0003-4975
https://doi.org/10.1016/j.athoracsur.2022.06.052

NEW TECHNOLOGY

Mechanical Cardiac Support With an Implantable Direct Cardiac Compression Device: Proof of Concept

George V. Letsou, MD, Christina M. Bolch, PhD, Erica C. Hord, PhD, William C. Altman, MBA, Brad L. Youngblood, DVM, Boris Leschinsky, BA, and John C. Criscione, MD, PhD

Baylor St Luke's Medical Center, Houston, Texas; Department of Surgery, Texas Heart Institute, Houston, Texas; CorInnova, Inc, Houston, Texas; Department of Veterinary Preventive Medicine, College of Veterinary Medicine, The Ohio State University, Columbus, Ohio; and Department of Biomedical Engineering, Texas A&M University, College Station, Texas

ABSTRACT

PURPOSE We examined the hemodynamic effects of a new, implantable, direct cardiac assist device in an ovine heart failure model.

DESCRIPTION The device, which encompasses both left and right ventricles, is inserted through the pericardial apex and self-expands to encompass the heart without suturing. The intact pericardium anchors the device in place. The device has 2 concentric chamber layers: an internal chamber layer filled with fluid to conform to the heart and an external chamber layer filled with air that provides external compression and negative pressure to aid relaxation.

EVALUATION The device was implanted in 7 sheep with heart failure induced by microsphere embolization. Cardiac performance was assessed for 6 to 8 hours. The cardiac assist device provided cardiac systolic and diastolic assistance, as shown by pressure tracings of the left ventricle and aorta, pulmonary artery flow, and +dP/dt. Central venous pressure decreased during cardiac assistance. No anatomic damage was noted postmortem.

CONCLUSIONS Systolic and diastolic cardiac assistance can be achieved with this device that compresses and relaxes in synchrony with the native cardiac cycle.

(Ann Thorac Surg 2022;114:1944-50)

TECHNOLOGY

Direct cardiac compression provides cardiac output in the absence of cardiac contraction during cardiopulmonary resuscitation. However no implantable device has been able to provide patients with direct mechanical cardiac compression that is effective and reproducible.[1-4] The experimental implantable CorInnova device (CorInnova, Inc, Houston, TX) that we describe here provides direct cardiac compression and aids cardiac relaxation.

The device is based on a collapsible nitinol frame and has a dual-chamber design of thin-film polyurethane chambers (Figures 1A, 1B). The inner lining of saline-filled internal chambers allows the device to closely conform to the heart's epicardial surface. A second outer layer of polyurethane chambers fills with air and empties cyclically to provide systolic cardiac compression and diastolic relaxation (Figure 1C). Diastolic assistance is provided by the mechanical properties of nitinol in the frame, which applies an outward force to the cardiac ventricles, improving cardiac filling. A subcutaneously tunneled driveline transmits air for chamber expansion and deflation and the electrocardiogram.

An implantable direct cardiac compression device such as the CorInnova device offers several advantages over currently available mechanical cardiac

The Videos can be viewed in the online version of this article [https://doi.org/10.1016/j.athoracsur.2022.06.052] on http://www.annalsthoracicsurgery.org.

Accepted for publication Jun 21, 2022.

Address correspondence to Dr Letsou's current affiliation: Department of Surgery, St. Joseph's Medical Center, 1401 St Joseph Parkway, Houston, TX 77002; email: georgeletsou@gmail.com.

