Coronary Blood Flow: Comparison between in Vivo and Numerical Simulation Data

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Abstract

Computer simulation of cardiac haemodynamics represents an effective approach to the in vitro study of complex pathophysiological problems.

Aim of our work was to reproduce, using a numerical simulator of the cardiovascular system, experimental waveforms of cardiac pressure and volumes, coronary blood flow and aortic pressure obtained in two anaesthetised open chest pigs. The computer simulator we used adopted a lumped parameters model to reproduce circulation. Variable elastance model reproduced the Starling's law of the heart. In pig#1 the correlation factors between in vivo and simulated instantaneous waveforms of systemic arterial pressure and coronary blood flow were 0.95 and 0.91 respectively. In pig#2 the correlation factors for the same waveforms were 0.97 and 0.98.

1. Introduction

Computer simulation is a valid approach to the *in vitro* study of cardiac haemodynamics and coronary blood flow mimicking a defined number of experimental variables [1,2]. Mosher et al. [3] studied coronary autoregulation and featured the coronary pressure-flow diagram being the best way of describing coronary vascular reserve. The graphic representation of the relation between instantaneous aortic pressure and coronary blood flow permits to study the different phases of the coronary flow during the cardiac cycle [4,5] in different circulatory conditions. The purpose of the present work was to reproduce by a computer simulator, haemodynamic and coronary blood flow waveforms obtained during in vivo experiments in two anaesthetised open chest pigs (performed at the Institute of Clinical Physiology in Pisa - Italy). During the experiments, ECG, left ventricular pressure, aortic pressure and left ventricular volume were monitored together with the coronary blood flow.

To reproduce the circulatory conditions obtained during the *in vivo* experiment we used a simulator of the cardiovascular system (CARDIOSIM©) [6-8].

In the first step of the procedure we tried to reproduce by the computer simulator the morphology of the instantaneous waveforms of the relevant experimental haemodynamic signals. In the second step we focused our attention on the curves representing the instantaneous relationships among related variables, i.e. the left ventricular pressure-volume loops and the aortic pressure-LAD (left anterior descending) coronary blood flow loops.

2. Methods

In two anaesthetised open chest pigs LAD phasic coronary blood flow was monitored by electromagnetic flowmeter (BL 613, Biotronex Laboratory, Inc., Silver Spring, Md.). ECG, aortic and left ventricular pressure were measured by a pigtail catheter with double microtip manometers (Mikrotip Catheter, Millar Instruments, Houston, Texas) together with conductance sensors for volume monitoring (Leycom, Sigma 5 DF mod., Leiden, The Netherlands). Through a small fluid filled cannula inserted into the LAD adenosine infusion was administered to abolish functional coronary resistances. By using the Po-nemah Physiology Platform (Gould Instrument Systems, Inc., Valley View, Ohio) system the following signals were acquired continuously: ECG, left ventricular pressure and volume, systemic arterial pressure, coronary blood flow and coronary pressure. The *off-line* data analysis was performed by a proprietary bio-signal processing software package [9].

In order to reproduce the same *in vivo* data an *in silico* software (CARDIOSIM©) was employed; this software is able to represent the entire circulation in the cardiovascular system with a lumped parameters model. Figure 1 shows the electric analog of the simulator.

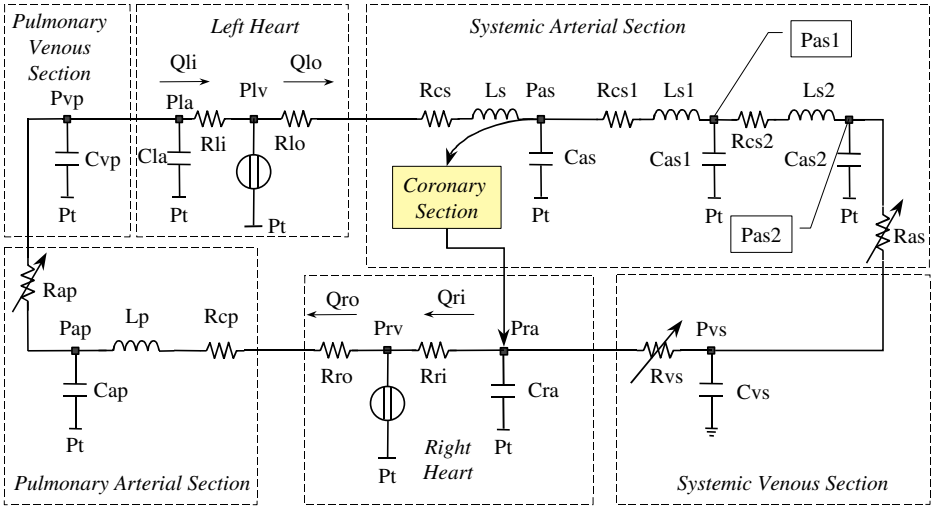

Figure 1. Electric analog of the cardiovascular system. The legend of parameters is presented in Table 1.

