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ORIGINAL ARTICLE

Cerebral Vascular Changes During Acute Intracranial Pressure Drop

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Abstract

Objective: This study applied a new external ventricular catheter, which allows intracranial pressure (ICP) monitoring and cerebral spinal fluid (CSF) drainage simultaneously, to study cerebral vascular responses during acute CSF drainage.

Methods: Six patients with 34 external ventricular drain (EVD) opening sessions were retrospectively analyzed. A published algorithm was used to extract morphological features of ICP recordings, and a template-matching algorithm was applied to calculate the likelihood of cerebral vasodilation index (VDI) and cerebral vasoconstriction index (VCI) based on the changes of ICP waveforms during CSF drainage. Power change (ΔP) of ICP B-waves after EVD opening was also calculated. Cerebral autoregulation (CA) was assessed through phase difference between arterial blood pressure (ABP) and ICP using a previously published wavelet-based algorithm.

Results: The result showed that acute CSF drainage reduced mean ICP ($P=0.016$) increased VCI ($P=0.02$) and reduced ICP B-wave power ($P=0.016$) significantly. VCI reacted to ICP changes negatively when ICP was between 10 and 25 mmHg, and VCI remained unchanged when ICP was outside the 10–25 mmHg range. VCI negatively ($r=-0.44$) and VDI positively ($r=0.82$) correlated with ΔP of ICP B-waves, indicating that stronger vasoconstriction resulted in bigger power drop in ICP B-waves. Better CA prior to EVD opening triggered bigger drop in the power of ICP B-waves ($r=-0.612$).

Conclusions: This study demonstrates that acute CSF drainage reduces mean ICP, and results in vasoconstriction which can be detected through an index, VCI. Cerebral vessels actively respond to ICP changes or cerebral perfusion pressure (CPP) changes in a certain range; beyond which, the vessels are insensitive to the changes in ICP and CPP.

Keywords: Cerebral autoregulation, Cerebrospinal fluid drainage, Cerebral vascular changes, Intracranial pressure waveform, ICP B-waves

Introduction

Measurement of intracranial pressure (ICP) is used to guide targeted therapy of acute brain injury during a patient's stay in a neurological intensive care unit (NICU) [1–6]. External ventricular drain (EVD) remains the gold standard for both monitoring ICP and diverting cerebrospinal fluid (CSF) from the ventricles in clinical situations requiring the management of acute hydrocephalus

or temporary CSF drainage [7–9]. Several studies have critically examined the effect of ventriculostomy drainage on elevated ICP [10–13]. It has been proved that CSF drainage significantly reduced ICP and increased cerebral perfusion pressure (CPP) in traumatic brain injury (TBI) patients [10, 14, 15]. However, how cerebral vessels respond to acute CSF drainage still remains unknown, partly due to the inability of conventional EVD to simultaneously detect ICP waveforms during CSF drainage [7, 16], and partly due to the fact that we lack an efficient tool to evaluate cerebral vascular changes continuously. To tackle the first problem, a novel Integra® Camino®

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FLEX Ventricular Catheter (Integra Lifesciences, County Offaly, Ireland) has been introduced into the market recently [17]. This double-lumen catheter uses one lumen to divert CSF and the other to embed a pressure sensor at the tip to obtain ICP pulse waveforms, thus enabling continuous ICP monitoring even when EVD is open [18–20]. The FLEX catheter could provide a unique opportunity to derive clinically meaningful information even during CSF drainage. Regarding the second issue (i.e., we need an efficient tool to evaluate cerebral vascular changes), a few studies tried to evaluate vascular changes via changes in cerebral arterial blood flow (CBF). The results were inconsistent, with some studies showing significant increase in CBF velocity [21], while others did not find obvious changes in CBF velocity after CSF drainage [10].

Introduced by Hu et al. in 2009, a modern signal processing algorithm, morphological clustering and analysis of intracranial pulse (MOCAIP) algorithm has been proved an effective tool for ICP waveform detection in brain injury patients [18–20, 22–24]. The MOCAIP algorithm allows a comprehensive quantitative characterization of ICP pulse morphology, including pulse amplitude, time intervals among subpeaks, curvature, slope, and decay time constants through 128 pulse morphological metrics (shown in Supplementary Fig. 1). Based on MOCAIP algorithm, the same group applied a template-matching algorithm [19] to estimate the likelihood of cerebral vasodilation index (VDI) and cerebral vasoconstriction index (VCI) based on the changes in ICP waveforms extracted by MOCAIP [18, 19]. In the present study, we applied this method to evaluate cerebral vascular changes during acute CSF drainage through ICP recordings detected by the new FLEX catheter.

