

# Modelling in the study of interaction of Hemopump device and artificial ventilation

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## Abstract

The aim of this work is to evaluate in different ventricular conditions the influence of joint mechanical ventilation (MV) and Hemopump assistance. To perform this study, we used a computer simulator of human cardiovascular system where the influence of MV was introduced changing thoracic pressure to positive values. The simulation confirmed that haemodynamic variables are highly sensitive to thoracic pressure changes. On the other hand, Hemopump assistance raises, among the others, mean aortic pressure, total cardiac output (left ventricular output flow plus Hemopump flow) and coronary flow. The simulation showed that the joint action of Hemopump and positive thoracic pressure diminishes these effects.

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## 1. Introduction

Mechanical heart assistance has the aim to improve general circulatory conditions. If it is used for heart recovery, it has the additional aim to improve coronary circulation and unload the failing ventricle supporting, in this way, its recovery. Among the devices used for heart recovery, an important role is played

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by non-pulsatile devices as their characteristics make their use rather simple and competitive in comparison to other devices such as intraaortic balloon pump (IABP). Hemopump HP31 device (Medtronic, Inc., Minneapolis, MN, USA) is among them: it is a miniature rotary blood pump introduced into the left ventricular cavity through the aortic valve. This ventricular assist device (VAD) uses cannula inserted through the aortic valve to aspirate the blood from the left ventricular cavity and to eject it into the ascending aorta. The capability to be inserted into the circulatory system without major surgery makes the pump almost as safe and convenient as the IABP. This pump may be more effective than IABP in assisting failing left ventricle [1]. In contrast to IABP, this kind of ventricular assist device is not synchronized with the patient's ECG and therefore works properly even during arrhythmia or cardiac fibrillation. In this study, according to Bai's works [2,3], we modelled Hemopump type HP31. This VAD can be operated at seven different rotational speeds ranging from 17 000 to 26 000 rpm, with an increment of 1500 rpm [4].

The direct effects of the Hemopump on the haemodynamic variables of the circulatory system include an increase in mean aortic pressure, in total cardiac output (left ventricular output flow plus Hemopump flow), a decrease in the area of the pressure–volume loop of the left ventricle with consequent decrease in blood flow pumped out by the ventricle [5,6]. In addition, the pump produces a decrease in left atrial pressure [1]. The increase in mean aortic blood pressure increases the coronary blood flow, which in turn increases the oxygen supply to the heart. Even if what is considered here is a specific device, most of these considerations can be extended to any of the existing devices of the same type.

Mechanical circulatory assistance is often applied in conjunction with mechanical ventilation (MV) of the lungs. The studies of haemodynamic consequence of MV is a complex problem and is the subject of various studies [7–11]. The lungs, right and left ventricles as well as large vessels are inside the thorax, so that they are influenced by cyclic pressure variations that are connected with different breathing patterns. During the spontaneous breathing, the mean intrathoracic pressure ( $P_t$ ) is negative, which creates physiological conditions for blood to go through the pulmonary vessels and venous return of the blood is enhanced as well. On the contrary, during MV of the lungs, which is used as a necessary mean to support inefficient respiratory system, new non-physiological conditions occur. Positive airway pressure generated by the respirator is transferred into the thoracic cage and the mean intrathoracic pressure is always positive.

Positive intrathoracic pressure influences cardiac output, coronary blood flow, mean systemic and pulmonary pressures and left ventricular end diastolic volume [8,12,13].

MV of the lungs may often result in decrease of cardiac output, arterial pressure and venous return, which is quite contrary to the results expected by application of Hemopump assist device [14]. So, some measures have been undertaken recently by anaesthesiologists to limit these negative side-effects. One of the measures is to replace “total” artificial ventilation by partial ventilatory support, synchronized with patient's spontaneous breathing. In this way positive thoracic pressure generated by MV is to some extent, at least partially “balanced” by negative thoracic pressure produced by respiratory muscles. Another way to decrease pleural pressure is the so-called “permissive hypercapnia” approach, which is the effect of smaller tidal volume delivery (5 ml/1 kg body weight) by a respirator. Recently introduced into clinical practice, various modes of MV like proportional assist ventilation (PAV) or pressure support ventilation (PSV), combine spontaneous breathing and ventilatory assistance. They differ in timing and applied airway pressure amplitude.

Simultaneous application of VAD (Hemopump in this case) and mechanical ventilatory support creates therefore for the cardiovascular system a new situation determined by the complex interaction between

mechanical assistance, circulatory and respiratory systems. The goal of this study is to assess, using a computer simulator of cardiovascular system, the influence of Hemopump device on haemodynamic parameters (as cardiac output, coronary blood flow, mean systemic and pulmonary arterial pressures, mean left atrial pressure, mean systemic pressure and mean pulmonary pressure) when MV of the lungs is simultaneously applied.

## 2. Methods

Numerical simulation was used to evaluate which might be the major haemodynamic parameters changes during Hemopump application and as a function of mean intrathoracic pressure ( $P_t$ ) level. Table 1 reproduces all the abbreviations and symbols used in the text.

### 2.1. Model of cardiovascular system

In our study, we used a lumped parameter model of the circulatory system (CARDIOSIM<sup>®</sup>) [15–17] that permits to reproduce the most important circulatory phenomena in terms of pressure and volume relationships. Its general layout is shown in Fig. 1 which includes the six circulatory sections and the

Table 1  
Legend of abbreviations

Variables and abbreviations	Abbreviation and symbols
Mechanical ventilation	MV
Intraaortic balloon pump	IABP
Ventricular assist device	VAD
Intrathoracic pressure	$P_t$
Instantaneous ventricular pressure	$p(t)$
Instantaneous ventricular volume	$v(t)$
Ventricular volume at zero pressure	$V_0$
End systolic pressure–volume relationship line	ESPVR
End diastolic pressure–volume relationship	EDPVR
Ventricular filling coefficients	$C, D, E, K, J$
Proportional assist ventilation	PAV
Pressure support ventilation	PSV
Intrathoracic pressure during the inspiratory period	$p_i(t)$
Intrathoracic pressure during the expiratory period	$p_e(t)$
Inspiratory time	$T_i$
Expiratory time	$T_e$
Left ventricular elastance	$E_{VLEFT}$
Left ventricular volume	$V_{OLEFT}$
Right ventricular elastance	$E_{VRIGHT}$
Cardiac output	CO
Left ventricular end-diastolic volume	$V_{ed}$
Coronary flow	CF

