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The Critical Closing Pressure and Resistance Area Product of the Cerebral Circulation

U. G. Jayasekera
Department of Physics, The Open University of Sri Lanka, Nawala, Nugegoda

ABSTRACT

Estimating changes in critical closing pressure (CrCP) and resistance area product (RAP) provided better understanding of the nature of cerebrovascular regulation (arterial stiffening or narrowing). The critical closing pressure of the cerebral circulation indicates the value of the arterial blood pressure (ABP) at which cerebral blood flow (CBF) approaches zero. Measurements in animals and in humans have shown that the CrCP is significantly greater than zero. Studies of the cerebral circulation need to take CrCP and RAP into account, to obtain more accurate estimates of cerebrovascular resistance changes, and to reflect the correct dynamic relationship between instantaneous ABP and CBF. This analysis was performed on 48 healthy subjects and 11 hypertensive subjects. Due to the non-linear shape of the complete ABP-CBF curve, most methods proposed for estimation of CrCP and RAP can only represent the linear range of the pressure-flow (or velocity) relationship.

1. INTRODUCTION

Understanding the human cerebral circulation has been a considerable challenge due to its unique anatomical and physiological characteristics and the difficulty of access imposed by the skull. In last the 25 years, new non–invasive technologies, such as transcranial Doppler ultrasound (TCD) and near-infrared spectroscopy (NIBS) have allowed unprecedented opportunities to study human cerebral haemodynamics in health and disease. These new methods have helped to improve our understanding of key mechanisms, such as the dynamic behaviour of cerebral blood flow autoregulation in human [1-2], but in other areas progress has been much slower. One such area in which knowledge has not advanced as much as expected is our ability to quantify and characterise the passive properties of the cerebral vascular bed.

The concept of a CrCP (and RAP) of the cerebral circulation, which has generated considerable controversy in the literature is a good example of an aspect of the vascular plant that requires more investigation. On the other hand, for the human cerebral circulation as a whole, CrCP can be seen as a part of a 'black-box' model, lacking in physiological specificity, and impossible to measure with acceptable accuracy.

The main reason is the empirical observation that the single-parameter model only with cerebrovascular resistance-(CVR) cannot provide a realistic representation of pressure-flow/velocity relationship of the cerebral circulation. The inclusion of additional parameters, such as CrCP, RAP, lead to conceptual models that more closely reflect relationship extracted from measurements that are increasingly used for management of patients with cerebrovascular conditions.

2. METHODOLOGY

2.1 **Data Collection and Subjects**

Seventeen normotensive young subjects (9 Male, 8 Female, age 27 ± 2 years), 31 normotensive elderly subjects (15 Male, 16 Female, age 56 ± 15 years), and 11 hypertensive (7 Male, 4 Female, age 66 ± 12 years) were tested in the study. Ethical approval was obtained from the Leicestershire Ethics Committee and written informed consent was obtained before each study. Most of the data received for this study is already available as a part of a large database assembled by the Stroke and Medicine for Elderly (University of Leicester ,UK) group in the last six years.

2.2 **Procedures and Measurements**

Arterial blood pressure (ABP) was measured in the middle or annular finger of the hand that was kept at heart level by photoplethysmography (Finapres 2300 Ohmeda). Cerebral blood flow velocity (CBFV) in the middle cerebral artery (MCA) (Left MCA and Right MCA) was recorded bilaterally by Doppler ultrasound (2 MHz, Scimed QVL842X) with probes placed over the temporal bone and secured with an adjustable head frame. The surface ECG (Electrocardiography) was recorded with three standards chest leads and transcutaneous CO_2 (TINA, Radiometer, Copenhagen) was monitored continuously with an axillary probe overlying the Tail of Spence.

2.3 Data Analysis

Data was downloaded in real time onto a dedicated personal computer. First the raw data was examined for stationarity as well as other time domain behaviour. The data was visually inspected to select recordings that had good quality waveforms for CBFV channels, as well as ABP and ECG. MATLAB (version 7.2) was used for the calculations and to generate the plots needed to visualize the results.

