neurocritical care society Neurocrit Care (2012) 17:58–66
DOI 10.1007/s12028-012-9672-6

ORIGINAL ARTICLES

Transcranial Doppler Pulsatility Index: What it is and What it Isn't

Nicolás de Riva · Karol P. Budohoski · Peter Smielewski · Magdalena Kasprowicz · Christian Zweifel · Luzius A. Steiner · Matthias Reinhard · Neus Fábregas · John D. Pickard · Marek Czosnyka

Published online: 4 February 2012

Abstract
Background Transcranial Doppler (TCD) pulsatility index (PI) has traditionally been interpreted as a descriptor of distal cerebrovascular resistance (CVR). We sought to evaluate the relationship between PI and CVR in situations, where CVR increases (mild hypocapnia) and decreases (plateau waves of intracranial pressure—ICP).

Methods Recordings from patients with head-injury undergoing monitoring of arterial blood pressure (ABP), ICP, cerebral perfusion pressure (CPP), and TCD assessed cerebral blood flow velocities (FV) were analyzed. The Gosling pulsatility index (PI) was compared between baseline and ICP plateau waves ($n = 20$ patients) or short term (30–60 min) hypocapnia ($n = 31$). In addition, a modeling study was conducted with the "spectral" PI (calculated using fundamental harmonic of FV) resulting in a theoretical formula expressing the dependence of PI on balance of cerebrovascular impedances.
Results PI increased significantly ($p < 0.001$) while CVR decreased ($p < 0.001$) during plateau waves. During hypocapnia PI and CVR increased ($p < 0.001$). The modeling formula explained more than 65% of the variability of Gosling PI and 90% of the variability of the "spectral" PI ($R = 0.81$ and $R = 0.95$, respectively).
Conclusion TCD pulsatility index can be easily and quickly assessed but is usually misinterpreted as a descriptor of CVR. The mathematical model presents a complex relationship between PI and multiple haemodynamic variables.

Keywords Cerebral hemodynamics · Plateau waves · Transcranial doppler · Traumatic brain injury

N. de Riva · K. P. Budohoski · P. Smielewski · M. Kasprowicz · C. Zweifel · L. A. Steiner · M. Reinhard · J. D. Pickard · M. Czosnyka (✉)
Division of Neurosurgery, Department of Clinical Neurosciences, Addenbrooke's Hospital, University of Cambridge, Hills Road, Box 167, Cambridge CB2 0QQ, UK
e-mail: mc141@medschl.cam.ac.uk

N. de Riva · N. Fábregas
Department of Anesthesiology, Hospital Clinic, Universitat de Barcelona, Barcelona, Spain

M. Kasprowicz
Institute of Biomedical Engineering and Instrumentation, Wroclaw University of Technology, Wroclaw, Poland

C. Zweifel
Department of Neurosurgery, University Hospital of Basel, Basel, Switzerland

L. A. Steiner
Department of Anaesthesia, Lausanne University Hospital, Lausanne, Switzerland

M. Reinhard
Department of Neurology, University of Freiburg, Freiburg, Germany

M. Czosnyka
Institute of Electronic Systems, Warsaw University of Technology, Warsaw, Poland

Introduction

Transcranial Doppler (TCD) ultrasonography allows repeated, non-invasive investigations of rapid changes in cerebral perfusion. While mean flow velocity (FV) cannot be translated easily into volume blood flow [1] due to the unknown diameter of the insonated vessel, additional information on cerebral haemodynamics may be derived

from the TCD waveform. The most commonly used haemodynamic index is the Gosling pulsatility index [2] (PI), which describes the pulsatility of TCD waveforms. It is calculated as the difference between systolic and diastolic flow velocities divided by the mean velocity $[(FV_{sys} - FV_{dia})/FV]$.

For the last three decades many authors have investigated the usefulness of PI in the assessment of distal cerebrovascular resistance (CVR), non-invasive intracranial pressure (ICP) and cerebral perfusion pressure (CPP) in traumatic brain injury (TBI) [3], and hydrocephalus [4]. Conclusions regarding its accuracy and reliability remain controversial as far as clinical decisions are concerned [5, 6]. In subarachnoid hemorrhage (SAH), the role of PI is discussed by some authors as it seems to correlate better with outcome than with TCD-diagnosed cerebral vasospasm [7].

Many experimental and clinical studies have supported the interpretation of PI as a reflection of the distal CVR, attributing greater PI to higher CVR [8], and this assumption is still accepted nowadays [9].

A previous experimental study in rabbits [10] showed that in physiological conditions hypercapnia decreased both CVR and PI while a reduction in CPP in autoregulating animals caused a decrease in CVR but an increase in PI. These findings suggested a combined change in distal vascular resistance and compliance of the large cerebral arteries.

Our hypothesis is that PI is a complex function of various hemodynamic factors and not only of CVR as it is usually interpreted. To clarify the relationship between TCD pulsatility and CVR, we have retrospectively compared clinical data of two different physiological situations where PI increases. The first one is intracranial hypertension, represented by ICP plateau waves, where a major vasodilatory cascade takes place (i.e., CVR decreases) due to a time-dependent positive feedback loop between vasodilation caused by decreasing CPP and increasing ICP [11]. The second group involves patients submitted to a mild hypocapnic challenge, which is known to increase CVR [12] [13]. We also sought to compare measured PI in both groups with a mathematical formula, expressing PI as a function of cerebrovascular impedance.

Subjects and Methods

Patients

From a database of 345 head-injured patients with continuous recordings of ABP, ICP, and TCD (the median age of patients was 29 years [interquartile range (IQR) 20–44], with 75% being male) we have identified all patients where an ICP plateau wave occurred during the monitored period. This material was partially presented before [14], however not in the context of TCD pulsatility and waveform analysis. Plateau wave data were recorded during daily TCD investigations of cerebral autoregulation [15] performed in head-injured patients, which constituted a part of a standard clinical protocol. Data were retrospectively analyzed as a part of routine clinical audit, with approval of Neurocritical Care Users Committee.

