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Experimentally modified Fontan circulation in an adolescent pig model without the use of cardiopulmonary bypass

Authors' Contribution:

- A** Study Design
- B** Data Collection
- C** Statistical Analysis
- D** Data Interpretation
- E** Manuscript Preparation
- F** Literature Search
- G** Funds Collection

Meletios A. Kanakis^{1A,B,D,E,F}, Fotios A. Mitropoulos^{2A,D,G}, Michalis Katsimpoulas^{3B,C,E},
Constantinos Dimitriou^{3B,G}, Michalis Peroulis^{3B,D}, Nikolaos Kostomitsopoulos^{3B,D},
Achilleas Lioulis^{1D,E,G}, Alkiviadis Kostakis^{3D,G}

¹ Department of Thoracic Surgery, Sismanoglio General Hospital, Athens, Greece

² Department of Pediatric and Congenital Heart Surgery, Onassis Cardiac Surgery Center, Athens, Greece

³ Center for Experimental Surgery, Biomedical Research Foundation of the Academy of Athens, Athens, Greece

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Summary

Background:

The feasibility and the hemodynamic outcome of Fontan circulation, without the use of cardiopulmonary bypass, were studied on a beating heart of an adolescent pig model, using a modified total cavopulmonary connection.

Material/Methods:

Eight open-chest anesthetized pigs underwent a successful total cavopulmonary connection with the use of an appropriate Y-shaped Dacron-type conduit. Through a median sternotomy, the distal part of the superior vena cava was anastomosed end-to-end to one side of the conduit. The other side of the graft was anastomosed end-to-side to the main pulmonary artery. The conduit was tailored to an appropriate length and anastomosed end-to-end to the inferior vena cava. The hemodynamic status of the animals was recorded before and after the establishment of the total cavopulmonary connection.

Results:

Forty-five minutes after completion of total cavopulmonary connection, and for a total of 1 hour, hemodynamic measurements showed a decrease in mean arterial and mean pulmonary artery pressures, heart rate and cardiac output. The inferior vena caval pressure and total pulmonary vascular resistance were increased.

Conclusions:

A total cavopulmonary connection, performed on a beating heart, without extracorporeal circulation or other means of temporary bypass, although it is technically demanding, is feasible.

Key words:

Experimental Fontan operation • total cavopulmonary connection • beating heart surgery • extracorporeal circulation • bypass • congenital heart disease

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Author's address:

Meletios A. Kanakis, Department of Thoracic Surgery, Sismanoglio General Hospital, Athens, Greece,
e-mail: meletis_kanakis@yahoo.gr

BACKGROUND

During the past 4 decades, the Fontan operation has been performed for the surgical treatment of children with congenital heart disease in which repair into a 2-ventricle system was impossible [1].

The Fontan operation can be performed by a number of variants. Currently, the most acceptable methods are the extracardiac conduit and the lateral tunnel total cavopulmonary connection techniques, both being accepted for their hemodynamic supremacy [2–4].

The ideal age at which a patient should undergo a Fontan operation remains controversial; however, the best post-surgical results were achieved when the operation was performed from the age of 7 months, where the increased cyanosis and the deterioration of the hemodynamic parameters rendered the operation absolutely necessary [5].

Today, over 40 years since the first use of the Fontan operation [1], the perioperative mortality has decreased significantly, and is stabilized at around 5% [6]. Factors contributing to the improvement of survival from the surgical procedure include the more energy efficient circulation obtained after the application of total cavopulmonary connection techniques [2]. Moreover, the limited duration of cross-clamping of the aortic root, and the decrease in the use of extracorporeal circulation, have both contributed to the better surgical outcome. Mair et al. reported an increase in survival over the “surgical era”, with the most recent patient cohort having improved survival and decreased perioperative mortality compared to those patients in the 2 prior decades. The survival rates 5, 10 and 15 years after surgery have increased, and are 86%, 81% and 73%, respectively [7]. An important finding, from the socioeconomic aspect, is that many of those patients with a Fontan operation had, and continue to enjoy, a long and high quality of life [4,8].

