Heart transplantation in patients with previous Fontan operations

Amando Gamba, MD
Maurizio Merlo, MD
Roberto Fiocchi, MD
Amedeo Terzi, MD
Carmelo Mammana, MD
Roberta Sebastiani, MD
Paolo Ferrazzi, MD

Objective: The clinical features and outcomes of patients undergoing heart transplantation after a failed Fontan operation are still debated. The aim of this study was to retrospectively evaluate our experience in 14 patients undergoing heart transplantation after previous Fontan-type operations.

Methods: From 1990 to 2002, 14 patients underwent heart transplantation in our institution after a previous Fontan procedure. The mean age at the time of the Fontan operation and at transplantation was 7.3 ± 2.8 and 17.2 ± 6.3 years, respectively. The indication for transplantation was protein-losing enteropathy in 7 patients, arrhythmia with ventricular dysfunction in 5 patients, and heart failure in 2 patients. All patients received basic immunosuppressive therapy with cyclosporine (INN: ciclosporin) and azathioprine without induction therapy or maintenance steroids.

Results: Two hospital deaths occurred: one patient died on the fifth postoperative day of graft failure, and the second died on the 17th postoperative day after an acute neurologic event. Two patients died later, one 23 months after transplantation of acute rejection and the other after 90 months of chronic rejection and endocarditis. One patient underwent successful reintervention 2 years after heart transplantation for pulmonary vein obstruction. The 10 surviving patients are in New York Heart Association class I, with a mean follow-up of 64.5 ± 42 months. One of them was delivered of a healthy baby 5 years after transplantation. Patients with protein-losing enteropathy reached a normal protein level within a mean of 10 months (range, 6-18 months) after transplantation. Four patients required a temporary administration (3-6 months) of oral steroid therapy for recurrent rejection episodes. Currently, 7 patients are taking cyclosporine, and 3 are taking cyclosporine and azathioprine. The actuarial survival at 1, 5, and 10 years was $86\% \pm 9\%$, $77\% \pm 12\%$, and $62\% \pm 17\%$, respectively.

Conclusion: Heart transplantation is a good option for patients with a failing Fontan operation. We documented the reversibility of protein-losing enteropathy in all patients. No mortality caused by surgical complications was observed.

From the Departments of Cardiovascular Surgery, Ospedali Riuniti di Bergamo, Bergamo, Italy.

Received for publication April 16, 2003; revisions requested June 20, 2003; accepted for publication Aug 1, 2003.

Address for reprints: Amedeo Terzi, U.O. Cardiochirurgia, Ospedali Riuniti di Bergamo, Largo Barozzi 1, Bergamo 24100, Italy (E-mail: terzia@cyberg.it).

J Thorac Cardiovasc Surg 2004;127:555-62
0022-5223/\$30.00

Copyright © 2004 by The American Association for Thoracic Surgery

doi:10.1016/j.jtcvs.2003.08.016

Successful application of the so-called Fontan operation was accomplished in 1968 and reported in 1971.^{1,2} Fontan and colleagues^{1,2} treated a case of tricuspid atresia by surgically bypassing the right ventricle to obtain separation of the right and left circulation. Subsequently, this type of operation has been used in many other types of congenital heart diseases when a biventricular repair could not be performed. A wide variety of techniques has been developed to connect the venous systemic return to the pulmonary circulation. Since his first operation, Fontan and many other authors modified the original technique,^{3,4} and the direct atrial-pulmonary artery connection became popular.⁵⁻¹¹ However, intermediate and long-term results showed that the Fontan operation was associated with a high incidence of supraventricular arrhythmia, circulatory pathway obstruction, decreased ventricular function, increasing cyanosis, and protein-losing enteropathy (PLE). Total cavopulmonary artery connection (TCPC) has been introduced to reduce the incidence of supraventricular arrhythmia. This procedure involves the construction of a cavopulmonary anastomosis for the superior vena cava (Glenn) and either an intra-atrial tunnel¹²⁻¹⁴ or an extracardiac conduit for the drainage of the inferior vena cava into the pulmonary artery.¹⁵ The TCPC is currently the method of choice, and it has been widely applied, even in patients with a previous atriopulmonary connection, with or without associated arrhythmia surgery.^{16,17} Still, a considerable number of patients experience late failure, and in some cases heart transplantation remains the only solution to improve survival and clinical status. The purpose of this study was to evaluate the results of our experience with heart transplantation in patients with failing Fontan operations.

