Hemodynamical Evaluation of a New Surgically Implanted Pulsatile Right Ventricular Assist Device Driven by a Conventional Intra-Aortic Balloon Pump Console

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Severe right heart failure, often overlooked and challenging to manage, has prompted a growing interest in innovative approaches to provide functional support. This study uses experimentation in large porcine models to introduce a novel prototype of a pulsatile mechanical circulatory support device and document its effects when deployed as a right ventricular assist device (RVAD). The pulsatile ventricular assist platform (pVAP), featuring a membrane pump driven by an intra-aortic balloon pump console, actively generates pulsatile flow to propel right ventricular blood into the pulmonary artery. This novel prototype demonstrates promising potential in addressing the challenges of right heart failure management. After preliminary *in vitro* assessments, the pVAP was tested on seven porcine models in a healthy state and after the induction of right ventricular failure. During the procedure, a set of standard (*ie*, standard-of-care) hemodynamic measurements was obtained. Additionally, invasive pressure-volume loop analysis was employed to examine left ventricular hemodynamics. Results indicated that activation of the pVAP during right ventricular failure significantly improved systemic hemodynamics and enhanced left ventricular function. This study sheds light on the potential of the pVAP in managing right heart failure. *ASAIO Journal* 2024; XX:XX–XX

Key Words: paracorporal pulsatile pump, percutaneous RVAD, right heart failure, right ventricular assist device

Outcomes of heart failure patients supported by ventricular assist devices (VADs) have continually enhanced during the past decade, mainly due to improved patient management[1] and minimally invasive techniques for implantation.[2]

Right VADs (RVADs) are used less frequently than left VADs (LVADs) due to the relatively lower incidence of isolated right ventricular failure (RVF) and the additional risk of rupture of the RV walls, which are thinner compared to those of the LV.[3–5] The initial management of RVF is conservative, but severe cases may require the use of RVADs or extracorporeal membrane oxygenation (ECMO).

The primary goals of RVAD therapy are to improve the patient's outcomes by optimizing systemic perfusion and decongesting the venous circulation. As such, RVADs can be used as bridge-to-decision, bridge-to-transplantation, or bridge-to-recovery in treating acute and chronic RVF.[4,6] Regardless of the indication, healthcare providers must weigh the potential clinical benefits against the risk of complications resulting from different insertion techniques. Methods for inserting cardiac devices include surgical insertion through sternotomy or thoracotomy,[7] and percutaneous insertion using a large-bore central venous access. Although a percutaneous approach is associated with lower morbidity, this technique is currently limited to short-term devices.[8]

Studies on the use of RVADs show that mechanical circulatory support (MCS) can decrease instability risk in the cardiac operating room (OR) or catheterization laboratory (CathLab), thereby improving short-term survival.[9,10] The hemodynamic effect of MCS is dependent on various factors, including the type of output flow applied. According to evidence, pulsatile flow is more effective as a circulatory backup and more physiologic than continuous flow. Although the first generation of durable VADs was mainly composed of pulsatile pumps, contemporary short- and long-term devices rely on continuous flow.[11,12] Developing new pulsatile RVADs may, therefore, enhance the efficacy of MCS and potentially improve clinical outcomes.

This report presents the first use of a newly developed pulsatile ventricular assist platform (pVAP) as an RVAD in a small cohort of porcine models. The study aims to assess the feasibility, safety, and efficacy of an *in vivo* mockup model of acute RVF.