The establishment of the Fontan circulation in an adolescent pig experimental model is extremely difficult, a fact ultimately supported by the very few experimental studies reported in the English literature [9–16]. The present study tested the feasibility of performing the Fontan operation on an animal model, using a modified technique of an extracardiac total cavopulmonary connection (TCPC), without the support of cardiopulmonary bypass or other means of temporary bypass during the performance of the anastomoses. Furthermore, we evaluated acute hemodynamic changes for a period of 1 hour after the completion of the surgical procedure, and its effects on the cardiovascular system when the pulmonary blood flow is switched from normal circulation to Fontan circulation.

MATERIAL AND METHODS

Eight anesthetized Landrace x Large White male pigs with a mean body weight of 43 ± 3.8 kg and aged 4.5 months were used for the study. All animals received humane animal care in compliance with the European Directive 86/609 of the European Council and the Presidential Decree 160/91 of the relevant Greek Legal Framework. The protocol was approved by the Ethics Committee of the Biomedical Research Foundation (Permission Number A.03.1/5/10-05). All

animals underwent a 5-day quarantine and acclimatization period in the animal house of the Center for Experimental Surgery prior to placement in the study. The day before surgery, physical examination and pre-anesthetic blood work were performed in all animals. Food was withheld from pigs for 12 hours prior to the induction of anesthesia, and body weight was obtained before surgery to facilitate the drug dosage calculation.

Each animal was pre-medicated with an IM injection of ketamine (10 mg/kg, Imalgem, Merial), atropine (0.04 mg/kg, Atropine, Demo) and midazolam (0.4 mg/kg, Dormicum, Roche). An IV catheter was placed and secured in the auricular vein for drug and fluid administration. Anesthesia was induced with an IV injection of 0.9 mg/kg of propofol (Diprivan 1% w/v, Astra Zeneca). The animal was intubated and attached to a veterinary anesthesia machine (MDS Matrix, Model 2000, USA). Thereafter, anesthesia was maintained by a closed circuit system, with inhalation of a mixture of 3–5% sevoflurane (Sevorane, Abbott) and oxygen at a rate of 12–15 breaths/min. An anesthesia monitoring record, every 15 minutes, was maintained for the duration of the procedure and for 1 hour post-surgery, including heart rate, respiration and arterial blood pressure, initially with a non-invasive technique and subsequently through an arterial line. Body temperature, end-tidal carbon dioxide, peripheral oxygen saturation, inhalation anesthetic level, tidal volume, and ventilator pressure were also recorded for the entire period of the study. The Passport 2 (Datascope Corp., USA) and the LSI-8R LifeSense (MedAir, Sweden) monitors were used to obtain and record all data. Physical methods were also used to monitor the animals during surgery, including assessment of eye reflexes, muscle tone, peripheral pulses, capillary refill time and mucous membrane color.

Animals were placed in the supine position, and the right common carotid artery and the jugular vein were dissected through a small incision. A Millar catheter (SPR-524; Millar Instruments, USA) was introduced to the carotid artery, and connected to a digital acquisition system (Sonometrics System, Sonometrics Co., Canada) for the continuous recording of arterial pressure.

Through appropriate skin incisions, both femoral veins were recognized and dissected. Catheters 10F (Avanti +, Cordis, USA) were inserted to the jugular and in one of the femoral veins for the rapid administration of crystalloid and colloid fluids, when needed. A Millar catheter was inserted through the contralateral femoral vein and connected to a digital acquisition system for the continuous monitoring of pressure in the inferior vena cava. Through a median sternotomy, the superior (SVC) and the inferior vena cava (IVC), the azygos vein, the ascending aorta (AO) and the main pulmonary artery (PA) were carefully dissected.

An ultrasound flow probe (20 PAX, TS420; Transonic Systems, USA) was placed around the ascending aorta for the continuous monitoring of cardiac output. Millar catheters were placed into the left atrium, the right ventricle and the pulmonary artery for pressure measurements. Electrocardiogram and all hemodynamic parameters, including phasic aortic flow signals, systolic, diastolic and mean arterial and pulmonary pressures, mean inferior vena cava