Moreover, we hypothesize that cerebral autoregulation (CA) is a potential triggering mechanism that causes cerebral vascular responses to acute CSF drainage. With intact CA, a decrease in ICP leads to an increase in CPP which may subsequently cause VCI [24–26]. Therefore, an investigation of how the cerebral arterial bed responds to acute CSF diversion is important not only for understanding physiological relevance but also because of its practical implication as a potential status indicator of CA [27]. A robust metric of CA, the wavelet phase difference between ICP and arterial blood pressure (ABP) [28–30] was used to quantify the status of CA. This approach has been validated with a more established metric—pressure reactivity index (PRx), and is proved to be more robust with less variations [28]. Moreover, since the presence of ICP slow waves or B-waves (0.33 to 3 cycles per minute) reflects vasogenic activity of CA [31–33], we also studied the power changes in ICP slow waves during acute CSF drainage.

Materials and Methods

Patients and Data Collection

The data analyzed in this study were collected from adult patients admitted to University of California, Los Angeles Medical Center (UCLA, Los Angeles, CA, USA) during a period of evaluating Integra® Camino® FLEX Ventricular Catheter (Integra Lifesciences, County Offaly, Ireland) between February and April, 2016. Three patients with severe TBI, two patients with aneurysmal subarachnoid hemorrhage, and one patient with intraventricular hemorrhage were enrolled in the study. Continuous ICP was detected through the FLEX catheter. The continuous ICP, ABP (3 of 6 patients) and electrocardiograph signals were obtained from bedside monitor (GE Solaris 8000) through BedMaster™ (Excel Medical, Jupiter, Florida, USA) system at a sampling rate of 240 Hz. The institutional review board approved the data analysis and waived the need for consenting patients because of the retrospective nature of the study. The decision to use FLEX catheters was clinically based without considering the needs of this study.

We retrospectively reviewed ICP recordings from each patient and selected the episodes associated with acute CSF drainage that caused ICP reduction (34 episodes in total from the 6 subjects). For each episode, we identified timing of EVD opening (t_0) and closure (t_1). A during-drainage segment is defined as the segment, while EVD is open to drainage, that is from t_0 to t_1 (Fig. 1a). A pre-drain segment is a segment of ICP prior to EVD open. A post-drainage segment is defined as the segment after EVD is closed again.

Data Analysis

Morphological Clustering and Analysis of Intracranial Pulse (MOCAIP)

MOCAIP algorithm was developed and validated in many of our previous publications [18–20, 34]. Briefly, this algorithm analyzes a segment of ICP signal to identify each cardiac pulse, clusters them, and forms an average pulse per each cluster. The average pulse of the biggest cluster is termed the dominant ICP pulse for the segment. The dominant pulse is further compared to validated ICP pulses in a pre-built ICP pulse library to determine if this pulse is legitimate. The morphology of a legitimate dominant pulse is further quantified using 128 systematically derived metrics based on an optimal designation of three subpeaks and the corresponding three valley points of a typical triphasic ICP pulse. The details of the algorithm should be referred to our published work [18]. What is relevant in this study is the ability of MOCAIP algorithm to provide a quantitative

Fig. 1 **a** An ICP recording of a traumatic brain injury patient through the Integra® Camino® FLEX Ventricular Catheter. The during-drainage segment refers to segment between $[t_0, t_1]$ sec, the pre-drainage segment is a segment of ICP prior to EVD open, and the post-drainage segment refers to the section after EVD is closed again. **b** An example of mean ICP, ABP, VCI, VDI, and ABP-ICP phase difference of one recording episode. Vertical lines correspond to EVD opening and closure, respectively. The three small charts in the upper panel represent dominant ICP pulses at pre-drainage (8 dominant pulses that were selected as baseline pulses to be compared to for VCI and VDI calculation), during-drainage, and post-drainage segments. *ABP* arterial blood pressure, *ICP* intracranial pressure, *VCI* vasoconstriction index, *VDI* vasodilation index, *EVD* external ventricular drains

characterization of ICP pulse waveform in terms of 128 MOCAIP metrics as illustrated in Supplemental Table 1 and Supplemental Fig. 1.

