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Scandinavian Real Heart (SRH) 11 Implantation as Total Artificial Heart (TAH)-Experimental Update

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Abstract

One Swedish Landrace pig weighting approximately 80 kg was used to implant the SRH11. In this experiment the main focus was on the details of anesthesia as well as the mechanical function of the SRH11. The main finding from this study is that the SRH11 can deliver a wide range of cardiac output with a pulsatile waveform similar to the flow pattern of the native heart. In the anesthesia the following issues are of major importance from clinical point of view: the fluid balance and the adequate perfusions pressure is a high priority; The kidneys may be protected by a moderate dose of furosemide and measurement of urine output is mandatory; The systemic inflammatory reaction has to be controlled; At the weaning from the CPB the animal needs transfusion, therefore fresh blood should be available.

Keywords: Mechanical circulatory support; Total artificial heart; Assist device

Introduction

Heart failure (HF) is estimated to affect more than 35 million patients worldwide [1]. 5-25% of patients are expected to progress to severe HF despite optimal medical management [2]. A donor heart is the only cure, but the 5000 heart transplants performed annually worldwide do not meet the clinical need [3]. Mechanical circulatory support can be used as a bridge-to transplant (BTT), to keep patients alive whilst on the waiting list, or as destination therapy (DT). The majority of patients are helped with a left ventricular assist device (LVAD), but the patients who have biventricular failure either require two continuous flow (CF) VADs or a total artificial heart (TAH), with a combined 1 year survival around 55% [4]. The only TAH currently on the market is the pneumatically-actuated Syncardia™, which has been implanted in >1,600 patients [5], and has successfully bridged about 80% of patients to transplant (with a 70% 1 year survival rate post-transplant) [6]. Limitations with pneumatics include noise, large diameter of the percutaneous drivelines [7], and restriction to mobility from carrying or wheeling around a pneumatic driver. Although the use of two CF-VADs offers a silent and mobile solution, the high morbidity and mortality means that there is still a clinical need for a superior solution for patients requiring biventricular support [8]. The electricallyhydraulically- actuated Carmat™ TAH which is currently in clinical trials [9] addressed many of pneumatically-related issues, but the large size is a disadvantage. By removing hydraulics from its design, ReinHeart has achieved a compact size which is being evaluated in chronic animal studies [10]. Similarly, Scandinavian RealHeart (SRH) has also opted for an electrically-actuated TAH design, and thus addresses all issues related to pneumatics. The first aim of our study was to test the hemodynamics generated by the prototype version SRH11 when both the stroke volume and stroke rate were manipulated. Our second aim was to observe the character of the arterial pulse curve during the testing and observe the clinically important moments during anesthesia.

Materials and Methods

Total artificial heart Real Heart prototype SRH11

The uniqueness in RealHeart's approach is that it mimics the design and the main pumping principle of the natural human heart. RealHeart is invented by Dr Azad Najar and consists of four chambers, two atria and two ventricles, separated by an atrioventricular (AV) plane with valves. AV-plane movement accounts for 60% of the left ventricular stroke volume in humans [11], and is the pumping principle employed in RealHeart. The TAH consists of two independently operated left and right pumps, which enables adjustment to the left flow=volume to compensate for the bronchial circulation. The two pumps create a synchronous pulsatile outflow, and continuous passive inflow. The atria are filled passively and are compliant to minimize upstream suction events, (Figures 1 and 2). The atria fill with blood both during systole and diastole, so there is no stop in blood flow during ventricle ejection as seen with other piston-pump designs. This should, in theory, reduce upstream pressure build-up, and thereby the risk for respiratory failure. The SRH11 prototype weighed 800 g and its inflow and outflow connections were optimized for the pig anatomy.

