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ORIGINAL ARTICLE

First evaluation of a novel pulsatile LVAD: Feasibility and haemodynamic impact in acute heart failure

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Abstract

Aims Non-pharmacological therapies for acute decompensated heart failure (HF) and cardiogenic shock have evolved considerably in recent decades. Short-term mechanical circulatory support (MCS) devices can be used as circulatory backup. While nearly all available devices use continuous flow, evidence indicates that pulsatile flow can be more effective. This study presents the first experimental use of a novel counter-pulsatile left ventricular (LV) assist device (LVAD) with a primary focus on assessing its feasibility and effectiveness.

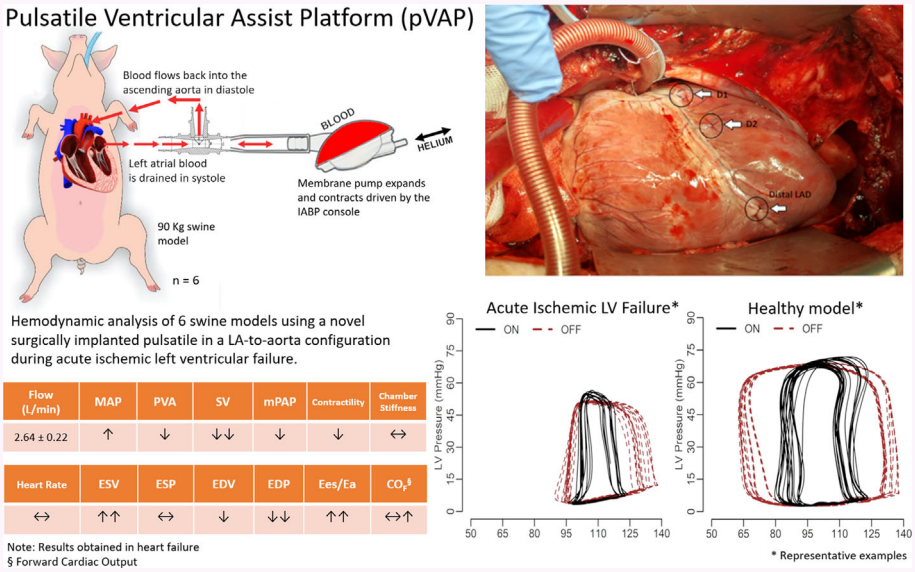
Methods The pulsatile ventricular assist platform (pVAP) was applied in six porcine models of acute ischaemic HF with the inlet in the left atrium and the outlet in the aorta. HF was induced through stepwise ligation of the left anterior descending artery and its diagonal branches. The pVAP functioned driven by a conventional IABP console while LV pressure–volume (PV) loops and standard haemodynamics with the device OFF and ON were recorded. Absolute values and percent variations were compared using Mann–Whitney's *U* test and Wilcoxon's sign-rank test.

Results The device's output flow is frequency dependent, with an output flow of 2.64 ± 0.22 L/min at 80 bpm. Activation reduced the EDV [132 (90–145) vs. 118 (83–130) mL, $P < 0.05$], EDP 9 (6–10) vs. 6 (5–9) mmHg, $P < 0.001$], native cardiac output [CO_N, 3.64 (2.88–6.71) vs. 1.67 (1.24–2.48) L/min, $P < 0.001$] and myocardial oxygen consumption [pressure–volume area * heart rate (PVA*HR), 4592 (2944–9272) vs. 2901 (1915–4437) mJ, $P < 0.001$]. Contractility decreased, with right-shifting the end-systolic PV relationship (ESPVR) while ESP and forward cardiac output CO_F were constant. The mean arterial pressure increased [54 (48–60) vs. 49 (42–55) mmHg, $P < 0.001$] and mPAP decreased [10 (8–11) to 9 (7–10) mmHg, $P < 0.01$]. The PV loop shifted left and downward. No changes occurred in the passive-elastic properties of the LV in diastole.

Conclusions The pVAP reduced the LV mechanical load while increasing systemic pressures and reducing pulmonary pressures. Its functionality as an LVAD is characterised by consistent and predictable performance. Further research is necessary to elucidate the physiological and clinical impact of the device in animals and, subsequently, in humans.

Graphical Abstract

The pulsatile ventricular assist platform (pVAP) was connected to a membrane pump in six large swine models. The system, driven by a conventional intra-aortic balloon pump console (IABP), was utilized to drain left atrial blood during systole and to eject the collected blood back into the ascending aorta during diastole. Following the induction of acute ischemic left ventricular failure, the system demonstrated an average flow of 2.64 L/min. The hemodynamic effect was characterized by an elevation of the mean arterial pressure, which coincided with a reduction in the mechanical and metabolic demands on the myocardium.



Keywords counter-pulsation; heart failure; left ventricular assist device; mechanical circulatory support; unloading

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Introduction

The global population is aging, leading to a rise in the overall incidence of heart failure (HF). Cardiogenic shock (CS) represents the natural evolution of acute and chronic HF, manifesting as a life-threatening state of hypoperfusion. The mortality rate associated with CS remains high, ranging from 42% to 60% at 30 days post-discharge. In the context of cardiac surgery, 27% of adult patients may develop some form of low cardiac output syndrome (LCOS), a fact that has been associated with a 25-fold increase in postoperative mortality.[1,2]

Studies indicate that the early management of CS is associated with reduced mortality. Despite the continued use of vasoactive drugs as a primary treatment option, their efficacy has been questioned more over the last years due to evidence pointing to worse survival rates.[3,4] Alternatively, doctors may employ short-term mechanical circulatory support (MCS) as a bridging therapy for several weeks. In the advanced stages of CS, MCS may mitigate the severity of haemodynamic compromise.[1] When initiated promptly, it can also preserve neurological function, maintain end-organ perfusion and reduce mortality.[5]

The primary objectives of MCS therapy are to enhance patient outcomes by optimizing systemic perfusion, unloading the LV and decongesting the venous circulation.[3,6,7] While factors such as ease of use, cost-effectiveness and low invasiveness are essential, it is crucial to consider whether the device is physiologically appropriate, including the type of flow it applies.

