European Heart Journal Supplements (2026) **28** (Supplement 1), i7–i16
The Heart of the Matter
https://doi.org/10.1093/eurheartjsupp/suaf088

ESC European Society of Cardiology

The fate of the Fontan circulation

Rosaria Barracano[1]*, Claudia Montanaro[2,3], Sebastien Hascoet[4], Nastasja M.S. de Groot[5], Raquel Prieto-Arévalo[6], Paul Clift[7], Marc Gewillig [8,9], Margarita Brida [3,10,11], and Giancarlo Scognamiglio[1]

[1]Adult Congenital Heart Disease Centre, Congenital and Familial Arrhythmias Unit, AORN Ospedale dei Colli, Monaldi Hospital, Naples 80131, Italy; [2]Congenital Heart Disease Unit, Cardiology, Cardiac Surgery and Heart Lung Transplantation: Bambino Gesù Hospital and Research Institute, IRCCS, Piazza St Onofrio, Rome 00192, Italy; [3]National Heart and Lung Institute, Imperial College Faculty of Medicine, London, UK; [4]Pediatric and Congenital Cardiology Department, M3C National Reference CHD Centre, Marie-Lannelongue Hospital, Le Plessis-Robinson, France; [5]Unit Translational Electrophysiology, Department of Cardiology, Erasmus University Medical Center, Rotterdam, The Netherlands; [6]Cardiology Unit, Hospital General Universitario Gregorio Marañón, Instituto de Investigación Sanitaria Gregorio Marañón, CIBERCV, Universidad Complutense, Madrid, Spain; [7]Adult Congenital Heart Disease Unit, Queen Elizabeth Hospital, Birmingham, UK; [8]Department of Pediatric and Congenital Cardiology, University Hospitals Leuven, Leuven, Belgium; [9]Department of Cardiovascular Sciences, Catholic University of Leuven, Leuven, Belgium; [10]Department of Medical Rehabilitation, Faculty of Medicine, University of Rijeka, Rijeka, Croatia; and [11]Adult Congenital Heart Centre and National Centre for Pulmonary Hypertension, Royal Brompton and Harefield Hospitals, Guy's and St Thomas' NHS Foundation Trust, London, UK

KEYWORDS
Fontan circulation;
Fontan failure;
Arrhythmias;
Heart transplant;
Fontan complications;
Adult congenital heart disease;
Fontan associated liver disease

Since the first operation performed in 1968, the worldwide population of patients living with Fontan circulation is dramatically growing, with 40% reaching adulthood in the current era. Despite this remarkable improvement in survival, some patients struggle with Fontan-related complications including heart failure, arrhythmias, end-organ dysfunction, and premature death. This review aims at describing common complications of the Fontan circulation, proposing a clinical and mortality risk score to better stratify this complex population as well as exploring the current state of art in catheter interventions and transplant.

Introduction

The Fontan palliation was introduced in 1968 to treat all types of congenital heart disease (CHD) with single-ventricle anatomy.[1,2] Consequently, the worldwide population of patients with Fontan circulation is dramatically growing, with 40% of patients >18 years of age, and a current estimate of 30-year survival of about 85%.[3,4] Despite this remarkable improvement in survival, ensuring these patients a normal duration and quality of life is not currently a reality, as multiple organ system dysfunction progresses. The hallmark of the Fontan circulation is a sustained, abnormally elevated central venous pressure combined with decreased cardiac output (CO), especially during periods of increased demands, resulting in a cascade of physiological consequences[5,6] (*Figure 1*). Major complications faced by these patients include heart failure, arrhythmias, and end-organ dysfunction such as protein losing enteropathy (PLE), plastic bronchitis (PB), pulmonary and liver disease[7–11] (*Figure 2*).

The aim of this review is to describe common complications of Fontan circulation, to propose a clinical

*Corresponding author. Tel: +34 06411801, fax: 081/7062501, Email: rosariabarracano@libero.it

and mortality risk score to better stratify this complex population as well as to explore the current state of art in catheter interventions and transplant.

Risk stratification in adults with a Fontan circulation: novel insights

The Fontan operation was first described in 1968 with the publication of three successful cases. Since then, numerous variations of the original procedure have been performed. Over the past 57 years, survival of patients with Fontan circulation has steadily improved. However, there remains ongoing debate regarding the optimal surgical technique, particularly comparing atriopulmonary connection vs. lateral tunnel vs. extracardiac total cavopulmonary connection. Increasingly, children not only survive the initial procedure but also constitute a growing adult population, with many reaching their 40s or beyond.[1,2]

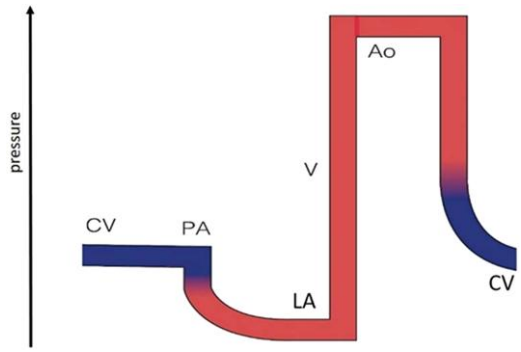

Figure 1 Pathophysiology of the Fontan circulation (courtesy of Dr Sébastien Hascoët). CV, central veins; PA, pulmonary artery; LA, left atrium; V, ventricle; Ao, aorta.

It would be highly valuable to be able to estimate survival at 5, 10, or 15 years in adults with a Fontan circulation.[3,4] Such prognostic information would guide long-term decisions regarding life planning and medical management, including referral time to cardiac transplant. Indeed, it is important to consider that complications related to the Fontan circulation are frequently multisystemic. The musculoskeletal system may be affected, with reduced bone mineral density, reduced lean mass, vitamin D deficiency, and growth hormone abnormalities. The lungs can be compromised by the presence of collaterals, arteriovenous malformations, PB, parenchymal lung disease, and increased pulmonary vascular resistance (PVR). Liver disease includes cirrhosis, portal hypertension, and tumour development. Kidney injury, often underestimated by creatinine measurements, is common and contributes to renal impairment. Fertility is reduced with a higher miscarriage rate and pregnancy is associated with increased morbidity and mortality risks. Chronically elevated venous pressure also contributes to splenomegaly, PLE, diarrhoea, and lymphatic dysfunction, all of which strain the lymphatic system and lead to progressive failure. The brain may be affected by the long-term cyanosis and surgical complications. From a cardiac perspective, complications include systolic and diastolic dysfunction of the systemic ventricle, valve disease, myocardial fibrosis, Fontan pathway stenosis, arrhythmias, and thrombosis.[5]

Multicentre studies have identified predictors of survival. Constantine *et al.* recently examined risk factors for freedom from death or transplantation in patients over 40 years old, highlighting low serum albumin, prior heart failure admissions, prior atrial arrhythmias, and pulmonary vasodilator therapy as adverse predictors.[12] Similarly, Diller *et al.* showed that age, arrhythmias, and symptoms of heart failure were associated with death, transplantation, or hospitalization,[13] while Cordina *et al.* identified echocardiographic predictors such as systolic/