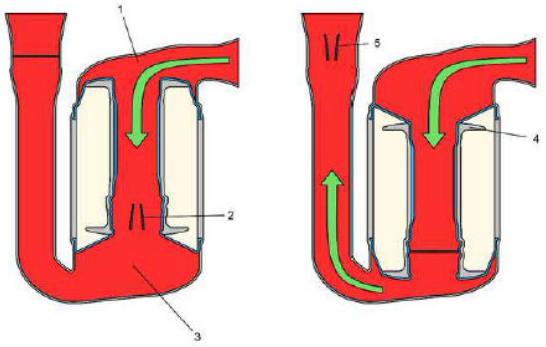

Figure 1: Prototype SRH11. A) Cross-section of a pump. Left: The diastolic phase. Blood enters the pump through the atria (1), passes the open bileaflet valve in the AV-plane (2),e and fills the ventricle (3). The outflow valve is closed. Right: The systolic phase. The AV plane containing the valve (4) moves downwards, the AV-plane valve closes due to the increased pressure in the ventricle, and the blood is ejected through the open valve in the outflow cannula and the valve(5).

Figure 2: SRH11 prior to the implantation. Two pumps are coupled together to create the total artificial heart.

Animal model

One 80 kg specially-bread Swedish land race pig (Sus Scrofa) was used for this research. The experiment was approved by the local ethical board [12].

Surgical procedure

After stress relief, the animal was premedicated with Zoletil®-Dexdomitor® (Zoletil® Virdac France, containing tiletamine 25 mg/ml, zolazepam 25 mg/ml, and Dexdomitor®, Orion Pharma, 0.5 mg dexmedetomidinehydrochloride, corresponding to 0.42 mg/ml dexmedetomidine). More details of the anesthetic technique are provided in our previous publication [12]. The pain relief was tested by pinching the pig's hind limbs. Intubation was carried out and the animal was ventilated throughout the experiment with FiO_2 21% using a Siemens Servo ventilator 900 D (Siemens, Siemens Healthcare, Stockholm, Sweden). The right carotid artery and the right internal jugular vein were also cannulated in the same wound on the neck. The arterial pressure was measured by strain gauge and the core temperature was recorded 30 cm from the nose in the esophagus. We monitored ECG lead II. Before starting the cardiopulmonary bypass (CPB) the animal was anticoagulated with heparin mg/kg BW. The anticoagulant effect was measured with ACT and a minimum 480 s was considered acceptable to start the CPB. After connecting the animal to CPB, bypass was instituted and the operation was then carried out on the empty beating heart. The right ventricle was incised 1 cm from the right atrium at the level of the right atrial appendix. The incision was extended along this border towards cava inferior and further 1 cm above the coronary sinus to the ventricular septum which was cut into the left ventricle. The incision was then carried out in the left ventricle (LV) 1 cm from the left atrium and to the left atrial appendix. The roof of the left atrium (LA) was cut towards the superior vena cava. Then the pulmonary trunk and aorta were transected distally and the heart removed. In this way we saved all tissue of the right atrium (RA) and LA for the connection with the TAH. Anastomoses were made with continuous suture between the atria and the pump cuffs and between the pump grafts and the pulmonary artery and aorta. The implantation of the SRH11 was done similar to earlier experience described detailed in our earlier publication [12].

