First Clinical Experience With the Pressure Sensor–Based Autoregulation of Blood Flow in an Artificial Heart

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The CARMAT-Total Artificial Heart (C-TAH) is designed to provide heart replacement therapy for patients with end-stage biventricular failure. This report details the reliability and efficacy of the autoregulation device control mechanism (auto-mode), designed to mimic normal physiologic responses to changing patient needs. Hemodynamic data from a continuous cohort of 10 patients implanted with the device, recorded over 1,842 support days in auto-mode, were analyzed with respect to daily changing physiologic needs. The C-TAH uses embedded pressure sensors to regulate the pump output. Right and left ventricular outputs are automatically balanced. The operator sets target values and the inbuilt algorithm adjusts the stroke volume and beat rate, and hence cardiac output, automatically. Auto-mode is set perioperatively after initial postcardiopulmonary bypass hemodynamic stabilization. All patients showed a range of average inflow pressures of between 5 and 20 mm Hg during their daily activities, resulting in cardiac output responses of between 4.3 and 7.3 L/min. Operator adjustments were cumulatively only required on 20 occasions. This report demonstrates that the C-TAH auto-mode effectively produces appropriate physiologic responses reflective of changing patients' daily needs and represents one of the unique characteristics of this device in providing almost physiologic heart replacement therapy. *ASAIO Journal* 2021; 67;1100–1108

Key Words: total artificial heart, autoregulation, physiologic, hemodynamics, pulsatile, bioprosthetic

Biventricular heart replacement pumps are used to support or substitute the cardiac output of patients suffering from severe biventricular failure. One of the key objectives of this therapy is to discharge a patient back to a home environment and associated usual activities that make for a normal quality of life. A central requirement for achieving this is to have a device that can be autonomous while requiring minimal attention. From a physiologic standpoint, the device should emulate the function of a native heart. This should preferably be accomplished by providing fully pulsatile flow with normal flow and pressure profiles, a Starling-like response to changes of input pressure by modifying the cardiac output, along with maintaining a low right atrial pressure so as to avoid edema without creating negative atrial pressures. Therefore, left/right cardiac outputs need to be balanced to avoid pulmonary edema, while providing adequate end-organ perfusion. From a patient management perspective, the device needs to require minimal interventions and the patient needs to require minimal medications.

The CARMAT-Total Artificial Heart (C-TAH) has been designed to achieve above objectives by the incorporation of proven biocompatible materials,[1] a pumping mechanism which mimics ventricular dynamics[2] and a control algorithm which has a Starling-like response.[3]

This report details the clinical experience with the entire first cohort of 10 patients enrolled in the ongoing CE Mark trial (protocol details at ClinicalTrials.gov Identifier: NCT02962973).

Materials and Methods

Device Description

The C-TAH is a single-unit device with bioprosthetic blood-contacting surfaces, designed for orthotopic placement. Each ventricle consists of two compartments, separated by a hybrid membrane (**Figure 1**). Two electrohydraulic rotary pumps create systolic and diastolic phases by rapidly reversing the direction of hydraulic fluid-flow that, alternately, pushes and pulls the membranes. Pressure sensors in each ventricle provide information on preload

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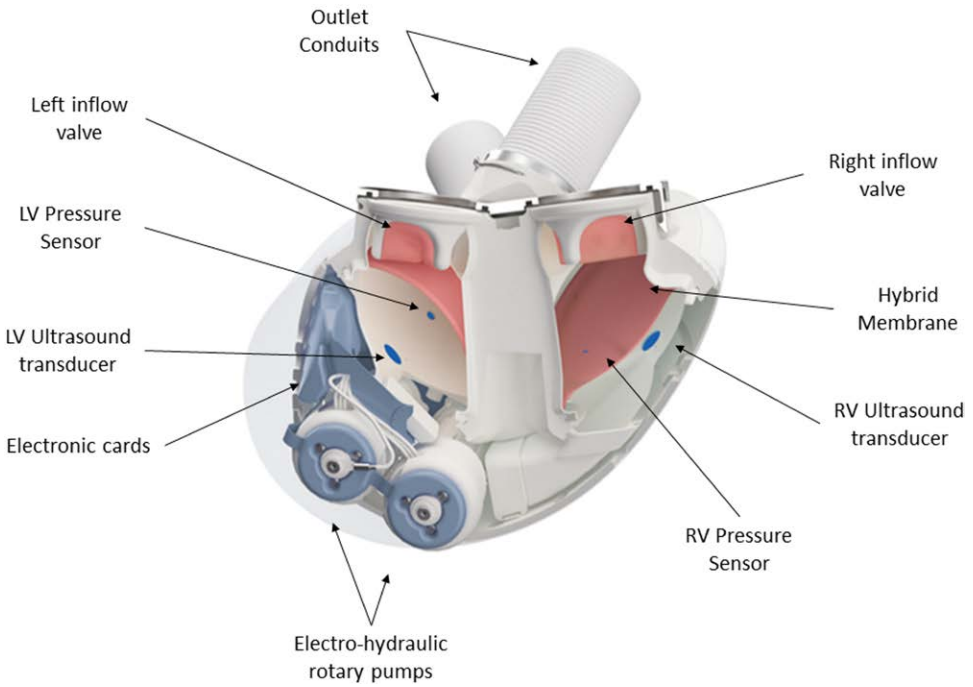

Figure 1. The CARMAT-TAH. LV, left ventricle; RV, right ventricle; TAH, total artificial heart.

