

Pulmono-atrial shunt and lung assist to treat right ventricular failure

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1. ABSTRACT

In right ventricular failure (RVF) a decrease of right ventricular afterload and improvement of left atrial filling could be achieved by a pulmonary artery-left atrial (PA)-shunt. To avoid cyanosis, artificial oxygenation is necessary. In 11 pigs a PA-shunt was created. An interventional lung assist device (ILA) was installed from the femoral artery to vein in 5 pigs (serial in relation to native lung: Group I) and into the PA-shunt in 6 pigs (parallel: Group II). RVF was induced by pulmonary artery banding. Right ventricular performance was determined by pulse contour analysis, pressure - and flow measurements. In both groups a stable RVF was generated. In Group I cardiac output trended to increase but neither right ventricular filling pressures nor arterial pressure changed significantly. The PaO₂ decreased significantly. In Group II cardiac output and arterial pressure increased significantly under a shunt flow of 2.3- 2.6 l/min and the animals recovered from cardiogenic shock. In conclusion a PA-shunt with a parallel lung assist can effectively reverse the deleterious effects of RVF.

2. INTRODUCTION

Right ventricular failure (RVF) following cardiac surgery is an often deleterious complication. It is now clear that the right ventricle is not only a passive conduit into the pulmonary vasculature (1). The pathophysiology of RVF is highly complex, reflecting the high mortality and challenges in treatment of RVF (2). Surgical options to treat RVF are limited. Besides assist device implantation and transplantation the only proven surgical option is a right ventricular exclusion with a “fontanisation” of the circulation (3, 4). Nevertheless the presence of pulmonary hypertension is a contraindication for fontanisation. We focused on the problem of a RVF caused by pulmonary hypertension, which occurs in different clinical settings and especially accounts for at least 19 % of early deaths in patients undergoing cardiac transplantation (5). In this context it is known that on the one hand pulmonary hypertension can decrease with correction of the underlying disease (6) and on the other hand the right ventricle can slowly adapt to pulmonary hypertension (1, 2). Besides several other mechanisms which lead to low cardiac output

in RVF a major feature is a reduced trans-pulmonary blood flow with reduced left atrial respectively ventricular filling (7, 8, 9). It is known that decompression of the right sided circulation with shunting of right sided blood to the left atrium for example by atrial septostomy is an option to palliate pulmonary artery hypertension and avoid RVF (10, 11). The idea of a pulmonary artery to left atrium shunt (PA-shunt) goes back to the sixties and was performed by Bilgutay and Lillehei (12). Gupta first evaluated a PA-shunt in pulmonary artery hypertension (13). He could demonstrate an effective decompression of the pulmonary artery circulation into the left atrium with a significant reduction of pulmonary artery pressure and contrariwise an increase of the femoral arterial blood pressure. Nevertheless the most important side effect of both atrial septostomy and PA-shunting is central cyanosis. In the study of Gupta the oxygen saturation fell down to 80% in an effective decompression of the pulmonary artery. Because adult individuals do not tolerate this cyanosis well and especially because the failing right ventricle is sensitive to ischemia (14, 15) PA-shunting plays no role in RVF. Our hypothesis was, that PA-shunting together with a today available, pumpless, low resistance lung assist could optimally reverse the deleterious effects of RVF because the problem of cyanosis may be avoided. To test this hypothesis we evaluated the effect of a PA-shunt together with a parallel and serial lung assist in a porcine, open chest model of hypertension-induced acute RVF.

3. MATERIALS AND METHODS

3.1. Animals and anaesthesia

11 female housepigs (Race: DL) of 70 +/- 3 kg were used in this study. The animal research protocol was approved by the local authorities (50.203.2-AC 14.42/03) in Cologne. Animals were treated according to the "Guide for the care and use of Laboratory animals" published by the US National Institutes of Health (National Institutes of Health publication no. 85-23, revised 1996). After premedication, anesthesia was maintained with pentobarbital in conjunction with fentanyl intravenously. Animals were intubated (8 Ch) and ventilated first with 100 % oxygen. Ventilation was adjusted with tidal volumes initially set to 10 ml/kg and ventilation rate was adjusted to maintain a PaCO₂ of 4.6–5.3 kPa. Oxygen concentration was maintained at 40%. Inflation pressures were below 10 mmHg and ventilation was adjusted according to the blood gas analyses. Before the skin incision an antibiotic prophylaxis was administered (Cefuroxime 1.5 g). With the beginning of the shunt surgery the animals were systemically heparinized (100 U/kg). Fluid (Ringers lactate) was given at a rate of 20 ml/kg. The temperature of the animal was maintained with a heating blanket and lamp.

3.2. Instrumentation

All animals received a right sided central venous access and a left sided sheath via the jugular veins, which were surgically dissected. A right sided femoral arterial line (Picco®-Catheter, Pulsion GmbH, Germany) was inserted under direct vision by a small incision in the groin. Via the right femoral vein a Swan-Ganz catheter (7.5-F, Model VS 1721; Ohmeda, UK) was inserted into the right ventricle.

With finished surgical procedures the REF Catheter (Pulsion GmbH, Germany) was advanced until shortly behind the pulmonary valve, position was controlled by palpation. Flow probes (Transsonic Inc. Ithaca, New York) were positioned around the descending aorta, the PA-shunt and the ILA tubes. Echocardiography was only available irregularly in the last experiments in group II (GE Healthcare: Vivid 5). For an adequate approach to display the right ventricle an additional small subxiphoid incision was performed.

