

# Acute right heart failure: future perspective with the PERKAT RV pulsatile right ventricular support device

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**Abstract:** Acute right heart failure is associated with impaired prognosis in cardiogenic shock. Since most pharmacological therapies are not evaluated for the failing right ventricle, or even contraindicated, there is a need for rapid minimal invasive circulatory right heart support. The PERKAT RV is such a device for acute therapy in congestive heart failure. It reduces the central venous pooling by pumping blood from the inferior vena cava into the pulmonary artery with flow rates of up to 4 litres/min. The device was evaluated in an animal model of acute pulmonary embolism after careful *in vitro* tests. PERKAT RV increased cardiac output by 59% in sheep suffering from acute right heart failure. We await the first human implantation in the near future. Based on the PERKAT concept, future development will also focus on left heart support.

**Keywords:** circulatory assist device, pulmonary embolism, right heart failure, shock

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More than 6 million people (2.4%) suffered from chronic heart failure in the United States (US) in 2016, with a projected increase up to 3% of the population within the next decade.<sup>1</sup> In 2016, there were nearly 340,000 deaths related to heart failure (acute decompensation or worsening of pre-existing condition). Between 15% and 24% of heart failure patients suffer mainly from right heart insufficiency.<sup>2</sup> Thus, acute right heart failure accounts for 50,000–80,000 deaths in the US per year. Right ventricular failure is a clinically challenging problem. While most therapeutic measures in emergency and intensive care medicine focus on left ventricular support, only a few have been evaluated for the right ventricle.<sup>3</sup> Thus, the role of the right ventricle in acute heart failure has been overlooked for many years, in particular because it was considered a so-called passive chamber.<sup>4</sup> Most drugs are approved only for use in acute left ventricular insufficiency, but not for the failing right ventricle.<sup>5</sup>

## Pathophysiology of right ventricular failure

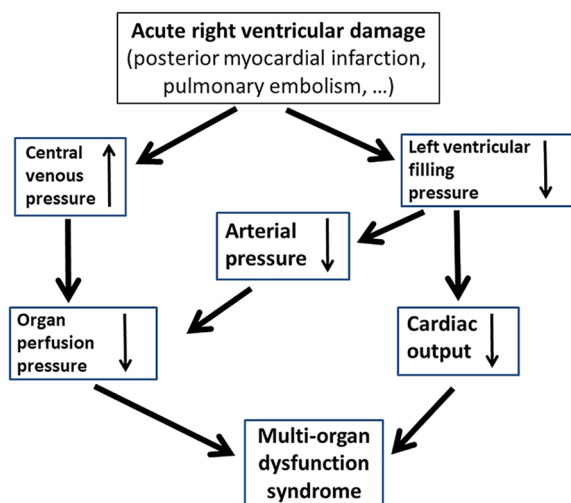
The left and right ventricles are closely linked regarding their function. While left ventricular

stroke work maintains the forward momentum of blood into a relatively rigid high pressure vasculature, the right ventricle generates minor systolic pressures in the low resistance circulatory vasculature of the pulmonary arteries. Systolic pressure is reduced in the case of acute right ventricular damage associated with an increase in right ventricular volume.<sup>6</sup> Acute deterioration of chronic right ventricular insufficiency is deleterious as the thinner wall of the right ventricle is unable to compensate for an acute increase in afterload.<sup>7</sup> Clinical studies have demonstrated that right ventricular failure increases short-term mortality in acute myocardial infarction.<sup>8</sup> Acute myocardial infarction of the right ventricle occurs in one-third of all myocardial infarctions.<sup>9</sup> Pulmonary embolism is the second most common reason for acute right heart failure. Other reasons include myocarditis, acute chronic pulmonary hypertension, postcardiotomy syndrome, pericarditis with pericardial effusion, cardiomyopathy including right ventricular dysplasia, left ventricular circulatory support devices and heart transplantation.

