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A dynamic nonlinear relationship between the static and pulsatile components of intracranial pressure in patients with subarachnoid hemorrhage

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Abstract

Object—In the search for optimal monitoring and predictive tools in neurocritical care, the relationship of the pulsatile component of intracranial pressure (ICP) and the pressure itself has long been of great interest. Higher pressure often correlates with a higher pulsatile response to the heartbeat, interpreted as a type of compliance curve. Various mathematical approaches have been used, but regardless of the formula used, it is implicitly assumed that a reproducible curve exists. The authors investigated the stability of the correlation between static and pulsatile ICPs in patients with subarachnoid hemorrhage (SAH) who were observed for several hours by using data sets large enough to allow such calculations to be made.

Methods—The ICP recordings were obtained in 39 patients with SAH and were parsed into 6-second time windows (1,998,944 windows in 197 recordings). The ICP parameters were computed for each window as follows: static ICP was defined as the mean ICP, and pulsatile ICP was characterized by mean ICP wave amplitude, rise time, and rise time coefficient.

Results—The mean ICP and ICP wave amplitudes were simultaneously high or low (the expected correlation) in only ~ 60% of observations. Furthermore, static and pulsatile ICP correlated well only over short intervals; the degree of correlation weakened over periods of hours and was inconsistent across patients and within individual patients over time. Decorrelation

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Disclosure

The software used for analysis of the ICP recordings (Sensometrics Software) is licensed by Department of Neurosurgery, Rikshospitalet University Hospital, and manufactured by a software company (dPCom AS, Oslo) wherein Per Kristian Eide, M.D., Ph.D., has a financial interest.

Supplemental online information:

Video 1: http://mfile.akamai.com/21490/wmv/digitalwbc.download.akamai.com/21492/wm.digitalsource-na-regional/Video_1.asx.

Video 2: http://mfile.akamai.com/21490/wmv/digitalwbc.download.akamai.com/21492/wm.digitalsource-na-regional/Video_2.asx.

originated with abrupt shifting and gradual drifting of mean ICP and ICP wave amplitude over several hours.

Conclusions—The relationship between the static and pulsatile components of ICPs changes over time. It evolves, even in individual patients, over a number of hours. This can be one reason the observation of high pulsatile ICP (indicative of reduced intracranial compliance) despite normal mean ICP that is seen in some patients with SAH. The meaning and potential clinical usefulness of such changes in the curves is uncertain, but it implies that clinical events result not only from moving further out on a compliance curve; in practice, the curve, and the biological system that underlies the curve, may itself change.

Keywords

intracranial pressure; static intracranial pressure; intracranial pulsatility; pressure-volume curve; compliance

The ICP-volume curve is crucial for understanding neurosurgical pathophysiology,^{7,8,16} the rationale for its interpretation and its implications for exploring ICP-volume relationships^{15,17–19} and the relationships between ICP and intracranial pulsatility.^{2–4,20–22} These relationships are indicated in Fig. 1. Under normal physiological conditions and good pressure-volume reserve capacity (high intracranial compliance), the mean ICP remains approximately constant as the total volume of fluid in the intracranial cavity changes. Consequently, small changes in intracranial volume associated with cardiac pulsations, probably in the range of 0.5–1 ml,¹ generate small-amplitude peaks (dP) in the ICP waveform. As the total volume of fluid in the intracranial cavity increases, intracranial compliance begins to decrease, and the mean ICP increases approximately exponentially with increases in intracranial volume. This failure is indicated by large-amplitude ICP waveform peaks (dP) in response to cardiac pulsations, shortening rise times (dT), and increasing ICP rise time coefficients (dP/dT). Several studies of the relationship between mean ICP and ICP pulse amplitude in humans and animals have proposed a linear relationship between these 2 parameters when the mean ICP is < 30–60 mm Hg.^{2–4,6,14,20,22} Current approaches to understanding ICP and its value as a clinical indicator thus tend to focus on the mean ICP as the primary parameter of interest, viewing other features of ICP as having less clinical relevance or postulating that they are captured by the behavior of the mean ICP.

