduit (Cond). Flow across the fenestration (fen) is shown by arrows in (a) and (b). Abbreviations are the same as those in* ***Figure 5****.*

to assure that they are normal prior to proceeding with Fontan completion. At some institutions, MRI is used for this assessment instead of catheterization and angiography; however, the author's preference is catheterization. During this catheterization, any significant collateral vessels that are present are also transcatheter-occluded by most cardiologists.

4.3.2 Stage IIIB

In the final stage, Stage IIIB, the fenestration is closed (**Figures 7b**, **8b**, and **9B** and **C**) by transcatheter methodology [27, 30–35], usually 6–12 months after Fontan Stage, IIIA. In the past, most devices used to occlude ASDs [32–35] were employed for this purpose, but at the present time, Amplatzer septal occluders are the most commonly used devices to accomplish such closures. If there are any other residual shunts, they should also be occluded (**Figure 10**) by device closure.

4.4 Interstage problems

In children who have one functioning ventricle requiring Fontan correction, the systemic and pulmonary circulations work in-parallel in place of the usual in-series circulation. A fragile equilibrium between the two circulations must be preserved so that adequate systemic and pulmonary perfusions are maintained. There is substantial interstage mortality ranging from 5 to 15% [66–68] which may be due to restrictive atrial communication, obstruction of the aortic arch, blockage of the shunt, distortion of the PAs, atrioventricular valve insufficiency, or a combination thereof [66]. Intercurrent illnesses such as dehydration, respiratory tract illness, or fever disturb this balance and make the patients to become critically ill and have been blamed for interstage mortality [66, 68]. The surgically created BT and Sano shunts may also get thrombosed producing severe hypoxemia [69]. Indeed, these abnormalities produce significant interstage mortality [67]; these appear to occur more frequently between Stages I and II than between Stages II and III. Consequently, extreme vigilance in managing these patients should be maintained by the caregiver [68, 70]; even trivial illnesses must be aggressively monitored and addressed as appropriate.

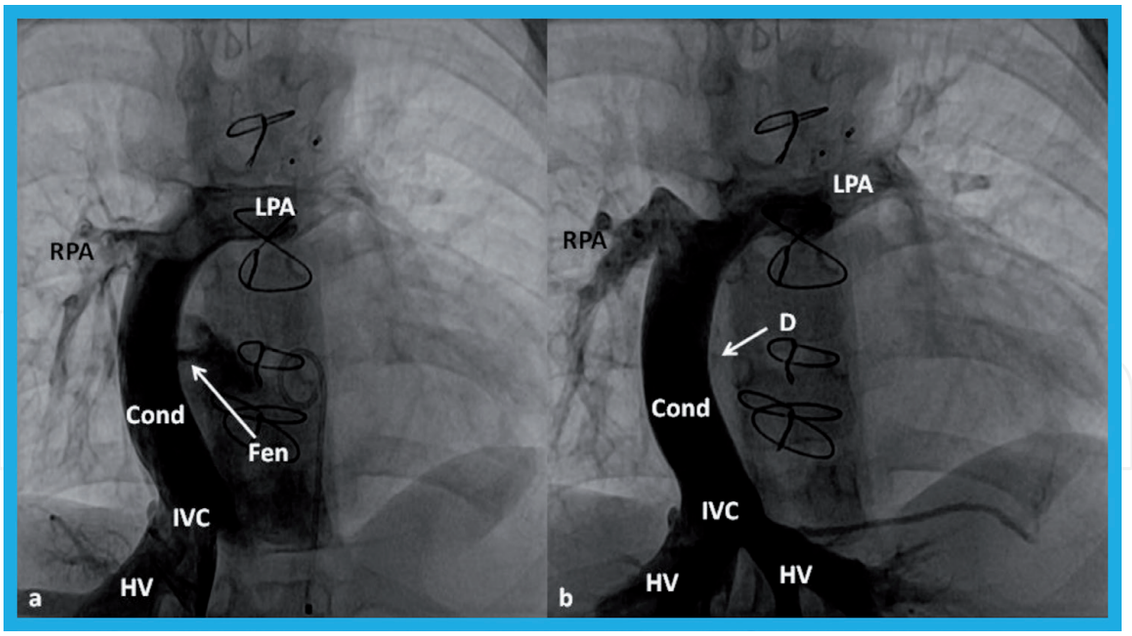

Figure 7.
Stage IIIB. (a) Selected frames from cineangiograms in anteroposterior projection illustrating Stage IIIA of the Fontan operation in which the inferior vena caval (IVC) flow is diverted into the pulmonary arteries by a non-valve conduit (Cond). The fenestration (fen) is shown by the arrow in (a). (b) Closure of the fenestration with an Amplatzer septal occluder device (D) is shown with an arrow in (b). HV, hepatic veins; LPA, left pulmonary artery; RPA, right pulmonary artery (Reproduced from [30]).

