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Completion of the Three-Stage Fontan Pathway Without Cardiopulmonary Bypass

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Abstract

Background: The three-stage surgical approach is now accepted as the standard for management of children born with functional single ventricle. However, there is little consensus on the cardiopulmonary bypass strategies employed for these procedures. We have attempted to avoid cardiopulmonary bypass in patients with single ventricle whenever possible to eliminate the adverse effects that are induced by this process. The purpose of this study was to review our experience in patients who underwent all three stages of the Fontan pathway without ever being exposed to bypass. **Methods:** A total of 52 patients with single ventricle underwent "off-pump" treatment at all three stages of their surgical management. The time period of the study was from 2002 to 2013. There were 31 males and 21 females. Anatomic diagnoses included double inlet left ventricle (n = 11), pulmonary atresia with intact ventricular septum (n = 11), tricuspid atresia (n = 10), double outlet right ventricle (n = 9), and other (n = 11). **Results:** There was no operative mortality in the 52 patients undergoing Fontan completion. The patients have been followed for an average of 5.1 ± 2.5 years, with one late mortality. The median length of hospital stay for the three stages was 17, 5, and 9 days, respectively. Of the 52 patients, 42 were able to undergo all three stages without the need for a blood transfusion. **Conclusions:** This series demonstrates the feasibility of achieving a Fontan circulation without patients exposed to cardiopulmonary bypass. There was no operative mortality and low mid-term mortality. It is notable that 80% of patients never required a blood transfusion with this approach. The elimination of cardiopulmonary bypass provides several potential clinical benefits in this highly select subset of patients with single ventricle.

Keywords

CHD, univentricular heart, cardiopulmonary bypass, CPB, inflammatory response, complications, Fontan, off-pump surgery

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Introduction

Achieving a Fontan circulation is a well-established goal for the management of children who are born with functional single ventricle. There is now a consensus for the three-stage surgical approach to patients with single ventricle. The majority of patients with single ventricle require a neonatal procedure predicated on the underlying anatomy and physiology. This is followed by a bidirectional Glenn procedure at three to six months of age. The third stage, frequently referred to as a "Fontan procedure," is completed between one and five years of age. This three-stage strategy has resulted in a significant reduction in morbidity and mortality over the past several decades.[1-4]

In spite of the consensus regarding a three-stage approach for the management of patients with single ventricle, there is little consensus with regard to the cardiopulmonary bypass strategies employed during these surgical procedures. The time-honored approaches include bypass without aortic cross-clamp, bypass with aortic cross-clamp (for completion of concomitant procedures), and circulatory arrest. In recent years, there have been several series reporting the experience with off-pump bidirectional Glenn[5-8] and also off-pump Fontan procedures.[9-13] It was presumed that the outcomes for off-pump surgery might exceed those for on-pump procedures. However, the outcomes for patients with single ventricle have improved to such an extent that it has been difficult to prove an advantage of any one cardiopulmonary bypass strategy. As a consequence, the divergent bypass strategies flourish in the absence of proof that one methodology is superior to another.

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Our group has been committed to developing an "off-pump" approach for management of patients with single ventricle.[14,15] This includes performing both the bidirectional Glenn and Fontan procedures without the use of cardiopulmonary bypass. The purpose of this study was to summarize our experience with patients who were able to undergo all three stages of the Fontan pathway without exposure to cardiopulmonary bypass.

Methods

This study was approved by the institutional review board at Stanford University. Patients were identified through the cardiac database, and the medical records were subsequently reviewed. The time period of this study was from 2002 through 2013.

This was a retrospective study summarizing our experience with 52 patients (31 males and 21 females) who underwent completion of all three stages of the Fontan pathway without the use of cardiopulmonary bypass. This represents approximately 25% to% of the overall number of patients with single ventricle undergoing management at our institution during this period. Anatomic diagnoses of these patients include double inlet left ventricle (n = 11), pulmonary atresia with intact ventricular septum (n = 11), tricuspid atresia (n = 10), double outlet right ventricle (n = 9), and other (n = 11).

Specifically, all patients with single ventricle who needed a neonatal procedure, which would require the use of cardiopulmonary bypass, were excluded from this study. The operations that would fall under this description include a Norwood or Damus-Kaye-Stancel procedure, repair of total anomalous pulmonary venous drainage, and atrial septectomy.

The strategy for performing an entirely off-pump approach begins at the time of the neonatal palliative procedure. We perform the majority of these procedures through a midline sternotomy approach, which provides an opportunity to comprehensively evaluate the anatomy of each patient. This approach is also quite versatile from a surgical standpoint and permits placement of a pulmonary artery band or systemic to pulmonary artery shunt. We usually perform a short, central shunt from the ascending aorta to the main or branch pulmonary artery, and in the presence of a single superior vena cava would place the shunt on the contralateral side. This facilitates performing the bidirectional Glenn procedure off pump at the next stage.

