How to improve flow during cardiopulmonary bypass in an acardia experimental model

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Abstract

OBJECTIVES: In extreme scenarios, such as hyperacute rejection of heart transplant, an urgent heart explantation might be necessary. The aim of this experimental study was to determine the feasibility and to improve the haemodynamics of a venoarterial cardiopulmonary bypass after cardiectomy.

METHODS: A venoarterial cardiopulmonary bypass was established in seven calves (56.4 ± 7 kg) by the transjugular insertion to the caval axis of a self-expanding cannula, with a carotid artery return. After baseline measurements (A), ventricular fibrillation was induced (B), great arteries were clamped (C), the heart was excised and the right and left atria remnants, containing the pulmonary veins, were sutured together leaving an atrial septal defect over the cannula in the caval axis (D). Measurements were taken with the pulmonary artery clamped and declamped.

RESULTS: Initial pump flow was 4.16 ± 0.75 l/min dropping to 2.9 ± 0.63 l/min (PAB < 0.001) 10 min after induction of ventricular fibrillation. After cardiectomy with the pulmonary artery clamped, the pump flow increased non-significantly to 3.20 ± 0.78 l/min. After declamping, the flow significantly increased close to baseline levels (3.61 ± 0.73 l/min, PAB = 0.009, PD = 0.017), supporting the notion that full cardiopulmonary bypass in acardia is feasible only if adequate drainage of pulmonary circulation is assured to avoid pulmonary congestion and loss of volume from the left-to-right shunt of bronchial vessels.

Keywords: ECMO • Cardiopulmonary bypass • Heart transplantation • Acardia

INTRODUCTION

Venoarterial bypass is commonly used for cardiorespiratory support in acute cardiac failure. In extreme scenarios, such as hyperacute rejection of heart transplant or in scenarios of uncontrollable bleeding during a cardiac surgery procedure, an urgent heart explantation, although never documented, might be the only option for survival, on condition that a cardiorespiratory support can be assured as a bridge to transplantation or artificial heart implantation. The use of extracorporeal membrane oxygenation (ECMO) is well documented for cardiac support in acute cardiac failure, as a bridge to therapeutic invasive procedure, to recovery, to implantation of a cardiac assistance device or as a bridge to transplantation [1–5]. Nevertheless, its feasibility has never been tested for cardiopulmonary support after a heart explantation. The aim of this experimental study was to determine the feasibility and to improve the haemodynamics of a venoarterial cardiopulmonary bypass after cardiectomy.

MATERIALS AND METHODS

After acceptance of the study protocol by the state veterinary office, seven bovine experiments (56.4 ± 7 kg) were performed under general anaesthesia (I.M. premedication and volatile medication for maintenance). All animals received humane care in compliance with the European Convention on Animal Care and the study was approved by the Institutional Ethics Committee. Following instrumentation for continuous monitoring (ECG, central venous pressure, systemic arterial pressure), a sternotomy was performed and a roller pump venaarterial cardiopulmonary bypass was established by the transjugular insertion to the caval axis of a wall-less venous cannula (Smartcannula, 24F), with return through the right carotid artery (19F), after full systemic heparinization (300 IU/kg bodyweight; ACT >480). This technique has been previously reported and termed temporary caval stenting, because the superior vena cava, the posterior part of the right atrium and the inferior vena cava are kept open despite continuous drainage [6].

Achievable pump flow with gravity drainage and baseline haemodynamic parameters (A) were recorded. Ventricular fibrillation (Fig. 1A) was induced by an external stimulator (B). Pump flow together with the haemodynamic consequences were recorded after 10 min as outlined above, including pressures of the cardiac cavities (direct puncture). After ventricular fibrillation measurements, the great arteries were clamped, the heart was excised (Fig. 1B) and right and left atria remants containing the pulmonary veins were sutured together leaving an atrial septal...
defect over the cannula in the caval axis. Measurements were taken with the pulmonary artery clamped (C) and declamped (D) (Fig. 1C and D). In order to avoid an air-lock into the cardio-pulmonary bypass system during the heart excision, the right atrial/central venous pressure was adjusted to 2 mmHg by partial clampage on the venous line. Furthermore, right and left atria were preserved and suspended during their anastomosis in order to have the caval axis cannula covered with blood. Blood flow was recovered with a pump sucker.

All continuous variables are expressed as mean ± 95% confidence intervals. The analysis of variance test for repeated measures with one degree of freedom was used to test the null hypothesis (H₀) that the mean pump flow is equal in the four groups of perfusion status (A, B, C and D). We used an α = 0.05 as the level of significance in the design of our study. The null hypothesis was rejected with a value of significance P < 0.001, so we proceeded in the pairwise comparisons of the difference of the mean pump flow in the four groups using a two-way paired t-test with Bonferroni adjustment for multi-comparison procedures.

Statistical analysis was performed using IBM SPSS 20.0.

