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**Artificial Heart and Cardiac Assist Devices**

# Circulatory assist with centrifugal pump as a bridge to recovery: Mathematical analysis

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*ABSTRACT: Mechanical circulatory support is an essential issue in the management of patients with end-stage cardiac failure. The aim of this study is to evaluate the efficacy of temporary support with a centrifugal blood pump as bridge to heart function recovery or bridge to transplantation.*
*Heart recovery is achieved by improving ventricular mechanical working conditions with proper modifications of preload and afterload.*
*This article assesses the advantages of a novel "cardiac chambers" cannulation setting versus the traditional one, in the case of biventricular or isolated right ventricular failure. The study was conducted using a numerical computer model based on the work by Guyton, Sagawa, Westerhof, and Noordergraaf . Simulation of the planned trials was achieved by changing the model parameters, the pump angular velocity, and the inflow and outflow settings. (Int J Artif Organs 2007; 30: 604-10)*

*KEY WORDS: Ventricular assist device, Centrifugal pump, Extracorporeal membrane oxygenator, Pressure-volume loops, Native ventricle and mechanical pump interaction, Circulatory support*

## INTRODUCTION

In recent years, thanks to technological improvements, centrifugal blood pump devices have been used in the treatment of heart failure not only for short-term support (one week) but also for mid-term support (30-40 days).

A mechanical cardiac assist device may provide an increase of myocardial ventricular energetic efficiency and a reduction of the wall stress as well, which is essential to both bridge-to-recovery and bridge-to-transplantation aims.

The goal of this study is to evaluate, through a numerical computer model, how different cannulation settings of cardiac chambers may improve both myocardial energetic efficiency and wall stress when providing isolated right ventricular or biventricular mechanical support.

Our study investigates the interaction between the centrifugal pump and the circulatory system, focusing on the relationship between pressure-volume loops (PV loops), energetic efficiency, wall stress, and ventricular preload-afterload flow rate balance according to Frank-Starling's law (7, 8).

## MATERIAL AND METHODS

A numerical computer model was used to reproduce two pathological situations: biventricular heart failure, and isolated right ventricular failure. Both conditions were evaluated by comparing two different, parallel designs of a mechanical support circuit with a centrifugal blood pump.

The traditional design drains the blood from the right atrium and reinfuses it into the ascending aorta (configuration RA---Ao), through the pump and the oxygenator. The second design, adopted by our institute, consists of draining the blood from both atria with the aid of two equally sized cannulae, through a "Y" branching connection, and reinfusing it into the ascending aorta (configuration RA+LA---Ao), through the pump (Jostra Rota Flow Pump, Maquet Cardiopulmonary AG,

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Hirrlingen, Germany) and the oxygenator (Quadrox Jostra D, Maquet Cardiopulmonary AG, Hirrlingen, Germany).

Conventionally, in the case of right ventricular support, the inflow cannula is placed in the right atrium and the outflow cannula in the pulmonary artery (configuration RA---PA). We suggest conveying the blood from the right atrium, as for traditional inflow cannula placement, to the pump (Jostra Rota Flow), the oxygenator (Quadrox) and, finally, to the left atrium, as the outflow placement (configuration RA---LA).

These clinical situations can be represented by a numerical model which uses a nonlinear lumped-parameter mathematical model, simulating the circulatory system and the ventricular assist device. Ventricles and atria are described by a time-varying elastance model with nonlinear end-systolic and end-diastolic pressure volume relations (ESPVR and EDPVR) (1-4). The systemic and pulmonary arterial loads follow the Westerhof (6) and Noordergraaf (4) models. The systemic and pulmonary venous return follows Guyton's model (5).

The oxygenator is a constant hydraulic resistance without inertance and compliance. The pump (with a velocity controller) is a flow-pressure relation which is a function of the angular velocity. Lumped parameters cells (RLC) are used for the cannulae.

Matlab Simulink software was used to implement the entire simulation model.

Figure 1 shows the scheme of the model. Dashed lines represent the cannulae and the various connections are created for each of the different experiments. One limitation is the propagation time of a pressure wave along the cardiovascular network, which is not well represented in lumped-parameter models as a limited number of cells. The numerical values of the model parameters were chosen based on the literature and our clinical experience. There was no planned, specific protocol for the measurement settings, and variable waveforms were created from standard measurements by following appropriate approaches based on well-described models and estimation methods, thereby making it possible to evaluate the proposed circuits with a centrifugal pump device.