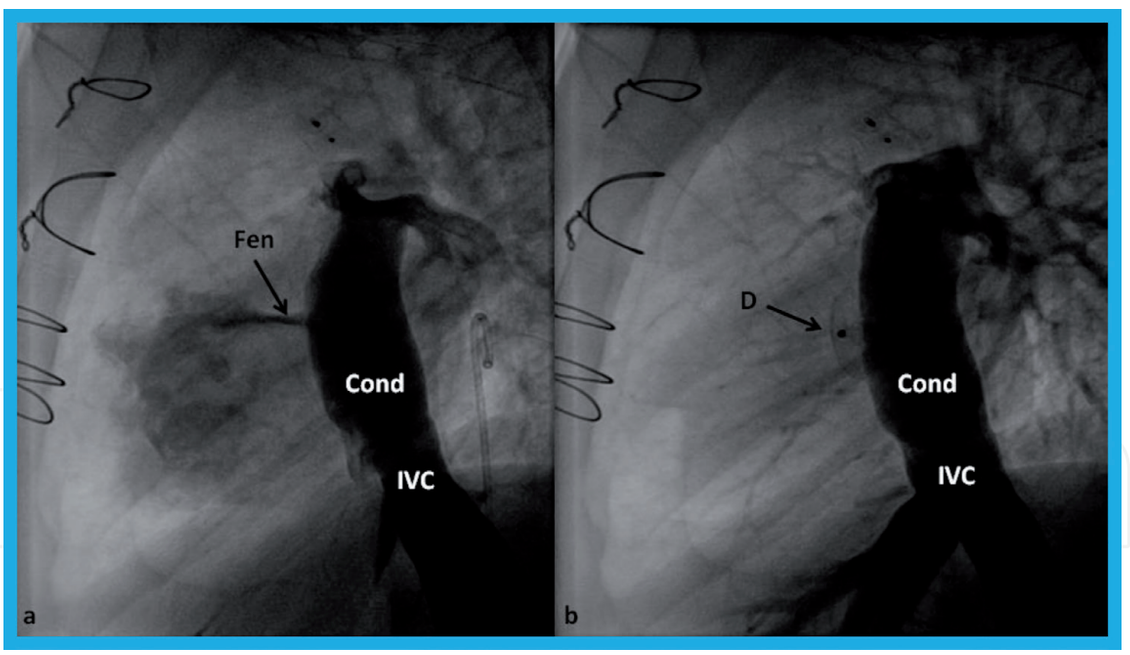

Figure 8.
Stage IIIB. (a) Selected frames from cineangiograms in lateral view of the same patient illustrated in **Figure 5** *showing Stage IIIA of the Fontan operation in which the inferior vena caval (IVC) flow is diverted into the pulmonary arteries by a non-valve conduit (Cond). The fenestration (fen) is shown by the arrow in (a). (b) Closure of the fenestration with an Amplatzer septal occluder device (D) is shown with an arrow in (b). (Stage IIIB). Reproduced from [30].*

5. Results of Fontan operation

Immediate and follow-up results of both older and current types of Fontan will be reviewed in this section.

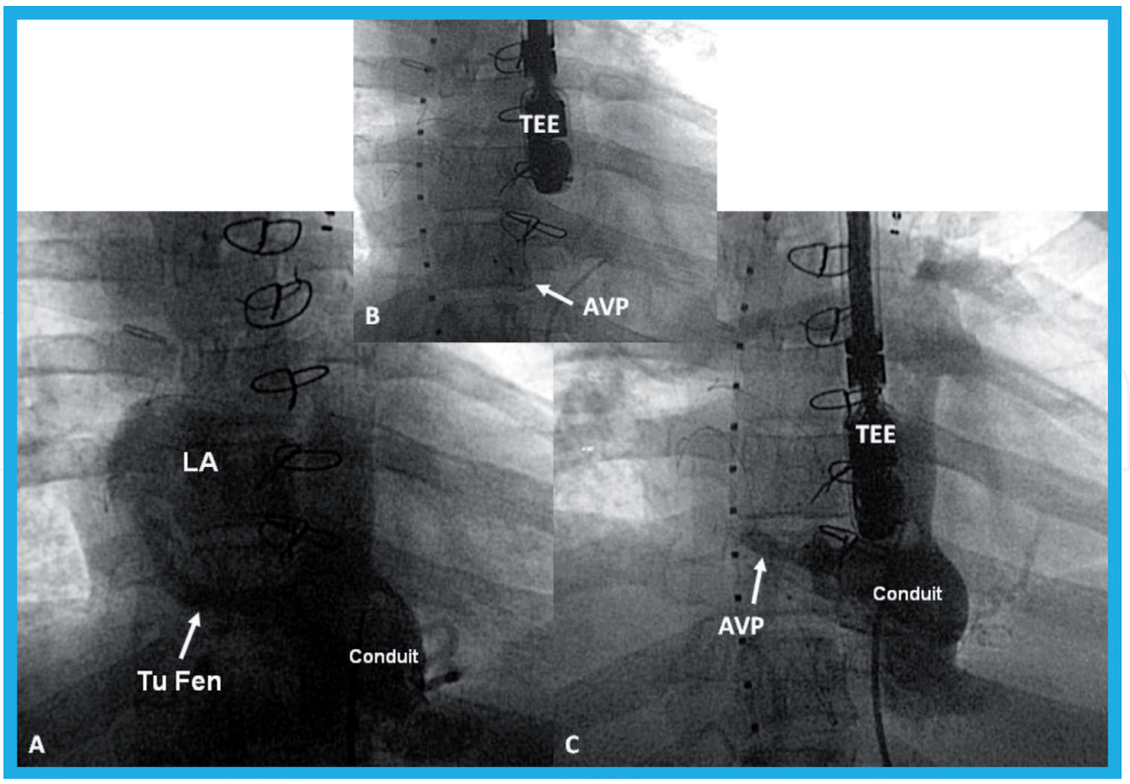

Figure 9.
(A) Selected cine frame from a Fontan conduit cineangiogram in anteroposterior view, demonstrating tubular fenestration (Tu fen) with opacification of the left atrium (LA). (B) The Tu fen is closed with an Amplatzer vascular plug (AVP). (C) A follow-up conduit cineangiogram after AVP implantation, showing complete occlusion of the Tu fen. TEE, transesophageal probe.