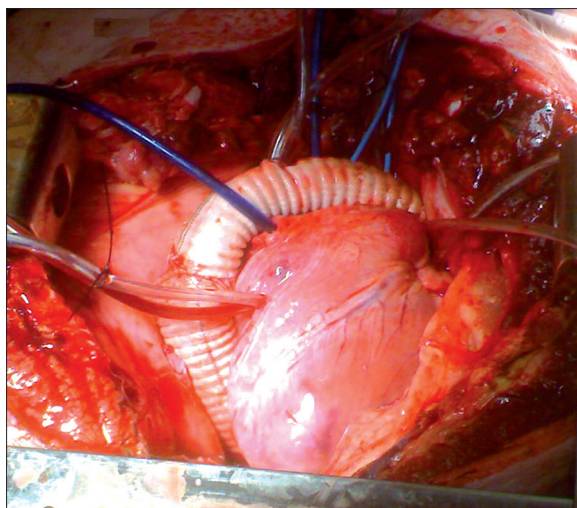


Figure 1. Intraoperative photo depicting the TCPC.

pressure, mean left atrium pressure, cardiac output and heart rate, were recorded.

An IV bolus of heparin (100 IU/kg) was given before the SVC was divided between 2 vascular clamps, and the cardiac end was oversewn using a continuous 5-0 polypropylene suture (Prolene; Ethicon, USA). The other portion of the SVC was anastomosed end-to-end to one of the upper sides of a Y-shaped Dacron type conduit with a 16mm diameter (Edwards Lifesciences, Switzerland) using a continuous 6-0 polypropylene suture. During this phase of the surgical procedure, animals were transfused through a femoral venous catheter with crystalloid and colloid fluids to retain normal arterial pressure. However, 3 of the animals needed inotropic support with dobutamine (2 µg/kg/min) due to hemodynamic instability. Inotropic support was discontinued after the completion of the anastomosis. The other upper side of the Y-shaped conduit was anastomosed end-to-side with the main pulmonary artery, using a continuous 6-0 polypropylene suture.

The IVC was recognized and the conduit was tailored to an appropriate length in order to be ready for end-to-end anastomosis. A suction device was used to raise the apex in order to more easily manipulate the IVC [17]. The vessel was then divided between 2 clamps and the distal end was anastomosed to the graft with a continuous 6-0 polypropylene suture. The proximal side of the vessel was oversewn, using a continuous 5-0 polypropylene suture. Animals were again supported by infusion of crystalloid and colloid fluids through the jugular venous catheter, while the 3 previously mentioned animals again needed inotropic support, which was discontinued after the completion of the anastomosis. The proximal remnant of the inferior vena cava, on the right atrium, was oversewn with the use of continuous 6-0 polypropylene suture, while the pulmonary artery trunk was ligated proximally to its anastomotic site with the graft. On performing all anastomoses, careful de-airing precautions were taken to avoid air embolism. A 12F diameter and 30 cm long vent-tube was introduced into the right ventricle, primarily to collect the coronary venous blood, which was directed into the pulmonary flow of the graft by use of a small roller pump, preventing the influence of

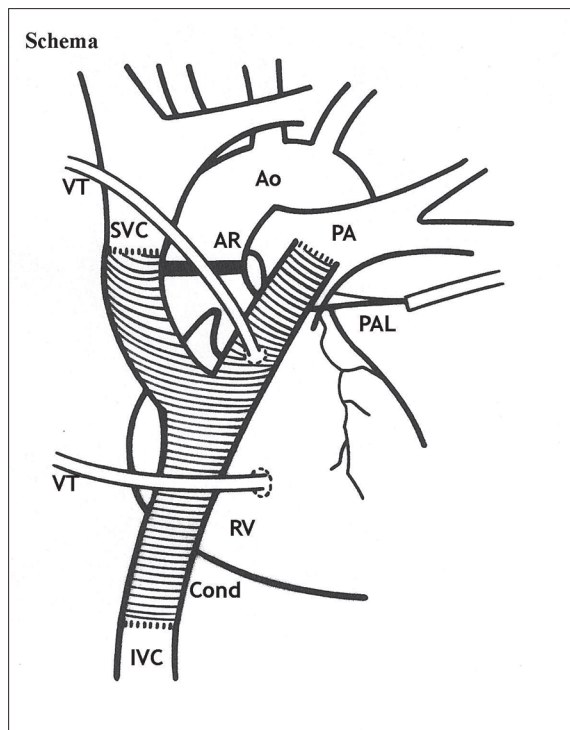


Figure 2. Schematic representation of the experimental design. (Ao: Aorta, PA: Pulmonary artery, SVC: Superior Vena Cava, IVC: Inferior Vena Cava, RV: Right Ventricle, VT: Vent tube, Cond: Conduit, PAL: PA ligation, AR: Aortic ring for cardiac output measurement).

right ventricular contractility on the left ventricular contractility (Figures 1, 2).