## RESULTS

The results obtained, following different approaches to treat the same pathologic situation, were compared:

1) Biventricular failure: our circuit, described as configuration RA+LA---Ao, compared to the conventional RA---Ao;
2) Right ventricular failure: our circuit, described as configuration RA---LA, compared to the conventional RA---PA.

### *Biventricular failure*

In the case of biventricular failure, the starting reference values of the parameters and variables were: mean right atrium pressure (RAP) = 15 mmHg; mean pulmonary artery pressure (PAP) = 30 mmHg; mean left atrium pressure (LAP) = 25 mmHg; maximal aortic pressure (AoP) = 80 mmHg; mean aortic pressure (AoP) = 60 mmHg; cardiac index < 2 liters/min/m$^2$.

The test was conducted as follows:

1) 0 - 35 seconds: pathological state; the pump is connected but not working; the outflow and the inflow cannulae are clamped.
2) 35 - 40 seconds: the cannulae are open; the pump starts to reach the steady state (transitory phase).
3) 40 - 55 seconds: the fluid-dynamic steady state has almost been achieved.
4) 55 - 70 seconds: left ventricle afterload is reduced by about 30%, due to the connection of an intra-aortic balloon pump (IABP) .

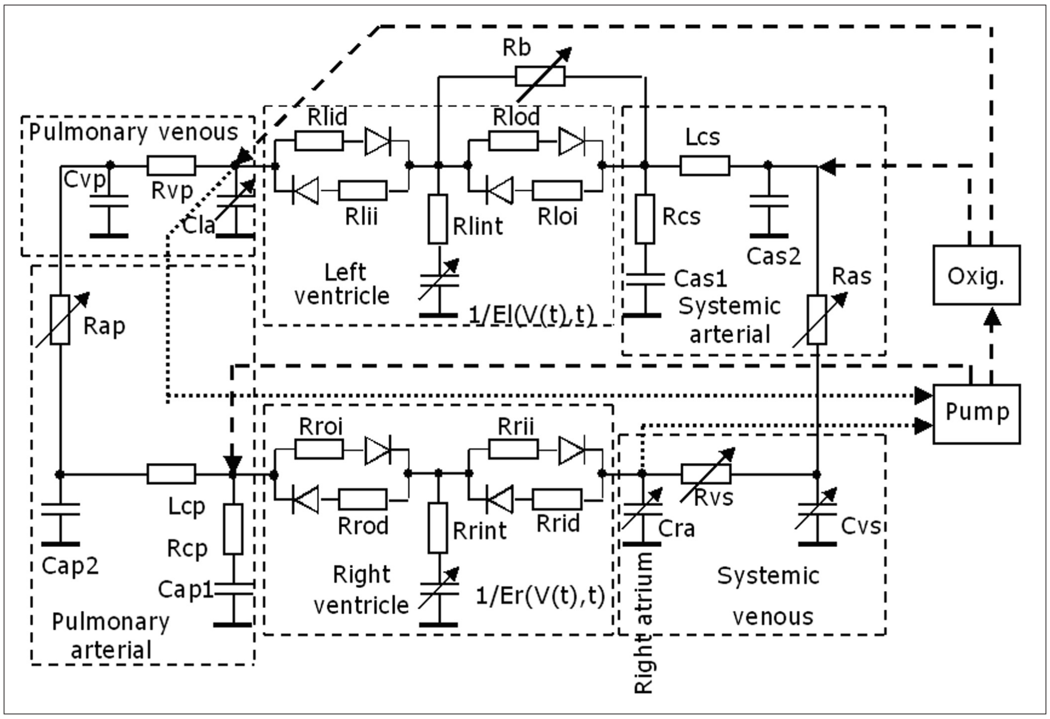
In configuration RA+LA---Ao, both atrial pressures decrease (RAP= 8 mmHg; LAP= 12 mmHg). The right atrium (RA) and left atrium (LA) outputs are not equal and the ratio changes during the working of the pump, depending on the system status and, especially, on the atria pressures (Figs. 2, 3).

