Fontan procedure on deep hypothermic circulatory arrest: Short-term results and technique

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ABSTRACT

Background: Various operative strategies are described for the Fontan procedure. In this study, we describe our short-term results and technique of Fontan procedure on cardiopulmonary bypass (CPB) and deep hypothermic circulatory arrest (DHCA).

Methods: This was a retrospective study of 32 patients, median age of 6 years (4–19 years) and median weight of 20 kg (13–51 kg), who underwent Fontan procedure on CPB and DHCA from July 2016 to July 2021.

Results: The median CPB time was 125 min (77–186 min), the median DHCA time was 42 min (27–50 min), and the median Fontan pressure was 14 mmHg (10–18 mmHg). The median time to extubation was 4 h (1–20 h), the duration of chest tube drainage was 8 days (5–24 days), and the median intensive care unit stay was 4 days (3–8 days). The presence of heterotaxy was associated with longer duration of pleural drainage ($P = 0.01$). There was no operative mortality and no major adverse events such as seizures, gross neurological deficits, or arrhythmias in the postoperative period.

Conclusions: Fontan procedure can be safely performed on CPB and DHCA with good operative results. This operative strategy may be used in special circumstances like in patients with situs and systemic venous anomalies and those requiring repair of a complex intracardiac defect. Long-term follow-up will be required to evaluate if this strategy has any impact on the neurodevelopmental outcome and the long-term sequelae of Fontan.

Keywords: Deep hypothermic circulatory arrest, Fontan operation, heterotaxy

INTRODUCTION

Since the original description of the Fontan procedure for univentricular physiology,[1] numerous technical modifications, notably the lateral tunnel and the extracardiac conduit Fontan with a tube graft, have led to a continuous improvement in clinical outcome.[2-5] Over the course of four decades, different operative strategies have been described for the Fontan procedure: off-pump, i.e., without using cardiopulmonary bypass (CPB);[6-8] on-pump[9] with beating heart; on-pump with arrested...
heart; or on-pump with deep hypothermic circulatory arrest (DHCA). The aim of this study was to present our results with the Fontan procedure on CPB and DHCA. This was not a comparative study, and the aim was not to differentiate one technique from the other.

Numerous patient and procedure-related factors have been identified as high risk for perioperative mortality, which is in the range of 2%–7%. Some procedure-related factors incriminated in increased operative mortality are long CPB time and/or aortic cross-clamping prompting many surgeons to even avoid the use of CPB. While it may be possible in some select patients to do off-pump Fontan, it may not be so in those patients who need concomitant intracardiac procedures such as atrioventricular (AV) valve repair and atrial septectomy or those who have small branch pulmonary arteries (PA) or PA confluence narrowing requiring PA plasty or those who have separate hepatic venous drainage. The safety of DHCA has been proven in many studies, and we hope this study will further help in adding information to the existing knowledge of DHCA in this subset of patients.

**METHODS**

This was a retrospective study, and the informed consent for data collection was waived by the hospital’s ethics committee. The end points for this analysis were Fontan failure (Fontan takedown, death, or transplantation) within 30 days of surgery, duration of intensive care unit (ICU) stay, duration of pleural drainage, and readmission to the hospital within 30 days of discharge. Other morbidities such as neurological events (stroke, seizures, speech disturbances, or limb weakness), arrhythmias, and re-examinations were also documented.

From July 2016 to July 2021, 32 patients who underwent the Fontan procedure on CPB and DHCA at our hospital were included in this study. Nineteen of these were male (60%), the median age was 6 years (range: 4–19 years), and the median weight was 20 kg (range: 13–51 kg). Preoperative peripheral oximetry ranged from 70% to 90% (median saturation: 83%). The safety of DHCA has been proven in many studies, and we hope this study will further help in adding information to the existing knowledge of DHCA in this subset of patients.

**Table 1: Anatomic diagnosis of study subjects (n = 32)**

| Diagnosis                                      | n (%) |
|------------------------------------------------|-------|
| Congenitally corrected TGA                     | 8 (25) |
| Tricuspid atresia or single ventricle with single AV valve | 8 (25) |
| Complex DORV                                  | 6 (18.7) |
| Unbalanced CAVC                               | 6 (18.7) |
| Double inlet left ventricle                    | 2 (6.2)  |
| Complex d-TGA, VSD with PS                     | 2 (6.2)  |

**Operative technique**

Uniform operative strategy was adopted in all the patients. Standard anesthetic induction was performed with radial arterial and left femoral venous line. CPB was established with aortic and right atrial cannulation after redo-sternotomy and mediastinal dissection. Both surface and core cooling were used and sodium nitroprusside was used as a vasodilator to ensure uniform cooling keeping the gradient between nasopharyngeal and rectal temperatures below 3°C. Alpha stat pH strategy was followed and near-infrared spectroscopy (NIRS) was used in 18 patients to monitor cerebral oxymetry (rSO2) with INVOS™ 5100C Cerebral Oximeter (Somanetics, Medtronic, Minneapolis, MN, USA). Three readings were recorded: baseline – after induction, peak – before the beginning of DHCA, and nadir – at the end of DHCA.