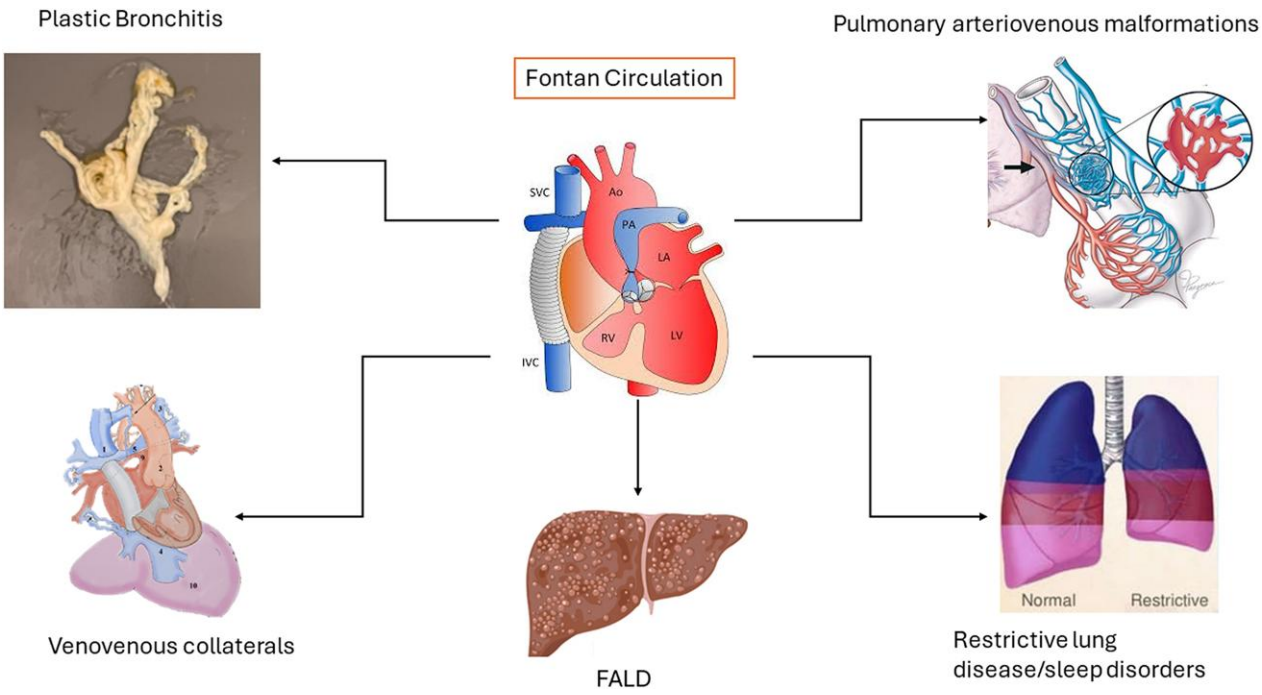

Figure 2 Lungs and liver complications in Fontan patients. SVC, superior vena cava; IVC, inferior vena cava; Ao, aorta; PA, pulmonary artery; RV, right ventricle; LV, left ventricle; LA, left atrium; FALD, Fontan associated liver disease.

diastolic ratios across atrio-ventricular valves and Tei index measurement.[14]

Several scoring systems have been developed to simplify risk assessment. Alsaied proposed a meta-analysis-derived score,[15] while Kramer *et al*. developed a more complex score including 15 variables, some requiring invasive measurements.[16] Most recently, Montanaro *et al*. published and externally validated a six-easy-to-obtain variable score to predict survival at 5, 10, 15, 20, and 30 years. The included predictors were age > 30 years at first visit, NYHA class > II, systolic blood pressure > 120 mm Hg, resting oxygen saturation < 85%, history of atrial tachyarrhythmia, and heart failure (defined as diuretic use). Each variable contributed one point, and a score ≥4 indicated extremely high risk of poor survival, even at 5 years. This score is designed for use at the first visit in an adult CHD centre, provided there is no PLE or Fontan pathway obstruction.[17]

Risk assessment in adults with Fontan circulation has evolved significantly, with validated clinical scores now available to support long-term prognosis. Their use can help clinicians identify high-risk patients early and guide personalized follow-up, medical management, and life planning.

Cardiac catheterization in Fontan patients: when and how?

The Fontan operation is typically described as the final stage of single-ventricle palliation. However, patients are frequently referred for cardiac catheterization (CC) both for diagnostic refinement as well as for percutaneous interventions.[18,19]

Diagnostic indications for CC include the presence of symptoms such as fatigue, cyanosis, ascites, oedema, syncope, PLE, PB, suspected Fontan pathway obstruction, or pulmonary artery hypoplasia; it may be useful to rule out the presence of collaterals or fenestration malfunction and in case of unexplained, disproportionate hepatic congestion. Last but not least, CC is crucial for haemodynamic assessment of transplant candidacy and prior to interventions.

In asymptomatic patients, indication for CC remains controversial due to the lack of clear evidence of its benefit and the absence of a uniform recommendation among current guidelines.[20] Indeed, European guidelines suggest that CC should be performed at a low threshold in cases of unexplained oedema, exercise deterioration, new onset arrhythmia, cyanosis, and haemoptysis.[21] On the other hand, American guidelines recommend CC in adults before initial Fontan surgery or revision of a prior Fontan connection to assess suitability of preintervention haemodynamics or when non-invasive testing is insufficient to guide therapy.[22]

According to current evidence, CC should be performed at each change in clinical condition and/or medication.[23]

CC in Fontan patients aims to provide a comprehensive assessment of the Fontan venous circuit, pulmonary vasculature, and ventricular function. This entails a thorough examination of venous, pulmonary, and ventricular filling pressures, along with an estimation of CO and PVR.

Venous pressure must be recorded across all venous and pulmonary circuits to rule out possible stenosis, and should include the superior and inferior vena cava, both pulmonary branches, and the Fontan conduit.

Ventricular filling pressures may be estimated recording pulmonary artery wedge pressure (PAWP), systemic atrial pressure if accessible through a previous fenestration, or, in the absence of atrioventricular valvulopathies, assessing the end-diastolic ventricular pressure.

The transpulmonary gradient (TPG) is defined as the difference between the mean pulmonary artery pressure and the ventricular filling pressure. The TPG carries the advantage of not being influenced by the estimation of CO. However, reference values for TPG are not clearly defined in Fontan patients and some authors propose a TPG ≥ 5 mm Hg as a value that could warn of a pre-capillary pulmonary vascular disease.[24]

Calculating CO is crucial in Fontan circulation, however, its measurement have some limitations. Indeed, as the thermodilution method is not valid due to the absence of a subpulmonary ventricle, estimation based on the Fick principle is often utilized. Typically, Fontan patients tend to have lower resting CO and a blunted increase with exercise.[25]

Accurate determination of PVR is critical in this labile circulation where even a slight increase can adversely affect ventricular preload and reduce CO. However, the coexistence of collateral blood flow, residual antegrade flow across a patent pulmonary valve or a patent fenestration could complicate the quantification of pulmonary blood flow and subsequent estimation of PVR.