At 0 - 35 seconds, the following flow rates balance is obtained: Qirv = Qorv = Qolv-Qb+Qpump (Qpump= 0) (Qivr and Qorv = input and output instantaneous volumetric flowrates of right ventricle; Qolv = output instantaneous volumetric flowrate of left ventricle; Qb = bronchial volumetric flowrate; Qpump = volumetric flowrate of the pump). The left and right ventricles (LV, RV) pressure-volume loops are not physiological as the stroke volume is low, average volumes are high, and consequently, the energetic efficiency ($\eta$) is low and ventricular wall stress ($\sigma$) is high.

At 35 - 40 seconds, the pump starts to work to reach the steady state.

At 40 - 55 seconds, the LV preload decrease, associated with the afterload increase, reduces the flow

**Fig. 1 -** *El(V(t),t) = pressure volume time relation in the left ventricle; Er(V(t),t) = pressure volume time relation in the right ventricle; Rlint, Rrint = generator resistances El(V(t),t), Er(V(t),t); Rlid, Rlii, Rlod, Rloi = direct and inverse resistances of the input / output left ventricle valves; Rrid, Rrii, Rrod, Rroi = direct and inverse resistances of the input / output right ventricle valves; Cas1, Cas2, Lcs, Rcs, Ras = compliances, inertance, resistances of 5 elements Noordergraaf systemic system model; Cap1, Cap2, Lcp, Rcp, Rap = compliances, inertance, and resistances of 5-element Noordergraaf pulmonary system model; Cvs, Rvs, Cra = compliances and resistance of the systemic venous system; Cvp, Rvp, Cla = compliances and resistance of the pulmonary venous system.*




rate to zero (Qilv=Qolv=0). Consequently, LV energetic efficiency (η) is zero and ventricular wall stress (σ) is high. The recovery of the left ventricle is unlikely.

Conversely, the RV improves while the stroke volume is almost the same, but the average volume decreases, consequently ventricular energetic efficiency (η) improves and wall stress (σ) decreases. Moreover, the pressures trend is towards normalization as AoP increases while LAP, RAP and PAP decrease. In order to avoid worsening LV function, an afterload reduction should be necessary and it can be accomplished using different approaches.

At 55 seconds, the value of systemic arterial resistance (Ras) is decreased, according to the Noordergraaf systemic arterial load model (Fig. 1). Consequently, the LV starts to work with an energetic efficiency (η) starting from zero. The stroke volume increases insignificantly and the average volume is high. The slope of the Frank-Starling's curve is much lower than the physiological one (1 liter/min/mmHg), while the differential elastance value of ESPVR (end-systolic pressure volume relation) is low due to an overly high volume for a pathological ventricle. The result strongly depends on the level of the afterload reduction.

The difference between configuration RA+LA---Ao and configuration RA---Ao is the lack of the cannula connecting the left atrium to the pump. The behavior of both ventricles is worsened as a consequence. When the pump starts, the LV is unable to pump blood into the aorta, as in the previous experiment, due to poor contractility shown by low ESPVR, and by an increase of its afterload (increase of aortic pressure) due to the pump flow.

Moreover, there is an increase of the blood volume and pressure in the pulmonary circulatory system until reaching a value at which even the RV flow rate is zero. At these conditions, the LAP is equal to the PAP, with possibly high values (in our experience more than 40 mmHg) (Figs. 2, 3). The evaluation of the LV and RV pressure-volume loops of both designs shows better results with configuration RA+LA---Ao when compared to those obtained conventionally (configuration RA---AO) (Figs. 4, 5).

In configuration RA+LA---Ao, the RV pressure-volume loops shift to lower volumes with consequent improvement of ventricular energetic efficiency and more sensitivity to preload, as well as decrease of the wall stress and less sensitivity to afterload (improvement of RV Frank-Starling, as opposed to the LV) (Fig. 5).

LV stroke volume at T = 55 is zero, as is, consequently, the energetic efficiency. In the case of a decrease of afterload, LV stroke volume increases (T=70) as does the