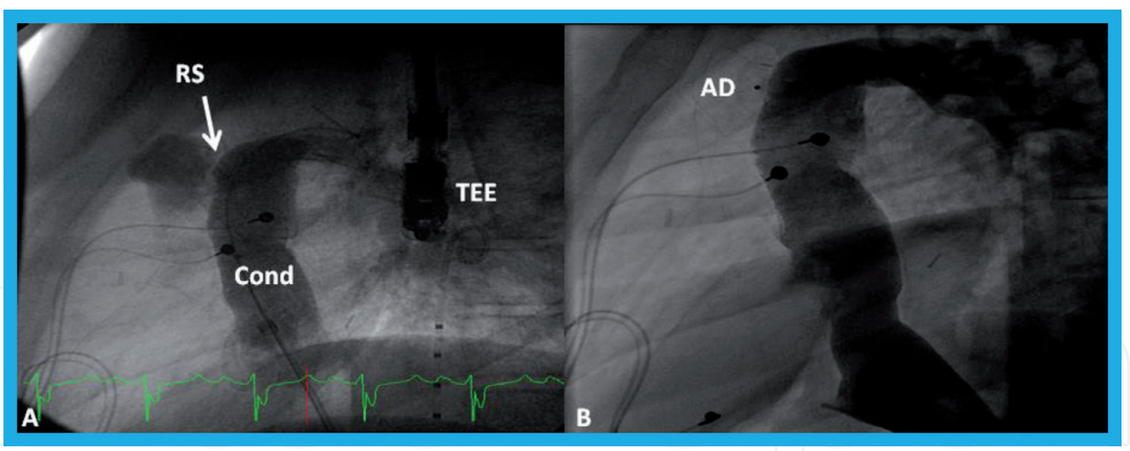

Figure 10.
(A) A selected cineangiographic frame showing the Fontan conduit in lateral view, demonstrating a residual shunt (RS) at the superior aspect of the conduit (Cond). (B) The RS was occluded with an Amplatzer septal occluder device (AD); the residual shunt is no longer seen. TEE, transesophageal echo probe.

5.1 Immediate results

The results of original Fontan [1, 2] and its earlier modifications, namely, RA-to-PA or RA-to-RV anastomosis either directly or via valved or non-valved conduits, revealed high initial mortality rates. The initial mortality rates ranged from 10 to 26% [9, 10, 71, 72]. Furthermore, the postoperative stay in the intensive care setting was prolonged.

The initial mortality following staged, total cavopulmonary connection has decreased remarkably [73–78]. Patients who had total cavopulmonary connection

without fenestration had initial mortality rates ranging from 8 to 10.5% [73–75], while subjects who had total cavopulmonary connection with fenestration had slightly lower (4.5–7.5%) initial mortality rates [76–78].

In one large single institutional study examining the results of 500 consecutive Fontan surgery patients [77], early failure was associated with high (≥19 mm Hg) mean PA pressure, young age at surgery, heterotaxy syndrome, a right-sided tricuspid valve as systemic atrioventricular valve, distorted pulmonary arteries, an atriopulmonary connection, no Fontan fenestration, and longer cardiopulmonary bypass time.

These investigators also observed that a significant improvement in morbidity and mortality from early (first quartile—early failures: 27.1%) to the more recent time (last quartile—early failures: 7.5%) occurred [77]. This progress appears to be related to increasing surgical and intensive care experience as well as to more recently introduced Fontan modifications.

5.2 Follow-up results

Long-term follow-up results were also poor with older types of Fontan [9, 10]. The late mortality rates varied from 1 to 11%, and when early and late mortality rates were combined, they varied between 11 and 25%. The need for reoperations was present in 1–11% of patients. Factors adversely influencing late mortality and reoperation rates are earlier calendar year of operation, age of patient at the time of surgery, type of prior palliative procedures, hypoplasia, distortion or obstruction of PAs, subaortic obstruction, significant mitral valve insufficiency, elevated PA pressure or resistance, decreased left ventricular function, increased left ventricular muscle mass, asplenia syndrome, and others [9, 10].

Following the introduction of staged cavopulmonary anastomosis (both lateral tunnel and extra-cardiac conduit diversion of IVC blood to the PA), the long-term outcomes have improved. In one study in which results of follow-up for 10.2 ± 0.6 years of 196 patients were examined, the estimated Kaplan-Meier survival was 93 and 91% at 5 and 10 years, respectively [79]. An equally impressive finding was freedom from supraventricular arrhythmias in 96 and 91% of patients at 5 and 10 years following surgery. In a different study, the actuarial survival 15 years following surgery was 85% [80]. But, late re-interventions were necessary in 12.7% of patients. When lateral tunnel and extra-cardiac conduit types of Fontan were compared, the outcomes were found to be similar for both groups [81, 82].

Using fenestration during Fontan appears to improve early mortality and morbidity, particularly demonstrated in high-risk patents [83]. A more recent analysis in a smaller group of patients did not demonstrate significant advantage of fenestrated Fontan over the non-fenestrated [84]. However, the general consensus is that using fenestration during Fontan decreases mortality and morbidity during the postoperative period [30, 76–78].

6. Follow-up protocol and complications

Periodic follow-up following Fontan is generally recommended. These patients are evaluated at 1, 6, and 12 months after Stage IIIB (device closure of fenestration) and yearly thereafter. During the follow-up, platelet-inhibiting doses of aspirin 2–5 mg/kg/day in children or clopidogrel 75 mg/day in adults to prevent thrombus formation and angiotensin-converting enzyme inhibitors for afterload reduction are generally prescribed. Electrocardiograms and echocardiograms are generally

performed during evaluation of these patients with additional imaging studies, as indicated. Any abnormalities, as and when detected, are addressed.

During follow-up, a number of complications were reported, and these include arrhythmias, obstructed Fontan pathways, cyanosis, paradoxical emboli, thrombi, development of collateral vessels, and protein loosing enteropathy [30, 31, 85]. These complications appear to be more frequent with older types of Fontan than with the currently used staged, total cavopulmonary connection with extra-cardiac conduit and fenestration. When such complications develop, they should be promptly investigated and treated. In the ensuing paragraphs, a brief review of some of these complications will be presented.