Hemodynamic measurements were performed 45 minutes after completion of total cavopulmonary connection, and for a total of 1 hour. Animals were in a steady hemodynamic status without the support of inotropic drugs or fluids, and were kept warm at 37°C. The mean time required for the establishment of the Fontan circulation was 38°C 17 min and the mean blood loss was 115±48 ml (volume accumulated in the suction device), while the total amount of crystalloid and colloid infused was about 2.500–3.000ml. Upon study completion, animals were euthanized with a bolus dose of sodium pentobarbital (Dolethal, Vetoquinol). A thorough autopsy of the great vessels and all cardiac cavities did not reveal the presence of clots.

Statistical analysis

All hemodynamic data were processed by SPSS 10 (IBM Co, U.S.A.) and expressed as mean ±SD. Results were evaluated using a paired Student t test, and differences of all recorded data before and after the Fontan circulation were considered to be significant at the level of $p < 0.05$.

RESULTS

The entire procedure was performed with a beating heart, without the use of extracorporeal circulation support. All animals tolerated the procedure well, although during the surgical establishment of total cavopulmonary connection

Table 1. Mean values of hemodynamic parameters at the baseline and after the Fontan circulation. All values are given as means \pm SE, (* $p < 0.05$).

Parameters	Baseline	Fontan circulation
HR(bpm)	90.81 \pm 3.61	71.61 \pm 2.67*
MAP(mmHg)	43.30 \pm 2.07	27.83 \pm 1.28*
IVCP(mmHg)	13.13 \pm 1.37	25.83 \pm 1.64*
LAP(mmHg)	5.32 \pm 0.69	4.28 \pm 0.40
PAP(mmHg)	18.28 \pm 0.52	10.68 \pm 0.90*
CO(lt/min)	3.24 \pm 0.28	1.29 \pm 0.13*
PVR(Wood's units)	3.56 \pm 0.25	6.22 \pm 0.70*
SVR(Wood's units)	11.62 \pm 0.86	16.56 \pm 1.68

3 of them needed inotropic support. The end-to-side anastomosis of the graft to the pulmonary trunk was performed uneventfully, while the end-to-end anastomosis of the inferior vena cava to the graft was the most difficult part of the experiment. Hemodynamic stability was sustained after the establishment of total cavopulmonary connection. All recorded hemodynamic data before and after Fontan circulation are presented in Table 1.

Heart rate at the control period was 90.81 \pm 3.61 bpm. During the 1-hour follow-up period after the establishment of the Fontan circulation, heart rate was 71.61 \pm 2.67 ($p < 0.05$). Sinus rhythm was sustained throughout the procedure in all animals.

Mean arterial pressure was 43.3 \pm 2.07 mmHg at the control period, and during the 1-hour follow-up period after the establishment of the Fontan circulation dropped to 27.83 \pm 1.28 mmHg ($p < 0.05$).

Mean inferior vena cava pressure at the control period was 13.13 \pm 1.37 mmHg, and increased to 25.83 \pm 1.64 mmHg ($p < 0.05$) during the 1-hour follow-up period after the establishment of the Fontan circulation.

Mean left atrial pressure. There is no significant difference in the LA pressure between measurements taken at the baseline (5.32 \pm 0.69 mmHg) and after Fontan circulation (4.28 \pm 0.40).

Mean pulmonary arterial pressure at the control period was 18.28 \pm 0.52 mmHg. During the 1-hour follow-up period after the establishment of the Fontan circulation, mean pulmonary arterial pressure was 10.68 \pm 0.90 mmHg ($p < 0.05$).

Right ventricular pressure: The right ventricle was decompressed with the pre-mentioned technique, and RVP was maintained at 20.56 \pm 0.84 mmHg throughout the procedure.

Cardiac output at the control period was 3.24 \pm 0.28 lt/min. During the 1-hour follow-up period after the establishment of the Fontan circulation, cardiac output dropped to 1.29 \pm 0.13 lt/min ($p < 0.05$).