Right ventricular failure results in impaired cardiac output (CO) due to insufficient left ventricular

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**Figure 1.** Deleterious cascade of acute right heart failure.

filling, and increased central venous pressure (CVP) with congestive heart failure. The organ perfusion pressure is the difference between mean arterial pressure (MAP) and CVP. A decrease in MAP due to impaired CO, in combination with increased CVP, finally leads to multi-organ hypoperfusion syndrome and profound cardiogenic shock (Figure 1). Thus, acute restoration and stabilisation of organ perfusion pressure is of utmost importance for patient recovery and survival. Acute circulatory support can overcome this deleterious haemodynamic situation. The right ventricle benefits from pulsatile support in the recovery phase as shown recently in animal experiments.<sup>10</sup> In addition, pulsatile circulatory support has certain advantages compared with continuous flow pumps regarding the microvasculature or coagulation state of the patient.<sup>10–12</sup> However, pulsatile devices like the intra-aortic balloon pump (IABP) have failed to improve overall mortality in cardiogenic shock due to relatively low circulatory support of <0.5 litres/min.<sup>13,14</sup>

Impaired right ventricular pulsatility is associated with an increase in mortality in end-stage heart failure patients.<sup>15</sup> Therefore, pulsatile support may be beneficial in acute right heart failure and may result in more rapid recovery. This offers a novel therapeutic option in acute myocardial infarction with right ventricular involvement or in acute pulmonary embolism providing a haemodynamically stable condition and avoiding

multi-organ failure syndrome. Therefore, we searched for a minimally invasive, pulsatile right ventricular support device providing rapid haemodynamic stabilisation in acute right heart failure with pump flows of >3 litres/min.