In this context, several studies suggest that pulsatile flow (PF) is a more effective and physiological modality of circulatory backup in comparison with continuous flow (CF). While the initial generation of durable ventricular assist devices (VADs) predominantly utilised pulsatile pumps,

contemporary short- and long-term devices primarily rely on CF. The preference for CF in long-term VADs is based on evidence indicating a lower incidence of adverse events due to technical failures.[6–18] Nevertheless, the administration of PF during surgery improves microcirculation and promotes a faster decrease in lactate levels postoperatively.[19] As such, the development of new, user-friendly PF devices that can be implanted without the necessity of cardiotomy may enhance the effectiveness of MCS, thereby potentially improving clinical outcomes.

This report details the experimental use of the novel pulsatile ventricular assist platform (pVAP) as a left ventricular assist device (LVAD) in large porcine models of acute ischaemic HF. The main goal is to evaluate the prototype's feasibility and to document its haemodynamic signature.

Methods

Device

The main features of the pVAP have been described previously (*Figure* 1). The pVAP is a counter-pulsatile VAD pneumatically driven by a conventional IABP console. It collects blood in systole into an extracorporeal membrane pump, which is subdivided into a blood and a helium chamber. In systole, the aspiration of gas from the helium chamber creates negative pressure and draws LV blood into the blood chamber, while in diastole the re-inflation of the helium chamber causes the blood to return to the arterial circulation driven by a two-way valve. It can operate synchronically with the patient's heart or autonomously at a pre-set pumping rate also referred to as internal mode, with a maximum pump stroke volume of 45 mL.[6,16]

Animals and monitoring

Six healthy pigs, with a weight range of 69 to 87 kg, were administered anaesthesia (isoflurane), sedation and continuously monitored. All animals were cared for in accordance with animal welfare ethics and guidelines. This study was approved by the Niedersächsische Landesamt für Verbraucherschutz und Lebensmittelsicherheit (LAVES) with approval number 23-00361 on 12 August 2023.

Instrumentation

Real-time LV pressure–volume (PV) data were recorded using a 7 Fr conductance catheter (CD Leycom B.V., Hengelo, the Netherlands) and a dedicated console (Inca® PV Loop System, CD Leycom B.V., Hengelo, the Netherlands). The conductance catheter was inserted through the carotid artery and positioned in the LV, with the pig-tail tip in the apex. Systemic arterial blood pressure was monitored via the carotid artery. Anticoagulation was maintained with unfractionated heparin, with an ACT $>$ 190 s. A Swan-Ganz catheter (Edwards Laboratories, Santa Ana, CA, USA) was introduced through the jugular into the pulmonary artery.

Implementation of the pVAP

The pVAP was configured in a left-atrium-to-aorta (LA-to-Ao) setup, utilizing two distinct cannulas with diameters of 28 Fr and 20 Fr, respectively (Bio-Medicus NextGen Cannulae, Medtronic, Meerbusch, Germany). The pump's outflow was directed through the 20 Fr cannula inserted and positioned in the ascending aorta. Concurrently, the pump inflow was directed through the 28 Fr cannula from the LA (*Figure* 1). The flow rate at the pump outlet was determined by means of a flowmeter (Em-tech GmbH, Finning, Germany). Haemodynamic assessments were conducted with the IABP console (Getinge, Sweden) in activated (ON) and deactivated (OFF) states. Multiple ON–OFF cycles were recorded at different pre-set pumping rates.

Left ventricular failure

Acute ischaemic LV failure was induced by the ligation of the D1 branch, followed by D2, and subsequently the distal LAD (*Figure* 2A). Aortic pressure, heart rate (HR), rhythm and pulse oximetry were continuously monitored. The pathophysiological model was established based on observing a clear and sustained decline in aortic pressure. Baseline measurements were taken with the pVAP deactivated before and after coronary ligation. Subsequently, the MCS device was activated, and haemodynamic responses were evaluated at varying IABP frequencies.

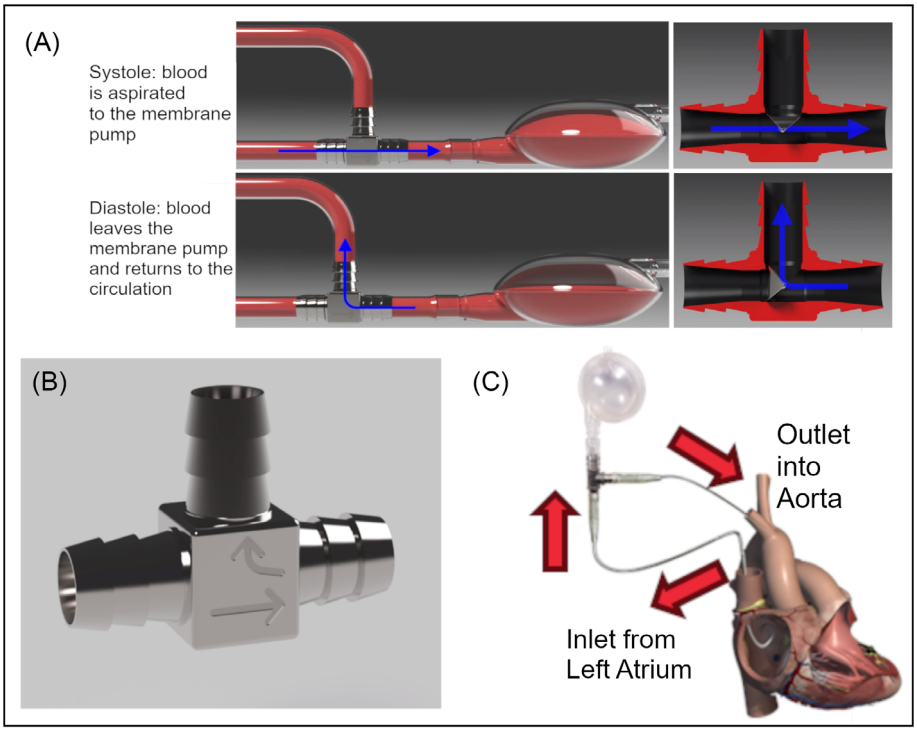
Video analysis

The residual volume of the pump was evaluated through a qualitative video analysis of the pump chamber. This analysis explored the relationship between residual volume and pump frequency under stable conditions: aortic pressure of 70/40 mmHg, HR of 80 bpm and 100% SpO_2.

Data analysis

Conductance data were collected and analysed using dedicated data acquisition and analysis software (Conduct NT, CDLeycom, Hengelo, the Netherlands). Video analysis was performed with ImageJ (Version 1.53, Wayne Rasband, National Institutes of Health, USA). Quantitative data are

Figure 1 (A) Schematic illustration of the pVAP design and operation. (B) External view. (C) Implantation method used in the experiment, with cannulation of the ascending aorta and left atrium.