Materials and Methods

Patients

From 1985, 575 heart transplantations have been performed at the Department of Cardiovascular Surgery of Ospedali Riuniti, Bergamo, Italy. Sixty-one of these patients underwent heart transplantation for congenital heart disease. Of these 61, between April 1990 and July 2002, 14 patients underwent transplantation after a previous Fontan operation and are the subject of our analysis.

The clinical characteristics of our patient population are detailed in Table 1. Overall, before transplantation, the 14 patients underwent 36 surgical procedures. Sixteen operations consisted of pre-Fontan palliative procedures, 14 were Fontan operations, 4 were redo Fontan operations, and 2 were second redo Fontan operations.

A variety of surgical strategies were used to perform Fontan operations:

- In 3 patients a conduit was initially implanted between the right atrium and the right ventricle. Subsequently, in 2 patients the conduits were replaced twice, and the third patient underwent conversion to Glenn anastomosis and direct atriopulmonary connection.

- In 8 patients a direct connection between the right atrium and the pulmonary artery was performed. Subsequently, one patient was converted to TCPC with a Glenn anastomosis and an intra-atrial baffle.
- In 3 patients a TCPC was performed with a Glenn anastomosis and an intra-atrial baffle. The procedures were performed in 2 stages in 2 patients.

The mean age at the time of the Fontan operation was 7.3 years (range, 3-30 years) and 17.6 years (range, 5.3-33.8 years) at the time of heart transplantation, with a mean weight of 42.8 kg (range, 13-90 kg).

Indications for heart transplantation were as follows:

- PLE in 7 patients. Concomitant ventricular dysfunction (ejection fraction, 30%) was present in only one of these patients. PLE was diagnosed on average 2.3 years after the Fontan operation (range, 0-9 years). Patients were listed for heart transplantation after requiring periodic albumin infusion for at least 1 year. One patient was receiving parenteral nutrition, and one was in congestive heart failure and receiving ventilatory support. At the time of heart transplantation, the mean serum protein level was 3.86 ± 0.48 mg/dL. The median time interval between the Fontan operation and heart transplantation was 6.3 years (range, 2.2-12.6 years). The average time on the waiting list was 5.5 months.
- Supraventricular arrhythmia in 5 patients. These patients were listed for heart transplantation after recurrent episodes of uncontrolled arrhythmia in the face of ventricular dysfunction, which caused very unfavorable hemodynamic consequences.
- Heart failure caused by ventricular dysfunction in 2 patients. Both patients needed hospitalization and inotropic medication when enrolled for heart transplantation.

A pretransplantation cardiac catheterization was performed in 12 patients. It is noteworthy that the 7 patients with PLE had a mean pulmonary pressure of 14.6 ± 2.5 mm Hg, and no gradient was detected in any segment of the Fontan connection. Five of the 7 patients with ventricular dysfunction, arrhythmias, or both had a mean pulmonary pressure of 19.4 ± 3.4 mm Hg. All patients with failing Fontan operations referred for cardiac transplantation were listed and underwent heart transplantation.

Surgical Technique

Harvesting the donor heart, we took as much donor conduits as possible to meet the needs for recipient reconstruction. Implant strategy was modified according to the variety of the anatomic situations encountered (different previous palliations and congenital abnormalities). In 2 patients cannulation of the femoral vessels was performed before sternotomy because of the proximity of the cardiovascular structure to the undersurface of the sternum; in these patients dissection proceeded uneventfully without extracorporeal circulation. In one patient emergency femorofemoral cardiopulmonary bypass was instituted because of right atrial hemorrhage during sternotomy: bleeding was eventually controlled, and the patient recovered uneventfully. All heart transplantations except 2, in which deep hypothermia was needed to control excessive collateral circulation, were performed under moderate hypothermia (24°C-28°C). After cardiectomy and takedown of the Glenn shunt, atriopulmonary anastomosis, or both, the pulmonary