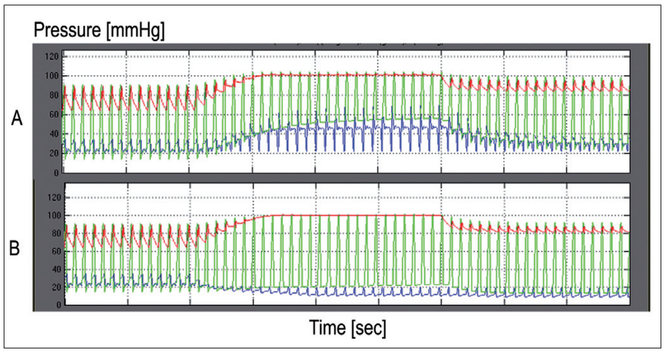



**Fig. 2 -** *A:configuration RA---Ao; B: Configuration RA+LA---Ao. AoiP = aortic instantaneous pressure (red); LviP = left ventricle instantaneous pressure (green); LaiP = left atrium instantaneous pressures (blue).*

energetic efficiency (η>0), but the average volume does not undergo change. The wall stress is high and there is no improvement of LV Frank-Starling function (Fig. 5).

In the case of the configuration RA---Ao, RV pressure-volume loops shift to lower volumes but there is no increase of ventricular energetic efficiency, due to the stroke volume decrease (zero at T=55). The wall stress decreases insignificantly (Fig. 4).

LV stroke volume at T=55 is zero, as is, consequently, the energetic efficiency (η=0). In the case of a decrease in afterload, the left ventricle stroke volume increases (T=70), as does the energetic efficiency (η>0), but not significantly. The average volume increases and the wall stress is high. The Frank-Starling function is worse than in the previous case (Fig. 4).

## *Right ventricular failure*

In the case of RV failure, the starting reference values of the parameters and variables were: mean right atrium pressure (RAP)= 15-20 mmHg; mean pulmonary artery pressure (PAP) at normal or low; mean left atrium pressure (LAP) = 5-7 mmHg; maximal aortic pressure (AoP) = 80 mmHg; mean aortic pressure (AoP) = 50 mmHg; cardiac index < 2 liters/min/$m^2$.

The test was conducted as follows:

1) 0 - 20 seconds: pathological state; the pump is connected, but not working; the inflow and outflow cannulae are clamped.
2) 20 - 40 seconds: the cannulae are open, the pump starts and reaches the steady state (transitory phase).
3) 40 - 70 seconds: the pump flow rate increases to reach the ideal flow rate (steady state).

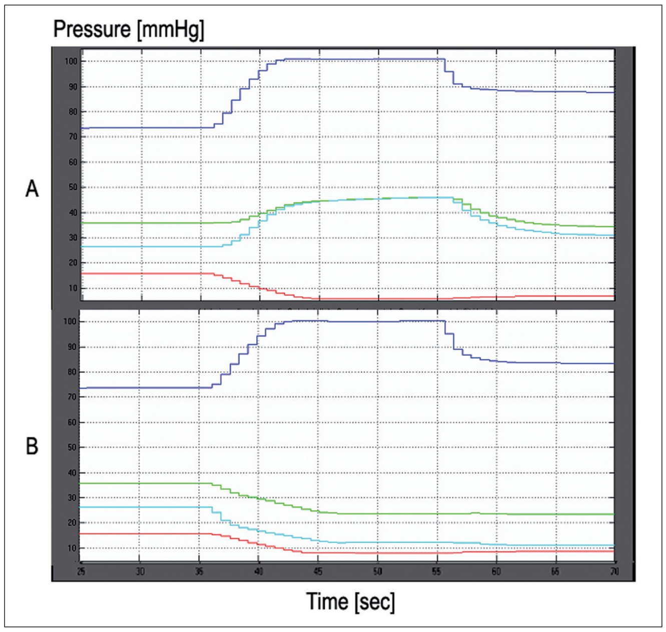



**Fig. 3 -** *A: Configuration RA---Ao; B: Configuration RA+LA---Ao. AoP= aortic mean pressure (blue); PAP= pulmonary artery mean pressure (green), RAP= right atrium mean pressure (red); LAP= left atrium mean pressure (light blue).*

In our circuit design (configuration RA---LA), at 20 - 40 seconds, the cannulae are open, the pump starts and reaches the steady state. RV flow decreases due to a reduction of RAP. PAP decreases depending on the reduction of the RV flow rate (Figs. 6, 7). LAP increases and leads to a rise in Qilv (input instantaneous volumetric flow rate of left ventricle) which is higher than Qolv (output instantaneous volumetric flow rate of left ventricle). LV mean volume and Qolv increase until reaching the same value as Qilv.