3.3. Surgical preparations

All animals were put in a supine position and fixed in a slightly rightward position. First the left groin was surgically dissected (Group I) with exposition of the femoral artery and vein. Using Seldingers technique under direct vision a 15 Fr cannula was inserted in the artery and a 17 Fr cannula into the vein (both Novalung, Germany). Until the connection with the ILA device they were sealed with heparin-saline. A left thoracotomy in the fourth intercostal space was performed and the fifth rib was resected for better exposure. After incising the pericardium, the pulmonary artery was dissected and exposed up to the bifurcation. By means of partial vascular clamp a segment of an aortic "homograft" (frozen aorta from another pig) was connected end to side with the very distal main pulmonary artery. Another donor segment was connected end to side with the lateral left atrium. Between the homografts a short tube (3/8) was inserted for the serial setting (group I). For the parallel setting (group II) the whole ILA device (with its 3/8 tubes) was inserted between the homografts. The systems were carefully vented and clamped.

3.4. Right ventricular failure model

To achieve RVF a banding of the very distal main pulmonary artery was performed. For banding we used a custom-made apparatus to reduce the diameter of the banding very slow by a screwing mechanism. The banding was persistent. RVF following pulmonary artery banding was defined as a profound decrease in systemic blood pressure (mean arterial pressure (MAP) < 2/3 of the beginning), an initial > 1/3 increase of systolic right ventricular pressure (RVP) and a depressed cardiac output (< 2/3 of baseline). Additionally right ventricular function was judged by inspection.

3.5. Lung assist

For all experiments we used the Novalung® (Novalung GmbH, Germany). This device consists of a polymethyl pentene membrane and offers an effective surface of 1.3 m² for gas exchange housed in a rigid 15 x 15 cm polyethlen box. Inflow and outflow are connected with each a 3/8 tube, at the top there is a connection for oxygen supply (Figure 1). The device is planned for a flow from 0.5–4.5 l/min and has a pressure decrease of 11 mmHg at 2.5 l/min. Oxygen was run with 6 L/ min during the whole experiments.

3.6. Experimental protocol

Two different settings of the placement of the ILA were evaluated. In group I the ILA was connected



Figure 1. Photograph of an ILA (Novalung®) with connected tubes.

peripherally with the right femoral artery and vein (serial setting). In this setting perfusion of the ILA was maintained by the pressure gradient from the femoral artery to the femoral vein. In group II the ILA was positioned centrally between the two homografts on the pulmonary artery and the left atrium (parallel setting) and thereby perfused by the gradient between the pulmonary artery and the left atrium (Figure 2). The major difference between the two groups was only the position of the ILA: in I it was positioned outside the thorax and perfused by arterial blood whereas in II it was positioned in the PA-shunt and thereby perfused by mixed venous blood. In principle the properties of the PA-shunt in conjunction with the ILA were investigated first without a RVF and thereafter with a RVF for 90 minutes (Figure 3). To exclude meantime changes in RVF conditions at the end of the study the shunt was clamped again and the following course observed. After euthanasia an autopsy was performed.

3.7. Data acquisition

Data were collected using the Datex AS-3 Compact Monitor (Datex Engstrom, USA) and recorded during the study on a laptop (HP). Additionally the Picco-VolEF Data Acquisition Software (Version 4.0; Pulsion, Germany) was used and stored on the laptop. For the measurements with the REF Catheter and the Picco Catheter 3 repeated measures were performed. Flow measurements were also collected and recorded on the laptop during the study. Data are expressed as means \pm SD. Statistical analyses were performed with SAS (Version 9.1, SAS, Germany). A Student 2 tailed paired t test was used. All statistical assumptions were performed to a level of significance of 0.05.

4. RESULTS

4.1. Surgery, common results

For no part of this PA-shunt operation cardiopulmonary bypass was necessary. No catecholamines had to be administered during the whole investigation. The method to use aortic homografts on the pulmonary artery and the left atrium to interposition a shunt proved beneficial because of its blood tightness and ease to use.

With the shunt in place it was even possible to close the thoracotomy (Figure 4). In one animal during insertion of the left atrial part of the shunt air was moved into the left atrium. Under clinical signs of myocardial infarction (ST Segment elevation) a rapidly worsening low cardiac output syndrome developed and the animal died. Autoptically there were no relevant changes: no thrombi or injuries to the heart could be detected. The anastomoses were fully open in all cases. The RVF failure model proved very reliable. In preliminary tests a relevant adaption (homeometric autoregulation) of the right ventricle to increased afterload (in our model very pronounced) could be excluded. Additionally to changed hemodynamic parameters in RVF the ECG showed characteristic and reproducible abnormalities: descending ST-segment depressions in part with a change into a right bundle block grossly correlated with the severity of RVF. A relevant observation in our model was, that with a progressive RVF causing a profound cardiogenic shock both right ventricular filling pressures and in consequence (proximal) pulmonary artery pressures decreased. In this situation the right ventricle seemed not to be able any more to generate adequate contraction. This phenomenon was observable both during the induction of RVF and after clamping of the shunt. When a sufficient therapy was instituted (e.g. opened shunt with lung assist or in the preliminary investigations a partial release of banding) the right ventricular filling pressures rose again parallel to a hemodynamic recovery. These observations are reflected only in part in the hemodynamic data shown in the tables.