Cardiac magnetic resonance (CMR) may be helpful in such patients. Indeed, combined CMR and CC allows for simultaneous measurement of invasive pressures and CMR-derived anatomy, function, and quantification of flow. Clinical validation studies have shown that combined CMR/CC is more accurate than standard Fick method for the assessment of PVR in pulmonary hypertension and CHD.[26]

Exercise can be performed in the catheterization laboratory, alone or in combination with a cardiopulmonary exercise test (CPET), to stress pulmonary vasculature. This method not only allows the determination of Fontan central venous pressure during exertion but also enables the measurement of CO using direct Fick method.[27]

The significant ongoing advancement in percutaneous interventions have also been successfully applied to Fontan population. A transcatheter approach can be performed to relieve cavopulmonary stenosis, close collaterals, as well as manage fenestration and impaired lymphatic circulation (*Table 1*). Obstruction relief includes balloon angioplasty and stenting of narrowed extracardiac conduits or pulmonary arteries as well as aspiration thrombectomy and covered stents which may be required for conduit obstruction. Collaterals may be treated by embolization or by vascular plug occlusion. Creating a fenestration may be a valuable option in selected patients with failing Fontan with low CO, PLE, or high central venous pressure, whereas fenestration closure may be considered in cyanotic patients when haemodynamics do not deteriorate after occlusion test. A fenestration can be created by puncture, usually along with stent implantation, whereas closure may be obtained with occlusion devices.[28]

Table 1 Indications and percutaneous therapeutic options in patients with Fontan circulation

Indications	Therapeutic options
Conduit/pulmonary branches obstruction	Balloon angioplasty/stenting/aspiration thrombectomy/covered stents
Collaterals	Embolization/vascular plug occlusion
Fenestration	Creation by puncture/closure with device
Lymphatic	Embolization/decompression
Severe AV valve regurgitation	High risk valve surgery (TEER in selected cases)
Hybrid strategies	Percutaneous Fontan
At each change in clinical condition and/or medication	See above

AV, atrio-ventricular; TEER, transcatheter edge-to-edge repair.

In highly selected patients with refractory PLE, interventional treatments of the lymphatic circulation may be an option. They include techniques of embolization of abnormal lymphatic vessels and decompression of the lymphatic system.[29,30]

Recent advancements in percutaneous treatments of the atrio-ventricular (AV) valve regurgitation and transcatheter cavopulmonary connections have also been described.[31]

Severe AV regurgitation increases the risk of Fontan failure. Traditionally, surgical interventions, including valve repair or replacement, have been the treatments of choice. Nonetheless, transcatheter edge-to-edge repair (TEER) represents a less invasive alternative, potentially reducing the associated surgical risks. Favourable short-term data have been reported in patients with systemic tricuspid regurgitation. A significant consideration is that accessing the systemic atrium can be challenging and might require puncturing the Fontan conduit. Therefore, a thorough prior evaluation with multimodal imaging is crucial for an accurate pre-procedural planning.[32,33]

For years, several hybrid strategies have been developed aiming at completing the Fontan circulation percutaneously. At the time of creating the bidirectional Glenn, a preparatory staging is performed for its subsequent percutaneous completion. The surgical technique consists of creating a lateral tunnel with a single large fenestration that communicates with the common atrium, closing the communication with the superior vena cava with a patch, thus maintaining the physiology of the bidirectional Glenn. Subsequently, in a second stage, the Fontan circulation could be completed percutaneously by perforating the patch through radiofrequency, stenting the conduit, and closing the fenestration with an occlusion device. Several experiences have been described but their uses have not been generalized. New prototypes are being developed using an extracardiac-type Fontan circuit pathway.[34-36]

In conclusion, CC remains central in diagnosing and managing Fontan complications, it should be targeted and requires expertise, careful technique, and individualized indications.

How to manage arrhythmias

Epidemiological data indicate that up to 50% of Fontan patients develop clinically significant arrhythmias during long-term follow-up, making them a leading cause of morbidity and mortality in this population. These arrhythmias are often very symptomatic and frequently contribute to heart failure, thromboembolic complications, and need for surgical or percutaneous reinterventions.[37]

The Fontan circulation constitutes a unique physiological state that predisposes patients to rhythm disturbances. Common arrhythmias include intra-atrial re-entrant tachycardia (IART), focal atrial tachycardia (FAT), cavo-tricuspid isthmus dependent atrial flutter (AFL), atrial fibrillation (AF), and sinus node dysfunction (SND). Long-term sequelae of the Fontan operation—such as atrial dilation, chronically elevated systemic venous pressures, and hypoxemia—further promote arrhythmogenesis. With the increasing survival of CHD patients, the management of arrhythmias has become a cornerstone of long-term care.

Among supraventricular tachycardias, IART accounts for approximately 75%, followed by FAT (15%) (*Figure 3*). AF is gaining prominence, with nearly half of patients referred for Fontan conversion presenting with this arrhythmia.[38] SND occurs in about 25% of those with lateral tunnel or extracardiac conduit procedures (*Table 2*).

Multiple factors contribute to post-surgery arrhythmia risk including atrio-pulmonary connections, elevated pulmonary artery pressures, older age at the time of surgery, low oxygen saturation, extended post-operative interval, pre-operative arrhythmias, and right atrial enlargement.[39]

The arrhythmogenic substrate in Fontan patients is highly complex. Surgical scarring, extensive suture lines, and multiple areas of intra-atrial conduction delay scattered across the atria, combined with atrial dilation, sinus node dysfunction, and structural remodelling create a fertile environment for both re-entrant and focal arrhythmias.[40] AF poses the greatest challenge, as its mechanisms occurs often in combination with chronic bradycardia due to sino-atrial node dysfunction.[41]

Therapeutic strategies require individualized planning. According to current ESC guidelines, anti-arrhythmic drugs are often used as initial therapy, though their efficacy is modest and side effects can be limiting. Catheter ablation is especially valuable for IART, demonstrating acute success rates of approximately 78% and long-term sinus rhythm maintenance around 72%.[4] However, high recurrence rates remain problematic, reflecting the presence of multiple arrhythmia mechanisms. Common challenges in ablation procedures are the non-inducibility of clinical arrhythmias, inducibility of multiple non-clinical arrhythmias and the complex arrhythmogenic substrates. Fontan conversion surgery, often combined with arrhythmia surgery, yields arrhythmia-free survival in 40-50% of patients at mid-term follow-up.[42] However, despite acceptable survival in carefully selected patients, the persistently high operative mortality following total

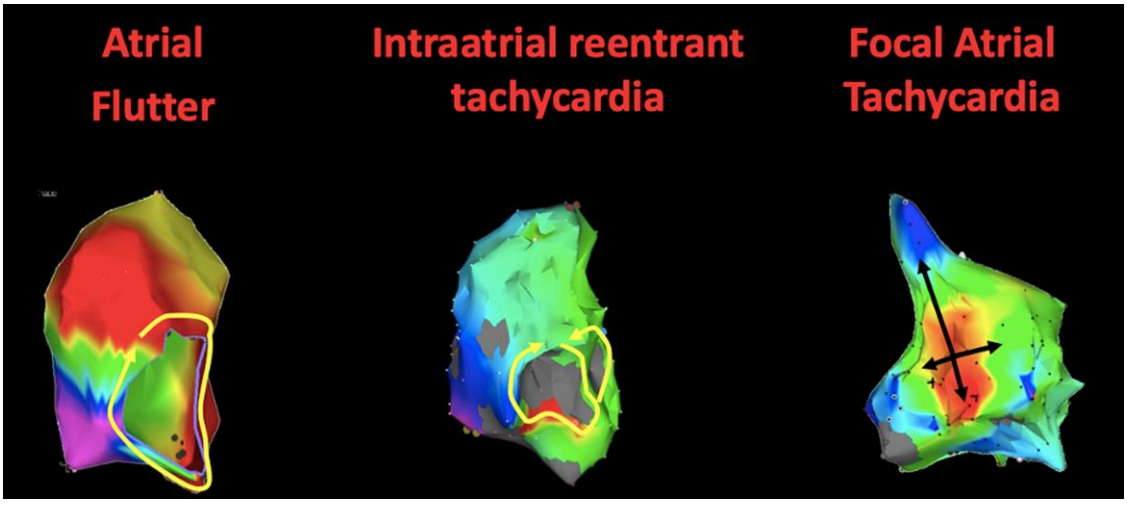

Figure 3 Regular atrial tachycardia: underlying mechanism.