Vasodilation and Vasoconstriction Index

We showed in a previous study that the cerebral vascular changes are reflected in morphological changes in ICP pulses [20]. In a carbon dioxide (CO_2) challenge experiment published previously [19], the authors identified 72 consistent MOCAIP metrics related to cerebral vasodilation and constriction, which were saved as a template of expected characteristic ICP pulse morphological changes

during cerebral vascular changes. In this study, we compared the changes in MOCAIP metrics of ICP between baseline and CSF drainage, and match them with the template defined above to detect whether the cerebral vasculature is in a vasodilatory, a vasoconstrictive, or a neutral state. Specifically, a VDI can be calculated as

$$VDI = \frac{N((S_+ \cap T_+^D) \cap (T_+^D \cap T_-^C)) + N((S_- \cap T_-^D) \cap (T_-^D \cap T_+^C))}{N(T_+^D \cap T_-^C) + N(T_-^D \cap T_+^C)} \quad (1)$$

In a similar way, VCI can be calculated as

Table 1 Mean values of different parameters pre- and during-EVD drainage session

	Patient #1	Patient #2	Patient #3	Patient #4	Patient #5	Patient #6
Age	38	22	25	40	75	47
Diagnosis	TBI	TBI	TBI	aSAH	IVH	IVH
Gender	M	F	M	F	M	F
No. of segments	5	9	2	5	12	1
Pre-drainage ICP	15.81 ± 3.28	14.75 ± 1.04	20.30 ± 1.54	16.03 ± 1.56	15.83 ± 4.46	14.09
During-drainage ICP	12.21 ± 1.28	9.65 ± 1.89	18.40 ± 2.77	11.10 ± 2.50	11.94 ± 3.49	9.48
Post-drainage ICP	13.31 ± 2.82	13.35 ± 2.83	17.16 ± 0.05	14.17 ± 1.82	12.36 ± 3.06	11.09
Pre-drainage ABP	N/A	90.47 ± 7.45	N/A	149.70 ± 2.50	N/A	112.58
During-drainage ABP	N/A	89.84 ± 7.87	N/A	150.0 ± 2.69	N/A	113.77
Post-drainage ABP	N/A	92.69 ± 8.71	N/A	147.8 ± 2.74	N/A	115.39
Pre-drainage VCI	0.51 ± 0.06	0.44 ± 0.08	0.18 ± 0.20	0.46 ± 0.03	0.48 ± 0.05	0.54
During-drainage VCI	0.59 ± 0.04	0.49 ± 0.12	0.23 ± 0.20	0.59 ± 0.03	0.56 ± 0.08	0.68
Post-drainage VCI	0.57 ± 0.07	0.51 ± 0.11	0.24 ± 0.24	0.48 ± 0.03	0.52 ± 0.08	0.67
Pre-drainage VDI	0.44 ± 0.05	0.40 ± 0.08	0.22 ± 0.18	0.49 ± 0.03	0.47 ± 0.06	0.41
During-drainage VDI	0.36 ± 0.02	0.29 ± 0.10	0.19 ± 0.21	0.37 ± 0.03	0.40 ± 0.07	0.31
Post-drainage VDI	0.38 ± 0.05	0.33 ± 0.08	0.14 ± 0.13	0.47 ± 0.03	0.43 ± 0.08	0.32
Pre-drainage phase	N/A	93.05 ± 20.99	N/A	79.63 ± 21.86	N/A	92.85
During-drainage phase	N/A	85.02 ± 24.78	N/A	80.45 ± 25.61	N/A	93.12
Post-drainage phase	N/A	98.04 ± 21.57	N/A	70.47 ± 24.37	N/A	63.34
Pre-drainage power of B-wave	505.86 ± 30.02	579.08 ± 89.27	460.04 ± 88.08	459.16 ± 65.60	711.35 ± 316.12	667.53
During-drainage ICP power of B-wave	405.66 ± 100.54	476.92 ± 110.51	446.10 ± 77.05	439.31 ± 62.80	652.08 ± 243.71	496.32
Post-drainage ICP power of B-wave	537.4 ± 181.87	741.06 ± 205.48	461.23 ± 195.27	805.60 ± 94.28	1197.94 ± 520.22	615.37