4.2. Overall hemodynamics and right ventricular performance

Group I (serial): An overview of the most important hemodynamic parameters is given in Table 1. The starting of the shunt along with the lung assist led to a moderate (but significant) decrease of the MAP at which the CO increased (ns). Right ventricular filling pressures and the all the rest of hemodynamic data remained grossly unchanged. The flow of the shunt and the lung assist was balanced at about one liter per minute. The data of the measuring points baseline I and II did not differ significantly. When the RVF was induced a massive (significant) decrease of the MAP (from 72 ± 6.1 to 50 ± 3.3 mm Hg) and the CO (from 5.7 ± 1.0 to 3.5 ± 0.5 l/min) could be observed. RVP and pulmonary artery pressure (PAP) as right ventricular filling pressures rose significantly to more than 50 mm Hg in systolic RVP. In parallel to a reduced (ns) right ventricular ejection fraction (RVEF) the stroke volume variation (SVV) rose significantly from 8 ± 3.2 to 15 ± 2.4 %. After beginning of the shunting the MAP trended to decline rather than to rise. Right ventricular filling pressures fell over the time of shunting only very little, the CO only trended to increase. The RVEF stayed low and the SVV stayed high both at the level of RVF. The flow through the PA-shunt as well as through the lung assist started with a little more than one liter per minute but declined with time to a little less than one liter per minute. With the shunts clamped again after 90 minutes MAP and CO slightly increased (ns), the right ventricular filling pressures also increased only slightly. In summary the animals exhibited a profound RVF, however by the

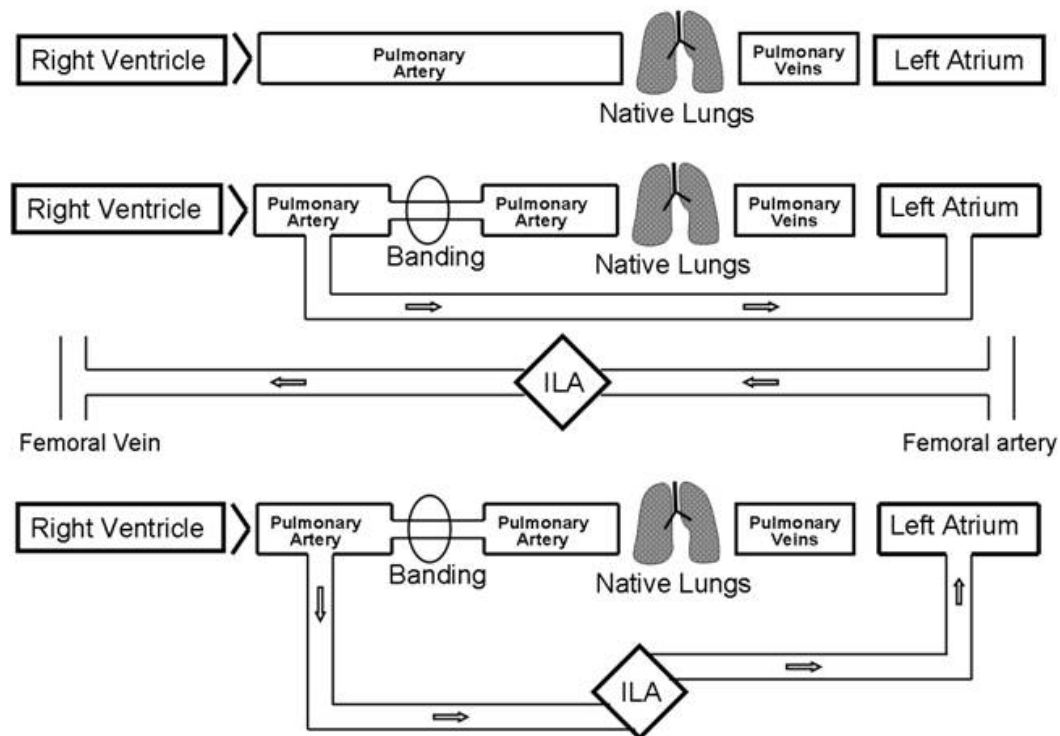


Figure 2. Configuration schema of the different arrangements of the PA-shunt and the ILA. The upper schema shows the native initial situation. The middle schema shows the serial setting with the peripherally connected ILA. The lower schema demonstrates the parallel setting with centrally connected ILA.

Table 1. Hemodynamic data group I. The ILA is peripherally connected: serial setting