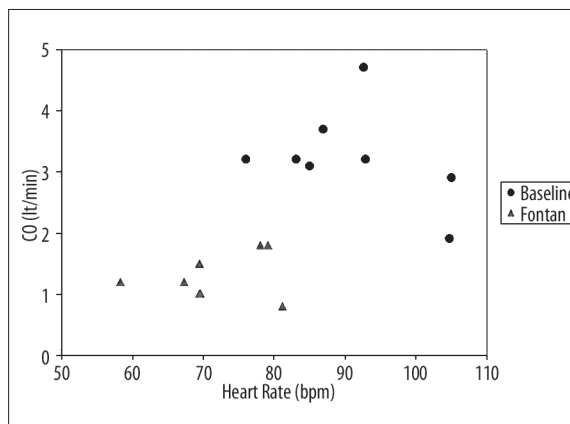


Figure 3. Cardiac output and heart rate correlation before and after the establishment of Fontan circulation were expressed on orthogonal coordinate system, in order to examine if there is a linear relation between the decrease of heart rate and cardiac output. No linear relation was found between these parameters.

Cardiac output and heart rate correlation before and after the establishment of Fontan circulation

Although heart rate sustained at sinus rhythm, it dropped significantly after the completion of Fontan circulation. In addition, cardiac output decreased significantly after the establishment of Fontan circulation. The above results were expressed on an orthogonal coordinate system in order to determine if there was a linear relation between the decrease of heart rate and cardiac output. No linear relation was found between these parameters (Figure 3).

Pulmonary vascular resistance was calculated as: $PVR = (PAP - LAP) / CO$. It was increased significantly from 3.56 \pm 0.25 Wood's units at the control stage to 6.22 \pm 0.70 Wood's units when Fontan circulation was established ($p < 0.05$).

Systemic vascular resistance was calculated as: $SVR = (MAP - RAP) / CO$, where RAP is the right atrial pressure. In the Fontan circulation, RAP was substituted by pulmonary arterial pressure. No significant changes were noticed in the SVR between the baseline and after the Fontan circulation (11.62 \pm 0.86 Wood's units vs. 16.56 \pm 1.68 Wood's units, respectively).

DISCUSSION

The experimental establishment of a total cavopulmonary connection, modified by the interposition of an artificial graft between the 2 vena cavae (end-to-end anastomosis) and the pulmonary artery (end-to-side anastomosis), on a beating heart without the use of extracorporeal circulation, has never before been described in the literature. Experimental data from the present study prove that although this procedure is demanding for an experienced cardiovascular surgeon, it is, however, feasible.

Haller et al. first described an experimental right heart bypass [9]. Years later, other investigators attempted to perform experimental Fontan circulation in animal models [10,11]. After the establishment of total cavopulmonary

connection with the use of an extracardiac conduit (2), new experimental studies were conducted using modifications of this method [12,13]. Several investigators have successfully established the Fontan circulation without the use of extracorporeal circulation [13–16].

Nawa et al. constructed a Y-shaped artificial conduit, with the end-to-side anastomosis of 2 separate conduits. They inserted and advanced the upper and lower ends of the conduit to the superior and inferior caval veins, respectively, performing only 1 end-to-side anastomosis of the other upper end of the conduit to the pulmonary trunk [13]. Kaku et al. performed end-to-side anastomosis of the graft to the caval veins using Satinsky vascular clamps [14]. Haneda et al. interposed an artificial conduit between the right atrium and the main pulmonary artery. Under temporary clamping of the caval veins, they placed a purse-string suture around the tricuspid annulus, which was driven out through the right atrium via a tourniquet. With this technique it was possible to alter volume flow characteristics of the Fontan circulation repeatedly by changing the degree of tricuspid valve stenosis every time [15]. Szabo et al. managed to introduce 2 polyethylene cannulas into the superior and inferior caval veins, and a third one into the distal main pulmonary artery [16].

In the present experimental study, the cavopulmonary bypass was achieved based on the experience gained from the extensive use of the extracardiac conduit techniques, mainly in the Fontan operation [2]. This technique takes into consideration the rheometry of blood in this particular anatomic area. The diameters of the conduits were similar to those of the superior and the inferior vena cavae [18]. Furthermore, with this technique anastomoses were performed by suturing the graft to the caval veins, rather than inserting the graft intraluminally [13,16]. Although a number of difficulties arose with this technique, its ability to maintain a higher volume of blood flowing from the caval veins to the pulmonary artery is a clear advantage. The size of the anastomotic area between the pulmonary artery and the graft was large enough not to interfere with blood volume flow.