RESULTS

During the initial period of venoarterial bypass (A), the mean pump flow was stabilized at 4.16 ± 0.75 l/min and the heart collapsed. After the electrical induction of ventricular fibrillation (B), the left heart dilated progressively (Fig. 1A) and pump flow dropped after 10 min to 2.9 ± 0.63 l/min (P₁₀ < 0.001). Endocavitary pressures were registered with a direct puncture of the right and left ventricles and the pulmonary artery. After left ventricle dilatation, they were equalized to a value of ≈30 mmHg. Following great vessels’ clamping (C) and heart explantation (Fig. 1B), the pump flow (3.2 ± 0.78 l/min) remained at ventricular fibrillation levels (P₁₂ = 0.436), being statistically significantly lower than baseline measurements (A) (P₁₃ = 0.025). After declamping the pulmonary artery, blood from the pulmonary circulation was aspirated and returned to the cardiopulmonary bypass machine, resulting in a significant rise of the pump flow, close to baseline values (3.61 ± 0.73 l/min, P₁₄ = 0.116). This value was statistically significantly greater than pump flow during ventricular fibrillation (B), P₁₅ = 0.009 and during the period that the pulmonary artery was clamped (C), P₁₆ = 0.017. The difference between the pump flow with the pulmonary artery

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**Table 1:** 95% confidence interval for mean pump flow in the four different groups of perfusion status

<table>
<thead>
<tr>
<th>Perfusion status</th>
<th>Mean pump flow in l/min</th>
<th>SE 95% confidence interval</th>
<th>Lower bound</th>
<th>Upper bound</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>4.157</td>
<td>0.285</td>
<td>3.461</td>
<td>4.854</td>
</tr>
<tr>
<td>VF</td>
<td>2.900</td>
<td>0.241</td>
<td>2.310</td>
<td>3.490</td>
</tr>
<tr>
<td>PA clamped</td>
<td>3.200</td>
<td>0.296</td>
<td>2.476</td>
<td>3.924</td>
</tr>
<tr>
<td>PA declamped</td>
<td>3.614</td>
<td>0.276</td>
<td>2.940</td>
<td>4.288</td>
</tr>
</tbody>
</table>

VF: ventricular fibrillation; PA: pulmonary artery.
Moreover, we can avoid an air-lock even in open right heart drainage of both the superior and inferior venae cavae (through a peripheral vessel) and provides a remarkable venous rerouting has the advantage to be easier to perform (cannulation of the caval axis with a wall-less venous cannula that keeps surgery without snares in our laboratory, we opted for a cannula model of remote single venous cannulation for open right heart implantation of an artificial heart. Having already worked on a model of remote single venous cannulation for open right heart surgery without snares in our laboratory, we opted for a cannulation of the caval axis with a wall-less venous cannula that keeps open the superior vena cava, the posterior part of the right atrium and the inferior vena cava (Smartcannula). This cannulation has the advantage to be easier to perform (cannulation through a peripheral vessel) and provides a remarkable venous drainage of both the superior and inferior venae cavae. Moreover, we can avoid an air-lock even in open right heart surgery by keeping a central venous pressure of 2 mmHg by partial clamping of the venous line. Blood overflow can be aspirated and returned to the venous line.

From a haemodynamic point of view, we showed that cardiopulmonary support in acardia is possible only if adequate pulmonary drainage is assured. In detail, after induction of ventricular fibrillation (B), the pump flow significantly decreased and the heart was dilated (Fig. 1A) due to the left-to-right shunt of the bronchial arteries to the pulmonary veins [9]. This flow, from the systemic to the pulmonary circulation, is responsible for the loss of volume into the left cardiac cavities and into the lungs when the heart loses its contractility, being unable to eject this volume back to the systemic circulation. As a result, the heart dilates and pulmonary congestion commences. Clinically, we can observe the continuous loss of volume and the need for continuous fluid replacement when, during ECMO, the left ventricle ejection fraction critically diminishes. Furthermore, after heart explantation and with the great vessels clamped (C), the pump flow did not rise above the levels of ventricular fibrillation (B), although the pulmonary veins were included into the atria conduit connecting the caval axis. Even though we only used gravity-based venous drainage, the suction created was probably enough to provoke the collapse of the pulmonary veins leading to an insufficient drainage of the pulmonary circulation. In contrast, with the pulmonary artery declamped and continuous aspiration in it, pump flow increased to baseline levels, suggesting that continuous drainage of the pulmonary circulation is pivotal for maintaining pump flow in acardia. This finding is consistent with the previous findings of our experimental team. We showed that ventricular fibrillation during cardiopulmonary bypass results in volume loss in cardiac cavities and pulmonary circulation. Remote drainage of the pulmonary artery by a femoral access significantly improves haemodynamics [10].

### DISCUSSION

Our current therapeutic approach is ill equipped to face clinical situations where emergency cardiac explantation is needed. An urgent need for heart explantation may be imagined in cases such as a hyperacute rejection of a heart transplantation [7, 8] or major, uncontrollable, perioperative bleeding where salvage of the heart is not possible. In such cases, given that urgent heart transplantation or artificial heart implantation is rarely available, an ECMO support after heart explantation as a bridge-to-heart transplantation or artificial heart implantation could be a solution. To our knowledge, the possibility of an ECMO support and its haemodynamic optimization in acardia has never been explored.