	Base-line 1	Shunt/ILA open	Base-line 2	RVF (0 Min)	I (5 Min)	II (15 Min)	III (60 Min)	IV (90 Min)	Shunt/ILA clamped
MAP ¹ (mmHg)	75 +/-4.6	57 +/-6.2	72 +/-6.1	50 +/-3.3	44 +/-7.6	44 +/-5.3	42 +/-4.2	40 +/-4.9	40 +/-5.9
RVP-S ² (mmHg)	35 +/-4.8	34 +/-4.2	35 +/-5.7	54 +/-9.8	51 +/-6.9	50 +/-7.3	48 +/-7.4	47 +/-6.9	52 +/-9.5
RVP-M ³ (mmHg)	17 +/-1.8	16 +/-1.7	16 +/-2.5	30 +/-5.6	28 +/-5.3	28 +/-5.5	28 +/-6.0	27 +/-5.9	30 +/-7.2
PAP-M ⁴ (mmHg)	23 +/-2.9	21 +/-2.8	22 +/-2.6	32 +/-5.6	30 +/-4.3	30 +/-4.3	29 +/-4.3	28 +/-4.5	31 +/-5.4
CVP-M ⁵ (mmHg)	7 +/-3.0	8 +/-1.9	7 +/-2.2	10 +/-2.0	10 ±2.3	10 +/-2.7	11 +/-2.6	11 +/-2.7	12 +/-2.8
LAP-M ⁶ (mmHg)	12 +/-3.1	13 +/-2.3	12 +/-2.9	8 +/-1.3	10 +/-1.6	10 +/-1.5	10 +/-1.4	10 +/-1.2	9 +/-1.4
CO(PC) ⁷ (l/min)	5.6 +/-1.1	6.7 +/-1.4	5.7 +/-1.0	3.5 +/-0.5	4.3 +/-0.7	4.3 +/-0.8	4.4 +/-0.9	4.3 +/-0.9	3.7 +/-0.8
Flow da ⁸ (l/min)	4.7 +/-0.9	5.9 +/-1.1	4.9 +/-0.8	3.1 +/-0.4	3.7 +/-0.5	3.8 +/-0.8	3.8 +/-0.9	3.8 +/-0.8	3.1 +/-0.8
Flow sh ⁹ (l/min)	0	1.4 +/-0.3	0	0	1.3 +/-0.3	1.3 +/-0.2	1.1 +/-0.1	1.2 +/-0.3	0
SV ¹⁰ (ml)	66 +/-14.3	80 +/-17.7	68 +/-12.6	39 +/-6.4	46 +/-10.0	47 +/-11.4	49 +/-12.2	46 +/-11.5	40 +/-11.8
SVV ¹¹ (%)	8 +/-3.3	9 +/-2.8	8 +/-3.2	15 +/-2.4	14 +/-0.9	13 +/-1.3	13 +/-1.5	14 +/-1.8	17 +/-2.0
RVEF ¹² (%)	32 +/-3.8	32 +/-4.6	32 +/-3.6	17 +/-2.3	16 +/-2.5	15 +/-3.2	16 +/-4.0	16 +/-4.0	14 +/-3.0
SvO2 ¹³ (%)	74 +/-10	66 +/-9.3	73 +/-9.8	43 +/-3.9	36 +/-2.7	36 +/-2.1	37 +/-2.7	36 +/-2.0	38 +/-4.3

¹ MAP: mean arterial pressure; ² RVP-S: systolic right ventricular pressure; ³ RVP-M: mean right ventricular pressure; ⁴ PAP-M: mean pulmonary artery pressure; ⁵ CVP-M: mean central venous pressure; ⁶ LAP-M: mean left atrial pressure; ⁷ CO(PC): cardiac output measured by pulse contour analysis; ⁸ Flow da: flow in the proximal descending aorta; ⁹ Flow sh.: Shunt flow; ¹⁰ SV: stroke volume; ¹¹ SVV: stroke volume variation; ¹² RVEF: right ventricular ejection fraction; ¹³ SvO2: mixed venous oxygen saturation.

Experimental protocol: Measuring points

Group I: serial setting
(ILA peripherally)

Group II: parallel setting
(ILA centrally)

Baseline 1: after surgery
Opened Shunt and ILA
Baseline 2: (Shunt/ILA clamped)
RVF (Pulmonary Artery banding)
I: 5 min after opened Shunt/ILA
II: 15 min after opened Shunt/ILA
III: 60 min after opened Shunt/ILA
IV: 90 min after opened Shunt/ILA
Clamped Shunt and ILA

Baseline 1: after surgery
Opened Shunt and ILA
Baseline 2: (Shunt/ILA clamped)
RVF (Pulmonary Artery banding)
I: 5 min after opened Shunt/ILA
II: 15 min after opened Shunt/ILA
III: 60 min after opened Shunt/ILA
IV: 90 min after opened Shunt/ILA
Clamped Shunt and ILA

Figure 3. Experimental protocol of the two groups.



Figure 4. Operative view: Left side demonstrating the connection of the tubes with the pulmonary artery (lower, dark tube) and the left atrium both via a homograft. Right side demonstrating a centrally connected ILA with closed thorax.

Table 2. Hemodynamic data group II. The ILA is centrally connected: parallel setting

