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Long-term safety and durability of novel intra-aortic percutaneous mechanical circulatory support device

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An unmet need exists for minimally invasive percutaneous mechanical circulatory support (pMCS) devices to provide partial support and promote cardiac rest and recovery in non−end-stage heart failure patients. This indication requires safe, long-term, ambulatory use with standard anticoagulation. The Aortix pump (Procyrion, Houston, Texas, USA) is a percutaneously deployed intra-aortic pump currently being clinically evaluated for subacute use and has the potential to provide extended therapy for non-end-stage heart failure patients. The device has demonstrated hemocompatibility and hemodynamic impact and has features well suited for home use. To evaluate the Aortix pump for long-term, ambulatory use, pumps were implanted in 4 untethered sheep. Pumps operated for 90 to 142 days and were stopped electively. Pump bearing components were found to have only superficial wear. No clinically significant hemolysis was observed and aorta and kidney histopathology showed no device-related findings or adhesions, suggesting Aortix is suitable for long-term (>6 months) ambulatory use.
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In non-end-stage heart failure patients, full left ventricular assist device support is not justified due to invasiveness, risk, expense, and impact on quality-of-life.[1] In these patients, months of pMCS may promote cardiac rest and reverse remodeling, improving disease state and outcomes and suggesting use of partial support as a bridge-to-recovery.[2-4] To be widely adopted, devices providing such therapy must be minimally invasive and safe for long-term ambulatory use without sacrificing quality-of-life. No such devices are currently available.[1]

The Aortix pump (Figure 1A) is an 18 Fr pMCS device implanted via the femoral artery and positioned in the descending aorta above the renal arteries (Figure 1B). No pump components reside in the left ventricle or across the aortic valve, mitigating risk of thrombotic stroke or cardiac damage. The device pumps 3.5 l/min at 25,000 rpm and uses fluid entrainment to augment native aortic flow (Figure 1B). Position is maintained during therapy by the combination of atraumatic struts and the power lead functioning as a tether opposing developed thrust.

The device is being clinically evaluated (NCT04145635) to provide up to 7 days of therapy for cardiorenal syndrome caused by acute decompensated heart failure wherein the pump's action increases distal perfusion and reduces cardiac afterload. In vitro and in vivo testing has demonstrated clinically acceptable hemocompatibility and significant hemodynamic impact (Figure 1C, D).[5] Prolonged cardiac afterload reduction and associated hemodynamic benefits may promote reverse remodeling, supporting pump use as a bridge-to-recovery in non−end-stage heart failure patients (Class 3b/ambulatory Class IV).

The major additional requirement for exploring longer-term human use is acceptable bearing performance and