The technique for performing an off-pump bidirectional Glenn has been well described.[5-8] Patients with bilateral superior vena cava can undergo an off-pump bilateral bidirectional Glenn by performing each side sequentially, solely with systemic heparinization. For patients with a single superior vena cava, we perform the bidirectional Glenn procedure utilizing a venovenous shunt constructed from the innominate vein to the systemic atrium (Figure 1). We monitor the upper compartment pressures with a temporary transthoracic line placed in the superior vena cava or innominate vein. These pressures should be less than 20 mm Hg when the venovenous shunt is functioning properly. Pressures higher than that value should prompt an investigation into the cause, which is usually attributable to malposition of one of the two cannulas. In addition to this pressure monitoring, we routinely use cerebral and visceral near-infrared spectroscopy for these procedures. The cavoatrial junction is clamped proximally and distally, and the atrial side oversewn. The cavopulmonary anastomosis is then constructed in a standard fashion (Figure 2).

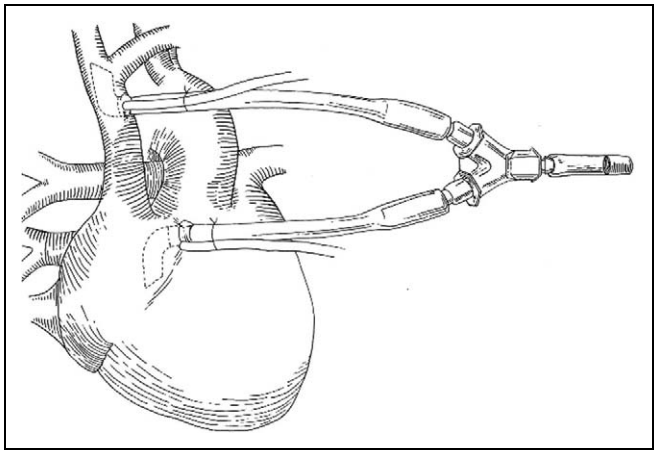

Figure 1. Artist's illustration demonstrating the technique for performing an off-pump bidirectional Glenn. The patient is heparinized and a venovenous shunt is constructed from the superior vena cava (SVC) to systemic atrium.

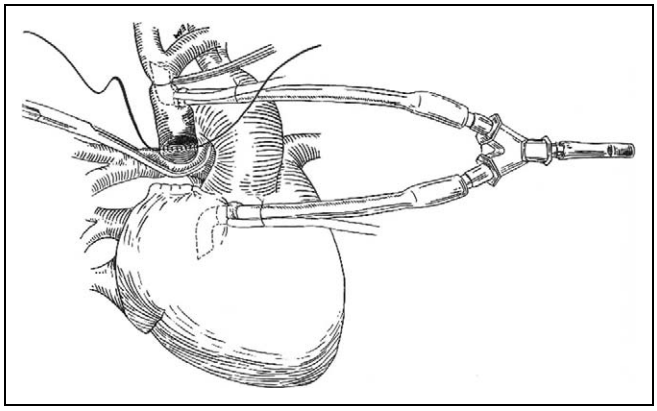

Figure 2. Illustration of the bidirectional Glenn procedure. The superior vena cava (SVC) is divided and the atrial side oversewn. A partial occlusion clamp is placed on the right pulmonary artery (RPA), and the anastomosis performed between the SVC and the RPA.

The Fontan procedure can be performed off-pump using an extracardiac conduit approach.[9-15] Our algorithm has been to wait until patients have achieved a weight of 12 to 15 kg and select a conduit to approximate the size of the adult inferior vena cava. The patients received full systemic heparinization, and the upper anastomosis to the underside of the pulmonary artery is performed first. Following complete mobilization of the superior vena cava and branch pulmonary arteries, a clamp is placed tangentially along the base of the cavopulmonary anastomosis, as illustrated in Figure 3. The upper compartment