The success of this surgical procedure entirely depends on the experience of the surgeon, with the most critical part of the experiment being the anastomosis of the graft to the inferior vena cava. During that period of time, the animals presented with severe hemodynamic instability. Some degree of hemodynamic compromise developed, also, during the anastomosis of the graft to the superior vena cava. To support the animals during these parts of the procedure, crystalloid and colloid fluids were infused, and 3 animals needed inotropic support. Once the anastomoses were completed and the right ventricle was decompressed, the animals were considered to be hemodynamically stable. From our pilot studies we concluded that decompression was imperative for the animals to survive.

The hemodynamic changes after the completion of the surgical procedure were significant. With the establishment of Fontan circulation, and through the 1-hour observation period, significant decreases in mean arterial pressure, mean pulmonary pressure, cardiac output, and heart rate were observed. In addition, a significant increase was noticed in

pulmonary resistance and in inferior caval pressure, with only borderline changes in left atrial pressure and systemic vascular resistance.

The recorded hemodynamic parameters confirmed the Fontan paradox; thus, the existence of venous hypertension coexists with hypotension in the pulmonary artery [4]. It must be emphasized that the experimental model described by the aforementioned parameters was hemodynamically stable and free from inotropic support. Furthermore, although the heart rate in the Fontan state decreased significantly, it remained in sinus rhythm.

The pressure in the inferior vena cava was considerably increased, which is in accordance with findings by Nawa et al. [13]. The surgical protocol applied by Haneda et al. [15] allowed pressure measurement in the right atrium, which correlated well with the central venous pressure. Left atrial pressure, in the present study, showed a mild, non-significant decrease, in agreement with the experimental results of Haneda et al. [15]. Nawa et al. and de Leval showed that left atrial pressure originally had a tendency to increase, then decrease, and finally return to a normal level [4,13,16,19]. Cardiac output, as was found in previous studies, displayed a significant decrease in all cases [12,13,15,16].

Systemic arterial resistance in our study demonstrated a relative increase, which was nearly statistically significant. Szabo et al. and Mace et al. found an increase in systemic arterial pressure, as well as in total vascular resistance [12,16], in contrast to data from Haneda et al., where the systemic vascular resistance presented a non-significant decrease [15]. An important finding in our study was the increased pulmonary resistance, which is in accordance with the results of Haneda et al. and Szabo et al. [15,16].

Hypoperfusion in the pulmonary capillary vasculature is responsible for the pulmonary hypertension, and consequently for the increased pulmonary vascular resistance, according to Haneda et al. De Leval considers these findings impressive, and questions whether patients having undergone a Fontan operation should be treated with medication to control pulmonary resistance [16]. In addition, the creation of a fenestration (a technique allowing systemic venous blood to shunt to the left atrium) seems to improve the preload, and indirectly assist with the above problem.

Due to the complex requirement for single-ventricle cardiac anatomy, a chronic animal model of unsupported Fontan physiology has never been produced. Myers et al. managed to achieve 24-hour stability by maintaining pulmonary perfusion and low systemic venous pressure by the use of a device in an animal model [20]. We believe that a modification in the cardiac anatomy of a swine model may permit the creation of a chronic Fontan circulation pattern. Moreover, the fenestration technique may be applied and hemodynamic, and other biochemical parameters could be continuously measured in order to study the experimental Fontan circulation more extensively. Furthermore, coronary blood flow patterns may be studied based on other animal model protocols [21].

In the design of this experimental protocol there are a few limitations that should be considered. It is important

to report that all animals used in the present study were healthy and free from any congenital heart diseases such as tricuspid atresia or univentricular heart condition. All experiments were acute, with a short survival period, and performed on animals with an open thoracic cavity, which might modify some hemodynamic parameters such as the venous blood return [4].

CONCLUSIONS

This study demonstrates the feasibility of a total cavopulmonary connection on a beating heart, without the use of circulatory support or bypass. This was achieved by the modified use of an appropriate size Y-shaped conduit connecting and draining the superior and inferior caval veins (end-to-end anastomosis) to the pulmonary trunk (end-to-side anastomosis). The obtained hemodynamic data confirmed the known Fontan paradox. The surgical procedure is challenging for a vascular or cardiac surgeon and requires extensive experience. Chronic survival experiments are needed to understand the physiology of the Fontan circulation and the plethora of hemodynamic questions arising from it.