During cooling, remaining dissection was performed and only aorta, right PA (RPA) with PA confluence, distal superior vena cava (SVC), and the inferior vena cava (IVC) were mobilized. Circumferential dissection around the SVC was avoided to prevent phrenic nerve injury. Appropriate size and length polytetrafluoroethylene (PTFE) tube graft (Gore-Tex, W. L. Gore and Assoc, Flagstaff, AZ) was selected. Its ends were beveled, and a 4-mm fenestration made with an aortic punch near its proximal end. Aortic cross-clamp was applied and antegrade del Nido cardioplegia (30 ml/kg) was delivered once the core temperature reached 20°C or if the heart fibrillated during cooling. If the antegrade flow was present, then the main PA was opened and the pulmonary valve was closed with 6-0 prolene.

Once the core temperature reached 18°C, pump flow was reduced and stopped, and venous cannula was removed. RA–IVC junction was transected and RA end was partially sutured with 5-0 prolene suture leaving an opening laterally, proximal end of the beveled PTFE graft was anastomosed to the IVC using 7-0 prolene continuous suture, and the RA opening was sutured around the fenestration, continuing with the same 5-0 prolene suture. RPA was incised longitudinally on the anterior surface and the incision was extended toward the PA confluence and then superiorly across the Glenn anastomosis over 8–10 mm into the distal end of SVC. Distal end of the beveled conduit was anastomosed to the RPA/SVC/PA confluence. Intra-atrial conduit Fontan was performed in a similar way except that right atriotomy was done and proximal anastomosis of the conduit to the IVC opening was done from within the RA and the right atriotomy was sutured around the tube graft leaving the fenestration inside the atrium followed by the distal anastomosis. RA
cannula was then repositioned and CPB and rewarming were started.

Rewarming was performed slowly with a temperature gradient of 6°C-10°C between Hemotherm and patient temperature. Alpha stat strategy was followed during rewarming and the aortic cross-clamp was released at 25°C. Once the core temperature reached 36°C, CPB was gradually weaned off and modified ultra-filtration was done for 15 min with the aim of increasing hemoglobin to 15 g/dl. Protamine was then administered, and decannulation and chest closure were performed.

Patients were shifted to the ICU on milrinone 0.5 mcg/kg/min and if required adrenaline 0.05 mcg/kg/min and exubated as early as possible. On postoperative day 1, inotrope weaning was begun, diuretics and aspirin (5 mg/kg) were started, and mediastinal drains were removed. Early mobilization was encouraged and pleural drains were removed when the drainage was <2 ml/kg/day.

**Statistical analysis**

Data are expressed as median with range and as mean ± standard deviation as appropriate. Independent variables analyzed included age, weight, duration of CPB, DHCA, Fontan circuit pressure, presence of fenestration, and pulse oximetry at discharge. Spearman correlation coefficient, Mann–Whitney U-test, and Fisher’s exact test were used as appropriate.

**RESULTS**

The tube graft was placed in an extra-cardiac position in 25 patients and as an intra-atrial conduit in 7 patients, size of the graft ranging from 18 to 22 mm (18 mm in 11, 20 mm in 16 and 22 mm in 5 patients). The median CPB time was 125 min (range: 77–186 min) and the median DHCA time was 42 min (range: 27–50 min) [Table 2]. Fontan circuit pressure was a median of 24 ± 10.72 mmHg (range: 50–3 mmHg) prior to the onset of DHCA, and rSO2 was 59.1 (range: 50–74), increased to a peak value of 88 (range: 82–95) prior to the onset of DHCA, and then decreased to a nadir value of 38.5 (range: 31–49) at the conclusion of DHCA.

Intra-atrial conduit Fontan was performed in 7 patients, 6 of whom had cardiac situs anomalies like dextrocardia or mesocardia which made conduit compression by the cardiac mass more likely in its usual extra-cardiac location. One patient had levocardia but with total anomalous pulmonary venous connection (TAPVC) and vertical vein on the right side which was left open and draining into the cardiac end of the SVC during the Glenn procedure. This patient underwent TAPVC repair with common chamber to common atrial anastomosis along with intra-atrial conduit Fontan with 20-mm PTFE tube graft and a 4-mm fenestration.