and afterload, while ultrasound transducers measure the position of the membranes. The pressure sensors have a low 1 year drift of 0.375 mm Hg that might influence the cardiac output. However, this can be managed by adjusting the device settings. The cardiac output is calculated as the product of the ejected ventricular volume and the beat rate. An algorithm responds to changes in preload and afterload by adjusting the beat rate (35–150 beats per minute) while stroke volume is maximized to 55-60 ml (autoregulation).[3] The resulting pulsatile blood flow ranges from 2 to 9 L/min[1] with automated adjustments on the left side to correct for the contribution of the bronchial circulation. Electronics and microprocessors are contained within the device. Bioprosthetic valves (Edwards Lifesciences, Irvine, CA), located at the inflow and outflow of each blood compartment, maintain unidirectional flow. The prosthesis is partially surrounded by a flexible polyurethane compliance bag, that contains the hydraulic fluid. A percutaneous driveline (8 mm diameter) delivers power to the C-TAH and retrieves information on the device performance. The driveline connects to a portable controller and battery pack while providing an uninterrupted power supply and to display device data and alarms. A pressure sensor is integrated inside the controller to automatically calibrate the pressure sensors located inside the device. The physician connects a medical console to the controller to access medical information and change settings, as required.

Autoregulation

Auto-mode is an operating mode in which the C-TAH behaves similarly to Starling's law: it automatically adapts ventricular outputs in response to changes in preload detected by the pressure sensors located inside the device. Changes in filling duration, ejection duration, and end-diastolic volume result in beat rate variation, while complying with the set target values.

Three main adjustments allow physicians to modify the C-TAH performance envelope (**Figure 2**). The first is the right ventricular inflow pressure (RVIP), which is the right ventricular target pressure during diastole; the objective is to achieve a near-empty right atrium without creating suction. The second is the average left-right inflow pressure gap (ALRIPG), which is the target for the difference between the average left and right inflow ventricular pressures; the objective is to achieve an unloaded left atrium, and to manage left/right balance, to take into account the bronchial circulation. Finally, the left minimal outflow pressure threshold (LMOPT) is the target for a minimum average of the left outflow pressure, designed to accommodate instances of low arterial pressure.

The CARMAT-TAH function is divided into a diastolic and a systolic phase, as described later and in **Figure 3**.

Diastolic Phase

The diastolic phase targets a maximum stroke volume of 60 ml according to the three periods.

Period 1: Each diastolic phase starts with a filling of around 4 ml of blood into the ventricle to open the inflow valve. This is achieved by an initial rapid movement of the membrane.

Period 2: The ventricular pressure sensor monitors the pressure inside the ventricle, providing an evaluation of the venous return. The speed of the membrane is dynamically adjusted every millisecond to initially fill up to half of the ventricular volume (30 ml), modulated by the difference between the ventricular pressure and the set RVIP. When this difference is low, the speed of the membrane is slowed down to avoid dropping below the RVIP.

Period 3: The speed of the membrane is decreased to target the end-diastolic position for a maximum stroke volume of 60 ml while taking into account the difference between the RVIP and the ventricular pressure.

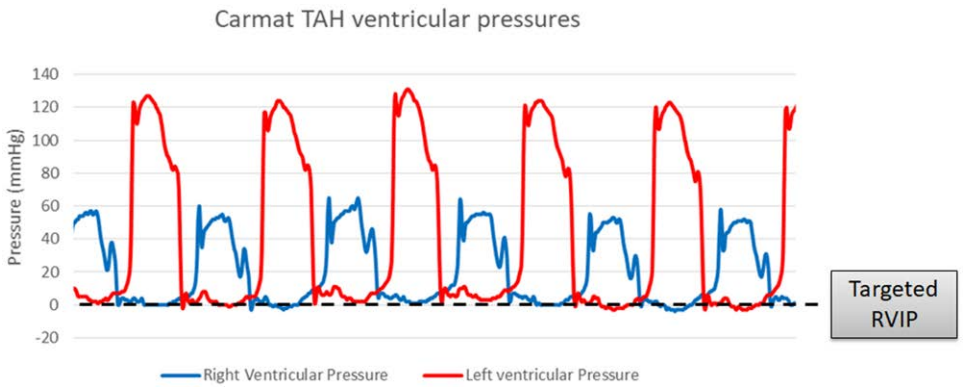

Figure 2. Real-time ventricular pressure curves with a RVIP set at 0 mm Hg. RVIP, right ventricular inflow pressure; TAH, total artificial heart.

In case of a negative pressure lower than 50 mm Hg developing during period 2 of the diastolic phase (due to inflow obstruction or severe hypovolemia), the diastolic phase is terminated early, as a safety measure to avoid atrial suction. The next systolic phase is then immediately initiated to minimize blood stasis.

Systolic Phase

The systolic phase is achieved in a time equivalent to a third of the full cardiac cycle and is designed to completely empty the ventricular blood volume. The speed of the membrane is increased until half of the blood volume (30 ml) is ejected and then decreased until reaching the end-systolic position at rest. That position of the membrane is controlled by an ultrasonic sensor located in the technical compartment of the ventricle. This enables the membrane to be adjusted at each beat to reach the optimal end-systolic position.

With respect to outflow pressures, only the left afterload influences the operation of the autoregulation algorithm. A low left afterload results in speeding up the systolic ejection time to eject the full volume in a shorter time and thus restore systemic blood pressure. Both ventricles are subject to a safety mechanism which halts systole early, and initiates the next diastolic phase, if the output pressures exceed 220 mm Hg.