First of all, MATLAB programme could be developed by using a simple algorithm to detect the beginning and end of each cardiac cycle, from the ECG as fiducial points (R-R interval). Several methods have been used to calculate CrCP and RAP. We used beat to beat linear regression analysis and harmonic methods [2].

2.4 Statistics

Changes in haemodynamics variables were compared by using one-way ANOVA and student's t-test. A value of $p < 0.05$ was accepted as statistically significant, and all data was represented as mean ± SD. All statistics were performed by using a 'Statistica version no: 6 (97 Edition) for Windows' software program.

3. RESULTS

3.1 Estimate of CrCP and RAP

Hypertensive elderly subjects had higher systolic, diastolic and mean pressures than the other two groups (see Table 1). Table 2 show the (mean ± SD) values of CrCP and RAP between the estimates obtained by linear regression and 1st harmonic methods. This result was confirmed by linear regression and 1st harmonic method for (left and right MCA) CrCP and RAP lead to approximately similar result. Table 3 gives the cerebral haemodynamic parameters (ANOVA result) of the 59 subjects.

Table 1: Demographic and baseline physiological parameters (n = 59)

variable	Normotensive Young	Normotensive Elderly	Hypertensive Elderly
n	17	31	11
Gender(Male: Female)	9:8	15:16	7:4
Mean age± SD, year	27 ± 2	55 ± 14	65 ± 11
Systolic BP, mmHg	118.4 ± 11.0	127.9 ± 12.4	153.4 ± 7.4
Diastolic BP, mmHg	71.1 ± 7.9	79.1 ± 9.1	85.8 ± 12.8
MAP, mmHg	86.8 ± 8.4	95.4 ± 9.4	112.3 ± 9.0
BMI, kg m^{-2}	22.9 ± 2.6	25.2 ± 2.9	26.0 ± 2.8

MAP-Mean blood pressure, BMI-Body mass index

Table 2: Distribution of CrCP and RAP estimates (mean ± SD) according to Linear regression and 1st Harmonic estimation method.

Variable	MCA	Linear Regression	1st Harmonic
CrCP (mmHg)	Left	35.41 ± 3.72	24.02 ± 5.76
	Right	34.25 ± 4.66	24.11 ± 7.58
RAP ($mmHg.s.cm^{-1}$)	Left	1.210 ± 0.220	1.267 ± 0.155
	Right	1.217 ± 0.146	1.316 ± 0.198

Table 3: Cerebral haemodynamic parameters

Variable		Young (n = 17)	Normotensive Elderly (n = 31)	Hypertensive Elderly (n = 11)	p (ANOVA)	F
Mean ABP, mmHg		86.9 ± 14.4	86.4 ± 12.2	92.1 ± 15.6	0.4692	0.7671
Mean CBFV ($cm\ s^{-1}$)	Left	55.1 ± 14.3	54.4 ± 16.9	41.7 ± 13.3	0.0286	3.789
	Right	55.1 ± 14.9	50.8 ± 14.1	45.8 ± 13.7	0.2459	1.438
Mean CrCP (mmHg)	Left	24.3 ± 12.1	25.5 ± 12.9	24.4 ± 9.2	0.9325	0.070
	Right	25.5 ± 12.1	24.8 ± 11.9	23.1 ± 12.6	0.8752	0.134
Mean RAP ($mmHg.s.cm^{-1}$)	Left	1.24 ± 0.54	1.36 ± 0.69	1.84 ± 0.67	0.0390	3.439
	Right	1.19 ± 0.41	1.35 ± 0.48	1.66 ± 0.60	0.0512	3.136
Mean HR , bpm		66.3 ± 10.2	64.8 ± 10.4	64.0 ± 7.5	0.8683	0.1416

* Values are group mean ± SD , HR-Heart rate(Beat per minute) **p* value indicates the ANOVA outcome