In order to explore the effect of hypocapnia we have used recordings from a previously published study evaluating the effect of moderate hyperventilation on ICP and FV [12]. Data were acquired as part of a research project investigating cerebral physiology and metabolism following TBI, which was approved by the Neurocritical Care Users Committee and the Institutional Research Ethics Committee.

Except for the period of the hypocapnic challenge to assess CO_2 reactivity patients were managed according to an ICP/CPP oriented protocol which aimed to keep CPP between 60 and 70 mmHg and ICP below 20–25 mmHg [16].

Monitoring and Data Analysis

ABP was monitored invasively from the radial artery using a pressure monitoring kit (Baxter Healthcare CA, USA; Sidcup, UK). ICP was monitored using an intraparenchymal probe (Codman & Shurtleff, MA, USA or Camino Laboratories, CA, USA). FV was monitored from the middle cerebral artery (MCA) with a 2 MHz probe (Multidop T, DWL, Germany) and using the Doppler Box (DWL Compumedics, Germany) or Neuroguard (Medasonic, CA, USA). TCD was performed daily for periods of 10 min to 1 h starting from the day of initiation of invasive monitoring. The decision to discontinue monitoring was made on clinical grounds.

Raw signals were digitized using an analog–digital converter (DT9801, Data Translation, Marlboro, Mass, USA) sampled at a frequency of 50 Hz and recorded using WREC (Warsaw University of Technology) or BioSAn (University of Cambridge, UK) software. ICM+ Software (Cambridge Enterprise, Cambridge, UK, http://www.neurosurg.cam.ac.uk/icmplus/) was used for final analysis. All signals were subjected to manual artifact removal. Artifacts consisted of three types: fast bimodal variations more than 20 mmHg from baseline which are related to tracheal suctioning; complete loss of diastolic FV (without signs of increased ICP) or fast, bimodal spikes on TCD due to a poor temporal bone window or incorrect gain settings; absence of the pulse waveform in ABP or ICP which were related to arterial line flushing or transducer malfunction.

The maximal and minimal values of FV from every 2 s period were calculated and treated as the peak-systolic and end-diastolic components, respectively. Second, FV and its peak-systolic and end-diastolic components were averaged over 10 s to give the mean values for FV (FV_m), peak-systolic FV (FV_s), and end-diastolic FV (FV_d). Discrete Fourier transform was used to calculate the fundamental harmonic components for pulse waveforms of ICP, ABP, and FV (denoted as $i1$, $a1$, and $f1$, respectively).

CVR was estimated as 10 s time-averaged CPP divided by the mean FV ($CVR = CPP/FV_m$) [15]. PI was calculated as the difference between FV peak-to-peak values divided by the mean FV [$(FV_s - FV_d)/FV_m$]. For analyzing TCD pulsatility at a fixed frequency the "spectral" PI was evaluated as $f1/FV_m$.

Finally, a mathematical model of cerebrovascular space, reduced to CVR and cerebral arterial compliance (Ca), was evaluated to express cerebrovascular impedance analytically. From this analysis PI was calculated for a fixed frequency equivalent to heart rate (HR). This relation is defined by the following formula (1) (please see "Appendix" for details of mathematical derivation).