Left/Right Balance Management

The stroke volume of each ventricle is continuously adjusted to avoid an imbalance between the average left and right inflow pressure of more than the LRIPG setting (2.5 mm Hg by default). If the actual difference is above the LRIPG, the right stroke volume is decreased to reduce the average left inflow pressure. When the average inflow pressure difference is below the LRIPG, the right stroke volume is maximized.

The above general functional description provides an overview of the algorithmic logic employed by the autoregulation of the device. The principle is to generate a cardiac output adjusted according to variations in the venous return. Therefore, the membrane speed is increased during the current cardiac cycle if the detected ventricular pressure (after opening the inflow valve) is higher than it has been in the previous cycle, thus creating a shorter diastolic phase. As a consequence, the beat rate increases while the stroke volume remains maximized, resulting in a higher flow.

Study Population

The first 10 consecutive patients enrolled in the European premarket clinical trial were included in this study (NCT 04475393). All patients were males with end-stage biventricular heart failure, predominantly in Interagency Registry for Mechanically Assisted Circulatory Support profile 3 at the time of implant (**Table 1**). The date of inclusion was the date of implantation for each patient. The follow-up end date was the May 31, 2019, or the time of device explantation before transplantation or death.

Data Collection

The autoregulation function was evaluated by examining how the device responds to changes in preload. Functional data are stored in the portable controller and the medical console and were collected throughout the study. Beat by beat cardiac output, stroke volume, beat rate, and pressures were evaluated after the switch from manual mode to auto-mode, while a 10 minute rolling average was used to analyze the behavior of the device, according to the venous return.

We also wanted to determine how often the physicians made autoregulation setting adjustments. Therefore, we analyzed all setting changes that were maintained for more than 24 hours. Temporary changes were excluded for two reasons. First, every single setting change is automatically stored by the device; thus, there can be several recorded lines for the same parameter change. Second, since less experienced physicians may change a parameter experimentally, to observe the effect, they will also cancel it on the same day.

Other clinical data, such as pre- and postoperative characteristics, were collected from the Case Report Forms. Preimplant data were recorded from the baseline or the screening data, if needed.

Analyses were performed with SAS software 9.4. Continuous data were expressed as mean ± standard deviation. Categorical variables were expressed by an absolute value and as a percentage.

Results

The device was successfully switched from manual mode to auto mode in the operating room, following weaning from cardiopulmonary bypass (CPB), in all patients. This resulted in an