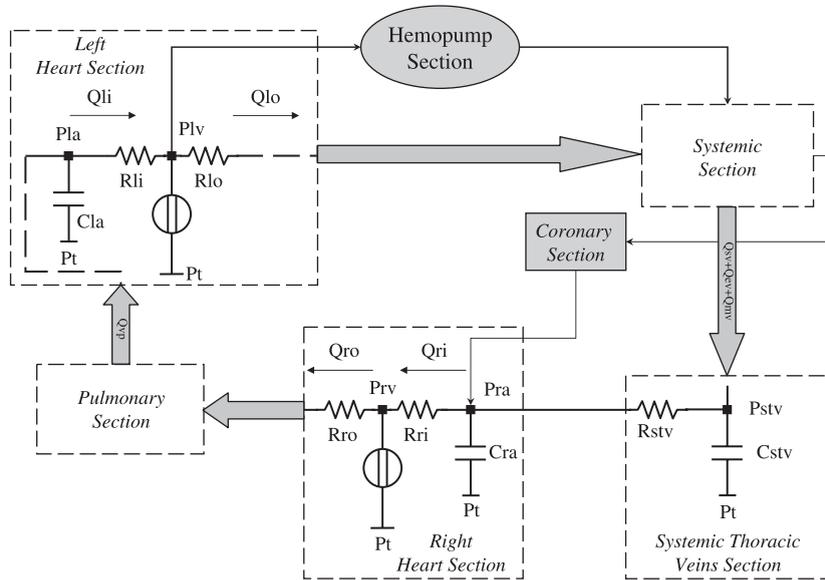


Fig. 1. The block diagram of the computer simulator of cardiovascular system CARDIOSIM<sup>®</sup>. In the left (right) heart section  $R_{li}$  ( $R_{ri}$ ) and  $R_{lo}$  ( $R_{ro}$ ) are the left (right) input and output valves resistance.  $Q_{li}$  ( $Q_{ri}$ ) and  $Q_{lo}$  ( $Q_{ro}$ ) are the left (right) input and output flows.  $P_{la}$  ( $P_{ra}$ ) is the left (right) atrial pressure.  $P_{lv}$  ( $P_{rv}$ ) is the left (right) ventricular pressure.  $P_t$  is the intrathoracic pressure. In the systemic thoracic veins compartment,  $P_{stv}$  is the systemic veins pressure,  $R_{stv}$  is the systemic veins resistance and  $C_{stv}$  is the systemic veins compliance.

Hemopump section. When present, ( $P_t$ ) represents intrathoracic pressure. The full nomenclature of the circulatory model is reported in Table 2.

2.1.1. Left and right heart sections

The left and right atria are represented using a single constant compliance ( $C_{la}$  and  $C_{ra}$ ). Both values are taken from Guyton [18]. The model chosen to represent the Starling’s law of the heart for each ventricle is based on the variable elastance model modified according to Sagawa’s studies [19]. The heart contraction and ejection phase is described by Eq. (1)

$$p(t) = E(t)[v(t) - V_0]F[v(t), \dot{v}(t), \dot{v}(t)_{max}], \tag{1}$$

where  $p(t)$  is the instantaneous ventricular pressure,  $v(t)$  is the instantaneous ventricular volume,  $V_0$  is the ventricular volume at zero pressure: it is defined as the intercept of the end systolic pressure–volume relationships (ESPVR) line with the volume axis. Changes in contractility are introduced by changes in maximum value of isovolumetric time-varying elastance  $E(t)$ . Function  $F[\dots]$  in Eq. (1) is a corrective function for the isovolumetric time-varying elastance taking into account the ejection rate, the maximal ejection rate and the ejected volume.

We simulated the filling conditions of the ventricle using the Gilbert’s [20] end diastolic pressure–volume relationships (EDPVR)

$$p(t) = Ce^{Kv(t)} + De^{-Jv(t)} + E \tag{2}$$

Table 2  
Legend of parameters and variables used in the CARDIOSIM<sup>®</sup> computer simulator

	Resistance (mmHg cm <sup>-3</sup> s)	Compliance (cm <sup>3</sup> mmHg <sup>-1</sup> )	Inertance (mmHg cm <sup>-3</sup> s <sup>2</sup> )	Pressure (mmHg)	Flow (l min <sup>-1</sup> )
<i>Left (right) heart</i>					
Left input (output) valve	$R_{li}$ ( $R_{lo}$ )				
Right input (output) valve	$R_{ri}$ ( $R_{ro}$ )				
Left (right) atrium		$C_{la}$ ( $C_{ra}$ )		$P_{la}$ ( $P_{ra}$ )	
Left input (output) flow					$Q_{li}$ ( $Q_{lo}$ )
Right input (output) flow					$Q_{ri}$ ( $Q_{ro}$ )
Left (right) ventricle				$P_{lv}$ ( $P_{rv}$ )	
<i>Systemic section</i>					
Systemic arterial section	$R_{as}$	$C_{as}$	$L_{as}$	$P_{as}$	$Q_{as}$
Splanchnic venous (peripheral) circulation	$R_{sv}$ ( $R_{sp}$ )	$C_{sv}$ ( $C_{sp}$ )		$P_{sv}$ ( $P_{sp}$ )	$Q_{sv}$
Extraspinal venous (peripheral) circulation	$R_{ev}$ ( $R_{ep}$ )	$C_{ev}$ ( $C_{ep}$ )		$P_{ev}$	$Q_{ev}$
Venous (peripheral) circulation inactive muscle compartment	$R_{mv}$ ( $R_{mp}$ )	$C_{mv}$ ( $C_{mp}$ )		$P_{mv}$	$Q_{mv}$
Systemic thoracic veins	$R_{stv}$	$C_{stv}$		$P_{stv}$	
<i>Pulmonary section</i>					
Pulmonary arterial section	$R_{ap}$	$C_{ap}$	$L_{ap}$	$P_{ap}$	$Q_{ap}$
Pulmonary peripheral (venous) section	$R_{pp}$ ( $R_{vp}$ )	$C_{pp}$ ( $C_{vp}$ )		$P_{pp}$ ( $P_{vp}$ )	$Q_{pp}$ ( $Q_{vp}$ )
<i>Mean thoracic pressure</i>				$P_t$	
<i>Coronary section</i>					
Coronary arterial (capillary) section	$R_{artery}$ ( $R_{arteryMicro}$ )	$C_{artery}$		( $P_{arteryMicro}$ )	$Q_{artery}$ ( $QR_{arteryMicro}$ )
Coronary venous (capillary) section	$R_{venous}$ ( $R_{venousMicro}$ )	$C_{venousMicro}$		( $P_{venousMicro}$ )	$Q_{venous}$ ( $QR_{venousMicro}$ )
Myocardium section		$C_{myocardium}$		$P_{myocardium}$	
<i>Hemopump section</i>					
Input (output) blood					$QH_{in}$ ( $QH_{out}$ )
Constant flow source (and resistance)	$R$				$Q_n$
Volumetric flow rate					$Q_L$
Inertial property of the blood			$L$		

In Eq. (2) the constants  $C$ ,  $D$ ,  $E$ ,  $K$ ,  $J$  represent the ventricular properties during the filling. The connection of the ventricle to the circulatory network is realized by means of valves, which are assumed to be ideal (when they are open the flow through is proportional to the pressure drop and there is no flow when they are closed). All the equations of the model are reported in Appendix A.