	Base-line 1	Shunt/ILA open	Base-line 2	RVF (0 Min)	I (5 Min)	II (15 Min)	III (60 Min)	IV (90 Min)	Shunt/ILA clamped
MAP ¹ (mmHg)	75 ±7.3	66 +/-7.8	69 +/-4.6	43 +/-5.2	61 +/-6.4	60 +/-6.1	60 +/-6.8	58 +/-5.6	36 +/-3.3
RVP-S ² (mmHg)	37 +/-3.0	32 +/-1.5	37 +/-4.1	54 +/-7.7	50 +/-7.4	49 +/-7.0	48 ±8.4	48 +/-8.3	52 ±8.1
RVP-M ³ (mmHg)	21 +/-4.1	17 +/-3.6	22 +/-5.3	29 +/-6.5	27 +/-6.4	27 +/-7.0	27 +/-7.9	26 +/-7.9	29 +/-7.9
PAP-M ⁴ (mmHg)	25 +/-2.7	21 +/-2.2	26 +/-2.0	36 +/-5.9	34 +/-4.6	33 +/-4.8	33 +/-4.6	33 +/-5.9	35 +/-6.4
CVP-M ⁵ (mmHg)	12 +/-1.0	10 +/-0.6	12 +/-1.5	14 +/-1.1	13 +/-0.6	12 +/-1.2	13 +/-0.1	12 +/-1.0	15 +/-0.6
LAP-M ⁶ (mmHg)	15 +/-6.0	13 +/-5.5	15 +/-6.2	12 +/-5.8	14 +/-7.1	15 +/-6.9	14 +/-7.0	15 +/-7.5	12 +/-6.2
CO(PC) ⁷ (l/min)	5.6 +/-0.6	5.8 +/-0.7	5.6 +/-0.7	3.0 +/-0.6	5.5 +/-0.7	5.4 +/-0.8	5.5 +/-0.8	5.3 +/-0.6	3.1 +/-0.6
Flow da ⁸ (l/min)	4.4 +/-0.5	5.0 +/-0.6	4.6 +/-0.5	2.5 +/-0.5	4.6 +/-0.6	4.6 +/-0.8	4.7 +/-0.7	4.6 +/-0.6	2.5 +/-0.5
Flow sh ⁹ (l/min)	0	1.5 +/-0.3	0	0	2.2 +/-0.3	2.3 +/-0.3	2.4 +/-0.4	2.3 +/-0.4	0
SV ¹⁰ (ml)	74 +/-4.3	72 +/-4.2	77 +/-3.8	38 +/-4.9	69 +/-6.9	69 +/-6.3	70 +/-5.7	71 +/-5.6	40 +/-5.1
SVV ¹¹ (%)	5.2 +/-2.2	4.7 +/-1.7	4.6 +/-1.5	12.9 +/-3.0	6.3 +/-2.2	6.3 +/-2.4	6.6 +/-2.4	6.7 +/-2.6	14 +/-3.4
RVEF ¹² (%)	32 +/-6.2	34 +/-4.2	32 +/-7.4	17 +/-3.1	28 +/-5.7	28 +/-4.9	27 +/-6.0	27 +/-5.2	15 +/-2.3
SvO2 ¹³ (%)	63 +/-2.6	69 +/-1.9	64 +/-1.7	41 +/-1.9	65 +/-2.0	63 4.3	64 +/-1.6	64 +/-2.4	44 +/-3.4

¹ MAP: mean arterial pressure; ² RVP-S: systolic right ventricular pressure; ³ RVP-M: mean right ventricular pressure; ⁴ PAP-M: mean pulmonary artery pressure; ⁵ CVP-M: mean central venous pressure; ⁶ LAP-M: mean left atrial pressure; ⁷ CO(PC): cardiac output measured by pulse contour analysis; ⁸ Flow da: flow in the proximal descending aorta; ⁹ Flow sh.: Shunt flow; ¹⁰ SV: stroke volume; ¹¹ SVV: stroke volume variation; ¹² RVEF: right ventricular ejection fraction; ¹³ SvO2: mixed venous oxygen saturation.

Table 3. Blood gas analyses group I. The ILA is peripherally connected: serial setting

	Base-line 1	Shunt/ILA open	Base-line 2	RVF (0 Min)	I (5 Min)	II (15 Min)	III (60 Min)	IV (90 Min)	Shunt/ILA clamped
PaO ₂ ¹ (kPa)	27.2 +/-9.7	14.7 +/-4.7	26.2 +/-7.9	29.2 +/-6.6	7.4 +/-1.5	7.9 +/-1.9	7.4 +/-1.1	7.4 +/-1.0	21.5 +/-4.7
PaCO ₂ ² (kPa)	5.1 +/-0.1	3.5 +/-0.3	5.4 +/-0.2	4.9 +/-0.4	3.5 +/-0.1	3.4 +/-0.3	3.3 +/-0.1	3.3 +/-0.2	4.6 +/-0.1
SvO ₂ ³ (%)	74 +/-10.6	66 +/-9.3	73 +/-9.8	43 +/-3.9	36 +/-2.7	36 +/-2.1	37 +/-2.7	36 +/-2.0	38 +/-4.3
Flow sh ⁴ (l/min)	0	1.4 +/-0.3	0	0	1.3 +/-0.3	1.3 +/-0.2	1.1 +/-0.1	1.2 +/-0.3	0

¹ PaO₂: oxygen partial pressure; ² PaCO₂: carbon dioxide partial pressure; ³ SvO₂: mixed venous oxygen saturation; ⁴ Flow sh: Shunt flow.