6.1 Arrhythmias

Arrhythmias were more frequently seen in patients with old Fontan (atriopulmonary connection) than with staged TCPC. The observed arrhythmias were typically atrial arrhythmias, namely, atrial flutter/fibrillation and supraventricular tachycardia. Initially, anti-arrhythmic medications are used to control the rhythm disturbance. This should be followed by hemodynamic and angiographic assessment to identify obstructive lesions in the Fontan pathways. The obstructive lesions should be treated with balloon angioplasty, stent, or surgery, as applicable. Continued rhythm abnormality calls for radiofrequency ablation. Although the success rate of radiofrequency ablation is high in 80% range [86], rates of recurrence range from 30 to 40%. In subjects who have resistant arrhythmias, reducing the atrial mass, switch to TCPC with concomitant Maize procedure is advisable [87]. A few patients develop atrioventricular block or sick sinus syndrome which may require pacemaker implantation. Fortunately, ventricular arrhythmias are less frequent.

6.2 Development of obstruction in Fontan pathways

Obstructions in Fontan circulation may occur. Obstructive lesions in the SVC or IVC may arise but are less frequently seen. However, branch pulmonary artery stenoses may be seen more often. Obstructions within the lateral tunnel or extra-cardiac conduit are also uncommon, but may occur due to thrombus formation and will be addressed in the section on "Thrombus formation." In the presence of signs and symptoms indicative of obstruction in the Fontan pathway, prompt investigation to confirm such obstruction should be made. While echo studies are useful in young children, poor echo windows in adolescents and adults may require MRI and CT, and/or angiographic studies to confirm or exclude such obstructive lesions. If the obstructive lesions are detected, they should be promptly relieved by balloon angioplasty or stent implantation (**Figure 11**) [88]. Surgery may be needed in rare occasions.

6.3 Residual arterial desaturation and paradoxical emboli

Sometimes connections between lateral tunnel and extra-cardiac conduit on the one hand and the atrium on the other persist. These residual defects and intentionally created Fontan fenestrations result in right-to-left shunt because the pressure in the Fontan conduit is higher than that of the atrial pressures. These residual defects will result in arterial desaturation and may become the site of paradoxical embolism with consequential transient ischemic attacks (TIAs), cerebrovascular accidents (CVAs), and systemic emboli. These residual defects as well as Fontan fenestrations should be occluded by transcatheter techniques

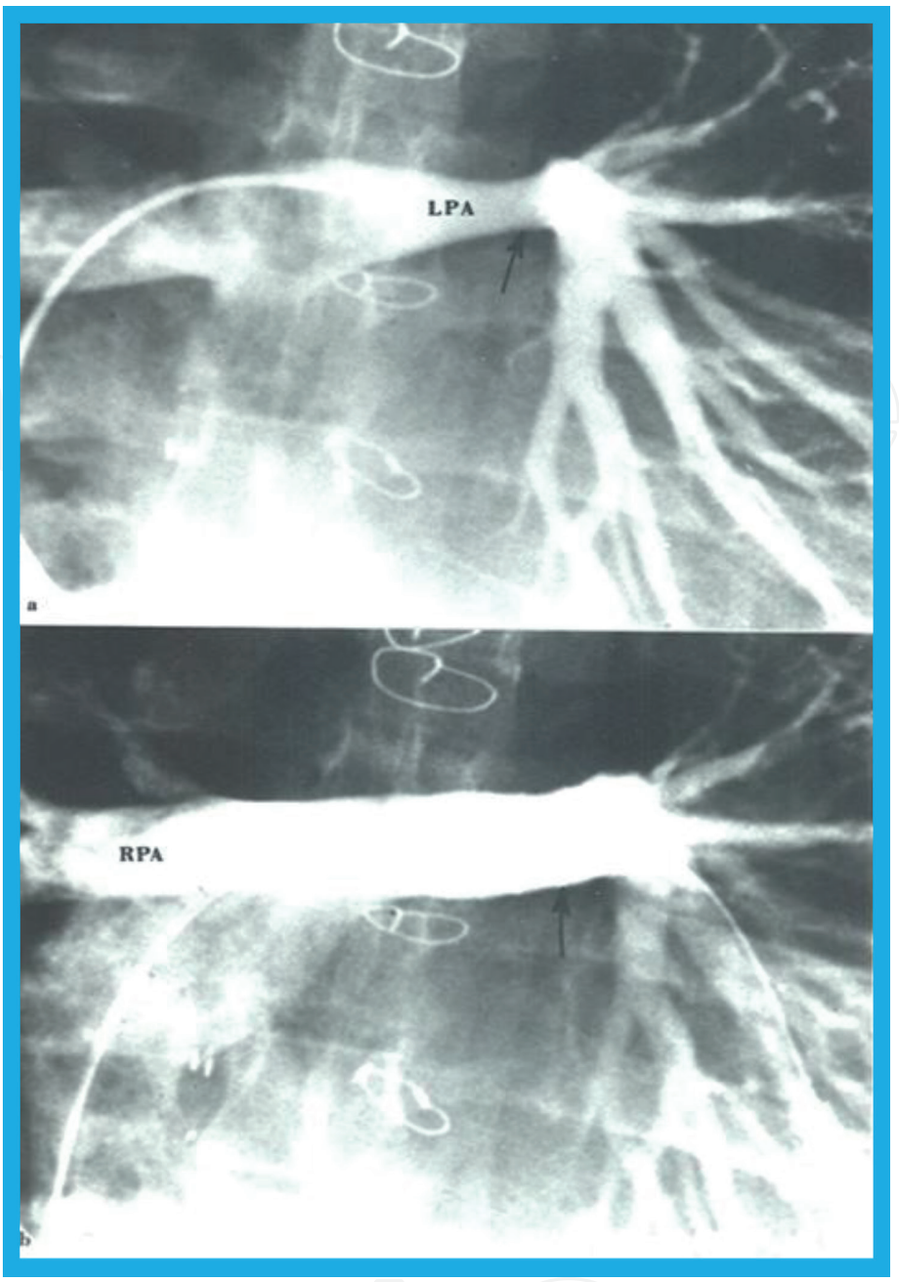

Figure 11.
Selected frames from cineangiograms of the pulmonary artery in posteroanterior view illustrating normal right pulmonary artery (RPA) and narrowed (arrow) left pulmonary artery (LPA) prior to (a) and after (b) stent (arrow) placement in an adolescent who had Fontan surgery several years earlier (Reproduced from [88]).