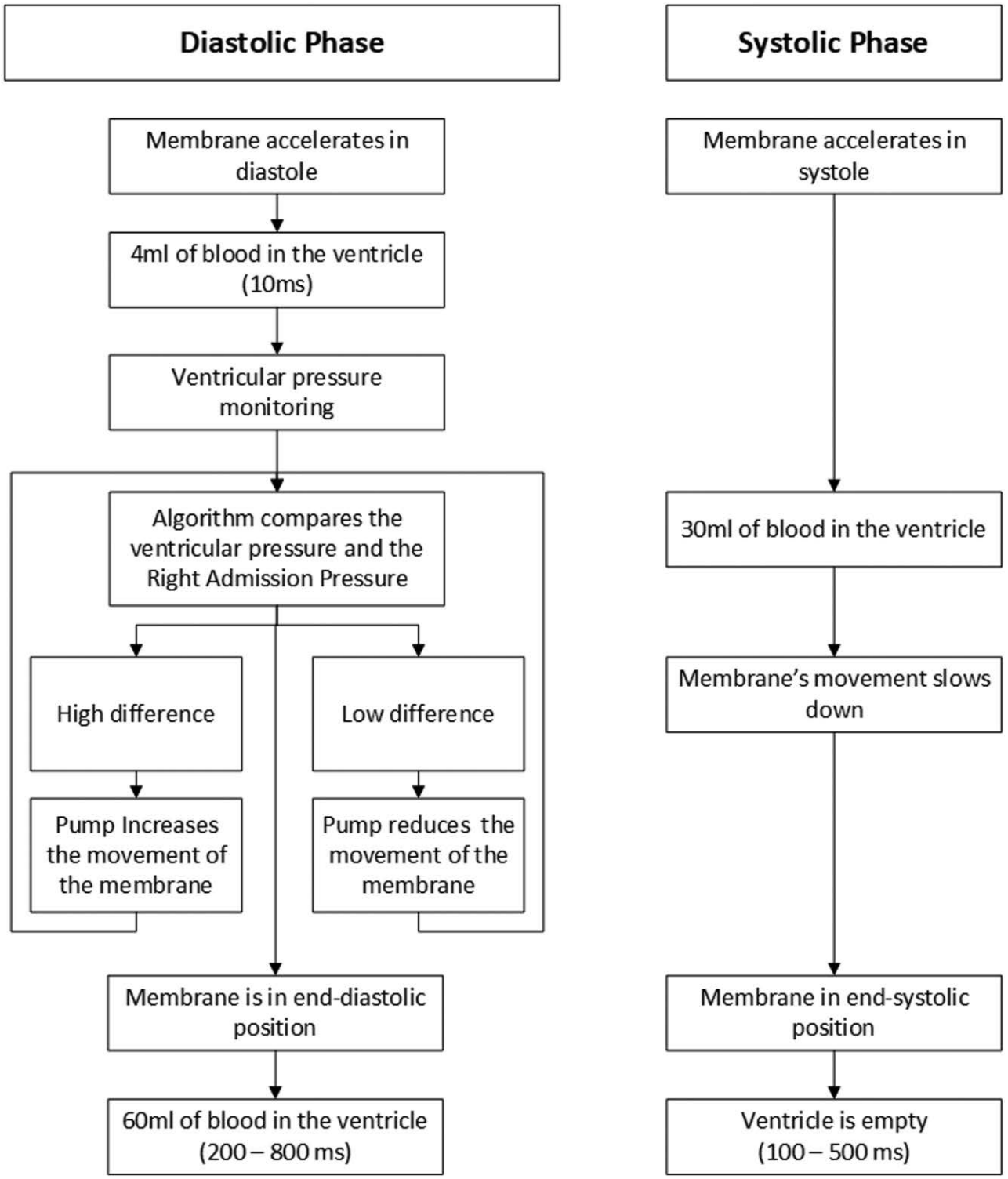

Figure 3. Flowchart describing the autoregulation mechanism of the CARMAT-TAH. TAH, total artificial heart.

immediate appropriate cardiac output response to the targeted RVIP and variations of venous return (**Figure 4**). In manual mode, the cardiac output is fixed. When switched to auto-mode, the cardiac output adapts to the venous return resulting in stable inflow pressures, according to the targeted left and right inflow pressure settings.

The cumulative auto-mode duration for all 10 patients throughout the study was 1,842 days. The default settings (RVIP = 0 mm Hg, average LRIPG = 2.5 mm Hg, LMOPT = 90 mm Hg) were most commonly used in these patients, for a cumulative duration of 1,580 days (86% of the time in auto-regulation). Analysis of the recorded device hemodynamic

Table 1. Patient Characteristics

Characteristics	Mean ± SD
Male	10 (100%)
Age at implant, years	60.1 ± 10.1
Weight, kg	82.9 ± 7.3
BSA, m^2	2.0 ± 0.1
INTERMACS patient profile	
2	1 (10%)
3	8 (80%)
4	1 (10%)
Indication	
Bridge-to-transplant	6 (60%)
Destination Therapy	4 (40%)
Cardiomyopathy	
Dilated	6 (60%)
Ischemic	4 (40%)

Continuous data are expressed as mean ± standard deviation and categoric data as a number with a percentage.

BSA, body surface area; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; SD, standard deviation.

trends show the expected variations in left and right ventricle outputs, corresponding to changes in the inflow pressures, as a consequence of beat rate variations, while stroke volumes were maximized (**Figure 5**). Left ventricular outputs ranges from 4.3 to 7.3 L/min for average left inflow pressures ranges of 6–19 mm Hg. On the right side, the ventricular output ranges from 4.2 to 7.2 L/min for average right inflow pressures ranging of 4–17 mm Hg. The average beat rate ranges from 78 to 128 bpm.

Management of Autoregulation Device Settings

Twenty auto-mode setting changes were performed by the medical teams during a cumulative implant duration of 5 years (**Table 2**). Nearly all the changes (n = 18) were related to the RVIP. One was related to the LRIPG and one was an adjustment to the LMOPT. Thirteen device setting changes were done during the first 30 days while 11 were done in the intensive care unit (ICU). After discharge, only four setting changes were made, on the seven outpatients, during more than 44 cumulative months. This represents approximately one setting change per 11 patient months.

Hemodynamic Recovery

Hemodynamic normalization was evident almost immediately after implantation (**Table 3**). The C-TAH provided a satisfactory cardiac index of 2.80 ± 0.33 L/min/m^2 as early as postoperative day 1 (*vs.* 1.57 ± 0.52 L/min/m^2 at the baseline) and with much lower preloads (central venous pressure 10.4 mm Hg on day 1 *vs.* 12.8 ± 6.8 mm Hg at the baseline and left atrial pressure 10.2 ± 2.9 mm Hg on day 1 *vs.* 23.3 ± 10.4 mm Hg at the baseline). The cardiac index was subsequently well maintained during the support duration with an average of 3.03 ± 0.27 L/min/m^2 at 6 months. Preloads continued to remain low, as indicated by the lower jugular vein diameter (12.8 ± 2.1 mm at 6 months *vs.* 15.0 ± 4.6 mm at baseline) and by device data recordings of mean