TABLE 1. Patient profiles

Patient no.	Sex	Diagnosis	Previous operations (age)	Indication to TXP	Age at HTx	Donor age	Weight at HTx	Donor weight	Ischemic time (min)	TXP outcome	Follow-up (mo)
1	F	Tricuspid atresia, pulmonary stenosis	1) Fontan: conduit RA/RV (14 y) 2) Conduit replacement (20 y) 3) Prosthesis RA/RV (22 y)	PLE	29.9 y	16 y	62	70	55	Alive	123
2	M	DILV, pulmonary stenosis	1) Left modified BT shunt (6 mo) 2) Right modified BT shunt (8 y) 3) Fontan: RA/PA (8 y), shunt (8 y)	Arrhythmias, LV dysfunction	18.5 y	23 y	60	70	51	Death neurologic complication	0.53
3	M	Tricuspid atresia, VSD+TGA	1) Pulmonary artery banding (6 mo) 2) Fontan: RA/PA + VSD enlargement (3 y)	PLE, LV dysfunction (EF 30%)	5.3 y	9 y	18	24	205	Death chronic rejection	91
4	F	Tricuspid atresia, pulmonary stenosis	1) Left modified BT shunt (6 mo) 2) Right modified BT shunt (6 y) 3) Fontan: RA/PA (7 y)	Atrial fibrillation, Right atrium thrombosis, LV dysfunction (EF 30%)	17 y	11 y	41	65	276	Death acute rejection	23.1
5	F	Tricuspid atresia, restrictive VSD, pulmonary stenosis + TGA	1) Left mod. BT shunt (2 y) 2) Fontan: RA/PA + VSD enlargement (5 y)	LV dysfunction (EF 30%), Arrhythmias	12.2 y	14 y	42	55	175	Alive	91.5
6	F	Tricuspid atresia, VSD	1) PA banding (3 y) 2) Fontan: conduit RA/RV (6 y) 2) Valved conduit 3) Conduit replacement (18 y), RA/RV (8 y)	PLE	22.4 y	20 y	54	70	52	Alive	117
7	M	DILV, pulmonary atresia	1) Left BT shunt (6 mo) 2) Right BT shunt (2 y) 3) Fontan: RA/PA (6 y) 4) Permanent pacemaker (12 y)	PLE	18.6 y	10 y	37	35	205	Alive	32.5

arteries were reconstructed by using different techniques. A bovine pericardium patch was used in 3 patients, a polytetrafluoroethylene patch was used in 2 patients, a recipient redundant right atrial wall was used in 2 patients, and donor pulmonary artery bifurcation tissue was used in 3 patients. Direct reconstruction of pulmonary artery continuity was easily done without patch interposition in the remaining 4 patients. Because patients with failing Fontan operations usually do not have conspicuous cardiomegaly, we tried to avoid significant weight

mismatch between donors and recipients, particularly when an extensive reconstruction of the pulmonary arteries was required or when diffuse pleural adhesions caused by a previous thoracotomy were present.

The implantation of the new heart was performed with atrial anastomoses in 7 patients and with direct caval anastomoses in the other 7 patients, according to surgeon's preference and anatomic suitability (TCPC). No patient had persistent bleeding after the operation.

TABLE 1. Continued

Patient no.	Sex	Diagnosis	Previous operations (age)	Indication to TXP	Age at HTx	Donor age	Weight at HTx	Donor weight	Ischemic time (min)	TXP outcome	Follow-up (mo)
8	F	Tricuspid atresia, pulmonary stenosis	1) Left modified BT shunt (1 mo) 2) Right modified BT 3) Fontan: RA/PA, (4 y), shunt (2 y)	PLE	16.3 y	12 y	43	48	186	Alive	33
9	F	Tricuspid atresia, pulmonary stenosis	1) Right BT shunt (3 mo) 2) Fontan: RA/PA (6 y) 3) Right PA angioplastic (9 y)	LV dysfunction (EF 26%), arrhythmias	19.1 y	11 y	47	70	180	Alive	69
10	M	DIRV, TAPVD, mitral atresia	1) TAPVD correction, Glenn (10 mo) 2) Conduit IVC/PA (6 y)	Ventricular dysfunction, severe heart failure	6.5 y	6 y	16	25	305	Alive	98
11	M	Tricuspid atresia, pulmonary stenosis	1) Davidson shunt (10 mo) 2) Fontan: conduit 3) Glenn + RA/PA connection (14 y), RA/RV (10 y)	LV dysfunction, atrial fibrillation, right atrial thrombosis	27.8 y	31 y	63	70	202	Alive	60
12	M	DIRV, VSD	1) PA banding + Glenn (9 mo) 2) Conduit IVC/PA (6 y)	PLE, heart failure/intubated	7.1 y	2 y	17	13	200	Death, graft failure	0.36
13	M	Tricuspid atresia, pulmonary stenosis, TGA	1) Fontan: RA/PA (18 y) 2) Total cavopulmonary 3) Permanent pacemaker connection (3 y)	PLE	33.8 y	29 y	72	90	193	Alive	12
14	F	Tricuspid atresia, VSD+TGA	1) PA banding (3 mo) 2) Total cavopulmonary connection (3 y)	LV dysfunction (EF 14%)	11.6 y	8 y	28	25	300	Alive	9