Table 4. Blood gas analyses group II. The ILA is centrally connected: parallel setting

	Base-line 1	Shunt/ILA open	Base-line 2	RVF (0 Min)	I (5 Min)	II (15 Min)	III (60 Min)	IV (90 Min)	Shunt/ILA clamped
PaO ₂ ¹ (kPa)	17.5 +/-4.9	29.9 +/-5.5	17.6 +/-6.5	18.8 +/-4.9	35.3 +/-5.9	34.1 +/-3.4	35.3 +/-5.7	34.0 +/-4.2	16.4 +/-4.3
PaCO ₂ ² (kPa)	5.1 +/-0.4	3.5 +/-0.8	4.9 +/-0.5	4.2 +/-0.4	2.9 +/-0.3	2.6 +/-0.1	2.6 +/-0.2	2.7 +/-0.3	3.7 +/-0.2
SvO ₂ ³ (%)	63 +/-2.6	69 +/-1.9	64 +/-1.7	41 +/-1.9	65 +/-2.0	63 +/-4.3	64 +/-1.6	64 +/-2.4	44 +/-3.4
Flow sh ⁴ (l/min)	0	1.5 +/-0.3	0	0	2.2 +/-0.3	2.3 +/-0.3	2.4 +/-0.4	2.3 +/-0.4	0

¹ PaO₂: oxygen partial pressure; ² PaCO₂: carbon dioxide partial pressure; ³ SvO₂: mixed venous oxygen saturation; ⁴ Flow sh: Shunt flow

institution of the PA-shunt with the (serial) lung assist no relevant hemodynamic improvement was achievable.

Group II (parallel): An overview of the most important hemodynamic parameters is given in Table 2. The starting of the shunt with the integrated lung assist led to a slight (just ns) decrease of the MAP with an also only slight increase of the CO. Right ventricular filling pressures and all the rest of hemodynamic data remained grossly unchanged. The flow through the shunt and thereby through the lung assist was around 1.25 liters per minute. The RVF appeared as pronounced as in group I. A significant decrease of the MAP (from 69 +/- 4.6 to 43 +/- 5.2 mm Hg) and the CO (from 5.6 +/- 0.7 to 3.0 +/- 0.6 l/min) could be observed. The right ventricular filling pressures rose (significance for systolic right ventricular pressure and for mean pulmonary artery pressures) from 37 +/- 4.1 to 54 +/- 7.7 and 26 +/- 2 to 36 +/- 5.9 mm Hg respectively. In parallel to a significantly reduced RVEF (from 32 +/- 7.4 to 17 +/- 3.1 %) the SVV rose from 4.6 +/- 1.5 to 12.9 +/- 3.0. After opening the shunt with the lung assist the MAP immediately increased significantly from 43 +/- 5.2 mm Hg in RVF to 61 +/- 6.4 mm Hg after 5 minutes of shunting. The CO also significantly increased immediately from 3.0 +/- 0.6 to 5.5 +/- 0.7. In parallel the RVEF significantly rose from 17 +/- 3.1 % to 28 +/- 5.7 %, the SVV decreased again to 6.3 +/- 2.2 %. All these parameters further improved slightly, but did not reach previous (baseline) values. The initial shunt flow 5 minutes after opening the shunt was 2.2 +/- 0.3. Amazingly the right ventricular filling pressures stayed nearly unchanged. Within the next 90 minutes of observation MAP slightly decreased whereas all other hemodynamic parameters stayed unchanged. The shunt flow slowly increased (ns) up to a maximum of 2.4 +/- 0.4 l/min after 60 minutes. When the shunt and thereby the lung assist was clamped again the RVF returned immediately with a significant decrease of MAP and CO. All the rest of the hemodynamic parameters

also indicated a recurrence of severe RVF. The right ventricular filling pressures stayed relatively stable. Taken together in this parallel approach the animals also exhibited a profound RVF but relevant hemodynamic improvement could be achieved by shunting. Even though the hemodynamic parameters improved significantly, they did not return to baseline values completely. This positive effect was neutralized by clamping the shunt again.

4.3. Gasexchange and lung assist

Group I (serial): An overview indicating the most important parameters of blood gas analysis is given in Table 3. The baseline values were within the normal range of an adjusted ventilation with an oxygen supply of 40 %. PaCO₂ is 5.1 +/- 0.1 kPa, the PaO₂ is 27.2 +/- 9.7. The mixed venous oxygen saturation (SvO₂) under the normal circulatory circumstances of baseline measurement is 74 +/- 10.6 %. With the opened shunt and serial lung assist a significant decrease of PaCO₂ down to 3.5 +/- 0.3 was detectable with a concomitant decrease of ph. The PaO₂ decreased with 14.7 +/- 4.7 kPa as well as the SvO₂ (66 +/- 9.3%) did. In RVF a dramatic (significant) decrease of the SvO₂ was detectable whilst the other parameters were relatively unchanged. When the shunt and the lung assist were open, the most obvious finding was a dramatic (significant) and constant decrease of the PaO₂ to 7.4 +/- 1.5 kPa. The SvO₂ stayed low with 36 +/- 2.7 over the whole time of shunting. PaCO₂ declined down to 3.3 +/- 0.1 kPa. With the shunt and lung assist clamped again the PaO₂ (significantly) rose again, the PaCO₂ and ph normalized again. The SvO₂ slightly increased up to 38 +/- 4.3 % again. Taken together in group I institution of the PA-shunt with a serial lung assist in RVF led to severe hypoxemia. Even the mixed venous saturation stayed lower than in RVF.