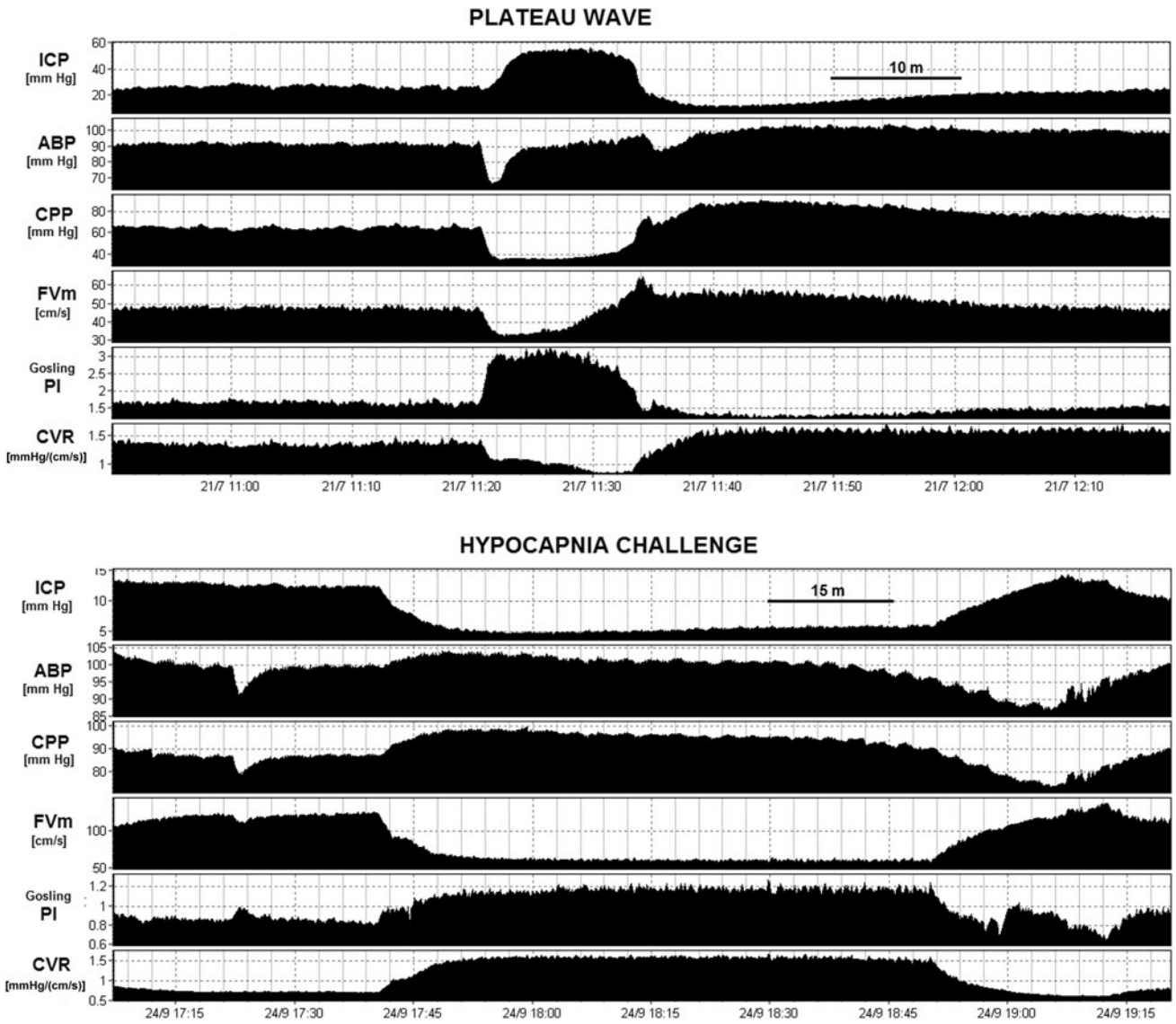

Fig. 1 Timetrends of intracranial pressure (ICP), arterial blood pressure (ABP), cerebral perfusion pressure (CPP), mean cerebral blood flow velocity (FV_m), pulsatility index (PI) and cerebrovascular resistance (CVR) in two different patients with head-injury. *Top panel* plateau wave of ICP. *Bottom* CO_2 vasoreactivity test (hypocapnia). The figure demonstrates an increase in PI in both situations while CVR decreases during the plateau wave due to the vasodilation but increases during the hypocapnic challenge due to the cerebral vasoconstriction

$$\mathrm{PI} = \frac{\mathrm{a1}}{\mathrm{CPP}} \times \sqrt{(\mathrm{CVR} \times \mathrm{Ca} \times \mathrm{HR} \times 2\pi)^2 + 1} \quad (1)$$

where $a1$ is the fundamental harmonic of arterial blood pressure pulse, CPP—mean cerebral perfusion pressure, CVR—cerebrovascular resistance, Ca—cerebral arterial compliance, HR—heart rate.

Statistical Analysis

Changes in ICP, CPP, CVR, and PI between baseline and the observed physiological condition (plateau or hypocapnia) were compared with the paired t test. Data are reported as mean ± SD. Calculations were performed using STATISTICA 6.0 (StatSoft, Inc.). $p < 0.05$ was considered significant.

Results

Fifty-one patients were included in the study on plateau waves and hypocapnia. The first cohort included 19 patients (mean age: 24.32 ± 6.02 years, range 17–35 years, five women, 14 men, median admission GCS 5, range 3–12) where 38 events of ICP plateau waves were registered. Studies were carried out 1–10 days after injury (median: day 4). Data obtained from an additional patient who exhibited four plateau waves has been included in the analysis although full demographics were unavailable. Total recording time equaled 30.3 h, with an average of 43.3 min per session (range 16.5–103.5 min).

The second group included 31 patients (mean age: 38 ± 15 years, range 17–70 years, five women, 26 men, median admission GCS: 5, range 3–12). Studies were carried out 1–10 days after injury (median: day 3). Patients were subjected to short term (30–60 min) controlled hyperventilation as part of a standard clinical CO_2 reactivity test.

Examples of time trends of recorded and calculated parameters are presented in Fig. 1.

Changes During Plateau Waves (group 1) and Hypocapnia (group 2)

During the plateau waves the increase in ICP from an average of 24.01 ± 6.91 to 43.53 ± 12.14 mmHg provoked a significant decrease in CPP, FV_m, and FV_d, but an increase in FV_s. The pulse amplitude of ICP and FV ($i1$ and $f1$, respectively) increased while the pulse amplitude of ABP ($a1$) did not change (Table 1). During the plateau waves PI increased significantly, whereas CVR decreased (Fig. 2a).

The increase in minute ventilation reduced $PaCO_2$ from 5.10 ± 0.35 to 4.40 ± 0.34 kPa inducing a small but significant decrease in mean ICP (from 16.59 ± 6.68 to 12.73 ± 6.25 mmHg, $p < 0.001$). CPP improved slightly with no significant change in ABP (Table 2). In this group of patients there was a steep decline in all parameters related to FV, however, PI as well as CVR increased significantly (Fig. 2B).

Table 1 Mean values of pressure and haemodynamic parameters found in 20 patients before and during plateau waves

Plateau waves ($n = 20$)			
Parameters	Baseline	Plateau	p value
ICP (mmHg)	24.01 ± 6.91	43.53 ± 12.14†	<0.001
CPP (mmHg)	71.64 ± 10.63	49.37 ± 11.64†	<0.001
FV_m (cm/s)	69.47 ± 29.97	57.94 ± 25.77†	<0.001
$i1$ (mmHg)	2.58 ± 0.85	6.01 ± 2.21†	<0.001
$f1$ (cm/s)	21.90 ± 6.87	25.92 ± 8.55†	<0.001
$a1$ (mmHg)	18.16 ± 3.50	17.31 ± 3.30	NS (0.062)
ABP (mmHg)	95.67 ± 9.15	92.91 ± 9.25*	0.014
HR (cycles/min)	74.26 ± 12.60	73.68 ± 12.26	NS (0.446)
FV_s (cm/s)	127.16 ± 41.05	132.03 ± 43.41	NS (0.055)
FV_d (cm/s)	42.10 ± 21.98	28.92 ± 18.30†	<0.001
PI	1.34 ± 0.38	2.01 ± 0.73†	<0.001
CVR [mmHg/(cm/s)]	1.25 ± 0.61	1.03 ± 0.50†	<0.001

