Non-Linear Modulation of Total Peripheral Resistance Due to Pulsatility: a Model Study

F Aletti[1], E Lanzarone[1,2], ML Costantino[2], G Baselli[1]

[1]Dipartimento di Bioingegneria, Politecnico di Milano, Milano, Italia
[2]Dipartimento di Ingegneria Strutturale, Politecnico di Milano, Milano, Italia

Abstract

Total Peripheral Resistance (TPR) is the resistance of the arterial tree, defined as the ratio between the mean systemic pressure and the cardiac output.

A lumped parameters model of the arterial tree with active and non linear peripheries was developed in order to show how mutual interactions between systemic and local responses characterize non-linear modulations of TPR.

Numerical simulations showed that TPR is lower in presence of pulsatile inputs, it decreases with the harmonic content of the input itself, as a consequence of local responses to pulsatility, and it is maximum in absence of pulsatility, a typical condition of Extra Corporeal Circulation (ECC) performed using continuous pumps.

TPR is therefore strongly affected by systemic conditions of circulation, but it is mainly determined by the nonlinear behaviour of peripheral networks.

1. Introduction

Total Peripheral Resistance (TPR) is a significant clinical parameter for the assessment of hypertension, ageing, arterial stiffness and disorders of the cardiovascular control.

The relationship between pressure and blood flow is often considered linear accordingly to the hydraulic analogue of the first of Ohm's laws:

$$p = R \cdot Q \quad (1)$$

where p is for pressure drop, Q is for flow and R is for resistance. Based upon this equation, TPR can be consequently expressed by this ratio:

$$TPR = \frac{MAP}{CO} \quad (2)$$

where MAP stands for Mean Arterial Pressure and CO stands for Cardiac Output.

The pressure-flow characteristic curve of the cardiovascular system is linear under the hypothesis of a constant value of the apparent TPR; this is a typical assumption of works [1,2] which do not take into account modulations of local resistances.

In physiology, a modulation of peripheral resistances on either pressure and metabolic status was observed. The propagation of pressure waves along the arterial tree and the degree of residual pulsatility at the inlet of peripheries depends on the input at the inlet of the arterial tree. As a consequence, a constant TPR, as hypothesised by a linear model, does not exist. On the contrary, changes of an apparent TPR result from the complex peripheral modulation, which responds not only to mean pressure and flow values but also to other dynamical factors such as the shape of the systemic input wave.

2. Methods

A lumped parameter model of the arterial tree inclusive of local controls of blood flow and of an analytical description of filtration through capillary walls was developed in order to investigate the role of local oscillations in the complexity of the system. This approach is the same of works aiming at combining active peripheries with classical models of the arterial tree [3].

The numerical integration of the model state differential equations was performed by an integration software (Simnon®, SSPA Sweden AB, Göteborg), which allows to choose the integration algorithm from a set of methods: in this study the Runge-Kutta algorithm with fixed step was applied to carry out the integration.

2.1. Model of the arterial tree

The lumped state model of the arterial tree [4] is an electrical network formed of as many RCL circuits, in π configuration in series one to another, as the number of segments in which large arteries were divided. Each vessel branch terminates with a peripheral district.

Blood pressure and blood flow are the state variables of the model. Segment equations describing blood flow and pressure wave propagation along the arterial tree derive from mass balance and energy conservation [4].

2.2. Model of microcirculation

All peripheral districts were modelled as purely resistive networks.

Peripheral resistances are not constant neither linear, as classically considered either with lumped parameters approaches [1,2] or structured tree approaches [5] to cardiovascular modelling, but they are non linear and active due to the presence of local controls of blood flow and to the effects of fluid transport through capillary walls.

The architecture of the generic peripheral network [6] is shown in Figure 1.

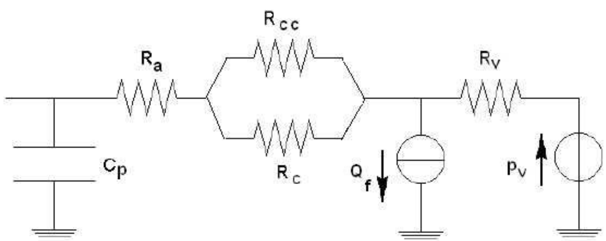

Figure 1. Peripheral district of the arterial tree.