Materials and Methods

The pVAP prototype is intended for short-term MCS in ORs and CathLab settings. The main component is a T-shaped splitter with a flow-driven, two-way valve on its lumen (Figure 1B). One opening of the splitter is connected into the membrane pump, whereas the other two openings serve as inlet and outlet
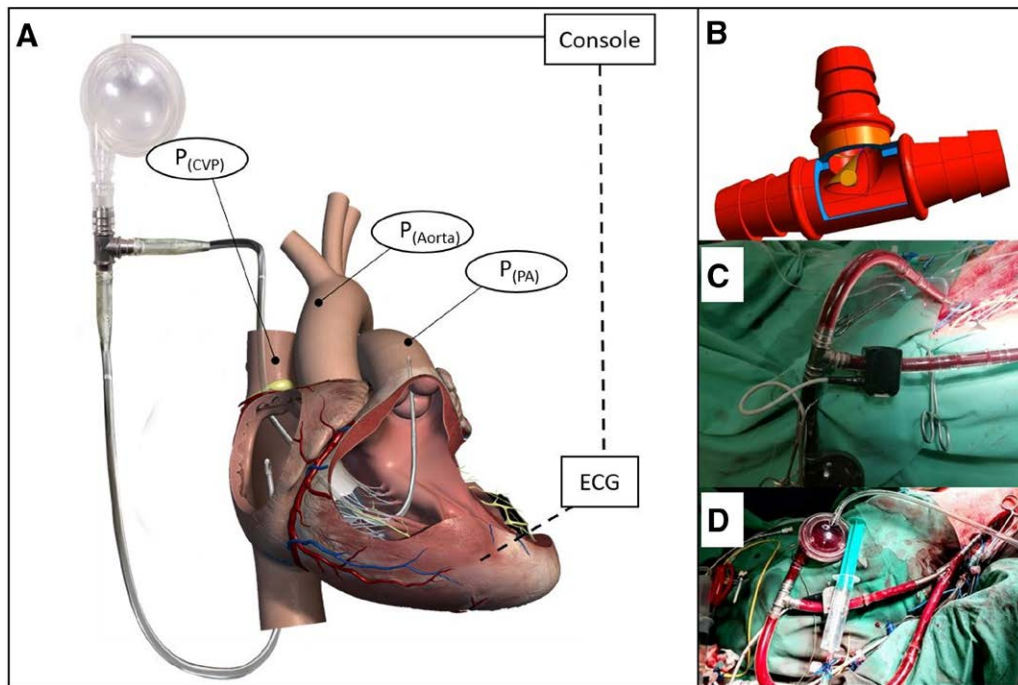
Figure 1. Schematic illustration of the circulatory setup. The membrane pump device and the interventional double-lumen catheter create a bypass of the right heart. Blood pressures are measured in the vena cava (CVP), in the PA, and in the aorta. **A**: Schematic illustration of the pVAP. **B**: Flowmeter clip at the outlet tubing of the paracorporeal pulsatile pump. **C, D**: Overall setup of the MCS device in the pig. CVP, central venous pressure; MCS, mechanical circulatory support; PA, pulmonary artery; pVAP, pulsatile ventricular assist platform.

ports for blood. The surgical operator places specific cannulas on the desired heart chambers or blood vessels and connects them to the splitter. Once positioned, they function as inlet and outlet conduits.

The membrane pump is connected to a conventional intra-aortic balloon pump (IABP) console. It is divided into a blood chamber and a helium chamber by a thin, flexible membrane. The two-way valve directs the flow by occluding the systolic outlet port and the diastolic inlet port. Gas aspiration from the helium chamber moves the flexible membrane during systole, and creates negative pressure on the blood chamber, which is filled with blood from the circulation. During diastole, the helium chamber inflates and compresses the blood chamber, expelling the blood back into circulation through the outlet cannula (Figure 1, A–D). The pVAP can eject a volume of 55 ml per stroke. The rate at which aspiration/ejection cycles occur can be set autonomously at the IABP console or matched with the native heart rate using the ECG or the blood pressure waveform. The ratio between the patient's heart rate and the pVAP's pumping rate can be set at 1:1 for full support or 1:3 in specific situations such as during arrhythmias or the weaning phase.

In Vitro Evaluation

A preliminary *in vitro* experiment was performed to evaluate the prototype's performance. A test medium consisting of a 35% glycerol/water mixture was used to reproduce the rheological properties of the blood at a hematocrit of 40%. The experimental setup comprised a tank filled with the test medium. The pVAP membrane pump was connected to a double-lumen cannula (ProtekDuo, CardiacAssist, Pittsburgh, PA). The

inflow and outflow cannulas were set at the corresponding water levels so that the inflow pressure could be adjusted to 6 mm Hg, representing the RV preload. The outflow pressure was set between 8 and 25 mm Hg, representing the pressure in the pulmonary artery. An IABP console (Getinge AB, Växjö, Sweden) was used to set the pump frequency to 80 bpm. The data were recorded using a flowmeter (em-tech GmbH, Finning, Germany).