Values are expressed as the mean ± SD. Significant levels of the differences between change in parameters before and during the plateau wave are given (paired t test)

a1 pulse amplitude (first harmonic) of ABP, *ABP* arterial blood pressure, *CPP* cerebral perfusion pressure, *CVR* cerebrovascular resistance, *f1* pulse amplitude (first harmonic) of blood FV, FV_m mean blood FV in the MCA, FV_d diastolic blood FV in the MCA, FV_s systolic blood FV in the MCA, *i1* pulse amplitude (first harmonic) of intracranial pressure, *ICP* intracranial pressure, *HR* heart rate, *NS* not significant, $PaCO_2$ carbon dioxide arterial partial pressure, *PI* Gosling pulsatility index

$^{*}p < 0.05$; $^{\dagger}p < 0.01$

Pulsatility Index and ICP/CPP

Regression between all points of PI and ICP indicates a correlation coefficient of $R = 0.7$ with linear model 95% prediction margin for ICP of 21 mmHg. Regression between CPP and PI suggests best reciprocal fit, with a correlation coefficient $R = 0.77$ and 95% prediction for CPP around 22 mmHg (Fig. 3).

Pulsatility Index and its Explanation Using the Mathematical Model

Analysis performed combining the results from both groups 1 and 2 showed that the correlation between the calculated

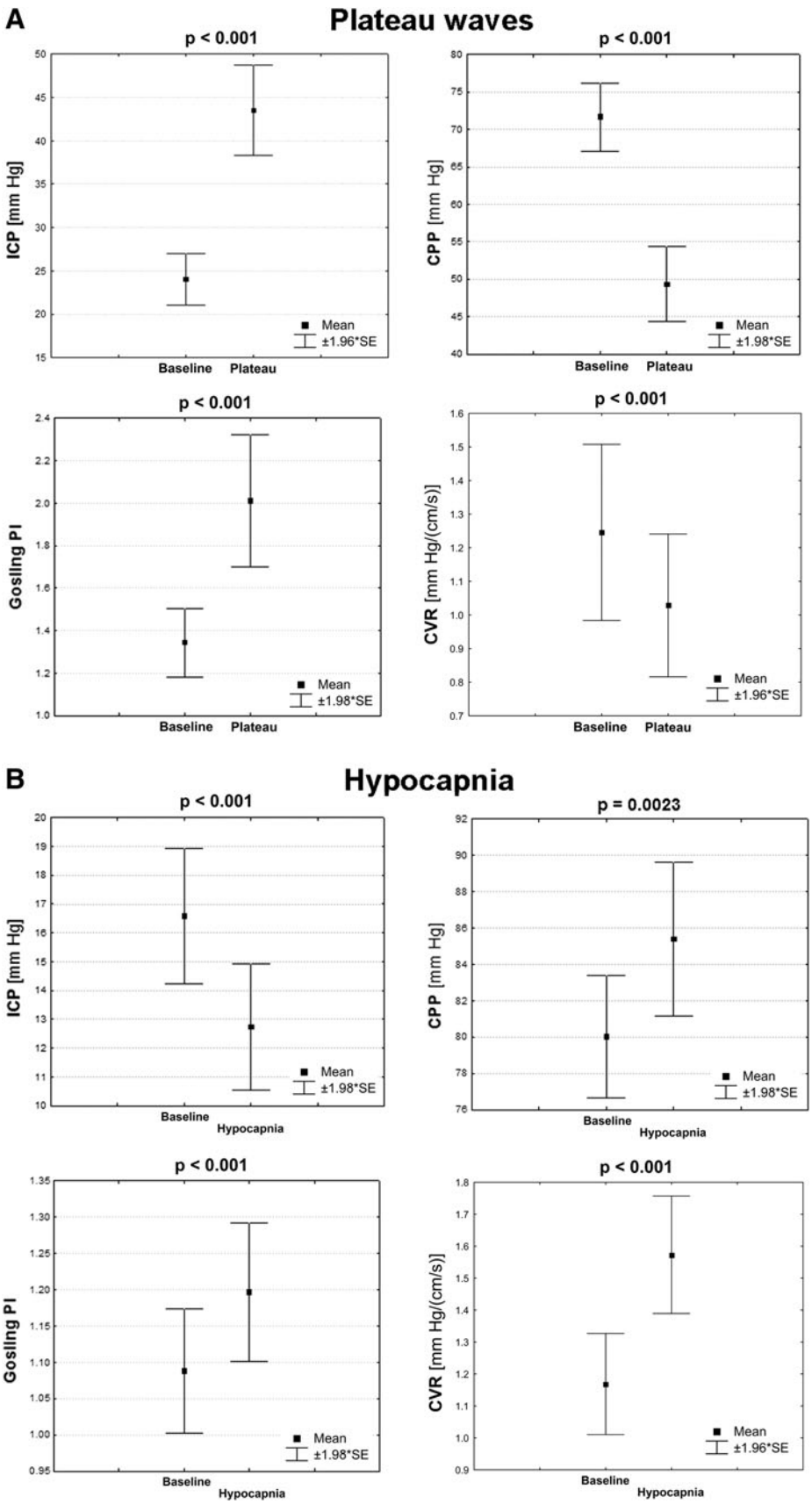

Fig. 2 **a** The differences in the mean intracranial pressure (ICP), cerebral perfusion pressure (CPP), Gosling pulsatility index (PI), and cerebrovascular resistance (CVR) between baseline and plateau wave of ICP. Data is averaged from recordings of 42 plateau waves encountered in 20 patients. **b** Differences in mean ICP, CPP, Gosling PI, and CVR between baseline and hypocapnic challenge. In all cases, PI significantly increased while CVR decreased in **a** and increased in **b**