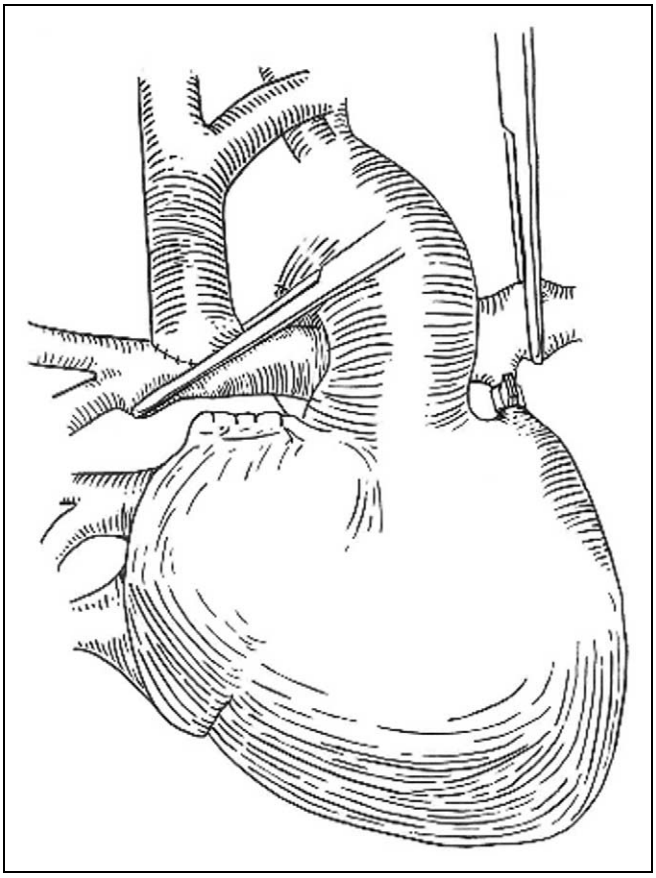

Figure 3. Artist's illustration demonstrating the technique for performing an off-pump extracardiac Fontan procedure. The branch pulmonary arteries and previously constructed bidirectional Glenn are fully mobilized. The patient is fully heparinized. A clamp is then placed tangentially across the pulmonary artery while still permitting flow to the ipsilateral lung.

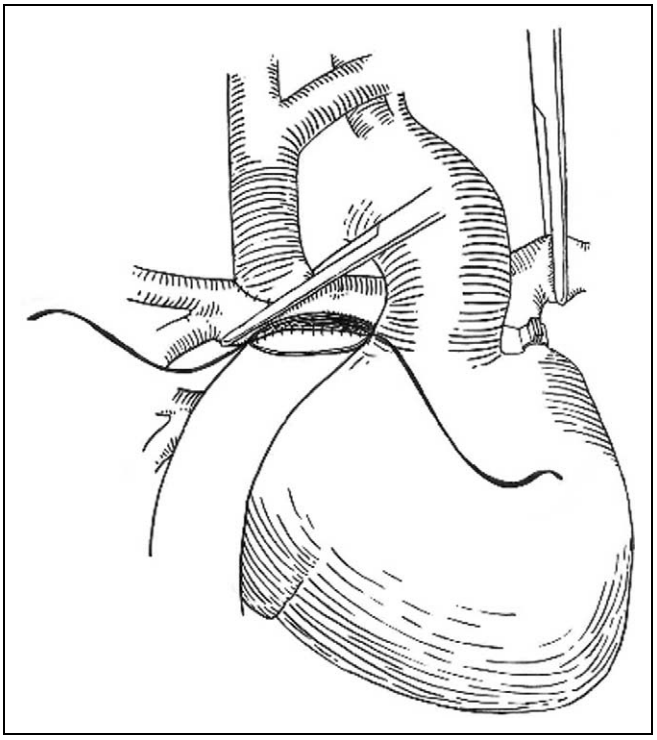

Figure 4. Illustration demonstrating construction of the upper anastomosis between the underside the branch pulmonary arteries and the Goretex tube graft. The anastomosis is performed with 6-0 Prolene.

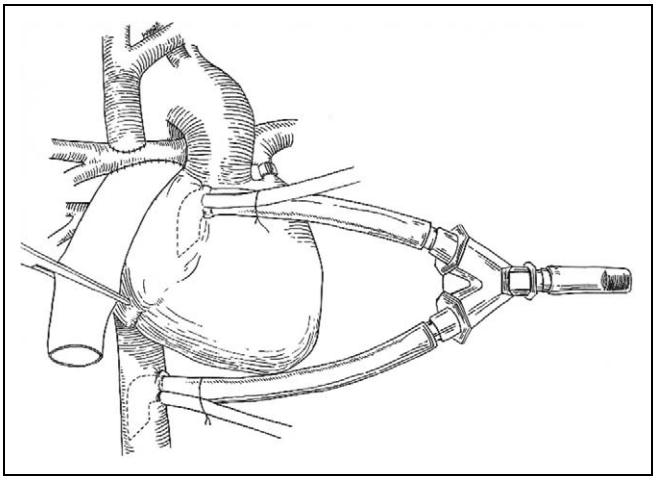

Figure 5. Illustration of the completed upper anastomosis. The clamp along the underside of the right pulmonary artery is removed and the Goretex graft deaired and clamped. A venovenous shunt is then constructed from the inferior vena cava to the systemic atrium. The two venous cannulas are deaired and connected together with a "Y" connector.

pressures are monitored, and the positioning of the clamp is guided by these pressures. The underside of the branch pulmonary artery is then incised. The anastomosis between the Goretex conduit and pulmonary artery is then performed (Figure 4). Following completion of the upper anastomosis, the clamp across the previously constructed cavopulmonary connection is removed, the conduit is deaired, and the conduit is then clamped in its mid-portion (Figure 5).