Concomitant intracardiac procedures performed included pulmonary valve closure in 24 patients, AV valve repair in 1 patient, and TAPVC repair in 1 patient. The median duration of mechanical ventilation was 4 h (range: 1–20 h), chest tube drainage was 8 days (range: 5–24 days), and the ICU stay was 4 days (range: 3–8 days). There was no operative mortality, and none of the patients required Fontan takedown or heart transplantation. There were no obvious gross neurological events such as seizures or limb weakness or speech or vision disturbances and no arrhythmias in the postoperative period. Twenty-five of the 32 patients (78%) had a patent fenestration at the time of discharge home with a mean peripheral saturation of 93.3% ± 2.0%. Those with a closed fenestration had a mean saturation of 96.7% ± 1.1% (P < 0.01). The discharge echocardiogram showed low velocity, continuous phasic flow in the Fontan circuit, and normal ventricular function in all the patients.

The duration of pleural drainage was significantly higher in patients with heterotaxy than those without [Table 3]. Moderate positive correlation (Spearman correlation coefficient) was seen between weight (r = 0.43), age at operation (r = 0.43), and duration of mechanical ventilation (r = 0.38) with duration of pleural drainage. The duration of DHCA, CPB, and Fontan circuit pressure had no correlation with either duration of pleural drainage or ICU stay. The presence of fenestration showed a moderate correlation (not statistically significant) with duration of pleural drainage. Patients with patent fenestration tended to have shorter duration of pleural drainage (P = 0.09).

One patient with permanent epicardial pacemaker before Fontan procedure continued with his previous

| Table 2: Intra- and perioperative data |
|--------------------------------------|
| **Median** | **Minimum** | **Maximum** |
| CPB (min)  | 125 | 77 | 186 |
| DHCA (min) | 42 | 27 | 50 |
| Mechanical ventilation (h) | 4 | 1 | 20 |
| Fontan circuit pressure (mmHg) | 14 | 10 | 18 |
| Pleural drainage (days) | 8 | 5 | 24 |
| Saturation on room air (%) | 94 | 90 | 98 |
| ICU stay (days) | 4 | 3 | 8 |
| Baseline rSO2 on NIRS | 59.1 | 50 | 74 |
| Peak rSO2 on NIRS | 88 | 82 | 95 |
| Nadir rSO2 on NIRS | 38.5 | 31 | 49 |

**Table 3: Association of heterotaxy syndrome with duration of pleural drainage and intensive care unit stay**

|                     | **Heterotaxy** | **P** |
|---------------------|----------------|-------|
| **Absent**          |                |       |
| Duration of pleural drainage (days) | 6.86±2.25 | 0.01 |
| ICU stay (days)     | 3.57±0.64 | 0.09 |
| **Present**         |                |       |
| Duration of pleural drainage (days) | 10.72±4.68 | <0.01 |
| ICU stay (days)     | 4.50±1.54 | 0.09 |

ICU: Intensive care unit
pacemaker settings and apparatus, while the remaining patients maintained sinus rhythm postoperatively. One patient was re-explored for mediastinal bleeding (within 6 h of surgery). There was no incidence of phrenic nerve paralysis or chylothorax, and no patient exhibited postoperative hepatic or renal insufficiency that required additional monitoring or medications or dialysis.

In the follow-up period (range: 6–60 months; median: 19 months), all patients are well and are in New York Heart Association functional Class I, except for one 15-year-old patient who had a high-risk intra-atrial conduit Fontan with TAPVC repair. He was readmitted 10 days after discharge with bilateral pleural effusions and underwent bilateral pleural drain placement followed by tetracycline pleurodesis. Diaphragmatic fenestration was performed after 4 days as effusions were persistent; the drains subsided 10 days later and were removed. None of the patients had any obvious gross neurological deficit/seizures or a change in behavior or deterioration in scholastic performance in this follow-up period. A formal neurological assessment was not done.

DISCUSSION

The Fontan procedure has undergone tremendous evolution since its inception in the 1970s and has now become the standard of care for children with single ventricle physiology as satisfactory long-term results are available. Our institutional preference is toward an extracardiac conduit Fontan when the patient is at least 3 years old or has a body weight of at least 15 kg. The extra-cardiac conduit Fontan procedure maximizes laminar blood flow, reduces atrial wall tension, and avoids intra-atrial suture lines.[16,17]

Planning and staging of the Fontan procedure is important in reducing the operative mortality.[18] Events associated with increased operative mortality include stroke or thromboembolism[19,20] and ventricular dysfunction,[21] while patient-related factors include right ventricle (RV) morphology,[22] heterotaxy syndrome,[23] pulmonary atresia with RV dependent coronary circulation,[24] and history of pacemaker dependence. Stroke or thromboembolism was not seen in any of our patients, and all were maintained on a single antithrombotic agent, aspirin, which was started on postoperative day 1. No heparin or oral anticoagulants were prescribed, even for patients with intra-atrial conduit Fontan. Heterotaxy was common in our study group, and it had a significant association with increased duration of pleural drainage and longer ICU stay. We routinely make a 4-mm fenestration in the conduit and did not experience any complication due to it, besides all patients had saturation more than 92% at the time of discharge, with seven patients demonstrating spontaneous closure of the fenestration. If we exclude the 15-year-old high-risk patient who had prolonged chest tube drainage, then patency of fenestration was found to have significant association with shorter duration of pleural drainage.