Group II (parallel): An overview of blood gas analysis in this group is given in Table 4. The baseline

values were within the normal range like in group I. When the shunt with the integrated lung assist was opened PaO₂ significantly increased up to 29.9 \pm 5.5 kPa, the PaCO₂ and pH decreased, mixed venous saturation slightly increased. The RVF displayed similar values of blood gas analysis like in group I especially with a dramatic (significant) decrease of the mixed venous saturation down to 41 \pm 1.9 %. When the shunt with the integrated lung assist was open, in contrast to group I, the PaO₂ increased significantly up to 35.3 \pm 5.9 kPa. Also the mixed venous saturation increased significantly back to normal values of 65 \pm 2.5 %. PaCO₂ and pH both decreased down to minimally 2.6 \pm 0.1 kPa. After clamping the shunt with the lung assist values like in RVF returned with a low mixed venous saturation and significantly lower pO₂. In summary in this group II the PA-shunt with the integrated lung assist in RVF led to an excellent, above-normal oxygenation status with restoration of normal values for mixed venous saturation.

4.4. Echocardiography

In group I no echocardiography was available. In group II for 3 of the 6 animals echocardiography could be performed. Initially (open thorax) the RV displayed grossly normovolemic with a tricuspid annular plain systolic excursion (TAPSE) of 18 mm and a tricuspid annular systolic velocity (TASV) of 10 cm/sec. When RVF was induced, a clearly enlarged RV with notably reduced TASV and septal shift to the left was detectable. During RVF TAPSE and TASV were reduced to 4 mm and 1.5 cm/sec respectively. Opening the shunt only reduced the size of the RV moderately. TAPSE and TASV improved markedly to 13 mm and 5 cm/sec respectively but therewith did not reach baseline values. The septal shift nearly disappeared. When the shunt was clamped again the echocardiographic appearance of the severe RVF returned again. Taken together in group II the echocardiographic findings indicated a recovery from RVF with the opened PA-shunt (and parallel lung assist). This included both an improvement of the right ventricular pump function and a change of septal geometry with repositioning to the right. Another relevant echocardiographic observation was that after an initial slight contamination of left ventricular cavities with air during the implantation procedure the whole further operation of the lung assist in central position did not cause any contamination with gas.

5. DISCUSSION

Right ventricular function is identified to be an independent risk factor for mortality in various diseases like COPD (16), pulmonary hypertension (17) or adult respiratory distress syndrome (18). Often the development of a RVF exhibits the final phase of the disease. In cardiothoracic surgery RVF seems to be a frequent cause for postoperative cardiogenic shock associated with a higher mortality than pure left ventricular failure (19, 20, 21). Surgical options to treat RVF are very limited and implantation of right sided assist devices is associated with a high mortality (22). Even though the whole pathophysiology of RVF is complex (20, 21) one important mechanism is reduced trans-pulmonary blood flow with

decreased left sided filling, what is called serial ventricular interdependence. The latter could be surgically approachable as historically already tried (12, 13). Nevertheless in these studies cyanosis was a major limitation. However today with an ILA a gas-exchange device with an extremely low resistance is available and may be a helpful tool to overcome the problem of cyanosis in this context. Our aim was to investigate whether a combination of right to left shunting (PA-shunt) and an ILA is able to treat RVF. This was approached by an experimental setting with two groups in the animal with a model of RVF. Group I represented a central PA-shunt on the one hand and the lung assist in an interventional position from the femoral artery to femoral vein on the other hand. Because the lung assist is arranged “after” the lung we called this setting serial. This arrangement would theoretically have the advantage of an easy reversal by removal of the lung assist and interruption of the shunt after recovery from RVF. In group II the lung assist was integrated into the PA-shunt and like the shunt driven by the pressure difference between the pulmonary artery and the left atrium. Because in this case the lung assist works in parallel with the native lungs we called this setting parallel.

In group I, the serial setting, the animals did not recover from cardiogenic shock in RVF. Despite sufficient shunting over the central PA-shunt the CO and MAP did not increase. The latter is to explain by the effects of peripheral shunting with a lung assist: At the second measuring point (open PA-shunt and ILA without RVF) it was detectable, that the combination of central shunting with peripheral shunting led to a decrease in MAP. Also in humans, in which a lung assist is installed in an arteriovenous mode, it is known, that because of the left-right shunt a decrease of MAP an increase of the CO results (23). This was also detectable in several pilot tests with the lung assist in pigs: the solely institution of a peripheral arteriovenous lung assist and thereby left-right shunt led to a relevant decrease of MAP and increase in CO due to the increased cardiac volume burden. These two effects seem to work against recovery from RVF: on the one hand decreased MAP worsens RVF by reduced coronary blood-flow and on the other hand increased volume burden to the RV in RVF further increases RV overdistension. The other important factor why in this setting RVF did probably not improve is the profound hypoxemia. The major goal of a peripheral lung assist is CO₂ removal to allow less invasive ventilation rather than oxygenation because the power to oxygenate blood by a pumpless arteriovenous lung assist is very limited due to the fact, that blood flowing through the device is already arterial (23). Although the amount of centrally shunted blood and the one flowing through the lung assist is nearly the same the peripheral lung assist could not provide sufficient oxygenation to balance the central hypoxemia. In contrast to this, in group II, the parallel setting, the animals recovered considerably from the cardiogenic shock caused by the RVF. The MAP and the CO increased significantly when the shunt was opened in RVF. In parallel all other parameters indicated recovery of the shock: the SV increased whereas the SVV decreased; the RVEF increased although baseline values were not reached again. The right ventricular filling pressures remained high during the whole time of shunting. However