Each resistive element of this network describes the mechanical properties of a specific kind of vessels:

- R_a represents the resistance of arterioles
- R_c and R_{cc} represent the capillary resistance in a capillary vessel shunt
- R_v represents the resistance of venules

As regards the other elements in this model, C_p is a capacitor preceding the peripheral network, Q_f represents the filtration flow through the capillary wall and p_v represents the pressure at the venous ending of the district. The capacitor C_p was included to model the compliance of tissues and to act as a low pass filter whose role is to cut off the high frequencies of the pulsatile regime of circulation in large vessels, so that the very low pulsatility of microcirculation can be reproduced.

2.3. Local controls of blood flow

This model includes the implementation of the metabolic control and of the myogenic control, which are responsible of local regulation of blood flow and of very low frequency vasomotion.

Although a few works attribute the metabolic regulation not only to venules but also to arterioles and some even individuate the arterioles as the only vessels interested by vasomotion [7], in this model each regulatory system acts on a different vessel of the peripheral network: the myogenic regulation controls the arteriolar radius, modulating it in function of the arterial pressure drop on the arterioles [4,6,8-10], while the metabolic regulation modulates the venular radius evaluating the specific O_2 consumption by the district [4,6,11] and comparing it to the oxygen need of the tissue under current conditions of circulation.

The feedback loops equations characterizing the two control systems are the same of [4].

2.4. Filtration through capillary walls

The filtration process through capillary walls is modelled by means of the flow generator Q_f (figure 1).

The fluid balance between the vascular compartment and the interstitial space determines the entity of the fluid transport [4,6].

Microcirculation was described by a capillary bed governed by the Hagen-Poiseuille Law (3):

$$R = \frac{8 \cdot \mu \cdot l}{\pi \cdot r^4} \quad (3)$$

where R is the resistance, μ is the viscosity of the blood, l is the length of the capillary vessels, r is the capillary radius and π is a constant. The radius however depends nonlinearly on the interstitial pressure.

This last aspect is of utmost importance in order to consider the additional effects of alterations in interstitial volumes on the peripheral activity and its contribution to the non linear modulation of peripheral resistances and to the systemic side effects of local phenomena.

2.5. Parameters of circulation

Simulations of circulation can be carried out imposing different values to the most significant parameters of circulation and of physical and chemical parameters of blood.

As regards blood parameters, physiological values were imposed for temperature (37 C), haematocrit (45%) and concentration of blood proteins (7.5 g / 100 ml of blood), which all contribute to determine other relevant blood parameters such as blood viscosity.

As to the main systemic parameters of circulation, values in the physiological range were adopted for heart rate (75 bpm) and cardiac output (5 l / min).

2.6. Inputs to the system

The arterial tree was solicited with a set of different inputs imposed at the inlet of the system in order to investigate the different responses in terms of TPR and, consequently, to analyse how these systemic differences are due to local activity.

The inputs were either pulsatile flow waves and non pulsatile ones.

Flow was constrained to zero during diastole, while several different shapes were simulated during systole:

- the Swanson and Clark wave [12], mimicking the physiologic cardiac blood flow wave
- a triangular wave
- four trapezoidal waves, each with a different length of the period of maximum ejection
- a rectangular wave
- a continuous wave

As regards the systole duration, it depends on heart rate accordingly to Katz and Feil equation (4):

$$T_s = \sqrt{\frac{0.096}{HR}} = \sqrt{\frac{0.096}{1.25}} \approx 0.277\,\text{s} \quad (4)$$

where:

- Ts is the systole duration in s
- HR is heart rate in Hz, which was set at 1.25 Hz

With respect to the continuous flow input, it simulates the typical regime of Extra Corporeal Circulation (ECC) as it is commonly performed in cardiac surgery during cardiopulmonary bypass.