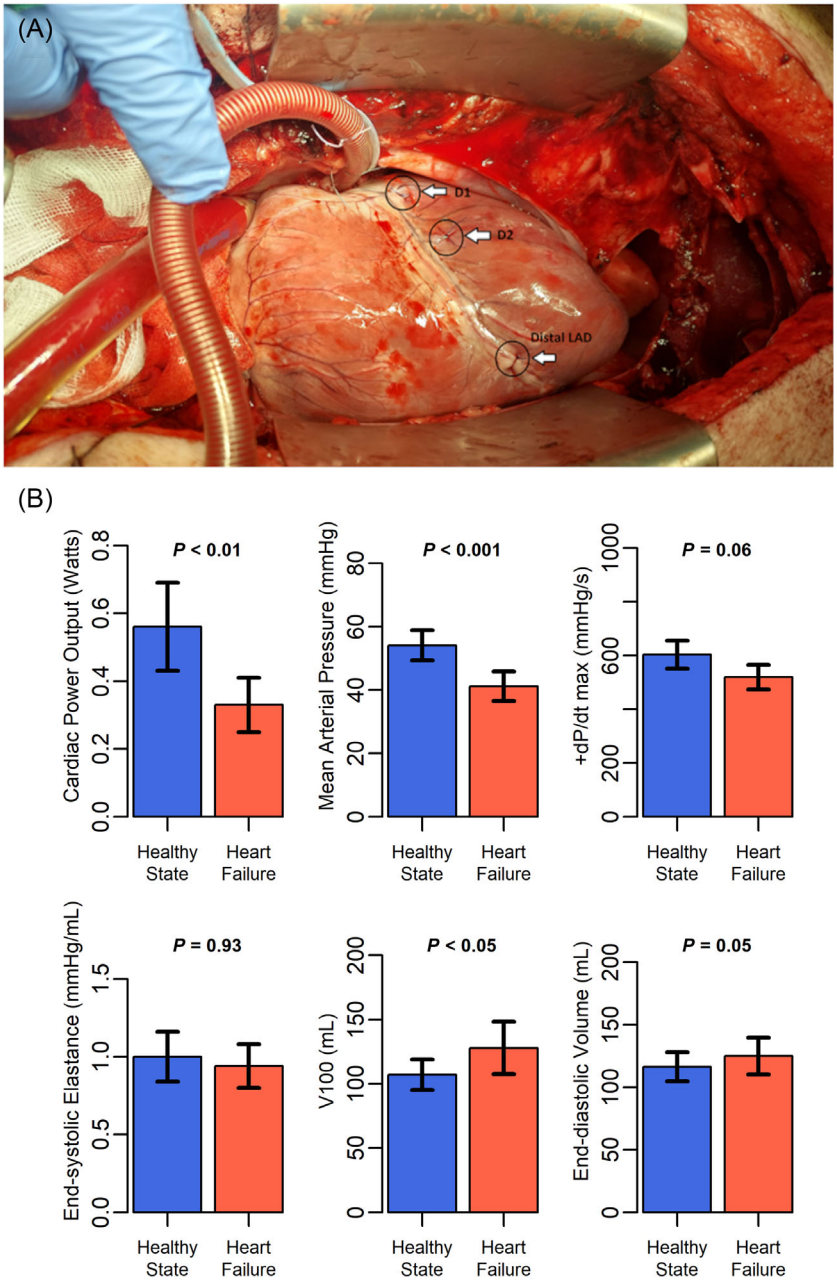
presented as mean ± standard deviation (*SD*), mean with 95% confidence interval (CI) or median with interquartile range (IQR), as appropriate. Categorical data are presented as frequencies and percentages. The pressure–volume area (PVA), a surrogate to the myocardial oxygen consumption (MVO_2), together with the end-systolic pressure–volume relationship (ESPVR) and the end-diastolic pressure–volume relationship (EDPVR) were obtained and analysed as described previously.[16,17] The MVO_2 estimation was calculated over a 1 min interval as HR * PVA, and the result was given in millijoules (mJ). Haemodynamic measurements obtained in a healthy state (HS) and a HF state (HF) were analysed using the Mann–Whitney's *U* test for absolute measurements and Wilcoxon's sign-rank test for percent variations. The changes in ESPVR and EDPVR were graphed by plotting the lines resulting from the mean and 95% confidence intervals of the slope of the ESPVR (end-systolic elastance, E_{es}) and the ESPVR-predicted end-systolic volume (ESV) at an end-systolic pressure (ESP) of 100 mmHg (V_{100}). For the EDPVR, the chamber stiffness coefficient (β) and V_{30} were used, where V_{30} represents the EDPVR-predicted end-diastolic volume (EDV) at a hypothetic end-diastolic pressure (EDP) of 30 mmHg. Cardiac power output (CPO) was calculated using the forward cardiac output (CO_F) and the mean arterial pressure (MAP) by the formula CPO = (CO_F * MAP)/451. The terms native cardiac output (CO_N) and native stroke volume (SV_N) were used to define the cardiac output and stroke volume produced by the LV, respectively. *P* values were adjusted using the false discovery rate and Bonferroni corrections. Tests were applied with a 5% alpha level using the R statistical package, version 4.3.2 (R Foundation, Vienna, Austria), and GraphPad Prism, version 10 (GraphPad Software, San Diego, CA, USA).

Results

HF model

Coronary ligation resulted in progressive haemodynamic deterioration. A decrease in contractility was evident with a rightward shift in the ESPVR, as demonstrated by a notable increase in V_{100} despite unchanged E_{es}, significant decreases in MAP, and a reduction in CPO (*Figure* 2B). The pressure–volume loops demonstrate a rightward shift, indicating an overall increase in LV volumes, a decrease in pressure build-up (downward displacement of the upper side of the PV loop) and a reduction in internal area, representative of stroke work (SW) and SV_N (*Figure* 4, dashed brown loops).

Figure 2 (A) Induction of acute left ventricular failure by ligation of the main epicardial arteries. (B) Haemodynamic changes from healthy to heart failure state. Data are shown as means and 95% confidence intervals. *P* values are obtained using Mann–Whitney's *U* test. The results demonstrate that acute left ventricular dysfunction was effectively induced.