Average ± SD. ABP arterial blood pressure, aSAH aneurysmal subarachnoid hemorrhage, EVD external ventricular drain, ICP intracranial pressure, IVH intraventricular hemorrhage, TBI traumatic brain injury, VCI vasoconstriction index, VDI vasodilation index

$$VCI = \frac{N((S_+ \cap T_+^C) \cap (T_+^C \cap T_-^D)) + N((S_- \cap T_-^C) \cap (T_-^C \cap T_+^D))}{N(T_+^D \cap T_-^C) + N(T_-^D \cap T_+^C)} \quad (2)$$

where S_+ denotes a set of MOCAIP metrics showing positive change from baseline, S_- a set of MOCAIP metrics showing negative change from the baseline, T_+^C (T_-^C) a set of MOCAIP metrics in the template showing positive (negative) changes during a cerebral vasoconstriction phase, and T_+^D (T_-^D) a set of MOCAIP metrics in the template showing positive (negative) changes during a cerebral vasodilation phase. $A \cap B$ refers to the intersection of two sets. It should be noted that the range of VCI and VDI is between 0 and 1.

To calculate VDI and VCI on a pulse-by-pulse basis, one only needs to compare the ICP pulse representing the current time to that recorded at a baseline and determine the direction of MOCAIP metric changes. In the present work, we applied MOCAIP algorithm to analyze and derive a dominant pulse from consecutive 12-second ICP signal segments. Instead of using only one baseline ICP pulse, we randomly selected 8 baseline pulses that

fell within the pre-drainage segment and reported the average VDI/VCI that was derived by comparing each consecutive dominant ICP pulse to the eight baseline ICP pulses. In this way, we smooth out the variations in VDI/VCI that are likely due to respiration.

Cerebral Autoregulation Parameter

Wavelet transform-based phase difference between ABP and ICP, in the low frequency of 0.005–0.08 Hz, was calculated through complex wavelet transform [29, 35–38]. Morlet mother wave was applied to extract the characteristics of ABP/ICP signals. The wavelet phase difference at each scale-frequency point was calculated, and wavelet transform coherence (WTC) was used as an indicator of a reliable phase relationship between input and output. Individual phase difference values with coherence higher than the threshold (decided through Monte Carlo simulations) were kept, while phase difference values with coherence lower than the threshold were deleted. Then, the average value along frequency at each time point was calculated. More details about the algorithm can be found in our previous publication [28].

In brief, the continuous wavelet transform W_n (3) describes the convolution of time series x_n with a Morlet mother wavelet (φ) (4) [39].

$$W_n(s) = \sum_{n'=0}^{N-1} x_{n'} \varphi^* \left[\frac{(n' - n)\delta t}{s} \right] \quad (3)$$

$$\varphi(\eta) = \pi^{-\frac{1}{4}} e^{i w_0 \eta} e^{-\eta^2/2} \quad (4)$$

$$\varphi \left[\frac{(n' - n)\sigma t}{s} \right] = \left(\frac{\delta t}{s} \right)^{\frac{1}{2}} \varphi_0 \left[\frac{(n' - n)\delta t}{s} \right] \quad (5)$$

where φ^* is the complex conjugate of the normalized wavelet function; n is the time series index, and δt is the sampling time s is scale, calculated as

$$f = f_0/s = w_0/2\pi s \quad (6)$$

w_0 is the reference coefficient ($w_0 = 2\pi f_0$), which shifts the balance between frequency resolution and time resolution.

The cross-wavelet transform of two time series x_n and y_n are defined as

$$W^{XY} = W^X W^{Y*} \quad (7)$$

where $*$ denotes complex conjugation. The complex argument $\text{pha}(W_{xy})$ can be interpreted as the instantaneous phase difference between x_n and y_n in time frequency space [35, 40, 41].