HTx, Heart transplantation; RA, right atrium, RV, right ventricle; PLE, protein-losing enteropathy; DILV/DIRV, double-inlet left/right ventricle; BT, Blalock-Taussig; PA, pulmonary artery; LV, left ventricle; VSD, ventricular septal defect; EF, ejection fraction; TGA, transposition of the great arteries; TAPVD, total anomalous pulmonary venous drainage; IVC, inferior vena cava.

The donor mean age was 14.2 ± 8.5 years, the mean weight was 52.1 ± 23.7 kg, and the mean ischemic time was 181 ± 83 minutes.

Immunosuppressive Therapy

According to our standard transplantation protocol, these patients started their immunosuppressive regimens with cyclosporine and azathioprine. Neither antithymocyte nor antilymphocyte globulin nor other induction therapies were administered. The rejection episodes were treated with a 3-day therapy of high-dosage intravenous meth-

ylprednisolone ($15 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{d}^{-1}$), followed by an oral course of prednisone in case of consecutive rejections.

Follow-up Monitoring

After discharge, the patients have been followed with physical examination, echocardiography, electrocardiography, and blood testing every 1 to 3 months in the first postoperative year and every 3 to 4 months subsequently. Myocardial biopsy was routinely performed only in patients aging more than 6 years during the first postoperative year.

Figure 1. Actuarial survival after heart transplantation in patients with failing Fontan operations. *CL*, Confidence limit.

Results

Early Results

There were 2 perioperative deaths. One patient (7.1 years, 17 kg, ventilated, low cardiac output) underwent an emergency operation, and we were urged to accept an undersized donor heart (2 years, 13 kg). He required extracorporeal membrane oxygenation implantation for severe low-output posttransplantation syndrome and died 5 days later of multiorgan failure. A second patient died 16 days after heart transplantation of cardiac arrest subsequent to a prolonged epileptic attack. The postmortem showed a large cerebral scar probably caused by an old and unrecognized cerebral infarct.

Of the 12 survivors, only one patient had inadequate cardiac output that required high inotropic support for a few days, and subsequently pancreatitis and cytomegalovirus and *Staphylococcus* species infection developed. He eventually recovered but underwent pacemaker implantation for a persistent atrioventricular block. A second patient required surgical plication of a paretic left diaphragm, and a third patient underwent successful reoperation 3 weeks after heart transplantation for acute thrombosis of the superior vena cava after a transjugular myocardial biopsy.

The intubation time was shorter than 24 hours in the 7 patients who had a remarkably straightforward recovery and between 2 and 16 days (mean, 6 days) in the remaining 7 patients. Intensive care stay was 2 to 23 days (mean, 6.5 days), and in-hospital recovery was 19 to 90 days (mean, 35 days).

Late Results

Two patients died after hospital discharge. The first died 23 months after heart transplantation of an episode of sudden acute rejection of the graft. She had been receiving treatment with cyclosporine and azathioprine, and of the 14 myocardial biopsies performed after heart transplantation, only 3 showed mild or moderate rejection.

The second death occurred in a patient waiting retransplantation for severe chronic rejection 90 months after the initial heart transplantation. The patient had been readmitted to the hospital in multiorgan failure and died of a concomitant acute aortic endocarditis.

The 10 remaining patients, with a mean follow-up of 64.5 ± 42 months (range, 9.2-123 months) are actually in good condition with normal heart function.