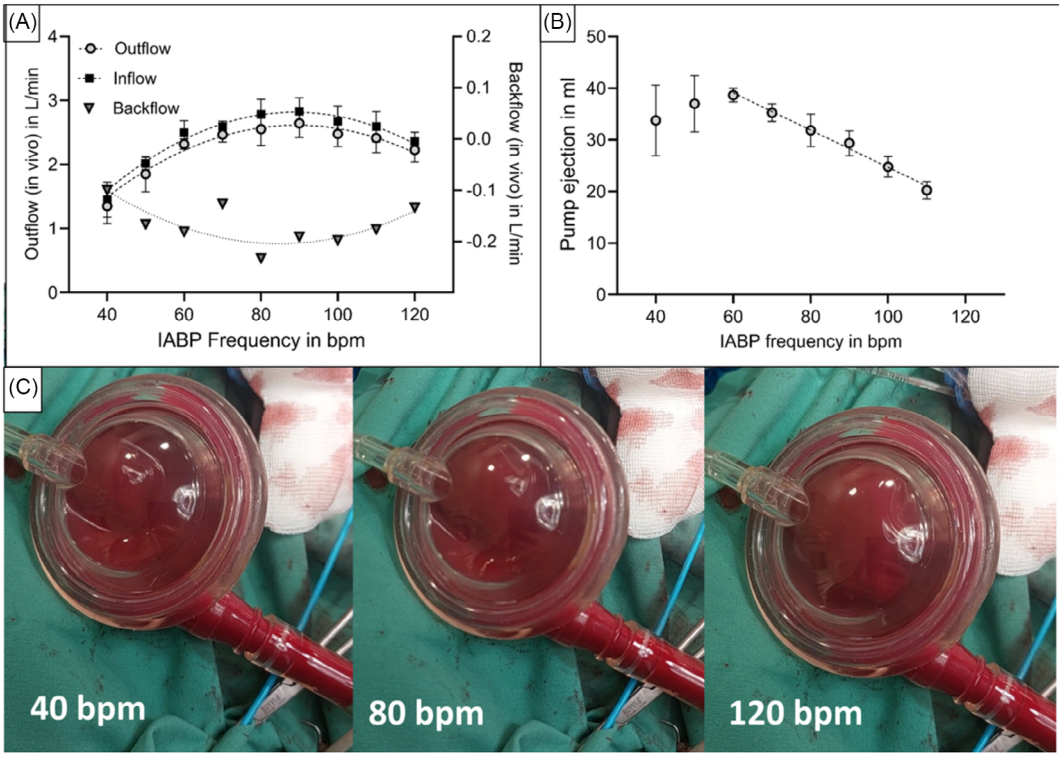
Pump flow

Figure 3A depicts the in vivo recordings of pump outflow and inflow, which reveal mean values of outflow ranging from 1.35 ± 0.27 L/min (40 bpm) to 2.64 ± 0.22 L/min (80 bpm). Similarly, the inflow reaches 2.8 L/min at an HR of 90 bpm. The backflow is 0.1 L/min at 40 bpm and reaches its maximum of 0.2 L/min at 80 bpm.

Pump stroke volume

The pump's stroke volume (i.e., the volume of blood expelled per pump cycle) tends to reach its peak at lower frequencies, around 40 to 50 bpm, and gradually decreases as the pump frequency rises (*Figure* 3B). The video analysis demonstrates that at 40 bpm, only a restricted area of the membrane extends outward into the gas chamber of the pump,

Figure 3 Relationship between IABP console's pumping rate and pump flow (A), pump's stroke volume (B) and residual volume (C). The different residual volumes can be appreciated in the three bottom panels, where lower frequencies lead to a smaller protrusion of the membrane pump at end-diastole.



indicating a minimal residual volume within the blood chamber. In contrast, at 120 bpm, a substantial portion of the membrane protrudes outward into the gas chamber, indicating a higher residual volume. The findings demonstrate a definitive correlation between pump outflow and frequency. At lower frequencies (40 bpm), the membrane has sufficient time for displacement, resulting in near-complete ejection of blood. Conversely, at higher frequencies, the pneumatic ejection of blood is constrained by the shorter diastolic times, resulting in incomplete emptying of the blood chamber.

Haemodynamic changes

The absolute haemodynamic changes observed with the activation of the pVAP (including before and after the induction of HF) are exposed in *Figures* 4 and 5. Before activating the pVAP, the EDV was 132 (90–145) versus 118 (83–130) mL after activation ($P < 0.05$); and the EDP was 9 (6–10) versus 6 (5–9) mmHg ($P < 0.001$). The ESV exhibited a more heterogeneous response, with a reduction observed in some cases. However, the predominant trend was toward increase, with a median value of 65 (42–81) mmHg at baseline versus 72 (53–99) mmHg post-activation ($P < 0.05$). The ESP remained constant with no statistically significant changes [55 (52–60) vs. 56 (51–63) mmHg, P = NS]. The mean pulmonary arterial pressure (mPAP) exhibited a mild reduction [10 (8–11) vs. 9 (7–10) mmHg, $P < 0.01$]. Conversely, the systemic circulation demonstrated the opposite trend, with a MAP of 54 (48–60) mmHg post-activation compared with 49 (42–55) mmHg pre-activation ($P < 0.001$). The pVAP resulted in a reduction in contractility, as evidenced by a significant decline in $+dP/dt_{MAX}$ and a notable decrease in the CO_N, from 3.64 (2.88–6.71) to 1.67 (1.24–2.48) L/min ($P < 0.001$). While the CO_F remained unaltered, a discernible decline was observed in the PVA * HR, which decreased from 4592 (2944–9272) to 2901 (1915–4437) mJ ($P < 0.001$). In the PV plane, the ESPVR exhibited a rightward shift, a characteristic indicative of negative inotropy (*Figure* 6, upper panels).

Differences between HS and HF states

HF has led to a distinct pattern of changes in relation to pre-ligation (HS), as exposed in *Figures* 6 and S1. The mPAP was significantly reduced in the HF state but not in HS. The observed increase in the MAP was statistically significant in both states but reached a greater numerical magnitude in HF. Even though CO_N significantly decreased in both states,

Figure 4 Invasively recorded left ventricular pressure–volume loops before and after activation of the pVAP.