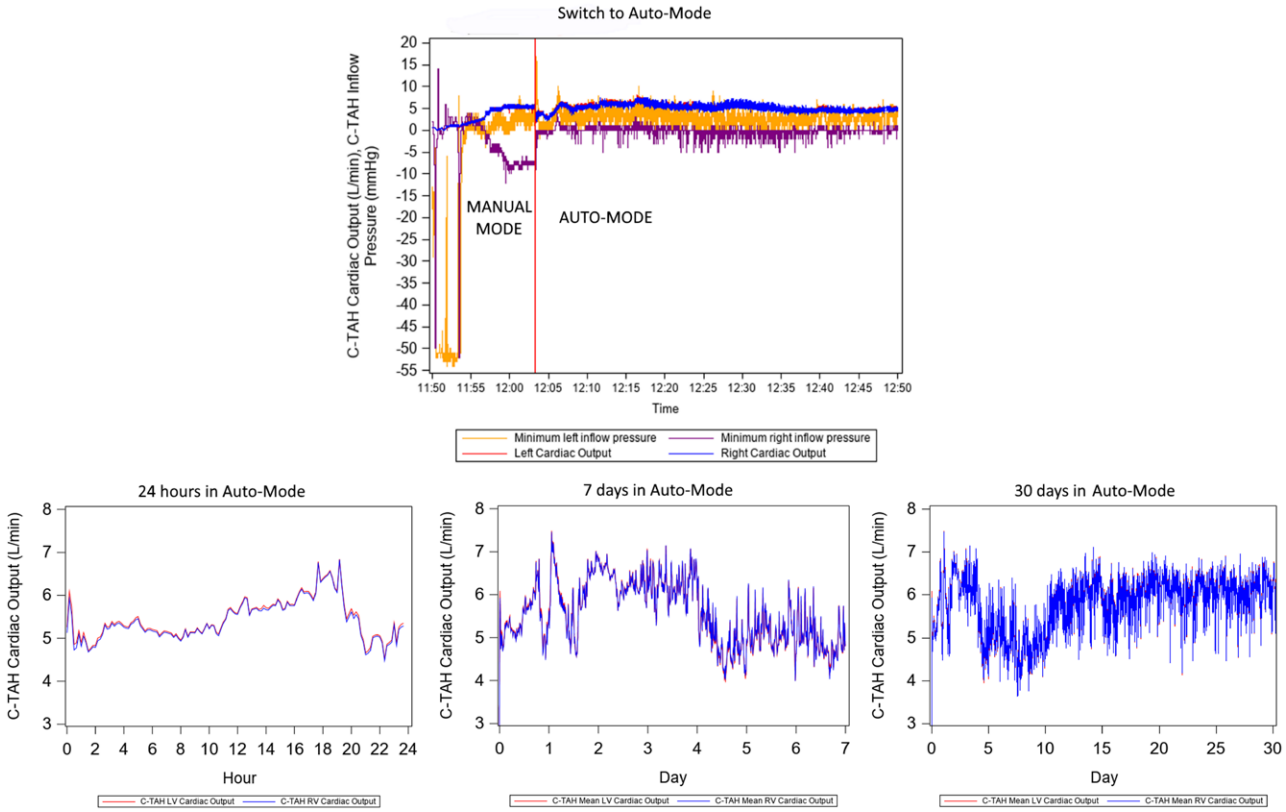

Figure 4. Responsiveness of the C-TAH when switched from manual to auto-mode with a targeted right ventricular inflow pressure of 0 mm Hg is demonstrated. Cardiac output in the first day, in the first week, and in the first month after the switch into auto-mode is shown for one patient in the three figures at the bottom. C-TAH, CARMAT-Total Artificial Heart; LV, left ventricle; RV, right ventricle.

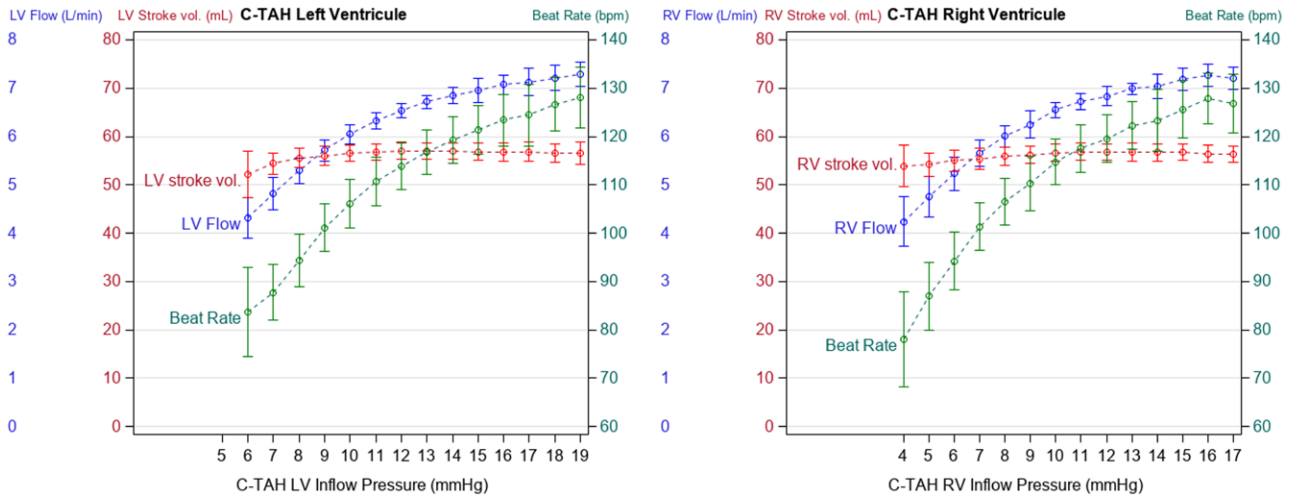

Figure 5. Pump output variation in response to inflow pressures is accomplished by beat rate changes while stroke volume (50–60 cc) is maximized. The C-TAH data of the device of the 10 patients when set at the default auto-mode setting were accumulated. C-TAH, CARMAT-Total Artificial Heart; LV, left ventricle; RV, right ventricle.

values throughout the study; C-TAH Right Inflow Pressure (9.9 ± 3.3 mm Hg) and C-TAH Left Inflow Pressure (12.0 ± 3.4 mm Hg) at 6 months *versus* 6.8 ± 1.5 mmHg and 9.56 ± 1.4 mm Hg at day 1. Patient's systolic blood pressures were satisfactory from postoperative day 1, with average pressures over 100 mm Hg, trending up by 20 mm Hg at 6 months.