cavo-pulmonary connection (TCPC) conversion highlights the critical importance of stringent patient selection and concentration of surgical expertise in specialized centres. Preventive strategies aimed at limiting atrial remodelling including fibrosis are increasingly recognized as essential components of care.

Innovative technologies such as pulsed field ablation are emerging as potential game changers, offering myocardial-selective ablation with reduced collateral damage.[43] Similarly, advances in imaging and electro-anatomical mapping techniques are expected to refine patient selection and improve procedural outcomes. Recent studies underscore the need for tailored hybrid approaches, integrating catheter-based and surgical interventions, particularly in patients with recurrent AF or complex substrates.

The risk of clinically significant bradycardia is particularly relevant in patients with Fontan physiology, in whom SND represents one of the most frequent rhythm disturbances. In this setting, junctional escape rhythms are often slow, unreliable, and poorly tolerated because of the absence of a functional subpulmonary ventricle and the dependency of CO on low central venous pressure and adequate atrial contraction. Even transient pauses can precipitate profound systemic desaturation, hypotension, or haemodynamic collapse. As a result, timely recognition and management of bradyarrhythmias are critical.[44] Pacing strategies—whether epicardial, transvenous, or hybrid—should be tailored to the individual patient, taking into account the specific Fontan anatomy, the presence of venous or baffle obstructions, and the potential need for atrial or ventricular pacing support.

In summary, arrhythmias remain a major determinant of outcomes in Fontan patients. While ablation provides effective control for regular atrial tachycardias, AF continues to represent the most formidable challenge. Future research should focus on the refinement of ablation strategies, preventive measures to reduce atrial remodelling, and the development of personalized management algorithms, supported by collaborative multicentre studies.

Pulmonary and liver complications

Pulmonary complications are common in Fontan patients, with a prevalence of up to 61% and include systemic to pulmonary venous collaterals/pulmonary arteriovenous malformations, restrictive lung disease, sleep abnormalities, and PB.[11]

The prevalence of cyanosis is high among patients with Fontan circulation. Contributing factors include veno-venous collaterals (VVCs) and pulmonary arteriovenous malformations (PAVMs). About one-third of Fontan patients develop VVCs. The increased venous pressure and the non-pulsatile venous circulation may lead to the formation of decompression VVCs from the systemic to the pulmonary veins. This decreases venous blood pressure and improves CO at the expense of oxygen desaturation. The diagnosis can be made by imaging or during CC. PAVMs can also occur in Fontan patients with flow preferentially to one lung rather than to both lungs. Several studies have theorized that the lack of hepatic venous blood flow to the pulmonary arteries is the primary reason for the development of PAVMs. The diagnosis can be made by transthoracic echo with microbubble contrast, computed tomography (CT) angiography, and CC. Both VVCs and PAVMs can be treated percutaneously by embolization or by vascular plug occlusion.[45,46]

Restrictive lung disease is common in Fontan patients, leading to decreased exercise capacity. Sleep abnormalities may result in hypoxia and increased PVR, which eventually contributes to low CO and Fontan failure.[47]

PB is a rare complication of the Fontan procedure and is defined as the leakage of proteinaceous material into the airways, resulting in episodic expectoration or bronchoscopic visualization of bronchial-shaped casts that can be associated with respiratory distress, wheezing, or significant airway obstruction. Imaging is crucial for diagnosis, individualized treatment, and outcome prediction. Contrast CT findings include bronchial casts seen in major or segmental bronchi along with atelectasis and consolidation without bronchiectasis. Magnetic resonance lymphangiography can detect abnormal lymphatic vessels, whereas

conventional lymphatic angiography might be a further option to delineate abnormal lymphatic vessels and guide lymphatic embolization.[9] Treatment includes relief of airway obstruction (bronchoscopy in cases of emergency, in non-emergent cases, bronchodilators, mucolytics, and inhaled plasminogen activators), anti-inflammatory treatment (corticosteroids and azithromycin) and improvement of haemodynamics (i.e. fenestration creation) and lymphatic interventions. Most patients receive a combination of these strategies.[48]

Some degree of Fontan-associated liver disease (FALD) is universally present after Fontan surgery. Liver damage can start even before the Fontan procedure and is present in patients without Fontan circulatory failure. The time elapsed from Fontan-type surgery is the main risk factor for developing advanced FALD. Liver fibrosis is nearly universal, with patchy distribution. The absence of a functional sub-pulmonic ventricle leads to chronic passive congestion of the liver which is the chief driver of the hepatic fibrosis and hepatomegaly observed in FALD. The elevation in systemic venous pressure caused by passive pulmonary blood flow results in increased systemic venous pressure, causing liver congestion. In addition, CO is reduced, and as a result, zone 3 hepatocytes may be compromised by decreased oxygen delivery to centrilobar cells. Chronic congestion causes shear stress on the hepatic vasculature, resulting in reactive fibrogenesis caused by centrilobular hepatocyte atrophy, sinusoidal fibrosis, and eventual bridging fibrosis and then cardiac cirrhosis.[49] According to the severity of the fibrosis on biopsy, these patients should undergo baseline magnetic resonance with continued surveillance to determine liver stiffness, establish initial anatomic features, identify concerning nodules, and evaluate for signs of portal hypertension and splenomegaly. Although liver laboratory values alone do not correlate with severity of fibrosis, monitoring these values over time will provide additional perspective for a liver specialist. In patients with cirrhosis, upper endoscopy may be useful to assess the presence of varices. Interventions for modifiable risk factors for chronic liver disease, including fatty liver, obesity, hepatotoxic medications, and alcohol use, should be considered in all patients with cirrhosis. Screening for hepatocellular carcinoma (HCC) is particularly challenging, but serial ultrasound and α-fetoprotein measurements to assess changes over time are reasonable.[50,51] For patients with concern for decompensating chronic liver disease, including those with ascites, splenomegaly, thrombocytopenia, gastrointestinal bleeding, jaundice, or failure to thrive/sarcopenia, collaboration with hepatology will be fundamental to fully assess the severity of liver disease and consider referral for liver transplantation evaluation.[52-54]

Fontan failure and transplant

Despite the significant improvement in survival, the Fontan operation remains a palliative surgery prone to several late complications.