Actuarial patient survival, according to Kaplan-Meier estimates, is $86\% \pm 9\%$, $77\% \pm 12\%$, and $62\% \pm 17\%$ at 1, 5, and 10 years, respectively (Figure 1).

Patient 10 (Table 1) underwent a successful operation in another center for stenosis of the pulmonary veins 2 years after heart transplantation. Before heart transplantation, at the age of 10 months, this patient had undergone surgical correction of a total anomalous pulmonary venous drainage.

Patient 1, a 35-year-old woman operated on 3 times for various Fontan modifications, was delivered of a healthy baby by means of caesarian section 5.5 years after heart transplantation.

Figure 2. Serum protein level before and after heart transplantation.

In the 6 patients with previous PLE, the protein level reached a normal value after 6 months in 4 patients and after 18 months in 2 patients (Figure 2). Mean serum protein levels were as follows during the 68 months of mean follow-up (range, 12-123 months): 3.91 ± 0.42 g/dL at 1 month, 6.26 ± 2.3 g/dL at 6 months, 6.38 ± 1.8 g/dL at 12 months, 7.06 ± 0.61 g/dL at 18 months, and 7.42 ± 0.6 g/dL at the last control.

Only 6 of the 12 early survivors had one or more episodes of acute rejection (total of 19 episodes), and 4 of them required, for a limited period of time (3-6 months), an oral course of prednisone.

Of the 10 late survivors, 7 patients are receiving monotherapy with cyclosporine for azathioprine intolerance. Two patients are taking cyclosporine and azathioprine, and one is taking cyclosporine and mycophenolate mofetil. The cyclosporine oral dose is, on average, 5 ± 1.6 mg $\cdot$ kg⁻¹ $\cdot$ d⁻¹. The mean blood creatinine level of the 10 patients was 1.12 mg/dL.

Discussion

The issue of failing Fontan operations is an ever increasing burden to univentricular patients. Most of the patients in this study were operated on in the past, when Fontan operations were performed at advanced age, and possibly the prolonged cyanosis played a role in the ultimate failure of the operation. Nonetheless, it appears inevitable that in any case some of the patients undergoing Fontan procedures will eventually require either mechanical or transplantation replacement. PLE is a life-threatening complication after the Fontan operation, the prevalence of which among the 30-day survivors ranges from 0% to 25%.¹⁸⁻²² This syndrome

has a very dismal prognosis, either with medical or surgical treatment, with a reported mortality of 46% to 64%.^{19,20} Pathophysiology is still debated. Chronic venous congestion always associated with the Fontan circulation might contribute to the intestinal protein loss. The mechanism should concern disturbed lymph drainage, increased lymph production, or both caused by intestinal congestion. Some sort of vicious circle on the basis of a chronic inflammatory response of the enteric system might be involved and related to individual factors. Certainly, PLE does not occur in all patients with increased venous pressure and does occur in some other patients with a favorable hemodynamic pattern (ie, a mean right atrial pressure of <15 mm Hg). As a matter of fact, our patients who required heart transplantation for PLE had a lower mean pulmonary artery pressure than those who received heart transplantation for ventricular dysfunction, arrhythmia, or both (14.6 vs 19.4 mm Hg). These data confirm the difficulty in dealing with this complication and the amount of uncertainty lingering on the different therapeutic options. The medical literature has scant information about heart transplantation and PLE. A multicenter study²³ regarding 10 patients who underwent heart transplantation for PLE after the Fontan operation with 7 long-term survivors reported that one patient had continuous problems with PLE despite excellent graft function. In another patient PLE temporarily improved but recurred after 1 year, despite normal graft function. Other reports of a few single cases showed a complete resolution of PLE after heart transplantation.^{24,25} The reason why PLE did not resolve after heart transplantation in the 2 cases reported in the multicenter study remains unknown. More detailed hemodynamic find-

ings other than the simple assessment of good graft function, such as right-side pressures or evaluation of diastolic function, could shed more light on this issue. It has also been postulated that some changes in the enteric system could become irreversible and therefore no longer responsive to hemodynamic normalization. Luckily, this has not been our experience, and all 6 patients discharged from the hospital had normalized serum protein levels within 18 months after heart transplantation. According to this, we are encouraged in pursuing a strategy of heart transplantation in the presence of PLE after the Fontan operation provided the medical therapy and surgical treatment aimed to resolve specific and well-identified hemodynamics problems has proved to be inefficacious. If heart transplantation is considered, we suggest it should be undertaken before nutritional debilitation becomes manifest.