Variable elastance model, according to Suga and Sagawa [10], reproduces the Starling's law of the heart for the contraction and the ejection phase (for both ventricles). To simulate the filling of the ventricle we used the End Diastolic Pressure-Volume Relationship (EDPVR) proposed by Gilbert and Glantz [11]. The right and left atria were described as linear capacities characterized by constant values of compliance (Cla and Cra) and unstressed volume, i.e. the contractile activity of the atrium was neglected. Three modified windkessel cells (Rcs, Ls, Cas, Rcs1, Ls1, Cas1, Rcs2, Ls2 and Cas2) [6] together with variable systemic arterial resistance (Ras) represent the systemic arterial tree.

Table 1. Legend of parameters used in the CARDIOSIM© computer simulator.

Parameter	Symbol	Unit
Left (right) heart		
Left input (output) valve resistance	Rli (Rlo)	[mmHg·cm^{-3}·sec]
Right input (output) valve resistance	Rri (Rro)	[mmHg·cm^{-3}·sec]
Left (right) atrial compliance	Cla (Cra)	[cm^{3}·mmHg^{-1}]
Left (right) atrial pressure	Pla (Pra)	[mmHg]
Left (right) ventricular pressure	Plv (Prv)	[mmHg]
Left input (output) flow	Qli (Qlo)	[l·min^{-1}]
Right input (output) flow	Qri (Qro)	[l·min^{-1}]
Systemic (pulmonary) arterial section		
Systemic (pulmonary) characteristic resistance	Rcs,Rcs1,Rcs2 (Rcp)	[mmHg·cm^{-3}·sec]
Systemic (pulmonary) inertance	Ls,Ls1,Ls2 (Lp)	[mmHg·cm^{-3}·sec^{2}]
Systemic (pulmonary) arterial compliance	Cas (Cap)	[cm^{3}·mmHg^{-1}]
Systemic (pulmonary) arterial resistance	Ras (Rap)	[mmHg·cm^{-3}·sec]
Systemic (pulmonary) arterial pressure	Pas, (Pap)	[mmHg]
Systemic (pulmonary) venous section		
systemic venous resistance	Rvs	[mmHg·cm^{-3}·sec]
systemic (pulmonary) venous compliance	Cvs (Cvp)	[cm^{3}·mmHg^{-1}]
systemic (pulmonary) venous pressure	Pvs (Pvp)	[mmHg]
Thoracic pressure	Pt	[mmHg]

Pulmonary section was modeled by modified windkessels (Rcp, Lp, and Cap) with adjustable resistor (Rap). Systemic venous section was represented by a capacitor (Cvs) and by a resistance (Rvs). Rvs value can be automatically adjusted according to the relationship proposed by Guyton [12]: Rvs=K/Pvs, where K is a constant.

Only a single compliance (Cvp) represents pulmonary venous section, as pulmonary venous resistance can be neglected [12]. The connection of the ventricle to the circulatory network is realised 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). The coronary bed is considered as a single branch which links the left ventricle output with the right atrium input as described in our previous work [13].

The model was fitted to experimental data through the following steps:

- Setting HR equal experimental value.
- Adjustment of systemic peripheral resistance to obtain mean arterial pressure equal to experimental value (Table 2).
- Setting left ventricular elastance to calculated value.
- Adjustment of coronary resistance to the value of the experimental total coronary resistance.

In the study we focused our attention on: mean (Pas), systolic (Pas_{SYS}) and diastolic (Pas_{DIAS}) systemic arterial pressure, left ventricular end-diastolic (EDV) and end-systolic volume (ESV) and coronary blood flow (CBF) during the cardiac cycle. We analysed also the instantaneous left ventricular pressure and volume, the instantaneous systemic arterial pressure and the instantaneous coronary blood flow.

3. Results

Table 2 shows the comparisons, in terms of mean values, between computer simulation and measured data. During the simulations the heart rate (HR) was fixed at the measured values (77 bpm in both experiments).

Figure 2 shows left ventricular pressure-volume loops obtained for the pig #2. Blue lines represent two cardiac cycles measured during *in vivo* experiments, red line represents the simulated cardiac loop.

In figure 3 the instantaneous left ventricular and systemic arterial pressures are reported. Green and yellow waveforms represent left ventricular and systemic arterial pressure respectively stored during *in vivo* experiment on pig #2. Red and blue waveforms are the result of simulation.

Table 2. Comparison between in vivo and simulation data for two different pigs.

	Pig #1	Simulation #1	Pig #2	Simulation #2
Mean Pas [mmHg]	94.7	93.8	66.8	65.7
Systolic Pas [mmHg]	106.8	109.4	91.2	95.0
Diastolic Pas [mmHg]	81.2	82.7	46.9	46.0
ESV [cc]	88.2	87.3	17.1	18.4
EDV [cc]	125.1	127.4	45.1	43.9
Stroke Volume [cc]	37.0	40.1	28.3	25.0
CBF [ml/min]	111.5	110.9	150.5	156.1

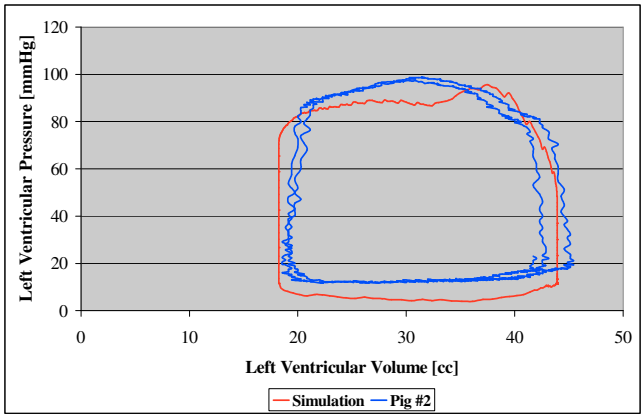

Figure 2. Left ventricular pressure-volume loops for measured (blue line) and simulated (red line) data.