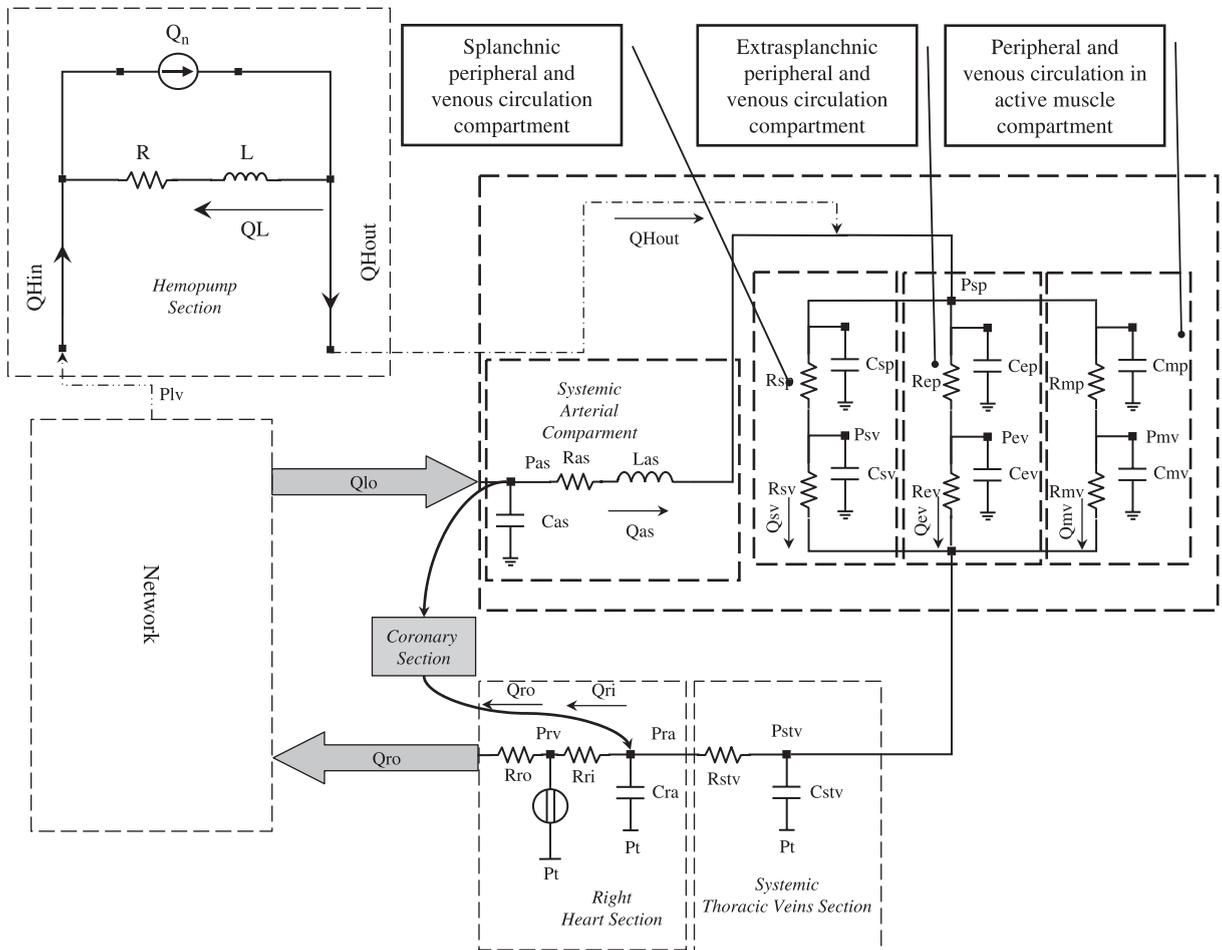


Fig. 2. Electric analog of systemic arterial pressure, of splanchnic and extrasplanchnic (peripheral and venous) circulation, of peripheral and venous circulation in active muscle compartment and of Hemopump assist device.  $P_{as}$ ,  $P_{sp}$ ,  $P_{sv}$ ,  $P_{ev}$ , and  $P_{mv}$  are, respectively, the systemic arterial, splanchnic peripheral, splanchnic venous, extrasplanchnic venous and venous in active muscle compartment pressures.  $Q_{as}$  is the systemic arterial flow.  $Q_{sv}$  ( $Q_{ev}$ ) is the splanchnic (extrasplanchnic) venous flow.  $Q_{mv}$  is the venous flow in the active muscle compartment.  $QH_{out}$  ( $QH_{in}$ ) is the output (input) pump flow.

### 2.1.2. Systemic and systemic thoracic veins sections

Mechanical properties of each section are modelled by RLC elements as in electric analogue circuits. Fig. 2 shows the four compartments that represent the systemic circulation [21,22]. Systemic arterial compartment, that includes the large arteries, is represented by a modified windkessel ( $R_{as}$ ,  $L_{as}$ ,  $C_{as}$ ). Resistances  $R_{sp}$  and  $R_{sv}$ , compliances  $C_{sp}$  and  $C_{sv}$  model splanchnic peripheral and venous compartment. Extrasplanchnic peripheral and venous compartment is represented by resistances  $R_{ep}$  and  $R_{ev}$  and compliances  $C_{ep}$  and  $C_{ev}$ . Finally, peripheral and venous circulation in active muscle compartment is modelled using resistances  $R_{mp}$  and  $R_{mv}$  and compliances  $C_{mp}$  and  $C_{mv}$ .

The representation of the systemic thoracic veins (Fig. 2) is very simple and contains a systemic venous compliance ( $C_{stv}$ ) and a systemic venous resistance ( $R_{stv}$ ).

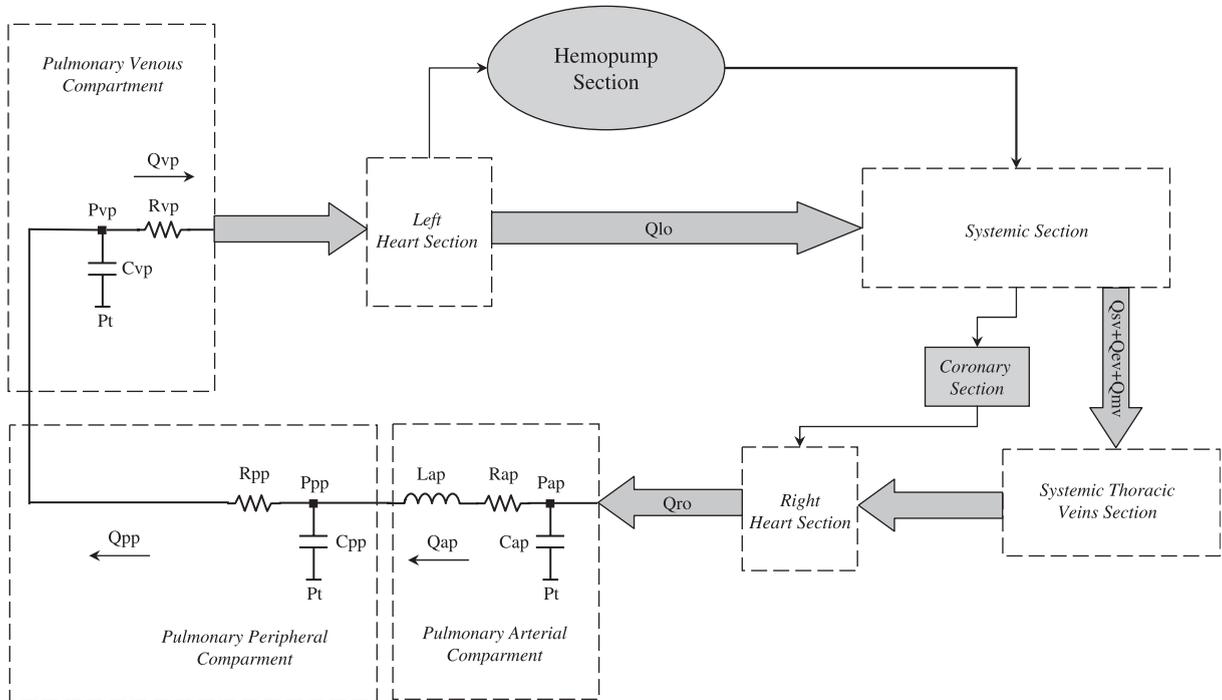


Fig. 3. Electric analog of the pulmonary section.  $P_{ap}$  ( $Q_{ap}$ ),  $P_{pp}$  ( $Q_{pp}$ ) and  $P_{vp}$  ( $Q_{vp}$ ) are, respectively, the pulmonary arterial, peripheral and venous pressures (flows).  $P_t$  is the intrathoracic pressure.