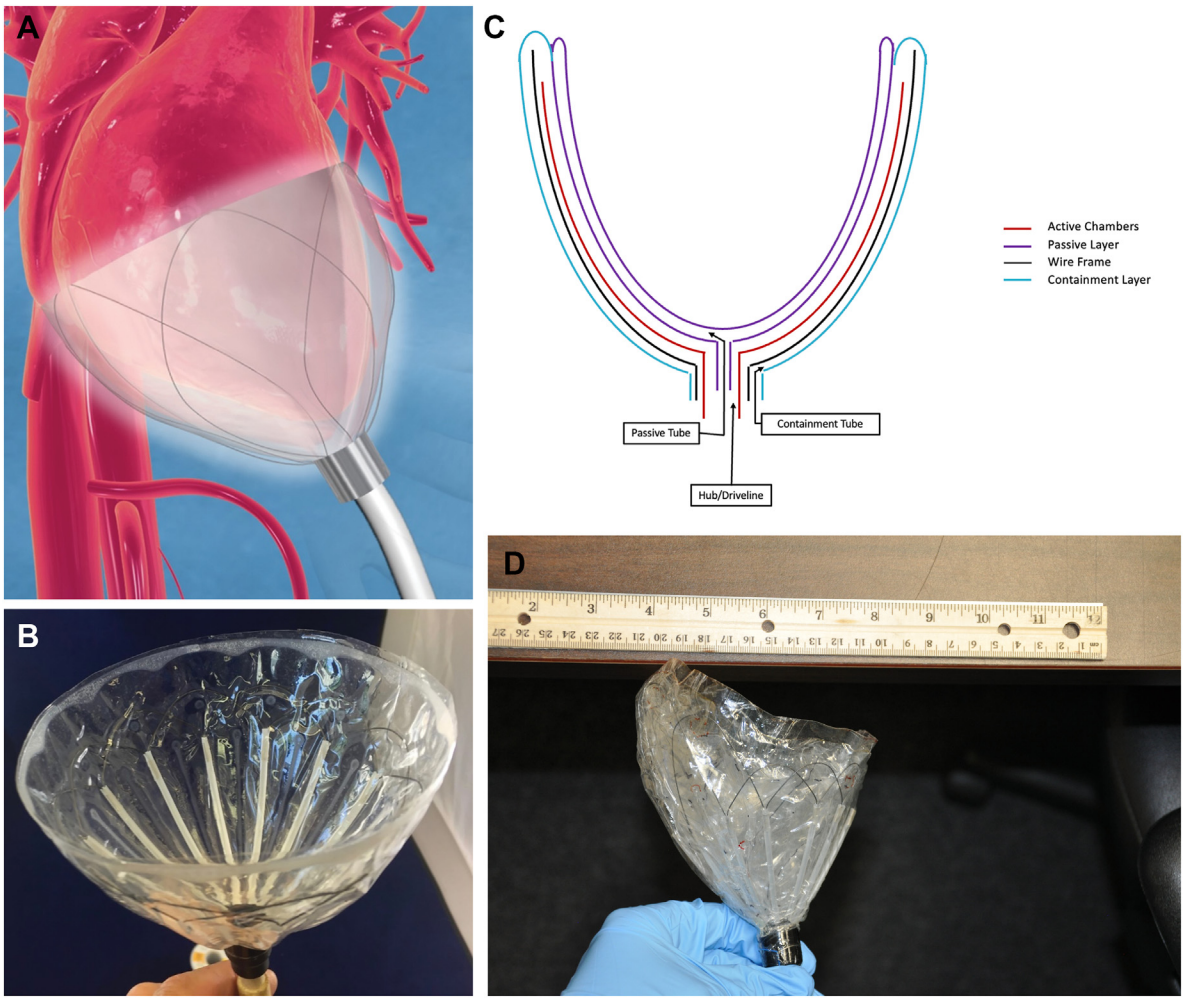

FIGURE 1 CorInnova device. (A) Line drawing of the CorInnova device. (B) Photograph of a symmetric device. (C) Cross-sectional diagram of the CorInnova device. The inner layer (purple) is the saline-filled passive chamber that conforms to the heart's surface and provides device–heart coupling to evenly transfer assist pressure from the active component to the ventricle. The middle layer (red) is the active chamber, which inflates and deflates to provide sequential compression and relaxation. The outer layers (blue and black) are the nitinol frame and a containment layer. (D) Photograph of an asymmetric device.

assist devices: It does not require anticoagulation, is suitable for patients with peripheral arterial disease, and provides biventricular assistance. In this proof-of-concept study we describe our initial results using the CorInnova device in an ovine model of chronic heart failure, documenting reproducible cardiac assistance.

TECHNIQUE

HUMANE ANIMAL CARE STATEMENT. All animals received humane care in compliance with the Guide for the Care and Use of Laboratory Animals. This study was approved by QTest Labs' Institutional Animal Care and Use Committee (QTest Labs study no. SPS16-008).

CREATION OF HEART FAILURE IN AN OVINE MODEL. Heart failure was induced in 7 sheep with microsphere embolization. Microspheres were 90-μm beads (6.24 × 104 particles/mL; Polysciences, Inc). Each injection was 1 mL (total of 2 mL injected). While each animal was under general anesthesia, a catheter was advanced into the circumflex coronary artery, and microspheres were injected. Electrocardiographic T-wave changes were used to determine the adequacy of embolization. One week later transthoracic echocardiography was performed. Two to 6 weeks afterward each animal underwent a second injection of microspheres and echocardiography.