4. DISCUSSION

CrCP is an alternative parameter of cerebral autoregulation [3] and RAP provided better understanding of the nature of cerebrovascular regulation (arterial stiffening or narrowing). RAP represents the relationship between estimated cerebral perfusion pressure and cerebral blood flow velocity [4], whereas CVR (CVR=mean ABP/mean CBFV) specifies the relationship between ABP and cerebral blood flow velocity. RAP [5] is a more sensible indicator of cerebrovascular resistance than the widely used CVR .RAP also reflected cerebralvascular resistance under different arterial pCO_2 tension [4]. According to our results, two methods (~10% differences) can be shown by CrCP. CrCP is a haemodynamic index that is affected in head injury patients. It is a poor estimator of mean intracranial pressure; it better explains cerebral vascular tone [6].

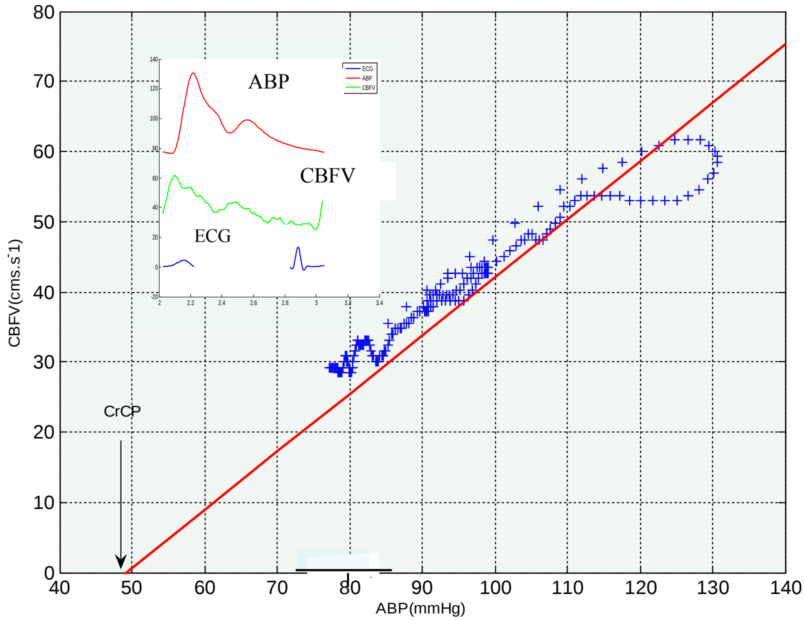

Figure 1: ABP -CBFV (beat- to -beat linear regression method) relationships for one selected cardiac cycle.

In some of the subjects, negative values were found for CrCP. The negative CrCP values are given from significant degrees of stenosis causing downstream falls in perfusion pressure [7]. We have used long data files in beat–to–beat linear regression method. In some cases it was very difficult to identify a loop as in figure 1, due to changes in measuring parameters. We had to change the time delay filter (ABP–CBFV delay) from subject to subject as well as within the same subject, which may affect the final results.

5. CONCLUSIONS

The results show that calculation of CrCP and RAP provided valuable information about the mechanisms and magnitudes of cerebrovascular regulation. The demonstration of a rise in CrCP is a very important factor in the control of cerebral blood flow, during clinical situation. We consider only linear velocity [8] (component (V_X) (1-D) for the CBFV (MCA artery). But in practical situation it is not possible. Therefore it is important to take into account using cylindrical polar coordinates (r,θ,ϕ) for the velocity component (Figure 2.) of the CBFV(3-D). But all the equations have been derived in classical mechanics (macroscopic scale). In the future work, this would be considered in Quantum mechanical point of view (Eg. Blood spin angular momentum, arteries wall vibration etc). We can introduce as a new concept 'Quantum Hemodynamics' for cerebral circulation (cerebral-micro circulation). According to this concept, we can identify very small changes (at very low frequency) in ABP-CBFV. We have to develop all these things by (using Neural Network and Wavelet theory) MATLAB programme.

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