While in the normal cardiovascular system the pulmonary and systemic circuits are connected in series and driven by two synchronized pumps, in the Fontan circulation, the absence of a sub-pulmonary ventricle functioning as a pump is associated with an elevated pressure in the caval system, a non-pulsatile blood flow in the pulmonary circuit and a reduction of the systemic output.[55]

Table 2 Epidemiology of arrhythmias in Fontan patients

Arrhythmia type	Prevalence in Fontan patients
Intra-atrial re-entrant tachycardia	≈75% of SVT
Focal atrial tachycardia	≈15% of SVT
Atrial fibrillation	Up to 50% of patients at referral for Fontan conversion
Sinus node dysfunction	≈25% in lateral tunnel/ extracardiac Fontan

SVT, supraventricular tachycardia

The pulmonary vascular bed represents the cornerstone of the Fontan circulation and PVR is the main determinant of the CO. Indeed, the higher the PVR, the lower the CO. On the other hand, in this non-physiologic circulation the venous flow through the cavo-pulmonary circuit is maintained via a combination of passive and weakly active forces. The central venous pressure must be higher than the pulmonary pressure in order to recruit the whole pulmonary vascular bed. At the same time, ideally it should be low enough to prevent lymphatic stasis and oedema. This concept is well known as the 'Fontan paradox'. The single ventricle pump drives the blood flow into the pulmonary vascular bed, mainly during systole. At the same time, the ventricle, pulling downwards the atrioventricular valve and expanding the atrial volume, acts as a suction force drawing blood forward. Similarly, passive ventricular filling is guaranteed by both normal diastolic compliance and low end-diastolic pressure (*Figure 4*).

PVR gradually increases in the normal population with age and will impact on the Fontan patient, and with a progressive increase in PVR there is a subsequent reduction of CO.[56] This, together with other poorly known mechanisms, leads to Fontan circulation failure. Overall, the incidence of Fontan failure has been estimated to be between 26% and 30% at 20 years.

There is still no evidence-based medical therapy for Fontan failure, mainly due to the lack of randomized controlled trials, as well as surgical and interventional procedures can be necessary but may carry a significant risk of complications. With this basis, the only effective treatment for Fontan circulatory failure and associated complications is transplant.[57]

An analysis of the Australia and New Zealand Fontan registry has demonstrated that only 2.5% of 1369 patients with Fontan circulation underwent transplantation at 20 years.[3] In addition, evaluation of referral patterns revealed that patients who were not treated at the national referral centre were less likely to be considered for transplantation. This indicates the need for standardized guidelines for assessment and management for these challenging patients. Patients with failing Fontan circulation require early referral for transplant evaluation at a centre of excellence where they can be assessed for all available treatment options, since early referral may reduce waiting list mortality and

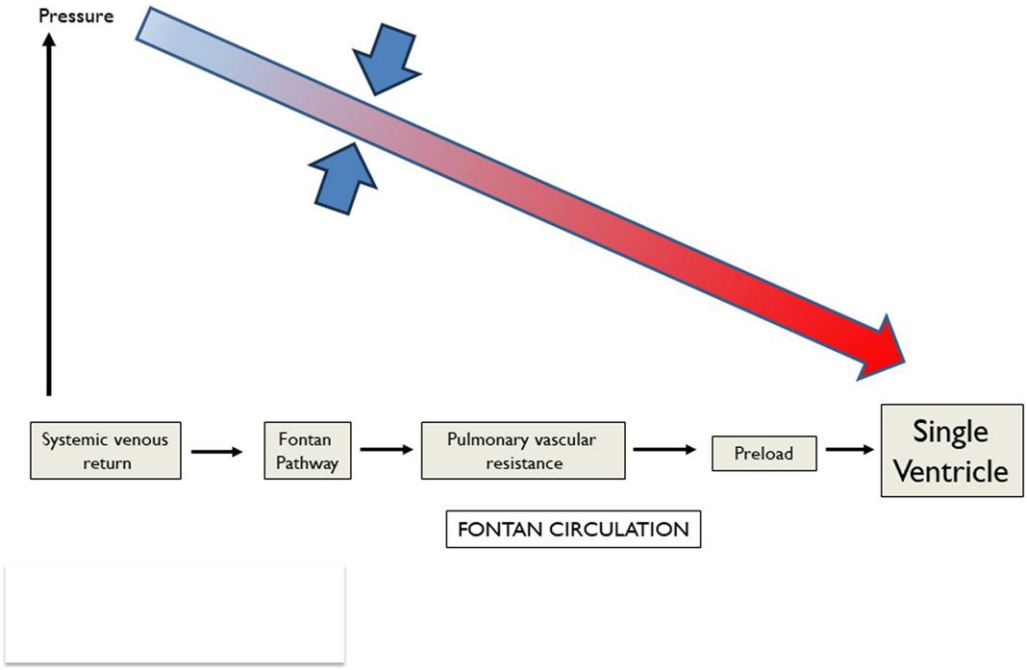

Figure 4 Mechanisms of Fontan failure (courtesy of Dr Paul Clift).

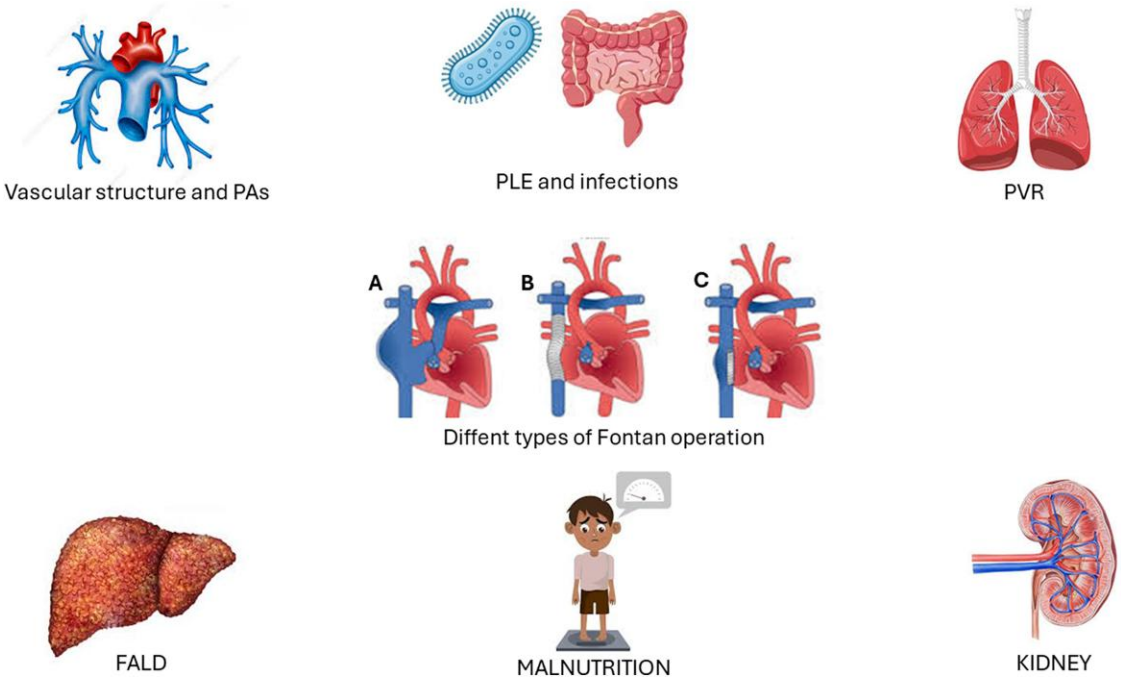

Figure 5 Pre-transplant assessment in Fontan patients. A, atrio-pulmonary Fontan; B, extracardiac Fontan; C, intracardiac Fontan. Pas, pulmonary arteries; PLE, protein losing enteropathy; PVR, pulmonary vascular resistance; FALD, Fontan associated liver disease.

improve outcomes post transplantation, bearing in mind that long-term survival after heart transplantation in Fontan patients is not different than that of patients with other forms of CHD.[58] Late referral after the onset of Fontan failure and select markers of failing Fontan physiology (i.e. worse functional status, cyanosis, bilateral lower extremity varicosities, and the presence of VVCs), has been demonstrated to be associated with higher post-transplant mortality.