NONSURVIVAL DEVICE ASSESSMENT. All animals underwent a nonsurvival study for device assessment while

under general anesthesia. Instrumentation included a Swan-Ganz catheter and arterial pressure monitoring with carotid artery cannulation. High-fidelity catheters (Millar, Inc) were used to record right ventricular (RV) and left ventricular (LV) pressures directly. A pulmonary artery (PA) flow probe was placed using a sternotomy before the animals were killed.

Five differently sized devices were available. Preoperative fluoroscopic imaging and direct intraoperative measurement of the distance from the atrioventricular groove to the cardiac apex were used to choose an appropriately sized device. The devices available had an axial height of 6.78 to 8.39 cm and a valve plane diameter of 9.68 to 11.88 cm.

The CorInnova assist device was placed through a small subxiphoid incision of approximately 2 inches. A 2-cm opening (the diameter of the insertion device) was created at the pericardial apex. The remainder of the pericardium was left entirely intact. For insertion the device was loaded into an introducer tube approximately 2 cm in diameter. The introducer tube was placed through the apical pericardiotomy (Video 1). The device was advanced under fluoroscopic guidance, and its base was positioned at the atrial-ventricular junction. The device's nitinol frame self-expanded to surround both cardiac ventricles (Video 2). After device expansion the intact pericardium secured the device in place. No sutures were necessary. The device's inner chambers were filled with saline to conform to the epicardial surface.

Device activation was timed by using an external controller triggered by the electrocardiographic QRS. Device inflation was timed to coincide with the initiation of the QRS and cardiac systole. The average length of systole was calculated. Device deflation was timed to occur with the onset of diastole. As with an intraaortic balloon pump, device inflation and deflation could be adjusted to optimize device performance. Device effectiveness was then determined. The device was activated for 1 hour. Central venous pressure, RV pressures, PA pressures, LV pressure, +dP/dt, -dP/dt, and cardiac output were determined before and 1 hour after device activation. Pressure and flow tracings with the device turned "on" and turned "off" were made by deactivating the device for 5 minutes after the 1-hour measurements had been completed. Animals were euthanized humanely at the end of the experiment.

CLINICAL EXPERIENCE

All 7 experimental animals responded well to embolism, showing substantial decreases in ejection fraction (Table 1). The average ejection fraction fell from 55.8% to 24.2%. Several conformations of the CorInnova device were assessed. A device with an asymmetric shape conforming to the asymmetric right ventricle was used in 5 animals (Figure 1D), and a device with a symmetric design was used in the remaining 2 animals (animals 3 and 7) (Figure 1B). The asymmetric device provided less pronounced hemodynamic alterations than the symmetric device. Because this was a proof-of-concept study, we did not average results among animals. Individual tracings demonstrating the hemodynamic effects of the 2 symmetric devices are shown.

To provide proof of concept we examined the symmetric device's effects on arterial pressure, LV pressure, RV pressure, cardiac output, +dP/dt, and -dP/dt. LV pressure tracings in the 2 animals with the symmetric device (animals 3 and 7) showed increases in LV pressure when the device was in assist mode. A representative LV pressure tracing in Figure 2A demonstrates effective increases in LV pressure, along with smaller decreases in diastolic LV pressure. As shown in Figure 2B, maximal LV pressure increased with device activation. Increases in aortic pressure occurred with increases in LV pressure (Figure 2C). Mean LV end-diastolic pressure decreased when the device was in assist mode compared

TABLE 1 Average Decrease in Left Ventricular EF and FS in the 7 Experimental Animals With Chronic Heart Failure

	Baseline		Heart Failure		Percent Change	
Animal	EF (%)	FS	EF (%)	FS	EF (%)	FS
1	55.4	28.1	30.5	14.5	–45.0	–48.6
2	56.8	29.5	21.8	10.1	–61.6	–65.8
3	43.2	20.6	30.7	14.3	–29.1	–30.8
4	49.9	24.4	19.0	8.6	–62.0	–64.9
5	60.2	31.3	23.4	10.9	–61.1	–65.3
6	58.4	30.9	28.1	13.2	–51.9	–57.2
7	66.4	36.2	16.0	7.2	–75.9	–80.2
Average	55.8	28.7	24.2	11.2	–55.2	–59.0
Standard error of the mean	2.8	1.9	2.1	1.1		

EF, ejection fraction; FS, fractional shortening.