Attention is then turned to the inferior anastomosis. A venovenous shunt is constructed from the inferior vena cava to the systemic atrium in order to decompress the lower compartment (Figure 6). The inferior vena cava is clamped proximally and distally and then divided. The atrial side is oversewn with 4-0 Prolene. The Goretex conduit to inferior vena cava anastomosis is performed with 5-0 Prolene (Figure 7).

We currently perform approximately 90% of our bidirectional Glenn and Fontan procedures without the use of cardiopulmonary bypass.[15] Indications for a planned on-pump approach would include the need for a concomitant intracardiac procedure such as atrioventricular valve repair, repair of pulmonary vein stenosis, atrial septectomy, or enlargement of a bulboventricular foramen. The indications for an unplanned on-pump approach could include injury to a cardiac structure during redosternotomy and hemodynamic instability during the off-pump approach.

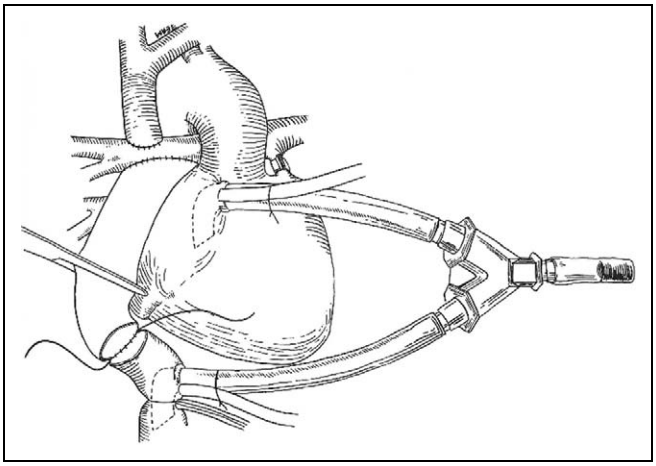

Figure 6. Illustration demonstrating construction of the lower anastomosis from the inferior vena cava (IVC) to the Goretex tube graft. The IVC is clamped and divided, and the atrial side oversewn with a running 3-0 Prolene. The cava to Goretex anastomosis is performed with 5-0 Prolene.

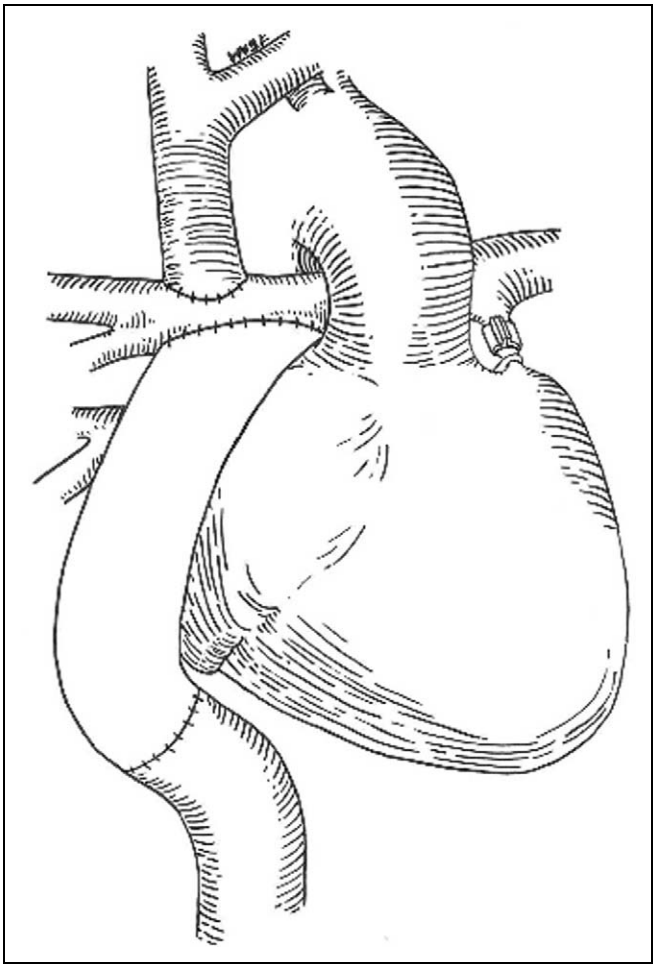

Figure 7. Illustration demonstrating the completed extra-cardiac Fontan. The venous cannulas have been removed and the heparin reversed with protamine.