In contrast to the traditional model, recent studies in patients with intracerebral hemorrhages have demonstrated reduced intracranial compliance in the presence of high pulsatile ICP but normal mean ICP.^{11–13} In patients with SAH, a worse clinical state was associated with high pulsatile ICP even though the mean ICP was normal.^{11–13} Moreover, when hypertonic saline was given to patients with SAH to reduce ICP, there was no significant correlation between the change in static and pulsatile ICPs.⁵ Thus, several clinical observations question the traditional model on the association between static and pulsatile ICPs, as traditionally understood in the pressure-volume curve.

In the present study, we reexamined the associations between the mean ICP and a set of parameters related to intracranial pulsatility: the mean ICP wave amplitude, the mean ICP

wave rise time, and the mean ICP wave rise time coefficient. In an analysis of nearly 2 million observations in 39 patients, we studied the associations between these pulsatility parameters and mean ICP and found that, in contrast with the prevailing model, mean (static) ICP was a poor indicator of intracranial pulsatility. That is, in nearly 40% of observations, a clinically low mean ICP was associated with a high mean wave amplitude and vice versa. Static and pulsatile ICP correlated well only over short intervals; the degree of correlation weakened over periods of hours and was inconsistent across patients and within individual patients over time. We investigated the sources of this decorrelation and found that they included abrupt shifting and gradual drifting of mean ICP and, independently, of ICP wave amplitude, over hours-long timescales. Because static and pulsatile ICPs correlate well over short intervals, we found that it was possible to use pulsatile ICP as an auxiliary parameter to distinguish between regular variations and irregularities in mean ICP over time. The results suggest that visualizing static and pulsatile ICPs simultaneously and investigating their relationship can be a potentially useful diagnostic tool. Our results demonstrate that ICP-volume relationships are not fixed in time. They evolve, even in individual patients, on timescales of hours. The use of pulsatile ICP as an auxiliary monitoring parameter may therefore facilitate more accurate clinical interpretation of ICP measurements recorded in patients over the course of many hours or days.

Methods

Intracranial Pressure Recordings

Between 2002 and 2004, 197 continuous ICP recordings were obtained in 39 patients (27 women and 12 men), who were hospitalized for SAH in the intensive care unit of Rikshospitalet University Hospital. The median patient age was 55.5 years (range 43–78 years). The ICP monitoring was done as part of routine clinical management, and the ICP recordings were stored in a hospital database (sampling frequency 100 Hz) for a retrospective, anonymous audit. Clinical information about our patients with SAH who underwent ICP monitoring has previously been reported.¹²

The ICP recordings were done using solid ICP sensors (Codman MicroSensor, Johnson and Johnson; or Camino OLM ICP Sensor, Camino Laboratories) placed 1–2 cm into the frontal brain parenchyma through a minimal opening in the dura.

Static and Pulsatile ICP Parameters Computed Over 6-Second Time Windows

The analysis of the continuous ICP waveforms was done using a previously published algorithm for automatic single-wave identification and analysis¹⁰ that has been implemented in software (Sensometrics Software, dPCom As). The algorithm was used to identify the cardiac beat-induced single ICP waves. The following different parameters were identified for every single ICP wave: dP, dT, and dP/dT (Fig. 1). The recordings were also parsed into 6-second time windows (that is, observations); for each window the static pressure (mean ICP) and the mean ICP wave amplitude, mean ICP wave rise time, and mean ICP wave rise time coefficient were determined. Only 6-second time windows of good quality and accepted according to the algorithm¹⁰ were used for the present analysis; 6-second time

windows with artifacts due to noise in the pressure signal (for example, patient movement or sensor movement or dysfunction) were not used in the analysis.

From the entire set of 197 ICP recordings, a total of 1,998,944 6-second time windows were available for analysis. Sets of windowed values of each of the 4 ICP parameters computed were analyzed pairwise for correlations using standard methods of linear regression, statistical significance testing, and multidimensional histograms. Multivariate regression techniques were used to assess relationships among groups of ICP waveform parameters.

Statistical Analysis

Data processing and statistical analysis were performed using PC-SPSS version 12.0 (SPSS, Inc.), MatLab version 7.0.4 (MathWorks, Inc.), and Mathematica version 6.0 (Wolfram Research, Inc.).