Discussion

One of the challenges of mechanical circulatory support (MCS) therapy has been the lack of devices with interactive control systems that automatically and physiologically adjust to the patients' hemodynamic changes. Normal cardiac physiologic control involves neural, hormonal, and intrinsic myocardial mechanisms. These mechanisms are obviously unavailable to an inanimate device.

The pneumatically powered SynCardia temporary Total Artificial Heart (TAH) is employed as a bridge-to-transplant (BTT) device in those patients with irreversible biventricular heart failure, at imminent risk of death. The beat rate, positive and negative pneumatic pressures, and the systolic duration are set manually. Thus, to respond to changes in the preload, the device is only partially filled at rest. Increases in output therefore rely on an increased preload causing an elevated stroke volume, up to a maximum of 70 ml. This results in a very truncated physiologic response due to a cardiac output increase of only 9% during exercise.[4]

In the case of the off-label use of two implantable continuous flow left ventricular assist devices (CF-LVADs), physiologic interaction with the patient is more complicated because both devices are placed in parallel to the existing cardiovascular system, where the patient's heart makes a variable contribution within the combined system. As LVADs are not designed to support the right ventricle, surgical techniques are modified to address this need, such as shortening the length of the inflow cannula,[5] inserting the right inflow cannula in the right atrium, instead of the right ventricle free wall, to avoid thrombosis[6] or downsizing the right-sided outflow graft diameter to avoid an elevated right outflow.[5]

Table 2. Auto-Mode Device Settings Changes During Patient Follow-Up

Location	Cumulative Months	Number of Setting Changes	Number of Setting Changes/Patient Month
ICU (n = 10)	5.8	11	1.91
General ward (n = 8)	10.2	5	0.49
Out of hospital (n = 7)	44.4	4	0.09
Total	60.4	20	0.33

ICU, intensive care unit.

The C-TAH autoregulation aims to come closer to a natural physiologic interaction with the patient. The manual mode of the C-TAH used a nominal operating mode during the feasibility study[7] which is now only used during deairing and weaning from CPB. In all patients, observed in this study, the device was successfully switched to auto-mode perioperatively. The C-TAH produces a significant increase in cardiac output in response to increased venous return, by beat rate adjustments (more than 3 L/min as observed in **Figure 5**) without device setting changes, and diminishes the risk of blood stasis by targeting a full ejection. The only event which could lead to a decreased stroke volume is a reduced venous return, due to either severe hypovolemia or a cardiac tamponade.

The management of the left/right balance is a challenge when using biventricular MCS. After implantation of two CF-LVADs, speed optimization of the 2 independent pumps requires echocardiography guidance to achieve a neutral interventricular septal position.[8] Subsequently, any modification of speed implemented on one pump requires a matching speed modification of the other pump. Patients supported with two such pumps suffer a limited quality of life due to the necessity of two sets of external equipment, as well as two drivelines. This may not only increase the risk of infection but also lead to additional patient discomfort.

There is also growing evidence that a pulsatile flow brings some significant advantages[9,10] in MCS. Pulsatility is difficult to achieve with small rotary continuous flow pumps and is also negatively influenced by interactions with the native heart. Several methods to compensate such challenges have been used, including the variation of pump speed and the sensing of native ventricular pressures.[11] Additionally, the aforementioned

Table 3. Pre- and Postoperative Hemodynamic Characteristics

Variable	Preimplant (n = 10)	D1 (n = 10)	D7 (n = 10)	M1 (n = 9)	M3 (n = 7)	M6 (n = 5)
Patient hemodynamic characteristics						
Systolic blood pressure, mm Hg	99.0 ± 10.0	105.1 ± 16.2 (p = 0.389)	109.6 ± 12.1	115.2 ± 10.1	114.0 ± 6.6	124.6 ± 23.0
Diastolic blood pressure, mm Hg	65.9 ± 5.0	57.2 ± 6.7 (p = 0.016)	60.1 ± 10.7	67.3 ± 10.2	75.3 ± 7.7	79.4 ± 5.6
Mean blood pressure, mm Hg	76.7 ± 6.6	72.8 ± 9.5 (p = 0.719)	75.9 ± 10.9	82.9 ± 8.8	87.9 ± 4.9	94.0 ± 10.0
Central venous pressure, mm Hg	12.8 ± 6.8	10.4 ± 2.6 (p = 0.207)	11.7 ± 5.9 (n = 9)	N.A.	N.A.	N.A.
PCWP (preimplant)/left atrial pressure (postimplant), mm Hg	21.6 ± 7.8 (n = 9)	10.2 ± 2.9 (n = 9) (p = 0.221)	11.2 ± 6.1 (n = 5)	N.A.	N.A.	N.A.
Right cardiac output, L/min	3.14 ± 0.97	N.A.	N.A.	N.A.	N.A.	N.A.
C-TAH hemodynamic characteristics						
C-TAH left cardiac output, L/min	N.A.	5.73 ± 0.63	5.87 ± 0.79	6.11 ± 0.66	5.85 ± 0.57	6.15 ± 0.58
C-TAH right cardiac output, L/min	N.A.	5.64 ± 0.59	5.78 ± 0.74	6.03 ± 0.66	5.78 ± 0.62	6.09 ± 0.57
C-TAH R/L cardiac output ratio	N.A.	0.99 ± 0.01	0.99 ± 0.02	0.99 ± 0.02	0.99 ± 0.02	0.99 ± 0.01
C-TAH left stroke volume	N.A.	56.9 ± 1.7	55.8 ± 1.9	55.9 ± 2.8	57.2 ± 2.7	56.2 ± 2.1
C-TAH right stroke volume	N.A.	56.2 ± 2.2	55.0 ± 2.5	55.3 ± 3.6	56.5 ± 2.9	55.7 ± 2.4
C-TAH beat rate, bpm	N.A.	99.7 ± 13.3	104.4 ± 14.4	108.6 ± 13.9	101.6 ± 13.3	108.4 ± 9.5
C-TAH left inflow pressure, mm Hg	N.A.	9.6 ± 1.4	10.2 ± 2.1	10.2 ± 2.0	9.9 ± 2.3	12.0 ± 3.3
C-TAH right inflow pressure, mm Hg	N.A.	6.8 ± 1.5	8.2 ± 2.4	8.4 ± 1.8	7.4 ± 2.7	9.9 ± 3.4
C-TAH left outflow pressure, mm Hg	N.A.	97.8 ± 8.8	94.0 ± 6.3	95.0 ± 4.2	99.5 ± 4.2	105.3 ± 12.3
C-TAH right outflow pressure, mm Hg	N.A.	46.1 ± 7.4	48.5 ± 10.4	48.6 ± 9.4	43.9 ± 7.1	48.2 ± 10.3