In this experimental study, we tried to determine the feasibility and to improve the haemodynamics of venoarterial cardiopulmonary bypass after cardiectomy, using a surgical technique that does not compromise a future heart transplantation or the implantation of an artificial heart. Having already worked on a model of remote single venous cannulation for open right heart surgery without snares in our laboratory, we opted for a cannulation of the caval axis with a wall-less venous cannula that keeps open the superior vena cava, the posterior part of the right atrium and the inferior vena cava (Smartcannula). This cannulation has the advantage to be easier to perform (cannulation through a peripheral vessel) and provides a remarkable venous drainage of both the superior and inferior venae cavae. Moreover, we can avoid an air-lock even in open right heart surgery by keeping a central venous pressure of 2 mmHg by partial clamping of the venous line. Blood overflow can be aspirated and returned to the venous line.

From a haemodynamic point of view, we showed that cardiopulmonary support in acardia is possible only if adequate pulmonary drainage is assured. In detail, after induction of ventricular fibrillation (B), the pump flow significantly decreased and the heart was dilated (Fig. 1A) due to the left-to-right shunt of the bronchial arteries to the pulmonary veins [9]. This flow, from the systemic to the pulmonary circulation, is responsible for the loss of volume into the left cardiac cavities and into the lungs when the heart loses its contractility, being unable to eject this volume back to the systemic circulation. As a result, the heart dilates and pulmonary congestion commences. Clinically, we can observe the continuous loss of volume and the need for continuous fluid replacement when, during ECMO, the left ventricle ejection fraction critically diminishes. Furthermore, after heart explantation and with the great vessels clamped (C), the pump flow did not rise above the levels of ventricular fibrillation (B), although the pulmonary veins were included into the atria conduit connecting the caval axis. Even though we only used gravity-based venous drainage, the suction created was probably enough to provoke the collapse of the pulmonary veins leading to an insufficient drainage of the pulmonary circulation. In contrast, with the pulmonary artery declamped and continuous aspiration in it, pump flow increased to baseline levels, suggesting that continuous drainage of the pulmonary circulation is pivotal for maintaining pump flow in acardia. This finding is consistent with the previous findings of our experimental team. We showed that ventricular fibrillation during cardiopulmonary bypass results in volume loss in cardiac cavities and pulmonary circulation. Remote drainage of the pulmonary artery by a femoral access significantly improves haemodynamics [10].

### CONCLUSIONS

Our experimental study showed that full cardiopulmonary support in acardia is feasible only if adequate drainage of the pulmonary circulation is assured to avoid pulmonary congestion and loss of volume from the left-to-right shunt of the bronchial vessels. In our

### Table 2: Pairwise comparison of pump flow in the four different groups of perfusion status using paired t-test with Bonferroni’s adjustment for multiple comparisons

<table>
<thead>
<tr>
<th>(I) Pump flow in different perfusion statuses</th>
<th>(J) Pump flow in different perfusion statuses</th>
<th>Mean difference (I-J)</th>
<th>SE</th>
<th>Significant*</th>
<th>95% confidence interval for difference*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline VF</td>
<td>Baseline PA clamped</td>
<td>1.257</td>
<td>0.127</td>
<td>0.000</td>
<td>0.765 – 1.749</td>
</tr>
<tr>
<td>Baseline PA clamped</td>
<td>Baseline PA declamped</td>
<td>0.957</td>
<td>0.213</td>
<td>0.025</td>
<td>0.135 – 1.779</td>
</tr>
<tr>
<td>Baseline PA declamped</td>
<td>PA clamped VF</td>
<td>0.543</td>
<td>0.171</td>
<td>0.116</td>
<td>-0.119 – 1.205</td>
</tr>
<tr>
<td>PA clamped VF</td>
<td>PA declamped VF</td>
<td>0.300</td>
<td>0.138</td>
<td>0.436</td>
<td>-0.233 – 0.833</td>
</tr>
<tr>
<td>PA declamped VF</td>
<td>PA declamped VF</td>
<td>0.714</td>
<td>0.130</td>
<td>0.009</td>
<td>0.213 – 1.216</td>
</tr>
</tbody>
</table>

VF: ventricular fibrillation; PA: pulmonary artery.
Based on estimated marginal means.
*The mean difference is significant at the 0.05 level.

* Adjustments for multiple comparisons: Bonferroni.
model, this was obtained by direct aspiration into the pulmonary artery, since pulmonary vein drainage was insufficient.

We believe that further work must be done in order to assure adequate drainage of the pulmonary circulation through the venous cannula. In such a model, a full ECMO support in acardia through a femoro-femoral cannulation and closure of the chest cavity is possible. Moreover, we believe that the haemodynamic stability of this model must be proved with mid- and long-term haemodynamic support.

Conflict of interest: none declared.

REFERENCES