Conversion to TCPC with ablative surgery has been reported as an effective method to treat refractory atrial arrhythmia after the Fontan procedure.^{16,17} In our experience 14 patients affected by untreatable arrhythmia after Fontan correction underwent TCPC conversion and ablative surgery. One patient died early of bronchopneumonia, and 13 had good late results. The 5 patients who underwent heart transplantation for arrhythmia were definitively a different subset of patients because of the concomitant presence of ventricular dysfunction. One patient (no. 13) required heart transplantation because after conversion elsewhere to TCPC for arrhythmia, PLE developed. Our opinion is that when arrhythmias are associated to detectable ventricular dysfunction, the patients should preferably listed for heart transplantation.

Overall, compared with our global experience with heart transplantation, the patient undergoing heart transplantation after a failed Fontan operation had a lower incidence of acute rejection episodes despite a reduced immunosuppressive therapy. In the 12 early survivors, the incidence of acute rejections that needed treatment was 1.58 episodes per patient compared with 4.6 episodes per patient in our global heart transplantation experience during a comparable length of follow-up.²⁶ Currently, 7 patients are receiving cyclosporine monotherapy, and none is taking steroids. This is in contrast with our global experience, in which steroids had to be chronically introduced in 15% of the patients because of repeated rejection episodes. Because of the small number of patients, it is impossible to demonstrate a lower immunoreactivity in this group of patients. However, we would like to speculate that the low rejection rate could be a consequence of a long disease and repeated previous blood transfusion, plasma transfusion, or both. The presence of previous surgical operations and a long history of disease has not been shown to be an incremental risk factor. Heart transplantation in these patients is a long and complex operation in which the surgical experience in the congenital field

coexisting with the transplantation expertise of the surgical center might play a fundamental role.

In conclusion, this retrospective analysis is encouraging, showing that heart transplantation has satisfactory early and midterm results after a failed Fontan operation. Survivors have been shown to enjoy a good quality of life. We documented the reversibility of PLE in all cases, but a longer follow-up in a bigger number of patients is required to draw definitive conclusions.