Indications for transplant (*Table 3*) include moderate-to-severe systolic dysfunction with heart failure symptoms (fatigue, ascites, oedema, and exercise intolerance, especially if unresponsive to medical therapy), lymphatic failure (manifesting as PLE

Table 3 Indications for heart transplantation in Fontan patients

Moderate-to-severe systolic dysfunction
Lymphatic failure
Arrhythmias
Impaired haemodynamics
FALD

FALD, Fontan-associated liver disease.

or PB), arrhythmias (particularly ventricular arrhythmias presenting with syncope or cardiac arrest), impaired haemodynamics (high Fontan pressure, low cardiac index, progressive desaturation), and FALD (advanced fibrosis/HCC).

Pre-surgical evaluation is paramount for a successful transplant in Fontan patients (*Figure 5*). A detailed evaluation of anatomical characteristics and haemodynamic as well as end-organ assessment is crucial.[59] Pre-operative imaging should describe vascular structures, pulmonary arteries, and potential re-entry risks due to prior surgeries. Some patients, such as those with hypoplastic left heart syndrome who underwent Norwood procedure or those with azygos continuation, may need vessels reconstruction before transplantation. Vascular access may be challenging in Fontan patients and must take into account the multiple surgical procedure they underwent over the lifetime.

Measurement of PVR via CC is essential since even mildly elevated PVR increases the risk of post-operative graft failure. Assessment for FALD should include imaging, elastography, and hepatology consultation. Ascites, varices, and advanced cirrhosis/HCC suggest the need for possible heart–liver transplant. Renal evaluation is highly important as well, since combined heart–kidney transplant may be necessary in some patients. However, multiorgan transplantation is still extremely difficult to achieved in any country over the world. A thorough evaluation including CT and pulmonary function testing is mandatory to exclude pulmonary complications. Patients with PLE or recurrent infections need an immunologic assessment as well. Malnutrition is commonly seen in Fontan patients and should be corrected pre-transplant via enteral or parenteral supplementation. Inotropic support may be useful to stabilize patients prior to transplant.[60-62] If symptoms or end-organ dysfunction persist despite inotropes, mechanical circulatory support (MCS) with a ventricular assisting device (VAD) should be considered. Durable VADs have been used successfully as a bridge to transplant or destination therapy in select Fontan patients. Multidisciplinary collaboration including transplant surgery, cardiology, hepatology, nephrology, nutrition, psychology, and social work is paramount.[63-65]

Multiple studies have reported an early mortality after heart transplantation ranging from 14% to 30%, with main causes represented by infection and graft failure. On the other hand, long-term outcomes have significantly improved over time, with one-year survival now exceeding 90% in recent multicentre studies, and 5-year survival ranging between 70% and 80%.[66-70]

Combined heart–liver transplantation is occasionally used in patients with advanced cirrhosis. Fontan Outcomes Study to improve Transplant Experience and Results (FOSTER) investigators reported an overall survival of patients who underwent combined heart/liver transplant at 1 and 5 years of 87% and 66%, respectively.[71]

In conclusion, the number of patients presenting with Fontan failure is dramatically growing, with transplantation increasingly viewed as the final stage of palliation. Early recognition and standardized referral for transplant evaluation are crucial. Pre-transplant optimization including management of heart failure symptoms, PVR, nutrition, and psychosocial health improves surgical outcomes. Post-transplant survival has improved significantly in the modern era and is now not different from that of other CHDs. Continued innovation in mechanical support, perioperative strategies, and care standardization will be essential to improve outcomes and equity for this expanding population.

Conclusions

Despite the remarkable improvement in survival, Fontan patients still experience complications which are frequently multisystemic. Validated clinical scores for risk assessment are now available to support clinicians in identifying high-risk patients early and guide personalized follow-up, medical management, and life planning. Patient-tailored approach to complications such as arrhythmias, lung, and liver failure is essential. Early recognition, pre-transplant optimization including interventional strategies to optimize haemodynamics, and standardized referral for transplant evaluation are paramount to further the care and improve outcomes of this complex and growing population.

Funding

Nothing to declare.

Conflict of interests: None declared.

Data availability

The data underlying this article are available in the article and in its online supplementary material.

References

1. Fontan F, Baudet E. Surgical repair of tricuspid atresia. *Thorax* 1971;**26**:240–248.
2. Kreutzer G, Galíndez E, Bono H, De Palma C, Laura JP. An operation for the correction of tricuspid atresia. *J Thorac Cardiovasc Surg* 1973;**66**:613–621.
3. Schilling C, Dalziel K, Nunn R, Du Plessis K, Shi WY, Celermajer D *et al*. The Fontan epidemic: population projections from the Australia and New Zealand Fontan registry. *Int J Cardiol* 2016;**219**:14–19.
4. Khairy P, Fernandes SM, Mayer JE Jr, Triedman JK, Walsh EP, Lock JE *et al*. Long-term survival, modes of death, and predictors of mortality in patients with Fontan surgery. *Circulation* 2008;**117**:85–92.
5. Rychik J, Atz AM, Celermajer DS, Deal BJ, Gatzoulis MA, Gewillig MH *et al*. Evaluation and management of the child and adult with Fontan circulation: a scientific statement from the American Heart Association. *Circulation* 2019;**140**:e234–e284.