Results

Of the 52 patients, 42 required a neonatal palliative (off-pump) procedure to regulate pulmonary blood flow. This included systemic to pulmonary artery shunts in 33 patients and pulmonary artery bands in nine patients.

All 52 patients underwent an off-pump bidirectional Glenn procedure at an average age of 6 $\pm$ 1 months (range 2-118 months). In all, 38patients had a single superior vena cava and 14 had bilateral superior vena cava. Concomitant procedures were performed in 44 of the 52 patients, including takedown of a systemic to pulmonary artery shunt (n = 30), tightening of a previously placed band (n = 6), ligation of the native right ventricular outflow tract (n = 4), and placement of a new pulmonary artery band (n = 4). Approximately half of the patients had some form of antegrade pulmonary blood flow left after completion of the bidirectional Glenn, with measurement of the pulmonary artery pressures to facilitate the regulation of this flow.

The 52 patients underwent their off-pump extracardiac Fontan procedure at an average age of 4.1 $\pm$ 1.3 years (range of 2.5-14.1 years). There was no operative mortality for the 52 patients undergoing completion of their Fontan. None of the patients had fenestration of their Fontan. Conduit size was 18 mm in 16 patients, 20 mm in 32 patients, 22 mm in 2 patients, and 24 mm in 2 patients. Of the 52 patients, 18 underwent concomitant procedures, including ligation of the main pulmonary artery (n = 15) and ligation of a shunt (n = 8).

Of the 52 patients, 28 were extubated on the day of surgery. Twenty patients were extubated on the first postoperative day, and the remaining four were extubated on the second postoperative day.

The average length of time until all chest tubes were removed was 4 $\pm$ 2 days. Eight patients subsequently required reinsertion of pleural drainage tubes. In these eight patients, the duration of secondary pleural drainage was 5 $\pm$ 2 days.

The median duration of hospitalization from the day of surgery to day of discharge was nine days, with an average of 14 $\pm$ 5 days and a range of 5 to 40 days. The median length of hospital stay for all three stages is shown in Figure 8.

There were six patients who were subsequently readmitted to the hospital. The underlying reason for readmission was pleural effusion in four patients, wound infection in one patient, and viral respiratory infection in one patient.

There has been one (2%) late death in this cohort of 52 patients. This patient developed progressive cardiac dysfunction and underwent a cardiac transplant. The patient subsequently experienced rejection with allograft failure and became a late mortality six years following Fontan procedure.

None of the patients in this study demonstrated any overt evidence of postoperative neurologic injury. Specifically, no patient demonstrated a neurologic deficit, clinical seizure, or unexpected delay in regaining consciousness.

Of the 52 patients, 42 were able to undergo all three stages of the Fontan without a blood transfusion. There were four patients who received a transfusion of packed red blood cells

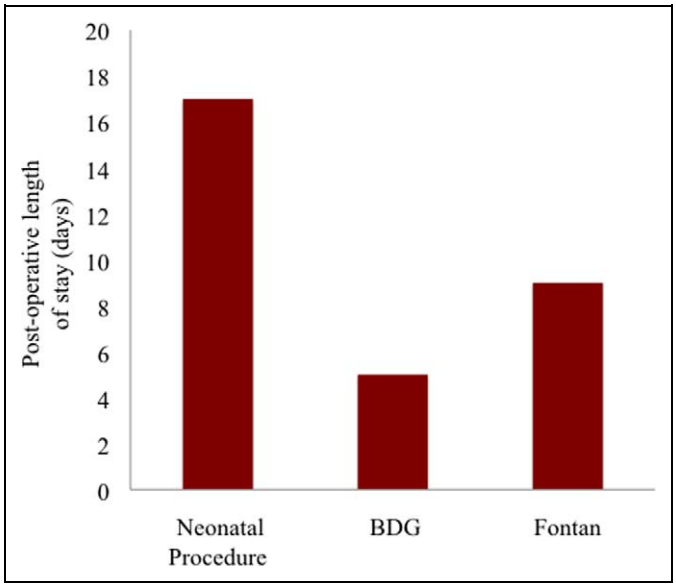

Figure 8. Bar graph demonstrating the median length of hospital stay for the three separate surgical stages.

(PRBCs) at the time of their initial palliative procedure. Five patients received PRBCs during the bidirectional Glenn procedure, and seven patients had a transfusion during the Fontan procedure. Six patients received a transfusion during two of their operations. Thus, 80% of cohort avoided blood transfusion at all three operations through the strategy of off-pump surgery.