Table 2 Mean values of pressure and haemodynamic parameters found in 31 patients before and during the hypocapnia challenge

Hypocapnia challenge ($n = 31$)			
Parameters	Baseline	Hypocapnia	p value
$PaCO_2$	5.10 ± 0.35	4.40 ± 0.34†	<0.001
ICP (mmHg)	16.59 ± 6.68	12.73 ± 6.25†	<0.001
CPP (mmHg)	80.02 ± 9.57	85.39 ± 12.08*	0.0023
FV_m (cm/s)	77.22 ± 26.33	58.99 ± 17.43†	<0.001
*i*1 (mmHg)	1.92 ± 1.63	1.37 ± 1.48†	<0.001
*f*1 (cm/s)	23.58 ± 10.45	19.22 ± 8.08†	<0.001
*a*1 (mmHg)	20.34 ± 5.09	20.86 ± 5.98	0.432 (NS)
ABP (mmHg)	96.62 ± 9.99	98.13 ± 12.65	0.339 (NS)
HR (cycles/min)	78.58 ± 16.64	78.75 ± 15.74	0.850 (NS)
FV_s (cm/s)	129.26 ± 41.03	103.94 ± 28.68†	<0.001
FV_d (cm/s)	47.86 ± 17.68	35.29 ± 11.03†	<0.001
PI	1.09 ± 0.24	1.20 ± 0.27†	<0.001
CVR [mmHg/(cm/s)]	1.17 ± 0.45	1.57 ± 0.52†	<0.001

Values are expressed as the mean ± SD. Significant levels of the differences between change in parameters before and during the hypocapnia challenge are given (paired t test)

a1 pulse amplitude (first harmonic) of ABP, *ABP* arterial blood pressure, *CPP* cerebral perfusion pressure, *CVR* cerebrovascular resistance, *f1* pulse amplitude (first harmonic) of blood FV, FV_m mean blood FV in the MCA, FV_d diastolic blood FV in the MCA, FV_s systolic blood FV in the MCA, *i1* pulse amplitude (first harmonic) of intracranial pressure, *ICP* intracranial pressure, *HR* heart rate, *NS* not significant, $PaCO_2$ carbon dioxide arterial partial pressure, *PI* Gosling pulsatility index

* $p < 0.05$. † $p < 0.01$

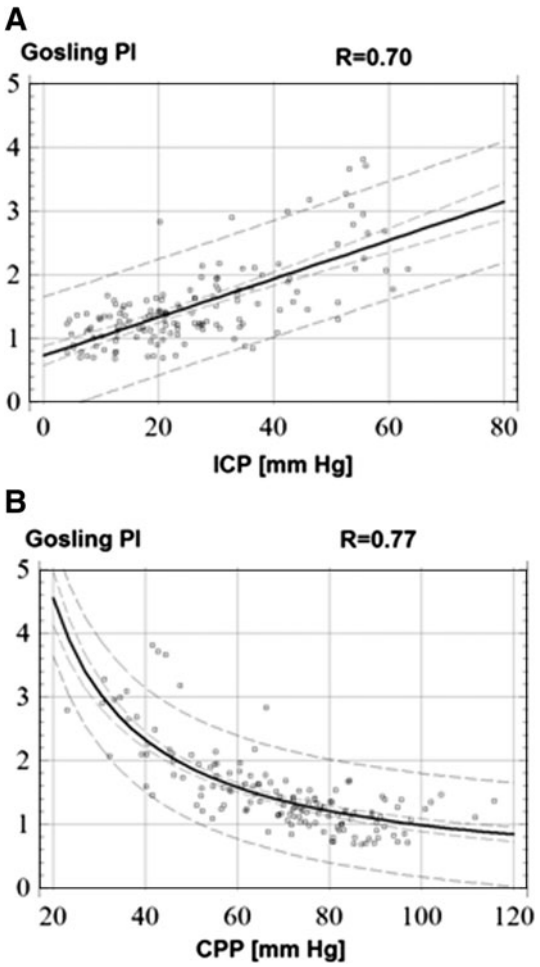

Fig. 3 The relationship between PI and **a** intracranial pressure (ICP) and **b** cerebral perfusion pressure (CPP). Combined data from recordings of plateau waves and hypocapnic challenge are presented. *Dashed lines* indicate 95% confidence limits for mean (inner) and 95% confidence limits for prediction (outer)

Gosling PI and the modeled PI (mPI) using the formula expressed in (1) is high ($R = 0.81$). This correlation improved further ($r = 0.95$) when PI was calculated by using the fundamental harmonic of FV (i.e., "spectral" PI) instead of the FV peak-to-peak pulse amplitude (Fig. 4a, b).

For confirmation of the obtained results the correlations between the mPI with the Gosling PI and the "spectral" PI were analyzed using our whole head-injury database ($n = 345$), achieving comparable average fit (Fig. 4c).

Discussion

The TCD-based pulsatility index is often interpreted as a descriptor of the distal cerebrovascular resistance [9]. However, our study suggests that this concept should be viewed with caution. We have analyzed two clinical situations, plateau waves, and hypocapnia, where opposite changes in CVR are observed. During plateau waves vasodilatation leads to decrease in CVR, increase in cerebral blood volume (CBV) and increase in ICP. During hypocapnia vascular constriction leads to an increase in CVR, decrease in CBV, and slight decrease in ICP. Despite opposite changes in CVR we observed that PI in both cases increased, reinforcing the concept that PI cannot be interpreted as an index of CVR alone. Also, in both situations ICP changed inversely (i.e., dramatically increased during plateau waves and slightly decreased during hypocapnia), therefore universal description of rising ICP by rising PI is also questionable.

We have demonstrated by using a mathematical model of cerebrovascular impedance the possible input signals determining the reactions of PI. Analysis of the model suggests that PI is determined by the interplay of the value of CPP, the fundamental harmonic of ABP pulse (*a*1), CVR, compliance of the cerebral arterial bed (Ca), and heart rate.