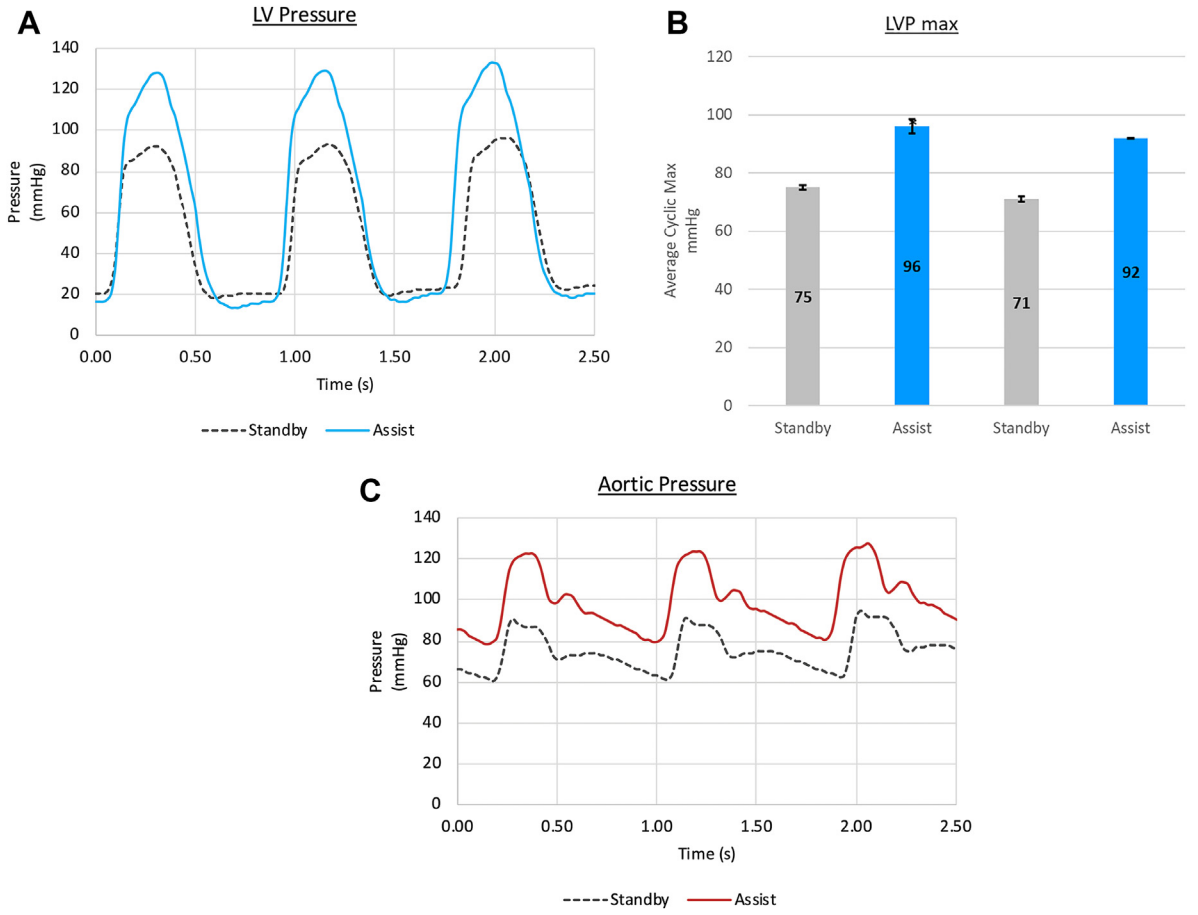

FIGURE 2 Left ventricular pressure (LVP) and aortic pressure measurements. (A) LVP in animal 3 determined by using a Millar catheter with the device in standby mode (dotted line) or assist mode (blue line). (B) Average LVP in animals 3 and 7 with the symmetric assist device in standby mode or activated for 1 hour. (C) Aortic pressure in animal 7 determined by using an arterial catheter when the symmetric device was in standby mode (dotted line) or activated (red line).

with when it was in standby mode (Figure 3A). When the device was in active mode, +dP/dt increased (Figure 3B).