WTC is defined as the squared absolute value of the smoothed cross-wavelet spectrum, normalized by the smoothed wavelet power spectrum of the two signals (8)

$$C_n^2(s) = \frac{\left| \langle W_n^{xy}(s) \cdot s^{-1} \rangle \right|^2}{\langle |W_n^{xx}(s)| \cdot s^{-1} \rangle \langle |W_n^{yy}(s)| \cdot s^{-1} \rangle} \quad (8)$$

where W_n^{xx} and W_n^{yy} are the wavelet spectral density functions; W_n^{xy} is the cross-wavelet spectrum; and the angular brackets indicate the smoothing operator [29, 38, 42].

The wavelet threshold was decided through Monte Carlo simulations (10000 simulations) and was used to evaluate the distribution of estimated wavelet coherence values corresponding to two uncorrelated signals. In this study, we applied coherence of 0.48 as the threshold. Additional details can be found in a previous publication showing high wavelet phase shift refers to good CA and low phase shift indicates bad CA [28, 43].

Power Spectrum Analysis to Quantify B-Wave Power Reduction

Power spectra were calculated using multiple taper approach [44, 45] for ICP B-waves (0.005–0.08 Hz) in pre-, during-, and post-drainage section, respectively. The relative power change of ICP B-waves (ΔP) from baseline (pre-drainage) to during-drainage section was calculated.

Statistical Analysis

Statistical analysis was performed using the IBM SPSS Statistics (version 21) software. The Wilcoxon paired t test (one side) was used to analyze the ability of different parameters (VCI, VDI, ABI-ICP phase difference and power of ICP B-wave) in distinguishing low (pre-drainage) and high (during-drainage) CPP states. Results were considered significant with $P < 0.05$. The relationships between baseline CA, the mean VCI (VDI), and relative power changes in ICP B-waves during CSF drainage were studied using Spearman's correlation coefficient (r).

Results

The mean age of the six (three males) patients enrolled in the study was 41.2 ± 19.1 (mean $\pm$ SD) years old. The mean duration of selected EVD open/close recordings was 47.8 ± 9.4 min (25.3 ~ 60.2 min, mean $\pm$ SD). Table 1 shows mean values of ABP, ICP, VDI, VCI, ABP-ICP phase difference and ICP B-wave power pre-, during-, and post-CSF drainage. The Wilcoxon test showed a significant increase in VCI ($P = 0.02$) and significant decrease in VDI ($P = 0.02$), mean ICP ($P = 0.016$), and ICP B-wave power ($P = 0.016$) after EVD opening. Figure 1b displays one example of the parameters we tested in this study with EVD opened for draining CSF at t_0 and then closed at t_1 .

Relationship Between VCI (or VDI) and ICP (or CPP)

To study the vascular changes in response to acute ICP or CPP changes, we created various bins based on median ICP (or median CPP) with a bin width of 5 mmHg. Mean values and standard errors of VCI and VDI falling in each bin were calculated and plotted against the median ICP value (or median CPP) of each bin. The result showed an inverse 'S' curve between ICP and VCI and an 'S' curve between ICP and VDI (Fig. 2a–b). Interestingly, when ICP was between 10 and 25 mmHg, VDI was positively and VCI was negatively correlated with ICP; while outside this ICP range, VDI and VCI were independent from ICP.

VDI started to increase when CPP dropped below 80 mmHg (Fig. 2c), and VCI started to increase when CPP increased above 80 mmHg (Fig. 2d).

Fig. 2 **a** Binned scatter plots of ICP versus VDI; **b** Binned scatter plots of ICP versus VCI; **c** Binned scatter plots of CPP versus VDI; **d** Binned scatter plots of CPP versus VCI. When ICP is between 10 and 25 mmHg, VDI is **(a)** positively and VCI is **(b)** negatively correlated with ICP. Outside this limit, VDI and VCI are insensitive to changes in ICP. **c** VCI increases, while CPP increases above 80 mmHg; **d** VDI increases with the decrease in CPP. ICP intracranial pressure, VCI vasoconstriction index, VDI vasodilation index, CPP cerebral perfusion pressure, ABP arterial blood pressure. Error bar standard error

Optimal Cerebral Perfusion Pressure

Previous publications already defined optimal CPP as the CPP level where the best CA is achieved by plotting CA parameters (such as PRx, wavelet phase difference) against CPP [28, 46]. In the present study, we created various bins based on median CPP with a bin width of 5 mmHg. Mean values and standard errors of ABP-ICP phase difference falling in each bin were calculated and plotted against the median CPP of each bin. An inverse 'U'-shaped curve was obtained, and the best CA (the largest phase difference)[28] was located at $CPP \approx 80$ mmHg (Fig. 3).