Plateau waves are defined as any sudden elevation of ICP above 50 mmHg that lasts longer than 5 min and

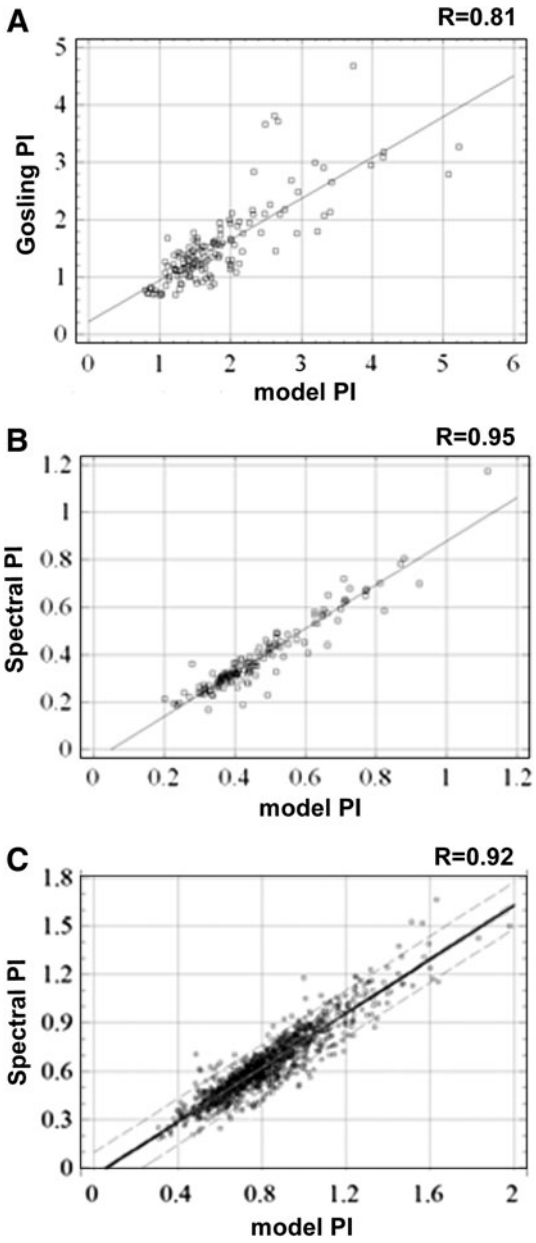

Fig. 4 Scatter plots of the relationship between Gosling PI and the modeled PI calculated using a mathematical model (1). **a** Strong relationship between the predicted Gosling PI and a real Gosling PI and **b** predicted and real "spectral" PI is seen ($R = 0.81$ and $R = 0.95$, respectively). **c** The relationship between "spectral" PI and modeled PI when applied to the whole head-injury database ($N = 345$; $R = 0.92$)

terminates spontaneously or in response to treatment. They are thought to be caused by a vasodilatory cascade, which may be triggered by a sudden decrease in CPP in the presence of functioning cerebral autoregulation [11, 17]. During plateau waves the profound reduction in CPP is accompanied by a decreased cerebral blood flow [15]. On the other hand, the vasodilatation leads to an increase in CBV, which is associated with an increase in cerebral arterial compliance (Ca) [14]. As the pulse amplitude of ABP ($a1$) remains fairly stable, during plateau waves PI changes inversely to the changes in CPP. Most probably, changes in both Ca and CVR balance each other therefore none of them play a major role in determining PI.

The second group involves patients submitted to short term hypocapnia to assess CO_2 reactivity. Based on the available evidence, the most recent "Guidelines for the management and prognosis of severe traumatic brain injury" still include moderate manipulation of the arterial partial pressure of CO_2 ($PaCO_2$) as an option to treat raised ICP [18]. The beneficial effect of hyperventilation is due to a reduction in CBV, through vasoconstriction [19]. Therefore, the observed increase in CVR was expected in this group of patients. It has been already shown that changes in CVR are stronger than changes in Ca during controlled changes of $PaCO_2$ in an experimental setup [20]. Most likely, a similar situation exists during hypocapnia in clinical conditions, therefore the observed increase in PI follows an increase in the product of CVR and Ca combined with a slight decrease in CPP.

According to the described mathematical model (1) (please see "Appendix") PI is a complex function of many mutually interdependent hemodynamic parameters. PI increases when the amplitude of ABP ($a1$) increases as well as during arterial hypotension and intracranial hypertension through changes in CPP. PI also increases when the product of CVR, Ca, and HR increases [14, 21], which has not been studied thoroughly before. Theoretically, the product of CVR and Ca expresses the time constant of the cerebral arterial bed [21]. The longer this time constant, the longer the time interval which is needed for arterial blood volume to arrive (from the point of TCD insonation) at the cerebral resistive vessels. In the experimental study mentioned above [21], the time constant has been shown to increase with hypocapnia and with reductions in cerebral perfusion pressure (caused by both arterial hypotension and rise in ICP). Similarly the PI in these scenarios will increase.

There are several limitations of this study. First, the sides of TCD insonation and of the ICP probe were not standardized. Although in most of the cases the ICP probe was placed in the right anterior frontal lobe, the side of the analyzed TCD signal depended on the qualities of both the insonated window and the recording. However, we cannot exclude that our data might have been more reliable if it had been based on the average of bilateral TCD readings. Neither can we exclude the influence in cases with unilateral lesions.

