Brain pulsations enlightened

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Scientists in the 1970s, or even earlier, initiated studies on the pulsatile component of intracranial pressure (ICP), suggesting that its possible origin was a pulsation of cerebral blood volume [19]. With a magnetic flow-meter, Avezaat and Eijndhoven [5] first attempted to quantify pulsations of cerebral blood volume (CBV) in an experimental setup. Later, transcranial Doppler ultrasonography (TCD) [13] alongside phase-contrast MRI (PCMRI) [2, 8] was utilized. It is worthwhile to emphasize that MRI is far more precise than TCD, as it takes into account all three fast components of cerebral volume: arterial blood, venous blood, and CSF oscillations. On the other hand, unlike TCD, MRI cannot be used by the bedside, cannot monitor changes in CBV over longer time (it is rather a snapshot), and is far more expensive.

Theoretically, the change in ICP is equal to the cerebral volume change multiplied by the intracranial elastance [5, 19]. Total cerebral volume (CV; blood plus CSF) can change (slightly; against golden rule sealed in the Monro-Kellie Doctrine) in few seconds during plateau waves of ICP, hyperventilation, reactions to vasoactive drugs, etc. But CV also changes continuously during each heart cycle, as the arterial blood pulsations prevail over venous pulsatile outflow, and additionally because intracranial CSF oscillations through the spinal canal do not completely balance intracranial blood volume changes [1]. The ICP pulse waveform is highly variable and can be directly measured by an invasive

pressure sensor. ICP pulse amplitude is a function of physiological body position, blood circulation, and respiratory movement which also modifies the CSF and blood flows [14]. Moreover, ICP pulse amplitude is affected in many brain diseases; therefore, its role is appreciated in hydrocephalus [15, 17], traumatic brain injury [4, 16], subarachnoid hemorrhage, and many other diseases. The ICP signal over time is comprised of components of low and high frequencies. In the short time window of a cardiac cycle, the ICP pulse wave is shaped by three main peaks: P1, P2, and P3 [13]. The ratio of P1 to P2 has been suggested to be proportional to brain compliance. Previous works have shown that the shape of ICP is a signature of the interactions between arterial, venous, and CSF void flow modified by intracranial elasticity [6]. For example, a simple time delay of the intracranial venous flush can induce an increase in the intracranial volume change during one cardiac cycle [7], therefore increasing the pulse amplitude of ICP.

Here, we have a good opportunity to provide a short synopsis of the applications of ICP pulse amplitude studied in specific clinical scenarios:

- Excessive ICP pulse amplitude is a marker of probable improvement after shunting in normal pressure hydrocephalus [15].
- Pulse amplitude plotted against diastolic (and also mean) ICP during infusion testing usually shows a straight line. If its slope is above 0.3 or 0.5, an improvement after shunting in hydrocephalus is almost certain [3].
- The shape of the pulse waveform correlates with cerebral blood flow after head injury [16].
- The “high frequency centroid” [20] of the ICP pulse waveform correlates with fatal outcome after TBI.
- The correlation coefficient between slow changes of amplitude and mean ICP (RAP index) shows where on the pressure-volume (P-V) curve that the “working point” lies. RAP = 0 indicates good compensatory

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reserve (the linear part of the P-V curve at low ICP), whereas RAP close to +1 shows poor compensatory reserve (the exponential part of the P-V curve) [17].

- Negative RAP at ICP > 25 mmHg indicates the critical closing of cerebral arterioles due to intracranial hypertension [12].
- The correlation coefficient between slow waves of arterial blood pressure and the pulse amplitude of ICP (the so-called PAX index) provides information about the autoregulation of CBF, and is an alternative to PRx, the pressure-reactivity index [4].

Conversely, most sound findings about pulsatile CSF flow can be summarized as below:

- Brain and CSF movements are influenced by the anatomy and mechanical properties of intracranial tissues, as well as by the waveforms of driving vascular pulsations [1, 2]
- CSF flow waveforms are sensitive to alterations in the cranial venous outflow. [10]
- Patients with NPH showed lower pulsations in the superior sagittal sinus than healthy subjects [9]
- Venous vessel compression and/or changes in intracranial subarachnoid CSF flow produce an increase in ventricular CSF flush that compensates for vascular brain expansion in patients with cerebral hemorrhage. [7]
- Patients presenting with clinical normal pressure hydrocephalus who have hyper dynamic CSF flow have been found to respond better to ventriculoperitoneal shunting than those with normal or decreased CSF flow. [11]. However, controversies about this point exist. Among patients who were shunted, measurement of CSF flow through the cerebral aqueduct did not reliably predict which patients would improve clinically [18].

PCMRI is a tool uniquely able to reconstruct CSF and intracranial blood flows [8]. In freshly printed paper [22] about comparison of ICP pulse, PCMRI [22] is not acquired in real-time. PCMRI reconstructs a mean period from many cycles over a few minutes of acquisition time. It is not possible to directly compare intracerebral volume with the real-time ICP pulses.

PCMRI accuracy could be a point of discussion because of small pulsatile changes in intracranial net volume, smaller than 1 ml. Nevertheless, in the literature for many years, others authors have already published volumetric changes in the same range of small volumes [8]. In the discussed paper [22], we don't have all of the information describing the total post-processing, which is an important potential source of error. It is also frustrating not to have access to the mean cerebral blood flows, the venous corrections parameters [21], and the CSF stroke volumes, all of which are important parameters playing a role in the dynamics of the system

investigated [8]. Is intracranial blood volume change related to the intracranial CSF volume change? In the same way, temporal organization of the arterial, venous, and CSF flows peaking along the cardiac cycle could also be source of interest in front of P1, P2, and P3 peaks.

Nevertheless, the paper presented by Unnerback et al. [22] is the first one to try to approach PCMRI and ICP measurements simultaneously, following a linear trajectory towards understanding and investigating the complex mechanism describing the origin of ICP. With this new kind of approach, the combination of ICP monitoring with intracranial blood and CSF volume dynamics in physiological behavior or in stress situations (as during infusion tests), knowledge of pathophysiology should increase in the near future.

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