Results

Summary Frequencies Binned According to Clinically Useful Parameter Thresholds

Table 1 shows the distribution of ICP pulsatility parameters categorized according to whether the mean ICP fell above or below the threshold value of 15 mm Hg. Summing the off-diagonal entries indicates that in 37.6% of observations, either high mean ICP (≥ 15 mm Hg) was observed in the context of low mean ICP wave amplitude (< 5.0 mm Hg) or vice versa. The expected association (high ICP with high wave amplitude or low ICP with low wave amplitude) was maintained only in the remaining 62.4% of observations. A mean ICP ≥ 15 mm Hg predicted a mean ICP wave amplitude ≥ 5 mm Hg with a sensitivity of 46% and specificity of 80% (positive and negative predictive values of 70 and 59%, respectively).

Lack of Linear Correlations Between Mean ICP and ICP Wave Amplitude

For each patient, the mean ICP wave amplitude was regressed against mean ICP using a standard linear model. Resulting best-fit lines are plotted together in Fig. 2A, while Fig. 2B shows a histogram of the correlation coefficients (R values) corresponding to the entire set of linear regressions. Data from the entire set of 39 patients were then pooled and used to approximate the distribution of mean ICP and mean ICP wave amplitude value pairs. Table 2 presents a coarse-binned partitioning of the data. Figure 3 presents the same data visually as a 2D density plot binned at a resolution sufficiently fine to convey the shape of the 2D frequency distribution within this patient population. The plot shows bimodal behavior of ICP pulse amplitude with respect to the mean ICP for a mean ICP greater than ~ 12 mm Hg, demonstrating that in practice there is not a functional (one-to-one) relationship between static and pulsatile ICPs.

Multivariate Relationships Among Waveform Shape Parameters

We performed a multivariate analysis of the data to determine whether variation in waveform shape might account for the observed decorrelation between mean ICP and ICP wave amplitude. This analysis was motivated by the observation that, if the waveform shape is permitted to vary, waveforms with identical amplitudes can have different means, and waveforms with identical means can have different amplitudes, so that the degree to which

waveform shape can be physiologically altered might reflect the degree of decorrelation between mean ICP and ICP wave amplitude. We therefore explored a model accounting for waveform shape changes by relating mean ICP to ICP wave amplitude and ICP wave rise time.

For each patient, the mean ICP wave amplitude and the mean ICP wave rise time were regressed against mean ICP using a standard multilinear model of the following formula: $\text{mean ICP} = C_A \times (\text{mean ICP wave amplitude}) + C_T \times (\text{mean ICP wave rise time}) + C_O$, where C_A and C_T are best-fit coefficients and C_O is a best-fit offset pressure. As in our 1D regression analysis, the best-fit coefficients exhibited a wide range of variation within individual patients observed at different times and across patients. Coefficients of determination for the 2D regressions remain nearly as poor as in the 1D regression, indicating that the poor correlation between mean ICP and ICP waveform amplitude cannot be explained on the basis of changes in waveform shape.

Impact of Pressure Offset Shifts and Drifts

The major reasons for the poor correlation between mean ICP and ICP wave amplitude, (that is, abrupt shifting and gradual drifting of mean ICP and ICP wave amplitude over several hours) are illustrated in Figs. 4 and 5 and Videos 1 and 2.