3. Results

Computation of TPR (1) for all the applied inputs shows that TPR decreases with the harmonic content of the input wave (figure 2).

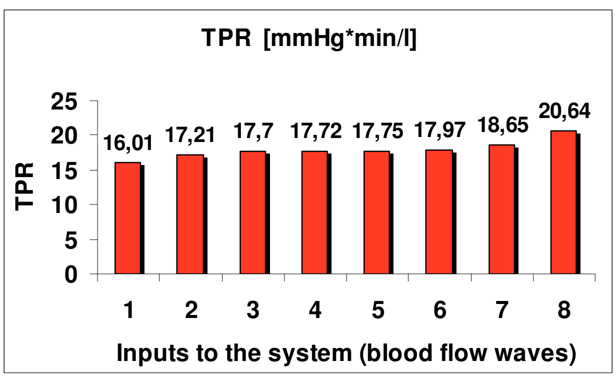

Figure 2. TPR of the arterial tree (in mmHg·min/l) for different flow waves at the aortic valve. Shapes are ordered with a decreasing harmonic content: 1) triangular wave; 2) Swanson and Clark's wave; 3-6) trapezoidal waves; 7) rectangular wave; 8) continuous wave.

TPR shows a minimum for a triangular input (1), increases for the Swanson and Clark input (2), it further increases for trapezoidal inputs while the trapezoidal shape tends to a rectangular shape (3, 4, 5, 6, 7) and finally, TPR has its maximum when the input is represented by a continuous flow wave.

The peripheral effects contributing to TPR with a non pulsatile regime of circulation were further investigated by extracting the pressure-flow characteristic curve of the system when the input is given by a steady pressure.

As expected, the flow increase with increasing pressure is limited by the action of controls, which tend to stabilize metabolic parameters. The pressure-flow characteristic curve with active peripheral controls is represented by the dark line in figure 3, while the tracing representing the same characteristic in absence of local activity is the light line. A comparison between the two curves allows to point out the overall contribution of local controls to the systemic behaviour.

The intersection between the two curves is given by the physiological reference working point of the system.

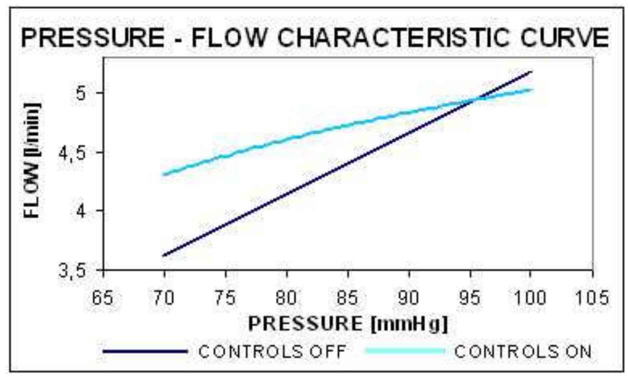

Figure 3. Pressure-Flow characteristic curve of the arterial tree, when local controls are active (dark line) and when no local activity is considered (light line).

4. Discussion and conclusions

TPR assessment under inputs differing for shapes and harmonic contents basically depends on the peripheral response, since TPR results from the apparent superposition of all peripheral resistances.

The analysis of the response of controls suggests that the metabolic regulation has no effects on the local response: all simulations were carried out imposing the same cardiac output and the same parameters of circulation, so that the physiological needs of tissues for oxygen and nutrients were matched by blood flow in all simulations.

On the other hand, the myogenic control is the unique control mechanism which is responsible for different local responses to the inputs of the system and, therefore, of the modulation of apparent peripheral resistances in response to pressure fluctuations.

TPR appears to be related with the spectral characteristics of the input wave and in particular TPR is higher with smoother input flow waves as their harmonic content decreases.

A comparison between the dynamics of peripheral resistances and in particular of arteriolar radiuses in presence and in absence of pulsatility shows that arteriolar radiuses oscillate around an equilibrium value which is larger when flow is pulsatile. That is to say, when circulation is non pulsatile, myogenic regulation constraints arteriolar lumen thus increasing peripheral resistances; as a consequence, TPR is higher than it is with a physiological regime of circulation.