to return O2 saturations to normal and decrease the likelihood for paradoxical embolism [30, 32, 33, 83, 88, 89]. Amplatzer septal occluder (St. Jude Medical, Inc., St Paul, MN) is currently most common device used to accomplish this (**Figures 7, 8**, and **10**). Tubular fenestrations may be closed with Amplatzer vascular plug devices (St. Jude Medical, Inc.) (**Figure 9**). Test occlusion of the residual defect or fenestration is suggested to ensure that adequate cardiac output is maintained following defect occlusion [89, 90], especially if the procedure is performed shortly after fenestrated Fontan. Late follow-up results of fenestration closure are good [33].

6.4 Thrombus formation

There is a tendency for thrombus formation in the Fontan pathway; the reported prevalence was 15–30% [91, 92]. Regrettably the usual transthoracic echo-Doppler

evaluation may not discover these thrombi. However, transesophageal echocardiography, MRI, or CT studies may be necessary to detect these thrombi. In an attempt to prevent thrombus formation in the Fontan circuit, thromboprophylaxis is commonly recommended; both warfarin and aspirin have been utilized in the past for this purpose. A multicenter, randomized trial was conducted to compare the efficacy of these two drugs; results showed less than optimal results with both drugs and no significant difference between the two regimens [93]. In the author's experience, most children are prescribed with aspirin for thromboprophylaxis which may be switched to clopidogrel (Plavix) as the children approach adulthood.

Despite seemingly adequate thromboprophylaxis, some patients develop thrombosis of the Fontan conduits (**Figure 12A**). We initially employ thrombus dissolving drug therapy (tPA, heparin, etc.). If the thrombi do not resolve, we have employed stenting of the conduit to compress the thrombi against the conduit wall [94]. An example from our experience is shown in **Figure 12**.

6.5 Development of collateral vessels

Systemic venous to pulmonary venous and systemic arterial to pulmonary arterial collateral vessels may develop in some patients after the Fontan procedure [88, 95]. These may develop both shortly after the procedure and during late follow-up. Systemic venous to pulmonary venous collateral vessels produce arterial hypoxemia. In addition, they may also become potential sites for paradoxical embolism.

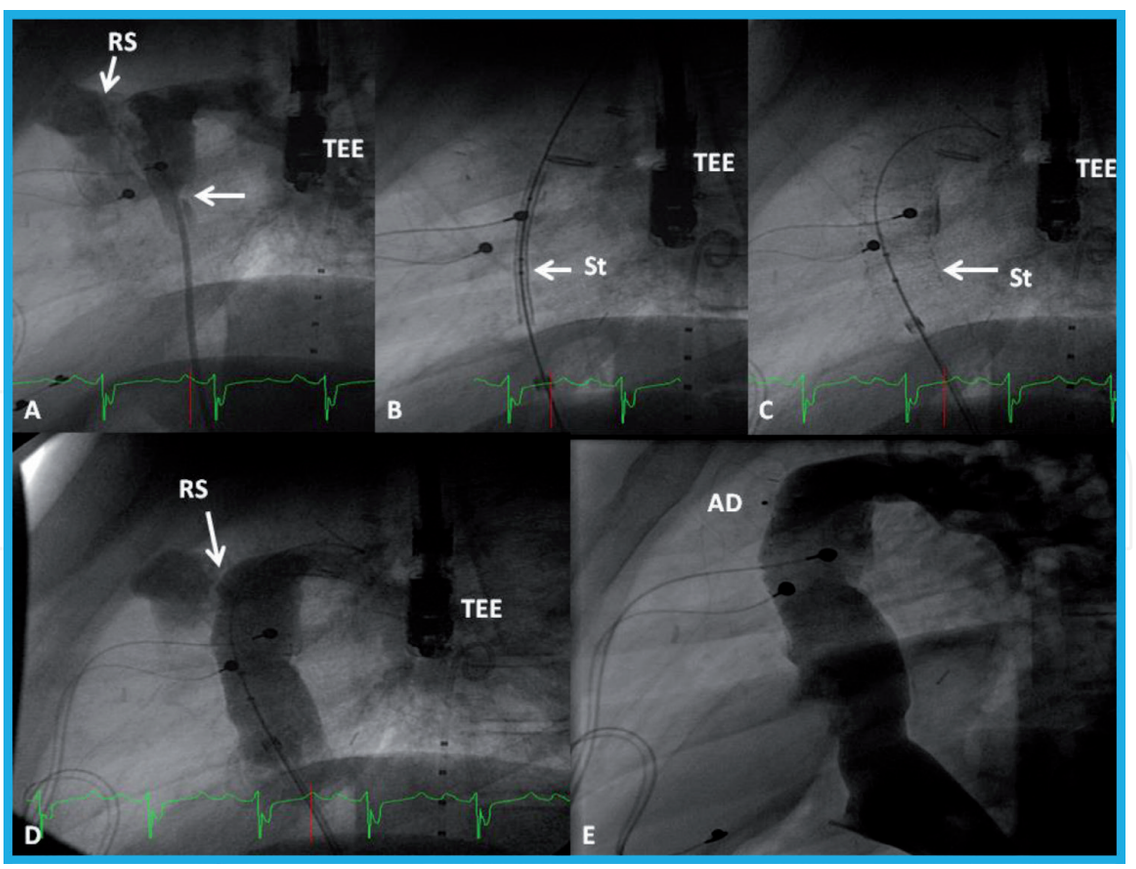

Figure 12.
(A) Selected frame from a cineangiogram of a Fontan conduit in lateral view, illustrating a thrombus (arrow in (A)). (B) and (C) position of a stent (St) before (B) and after (C) its complete expansion. (D) Cineangiographic frame demonstrating the widely patent stent after stent deployment. Also, note the residual shunt (RS) at the superior aspect of the conduit (seen in (A) and (D)). The RS was occluded with an Amplatzer septal occluder device (AD) shortly after the cine shown in (D). (F) A follow-up cineangiogram 1 year later shows the continued patency of the conduit with no RS. TEE, transesophageal echo probe (Reproduced from [94]).