p value denotes difference at D1 from preimplant value.

C-TAH, CARMAT-total artificial heart; D1, day 1; D7, day 7; M1, month 1; M3, month 3; M6, month 6; N.A., not available; PCWP, pulmonary capillary wedge pressure.

approaches may result in additive blood trauma due to rapid speed modulation and associated shear rates.[12]

For the SynCardia TAH, the left/right balance is managed semiautomatically by the device, using the mechanism of partial-fill, along with independent negative pressure settings for each ventricle. However, with this device a higher risk of stroke and bleeding is incurred due to the combination of partial ventricular fill and mechanical valves.[13] Furthermore, the driving system is, despite its refinements, still relatively noisy[14] thus negatively impacting the patients' quality of life.

The C-TAH, in comparison, automatically manages the left/right balance by maintaining a preset difference between right and left inflow pressures. Thus, the left and right outputs are automatically adjusted to always maintain an optimal inflow pressure difference, compensating for the bronchial flow. This preset difference (ALRIPG) was only modified for the first autoregulated patient, 3 days after implantation. It was not modified for any other patient. The reduced need for device management changes may contribute to greater autonomy for patients outside of the hospital environment and thus improve their quality of life.

The modification of settings of biventricular MCS systems can be required in several situations. Mitigation of this need is appreciated by both the medical team and the patient. Conversely, LVAD management requires optimization of pump speed according to the patient's hemodynamic status to unload the left ventricle, without inducing suction or right ventricular dysfunction.[15]

On the C-TAH, most setting changes were executed during the first 30 days postoperative, predominantly in ICU, while only four were performed after discharge. Among the 20 changes, 18 concerned the RVIP. This corresponds to the targeted right venous return pressure. It has been suggested that an abrupt increase in blood flow in some patients adapted to chronic low cardiac outputs may result in a renal reperfusion injury, during the early postoperative recovery phase,.[7] It is therefore possible that lifting the RVIP parameters up during this early phase might bring some benefits (**Figure 6**). Adjustments to the RVIP were also made for hypovolemic episodes while clinical interventions (diuretics dose adjustments, volume infusion, *etc.*) were optimized. After the restoration of optimal intravascular volume, the device was generally set back to the default setting. Seven patients were discharged home with the default device settings, demonstrating that, despite temporary setting modifications while the patient is in hospital, the clinicians considered that default settings provide an optimum function. In addition, two patients did not require setting adjustments at any time throughout their entire support. For illustrative purposes, the 1 year hemodynamic trends of one of these patients are shown in **Figure 7**. This depicts the autonomous variation of the cardiac output according to the average inflow pressure.

The current study has several limitations. It is a nonrandomized observational study recording the first clinical experience with the new autoregulation system. The small number of patients (n = 10) and the low number of only 3 study centers may limit the significance of the data. All patients were male, however this is common in biventricular support.[13] Since this is an ongoing study, total cohort outcomes were not available at the time of submission of this article. Additionally, the minimal long-term drift might have an effect on the accuracy of the autoregulation response. However, there was no clinical situation on any patient in the current study requiring adjustment of auto-mode device settings that might have been caused by this drift.

Nevertheless, it represents a significant experience of more than 4 years of device performance with an overall positive and promising outcome for the patients yet requiring only minimal intervention from the clinicians.

In fact, this experience will allow further improvements of the system. Although an observation on exercise response was not part of this study, we intend to do so in the future.