In Fontan on DHCA, by avoiding direct cannulation of SVC and the IVC, there is a reduced risk of local site thrombus formation; by avoiding looping and snaring of the VC, there is a reduced risk of phrenic nerve injury. Patients with hemi-diaphragmatic paralysis have a significantly higher Fontan pressure, longer duration of chest tube drainage, and a greater likelihood of readmission for related issues.[25] Further, PA confluence narrowing or constriction at the Glenn anastomosis (old suture line) can be relieved by doing Fontan on DHCA as the RPA, PA confluence, and the distal SVC across Glenn anastomosis are opened up and the widest possible anastomosis achieved without any clamp in situ. Off-pump Fontan is not suitable for patients with small branch PAs, abnormal IVC, and hepatic venous drainage and those with intracardiac defects.

There are concerns that hypothermia causes an increase in the pulmonary vascular resistance (PVR) and coagulopathy, which may not be suitable for Fontan physiology. Both the increased PVR and the coagulopathy get reversed once the temperature returns to normal. As seen in our study, all patients had Fontan circuit pressure between 10 and 18 mmHg, which was within the acceptable range, and only one patient required re-exploration for bleeding. All patients were extubated within 24 h of surgery, and none of the patients required re-intubation.

There is a concern regarding the impact of DHCA on long-term neurodevelopmental outcomes. During DHCA, on the one hand, there is cell death due to lactate released from anaerobic glycolysis and glutamate released due to hypoxia, while on the other hand, there is cerebral protection by reduction in the rate of cerebral metabolism; at 18°C, the basal metabolic rate is 12%–25% of normal. In the Boston Circulatory Arrest Trial,[26,27] early results showed that the circulatory arrest (TCA) group had more neurological damage than the low-flow bypass (LF-CPB) group. However, Long-term results at 8-year follow-up,[28] showed that the primary end points of intelligence quotient and overall neurological status was similar in both groups, while the entire cohort, regardless of TCA or LF-CPB support, performed below the general population. It is a well-known fact that maximal human brain development occurs during gestation and in the first 2 years of life.[29,30] Briefly, neurogenesis peaks at 21-week gestational age (GA), cortical plate differentiation peaks at 22–28-week GA, myelination occurs between 20-week GA and 2 years of age, synaptogenesis occurs between 22- and 47-week GAs, and synaptic pruning continues from 2 years.
forward to adolescence. It seems logical, therefore, to assume that the maximum vulnerability of the brain is \textit{in utero} to 2 years of age, and if the DHCA is performed at a median age of 6 years (our series), there may be less of an impact on the neurodevelopmental outcome. Other patient factors such as birth weight, preoperative mechanical ventilation, and socioeconomic status are more important predictors of neurodevelopmental outcomes than the use of DHCA.\textsuperscript{[31]}

The baseline and the peak \textit{rSO}_2 values on NIRS were in the acceptable range.\textsuperscript{[32]} but there was greater fall in nadir \textit{rSO}_2 at the end of DHCA, the lowest value of 31 and a median of 38.5. Even with these low values, there were no clinically discernible neurological deficits, possibly due to much older patient cohort with more cerebral maturity.

\textbf{Limitation}

The retrospective nature of the study and the limited number of patients are the main drawbacks of the study. Lack of long-term follow-up is also a major drawback. Possible neurodevelopmental sequelae of DHCA need to be studied by formal testing of the patients.

\textbf{CONCLUSIONS}

Fontan procedure on CPB and DHCA is a safe and effective operative strategy for achieving total cavopulmonary connection and may be considered in certain complex anatomies. Benefits include a bloodless operative field, secure myocardial protection, simultaneous intracardiac repair, lesser incidence of phrenic nerve injury, prevention of nidus and clot formation in major systemic veins, and acceptable mortality and morbidity. This operative strategy can be used in special circumstances like in patients with situs and systemic venous anomalies, those requiring intra-atrial conduit Fontan, and those requiring repair of complex intracardiac defect like TAPVC, common AV valve regurgitation, etc. Long-term follow-up will be required to evaluate if this strategy has any impact on the neurodevelopmental outcome and the long-term sequelae of Fontan.

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\textbf{Conflicts of interest}

There are no conflicts of interest.

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