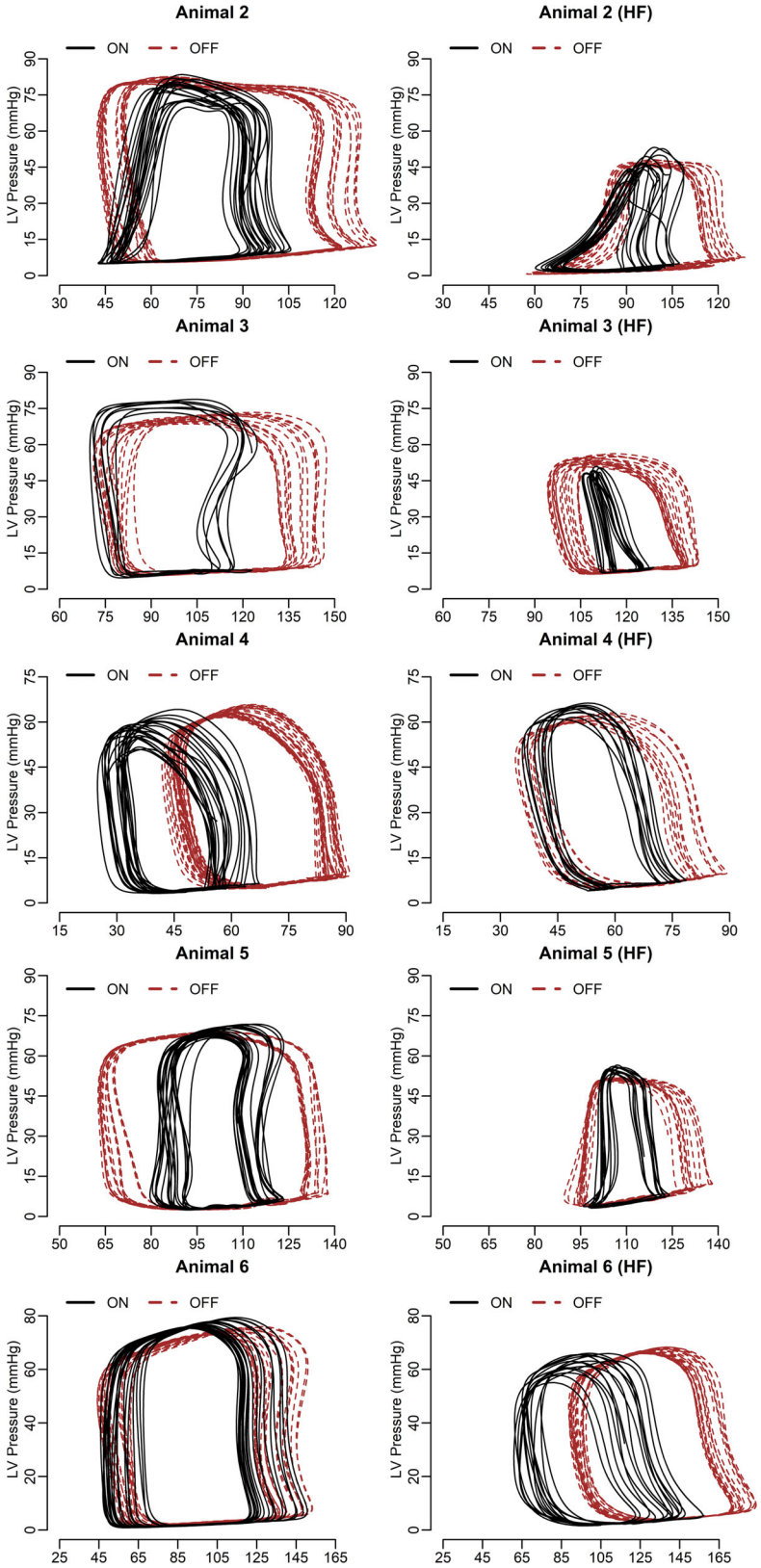
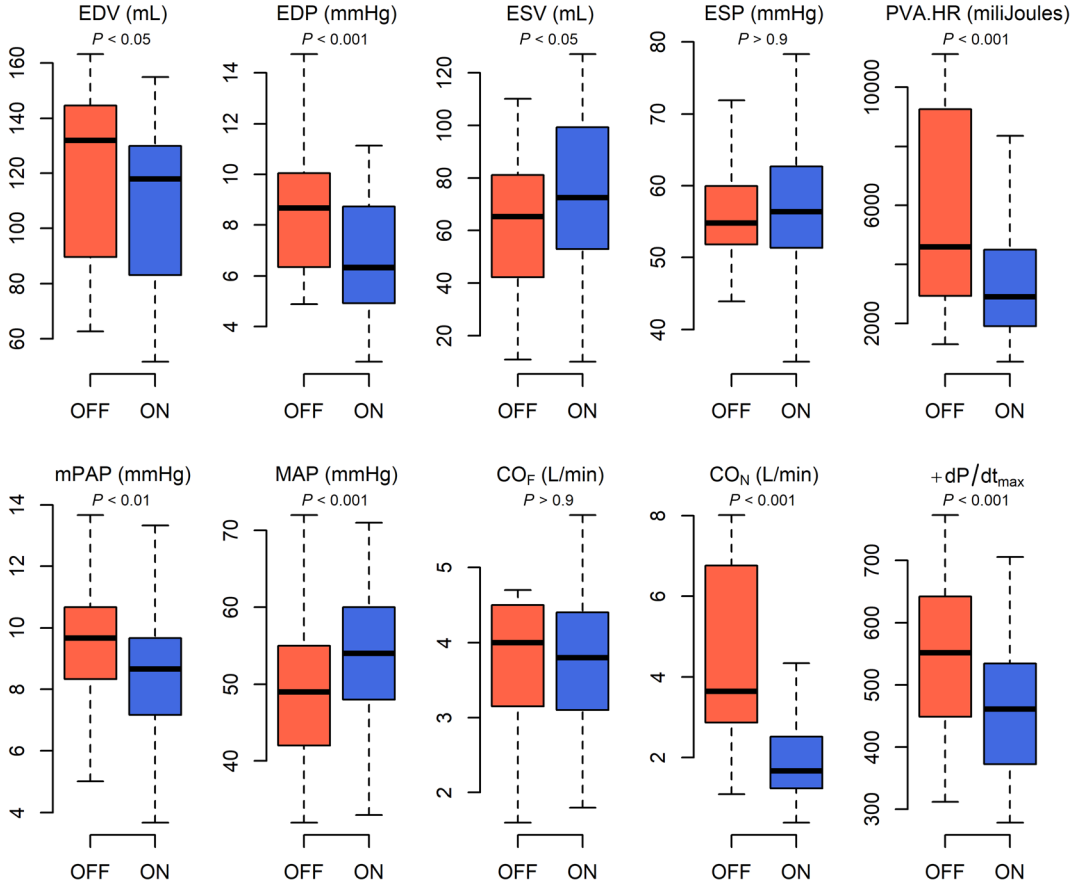