Systemic arterial to pulmonary arterial (or venous) collateral vessels produce left ventricular volume overload. These abnormal vessels should be transcatheter-occluded with coils, vascular plugs, and ductal occluding devices depending upon the size and accessibility. Examples from the author's experience of occluding these vessels are shown in **Figures 13–16** [88, 95, 96].

6.6 Protein loosing enteropathy

Protein losing enteropathy (PLE) is a grave long-term complication of Fontan with a prevalence of 11.1% in older types of Fontan [85, 97]. However, the incidence appears to have come down to 1.2% with staged TCPC [85, 98]. The reason for development of PLE is not understood. Intestinal protein loss secondary to lymphatic distension which in turn may be due to elevated pressure in systemic veins is considered to be a pathogenic mechanism. But, PLE has been seen even in patients with "normal" Fontan circuit pressures. Therefore, the true cause of PLE remains a mystery. The symptoms and signs of PLE are diarrhea, edema, ascites, and/or pleural effusions. Laboratory abnormalities include reduced serum albumin and elevated fecal alpha-1 antitrypsin levels. The PLE diagnosis may be confirmed with technetium 99m-labeled human serum albumin scintigraphy [99].

Because of high mortality rate seen with PLE, speedy diagnosis and implementing aggressive management strategies are important [85]. At first, supportive therapy such as medium-chain triglycerides diet, infusion of intravenous albumin, and replacement of immunoglobulins should be undertaken. Obstructive lesions in the Fontan pathway should be scrutinized, and aortopulmonary connections should be screened for. If identified, they should be treated with appropriate transcatheter measures. Surgical therapy is indicated if they cannot be adequately addressed with transcatheter intervention. A variety of other treatment regimens, including prednisone, elementary diet, calcium replacement, regular high-molecular-weight heparin, low-molecular-weight heparin, somatostatin, high-dose spironolactone, sildenafil, and resection of localized intestinal lymphangiectasia, have been utilized in the past with varying degrees of success [85].

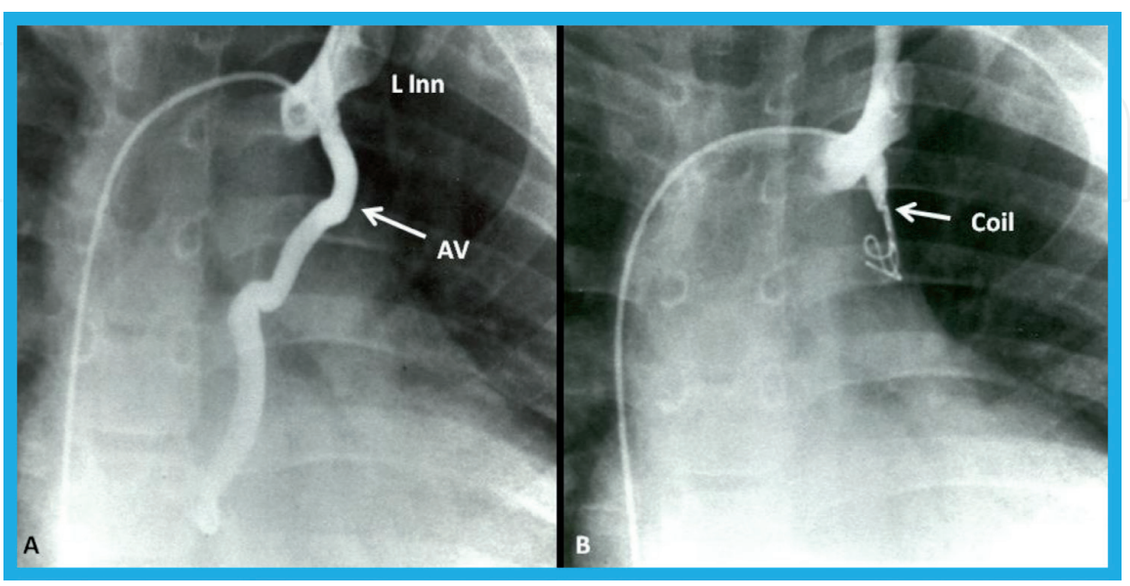

Figure 13.
(a) Selected frame from a left innominate vein (L inn) cineangiogram in posteroanterior view demonstrating an anomalous vein (AV) opacifying the atrial mass (not marked). (b) Following occlusion with Gianturco coil (arrow), the AV is completely occluded and the systemic arterial saturation improved (Reproduced from [88]).