According to the traditional circuit design (configuration RA---PA), RV flow is zero due to a reduction of RAP and an increase of PAP. The pump flow leads to an increase of LAP and a pressure drop across the pulmonary resistance (Rap). A lack of RV isotonic contraction is observed. The opposite situation could be present only in the event of tricuspid valve incompetence. In our configuration, isotonic and isometric contraction are obtained (Figs. 6, 7).

A comparison of the pressure-volume loops shows good RV behavior in the first case (configuration RA---LA).

Using configuration RA---LA, the RV pressure-volume loop shifts to lower volumes and we observe an

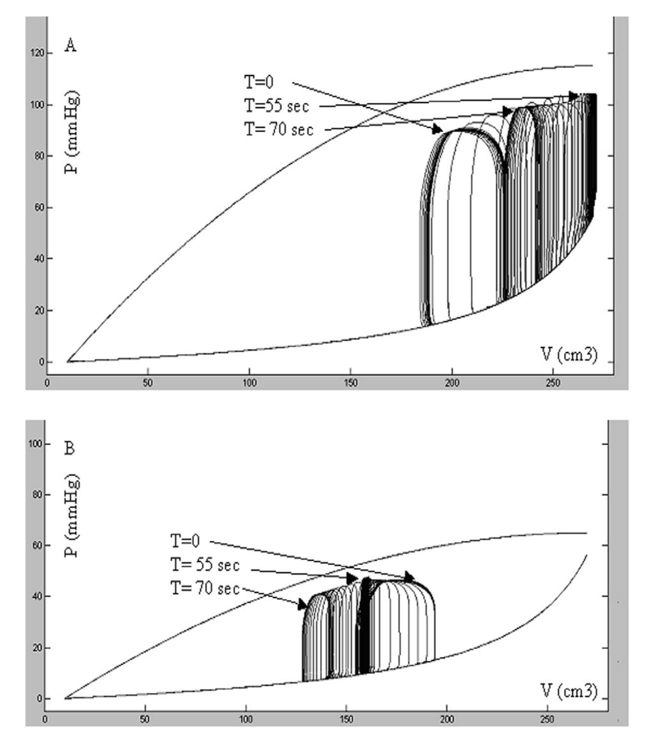



**Fig. 4 -** ***A:*** *left ventricle Pressure-Volume loops;* ***B:*** *right ventricle pressure-volume loops in configuration RA---Ao.*
*P = pressure (mmHg), V= volume (cm³), T = time (sec).*

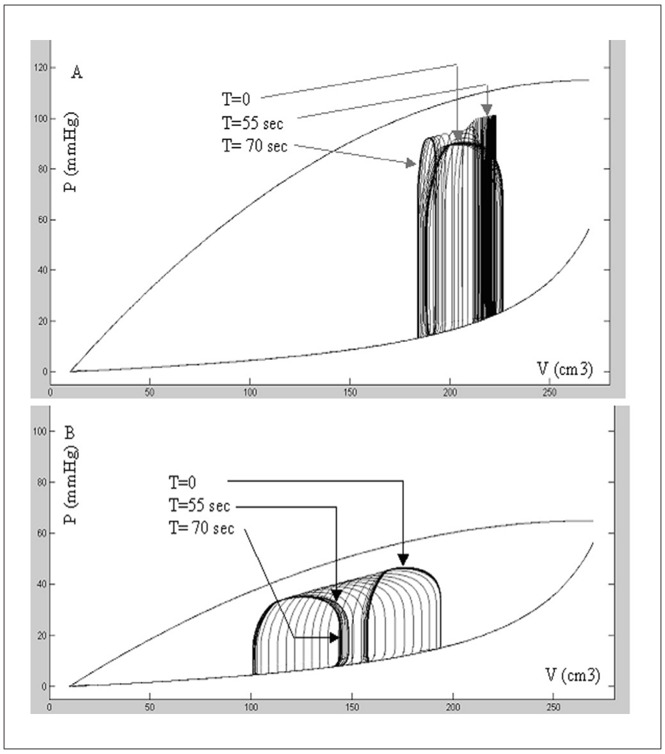



**Fig. 5 -** ***A:*** *left ventricle Pressure-Volume loops;* ***B:*** *right ventricle pressure-volume loops in configuration RA+LA---Ao.*
*P = pressure (mmHg), V = volume (cm³), T = time (sec).*