Figure 4 shows scatter plots of the mean ICP and ICP wave amplitude in long-term recordings obtained in 4 different patients. These scatter plots illustrate several classes of behavior observed in long-term ICP recordings. Figure 4a is a rare example illustrating a nearly ideal, constant linear relationship between static and pulsatile ICPs over a period of 21 hours. Even in this nearly ideal example, however, one discerns clusters of data points (for example, mean ICP and ICP wave amplitude). Data points within each cluster belong to a definite time interval and exhibit a particular intracluster linear trend. In Fig. 4a the trends exhibited by the various clusters are similar, and thus the clusters exhibit a large degree of overlap. Moreover, the linear trend within each cluster is strong, so the within-cluster correlation coefficient is close to unity; and since the linear trends across clusters are very similar, the correlation coefficient over the entire 21-hour observation period is also close to unity. In Fig. 4b, a more typical example, the clusters are more diffuse than in Fig. 4a, exhibiting weaker but still discernible linear trends on time scales up to ~ 3 hours. Yet over the course of 12 hours, the mean ICP gradually drifts to higher values while the ICP wave amplitude remains within the same range. This upward drift in mean ICP leads to a smearing of clusters that obscures the correlation between static and pulsatile ICPs: the correlation between mean ICP and ICP wave amplitude is nearly zero when taken over the entire observation period. Figure 4c illustrates a second phenomenon we frequently observe in long-term ICP recordings, that is, abrupt shifting of ICP parameters. The recording plotted in Fig. 4c contains distinct data clusters exhibiting strong within-cluster linear correlations. The many clusters have similar slopes, indicating that a similar linear relationship between static and pulsatile ICPs is maintained over time. However, the offset value of wave amplitude falls suddenly by a fraction of 1 mm Hg every few hours, leading to the formation of distinct data clusters. As in Fig. 4a, the within-cluster correlation coefficients are close to unity; however, the shifting behavior that leads to the separation of clusters greatly reduces

the overall correlation coefficient and numerically obscures the correlation between static and pulsatile ICPs. The abrupt downward shifting in pulsatile ICP observed in Fig. 4c is analogous to the gradual upward drift in the mean ICP observed in the recording of Fig. 4b, although in Fig. 4c the data clusters are more distinctly separated due to a higher degree of linear correlation. We also observed gradual drifts and sudden shifts in static and pulsatile ICPs in individual patients, as the data in Fig. 4d illustrate. In the recording plotted in Fig. 4d, data from 4 intervals clustered along 4 corresponding and connected line segments; the first and last of these segments have nearly identical slopes but are offset by ~ 18 mm Hg in mean ICP (the range of ICP wave amplitudes explored increases by approximately one-third over the course of the recording). While the data within each of the 4 intervals exhibited strong linear correlations, the gradual shifts in the linear relationship over the observation period resulted in a weak overall correlation between static and pulsatile ICPs.

In a subset of the 197 ICP recordings, 2 simultaneous ICP signals from different ICP sensors were present, providing the opportunity to verify that neither gradual drift nor abrupt shifts could be attributed to sensor measurement artifacts. Sensor-associated and physiological noise sources were present in all recordings (as confirmed by comparing the variances in sensor measurements made before and after removal from brain parenchyma).

Two examples confirm that the phenomena described here were robust to both sources of noise. First, we reexamined 3 ICP recordings containing simultaneous ICP signals from 2 different ICP sensors (Codman MicroSensor and Camino OLM ICP Sensor) placed nearby in the frontal lobe in 3 patients.⁹ Shift and drift phenomena were observed while using both types of sensors. Notably, however, the mean correlation coefficient between measurements of static ICP by the 2 sensors was 0.37, whereas the corresponding correlation coefficient for pulsatile ICP was 0.85.

Second, we further analyzed one of the ICP recordings that contained 2 simultaneous ICP signals from identical Codman MicroSensors placed in the left and right frontal lobe parenchyma. To quantify physiological variability, 24 hours of data from this recording are shown accumulating over a series of time points in Fig. 5. In each subfigure of Fig. 5, recent data points are plotted in color against a background of past data (red and blue points correspond to data from the right and left hemispheres, respectively), with past data plotted in shades of gray (darker shades of gray indicate later data points). The data shown in Fig. 5 indicate that even within an individual patient the short-term linear relationship between static and pulsatile ICPs undergoes both gradual drifts and abrupt shifts. The drift phenomenon is illustrated by the movement of recent data points relative to the background of past data, while the shift phenomenon is evident from the relative movement of the right- and left-hemisphere trend lines from one frame to the next. Notably, the mean correlation coefficient between measurements of mean ICP made in the right and left frontal lobes was 0.61, while the corresponding mean correlation coefficient for pulsatile ICP was 0.93.

In this data set of 197 ICP recordings, ICP shifts defined as change in mean ICP > 2.5 mm Hg combined with change in ICP wave amplitude < 2.0 mm Hg between successive 6-second time windows occurred approximately every 2.3 hours, while ICP shifts defined as change in ICP wave amplitude > 2.0 mm Hg combined with change in mean ICP < 2.5 mm

Hg between successive 6-second time windows occurred less frequently, approximately every 3.3 hours.