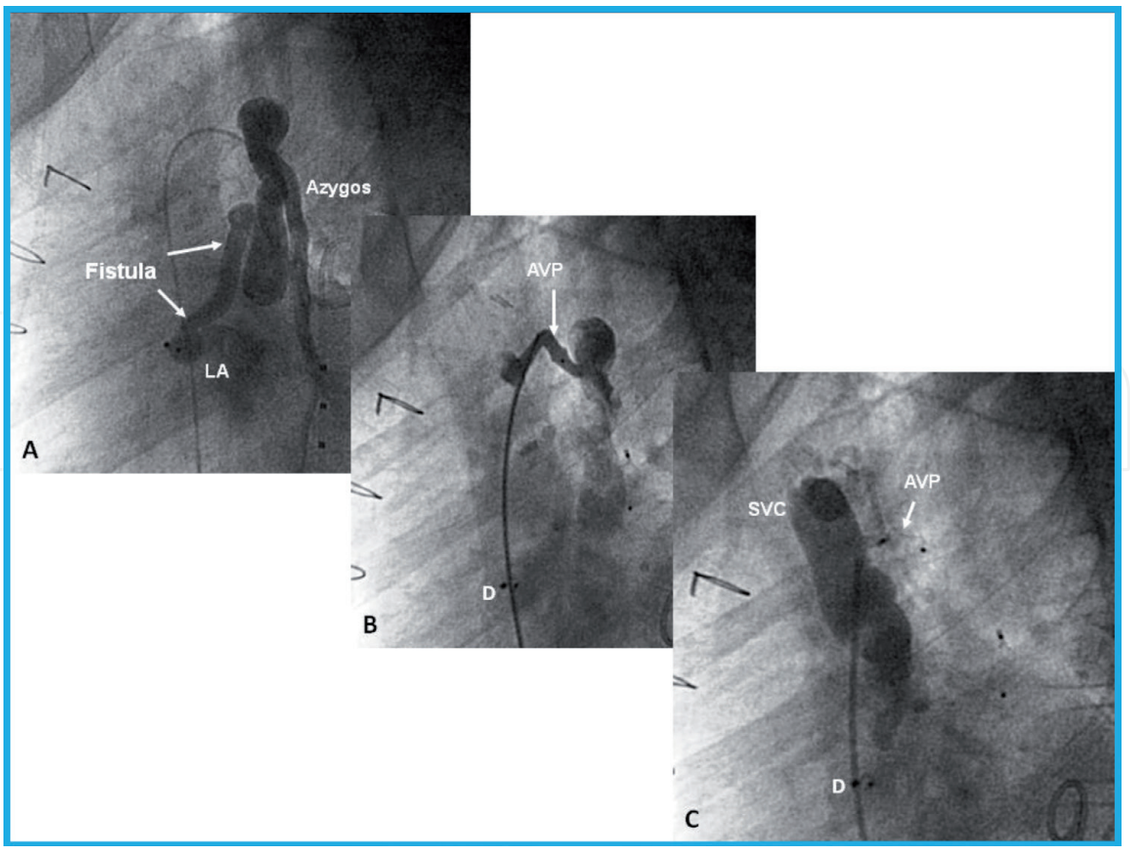

Figure 14.
(A) Selected frame from a cineangiogram in lateral view with the catheter positioned at the superior vena cava/azygos junction illustrating a fistula which results in opacification of the left atrium (LA). (B) The fistula was occluded with an Amplatzer vascular plug (arrow—AVP) with some residual flow. (C) Follow-up SVC injection shows complete occlusion by the AVP (Reproduced from [96]).

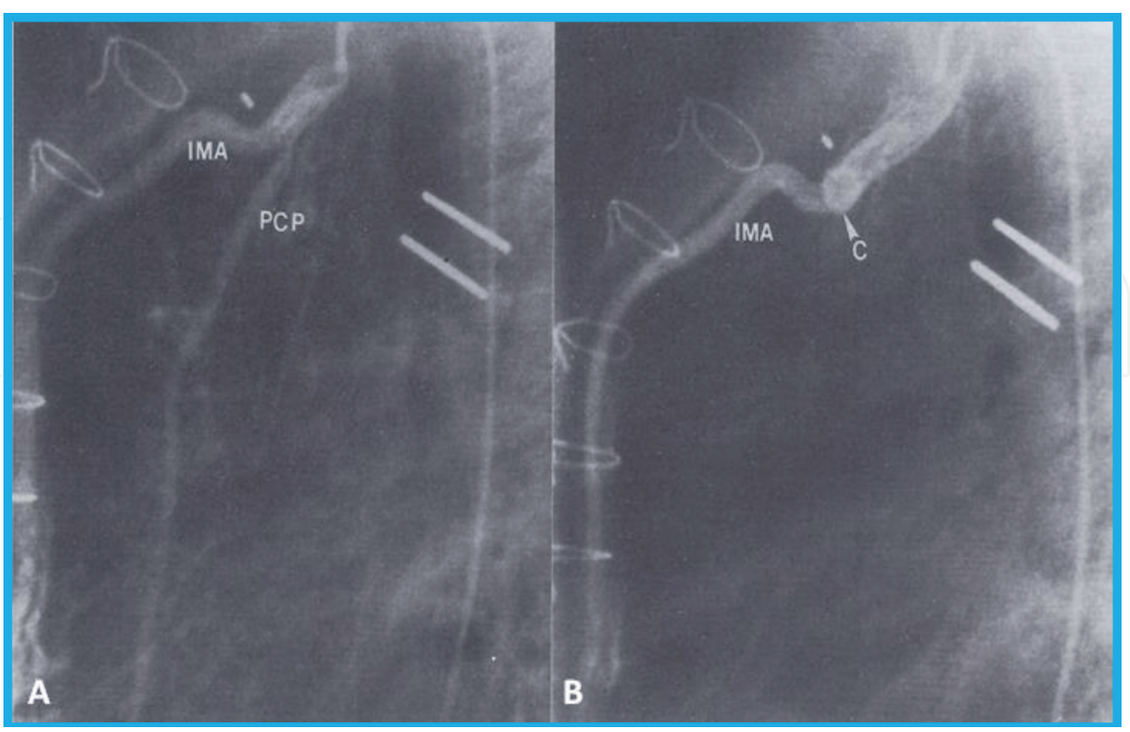

Figure 15.
(A) Selected cine frame from an internal mammary artery (IMA) cineangiogram in the lateral view, demonstrating multiple small collateral vessels arising from the pericardiophrenic (PCP) branch, which resulted in a significant levophase (not shown). (B) Following occlusion with a Gianturco coil (C), there is complete occlusion of this vessel (Reproduced from [95]).