Improved PA blood flow consistent with improved systolic RV function occurred with device activation. PA blood flow decreased during diastole with the device in assist mode compared with standby mode, consistent with decreased RV diastolic pressure (Figures 4A, 4B). Increased PA systolic flow and decreased PA diastolic flow with the device in assist mode were consistent with the systolic augmentation and diastolic unloading seen in the left ventricle.

A decrease in central venous pressure indicative of improved cardiac performance was observed when the device was in assist mode for 1 hour compared with standby mode (Figure 5A). Mean aortic pressure increased as well (Figure 5B).

Postmortem examination was performed after 1 hour of cardiac assist and euthanasia. No gross evidence of myocardial contusion, myocardial ischemia, or valvular damage was detected in any animal. Superficial inflammation of the epicardium was the only abnormality noted (Figure 6).

COMMENT

In this proof-of-concept trial the CorInnova direct cardiac compression device reliably reproduced hemodynamic improvements in LV pressure, LV +dP/dt, and aortic pressure and decreases in LV end-diastolic pressure in an ovine heart failure model. Increases in PA flow consistent with RV assist were also reproducible.

As described above the CorInnova device is constructed on a compliant nitinol frame, which is different from previous devices. The Anstadt Cup was constructed on a rigid frame; compression inverted the ventricles, compromising cardiac function.[1] The CorInnova device

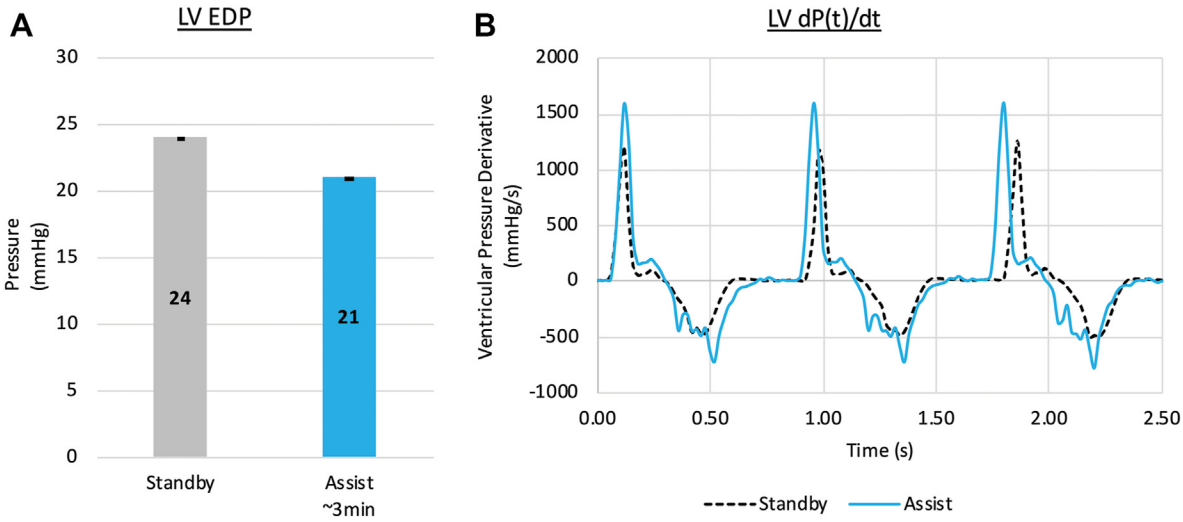

FIGURE 3 Mean left ventricular end-diastolic pressure (LV EDP) and +dP/dt measurements. (A) LV EDP in animal 6 after the device was in assist mode for 1 hour. (B) +dP/dt in an animal with heart failure with the device in standby mode (dotted line) or assist mode (blue line). The assist mode measurements were taken after 1 hour of assistance.

does not invert the ventricles. Furthermore, unlike other previous devices, the CorInnova device is anchored by the intact pericardium and inner layer of saline-filled chambers, allowing effective compression with each cycle. Maintenance of the intact pericardium is an extremely important device feature.[5]

Although we initially hypothesized that an asymmetric device may be more effective and less traumatic than a symmetric device, an asymmetric device produced less reliable hemodynamic effects. Cardiac contusion and bruising were not identified after assist with either symmetric or asymmetric devices. The availability of 5 differently sized devices avoids undersizing or oversizing. Echocardiography and intraoperative measurement reliably predicted appropriate device size.