Limitations of the method used to calculate CaBV, Ca, and CVR from pulsatile waveforms of FV and ABP for the calculation of the cerebrovascular time constant have been discussed in previous publications [14, 22]. Monitoring the changes in cerebrovascular compliance is difficult to obtain

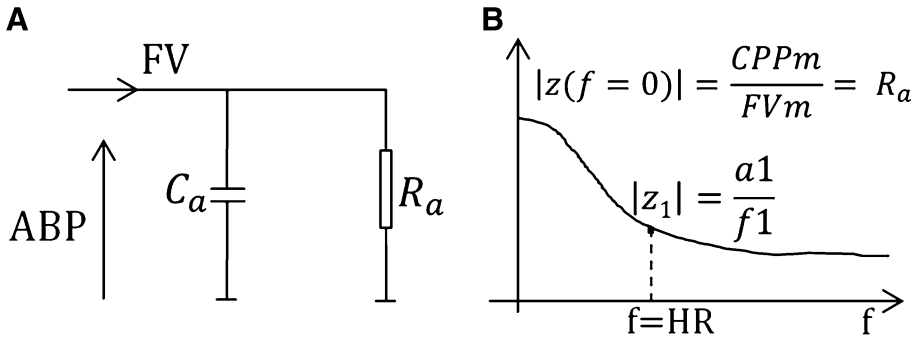

Fig. 5 Simplified input circuit used for the derivation of the formula (4) describing PI (calculated for fixed frequency of heart rate). **a** Input circuit representing a model of cerebral circulation. **b** Diagram of cerebrovascular impedance |Z(f)| as a function of frequency. Two frequencies are considered: $f = 0$ (i.e., DC component) and $f =$ HR. Module of impedance for $f = 0$ is equal to R_a, and may be estimated as CPPm/FV_m. *a1* pulse amplitude (first harmonic) of ABP, *ABP* arterial blood pressure, C_a cerebrovascular compliance, *CPPm* mean cerebral perfusion pressure, *f* frequency, *f1* pulse amplitude (first harmonic) of blood FV, FV_m mean blood flow velocity in the middle cerebral artery, *HR* heart rate, *PI* Gosling pulsatility index, R_a cerebrovascular resistance (in the main part of manuscript expressed as CVR), |z| cerebrovascular impedance, $|z_1|$ cerebrovascular impedance with frequency equal to HR

absolute measures, which requires the application of phase-contrast MRI [23, 24]. Recently Kim et al. developed a computational method allowing a continuous assessment of relative changes in cerebral compartmental compliances based on the relationship between pulsatile components of ABP, ICP, and the cerebral arterial blood volume (CaBV) [14]. This method is estimation only; it does not allow assessing absolute values of Ca but only its relative changes.

In the past another mathematical model was proposed, linking TCD pulsatility index and critical closing pressure [25]. But these formulas differ as the one we present links PI with physiological model parameters.

Conclusion

A mathematical formula describing PI is proposed and it shows a good correlation with the measured values of PI, and hence it is able to explain the major factors influencing PI. The pulsatility index is not dependent solely on CVR but it is a product of the interplay between CPP, pulse amplitude of arterial pressure, cerebrovascular resistance and compliance of the cerebral arterial bed as well as the HR. PI is not an accurate estimator of ICP; it describes CPP in a more accurate manner.

Acknowledgment This study was supported by the National Institute of Health Research, Biomedical Research Centre (Neuroscience Theme), the Medical Research Council (Grants G0600986 and G9439390), and NIHR Senior Investigator Awards (JDP); the Hospital Clinic Grant, Barcelona, Spain (NR) and also by the Swiss National Science Foundation (PBBSP3-125550 to CZ), Bern, Switzerland.

Disclosures ICM+ Software is licensed by Cambridge Enterprise, Cambridge, UK, http://www.neurosurg.cam.ac.uk/icmplus/. MC and PS have a financial interest in a fraction of the licensing fee.

Appendix

Mathematical Methods

The input circuit to cerebrovascular space (Fig. 5) can be reduced to cerebrovascular resistance (R_a) and compliance (Ca) of arteries. Under the assumption that input pressure is low, and systolic–diastolic distance is totally contained within the range of autoregulation, the system may be treated as semi-linear.

The pulsatility of the flow (PI), described as the ratio of the fundamental amplitude of the FV waveform divided by mean FV (1)

$$\mathrm{PI} = \frac{\mathrm{f1}}{\mathrm{FV_m}} = \frac{a1}{\mathrm{CPP_m}} \times \left|\frac{\mathrm{z(0)}}{\mathrm{z(HR)}}\right| \qquad \left|\begin{array}{l} \mathrm{f1} = \dfrac{a1}{|\mathrm{Z(HR)}|} \\ \mathrm{FV_m} = \dfrac{\mathrm{CPP_m}}{|\mathrm{Z(0)}|} \end{array}\right. \qquad (1)$$

where $f1$ is the fundamental harmonic of FV, $\mathrm{FV_m}$ is the mean FV, $a1$ is the fundamental harmonic of arterial pulse pressure, $\mathrm{CPP_m}$ is the mean cerebral perfusion pressure, |z(0)| is the cerebrovascular impedance at zero frequency, |z(HR)| is the cerebrovascular impedance at frequency equal to heart rate.

Cerebrovascular impedance ($Z(j\omega)$) can be described as a complex function of frequency (2).

$$z(j\omega) = \frac{\frac{R_a}{j\omega Ca}}{R_a + \frac{1}{j\omega Ca}} = \frac{R_a}{j\omega R_a Ca + 1} \quad (2)$$

where ω is the $2\pi f$, j is the imaginary unit, R_a is the cerebrovascular resistance, Ca is the compliance of arteries and arterioles.

Z(f)| is described in (3)

$$|z(j\omega)| = \frac{R_a}{\sqrt{R_a^2 Ca^2 \omega^2 + 1}} \quad (3)$$

where R_a is the cerebrovascular resistance, Ca is the compliance of arteries and arterioles.