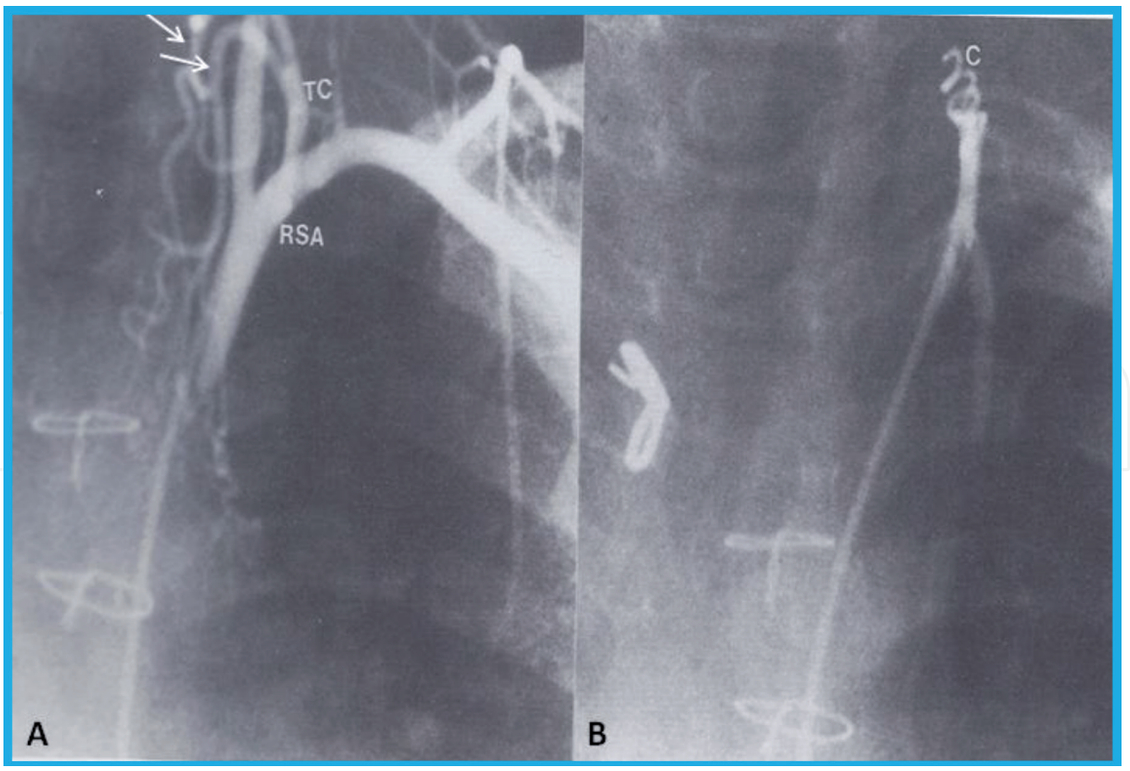

Figure 16.
(A) Selected cine frame from a right subclavian artery (RSA) cineangiogram showing branches (white arrows) of the thyrocervical (TC) trunk which supplied a number of small vessels, giving a good degree of levophase. (B) Complete occlusion occurred following the implantation of a Gianturco coil (C) (Reproduced from [95]).

Following a short trial of any of the above treatment modes, largely on the basis of the cardiologist's preference, a more definitive treatment methods such as lessening the conduit pressure by creating a fenestration between the conduit and the atrium [99–101], converting atriopulmonary type of Fontan to TCPC [87, 102, 103], instituting sequential atrioventricular pacing [104, 105], and performing cardiac transplantation [106–108] should all be considered. Again, it is essential to emphasize that timely treatment should be instituted as soon as PLE is identified [85]. Fortunately, the need for use of these methods has progressively diminished since the wide use of staged TCPC.

7. Summary and conclusions

Since the initial description of the Fontan operation in the early 1970s by Fontan, Kruetzer, and their associates, several modifications have been introduced. These include avoiding classic Glenn anastomosis; not using a prosthetic valve in the IVC; RA-PA anastomosis, direct or through a non-valved conduit; RA-PA anastomosis through a valved conduit; RA-RV anastomosis, direct or non-valved anastomosis; RA-RV anastomosis through a valved conduit; bidirectional Glenn procedure (cavopulmonary anastomosis); lateral tunnel; total cavopulmonary connection; extra-cardiac conduit, staged Fontan; fenestrated Fontan; and closure of Fontan fenestration. Currently staged, total cavopulmonary connection with extra-cardiac conduit and fenestration has become the most commonly used multistage surgery in accomplishing the Fontan.

The indications for Fontan are patients who have one functioning ventricle, and these include tricuspid atresia, double-inlet left ventricle, HLHS, mitral atresia with normal aortic root, unbalanced AVSDs, pulmonary atresia with intact ventricular

septum with markedly hypoplastic right ventricle, and other complex heart defects with one functioning ventricle. Recently there has been a trend for biventricular repair, particularly for patients with unbalanced AVSDs.

Stage I consists of performing palliative procedures on the basis of pathophysiology of the defect complex at presentation, usually in the neonatal period. Stage II involves performing a bidirectional Glenn procedure (diversion of the superior vena caval blood flow into both lungs) usually at about the age of 6 months. During stage IIIA diversion of the IVC blood flow into the lungs, usually by an extra-cardiac conduit plus a fenestration, usually at about the age of 2 years. Stage IIIB consists of transcatheter closure of the fenestration 6–12 months after Stage IIIA.

Both the immediate and follow-up results have remarkably improved, both in terms of mortality and morbidity, following the introduction of staged total cavo-pulmonary connection with extra-cardiac conduit and fenestration with subsequent catheter closure of Fontan fenestration. Complications do occur during follow-up, and they should be addressed as and when they are detected.

Conflict of interest

The author declares no conflict of interest.

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