6. Gewillig M, Goldberg DJ. Failure of the fontan circulation. *Heart Fail Clin* 2014;**10**:105–116.
7. Okólska M, Karkowski G, Kuniewicz M, Bednarek J, Pająk J, Róg B *et al*. Prevalence of arrhythmia in adults after Fontan operation. *J Clin Med* 2022;**11**:1968.
8. Barracano R, Merola A, Fusco F, Scognamiglio G, Sarubbi B. Protein-losing enteropathy in Fontan circulation: pathophysiology, outcome and treatment options of a complex condition. *Int J Cardiol Congenit Heart Dis* 2022;**7**:100322.
9. Mackie AS, Veldtman GR, Thorup L, Hjortdal VE, Dori Y. Plastic bronchitis and protein-losing enteropathy in the Fontan patient: evolving understanding and emerging therapies. *Can J Cardiol* 2022; **38**:988–1001.
10. Gozzi A, Vedovelli L, Bergonzoni E, Cao I, Angeli E, Zanoni R *et al*. Fontan-associated liver disease (FALD) in the EUROFontan experience. An insight into European awareness. *Pediatr Cardiol* 2025; doi:10.1007/s00246-025-03781-0
11. Abdulkarim A, Shaji S, Elfituri M, Gunsaulus M, Zafar MA, Zaidi AN *et al*. Pulmonary complications in patients with Fontan circulation: JACC review topic of the week. *J Am Coll Cardiol* 2023;**81**:2434–2444.
12. Constantine A, Ferrero P, Gribaudo E, Mitropoulou P, Krishnathasan K, Costola G *et al*. Morbidity and mortality in adults with a Fontan circulation beyond the fourth decade of life. *Eur J Prev Cardiol* 2024;**31**:1316–1323.
13. Diller GP, Giardini A, Dimopoulos K, Gargiulo G, Müller J, Derrick G *et al*. Predictors of morbidity and mortality in contemporary Fontan patients: results from a multicenter study including cardiopulmonary exercise testing in 321 patients. *Eur Heart J* 2010;**31**:3073–3083.
14. Cordina R, von Klemperer K, Kempny A, West C, Senior R, Celermajer DS *et al*. Echocardiographic predictors of mortality in adults with a Fontan circulation. *JACC Cardiovasc Imaging* 2017;**10**:212–213.
15. Alsaied T, Bokma JP, Engel ME, Kuijpers JM, Hanke SP, Zuhlke L *et al*. Predicting long-term mortality after Fontan procedures: a risk score based on 6707 patients from 28 studies. *Congenit Heart Dis* 2017;**12**: 393–398.
16. Kramer P, Schleiger A, Schafstedde M, Danne F, Nordmeyer J, Berger F *et al*. A multimodal score accurately classifies fontan failure and late mortality in adult Fontan patients. *Front Cardiovasc Med* 2022;**9**: 767503.
17. Montanaro C, Arvanitaki A, Kerrigan W, Kadani Z, Barracano R, Scognamiglio G *et al*. The Fontan adult Brompton clinical score and mortality risk. *Eur Heart J* 2025;**46**:1933–1945.
18. Brida M, Diller GP, Nashat H, Barracano R, Kempny A, Uebing A *et al*. Cardiac catheter intervention complexity and safety outcomes in adult congenital heart disease. *Heart* 2020;**106**:1432–1437.
19. Gagliardi MG, Formigari R, Perrone MA, Pomiato E, Fanisio F, Panebianco M *et al*. Changes in the Cath lab in the treatment of adult patients with congenital heart disease: a 12-year experience in a single referral center with the establishment of a dedicated working group. *J Cardiovasc Dev Dis* 2023;**10**:314.
20. Miranda W, Hagler D, Connolly H, Kamath P, Egbe A. Invasive haemodynamics in asymptomatic adult Fontan patients and according to different clinical phenotypes. *J Invasive Cardiol* 2022; **34**:E374–E379.
21. Baumgartner H, De Backer J, Babu-Narayan SV, Budts W, Chessa M, Diller G *et al*. 2020 ESC guidelines for the management of adult congenital heart disease. *Eur Heart J* 2021;**42**:563–645.
22. Stout KK, Daniels CJ, Aboulhosn JA, Bozkurt B, Broberg CS, Colman JM *et al*. 2018 AHA/ACC guideline for the management of adults with congenital heart disease: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines. *Circulation* 2019;**139**:e698–e800.
23. Egidy Assenza G, Krieger EV, Baumgartner H, Cupido B, Dimopoulos K, Louis C *et al*. AHA/ACC vs ESC guidelines for management of adults with congenital heart disease: JACC guideline comparison. *J Am Coll Cardiol* 2021;**78**:1904–1918.
24. Stumper O, Penford G. Catheter hemodynamic assessment of the univentricular circulation. *Ann Pediatr Cardiol* 2017;**10**:167–174.
25. Shah AH, Qureshi SA, Krasuski RA. Invasive hemodynamic evaluation of the Fontan circulation: current day practice and limitations. *Curr Cardiol Rep* 2022;**24**:587–596.
26. Egbe AC, Connolly HM, Miranda WR, Ammash NM, Hagler DJ, Veldtman GR *et al*. Haemodynamics of Fontan failure: the role of pulmonary vascular disease. *Circ Heart Fail* 2017;**10**:e004515.
27. Miranda WR, Jain CC, Borlaug BA, Connolly HM, Burchill LJ, Van De Bruaene A *et al*. Exercise catheterization in adults post-Fontan with normal and abnormal haemodynamic criteria: insights into normal Fontan physiology. *Eur J Heart Fail* 2024;**26**:314–323.
28. Jalal Z, Gewillig M, Boudjemline Y, Guérin P, Pilati M, Butera G *et al*. Transcatheter interventions in patients with a Fontan circulation: current practice and future developments. *Front Pediatr* 2022;**10**: 965989.
29. Dori Y, Keller MS, Rychik J, Itkin M. Successful treatment of plastic bronchitis by selective lymphatic embolization in a Fontan patient. *Pediatrics* 2014;**134**:e590–e595.
30. Maleux G, Storme E, Cools B, Heying R, Boshoff D, Louw JJ *et al*. Percutaneous embolization of lymphatic fistulae as treatment for protein-losing enteropathy and plastic bronchitis in patients with failing Fontan circulation. *Catheter Cardiovasc Interv* 2019;**94**: 996–1002.
31. Guerin P, Jalal Z, Le Ruz R, Cueff C, Hascoet S, Bouvaist H *et al*. Percutaneous edge-to-edge repair for systemic atrioventricular valve regurgitation in patients with congenital heart disease: the first descriptive cohort. *J Am Heart Assoc* 2022;**11**:e025628.
32. Haeffele CL, Lui GK, Peng L, Chan F, Sharma RP. First described mitral clip in an adult extracardiac Fontan patient: a case report. *Eur Heart J Case Rep* 2022;**7**:ytac479.
33. Kumar P, Gordon BM, Kheiwa A, Abudayyeh I. A case report of percutaneous MitraClip implantation in an adult with a double-outlet right ventricle. *Eur Heart J Case Rep* 2023;**7**:ytad247.
34. Sivaprakasam MC, Ganesan R, Ramkishore S, Saranya A, Girija H, Arun V *et al*. Catheter-based Fontan completion without prior surgical preparation: is this the way forward? *JACC Case Rep* 2024;**29**:102657.
35. Prabhu S, Maiya S, Shetty R, Murthy K, Ramachandra P, Karl TR. Improved technique for interventional extracardiac Fontan. *World J Pediatr Congenit Heart Surg* 2020;**11**:488–492.
36. Crystal MA, Yoo SJ, Mikailian H, Benson LN. Images in cardiovascular medicine. Catheter-based completion of the Fontan circuit: a nonsurgical approach. *Circulation* 2006;**114**:e5–e6.
37. Egbe AC, Connolly HM, Khan AR, Niaz T, Said SS, Dearani JA *et al*. Outcomes in adult Fontan patients with atrial tachyarrhythmias. *Am Heart J* 2017;**186**:12–20.
38. Mavroudis C, Deal BJ. Fontan conversion: literature review and lessons learned over 20 years. *World J Pediatr Congenit Heart Surg* 2016;**7**: 192–198.
39. Gewillig M, Brown SC. The Fontan circulation after 45 years: update in physiology. *Heart* 2016;**102**:1081–1086.
40. de Groot NMS, Bogers AJJC. Development of tachyarrhythmias late after the Fontan procedure: the role of ablative therapy. *Card Electrophysiol Clin* 2017;**9**:273–284.
41. Moore JP, Burrows A, Gallotti RG, Shannon KM. Electrophysiological characteristics of atrial tachycardia recurrence: relevance to catheter ablation strategies in adults with congenital heart disease. *Heart Rhythm* 2022;**19**:272–280.
42. Mavroudis C, Deal BJ, Backer CL. The beneficial effects of total cavopulmonary conversion and arrhythmia surgery for the failed Fontan. *Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu* 2002; **5**:12–24.
43. Turagam MK, Neuzil P, Schmidt B, Reichlin T, Neven K, Metzner A *et al*. Safety and effectiveness of pulsed field ablation to treat atrial fibrillation: one-year outcomes from the MANIFEST-PF registry. *Circulation* 2023;**148**:35–46.
44. Balaji S, Rychik J, Moore JP. Fontan junctional rhythm-innocent bystander or silent killer? *JAMA Cardiol* 2024;**9**:495–496.
45. McElhinney DB, Reddy VM, Hanley FL, Moore P. Systemic venous collateral channels causing desaturation after bidirectional cavopulmonary anastomosis: evaluation and management. *J Am Coll Cardiol* 1997;**30**:817–824.
46. Nakamura Y, Yagihara T, Kagisaki K, Hagino I, Kobayashi J. Pulmonary arteriovenous malformations after a Fontan operation in the left isomerism and absent inferior vena cava. *Eur J Cardiothorac Surg* 2009;**36**:69–76; discussion 76.
47. Nanayakkara B, Lau E, Yee B, Gauthier G, Melehan K, Celermajer D *et al*. Sleep disordered breathing in adults living with a Fontan circulation and CPAP titration protocol. *Int J Cardiol* 2020;**317**:70–74.
48. Wilson J, Russell J, Williams W, Benson L. Fenestration of the Fontan circuit as treatment for plastic bronchitis. *Pediatr Cardiol* 2005;**26**: 717–719.