In summary, the C-TAH autoregulation system ensures a fully pulsatile cardiac output, that is automatically adjusted, according to the venous return. It allows an immediate and durable hemodynamic recovery, with low preloads, and

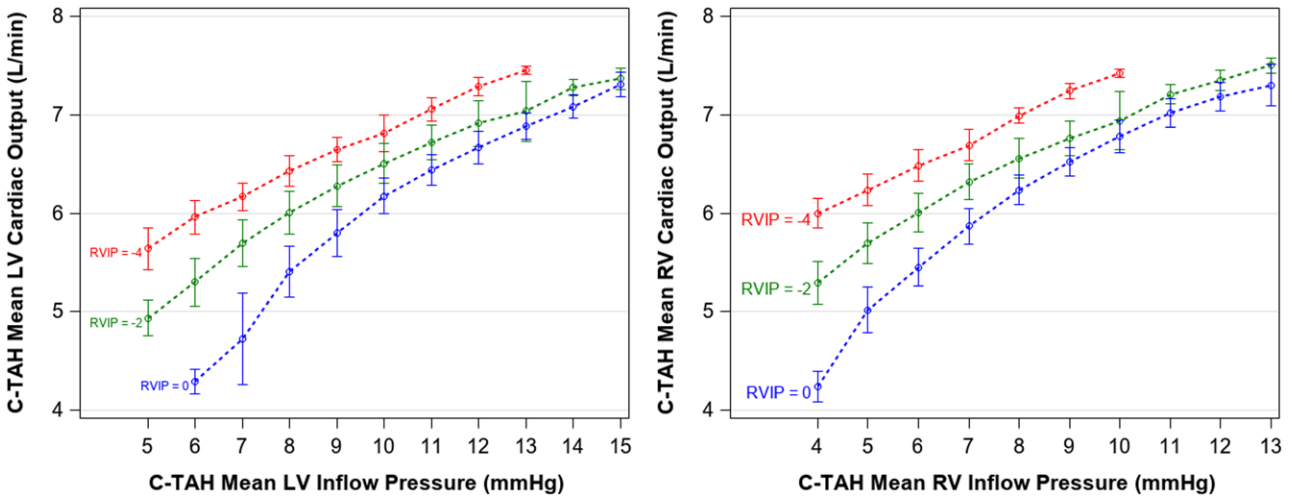

Figure 6. The left and right ventricular cardiac output variations in response to inflow pressures, at three RVIP settings, in a representative patient. A lower set RVIP resulted in a higher cardiac output, at the same averaged inflow pressure. C-TAH, CARMAT-Total Artificial Heart; LV, left ventricle; RV, right ventricle; RVIP, right ventricular inflow pressure.

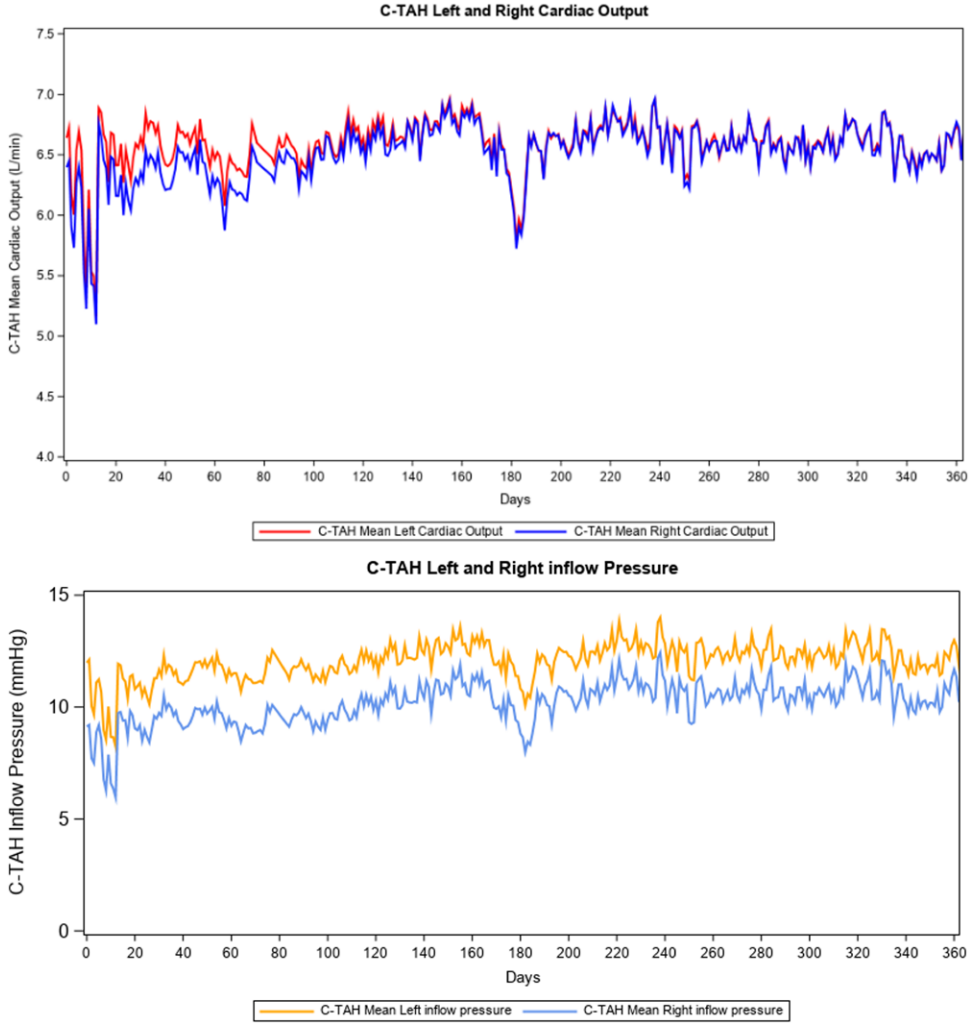

Figure 7. Daily average cardiac output and inflow pressure in autoregulation without setting changes, measured over 1 year of support. C-TAH, CARMAT-Total Artificial Heart.

normal systolic blood pressures. Whether the low number of device setting interventions will result in reduced readmission rates needs to be elucidated in broader scale future studies with the C-TAH.

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