The CorInnova device provided reproducible hemodynamic effects. Changes in pressure in the cardiac chambers, PA, and aorta were consistent with the time

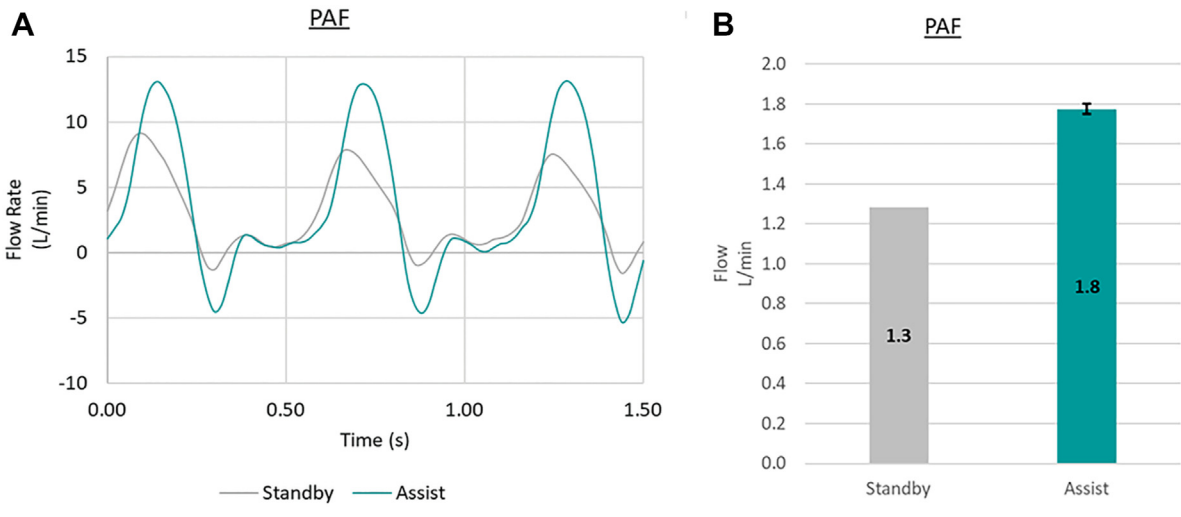

FIGURE 4 Pulmonary artery blood flow (PAF) measurements. (A) PAF in animal 7 determined by using a PAF probe with the device in standby mode (gray line) or assist mode (green line). (B) Mean PAF determined by when the device was in standby or assist mode. Assist mode measurements were taken after 1 hour of assistance. The device was then turned off for 5 minutes, and the measurements were repeated.