In Vivo Evaluation

Seven healthy pigs weighing between 69 and 87 kg were anesthetized, sedated, and continuously monitored. The seventh animal was monitored using a 7 Fr conductance catheter (CC) and a dedicated console (CD Leycom, Hengelo, the Netherlands). The CC was positioned in the LV to obtain real-time pressure-volume (PV) data. Anticoagulation was achieved using unfractionated heparin (activated clotting time (ACT) >190 seconds). After pulmonary catheterization, the pVAP was inserted. In the first two animals, a ProtekDuo double-lumen catheter (CardiacAssist in Pittsburgh, PA) was percutaneously inserted through the internal jugular vein without a sheath. The catheter has an outer diameter of 29 Fr and contains a 16 Fr catheter within its lumen. The remaining fraction of the lumen, which is not occupied by the inner catheter, is equivalent to a 14 Fr catheter. The inlet was positioned in the RV, and the outlet was set in the pulmonary artery (Figure 1A).

In the four remaining animals, the T-shaped splitter was connected to two separate catheters (Bio-Medicus NextGen Cannulae, Medtronic, Meerbusch, Germany) of 17 Fr (inlet) and 19 Fr (outlet). The 17 Fr inlet cannula was inserted into

the internal jugular vein and positioned in the vena cava. The 19 Fr outlet cannula was surgically placed in the pulmonary trunk *via* sternotomy. The device was driven by a standard IABP console in all animals. The console operated independently and asynchronously with respect to the native heart rate. The flow rate at the pump outlet was measured using a flowmeter. Blood pressure was measured in the ascending aorta and the pulmonary trunk. Measurements were taken with the device both on and off in a healthy state. Due to concerns regarding the structural stability of the used prototype, the frequency of the IABP console was limited to values between 40 and 85 bpm.

Right ventricular failure was simulated in animals 3–6. Instead of using primary RV systolic dysfunction, for ease of manipulation and control of extent of hemodynamic deterioration, we chose a model of augmented RV afterload by pulmonary arterial clamping[13] proximal to the device outflow site, wherein our device yet could provide assistance by augmenting blood flow into the PA, functionally "bypassing" the iatrogenic stenosis. Clamping was adjusted to produce a stenosis of 50%. Hemodynamic measurements were obtained with the device turned off and subsequently turned on. After the experiments were concluded, the animals were sacrificed. The study was conducted in strict adherence to the laws and regulations governing animal welfare stipulated by the German authorities. This study was approved by the Niedersächsische Landesamt für Verbraucherschutz und Lebensmittelsicherheit (LAVES) with approval number 23-00361 on August 12, 2023.

Pressure-Volume Loop Measurements

For animal 7, left ventricular (LV) PV loops and standard monitoring were recorded. The CC was introduced *via* the carotid artery and positioned across the aortic valve with the CC's tip in the LV apex. The pVAP prototype was placed on the right circulation, as in the other animals. Cardiac output (CO) was determined using the pulse pressure method (HemoSphere monitor, Edwards Lifesciences Corporation, Irvine, CA). Measurements were taken with the device both off and on.

Data Analysis

Continuous data are expressed as mean ± standard deviation (SD). Differences in hemodynamical measurements taken at different states were tested for statistical significance using Student's t-tests for two paired samples. All statistical analyses considered $p < 0.05$ as significant. Data input and analysis were conducted in Microsoft Excel 2019 (Microsoft Corporation, Redmond, USA).