References

- Fontan F, Mounicot FB, Baudet E, Simonneau J, Gordo J, Gouffrant JM. "Correction" of tricuspid atresia. 2 cases "corrected" using a new surgical technique. *Ann Chir Thorac Cardiovasc*. 1971;10(1):39-47.
- Fontan F, Baudet E. Surgical repair of tricuspid atresia. *Thorax*. 1971;26(3):240-8.
- Fontan F, Deville C, Quaegebeur J, Ottenkamp J, Sourdil N, Choussat A, et al. Repair of tricuspid atresia in 100 patients. *J Thorac Cardiovasc Surg*. 1983;85(5):647-60.
- Fontan F, Chaussat A, Brom A, Chauve A, Deville C, Castro-Cels A. Repair of tricuspid atresia—surgical considerations and results. In: Anderson RH, Shinebourne EA, editors. *Pediatric cardiology*. Edinburgh: Churchill Livingstone; 1978. p. 675-93.
- Kreutzer G, Galindez E, Bono H, De Palma C, Laura JP. An operation for the correction of tricuspid atresia. *J Thorac Cardiovasc Surg*. 1973;66(4):613-21.
- Kreutzer GO, Vargas FJ, Schlichter AJ, Laura JP, Suarez JC, Coronel AR, et al. Atriopulmonary anastomosis. *J Thorac Cardiovasc Surg*. 1982;83(3):427-36.
- Bowman F, Malm J, Hayes C, Gersony W. Physiological approach to surgery for tricuspid atresia. *Circulation*. 1978;58(suppl 1):1-83.
- Doty DB, Marvin WJ Jr, Lauer RM. Modified Fontan procedure. Methods to achieve direct anastomosis of right atrium to pulmonary artery. *J Thorac Cardiovasc Surg*. 1981;81(3):470-5.
- Henry JN, Devloo RA, Ritter DG, Mair DD, Davis GD, Danielson GK. Tricuspid atresia. Successful surgical "correction" in two patients using porcine xenograft valves. *Mayo Clin Proc*. 1974;49(11):803-10.
- Neveux JY, Dreyfus G, Leca F, Marchand M, Bex JP. Modified technique for correction of tricuspid atresia. *J Thorac Cardiovasc Surg*. 1981;82(3):457-60.
- Gale AW, Danielson GK, McGoon DC, Wallace RB, Mair DD. Fontan procedure for tricuspid atresia. *Circulation*. 1980;62(1):91-6.
- Puga FJ, Chiavarelli M, Hagler DJ. Modifications of the Fontan operation applicable to patients with left atrioventricular valve atresia or single atrioventricular valve. *Circulation*. 1987;76(suppl):III53-60.
- de Leval MR, Kilner P, Gewillig M, Bull C. Total cavopulmonary connection: a logical alternative to atriopulmonary connection for complex Fontan operations. Experimental studies and early clinical experience. *J Thorac Cardiovasc Surg*. 1988;96(5):682-95.
- Jonas RA, Castaneda AR. Modified Fontan procedure: atrial baffle and systemic venous to pulmonary artery anastomotic techniques. *J Card Surg*. 1988;3(2):91-6.
- Marcelletti C, Corno A, Giannico S, Marino B. Inferior vena cavopulmonary artery extracardiac conduit. A new form of right heart bypass. *J Thorac Cardiovasc Surg*. 1990;100(2):228-32.
- Mavroudis C, Backer CL, Deal BJ, Johnsrude CL. Fontan conversion to cavopulmonary connection and arrhythmia circuit cryoblation. *J Thorac Cardiovasc Surg*. 1998;115(3):547-56.
- Kao JM, Alejos JC, Grant PW, Williams RG, Shannon KM, Laks H. Conversion of atriopulmonary to cavopulmonary anastomosis in management of late arrhythmias and atrial thrombosis. *Ann Thorac Surg*. 1994;58(5):1510-4.
- Gentles TL, Gauvreau K, Mayer JE Jr, Fishberger SB, Burnett J, Colan SD, et al. Functional outcome after the Fontan operation: factors influencing late morbidity. *J Thorac Cardiovasc Surg*. 1997;114(3):392-403; discussion 04-5.
- Feldt RH, Driscoll DJ, Offord KP, Cha RH, Perrault J, Schaff HV, et

- al. Protein-losing enteropathy after the Fontan operation. *J Thorac Cardiovasc Surg.* 1996;112(3):672-80.
20. Mertens L, Hagler DJ, Sauer U, Somerville J, Gewillig M. Protein-losing enteropathy after the Fontan operation: an international multicenter study. PLE study group. *J Thorac Cardiovasc Surg.* 1998;115(5):1063-73.
21. Kaulitz R, Luhmer I, Bergmann F, Rodeck B, Hausdorf G. Sequelae after modified Fontan operation: postoperative haemodynamic data and organ function. *Heart.* 1997;78(2):154-9.
22. Crupi G, Locatelli G, Tiraboschi R, Villani M, De Tommasi M, Parenzan L. Protein-losing enteropathy after Fontan operation for tricuspid atresia (imperforate tricuspid valve). *Thorac Cardiovasc Surg.* 1980;28(5):359-63.
23. Mertens L, Canter C, Parisi F. The outcome for heart transplantation for protein-losing enteropathy after the Fontan operation. *Circulation.* 1999;100(suppl 1):1602.
24. Holmgren D, Berggren H, Wahlander H, Hallberg M, Myrdal U. Reversal of protein-losing enteropathy in a child with Fontan circulation is correlated with central venous pressure after heart transplantation. *Pediatr Transplant.* 2001;5(2):135-7.
25. Sierra C, Calleja F, Picazo B, Martinez-Valverde A. Protein-losing enteropathy secondary to Fontan procedure resolved after cardiac transplantation. *J Pediatr Gastroenterol Nutr.* 1997;24(2):229-30.
26. Gamba A, Mamprin F, Fiocchi R, Senni M, Troise G, Ferrazzi P, et al. The risk of coronary artery disease after heart transplantation is increased in patients receiving low-dose cyclosporine, regardless of blood cyclosporine levels. *Clin Cardiol.* 1997;20(9):767-72.