Each element value (resistance, compliance and inertance) was taken from the literature [21–23].

### 2.1.3. Pulmonary section

The pulmonary system is rather simply represented (Fig. 3) by three different compartments [21–24]. Pulmonary arterial compartment is represented by means of a modified windkessel ( $R_{ap}$ ,  $C_{ap}$  and  $L_{ap}$ ). Pulmonary peripheral and venous compartments contain a pulmonary peripheral compliance  $C_{pp}$ , a pulmonary peripheral resistance  $R_{pp}$ , a pulmonary venous compliance  $C_{vp}$  and a pulmonary venous resistance  $R_{vp}$ , respectively. Each element value (resistance, compliance and inertance) was taken from the literature [22].

### 2.1.4. Coronary section

In CARDIOSIM<sup>®</sup> we considered the coronary bed as a single branch which links the left ventricle output with the right atrium input [25,26]. Fig. 4 shows the electrical analogue of the coronary model. The natural coronary bed is composed of two main branches perfusing left and right ventricle. In the model there are a single arterial section (composed by  $R_{artery}$ ,  $R_{arteryMicro}$  and  $C_{arteryMicro}$ ) and a single venous section (composed by  $R_{venous}$ ,  $R_{venousMicro}$  and  $C_{venousMicro}$ ).  $R_{artery}$  is the input resistance of the coronary arteries,  $C_{artery}$  represents the compliance of the arterial bed,  $R_{arteryMicro}$  is the arterial capillary resistance,  $R_{venousMicro}$  and  $C_{venousMicro}$  are the capillary resistance and the compliance of the venous bed, respectively.  $R_{venous}$  is the resistance of the coronary veins and  $C_{myocardium}$  represents the

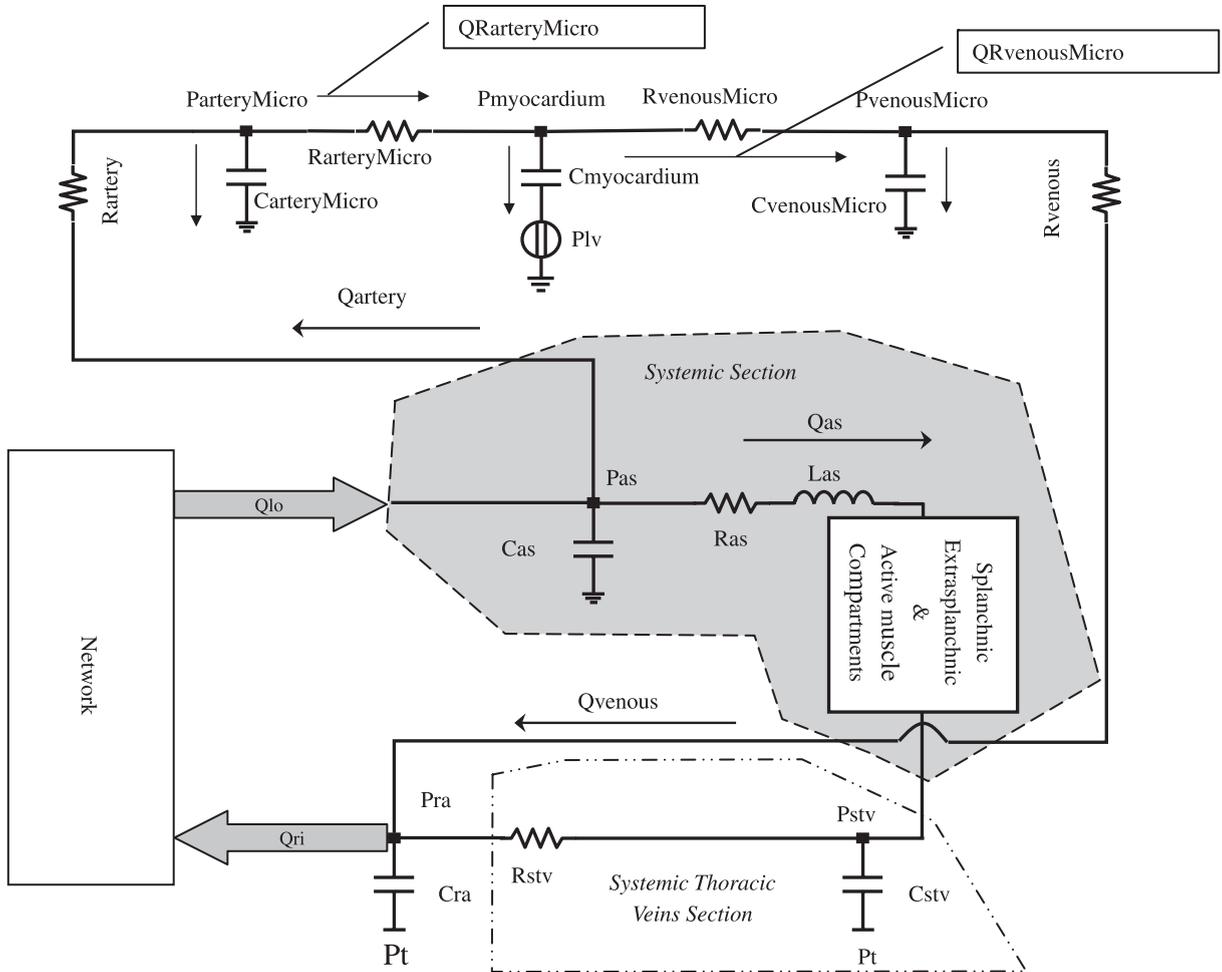


Fig. 4. Electric analog of the coronary bed.  $Q_{artery}$  and  $Q_{RarteryMicro}$  ( $Q_{venous}$  and  $Q_{RvenousMicro}$ ) are the flows, respectively, in the arterial (venous) and capillary bed.  $P_{arteryMicro}$  ( $P_{venousMicro}$ ) and  $P_{myocardium}$  are the pressures in the arterial (venous) capillary and myocardium compartments.

myocardial compliance. The values of coronary parameters [25] can be adjusted, if necessary, during the model run.