Figure 5 Absolute values of haemodynamic measurements taken before and after activation of the pVAP. *P* values were calculated using the Mann–Whitney *U* test for two samples. Pressure and volume unloading are denoted by significant reductions in EDP and EDV, as well as in the CO_N. Pulmonary pressures decreased, and systemic pressures increased, while the myocardial oxygen consumption was reduced. A significant reduction in CO_N also indicates LV unloading while CO_F is kept constant. The reduction in $+dP/dt_{MAX}$ suggests both the presence of LV unloading and contractility reduction. EDV: End-diastolic Volume. EDP, end-diastolic pressure; ESV, end-systolic volume; ESP, end-systolic pressure; PVA * HR, product of the pressure–volume area and heart rate; mPAP, mean pulmonary artery pressure; MAP, mean arterial pressure; CO_F, forward cardiac output.



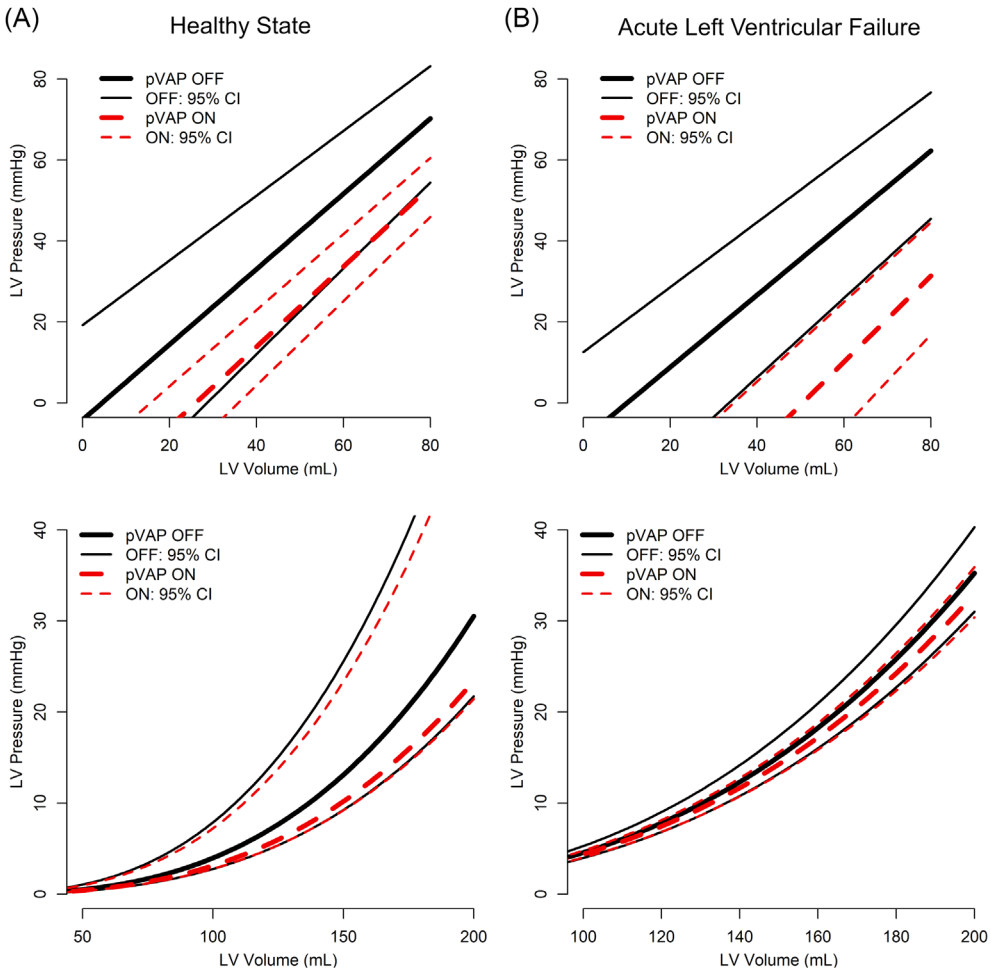
CO_F showed a trend toward a slight increase in HF, whereas in HS, it remained unchanged. Despite showing significantly higher slopes, the net effect over the ESPVR was a shift to the right in both states, as indicated by significant increases in V_{100}. However, this effect was non-significant in the HS state (*Figures* 6A). Despite this discrepancy, the PVA*HR significantly decreased in both states, and a similar phenomenon was observed in SV_N (Figure S2). Ventricular–arterial coupling, represented by the ratio E_{es}/E_a, where E_a stands for end-systolic arterial elastance, significantly improved in both states, with the best results observed in HF. The activation of MCS in HF or HS did not change the lusitropic performance during the ventricular filling phase. Although significant changes were observed in the chamber stiffness constant (β), they did not significantly shift the EDPVR in the pressure–volume plane, as demonstrated by the unchanged values of V_{30} and by the overlapping EDPVR curves and 95% confidence intervals in *Figure* 6B. Nevertheless, the active relaxation phase, as described by the time constant of pressure decay in the active relaxation phase (*Tau*) was significantly prolonged by up to 14% (*Figure* S1).

IABP cycling rate

Figure S3 illustrates that the haemodynamic response is contingent upon the pumping rate. The mPAP only decreased in the HF state, with a peak effect around 90 bpm. The pumping rate did not modify the MAP, CPO, EDV, ESP and SV_N effects. mPAP, ESV, EDP and PVA * HR showed more evident changes between 80 and 100 bpm.

In both cases, with and without LV failure, the activation of pVAP induced a sudden shift of the PV-loops to the left and downward, as illustrated in *Figure* 4. This leftward shift is more consistently observable on the right side of the PV loop, representing the isovolumetric contraction phase and the LV preload. The left side of the loop, representing the isovolumetric relaxation phase, may either shift in

Figure 6 Graphic evaluation of the mechanical properties of the left ventricle before and after activation. The two left plots show the ESPVR (top) and EDPV (bottom) lines before (black) and after (dashed red) activation, with 95% confidence intervals. The intervals overlap, indicating the absence of changes in a healthy state. On the right, the same disposition after coronary ligation indicates diverging ESPVR intervals. This points to lower contractility once the device is activated during acute ischaemia.



alignment with the right side or, paradoxically, shift to the right, resulting in the centralization of the ESV relative to the PV loop. This phenomenon was observed more clearly in HF cases than in cases without HF (HS), as evidenced in Figure S3.