Results

In Vitro

When the IABP console was set to a rate of 80 bpm, sequential increases in the outflow pressure within the range of 8–25 mm Hg consistently decreased the pump outflow (Figure 2). The pump exhibited a backflow of 0.1 L/min regardless of the outflow pressure. At 25 mm Hg, the observed pump outflow was 2.7 L/min.
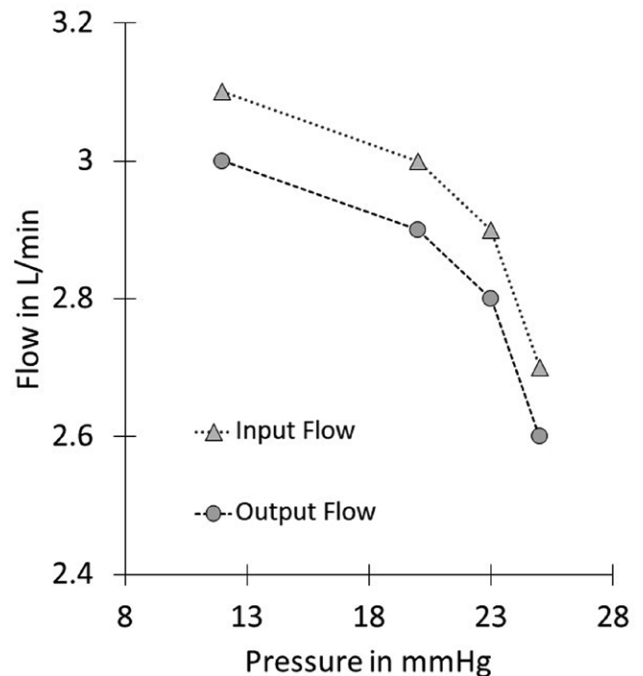

Figure 2. Dependence of device's inflow and outflow on the pressure that is applied to the outlet opening, representing the pulmonary artery pressure, at a constant pressure of 6 mm Hg on the inlet opening. The difference between the inflow and the outflow curves indicates the backflow.

In Vivo

Blood pressure at different pumping rates set on the IABP console is shown in Figure 3, A and B. A nonsignificant trend toward an increase in blood pressure was observed in the aorta. The systolic blood pressure (SBP) increased by +5.1±3.1 mm Hg ($p = 0.06$); the diastolic blood pressure (DBP) by +3.1±1.8 mm Hg ($p = 0.09$); and the mean arterial pressure (MAP) by +4.2±1.7 mm Hg ($p < 0.05$). In the pulmonary system, pressures remained stable (pulmonary artery systolic pressure [PASP]: +1.2±2.5 mm Hg, $p = 0.4$; pulmonary artery diastolic pressure [PADP]: −0.3±1.3 mm Hg, $p = 0.5$; mean pulmonary artery pressure [Mpap]: +0.6±4.8 mm Hg, $p = 0.17$).

Activation of the pVAP in a healthy state resulted in a rightward and upward shift of LV PV loops compared to the "off" state. Left ventricular systolic pressures and end-diastolic volume increased, resulting in higher stroke volume. The end-systolic volume increased slightly. Phase shift was observed in the isovolumetric contraction phase of the cardiac cycle after activation (Figure 4A).