As to the pressure-flow characteristic relation, the comparison between the two tracings in figure 3 shows that the nonlinearity of the systemic response is due to peripheral activity, as expected. When local controls are not active, the arterial tree is passive and peripheral dynamics are linear. Thus, the pressure-flow relationship itself is linear as expected considering equation (1).

The general conclusion which can be drawn from both the presented results is that pulsatility and mean peripheral flow are not linearly superimposed, because of the nonlinearity underlying the dynamics of peripheral resistances.

A remarkable clinical condition which is characterized by a continuous flow is Extra Corporeal Circulation (ECC) performed in cardiac surgery using either centrifugal or roller pumps.

A number of studies focused on the alteration induced by this regime of circulation on the patient, suggesting the development of newly designed pulsatile pumps to be expressively destined to ECC. Our simulations showed that TPR is considerably lower in presence of a pulsatile flow rather than in its absence, indicating that lack of pulsatility strongly affects the non physiological response of the system during ECC.

Since some of the technical limitations of ECC, such as the priming of the heart-lung machine and the consequent haemodilution cannot be solved, these results give further evidence that the transition to a pulsatile ECC may significantly reduce the invasiveness of this practice in cardiac surgery and more in general in the domain of life assistance devices.

Acknowledgements

This study was supported by the My Heart project IST 507816 of the European Community.

References

[1] Westerhof N, Bosman F, De Vries CJ, Noordergraaf A. Analogue studies of the human systemic arterial tree. Journal of Biomechanics 1969;2:121–43.

[2] Burattini R, Gnudi G. Computer identification of models for the arterial tree input impedance: comparison between two new models and first experimental results. Medical & Biological Engineering & Computing 1982;20:134–44.

[3] Baselli G, Porta A, Pagani M. Coupling Arterial Windkessel with Peripheral Vasomotion: Modeling the effects on Low Frequency Oscillations. IEEE Transactions on Biomedical Engineering 2006;53:53-64.

[4] Lanzarone E, Liani P, Baselli G, Costantino ML. Model of Arterial Tree and Peripheral Control for the Study of Physiological and Assisted Circulation. Medical Engineering & Physics, in press

[5] Olufsen M, Peskin C, Kim WY, Pedersen E, Nadim A, Larsen J. Numerical simulation and experimental validation of blood flow in arteries with structured-tree outflow conditions. Annals of biomedical engineering 2000;28:1281-99.

[6] Aletti F, Lanzarone E, Costantino ML, Baselli G. Effects of Pulsatility on Apparent Peripheral Resistance with Edema. ESGCO Proceedings 2006;264-5.

[7] Cornelissen AMJ, Dankelman J, Van Bavel E, Spaan JAS. Balance between myogenic, flow-dependent and metabolic flow control in coronary arterial tree: a model study. American Journal of Physiology, Heart and Circulation Physiology 2002;282:2224-37.

[8] Cavalcanti S, Ursino M. Chaotic oscillations in microvessel arterial networks. Annals of biomedical engineering 1996;24:37–47

[9] Davis MJ, Myogenic response gradient in arteriolar network. American Journal of Physiology 1993;264:2168-79.

[10] Ursino M, Fabbri G, Belardinelli E. A mathematical analysis of vasomotion in the peripheral vascular bed. Cardioscience 1992;3:13–25.

[11] Groebe K. Precapillary servo control of blood pressure and postcapillary adjustment to tissue metabolic status; a new paradigm for local perfusion regulation. Circulation 1996;94:1876–85.

[12] Swanson WM, Clark RE. Cardiovascular system simulation requirements, design and performance. Journal of Bioengineering 1977;1:121-33.

Address for correspondence

Federico Aletti
Politecnico di Milano
Dipartimento di Bioingegneria
Piazza Leonardo da Vinci, 32
20133 Milano, Italy
federico.aletti@polimi.it