Discussion

This study reports the first experience with a novel pulsatile MCS device and demonstrates it to be feasible and effective as an LVAD. With a median output flow of 2.64 L/min, the pVAP unloaded the LV and optimized systemic and pulmonary pressures. The pVAP was more effective at pumping rates between 80 and 90 bpm during acute ischaemic LV failure.

Given that the pressure head is greater in the ascending aorta than in the pulmonary trunk, the LVAD configuration required larger cannulas than the RVAD configuration so as to achieve a matching output flow, which is shown in a previous study.[6] The larger diameters created less resistance against the blood flow, enabling the pVAP to generate a comparable output despite overcoming higher pressures. The findings consistently demonstrated a close relationship between pumping rate and output flow in this context. Low rates were observed to increase the volume ejected per cycle while reducing the number of cycles per minute. In contrast, high rates exhibited the opposite effect. In both situations, the output was lower than in the optimal range, which stays between 80 and 90 bpm. This interplay is driven by the material properties of the membrane pump.[18] Moreover, the inverse relationship between the device's output flow and output pressure, which is the pressure at the outlet chamber

(i.e., the aorta), may explain the enhanced performance observed in acute HF.[6] Notably, the pathophysiology of the LV failure condition results in lower output pressures in combination with higher inlet pressures inside the congested ventricle. This facilitates flow generation by the device, resulting in slightly higher output flows compared with the same device under healthy conditions.[6,7,9]

The pVAP resulted in a notable and prompt reduction in the EDP (*Figures* 5, S1 and S3). When considered alongside the observed increase in the MAP, this suggests an enhancement in the myocardial perfusion pressure, which in turn is a therapeutic goal in ischaemic conditions.[14] Notably, the pVAP optimized both the EDP and the MAP irrespective of the pathophysiological state (HS or HF) and the effect was resilient against alterations in the pumping rate (Figure S3).

Similarly, pronounced reductions in SV_N were observed in both states and at varying pumping rates. In conjunction with CO_N, SV_N exhibited the most substantial reductions compared with the 'off' state, decreasing by up to 50% at 90 bpm. This finding aligns with previous observations with short-term LVADs.[16] Moreover, the lack of variation in CO_F suggests that the device effectively replaced the native heart by taking over a relevant fraction of its mechanical load. Negative inotropy was demonstrated by multiple parameters, including right-shifting of the EPSVRs and significant reductions in the $+dP/dt_{MAX}$. The latter is more widely adopted as a marker of contractility despite its load dependence. This reduction contrasts with the observed absence of change in the ESP, which might be attributed to the concurrent increase in MAP. This finding is consistent with previous reports on micro-axial flow devices.[20]

It should be mentioned that most measurements in the present study were taken using non-synchronized pulsatile support instead of synchronized support. The use of non-synchronized support was more frequent than expected because the pVAP's performance is rate-dependent, while the native HR was not uncommonly out of that ideal range. As consistently demonstrated in the present study and in previous experiments with the same device, pumping rates below 70 and above 90 bpm substantially reduce the pump's stroke volume. In situations of tachycardia or bradycardia with instability, the device should be set to non-synchronized mode with a self-triggering rate of 80 bpm.[6,7,16] The lack of synchronization may have attenuated the unloading effect on intraventricular end-systolic pressures due to phase shift, a phenomenon whereby the systolic stroke of both the device and native heart coincide and diverge at regular periods due to different frequencies. The result is an increase in aortic impedance and, consequently, higher afterload with less effective end-systolic unloading.[6,21] Additionally, the absence of ESP variation in the presence of a 6% to 25% increase in the MAP (*Figures* S1 and S3) indicates pressure decoupling between the LV and the ascending aorta, which is the hallmark of a functioning LVAD.[9]

The pVAP shares several similarities with the iVAC2L, a CE-marked percutaneous transvalvular LVAD that uses the same design of membrane pump connected to a bi-directional flow catheter to propel LV blood using counterpulsation. Two prospective cohorts and one large retrospective registry including patients undergoing iVAC2L-assisted HR-PCI reported increases in both MAP and CO.[10] In 2022, Bastos et al. documented the effects of the iVAC2L on the cardiac dynamics of 27 patients receiving iVAC2L with the same indication (elective high-risk PCI in stable patients), showing that iVAC2L reduced the PVA while increasing the MAP and the CPO. Decreases were documented in ESP, EDV and PVA, which aligns with the changes observed with the pVAP with the exception of the ESV, which diverged. The current results also did not replicate the increments in EDP, SV_N (also referred as SV_{GLOBAL}) and in the pulmonary pressures documented in the PULSE trial.[9]

The ESV increase observed in the current experiment is similar to previous results with a LA-to-Ao configuration.[22,23] Methodological differences explain such discrepancies. In the PULSE, measurements were taken before and after PCI in stable compensated human subjects, who were revascularized according to the latest standards of care. While it is well established that the effects of VADs have better detectability in dysfunctional and overloaded ventricles, especially when it concerns partial support, several individuals had normal LV function despite having a high-risk profile.[6] This fact, added to the increase in venous return caused by the MCS, the use of preload-boosting interventions (IV fluid bolus) to treat transitory post-puncture vasovagal reflexes and the increased risk of periprocedural aortic regurgitation due to the transvalvular setup,[24] may have reduced the magnitude of the end-diastolic unloading in the PULSE study.[9]

The present results, in contrast, were obtained in a pre-clinical experimental setting where the device could be applied with better assessment and control of confounders. Measurements were taken in a decompensated state thus adding detectability. Moreover, there was no need for crossing the aortic annulus which prevented the occurrence of iatrogenic aortic regurgitation. Since the cardiovascular response to MCS reflects the physiological conditions within which it is applied, the pVAP only reduced the mPAP in the HF state (Figure S3).[22] The findings of the present study alongside those from the PULSE trial suggest that the observed differences are most likely a result of different haemodynamic contexts, different support modalities (LV-to-Ao vs RA-to-Ao) and different pump outflows (1.4 vs 2.6 L/min).[9]

The activation of the pVAP resulted in a significant reduction in the PVA, which is a strong positive correlate of MVO_2. MVO_2 reduction is a desirable strategy in the treatment of myocardial ischaemia. Two decades ago, Meyns

et al. demonstrated in ovine models of acute left anterior myocardial infarction that LV assist devices significantly reduced MVO_2. That reduction correlated strongly with a reduction in infarct size. Moreover, the application of partial support equivalent to 50% of the baseline CO was sufficient to achieve a notable reduction in MVO_2, as previously described.[6,9,16,18,25] In light of the aforementioned evidence, the hypothesis that the pVAP may hypothetically reduce infarct size in average-sized human beings should warrant confirmatory studies.