Heart Failure Model

Figure 5A illustrates the changes in aortic pressures before clamping, during 50% clamping, and after activation of the pVAP. In the aorta, 50% pulmonary artery clamping significantly decreased SBP (−18.2±6.1 mm Hg, $p < 0.01$), DBP (−12.7±3.6 mm Hg, $p < 0.001$), and MAP (−15.0±3.8 mm Hg, $p < 0.001$). After the clamp was applied, activating the pump resulted in a significant increase in SBP by +15.0±6.9 mm Hg ($p < 0.01$), DBP by +10.0±4.8 mm Hg ($p < 0.05$), and MAP by
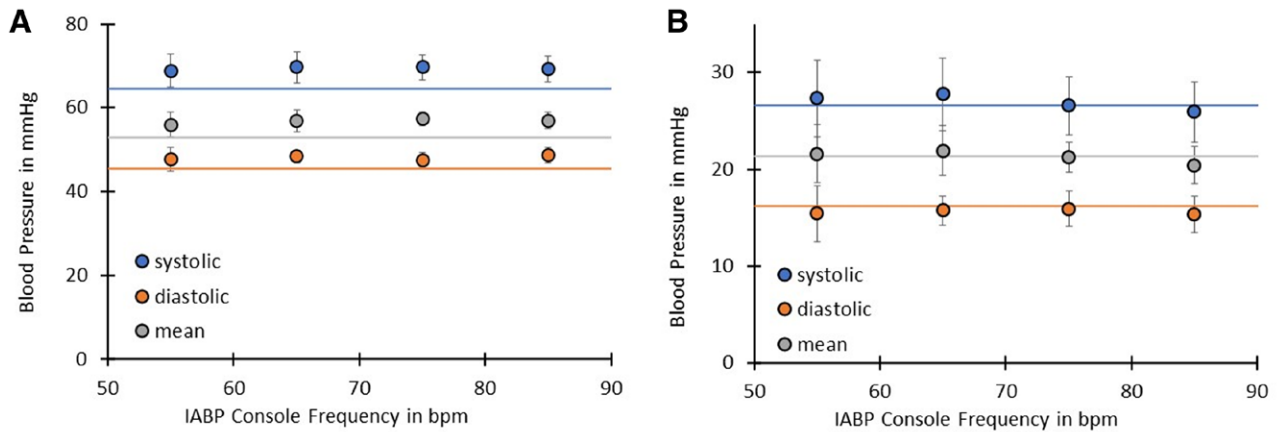
Figure 3. Response of the aortic blood pressure (**A**) and pulmonary artery blood pressure (**B**) to different pumping rates in healthy pigs. The lines represent the baseline pressure of the healthy animals with the pump OFF.
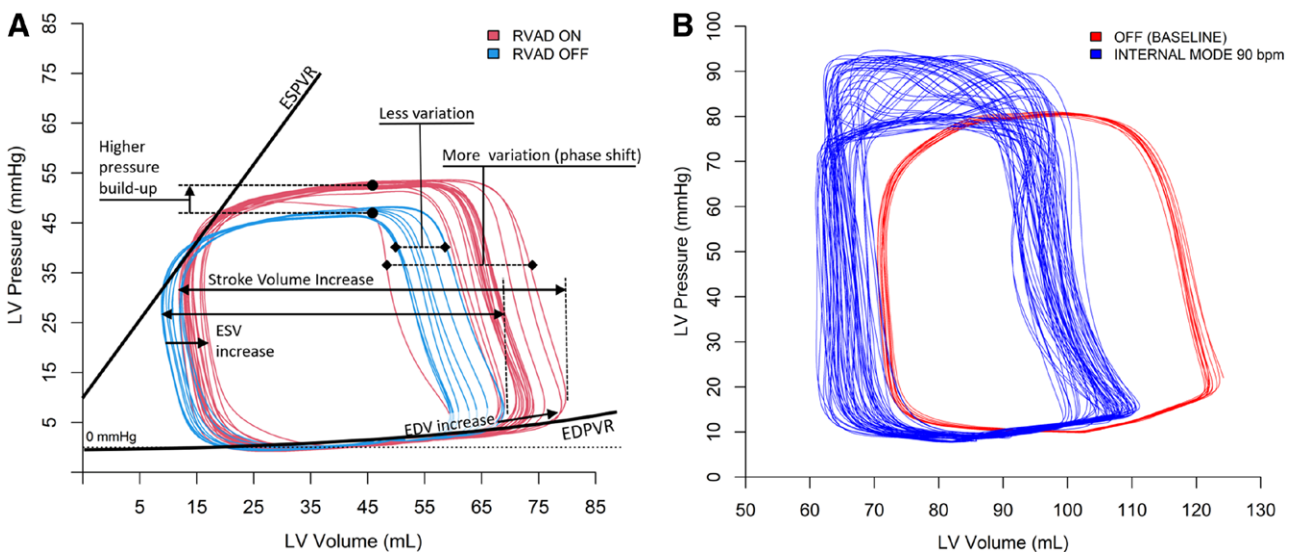

Figure 4. LV PV loops from animal 7. **A**: A shift to the right and upward indicates that a sudden increase in LV load occurred when the RVAD was activated. The isovolumetric contraction phase (right side of the PV loop) shows a more remarkable shift in the volume dimension than the isovolumetric relaxation phase (left side of the PV loop). This indicates that the additional load is most likely due to additional preload. A broader postactivation PV loop indicates that SV also increased, and the elevation of the upper side of the PV loop indicates increased systolic pressures. Both changes are directly related to the RVAD-mediated increase in preload. The morphology of the PV loop and the end-diastolic pressures remain relatively unchanged, indicating that LV loading remains in the physiologic range. **B**: Left ventricular PV loops recorded with the pVAP positioned and activated in the LV (data not published). With the device deactivated, the PV loops are structurally uniform. When the device is activated in internal mode, the PV loops shift to the left but two morphologies appear in the ejective phase (upper side), evidencing phase shift. EDPVR, end-diastolic pressure-volume relationship; EDV, end-diastolic volume; ESPVR, end-systolic pressure-volume relationship; ESV, end-systolic volume; LV, left ventricle; PV, pressure-volume; RVAD, right ventricular assist device; SV, stroke volume.