Baseline CA Versus VCI, VDI and ΔP

Figure 4a and b shows the relationship between VCI, VDI and ΔP (relative change of ICP B-wave power after EVD opening). VCI negatively ($r = -0.44$, $n = 34$) and VDI positively ($r = 0.82$, $n = 34$) correlated with ΔP , indicating that stronger vasoconstriction resulted in bigger drop in ICP B-wave power during CSF drainage. We further studied how the baseline (prior to EVD opening) CA was related to VCI or ΔP . The result showed a negative

Fig. 3 Binned scatter plots of CPP versus ABP-ICP phase difference; ABP-ICP phase difference reaches the peak (indicating the best cerebral autoregulation), while CPP equals 80 mmHg. ICP intracranial pressure, VCI vasoconstriction index, VDI vasodilation index, CPP cerebral perfusion pressure, ABP arterial blood pressure

relationship between CA (depicted by ABP-ICP phase difference) and ΔP ($r = -0.612$, $n = 16$, Fig. 4c). Larger phase difference prior to EVD open, indicating better

autoregulation, introduced larger power drop in ICP slow waves during CSF drainage. However, no relationship existed between ABP-ICP phase difference and VCI ($r \approx 0$) or VDI ($r = 0.05$).

Discussion

Continuous ICP monitoring remains a useful tool in the management of patients in NICU [47, 48]. In this study, we used a new ventricular catheter which enables continuous ICP monitoring even during CSF drainage to study cerebral vascular changes during acute ICP drop. There are three major findings in this study: (1) An acute decrease in ICP or increase in CPP would result in vasoconstriction which can be detected through an index, VCI; (2) cerebral vessels actively respond to acute ICP changes or CPP changes in a certain range; beyond which, the changes in ICP or CPP cannot cause further vascular responses; and (3) the drop of ICP B-wave power during CSF drainage is positively related to VCI and to CA states at baseline.

First, this study shows a significant increase in VCI during CSF drainage, indicating that an acute decrease in ICP, resulting in increased CPP, leads to cerebral vasoconstriction. CA is a compensatory mechanism which can maintain stable cerebral blood flow despite fluctuating CPP within certain limits [26, 49–51]. With intact CA, an increase in CPP leads to vasoconstriction (probably due to a direct ‘myogenic’ effect on the vascular smooth muscle) thereby maintaining flow; on the contrary, a decrease in CPP causes vasodilation [52–54]. This study provides further evidence that the two parameters, VCI and VDI, can be applied to assess acute cerebral vascular changes.

Second, the inverse ‘S’-shaped relationship between ICP and VCI is an interesting finding. In this cohort of patients, VCI (VDI) decreases (increases) when ICP

increases within the range of 10–25 mmHg. The vessels seem to reach their maximum constriction, while ICP decreases below 10 mmHg; and inversely, vessels cannot dilate any more, while ICP is higher than 25 mmHg. Since CPP is the driven force of cerebral blood flow into the brain and in the present study, the CPP changes are mainly caused by the changes in ICP due to CSF drainage, it is plausible to get this inverse ‘S’-shaped relationship between VCI and ICP. The result may suggest within a certain range of ICP, the vessels response to ICP changes quickly to maintain relatively stable cerebral blood flow. The result indicates that the range (ICP: 10–25 mmHg) may correspond to a safe and effective range of ICP, where CPP can be manipulated to achieve optimal perfusion pressure. Further studies are needed to confirm or invalidate this speculation.

Wavelet phase difference measures the delay between input (ABP) and output (ICP) over a range of frequencies and time [55], with high phase difference indicating good CA [56–58] and low phase difference reflecting direct changes in ICP following ABP changes because of impaired CA function [28, 59]. A recent study already suggests that wavelet method produces more robust and stable assessment of CA than a well-established metric—PRx [28]. Therefore, we chose wavelet method to assess CA in the current study. With the help of a curve fitting algorithm, the optimal CPP (CPPopt) can be continuously estimated [46, 60–62] by plotting wavelet phase difference against CPP, which produces a reverse U-shaped curve and CPP value at the maximum phase difference is associated with the strongest autoregulatory ability [28]. In the current cohort, the optimal CPP value (around 80 mmHg) matches the result of our previous study of 515 TBI patients [28]. Interestingly, the optimal CPP value of 80 mmHg corresponds to the turning point of VCI-CPP curve (Fig. 2d). While CPP increases above