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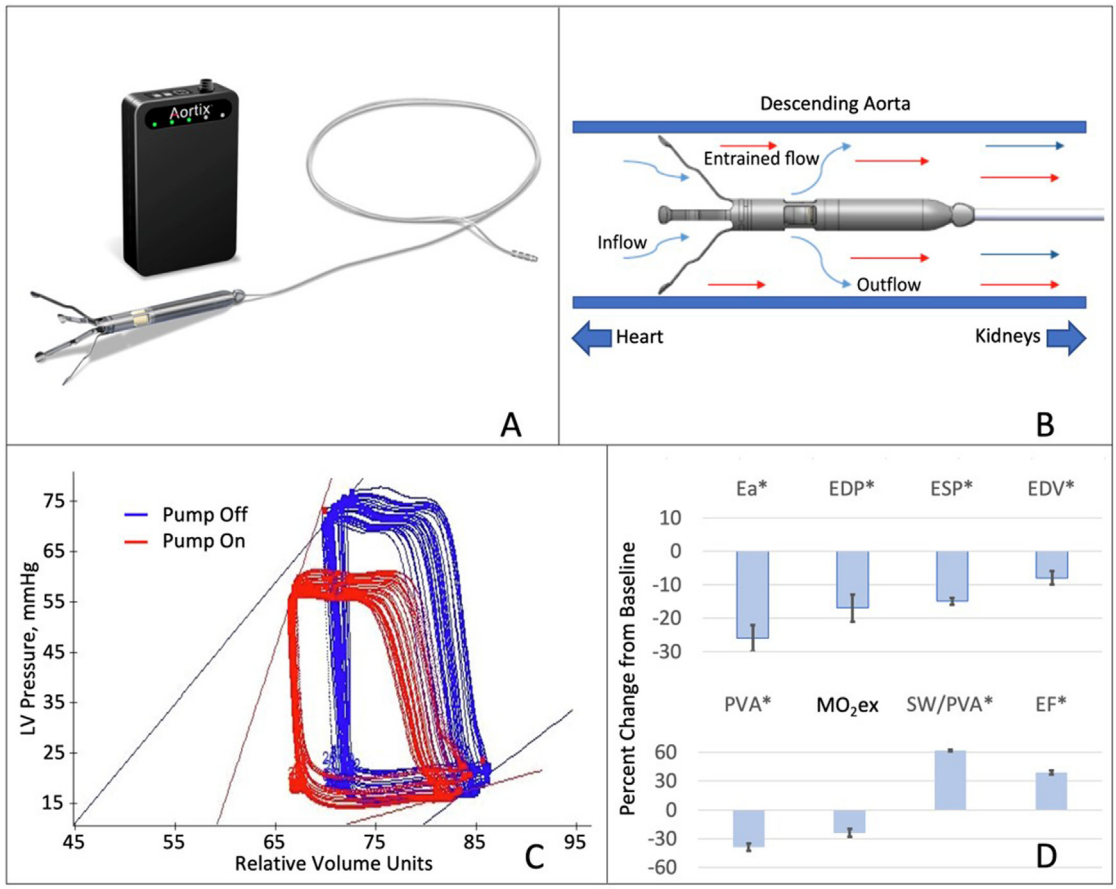

Figure 1 . Overview of Aortix system and hemodynamic impact. Pump and controller **(A),** pump sits in descending aorta and reduces cardiac afterload by assisting the heart in perfusing distal organs **(B),** pressure-volume loops showing LV function from previous work in a preclinical animal model of heart failure before (blue) and after (red) pump activation **(C),** and change in key hemodynamic parameters due to pump activation in the same preclinical animal model of heart failure **(D).** Ea indicates arterial elastance; EDP, end diastolic pressure; ESP, end systolic pressure; EDV, end diastolic volume; PVA, pressure-volume area; $M0_2ex$, myocardial oxygen extraction; SW, stroke work; and EF, ejection fraction.

freedom from embolic events over longer operating durations. To this end, we proposed to demonstrate safe, >90 day, untethered, and infusion-free Aortix pump use in an ovine model.

Material and methods

Devices were implanted in the descending thoracic aorta of 4 male Polypay sheep (57-59 kg) via the femoral artery. The pump power lead was externalized through the arteriotomy, tunneled, and secured on the animal's flank. Support vests were used to secure the pump controller and battery.

Animals were initially cross-tied; 5 to 10 days after implantation, the cross-ties were removed and animals transitioned from constant-rate infused heparin to twice-daily subcutaneous enoxaparin while monitoring effectiveness with anti-Xa assays. For the remainder of the study, pumps were powered by 450-gram batteries that each provided 10-12 hours of operation. Animals were assessed weekly via clinical pathology, physical examination, and blood labs.

At support completion, animals were given heparin boluses and euthanized. Pumps were recovered via necropsy. Clinical pathology, gross pathology, histopathology, hemocompatibility, and pump operation were assessed. Following gross inspection, recovered pumps were hydraulically characterized *in vitro* to assess performance and disassembled to characterize bearing component wear.

All animals received humane care complying with the 'Principles of Laboratory Animal Care' formulated by the National Society for Medical Research and the 'Guide for the Care and Use of Laboratory Animals' prepared by the Institute of Laboratory Animal Resources and published by the National Institutes of Health.