$+11.0 \pm 4.7$ mm Hg ($p < 0.01$). The aortic pressure returned to levels up to 93% of the initial preclamping state.

In the pulmonary circulation, clamping the pulmonary artery by 50% significantly decreased PASP by -6.6 ± 2.5 mm Hg ($p < 0.05$) and mPAP by -4.5 ± 3.0 mm Hg ($p < 0.05$). The PADP nonsignificantly decreased by -3.6 ± 3.4 mm Hg ($p = 0.1$). When the pVAP was activated while the pulmonary artery was clamped, it caused a significant increase in the PASP by $+5.7 \pm 2.5$ mm Hg ($p < 0.05$), in the PADP by $+4.3 \pm 3.1$ mm Hg ($p < 0.05$), and in the mPAP by $+5.6 \pm 3.7$ mm Hg ($p < 0.01$). Upon activation of the pVAP, the blood pressure values in the pulmonary artery returned to preclamping levels (Figure 5B).

Fifty percent of pulmonary artery clamping increased central venous pressure (CVP) by $+2.6 \pm 1.0$ mm Hg ($p < 0.05$). After activation of the pVAP, the CVP nonsignificantly decreased by -1.9 ± 1.4 mm Hg ($p = 0.13$). CVP results are shown in Figure 6.

Discussion

This study describes the development and experimental testing of a new pulsatile VAD specifically configured for right ventricular support. The platform was evaluated in large animal models, focusing on its performance and efficacy in the context of RVF. The pVAP was pneumatically driven by a standard
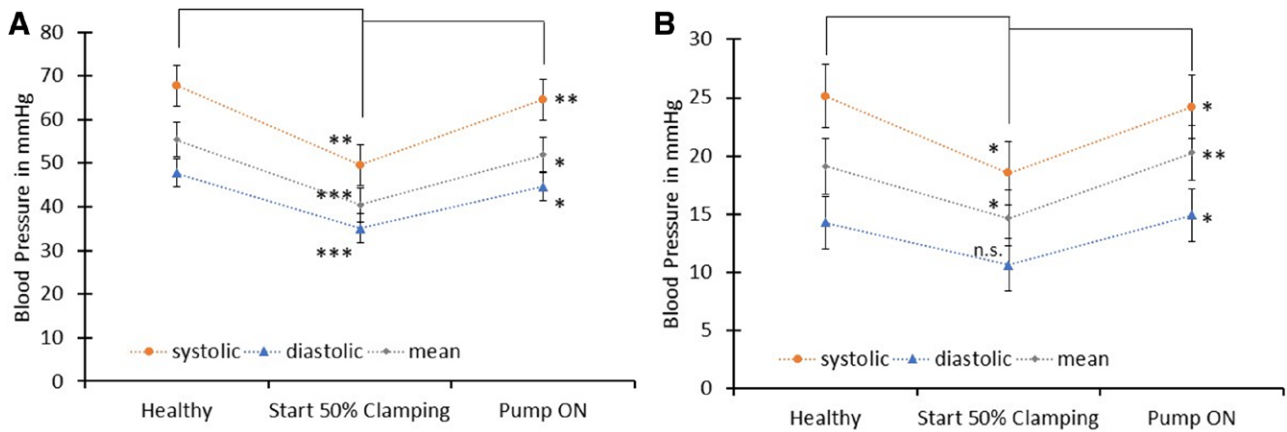
Figure 5. Variation of blood pressure in the systemic circulation (**A**) and in the pulmonary circulation (**B**) from healthy state through clamping and subsequent recovery after the device is activated. Activation of the right ventricular assist device resulted in significant increases in blood pressure and optimized hemodynamics back into preclamping values. (* < 0.05; ** < 0.01; *** < 0.001), (n = 4). n.s., not significant.
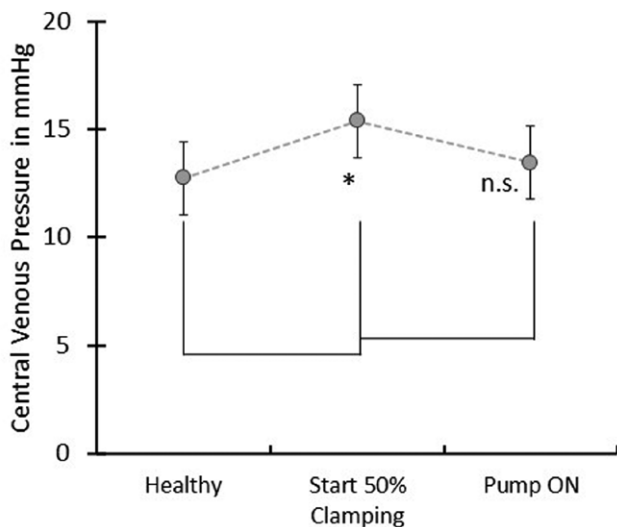