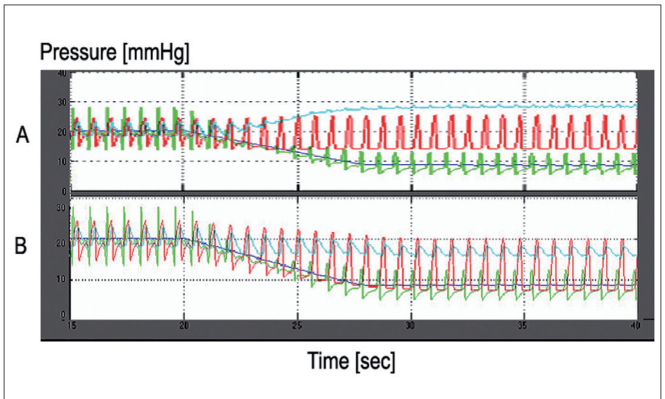



**Fig. 6 -** *A: Configuration RA---PA; B: Configuration RA---LA.*
*PAP = pulmonary artery instantaneous pressure (light blue); RVP = right ventricle instantaneous pressure (red); RAP = right atrium instantaneous pressure (green); CVP = central venous pressure (blue).*

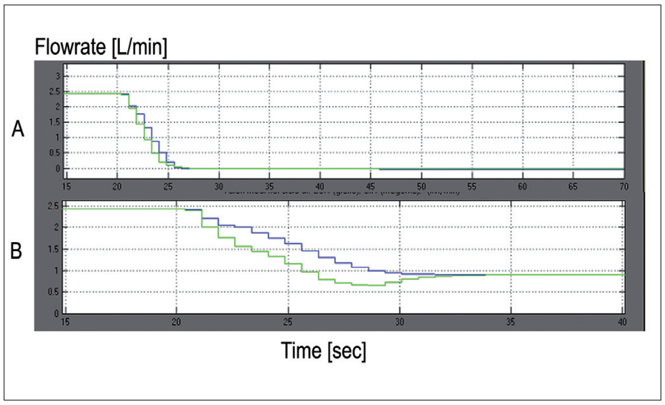



**Fig. 7 -** *A: Configuration RA---PA; B: Configuration RA---LA.*
*Oorv = output volumetric flowrates of right ventricle (blue); Oirv = input volumetric flow rates of right ventricle l/min (green).*

improvement in energetic efficiency (η), more sensitivity to the preload, a decrease in the wall stress (σ) and less sensitivity to the afterload (improvement of Frank-Starling function) (Fig. 8).

In configuration RA---PA, RV stroke volume becomes zero (T=40) as does the energetic efficiency (η=0), the average volume does not undergo change, the wall stress (σ) is high, and the Frank-Starling function is poor at the beginning, becoming progressively worse (Fig. 8).

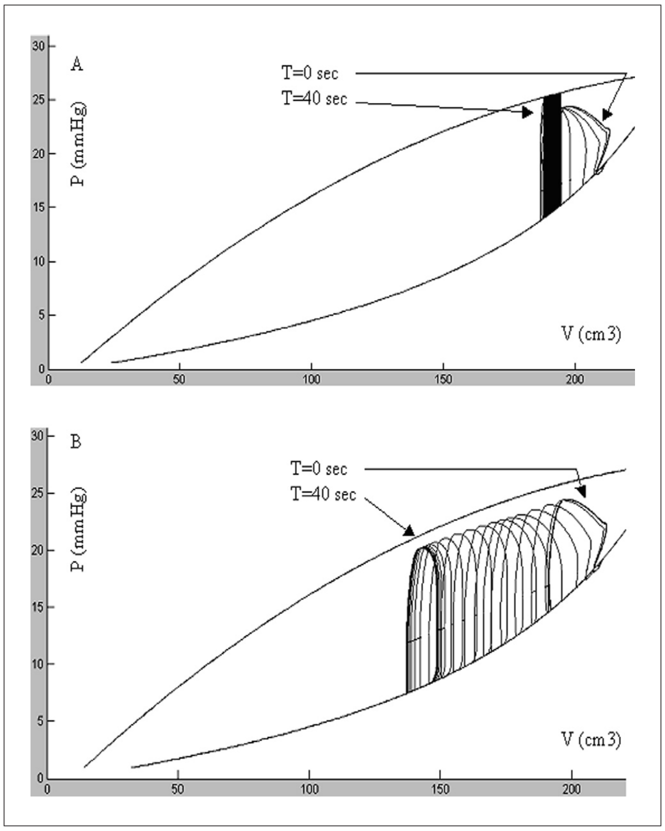



**Fig. 8 -** *Right ventricle pressure-volume loops.*
***A:*** *Configuration RA---PA;* ***B:*** *Configuration RA---LA.*
*P = pressure (mmHg); V= volume (cm³); T= time (sec).*