From here we can derive formula describing the pulsatility index:

$$PI = \frac{a1}{CPP_m} \times \sqrt{(R_a Ca)^2 HR^2 (2\pi)^2 + 1} \quad (4)$$

where PI is the pulsatility index (for fundamental component of HR), $a1$ is the pulse amplitude (first harmonic) of ABP, CPP_m is the mean cerebral perfusion pressure, R_a is the cerebrovascular resistance, Ca is the compliance of arteries and arterioles, HR is the heart rate.

For the Gosling pulsatility index (PI) $a1$ should be substituted by the peak-to-peak amplitude of the ABP pulse. Also, Ca should be derived in a far more complex way, taking into account all harmonics of the ABP pulse and modules of impedances at these frequencies. But the general description of TCD pulsatility as a function of cerebral haemodynamic parameters remains the same.

References

1. Kontos HA. Validity of cerebral arterial blood flow calculations from velocity measurements. Stroke. 1989;20(1):1–3.
2. Gosling RG, King DH. Arterial assessment by Doppler-shift ultrasound. Proc R Soc Med. 1974;67(6 Pt 1):447–9.
3. Bellner J, Romner B, Reinstrup P, Kristiansson KA, Ryding E, Brandt L. Transcranial Doppler sonography pulsatility index (PI) reflects intracranial pressure (ICP). Surg Neurol. 2004;62(1):45–51.
4. Behrens A, Lenfeldt N, Ambarki K, Malm J, Eklund A, Koskinen LO. Transcranial Doppler pulsatility index: not an accurate method to assess intracranial pressure. Neurosurgery. 2010;66(6):1050–7.
5. Figaji AA, Zwane E, Fieggen AG, Siesjo P, Peter JC. Transcranial Doppler pulsatility index is not a reliable indicator of intracranial pressure in children with severe traumatic brain injury. Surg Neurol. 2009;72(4):389–94.
6. Melo JR, Di Rocco F, Blanot S, et al. Transcranial Doppler can predict intracranial hypertension in children with severe traumatic brain injuries. Childs Nerv Syst. 2011;27(6):979–84.
7. Soehle M, Chatfield DA, Czosnyka M, Kirkpatrick PJ. Predictive value of initial clinical status, intracranial pressure and transcranial Doppler pulsatility after subarachnoid haemorrhage. Acta Neurochir (Wien). 2007;149(6):575–83.
8. Giller CA, Hodges K, Batjer HH. Transcranial Doppler pulsatility in vasodilation and stenosis. J Neurosurg. 1990;72(6):901–6.
9. Lim MH, Cho YI, Jeong SK. Homocysteine and pulsatility index of cerebral arteries. Stroke. 2009;40(10):3216–20.
10. Czosnyka M, Richards HK, Whitehouse HE, Pickard JD. Relationship between transcranial Doppler-determined pulsatility index and cerebrovascular resistance: an experimental study. J Neurosurg. 1996;84(1):79–84.
11. Rosner MJ, Becker DP. Origin and evolution of plateau waves. Experimental observations and a theoretical model. J Neurosurg. 1984;60(2):312–24.
12. Steiner LA, Balestreri M, Johnston AJ, et al. Sustained moderate reductions in arterial CO2 after brain trauma time-course of cerebral blood flow velocity and intracranial pressure. Intensive Care Med. 2004;30(12):2180–7.
13. Hsu HY, Chern CM, Kuo JS, Kuo TB, Chen YT, Hu HH. Correlations among critical closing pressure, pulsatility index and cerebrovascular resistance. Ultrasound Med Biol. 2004;30(10):1329–35.
14. Kim DJ, Kasprowicz M, Carrera E, et al. The monitoring of relative changes in compartmental compliances of brain. Physiol Meas. 2009;30(7):647–59.
15. Czosnyka M, Smielewski P, Piechnik S, et al. Hemodynamic characterization of intracranial pressure plateau waves in head-injury patients. J Neurosurg. 1999;91(1):11–9.
16. Helmy A, Vizcaychipi M, Gupta AK. Traumatic brain injury: intensive care management. Br J Anaesth. 2007;99(1):32–42.
17. Lundberg N. Continuous recording and control of ventricular fluid pressure in neurosurgical practice. Acta Psychiatr Scand Suppl. 1960;36(149):1–193.
18. Brain Trauma F, American Association of Neurological Surgeon, Congress of Neurological Surgeons, et al. Guidelines for the management of severe traumatic brain injury. XIV. Hyperventilation. J Neurotrauma 2007; 24 Suppl 1:S87–S90.
19. Raichle ME, Posner JB, Plum F. Cerebral blood flow during and after hyperventilation. Arch Neurol. 1970;23(5):394–403.
20. Czosnyka M, Richards HK, Reinhard M, et al. Cerebrovascular time constant: dependence on cerebral perfusion pressure and end-tidal carbon dioxide concentration. Neurol Res. 2012;34(1):17–24.
21. Czosnyka M, Piechnik S, Richards HK, Kirkpatrick P, Smielewski P, Pickard JD. Contribution of mathematical modelling to the interpretation of bedside tests of cerebrovascular autoregulation. J Neurol Neurosurg Psychiatry. 1997;63(6):721–31.
22. Carrera E, Steiner LA, Castellani G, et al. Changes in cerebral compartmental compliances during mild hypocapnia in patients with traumatic brain injury. J Neurotrauma. 2011;28(6):889–96.
23. Alperin N, Sivaramakrishnan A, Lichtor T. Magnetic resonance imaging-based measurements of cerebrospinal fluid and blood flow as indicators of intracranial compliance in patients with Chiari malformation. J Neurosurg. 2005;103(1):46–52.
24. Baledent O, Fin L, Khuoy L, et al. Brain hydrodynamics study by phase-contrast magnetic resonance imaging and transcranial color doppler. J Magn Reson Imaging. 2006;24(5):995–1004.
25. Michel E, Zernikow B. Goslig's Doppler pulsatility index revisited. Ultrasound Med Biol. 1998;24(4):597–9.