Figure 6. Central venous pressure progression from healthy state through clamping and subsequent recovery of blood pressure through the pump. (* < 0.05; ** < 0.01; *** < 0.001), (n = 4). n.s., not significant.

IABP console. The main findings indicate that the pVAP is feasible and effective. The following points summarize the findings: 1) the output flow of the pVAP is directly influenced by the pressure in the output chamber; 2) the pVAP produces an output of 2.7 L/min; 3) the pVAP has a minor, but observable, hemodynamic effect in healthy individuals; and 4) in cases of acute RVF, activating the pVAP significantly improves hemodynamics in both the pulmonary and aortic circulations.

The pVAP is based on the iVAC system (PulseCath BV, Arnhem, the Netherlands). The iVAC system is a percutaneous LVAD used for short-term support during high-risk interventions. The iVAC system can be operated using a standard IABP console and can function in either synchronized or nonsynchronized modes. In synchronized mode, the IABP console follows the cardiac cycle and is triggered by either the ECG signal or the arterial pressure waveform. In the internal mode, the pumping rate is autonomously set at the IABP console which operates independently of the heart's rhythm. The output flow of the pump is rate-dependent and works best at rates around

80–90 bpm. If the patient's heart rate deviates from the optimal range while using the device in synchronized mode, it may result in reduced performance. Operators should then consider switching the IABP console to internal mode to avoid any loss of performance. The relationship between pump output and pumping rate has already been explained in the previous versions of the iVAC system (iVAC3L and iVAC2L). Reportedly, the best performance for iVAC2L has been observed between 70 and 90 bpm.[14] The iVAC devices and the pVAP are both membrane pumps with frequency-dependent outputs. They have similar designs and materials, which lead to a similar optimal operation range between 80 and 90 bpm.

The RVF model clearly evidenced the effect of pVAP on left circulation when used as an RVAD. A comparable pattern was also be observed in the healthy state, albeit with a smaller magnitude. This could be attributed to certain aspects of MCS physiology. First, the hemodynamic effects of MCS are influenced by the pump output in liters per minute, and by the patient's preassist ventricular function. The data show an output of approximately 2.7 L/min, which corresponds to partial support. Second, in the MCS setting, it is important to consider that the standard measurements provide the total (or forward) CO (CO_T), which comprises the native heart's output (CO_N) added to the pump's output. When MCS is activated, the device unloads the heart chamber where the inlet is located and ejects blood into the arterial system thus increasing the MAP. Compensatory reflexes such as those mediated by carotid baroreceptors often down-regulate the heart's autonomic tone, causing CO_N to decrease and consequently reducing the myocardial oxygen demand. This concept is critical in understanding the physiologic response to MCS in both health and disease.