Comment

This study demonstrates the feasibility of achieving completion of all three stages of the Fontan pathway without the use of cardiopulmonary bypass. To accomplish this, a number of specific features must be present. Specifically, the anatomy must be favorable so that the patients require only an off-pump palliative procedure as neonates (or no palliative procedure at all). In addition to these anatomic constraints, the patients must also receive their surgical care at an institution committed to performing the bidirectional Glenn and subsequent Fontan procedures without cardiopulmonary bypass. Thus, the number of patients and the number of institutions that could achieve a three-stage Fontan without cardiopulmonary is limited. We believe this is the first report describing the longitudinal care of patients across all three surgical stages leading to Fontan completion in whom cardiopulmonary bypass was avoided at each and every procedure.

McAmmond et al recently published a report from our institution summarizing a comparison of outcomes between patients undergoing Fontan with or without cardiopulmonary bypass.[16] This series included 73 patients who underwent Fontan surgery from 2001 to 2006. The results of this comparison were notable for nearly identical results in the two groups in most measures of outcome, including mortality, length of hospital stay, duration of effusions, and length of intensive care unit (ICU) stay. There was a significant difference noted with regard to intraoperative physiology, where the off-pump group had significantly lower Fontan pressures compared with the on-pump group. However, this difference in a key physiologic parameter had dissipated by the six-hour postoperative measurement point. The authors concluded that an off-pump Fontan had early physiologic advantages that were short lived and did not appear to confer a significant clinical advantage.

The 52 patients in the current study experienced no operative mortality and one late mortality. We also tracked a number of "surrogate markers" of outcome, including length of time on the ventilator, length of stay in the ICU, and length of stay in the hospital, all of which were reasonably comparable to previously published results for the on-pump Fontan. As in many previous series, the current study does not prove a superiority of the off-pump approach. However, the express purpose of this study was to demonstrate the feasibility of an entirely off-pump approach for a select group of patients with single ventricle. It would, in fact, be difficult to prove an advantage of an off-pump versus on-pump approach from a statistical standpoint, given the rarity of these adverse events in the modern era. To provide an example, if one assumed a mortality rate of 0% for an off-pump Fontan and a 3% mortality rate for on-pump Fontan, it would require 257 patients in each arm of the study (or a total of 514 total patients) to reach statistical significance. Many of the studies that have published on off-pump single ventricle surgery have probably been underpowered from a statistical basis, but it is likely that any difference in short-term measures of outcome will be unprovable based on the low incidence of adverse events.

One potentially significant finding of this study was that 80% of the patients were able to avoid exposure to PRBCs. This is a direct consequence of eliminating the cardiopulmonary bypass circuit, which usually requires the addition of blood in the prime solution to avoid hemodilution in pediatric patients. Nearly, all infants undergoing an on-pump bidirectional Glenn will require the addition of blood to the cardiopulmonary bypass circuit to avoid excessive hemodilution. The patients undergoing a Fontan completion are obviously older and larger than they were at the time of their bidirectional Glenn but may still require blood added to the pump. In the study by McAmmond comparing on- and off-pump Fontans, the patients who underwent an on-pump Fontan received a blood transfusion in the nearly all cases and received twice the total amount of blood products compared to the off-pump group.[16] There has been quite convincing evidence that exposure to blood is an independent risk factor for adverse outcome in adults.[17,18] In contrast, transfusion has historically not been considered to have the same adverse effects in pediatric cardiac surgery, and indeed, there was some evidence to suggest that on-pump anemia posed a greater risk than transfusion.[19] However, several recent publications have reevaluated the association between blood transfusion and outcomes in pediatric patients with cardiac disease. These studies found an association between blood transfusion and both increased length of time on the ventilator and increased duration of ICU stay

Table 1. Literature summary for circulating mediators.

Author	Reference	Year Published	Circulating Mediator
Mainwaring et al	24	1994	Renin/angiotensin
Mainwaring et al	25	1995	Renin/angiotensin
Mainwaring et al	26	1997	Thyroid hormone
Mainwaring et al	27	2000	Thyroid hormone
Mainwaring et al	28	1998	Complement/cytokine
Seghaye et al	29	1993	Complement
Tarnok et al	30	1999	Complement/cytokines
Kawahira et al	31	2006	Complement/cytokine

following congenital heart operations.[20,21] In addition, blood transfusion has been shown to increase infection rates and increase the incidence of allogeneic sensitivity.[22,23] The avoidance of blood transfusion through the off-pump approach may confer important advantages through the elimination of risks associated with transfusion.