The evidence on effectiveness gathered in this experiment adds to previous works, where the pVAP has been successfully used to support the right ventricle.[6] The easiness of implantation, customizability, and compatibility with standard IABP consoles may increase the availability of MCS to a broader range of patients and geographies, adding one more option to the devices already in the market. The Berlin Heart (BH) EXCOR (Berlin Heart, GmbH, Berlin, Germany) uses a similar membrane-pump-based system that is available for bi-ventricular support (BiVAD). The BH has been used in paediatric and adult patients. Current evidence on the use of BH in adults shows favourable survival rates between 50% and 80%, but also points to high rates of haemorrhagic and thrombo-embolic events.[26] The Heartmate 3 (Abbott Laboratories) is a centrifugal CF LVAD that is primarily intended for durable support but can also serve as a temporary bridge to transplant or to decision. It is not intended as a BiVAD, even though it can be applied 'off-label' in the RV[27]; and it cannot receive an oxygenator to provide VA-ECMO. The pVAP, in contrast, stands out for its versatility and a potentially higher benefit–cost ratio as it can be used according to the patient's needs as LVAD, RVAD,[6] BiVAD or VA-ECMO (data in press); and is compatible with any standard IABP consoles, circumventing the additional costs associated with training personnel and handling the system at local level.

Even though the present study did not include a systematic assessment of safety parameters, several remarks can be placed in this aspect. First, no signs of significant haemolysis were observed. This goes in line with previous results with the iVAC2L, where the maximum observed levels of plasma free haemoglobin (pFHb) recorded in healthy porcine models was 1.29 mg/dL using centrifugation-based pFHb detection (data not published). In humans, the use of iVAC2L has been associated with a non-significant increase in median pFHb from 26 to 38 mg/dL.[3] According to evidence, pneumatic systems such as the iVAC are less haemolytic than micro-axial pumps.[8] As an example, in the ISAR-shock trial, the median levels recorded with micro-axial pumps stayed around 45 to 50 mg/dL and the difference was statistically significant compared with baseline pre-activation.[28] According to recent ELSO definitions, levels of pFHb between 50 and 100 mg/dL are considered moderate haemolysis.[29] Anecdotal evidence shows that replacing a micro-axial flow device with an iVAC2L halved the pFHb levels when severe haemolysis (130 mg/dL pFHb) developed in a patient who used VA-ECMO for several days due to an acute myocarditis complicated by CS.[8]

In general, the pVAP may be useful for peri- and post-operative MCS during open cardiac surgery in patients who show a greater likelihood of circulatory collapse. It can also help as a bridging tool for the treatment of ongoing CS due to LV failure, especially in cases where the conventional trans-aortic approach is contra-indicated due to factors such as aortic stenosis or aortic valve prostheses. Due to the surgical implantation, the pVAP is not primarily suitable for the catheterization laboratory but can be helpful in operating rooms and intensive care units.

The HF model employed in this study effectively reproduced acute ischaemic LV failure with haemodynamic instability. The swine model is especially advantageous in this context, given its remarkable organ size, coronary anatomy and physiology similarities to humans.[30] Furthermore, intracardiac monitoring allowed for a more comprehensive evaluation of the haemodynamic effects of the new device. However, the unloading performance may have been underestimated due to using non-synchronized support as the animal's HR occasionally reached values out of the optimal range for the device's performance. In order to avoid this issue, future studies should include pacing at 80 bpm in all measurements.

It is currently unclear whether synchronized counter-pulsatile support could result in more pronounced levels of LV unloading compared with non-synchronized or CF support. This is a question that should be addressed in future investigations. Such data could also offer insights over a longer time frame, during which changes in chamber stiffness—absent in the current study—might become more detectable. Furthermore, additional elucidation of the influence of this MCS modality on cerebral and microvascular perfusion at the end organs is imperative, as is a comprehensive assessment of its safety and efficacy profile when utilised in human subjects. And finally, results of experiments testing the pVAP's performance as VA-ECMO and as BiVAD, as well as its safety profile in the short and long term, are expected to provide additional evidence in the near future.

Conclusions

The pVAP exhibited favourable performance in large animal models of acute LV failure, demonstrating consistent and predictable haemodynamic support when used in a LA-to-Ao LVAD configuration. Further research is required to elucidate its safety and efficacy in the long term under different configurations.

Clinical perspectives

- The pVAP is a new surgically implanted VAD capable of providing approximately 2.6 L/min on top of the patient's cardiac output.
- The device effectively unloads the LV, reduces myocardial metabolic needs and elevates systemic pressures.
- Its simple design allows for fast implantation after which it can be driven by a conventional IABP console. This feature expands its availability to most hospitals.
- This is a pre-clinical study. Additional questions that require further clarification include the effect of its pulsatility on the heart and end-organs compared with devices applying CF in the short and long term, and its safety profile including its potential for vascular complications and its potential for haemolysis.

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Conflict of interest statement

Oren Malchin is the CEO of PulseCath BV. Marcelo B. Bastos receives personal fees from PulseCath BV. The remaining authors have no conflicts of interest to declare.

Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Figure S1. Absolute values of haemodynamic measurements pre- and post-activation, with percent variations. *P*-values were obtained using the Wilcoxon's Rank-sum test against a null hypothesis of zero variation. Data is exposed as medians and interquartile range. The intervals show means and 95% confidence intervals for the percent variations.
Figure S2. The Density plot shows that the pVAP reduced SV_N similarly in the healthy state and after coronary ligation. The device did not change CO_F, and a greater proportion of positive values were observed after coronary ligation.
Figure S3. Absolute values of haemodynamic measurements in relation to pumping rate.

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