Heart failure and cardiogenic shock are conditions that may worsen with persistent hypotension and peripheral vasoconstriction. These changes may affect the autonomic response to MCS, making compensatory mechanisms less likely to down-regulate the already depressed CO_N. As a result, there may be more noticeable increases in CO_T in response to MCS.[15,16] As such, when activated during simulated RVF, the pVAP significantly improved arterial and pulmonary pressures, whereas having only a minor effect on the healthy state. This optimization of the cardiac function back to nearly physiologic levels

and the reduction in venous congestion observed in the current study are well-documented in the literature as known effects of MCS.[17,18]

These findings are supported by the changes recorded in the PV plane. Upon device activation, the LV PV loops shifted to the right and upward due to a sudden increase in preload. Preload is indicated in the PV plane by the bottom-right corner of the PV loop. This corner is the end-diastolic point within a cardiac cycle and represents the ventricular pressure and volume at this time point. In cases of isolated RVF, this increase in preload optimizes the LV function and leads to improved pressure buildup, resulting in increased stroke volume and potentially improved CO.

At the beat level, sequences of consecutive beats exhibit greater variation in preload when the pVAP is turned on, as shown in Figure 4A. The IABP console operates in internal mode, causing it to fall out of sync with the native heart rhythm. This situation results in cyclic interbeat variations in LV pressures or volumes, which are known as phase shifts. This phenomenon may indicate that the use of asynchronous support, as provided by the internal mode, may partially affect the device's effectiveness in managing the cardiac load.

The PV loops were recorded in the LV, whereas the pump was located downstream in the RV. As a result, the occurrence of phase shift primarily affected LV preload. Conversely, when the pVAP is used in an LVAD configuration (data not published), it may increase systolic pressures. This can lead to an increase in afterload rather than preload. An increase in afterload is indicated by an elevation of the upper side of the PV loop (Figure 4B), and points to some reduction in the device's ability to reduce LV systolic pressures. Hence, operators should consider using synchronized mode whenever possible to maximize performance.

Similar to nonsynchronized pulsatile flow, the use of continuous flow results in the device ejecting simultaneously with the assisted ventricle. It is possible that synchronized pulsatile support, as provided by the pVAP, may require lower flow rates than MCS with continuous flow to achieve the same level of LV unloading. The reason for this is that in systole, the ejection of blood into the ascending aorta by an MCS device simultaneously with the LV systolic stroke will tend to magnify the resistance against the blood ejected by the LV. This may partially hinder LV unloading in a failing heart.

Currently, there are several devices available to operators. One such device is the Impella RP (Abiomed, Danvers, MA), a 22 Fr axial-continuous flow RVAD that can be inserted through the femoral vein and is approved for use for up to 14 days. Its disadvantages include the use of continuous flow and the inability to accommodate an oxygenator. For biventricular support with an oxygenator, peripheral venous-arterial (VA) ECMO and left atrial VA (LAVA) ECMO can be used up to 9 days. The ProtekDuo kit (CardiacAssist Inc., Pittsburgh, PA) also supports an oxygenator, but its usage is limited to 24 hours. It is important to note that all contemporary short-term RVADs rely on continuous flow, despite their different designs. Although continuous flow may ensure a certain level of efficacy in supporting hemodynamics, previous research has shown that it is also less effective in transferring mechanical energy to the arterial system and ensuring

adequate end-organ perfusion.[11,14,19] Notably, the pVAP prototype operates on pulsatile flow, which represents a major advantage.

This animal study accurately replicates hemodynamics of acute hypocontractile RVF and demonstrates the efficacy of the pVAP. The data indicate that the device can have a positive impact on hemodynamics by providing partial support with 2.7 L/min of pulsatile flow. As such, this report serves as a foundation for future improvements in the design, operation, and application of the new prototype.

Further investigations are necessary to better define the risk of hemolysis by measuring plasma-free hemoglobin in compliance with hemolysis test standards.[20] The size of the cannulas should be reassessed, aiming for an optimal balance between diameter and output flow, and possibly considering percutaneous use. Further information on the unloading capabilities of the device should be investigated by intracardiac monitoring using the PV framework. And finally, upgrading the pathophysiological model with induced ischemia of the RV may provide additional insights into the cardioprotective capabilities of this new device.

Conclusion

This initial experience with the pVAP prototype demonstrates its feasibility as a VAD and effectiveness in restoring hemodynamics in porcine models of acute RVF.

Acknowledgment

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