Results

Devices remained implanted for at least 90 days (range 90 to 142 days). All 4 animals were electively terminated and appeared healthy throughout the study as evaluated by board-certified, independent veterinary pathologists. Blood labs were unremarkable, and no clinical signs or symptoms of hemolysis were observed. No driveline related or other infections were noted, and kidneys appeared normal with no evidence of emboli. No aortic or vascular damage, bleeding complications, or adhesions were observed, indicating the feasibility of catheter-based retrieval in the future.

Table 1 summarizes pump implant time, uptime, and condition. Pump location in each animal was assessed with fluoroscopy after a minimum of 90 days. In Animals 1 and

Table 1 Study Summary

Animal	Implant duration (days)	Pump uptime (days)	Days before pump displacement	**Thrombus**
1	90	88	25	No
2	104	98	55	Yes
3	128	126	120	No
4	142	140	N/A	No

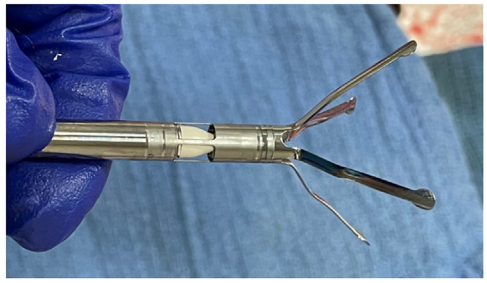

Figure 2 Pump from Animal 4 immediately post-explant with no evidence of thrombus.

2, this revealed animal behavior (chewing and pulling the power lead) had pulled pumps from their original position to the arteriotomy, so these animals were terminated. In Animal 2, displacement into the femoral artery occluded the pump outlet, interrupting flow through the pump and causing thrombus formation. Pumps in Animals 3 and 4 remained in their original positions. We subsequently monitored the length of exposed power lead to identify further displacement. Animal 3 was terminated following an increase in exposed lead length. Animal 4 was terminated at the same time so that the pump remained superior to the renal arteries for the entire implant time. Pump displacement left no observable signs on the intimal surface of the aorta. Aside from the single thrombus formed due to outlet occlusion, recovered pumps showed no evidence of thrombus formation (Figure 2).

Several pump stops of 30 to 90 minutes occurred due to animal-caused disconnections or delayed battery changes. One stop of 96 hours was caused by a controller software issue that was corrected early in the study. No adverse events resulted from these stops. Pump performance was evaluated in vitro after explant and met normal operating requirements. Bearing surface thicknesses of the explanted pumps (n = 4, −3 to +15 μm from nominal) were within the range of those from new, unused components (n = 5, −5 to +25 μm from nominal). No pump factors were observed that would limit intended duration of use.

Discussion

The absence of thromboembolic events, hemolysis, or measurable bearing wear combined with an anticoagulation regime compatible with outpatient care suggest the Aortix pump is suitable for long-term (>6 months) ambulatory use.

Other features enhance the possibility of effective home therapy with this device. Pump operation does not interfere with natural cardiac contraction or valve function, and its location eliminates the risk of thrombotic stroke. The pump's design appears tolerant to stopping and restarting without performance loss, thrombosis, or embolic risk. Since the power lead requires no purge or mechanical or optical elements, it is more flexible and allows for improved mobility. Atraumatic localization without observed endothelialization should allow for nonsurgical pump retrieval. Finally, the pump's low power requirement makes transcutaneous energy transfer feasible, substantially lowering the risk of infection or pump displacement.

To our knowledge, this is the first published account of a pMCS device demonstrating over 90 days of mobile, infusion-free, in vivo operation. Such a device may provide new, minimally invasive home ambulatory therapy for non −end-stage heart failure patients that increases quality-of-life while allowing cardiac rest and recovery.

Author contributions

All authors contributed to the writing of this manuscript and data analysis. Jace Heuring, Aaron Palmer, Chris Durst, and Av Edidin contributed to the study design.

Conflicts of interest statement

All authors are employees of Procyrion and have stock/option interest in Procyrion. Jace Heuring is an officer of Procyrion. No funding organizations had any role in the collection of data, its analysis and interpretation, or in the right to approve or disapprove publication of the finished manuscript.

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