Fig. 4 Scatter plots of relative changes (percentage) in power of ICP B-waves versus VCI (a) or VDI (b) or ABP-ICP phase difference (c). ICP intracranial pressure, VCI vasoconstriction index, VDI vasodilation index, CPP cerebral perfusion pressure, ABP arterial blood pressure

80 mmHg, VCI starts to increase; and when CPP is below 80 mmHg, VDI starts to increase. Further study needs to be carried out to validate the possibility of using VCI to estimate optimal CPP in the future.

Furthermore, the positive relationship between VCI and the decrease in ICP B-wave power further suggests that ICP B-waves reflect vasogenic activity [31–33, 63] and the main reason of B-wave reduction during CSF drainage is cerebrovascular constriction.

Finally, in this study, we found a negative relationship between ABP-ICP phase difference at baseline and the decrease in ICP B-wave power during CSF drainage. A possible explanation is that a preserved autoregulation before acute CSF drainage is a prerequisite for observing cerebral vasoconstriction as a response to increased CPP after reducing ICP acutely. The better the CA prior to EVD opening (indicated by bigger ABP-ICP phase difference), the bigger the cerebral vascular responses and the greater decrease in ICP B-wave power it may cause. However, we could not establish a significant correlation between CA of pre-drainage period and VCI (or VDI) during CSF drainage. This phenomenon could potentially be due to the fact that VCI is more of a state indicator than being a metric of degree of cerebrovascular vasoconstriction. Another potential explanation is that a highly nonlinear relationship exists between the actual strength of autoregulation and the extent of cerebral vasoconstriction.

Limitations

We acknowledge the following limitations of the study. The analysis and conclusion of this study heavily relied on our previously proposed VCI and VDI algorithm. The calculation of VCI/VDI was based on the ICP pulse morphological change patterns established using data from CO₂ challenge that was performed on patients with chronic hydrocephalus with an indwelling shunt [19]. Therefore, our assumption is that CO₂-induced cerebral vasodilation is equivalent to cerebral vasodilation that is induced by the reduction in CPP and that this equivalence is of a physiologic nature and not disease-dependent. Although we were not able to validate these two assumptions, the results we obtained are plausible and future work can be readily performed to establish perhaps more relevant templates of cerebral vasodilation and vasoconstriction for this patient population and the triggering mechanism of cerebral vascular changes. Second, we lack an efficient tool to test cerebral blood flow currently, which is important for brain injury patients. In our study, we noticed that the vessels tried to maintain stable cerebral blood flow by responding to ICP changes in a certain range. It will be of great potential if we can validate the relationship between VCI and VDI and

cerebral blood flow, and thus VCI/VDI might be used to detect cerebral blood flow in the future. Finally, the data analyzed in the present study only included 6 patients. The method needs to be tested in more patients. However, the small cohort allows us to be able to study information in details.

Conclusions

This study showed that acute CSF drainage reduced mean ICP, increased CPP, and reduced ICP B-wave power. A plausible explanation of this observation is cerebral vasoconstriction as an autoregulatory response to acute ICP decrease and CPP increase. The study validated VCI as an index to assess cerebral arterial changes for acute brain injury patients. Better CA at baseline and stronger vasoconstriction would result in bigger decrease in power of ICP B-waves during CSF drainage.

Electronic supplementary material

The online version of this article (<https://doi.org/10.1007/s12028-018-0651-4>) contains supplementary material, which is available to authorized users.

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Author Contributions

The concept and study design were formed by X.H., X.Y.L., P.V., L.Z. and X.L.L. Data acquisition was conducted by P.V., N.H. and L.Z. Data analysis was conducted by X.Y.L., N.H., X.L.L. and X.H. Drafting of the manuscript and figures was contributed by X.Y.L., X.H., L.Z., P.V., N.H. and X.L.L.

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Compliance with Ethical Standards

Conflict of interest

The authors declare that they have no conflict of interest.

Ethical Approval

The institutional review board (IRB) approved the data analysis and waived the need for consenting patients because of the retrospective nature of the study.

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