## 2.2. Hemopump section

Fig. 2 shows the Hemopump electric analogue. The pump model is connected to the circulation model in such a way that it aspirates blood from inside the ventricular model ( $QH_{in}$ ) and expels the blood into the systemic section ( $QH_{out}$ ). In the model represented in Fig. 2 [2,3]  $R$  is a resistance and  $L$  is an inductance.  $Q_n$  is a constant flow source: its value depends on the rotational speed of the pump.  $L$  represents the effects of the inertial properties of the blood in the pump. Changing the resistance ( $R$ ) value (and  $Q_n$  value) it is possible to simulate seven different rotational speeds [3] from 17 000 to 26 000 revolutions  $\text{min}^{-1}$ .

### 2.3. Mechanical ventilation section

In order to simulate the influence of MV on haemodynamics, the mean thoracic pressure ( $P_t$ ) was introduced into “CARDIOSIM<sup>®</sup>” in those sections where it has an impact on the cardiovascular system [15]. Mean thoracic pressure is defined as

$$P_t = \frac{1}{T_i + T_e} \left( \int_0^{T_i} p_i(t) dt + \int_{T_i}^{T_i+T_e} p_e(t) dt \right), \quad (3)$$

where  $p_i(t)$  and  $p_e(t)$  are the intrathoracic pressure changes during the inspiratory and the expiratory period respectively,  $T_i$  and  $T_e$  are the inspiratory and the expiratory time, respectively.

Using  $P_t$  expressed by (3) it is possible to take into account both the actual amplitude of the intrathoracic pressure and the time period when this pressure is applied. In this hypothesis,  $P_t$  is a good index of the influence of MV of any type on cardiovascular system.

### 2.4. Experimental method

Experiments were performed in two steps. In each step the influence of the MV support was introduced by changing levels of the intrathoracic pressure ( $P_t$ ) from  $-2$  to  $+5$  mmHg [21,27].

In the first step, the pathological condition of the heart was reproduced by setting left ventricular elastance to  $E_{v_{LEFT}} = 0.7$  mmHg cm<sup>-3</sup>, left ventricular rest volume  $V_{0_{LEFT}} = 15$  cm<sup>3</sup> and right ventricular elastance to  $E_{v_{RIGHT}} = 0.3$  mmHg cm<sup>-3</sup>, like in the ischaemic heart disease. The values of the parameters represented in Figs. 1–4 are reported in literature [15,16,20–25]. In the second step Hemopump assistance was applied to the pathological condition. The rotational speed of the pump was changed in steps and was assumed to be constant during each step. We have chosen three different rotational speeds:

- 17 000 rpm—Assisted#1,
- 20 000 rpm—Assisted#2,
- 23 000 rpm—Assisted#3.

The following variables were computed and presented for each step: total cardiac output (CO), left ventricular end-diastolic volume ( $V_{ed}$ ), coronary blood flow (CF), mean systemic and pulmonary arterial pressure ( $P_{as}$  and  $P_{ap}$ ), mean left and right atrial pressure ( $P_{la}$  and  $P_{ra}$ ), mean systemic and pulmonary pressure ( $P_{ms}$  and  $P_{mp}$ ), Hemopump flow and the left ventricular output flow. Total cardiac output is left ventricular flow plus, when present, Hemopump flow.

## 3. Results

Figs. 5–7 show the effects of the two experimental steps (pathological and assisted) on some haemodynamic variables. Fig. 5 shows that the transition from pathological to assisted condition increases total cardiac output (CO) and coronary blood flow (CF). Left ventricular end-diastolic volume ( $V_{ed}$ ) drops in relation to the rotational speed of the pump (thus reducing oxygen consumption) [3]. Left ventricular end-systolic volume ( $V_{es}$ ) with constant  $P_t$ , appears to be no or little sensitive to the Hemopump assistance. The same trends have been reported in clinical experiments [28–30].

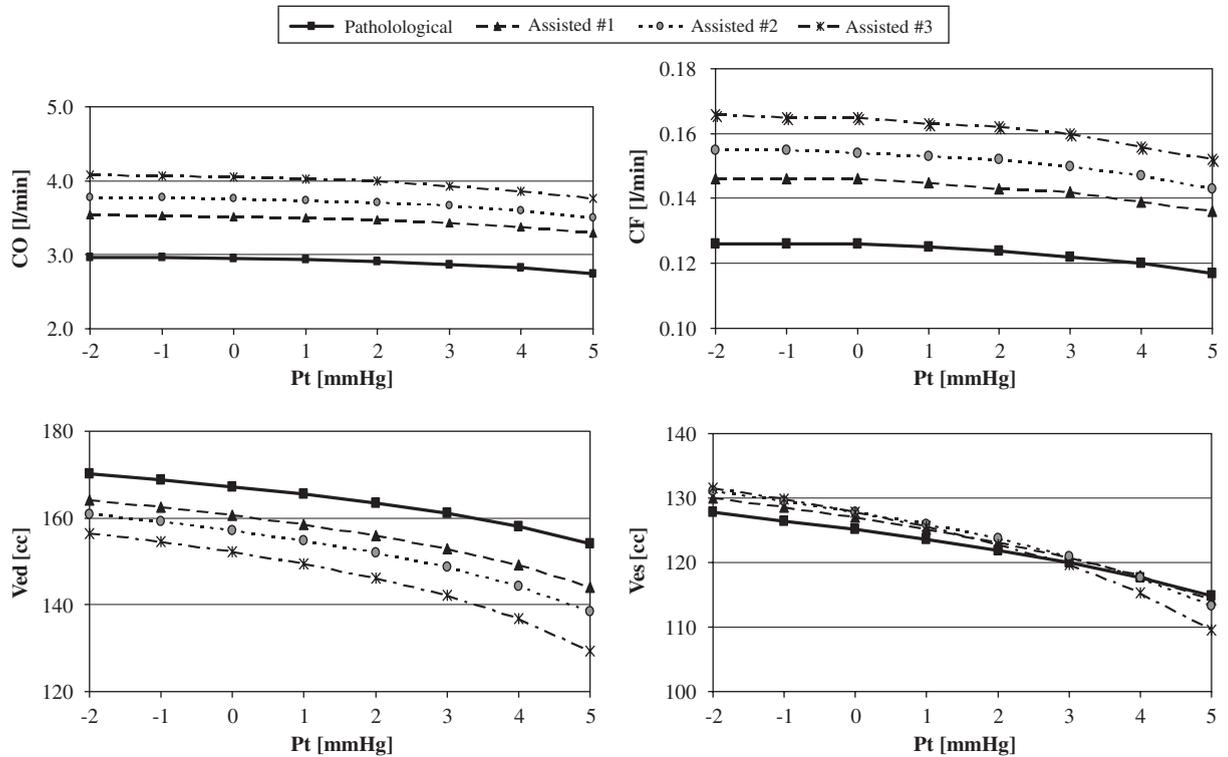


Fig. 5. Static characteristics of total cardiac output (CO), coronary flow (CF), left end-diastolic volume ( $V_{ed}$ ) and left end-systolic volume ( $V_{es}$ ) versus  $P_t$  (ranging from  $-2$  to  $5$  mmHg) for pathological and assisted (by Hemopump) conditions. Total cardiac output is left ventricular flow plus, when present, Hemopump flow. In the assisted conditions, the rotational speed of the pump was fixed, respectively to 17 000 (Assisted #1) 20 000 (Assisted #2) and 23 000 rpm (Assisted#3).