There are numerous physiologic consequences induced by the use of cardiopulmonary bypass in the setting of a bidirectional Glenn and/or Fontan procedure. These effects can be divided into those measurable at a whole organism level and those measurable at a cellular level. Several examples of the physiologic changes that have been documented in patients with single ventricle include an increase in lung water, decrease in ventricular compliance, and immune suppression. The physiologic consequences at a cellular level are quite extensive,[24-31] as summarized in Table 1. These changes in circulating mediators would generally be thought to have adverse effects, and yet there has been little evidence to support the conjecture that these physiologic changes result in negative clinical effects. This dissociation between circulating mediators and outcomes is similar to the literature in adult patients undergoing off-pump coronary bypass surgery. Thus, although a host of physiologic changes occur following the use of cardiopulmonary bypass in patients with single ventricle, it is evident that the majority of these changes do not have a demonstrable influence on overall recovery.

Although studies have not demonstrated significant short-term benefits of an off-pump surgical approach, it is conceivable that there may be some late benefits. Specifically, longer term areas of concern for patients with single ventricle have been limitations in exercise capacity and neurologic performance, factors which play a critical role in determining quality of life. Numerous studies in adult patients have demonstrated better neurologic outcomes in patients undergoing off-pump versus on-pump coronary bypass surgery.[32] This facet of long-term outcome has not been studied to date in pediatric patients. In addition, many studies have demonstrated that patients undergoing multiple operations using cardiopulmonary bypass ($\pm$ cross-clamp and $\pm$ hypothermic circulatory arrest) are predisposed to late decreased systolic and diastolic function. Finally, it is possible that avoidance of blood transfusions through an off-pump approach will have late benefits for the reasons cited in the literature on this subject. In the future, it is our goal to implement a systematic program for testing exercise and neurologic performance in these patients to evaluate whether an off-pump approach does have late benefits in these areas.

In summary, this manuscript summarizes our experience with 52 patients who were able to complete all three stages of the Fontan pathway without ever being exposed to cardiopulmonary bypass. This is a descriptive report emphasizing the feasibility of employing this philosophy and the surgical techniques that are utilized. Whether this approach will translate into clinical benefits remains unproven, but we would speculate that avoidance of bypass and avoidance of blood transfusions will ultimately prove to have long-term benefits.

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Declaration of Conflicting Interests

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References

1. Anderson PA, Sleeper LA, Mahoney L, et al. Contemporary outcomes after the Fontan procedure. *J Am Coll Cardiol*. 2008;52(2): 85-98.
2. Said S, Burkhart HM, Dearani JA. The Fontan connections: past, present, and future. *World J Pediatr Congenit Heart Surg*. 2012; 3(2): 171-182.
3. Rogers LS, Glatz AC, Ravishankar C, et al. 18 years of the Fontan operation at a single institution. *J Am Coll Cardiol*. 2012;60(11): 1018-1025.
4. Jacobs ML, Pelletier GJ, Pourmoghadam KK, et al. Protocols associated with no mortality in 100 consecutive Fontan procedures. *Eur J Cardiothorac Surg*. 2008;33(4): 626-632.
5. Liu J, Lu Y, Chen H, Shi Z, Su Z, Ding W. Bidirectional Glenn procedure without cardiopulmonary bypass. *Ann Thorac Surg*. 2004;77(4): 1349-1352.
6. Luo XJ, Yan J, Wu QY, Yang KM, Xu JP, Liu YL. Clinical application of bidirectional Glenn shunt with off-pump technique. *Asian Cardiovasc Thorac Ann*. 2004;12(2): 103-106.
7. Hussain ST, Bhan A, Sapra S, Juneja R, Das S, Sharma S. The bidirectional cavopulmonary (Glenn) shunt without cardiopulmonary bypass: is it a safe option? *Interact Cardiovasc Thorac Surg*. 2007;6(1): 77-82.
8. LaPar DJ, Mery CM, Peeler BB, Kron IL, Gangemi JJ. Short and long-term outcomes for bidirectional Glenn procedure performed with and without cardiopulmonary bypass. *Ann Thorac Surg*. 2012;94(1): 164-171.
9. Tireli E, Ugurlucan M, Basaran M, et al. Extracardiac Fontan operation without cardiopulmonary bypass. *J Cardiovasc Surg (Torino)*. 2006;47(6): 699-704.