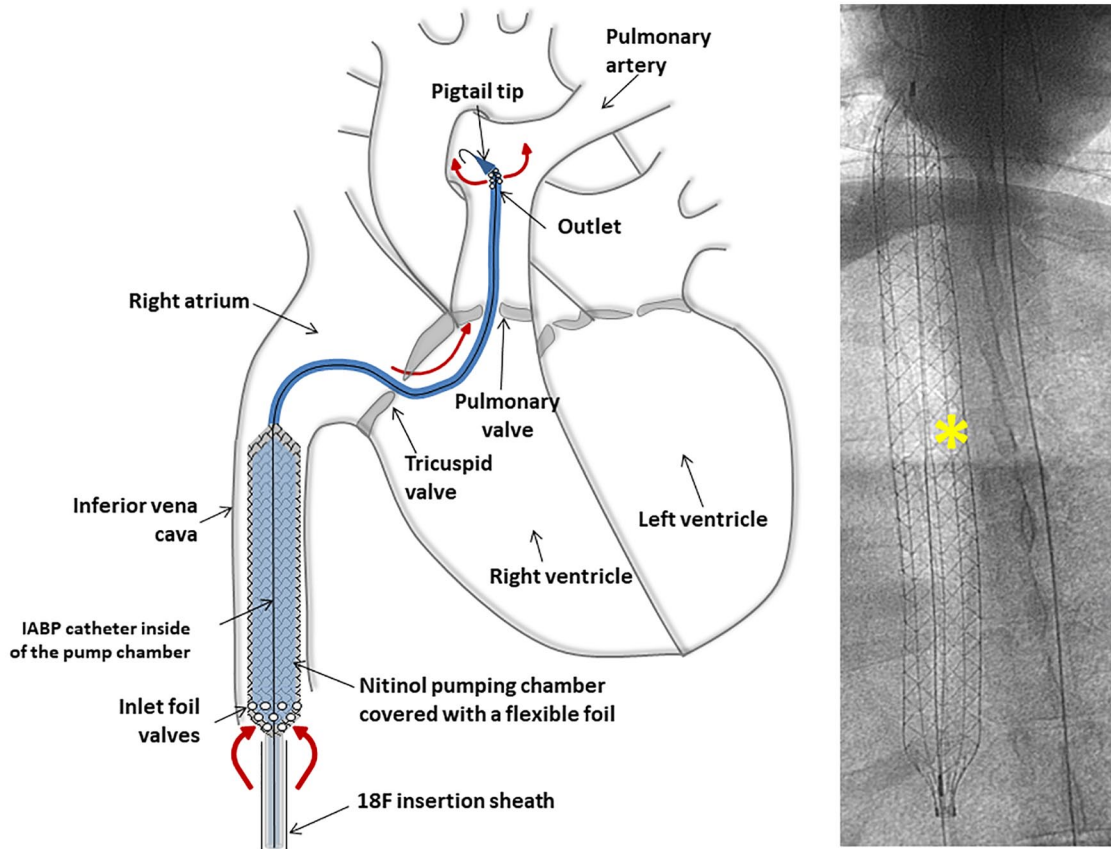
### Design of the PERKAT RV

The implantation process of PERKAT RV requires insertion of a 260 cm stiff guidewire into the pulmonary artery for rapid percutaneous implantation of the pump device. The folded device comes premounted inside the 18F insertion sheath. The device consists of a flexible catheter with a self-expanding pump chamber, which is placed by percutaneous insertion from the femoral vein into the inferior vena cava.<sup>16</sup> Pulling back the external implantation sheath results in unfolding of the flexible pump chamber. In a second implantation step, a standard IABP balloon is inserted into the nitinol pump chamber. This balloon is inflated with helium gas and deflated by an external standard IABP console. The pump chamber is covered with foil, which includes multiple foil valves allowing blood inflow from the vein during deflation of the IABP balloon. Inflation of the balloon pumps the blood into the pulmonary artery trunk through a flexible outlet tube, bypassing the right atrium and right ventricle (Figure 2). The pigtail tip provides angiographic visualisation and a stable position of the outlet of the pump device in the pulmonary artery. The tapered pigtail tip allows percutaneous insertion over a 0.035 inch guide wire. The pump chamber can be removed by refolding into the femoral sheath.

### Experimental evaluation of the device

The PERKAT RV device was intensively tested *in vitro* and *in vivo*.<sup>17</sup> The inlet foil valves and the outlet tubing were optimised based on the results of *in vitro* tests. We measured flow rates of nearly 4 litres/min by variation of afterload, inflation/deflation rate, balloon size and fluid medium.<sup>18</sup>

First *in vivo* evaluation focussed on an animal model of acute right heart failure. We induced acute pulmonary embolism in eight sheep by repetitive injection of Sephadex microspheres (diameter 40–120 µm) through a pigtail catheter into the pulmonary artery until an increase in pulmonary artery pressure of at least twofold and a



**Figure 2.** Concept and X-ray of the PERKAT RV device. The blood is pumped from the inferior vena cava into the pulmonary artery trunk through a flexible outlet tube. An IABP balloon catheter is deflated and inflated with helium gas inside the pump chamber [\*]. IABP, intra-aortic balloon pump.

decrease of cardiac output by  $>50\%$  to  $<2.5$  litres/min occurred.<sup>19</sup> Unfortunately, one animal died of severe arrhythmias before implantation of the device. In the remaining seven sheep, it was possible to insert the PERKAT RV device through the femoral vein using Seldinger's technique within less than 5 minutes. It was possible to puncture the vein directly after inguinal skin incision. We administered 5000 IU of heparin after insertion of the 18F system. Blood samples were taken every hour for measurement of activated clotting time (ACT). We maintained  $ACT > 250$  s by additional heparin bolus injections of 2000 IU. Anticoagulation management in humans will use an  $ACT > 250$  s as long as the device is in place. However, it will be necessary to avoid any longer periods of pump arrest to prevent thrombus formation. We inspected the device for any thrombus formation at the end of the experiment after 4 h (three animals), and after 8 h (four animals) of support. There were

no signs of any thrombus formation in all 7 samples at the end of the experiment.

Starting the pump resulted in immediate hemodynamic stabilisation. CO increased by 59% upon starting pump support. Urine output was measured hourly with a bladder catheter during the experiment; there was no relevant change in urine volume during the 4 h duration of the experiment. We were able to remove the device in all sheep through the percutaneous sheath at the end of the experiment without any relevant damage to the access site in the groin. We did not observe any relevant haemolysis in the blood samples taken, no macroscopic thrombus formation or other adverse side effects in this series of acute experiments.

Based on the successful development of the minimal-invasive pulsatile PERKAT concept, we elaborate a left heart support device pumping

blood from the left ventricle into a pump chamber with outlet valves in the descending aorta. Preliminary *in vitro* tests revealed flow rates in the arterial circulation of up to 4 litres/min when using a similar diameter of the device.

The percutaneous rapid implantation and the easy removal of the PERKAT RV might give an option in acute cardiac care and intensive care medicine for acute right heart failure even in multimorbid patients. We await first human implantation in the next year based on promising *in vitro* and *in vivo* experiments. Clinical studies will allow precise definition of indications and contraindications for this novel circulatory assist device.


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### Conflict of interest statement

MWF is cofounder and shareholder of Novapump Inc., PCS, and DK declare no conflicts of interest.

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