REFERENCES:

- Fontan F, Baudet E: Surgical repair of tricuspid atresia. *Thorax*, 1971; 26: 240-48
- de Leval MR, Kilner P, Gewillig M et al: Total cavopulmonary connection: a logical alternative to atriopulmonary connection for complex Fontan operations. *J Thorac Cardiovasc Surg*, 1988; 96: 682-95
- Kanakis MA, Petropoulos AC, Mitropoulos FA: Fontan operation. *Hellenic J Cardiol*, 2009; 50: 133-41
- de Leval MR: The Fontan circulation: a challenge to William Harvey? *Nat Clin Pract Cardiovasc Med*, 2005; 2: 202-8
- Pearl JM, Laks H, Drinkwater DC et al: Modified Fontan procedure in patients less than 4 years of age. *Circulation*, 1992; 86(Suppl): II 100-5
- van Arsdell GS, McCrindle BW, Einarson KD et al: Interventions associated with minimal Fontan mortality. *Ann Thorac Surg*, 2000; 70: 568-74
- Mair DD, Puga FJ, Danielson GK: The Fontan procedure for tricuspid atresia: early and late results of a 25-year experience with 216 patients. *J Am Coll Cardiol*, 2001; 37: 933-39
- Trojnarska O, Gwizdała A, Katarzyński S et al: Evaluation of exercise capacity with cardiopulmonary exercise testing and BNP levels in adult patients with single or systemic right ventricles. *Arch Med Sci*, 2010; 6(2): 192-97
- Haller JA Jr, Adkins JC, Worthington M et al: Experimental studies on permanent bypass of the right heart. *Surgery*, 1966; 59: 1128-32
- Shemin RJ, Merrill WH, Pfeifer JS et al: Evaluation of right atrial-pulmonary artery conduits for tricuspid atresia. Experimental study. *J Thorac Cardiovasc Surg*, 1979; 77: 685-90
- Matsuda H, Kawashima Y, Tanaka H et al: Experimental evaluation of atrial function in right atrium-pulmonary artery conduit operation for tricuspid atresia. *J Thorac Cardiovasc Surg*, 1981; 81: 762-67
- Mace L, Dervanian P, Weiss M et al: Hemodynamics of different degrees of right heart bypass: Experimental assessment. *Ann Thorac Surg*, 1995; 60: 1230-37
- Nawa S, Irie H, Takata K et al: Development of a new experimental model for total exclusion of the right heart without the aid of cardiopulmonary bypass. *J Thorac Cardiovasc Surg*, 1989; 97: 130-34
- Kaku K, Matsuda H, Kaneko M et al: Experimental complete right heart bypass. Proposal of a new model and acute hemodynamic assessment with vasoactive drugs in dogs. *J Thorac Cardiovasc Surg*, 1990; 99: 161-66
- Haneda K, Konnai T, Sato N et al: Acute hemodynamic changes after Fontan operation: an experimental study. *Tohoku J Exp Med*, 1993; 19: 113-19
- Szabo G, Buhmann V, Graf A et al: Ventricular energetics after the Fontan operation: Contractility-afterload mismatch. *J Thorac Cardiovasc Surg*, 2003; 125: 1061-69
- Mitropoulos F, Odum J, Laks H: Use of apical suctioning device for placement of posterior epicardial defibrillator patch. *Heart Surgery Forum*, 2006; 9(3): E641-42
- Allan JS, Rose GA, Choo JK et al: Morphometric analysis of miniature swine hearts as potential human xenografts. *Xenotransplantation*, 2001; 8: 90-93
- de Leval MR: The Fontan Circulation: What have we learned? What to expect? *Pediatr Cardiol*, 1998; 19: 316-20
- Myers CD, Mattix K, Presson RG et al: Twenty-four hour cardiopulmonary stability in a model of assisted newborn Fontan circulation. *Ann Thorac Surg*, 2006; 81: 264-71
- Ootaki Y, Ootaki C, Kamohara K et al: Phasic coronary blood flow patterns in dogs vs pigs: an acute ischemic heart study. *Med Sci Monit*, 2008; 14(10): BR193-97