In figure 4 both *in vivo* and simulated coronary blood flow waveforms are represented for the same pig #2, while figure 5 shows the aortic pressure-coronary flow loops.

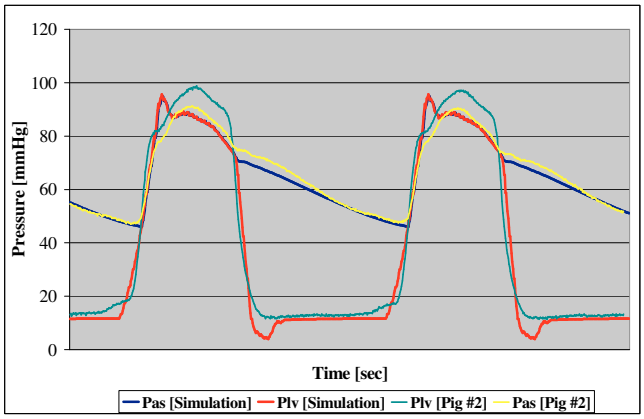

Figure 3. Left ventricular and systemic arterial pressures waveforms for measured (green and yellow lines) and simulated (red and blue lines) data.

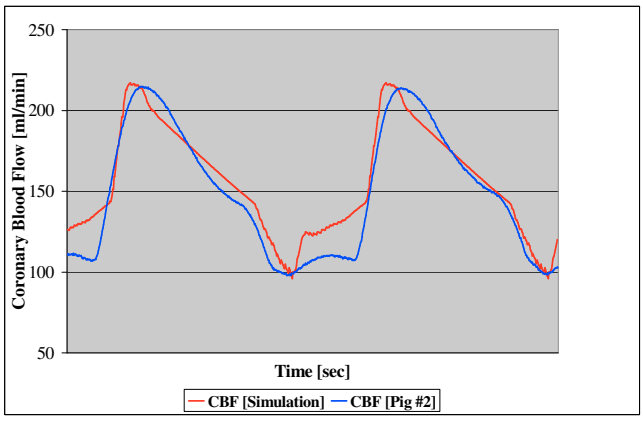

Figure 4. Coronary blood flow waveforms for measured (blue line) and simulated (red lines) data.

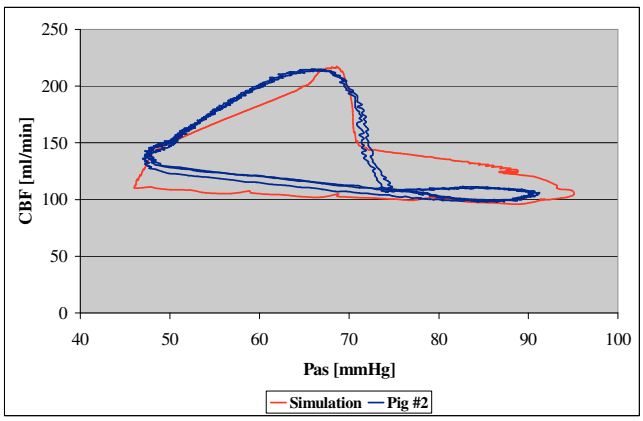

Figure 5. Relation between instantaneous aortic pressure and coronary flow for *in vivo* (blue lines) and simulated (red line) conditions.

Finally table 3 summarises the correlation factors between *in vivo* and simulated waveforms.

4. Discussion and conclusions

The results of the study suggest that the employed electric analog model of the cardiovascular system is capable of reproducing *in vivo* data together with the relations among different variables. Correlation function (Table 3) confirms the correspondence between in vivo simulated variables in steady state conditions. Moreover the analysis of waveforms at different times during the cardiac cycle shows that some differences exist between experimental and simulated left ventricular volume curves during diastole; probably due to the left atrium simulated as passive reservoir and to the neglected active components of the atrial contraction.

Table 3. Correlation factors between in vivo and simulated instantaneous waveforms.

	Pig #1	Pig #2
Systemic Arterial Pressure	0.95	0.97
Coronary Blood Flow	0.91	0.98
Left Ventricular Volume	0.85	0.92
Left Ventricular Pressure	0.95	0.98

An additional difference is present in the coronary blood flow waveform: during systole the simulated flow seems to be exclusively dependent on the left ventricular pressure, in presence of fixed coronary resistance and compliance. We prospect the possibility of validating the simulation in unsteady conditions.

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