The effect of increasing  $P_t$  on the pathological condition is to reduce total cardiac output, coronary blood flow,  $V_{ed}$  and  $V_{es}$  as it is confirmed by literature [7,8,12]. The presence of the assistance does not change this trend even if, for each  $P_t$  value, it produces effects similar to those described above.

Fig. 6 shows left and right atrial pressures and systemic and pulmonary arterial pressures. The transition from pathological to assisted condition reduces left atrial pressure [30–32] and pulmonary arterial pressure. Right atrial and systemic arterial pressures are, on the contrary increased.

The effect of increasing the thoracic pressure on the pathological condition is to reduce  $P_{la}$ ,  $P_{ap}$  and  $P_{as}$ . Right atrial pressure is, on the contrary, increased. In this case too, the presence of the Hemopump produces its typical effects without changes the trend.

Finally, Fig. 7 shows mean systemic and pulmonary pressures along with Hemopump flow and left ventricular output flow.

The transition from pathological to assisted condition increases mean systemic pressure and decreases mean pulmonary pressure. Left ventricular output flow is decreased by the assistance.

Positive intrathoracic pressure shifts blood from pulmonary to systemic circulation reducing  $P_{mp}$  and increasing  $P_{ms}$ . The presence of the assistance emphasizes these phenomena. Increasing  $P_t$  decreases left ventricular output flow while Hemopump flow is insensitive to intrathoracic pressure variations.

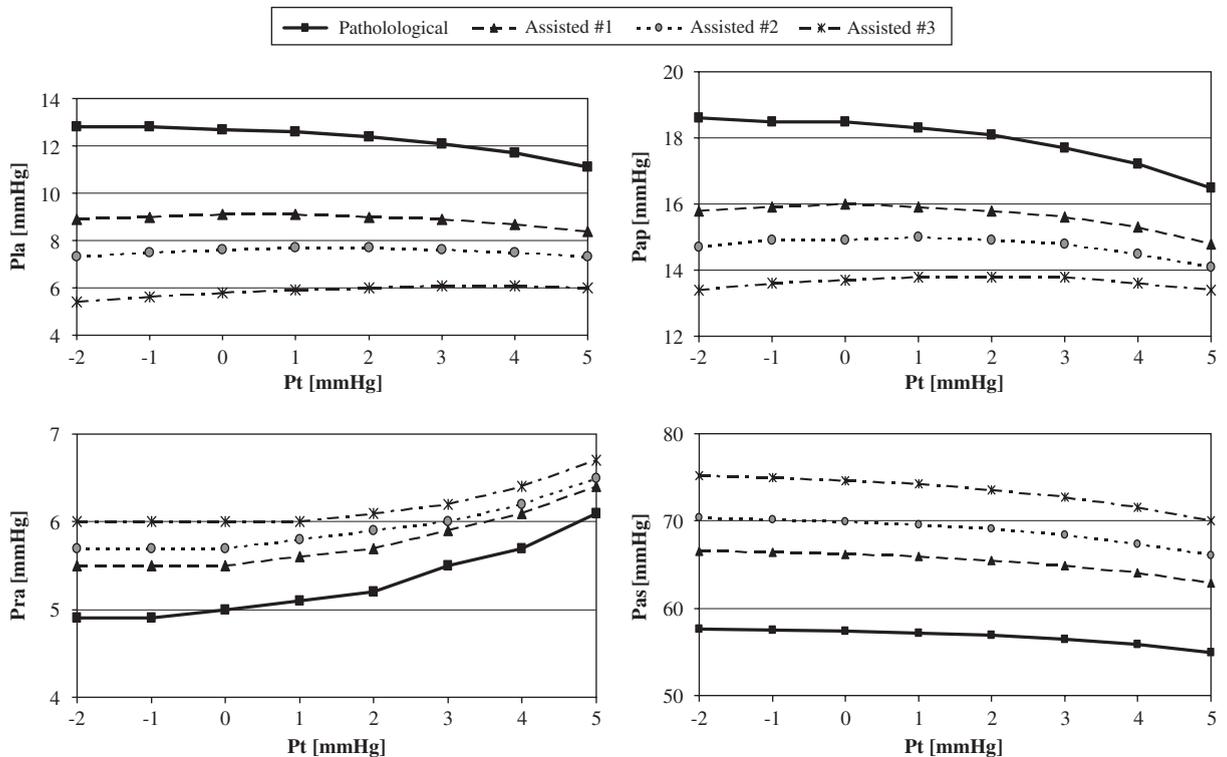


Fig. 6. Static characteristics of mean left atrial pressure ( $P_{la}$ ), mean pulmonary arterial pressure ( $P_{ap}$ ), mean right atrial pressure ( $P_{ra}$ ) and mean aortic pressure ( $P_{as}$ ) versus  $P_t$  (ranging from  $-2$  to  $5$  mmHg) for pathological and assisted (by Hemopump) conditions. In the assisted conditions, the rotational speed of the pump was fixed, respectively to  $17\,000$  (Assisted#1)  $20\,000$  (Assisted#2) and  $23\,000$  rpm (Assisted#3).

#### 4. Discussion

If the effects of Hemopump and MV of the lungs are considered separately, the assistance shifts blood from pulmonary to systemic circulation as it is shown by the changes in mean systemic and pulmonary pressures (upper part of Fig. 7 –  $P_t = -2$  mmHg). This is undoubtedly the expected effect of Hemopump application as it is also reflected by the changes in all pressures (Fig. 6). Considering the ventricle, the main effect of the assistance is a strong reduction of left ventricular output flow (Fig. 7) while total cardiac output is remarkably increased (Fig. 5). The consequence of Hemopump action on ventricular volumes consists of a reduction of end-diastolic volume, while end-systolic volume is almost constant. This is confirmed by literature [3,4,29–32] and, in terms of ventricular energetics, means a reduction of ventricular work and of oxygen consumption [3]. The effect on cardiac mechanical efficiency (defined by the ratio of ventricular work to oxygen consumption) is rather limited. As a matter of fact, if circulatory and ventricular parameters are constant, the natural ventricle flow can be maintained only by an increase of end-systolic volume and end-systolic pressure. These conditions are for sure not optimal for ventricular recovery, at least by the point of view of ventricular energetics. On the other hand, this type of assistance implies that average ventricular volume is always enough to permit Hemopump flow without risks for the natural ventricle.