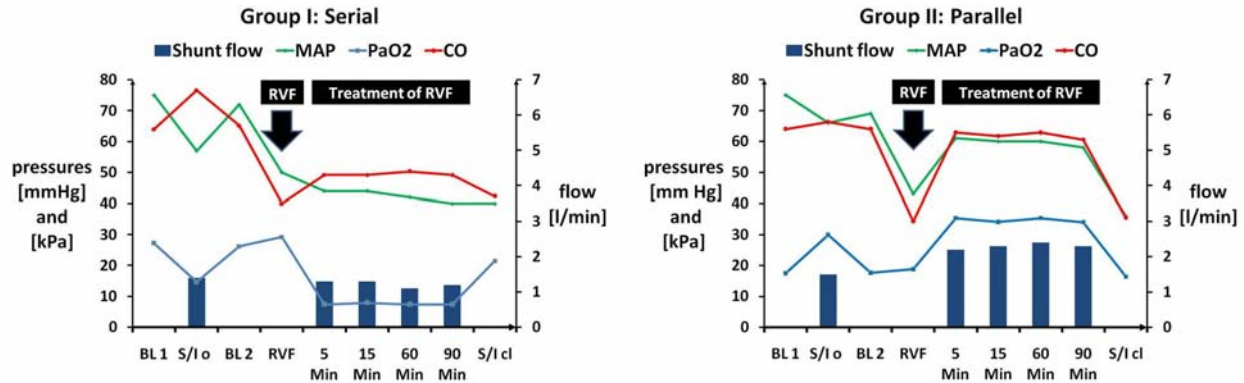


Figure 5. Overview showing the course of the most important hemodynamic data combined with gas exchange parameters for the two groups: Note, that in Group I with open shunt and ILA the PaO₂ is critically lowered whereas in Group II it is increased to supra normal values.

this seems not to be a refutation against recovery from RVF because in our model in further untreated profound RVF with cardiogenic shock these pressures even decreased. In this case with recovering MAP and CO the still high right ventricular filling pressures seem to be an indication for the fact that the RV is still able to produce high filling pressures and is not failing. With the shunt open the mixed venous oxygen saturation reached baseline values again also indicating recovery from cardiogenic shock. To our surprise the blood gases developed exciting: in this setting with an inflow of mixed venous blood with low oxygen content into the lung assist besides to a strong CO₂ elimination a powerful oxygenation of centrally shunted blood could be obtained leading to supra normal PaO₂ values. These latter findings certainly contributed to overall recovery from cardiogenic shock. Echocardiographically besides of a major recovery of the RV no relevant side effects of a central lung assist like for example air bubbles in the left sided cavities could be detected. Taken together the major reason for the different course of the RVF in the two groups seems to be a different influence of the lung assist on hemodynamics and even blood gasses which is only caused by the installation arrangement of the lung assist (Figure 5). Pathophysiologically the hemodynamic changes accord very well with the concept of serial ventricular interdependence: In group I the workload of the RV is not changed because the peripheral lung assist causes an additional volume load to the RV whereas in group II selectively right ventricular afterload is reduced combined with increased left ventricular preload. Very similar results like our group II could be obtained by Haft in 2001 (24), when he investigated their experimental artificial lung. He could demonstrate that an artificial lung reduces right ventricular load and improves ventricular efficacy in the setting of pulmonary hypertension. This concept to avoid serial ventricular interdependence by oxygenated shunting from the right sided heart to the left sided may also be successful in other aetiologies of RVF. Although the interventional lung assist has not been approved for a central implantation yet, during our experiments some sporadic cases have been published (25, 26, 27, 28) using this technique in different intentions.

In some cases successful bridging until lung transplantation was possible. Whereas the use of the interventional lung assist as a tool to treat pulmonary hypertension respectively RVF proved mainly successful its use as artificial lung proved difficult. Taking together our experimental results and present human cases a central implantation of an interventional lung assist may develop to a reasonable part in the therapy of RVF. A minimally invasive central implantation, at least explantation, should be possible to realize in the future.

Limitations: In this experimental study no high fidelity cardiopulmonary recording was used. Especially the different methods to determine the cardiac output with derived parameters have to be seen with caution; although the pulsecontour analysis measurements which could be obtained in these experiments were with a partial right to left shunt, they demonstrated quite coherent with the other measurements. This may be explained by a similar transit pattern of blood through the native lungs and the lung assist. Nevertheless all measurements taken together allow for a realistic evaluation of the overall picture. The use of other RVF models, the determination of long term results and more detailed echocardiographic investigations are a matter of further investigations.

Conclusion: In this study we could demonstrate, that a PA-shunt with an integrated lung assist (parallel setting) can effectively reverse most of the deleterious effects of hypertension-induced RVF probably by overcoming ventricular interdependence. Moreover, in this pumpless, centrally placed setting an excellent oxygenation of blood can be achieved, which augments reversal of RVF and opens options for further fields of application. More studies are needed to define exact clinical indications and the long term behavior of such a parallel "artificial lung".

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Abbreviations: CO: Cardiac Output; ILA: Interventional lung assist; l/min: liters per minute; MAP: Mean arterial pressure; mm Hg: Millimeters of mercury; ns: not significant; PA-shunt: Pulmonary artery to left atrium shunt; RV: Right ventricle; RVF: Right ventricular failure; SD: Standard deviation

Key Words: Right ventricular failure, shunt; pulmonary artery, lung assist, left atrium, cyanosis, oxygenation, parallel

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