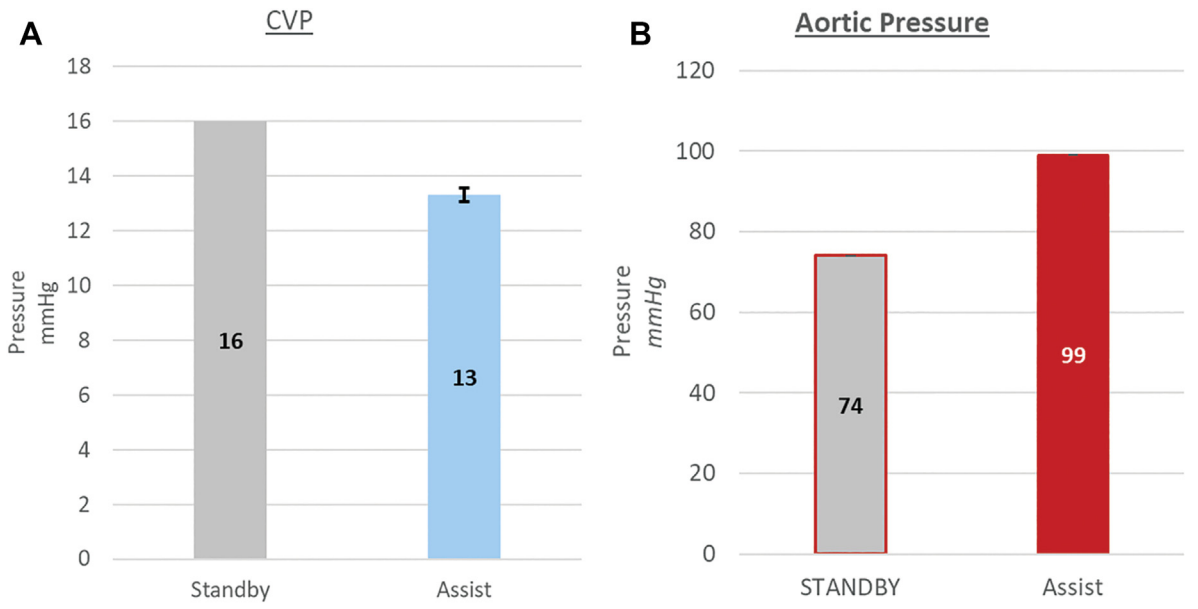

FIGURE 5 Improved hemodynamics with the device in assist mode compared with standby mode in animal 3. (A) Central venous pressure (CVP) determined by using a Swan-Ganz catheter when the device was in standby or assist mode. (B) Aortic pressure determined in the same animal when the device was in standby or assist mode.

course of device activation. The device provided support to both RV and LV chambers.

Our study had limitations. Seven animals were studied, but only 2 were studied with the more effective symmetric device. RV function was not assessed experimentally. Microspheres were selectively injected in the left circumflex coronary artery, and LV ejection fraction decreased, as expected. However the right coronary artery was not injected with microspheres, and we did not objectively assess RV function. Long-term animal survival studies will be necessary to determine whether the device can cause substantial pericardial effusions or restrictive cardiac disease. In conclusion we showed in an ovine model of cardiac failure that the implantable CorInnova direct cardiac assist device alters LV pressures, RV pressures, PA flow, dP/dt, and overall hemodynamics in a fashion consistent with the amelioration of heart failure.

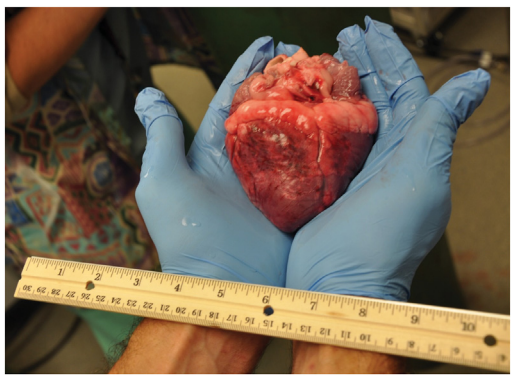

FIGURE 6 Gross ovine heart specimen demonstrating lack of gross injuries after cardiac assist for 1 hour with a CorInnova assist device.

FREEDOM OF INVESTIGATION

All authors had complete freedom of investigation as well as full control of the study design, outcome parameters, data analysis, and manuscript preparation.

DISCLAIMER

The Society of Thoracic Surgeons, Southern Thoracic Surgical Association, and *The Annals of Thoracic Surgery* neither endorse nor discourage the use of the new technology described in this article.

The authors thank Nicole Stancel, PhD, ELS(D), of the Department of Scientific Publications at the Texas Heart Institute, for her editorial contributions.

FUNDING

This work was funded by Wellcome Trust Translation Fund Award no. 104613, awarded to CorInnova, Inc (Houston, TX).

DISCLOSURES

Christina M. Bolch, Erica C. Hord, William C. Altman, Boris Leschinsky, and John C. Criscione are employees of CorInnova Inc. John C. Criscione also is a board member and consultant for and owns equity and stocks in CorInnova Inc. William C. Altman also is a board member for and owns equity and stocks in CorInnova Inc. All other authors have no conflicts of interest to disclose.

REFERENCES

1. Anstadt MP, Anstadt GL, Lowe JE. Direct mechanical ventricular actuation: a review. *Resuscitation*. 1991;21:7-23.

2. Letsou GV, Austin L, Grandjean PA, Braxton JH, Elefteriades JA. Dynamic cardiomyoplasty. *Cardiol Clin*. 1995;13:121-124.

3. Mann DL, Kubo SH, Sabbah HN, et al. Beneficial effects of the CorCap cardiac support device: five-year results from the Acorn Trial. *J Thorac Cardiovasc Surg*. 2012;143:1036-1042.

4. Schenk S, Reichenspurner H, Boehm DH, et al. Myosplint implant and shape-change procedure: intra- and peri-operative safety and feasibility. *J Heart Lung Transplant*. 2002;21:680-686.

5. Hord EC, Bolch CM, Tuzun E, Cohn WE, Leschinsky B, Criscione JC. Evaluation of the CorInnova heart assist device in an acute heart failure model. *J Cardiovasc Transl Res*. 2019;12:155-163.