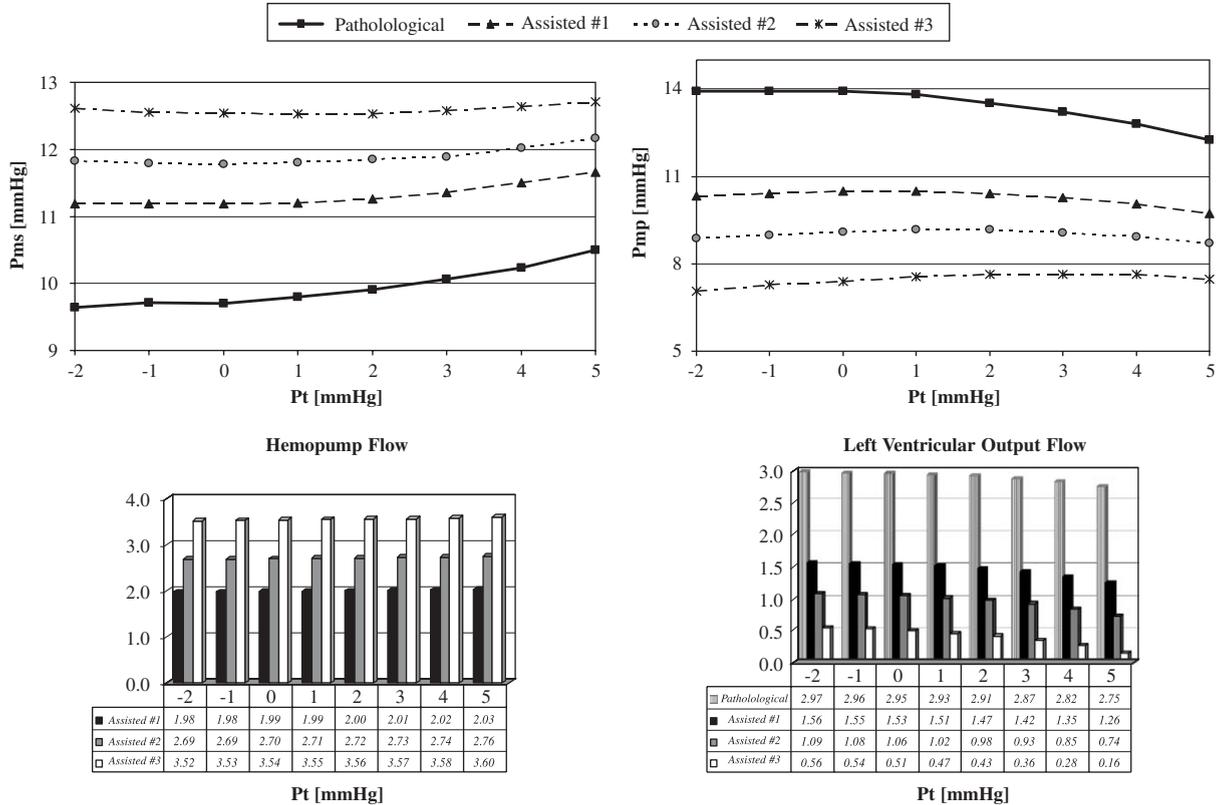


Fig. 7. Static characteristics of mean systemic pressure ( $P_{ms}$ ), mean pulmonary pressure ( $P_{mp}$ ), Hemopump and left ventricular output flow versus  $P_t$  (ranging from  $-2$  to  $5$  mmHg) for pathological and assisted (by Hemopump) conditions. In the assisted conditions, the rotational speed of the pump was fixed respectively to  $17\,000$  (Assisted#1)  $20\,000$  (Assisted#2) and  $23\,000$  rpm (Assisted#3).

By the point of view of flows, the inflow from the left atrium is divided between the Hemopump flow and the left ventricular output flow. The latter decreases with the increasing pump rotational speed. This situation affects also the morphology of the ventricular work cycle [29,32].

The use of positive thoracic pressure as it happens during MV of the lungs produces the same effects of Hemopump shifting blood from pulmonary to systemic circulation reducing mean pulmonary pressure and increasing mean systemic pressure (Fig. 7). The joint action of the assistance and MV emphasizes, in general, these effects as it can be observed by the strong reduction of  $P_{mp}$  at higher  $P_t$  values and pump rotational speed (Fig. 7). It is interesting to observe the effects of MV on left ventricular output flow during assistance: at higher  $P_t$  values left ventricular output flow is almost reduced to zero with remarkable effects on end-diastolic and end-systolic volume, which however, is almost insensitive to pump rotational speed variations.

It is not easy to justify the maximum in the mean pulmonary pressure versus  $P_t$  (Fig. 7): it clearly moves rightwards with increasing pump rotational speed. Something similar but opposite can be observed in mean systemic pressure. We computed right ventricular work for each  $P_t$  value and found that the maximum in  $P_{mp}$  correspond to a maximum in ventricular work. A possible explanation could be that the points

of maximum meet the conditions for maximum power transfer to the load (arterial elastance equal to ventricular elastance) [19]. If this last hypothesis could be verified, it could permit the analysis of right ventricular energetics during the joint action of mechanical circulatory assistance and MV of the lungs.

## 5. Conclusions

A numerical simulation of the interaction between a continuous flow ventricular assist device and the mechanical ventilation of the lungs has been presented. When Hemopump is applied, our simulation (in good agreement with the results of the literature [3,4,29–32]) shows an increase in mean aortic pressure, in total cardiac output (left ventricular output flow plus Hemopump flow), and in coronary blood flow, a decrease in blood flow pumped out by the left ventricle, a decrease in mean pulmonary pressure and in left atrial pressure. The simulation results also indicate that all the beneficial effects of the Hemopump are enhanced when the pump rotational speed increases. Increasing the intrathoracic pressure as in mechanical ventilation of the lungs emphasizes the effects of the Hemopump. The reduction in left ventricular output flow due to the increase in thoracic pressure is balanced by the Hemopump flow.

We are aware of the limitations of this model of the cardiovascular system. However, considering the lack of in vivo data and keeping in mind the above limitations, CARDIOSIM<sup>®</sup> can be a very suitable tool to predict at last trends of the major haemodynamic variables changes as a result of mechanical ventilation of the lungs and/or mechanical heart assistance (as Hemopump).

## 6. Summary

The aim of this work is to evaluate the influence of joint MV of the lungs and Hemopump assistance. To perform this study we used a computer simulator of human cardiovascular system in which lumped parameters models are used to reproduce the circulatory phenomena in terms of pressure and volume relationships. It is built up of seven different sections: left and right heart, systemic and pulmonary circulation, systemic thoracic veins, coronary circulation and Hemopump. Mechanical properties of each section are modelled by RLC elements as in electric analogue circuit. Variable elastance models reproduce the Starling's law of the heart, for each ventricle. Left and right ventricular elastance and left ventricular rest volume assumed the following values to reproduce pathological conditions:  $E_{V_{LEFT}} = 0.7$ ,  $E_{V_{RIGHT}} = 0.3$  mmHg cm<sup>-3</sup> and  $V_{0_{LEFT}} = 15$  cm<sup>3</sup>. We studied the assistance effects of the pump at three different rotational speeds (17 000, 20 000 and 23 000 rpm) when MV of the lung was applied or not. The influence of mechanical ventilation was introduced changing mean thoracic pressure ( $P_t$ ) from  $-2$  till  $+5$  mmHg. The results of computer simulations confirmed that the main haemodynamic variables (cardiac output, coronary blood flow, and systemic and pulmonary arterial pressures) are very sensitive to positive pressure changes in the thorax. The simulation shows, also, that the presence of the Hemopump in the case of heart failure produces an increase in the total cardiac output, in mean arterial pressure, in coronary blood flow and that these beneficial effects become more significant when the pump rotational speed increases. The presence of the Hemopump produces, also, a decrease in left ventricular end-diastolic volume, in blood flow pumped out by the left ventricle and in left atrial pressure and an increase in the right atrial pressure. This effect can be explained by the blood volume shift from pulmonary to systemic circulation due to the pump action. Hemopump effects are in general emphasized by mechanical ventilation of the lungs. The

reduction in left ventricular output flow is compensated by the Hemopump flow that is widely insensitive to positive  $P_t$  variations.