Results

The preparation for CPB took 33 min. A bolus of 2 mg i.v. metoprolol was needed before cannulation of the heart to prevent atrial fibrillation and ventricular arrhythmias. The duration of the CPB was almost 4 h. The ACT before the CPB was 750 sec and throughout the CPB it varied between 582 – and >999 sec. The temperature was kept at +36.7–36.8°C. At the end of the experiment the temperature dropped to +34.5°C despite warming with a thermal ceiling. The hematocrit as measured by the heart lung machine was 18-24%. No hemolysis in the urine was noted. During the CPB Noradrenalin 40 microgram/ml was needed at a rate of 1-3 ml/h. The fluid balance was +11,150 ml. Urine output: 1,950 ml. 10 mg intravenous furosemid was required to increase the urine output and decrease the renal tubular oxygen demand. Transfusion of 2,500 ml fresh blood from another pig was used to fill the animal during weaning from the CPB. Throughout the CPB support, an arterial pressure of 60-80 mmHg was maintained. The peripheral vasoconstriction made the arterial saturation´s measurement impossible. The filling pressure was measured in some points with wireless micro pressure sensors (ISS Inc., Ypsilanti, MI, US) which were checked with an antenna [13]. The measurement was of good quality and such devices can be safely used at the same time when SRH11 is implanted. At the weaning the experimental animal's hematocrit was 23%. The data of how the SRH11 was tested are shown in the (Table 1). The SRH11 was run for 65 min without problems. The mean systolic blood pressure in the aorta was 77 mmHg, and the diastolic blood pressure was slightly above 20 mmHg, likely due to hemodilution and relatively low pump output.

Stroke volume	Frequency	Cardiac output	Measurement of filling P in the pulm.
SRH 11	SRH11	SRH11	
ml	beat/minute	ml/min	artery/SAP
5	15	75	
10	20	200	

20	30	600	
25	30	750	
20	25	500	
20	35	700	
20	50	1000	
25	60	1500	
30	60	1800	
30	65	1950	
35	65	2275	
30	60	1800	
30	65	1950	
30	70	2100	
30	75	2250	
30	80	2400	
30	85	2550	*PA=30, Ao=97/72
30	90	2700	*PA=27, LAP=0
30	95	2850	
30	90	2700	
25	90	2250	
25	95	2375	
30	85	2250	
30	90	2700	
30	90	2700	
30	100	3000	
30	105	3150	
32	105	3360	
30	100	3000	
30	105	3150	
30	100	3000	
30	110	3300	
30	120	3600	
40	120	4800	
40	125	5000	

Table 1: Data under weaning measured on the SRH11 and some pressure values. *Are data obtained with IYSS pressure sensors.

Pump output

The curve generated by the SRH11 as measured in the left carotid artery is shown in (Figure 3). A pulsatile flow is generated with a waveform similar to the flow pattern of the native heart. With more detailed analysis you can also observe a dicrotic notch in the arterial recording.

Figure 3: The arterial curve on the pressure monitor. The curve form is similar to the pressure pattern generated by the native heart with a dicrotic notch.

Discussion

The main finding from this study is that the SRH11 can deliver a wide range of cardiac output with a pulsative waveform similar to the flow pattern of the native heart. However, the fluid overload may put an excessive burden on the lungs, as we measured 30 mmHg in the pulmonary artery, and 0 mmHg in the vena pulmonalis immediately before the left atrium. The balance of +11 liter was too much and needs to be better controlled in the future. More specifically, the systemic inflammatory reaction needs to be suppressed with corticosteroids, and the decrease in oncotic pressure with an infusion of albumin. The pump output has to be raised more promptly than we did here to reach the optimal cardiac output corresponding to the animal's weight and temperature. The systolic arterial pressure needs to be increased to around 70-80 mmHg, which is typically achieved in cardiac surgery patients after CPB.

Conclusion

The SRH11 can deliver a wide range of cardiac output with a pulsative waveform similar to the flow pattern of the native heart. The equilibrium between the fluid balance and the adequate perfusion pressures are a high priority. The kidneys may be protected by a moderate dose of furosemid and measurement of urine output is mandatory. Fresh blood has to be available at the weaning from CPB to fill the animal and the SRH11. The generated pressure curve is physiologic and displays a dicrotic notch. The systemic inflammatory reaction has to be controlled.

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Conflicts of Interest

Henrik Ahn and Zoltán Szabó received compensation from Scandinavian Real Heart for the experimental research work, but not for preparing the manuscript. Authors Azad Najar, Göran Hellers, and Ina Laura Pieper hold positions and own stock in Scandinavian Real Heart. Jonas Holm has no conflicts of interest.

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