## DISCUSSION

The analysis of the interaction between the circulatory system and the mechanical support shows that different inflow and outflow settings influence both the cardiac output, with the aim of achieving correct systemic perfusion and the energetic efficiency ($\eta$) of both ventricles. In the case of biventricular failure, the centrifugal pump device is traditionally connected to the right atrium and aorta (configuration RA---Ao). In this case, there is an increase of the aortic (mean) pressure and a lower RAP, thus reaching physiological values. In the case of severe heart failure, the increase of the aortic pressure reduces the LV flow rate to zero. Moreover, it allows an increase of LAP and PAP which, together with the RAP decrease, reduces the RV flow rate to zero. Under these conditions, the energetic efficiency ($\eta$) of both ventricles is zero, the wall stress is very high and, consequently, heart recovery is impeded.

A different cannulation setting may offer different advantages.

In the case of biventricular failure using the configuration RA+LA---Ao, RAP, which is directly correlated to RV flow rate, decreases with LAP, which is directly correlated to PAP. The RAP and LAP reductions can be achieved by removing blood from both atria with a proper flow-rate ratio. With the aim of bringing about a decrease in the mean aortic pressure, in order to have better LV performance, an IABP can be used.

In the case of isolated RV failure, the centrifugal pump is traditionally connected (without oxygenator) to the right atrium and the pulmonary artery (configuration RA---PA). RV flow rate and energetic efficiency decrease to zero, depending on a higher afterload and a lower preload.

We prefer to connect the centrifugal pump device to the right atrium as inflow, and to the left atrium as outflow (configuration RA---LA). Consequently, LAP increases and PAP decreases with a low RV flow rate, thus aiding recovery. The non-pathological LV flow rate increases. With the same preload, the RV stroke volume is proportional to the energetic efficiency.

## CONCLUSIONS

The aim of the proposed numerical computer model is to improve the management of cardio-circulatory support with centrifugal blood pumps according to different patient physio-pathological conditions. The numerical model applied to the device makes it possible using mathematical processing to assess and decide on a rational basis as to the correct blood drawing separately from the right and left atria, without having to consider the cannulae diameters, which in our experiment had the same size.

It is important to assist the left and right ventricles in a separate and independent fashion, knowing the different behaviour of each in terms of recovery.

The proper operation of a cardio-circulatory support involves fully benefiting from the cardiac share to optimize cardiac functioning, according to the previsions of the mathematic model, the ventricular PV loop calculations, and the parameter estimation methods, consequently minimizing invasive clinical measurements.

Computer analysis results are in agreement with clinical measurements. The use of a computer model in the selection of the correct parameters to use for optimal operation of mechanical support devices, and the suitability of the latter for various clinical conditions will likely offer significant assistance in employing such devices for their intended aims.

## ABBREVIATIONS AND SYMBOLS

- LV, RV = left ventricle, right ventricle
- LA, RA = left atrium, right atrium
- LAiP, RAiP = LA, RA instantaneous pressures
- LViP, RViP = LV, RV instantaneous pressures
- AoiP, PAiP = aortic and pulmonary artery instantaneous pressures
- LAP, RAP = mean LA, RA pressures
- PAP = mean pulmonary artery pressure
- CVP = mean central venous pressure
- LViV, RViV = LV, RV instantaneous volumes
- LAiV, RAiV = LA, RA instantaneous volumes
- LVESV, LVEDV = end-systolic and end-diastolic LV volumes
- RVESV, RVEDV = end-systolic and end-diastolic RV volumes
- Qilv, Qolv = input and output instantaneous volumetric flow rates of the left ventricle
- Qirv, Qorv = input and output instantaneous volumetric flow rates of the right ventricle
- Qb = bronchial volumetric flow rate
- Qpump = volumetric flow rate of the pump
- $\eta$ = ventricular energetic efficiency
- $\sigma$ = instantaneous wall stress of ventricle

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