49. Emamaullee J, Zaidi AN, Schiano T, Kahn J, Valentino PL, Hofer RE *et al*. Fontan-associated liver disease: screening, management, and transplant considerations. *Circulation* 2020;**142**:591–604.
50. Keung CY, Zentner D, Gibson RN, Phan DH, Grigg LE, Sood S *et al*. Fontan-associated liver disease: pathophysiology, investigations, predictors of severity and management. *Eur J Gastroenterol Hepatol* 2020;**32**:907–915.
51. Dillman JR, Trout AT, Alsaied T, Gupta A, Lubert AM. Imaging of Fontan-associated liver disease. *Pediatr Radiol* 2020;**50**:1528–1541.
52. Cieplucha A, Budts W, Gewillig M, Van De Bruaene A. Fontan-associated liver disease in adults: what a cardiologist needs to know. A comprehensive review for clinical practitioners. *US Cardiol* 2022;**16**:e25.
53. Téllez L, Rincón D, Payancé A, Jaillais A, Lebray P, Rodríguez de Santiago E *et al*. Non-invasive assessment of severe liver fibrosis in patients with Fontan-associated liver disease: the VALDIG-EASL FONLIVER cohort. *J Hepatol* 2025;**82**:480–489.
54. D'Amato J, Bianco EZ, Camilleri J, Debattista E, Ellul P. Hepatocellular carcinoma in Fontan-associated liver disease. *Ann Gastroenterol* 2025;**38**:133–142.
55. Mazza GA, Gribaudo E, Agnoletti G. The pathophysiology and complications of Fontan circulation. *Acta Biomed* 2021;**92**:e2021260.
56. Chowdhury UK, George N, Sankhyan LK, Pradeep D, Chittimuri C, Chauhan A *et al*. Fontan failure: phenotypes, evaluation, management, and future directions. *Cardiol Young* 2022;**32**: 1554–1563.
57. Lubert AM, Cedars A, Almond CS, Amdani S, Conway J, Friedland-Little JM *et al*. Considerations for advanced heart failure consultation in individuals with Fontan circulation: recommendations from ACTION. *Circ Heart Fail* 2023;**16**:e010123.
58. Griffeth EM, Burchill LJ, Dearani JA, Oberoi M, Abdelrehim AA, Leary O *et al*. Optimizing referral timing of patients with Fontan circulatory failure for heart transplant. *Transplant Proc* 2023;**55**: 417–425.
59. Dipchand AI, Honjo O, Alonso-Gonzalez R, McDonald M, Roche SL. Heart transplant indications, considerations, and outcomes in Fontan patients: age-related nuances, transplant listing, and disease-specific indications. *Can J Cardiol* 2022;**38**:1072–1085.
60. Schumacher KR, Rosenthal DN, Batazzi A, Yu S, Reichle G, Bano M *et al*. The impact of Fontan circulatory failure on heart transplant survival: a 20-center retrospective cohort study. *Circulation* 2025;**152**:508–518.
61. Ghelani SJ, Harrild DM, Gauvreau K, Geva T, Rathod RH. Comparison between echocardiography and cardiac magnetic resonance imaging in predicting transplant-free survival after the Fontan operation. *Am J Cardiol* 2015;**116**:1132–1138.
62. Kearney K, McDonald M, Roche L. Collaborative care models in adult congenital heart disease transplant. *Curr Opin Organ Transplant* 2024;**29**:420–427.
63. Mascio CE. Mechanical support of the failing Fontan circulation. *Semin Thorac Cardiovasc Surg* 2021;**33**:454–458.
64. Zwischenberger JB, Breetz KA, Ballard-Croft C, Wang D. Failing Fontan cardiovascular support: review. *J Card Surg* 2022;**37**:5257–5261.
65. Moosmann J, Dittrich S, Purbojo A, Cesnjevar R. RVAD implantation in a Fontan patient with protein-losing enteropathy as a bridge to transplant: Prêtre modification. *J Card Surg* 2020;**35**:1721–1724.
66. Monaco J, Khanna A, Khazanie P. Transplant and mechanical circulatory support in patients with adult congenital heart disease. *Heart Fail Rev* 2020;**25**:671–683.
67. Konstantinov IE, Schulz A, Buratto E. Heart transplantation after Fontan operation. *JTCVS Tech* 2022;**13**:182–191.
68. Hogue SJ, Greenberg JW, Mehdizadeh-Shrifi A, Villa CR, Chin C, Lorts A *et al*. Heart transplantation outcomes for Fontan patients when using contemporary strategies: heart-liver transplantation and ventricular assist device therapy. *World J Pediatr Congenit Heart Surg* 2025;**16**: 368–375.
69. Davies RR, Sorabella RA, Yang J, Mosca RS, Chen JM, Quaegebeur JM. Outcomes after transplantation for "failed" Fontan: a single-institution experience. *J Thorac Cardiovasc Surg* 2012;**143**: 1183–92.e4.
70. Bhama JK, Shulman J, Bermudez CA, Bansal A, Ramani R, Teuteberg JJ *et al*. Heart transplantation for adults with congenital heart disease: results in the modern era. *J Heart Lung Transplant* 2013;**32**:499–504.
71. Lewis MJ, Reardon LC, Aboulhosn J, Haeffele C, Chen S, Kim Y *et al*. Morbidity and mortality in adult Fontan patients after heart or combined heart-liver transplantation. *J Am Coll Cardiol* 2023;**81**: 2161–2171.