## Appendix A.

The equations for the left (right) atrium, systemic arterial section, splanchnic (extrasplanchnic) peripheral and venous circulation, peripheral and venous circulation in active muscle compartment, systemic thoracic veins and pulmonary arterial, peripheral and venous sections are the following:

$$Q_{lo} = \frac{P_{lv} + P_t - P_{as}}{R_{lo}}, \quad Q_{ro} = \frac{P_{rv} - P_{ap}}{R_{ro}},$$

$$Q_{lo} = \dot{P}_{as} \cdot C_{as} + Q_{as} + Q_{artery}, \quad Q_{sv} = \frac{P_{sv} - (P_{stv} + P_t)}{R_{sv}},$$

$$P_{as} - P_{sp} = Q_{as} \cdot R_{as} + \dot{Q}_{as} \cdot L_{as}, \quad Q_{ev} = \frac{P_{ev} - (P_{stv} + P_t)}{R_{ev}},$$

$$Q_{li} = \frac{P_{la} - P_{lv}}{R_{li}}, \quad Q_{mv} = \frac{P_{mv} - (P_{stv} + P_t)}{R_{mv}},$$

$$Q_{ri} = \frac{P_{ra} - P_{rv}}{R_{ri}}, \quad Q_{sp} = \frac{P_{sp} - P_{sv}}{R_{sp}},$$

$$Q_{ri} + \dot{P}_{ra} \cdot C_{ra} = \frac{P_{stv} - P_{ra}}{R_{stv}} + Q_{venous}, \quad Q_{ep} = \frac{P_{sp} - P_{ev}}{R_{ep}},$$

$$P_{rv} - P_{ap} = Q_{ro} \cdot R_{ro}, \quad Q_{mp} = \frac{P_{sp} - P_{mv}}{R_{mv}},$$

$$\frac{P_{stv} - P_{ra}}{R_{stv}} = \dot{P}_{vs} \cdot C_{vs} + Q_{sv} + Q_{ev} + Q_{mv}.$$

$Q_{sp}(Q_{ep})$  is the splanchnic (extrasplanchnic) peripheral flow.  $Q_{mp}$  is the peripheral flow in the active muscle compartment.

$$Q_{ep} = Q_{ev} + \dot{P}_{ev} \cdot C_{ev}, \quad \dot{Q}_{ap} \cdot L_{ap} = P_{ap} - P_{pp} - Q_{ap} \cdot R_{ap},$$

$$Q_{mp} = Q_{mv} + \dot{P}_{mv} \cdot C_{mv}, \quad \dot{P}_{ap} \cdot C_{ap} = Q_{ro} - Q_{ap},$$

$$Q_{as} + QH_{out} = (Q_{sp} + \dot{P}_{sp} \cdot C_{sp}) + (Q_{ep} + \dot{P}_{sp} \cdot C_{ep}) + (Q_{mp} + \dot{P}_{sp} \cdot C_{mp}),$$

$$\dot{P}_{pp} \cdot C_{pp} = Q_{ap} - Q_{pp},$$

$$Q_{vp} = \frac{P_{vp} - P_{la}}{R_{vp}}, \quad Q_{pp} = \frac{P_{pp} - P_{vp}}{R_{pp}}, \quad \dot{P}_{vp} \cdot C_{vp} = Q_{pp} - Q_{vp}.$$

$$\dot{P}_{la} \cdot C_{la} + Q_{li} = Q_{vp}, \quad \dot{V}_{lv} = Q_{li} - (Q_{lo} + QH_{in}), \quad \dot{V}_{rv} = Q_{ri} - Q_{ro}.$$

$V_{lv}$  ( $V_{rv}$ ) is the left (right) ventricle volume.

$$P_{sv} = \frac{1}{C_{sv}} [V_{TOT} - C_{as} \cdot P_{as} - (C_{sp} + C_{ep} + C_{mp}) \cdot P_{sp} - C_{ev} \cdot P_{ev} - C_{mv} \cdot P_{mv} - C_{ra} \cdot (P_{ra} + P_t) - C_{ap} \cdot (P_{ap} + P_t) - C_{pp} \cdot (P_{pp} + P_t) - C_{pv} \cdot (P_{pv} + P_t) - C_{la} \cdot (P_{la} + P_t) - C_{stv} \cdot (P_{stv} + P_t) - V_{rv} - V_{lv} - V_u],$$

$$V_u = V_{uAS} + V_{uSP} + V_{uEP} + V_{uSV} + V_{uEV} + V_{uRA} + V_{uAP} + V_{uPP} + V_{uPV} + V_{uLA} + V_{uAMP} + V_{uAMV} + V_{uSTV}.$$

$V_{TOT}$  is the total blood volume (5300 ml),  $V_{uLA}$  ( $V_{uRA}$ ) is the left (right) atrium unstressed volume,  $V_{uAS}$  ( $V_{uAP}$ ) is the systemic (pulmonary) arterial unstressed volume,  $V_{uSP}$  ( $V_{uSV}$ ) is the splanchnic peripheral (venous) unstressed volume,  $V_{uEP}$  ( $V_{uEV}$ ) is the extrasplanchnic peripheral (venous) unstressed volume,  $V_{uAMP}$  ( $V_{uAMV}$ ) is the active muscle peripheral (venous) unstressed volume,  $V_{uPP}$  ( $V_{uPV}$ ) is the pulmonary peripheral (venous) unstressed volume and  $V_{uSTV}$  is the systemic thoracic venous unstressed volume.

The equations for the coronary sections (Fig. 4) are the following:

$$Q_{artery} = \frac{P_{as} - P_{arteryMicro}}{R_{artery}},$$

$$Q_{artery} = \dot{P}_{arteryMicro} \cdot C_{arteryMicro} + QR_{arteryMicro},$$

$$QR_{arteryMicro} = \frac{P_{arteryMicro} - (P_{myocardium} + P_{lv})}{R_{arteryMicro}},$$

$$QR_{arteryMicro} = QR_{venousMicro} + \dot{P}_{myocardium} \cdot C_{myocardium},$$

$$QR_{venousMicro} = \frac{(P_{myocardium} + P_{lv}) - P_{venousMicro}}{R_{venousMicro}},$$

$$QR_{venousMicro} = Q_{venous} + \dot{P}_{venousMicro} \cdot C_{venousMicro},$$

$$Q_{venous} = \frac{P_{venousMicro} - (P_{ra} + P_t)}{R_{venous}}.$$

The equations for the Hemopump numerical model (Fig. 2) are the following:

$$QH_{in} + QL = Q_n, \quad QH_{out} + QL = Q_n, \quad P_{as} - P_{lv} = QL \cdot R + \dot{QL} \cdot L.$$

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