10. Shikata F, Yagihara T, Kagisaki K, et al. Does the off-pump Fontan procedure ameliorate the volume and duration of pleural and peritoneal effusions? *Eur J Cardiothorac Surg*. 2008;34(3): 570-575.
11. Tam VK, Miller BE, Murphy K. Modified Fontan without use of cardiopulmonary bypass. *Ann Thorac Surg*. 1999;68(5): 1698-1704.
12. Navabi MA, Rastegar SM, Kiani A, et al. Avoiding cardiopulmonary bypass in extracardiac cavopulmonary connection: does it really matter? *J Thorac Cardiovasc Surg*. 2010; 139(5): 1183-1188.
13. Shinkawa T, Anagnostopoulos PV, Johnson NC, et al. Early results of the "Clamp and Sew" Fontan procedure without the use of circulatory support. *Ann Thorac Surg*. 2011;91(5): 1453-1459.
14. McElhinney DB, Petrossian E, Reddy VM, Hanley FL. Extracardiac conduit Fontan procedure without cardiopulmonary bypass. *Ann Thorac Surg*. 1998;66(5): 1826-1828.
15. Petrossian E, Reddy VM, Collins KK, et al. The extracardiac conduit Fontan operation using minimal approach extracorporeal circulation: early and mid-term outcomes. *J Thorac Cardiovasc Surg*. 2006;132(5): 1054-1063.
16. McCammond AN, Kuo K, Parikh VN, et al. Early outcomes after extracardiac conduit Fontan with cardiopulmonary bypass. *Pediatr Cardiol*. 2012;33(7): 1078-1085.
17. Koch C, Li L, Figueroa P, Mihaljevic T, Stevensson L, Blackstone EH. Transfusion and pulmonary morbidity after cardiac surgery. *Ann Thorac Surg*. 2009;88(5): 453-459.
18. Paone G, Likosky DS, Brewer R, et al. Transfusion of 1 and 2 units of red blood cells is associated with increased morbidity and mortality. *Ann Thorac Surg*. 2014;97(1): 87-94.
19. Newburger JW, Jonas RA, Soul J, et al. Randomized trial of hematocrit 25% versus 35% during hypothermic cardiopulmonary bypass in infant heart surgery. *J Thorac Cardiovasc Surg*. 2008; 135(2): 347-354.
20. Redlin M, Kukucka M, Boettcher W, et al. Blood transfusion determines postoperative morbidity in pediatric cardiac surgery applying a comprehensive blood-sparing approach. *J Thorac Cardiovasc Surg*. 2013;146(3): 537-542.
21. Iyengar A, Scipione CN, Sheth P, et al. Association of complications with blood transfusions in pediatric cardiac surgery patients. *Ann Thorac Surg*. 2013;96(3): 910-916.
22. Szekely A, Cserep Z, Sapi E, et al. Risks and predictors of blood transfusion in pediatric patients undergoing open heart operations. *Ann Thorac Surg*. 2009;87(1): 187-197.
23. Salvin JW, Scheurer MA, Laussen PC, et al. Blood transfusion after pediatric cardiac surgery is associated with prolonged hospital stay. *Ann Thorac Surg*. 2011;91(1): 204-210.
24. Mainwaring RD, Lamberti JJ, Moore JW, Billman GF, Nelson JC. A comparison of the hormonal response following bidirectional Glenn and Fontan procedures. *Ann Thorac Surg*. 1994;57(1): 59-64.
25. Mainwaring RD, Lamberti JJ, Carter TL, Moore JW, Nelson JC. Renin, angiotensin II, and the development of effusions following bidirectional Glenn and Fontan procedures. *J Card Surg*. 1995; 10(2): 110-118.
26. Mainwaring RD, Lamberti JJ, Nelson JC, Billman GF, Carter TL, Schell K. Effects of Triiodothyronine supplementation following modified Fontan procedure. *Cardiol Young*. 1997;7(2): 194-200.
27. Mainwaring RD, Caparelli E, Schell K, Nelson JC. Pharmacokinetic evaluation of triiodothyronine supplementation following modified Fontan procedure. *Circulation*. 2000;101(12): 1423-1429.
28. Mainwaring RD, Lamberti JJ, Hugli TE. Complement activation and cytokine generation after modified Fontan procedure. *Ann Thorac Surg*. 1998;65(6): 1715-1720.
29. Seghaye MC, Duchateau J, Grabitz RG, et al Complement activation during cardiopulmonary bypass in infants and children: relation to postoperative multiple system organ failure. *J Thorac Cardiovasc Surg*. 1993;106(6): 978-987.
30. Tarnok A, Hambsch J, Emmrich F, et al. Complement activation, cytokines, and adhesion molecules in children undergoing cardiac surgery with or without cardiopulmonary bypass. *Pediatr Cardiol*. 1999;20(2): 113-125.
31. Kawahira Y, Uemura H, Yagahira T. Impact of the off-pump Fontan procedure on complement activation and cytokine generation. *Ann Thorac Surg*. 2006;81(2): 685-689.
32. Selke FW, DiMalo JM, Caplan LR, et al. Comparing on-pump and off-pump coronary artery bypass grafting. *Circulation*. 2005;111(21): 2858-2864.