Discussion

Clinical Correlation

The present data help explain several clinical observations that are incompatible with the traditional view of the relationship between static and pulsatile ICPs. Recent observations have indicated that pulsatile ICP may be high (> 5 mm Hg), indicating impaired intracranial compliance, even when the mean ICP is low (< 15 mm Hg).^{5,11–13} In patients with SAH, the acute clinical state and final outcome were worse when pulsatile ICP was high even though the mean ICP was maintained within normal limits.^{12,13} Reducing pulsatile ICP improved the clinical state even though the mean ICP was within the normal range.¹³ When hypertonic saline was given to reduce ICP in patients with SAH, the target level of mean ICP (< 15 mm Hg) was reached in 65% while the target of ICP wave amplitude (< 5 mm Hg) was reached in only 35% of interventions, indicating that intracranial compliance was still reduced despite a normal mean ICP.⁵ Taken together, these observations are incompatible with the traditional model of the ICP-volume relationship, especially with regard to the prevailing clinical thresholds for static and pulsatile ICPs that are thought to indicate failure in intracranial compliance, as well as the notion that static and pulsatile ICPs are strictly correlated in a time-invariant, linear manner. The findings we present here highlight the need for a better understanding of the relationship between static and pulsatile ICPs.

Another still unanswered question is whether pulsatile ICP is more helpful than mean ICP in guiding patient care. An ongoing study is exploring how critical care management according to static and pulsatile ICP relates to outcome after SAH (<http://clinicaltrials.gov/ct2/show/NCT00248690>).

Other observations incompatible with a traditional understanding of the ICP-volume relationship are that different ICP sensors placed nearby within the brain parenchyma of an individual with SAH can show very different mean ICP values, even though the ICP wave amplitudes are identical.⁹ Such observations clinically validate the finding presented here, that there often exists a decorrelation between high mean ICP and high pulsatile ICP.

Mean ICP is traditionally interpreted as an indicator of intracranial compliance in the sense that mean ICP above a certain clinically defined threshold value is taken to indicate decompensated intracranial compliance. However, patient-to-patient variability in the data we present indicates that threshold ICP values marking the transition to decompensated intracranial compliance are very likely patient specific. Others²² have noted the importance of patient-to-patient variability in this context as well. It is probably not meaningful to define a clinical threshold for mean ICP above which any patient is considered to have experienced a failure in autoregulation and decompensation of intracranial compliance. The problem of determining whether a particular patient has experienced such decompensation can perhaps be approached by considering not only mean ICP but also additional physiological data obtained through continuous monitoring, such as the present state of the

pulsatile ICP and the historical correlation between static and pulsatile ICPs in the individual patient. For example, a recent history of strong correlation between static and pulsatile ICPs, combined with high mean ICP and large ICP waveform pulsations, provides a case for greater failure of intracranial compliance than high mean ICP alone.

Decorrelation Between Static and Pulsatile ICPs During Long-Term Monitoring

The traditional understanding of intracranial compliance through the ICP-volume curve holds that static and pulsatile ICPs typically exhibit a fixed linear relationship. In contrast to this view, we have found that the linear relationship between mean ICP and mean ICP wave amplitude changes, even in individual patients, on time scales of hours. Our findings are based on nearly 2 million observations made in a controlled clinical setting, during multiple sessions of multihour ICP recordings in a cohort of 39 patients with SAH.

A fixed linear relationship between static and pulsatile ICP would imply that a high mean ICP should correlate with a high mean ICP wave amplitude, while a low mean ICP should correlate with a low mean ICP wave amplitude. Contrary to this expected relationship, we found that in 37.6% of observations, either high ICP (≥ 15 mm Hg) was observed in the context of a low mean ICP wave amplitude (< 5 mm Hg) or vice versa (Table 1). The expected association (high ICP with high wave amplitude or low ICP with low wave amplitude) was maintained only in the remaining 62.4% of observations.

It may also be important to note an additional way in which static and pulsatile ICP can be decoupled. Mathematically, the window-averaged mean of a waveform does not depend on waveform amplitude. Theoretically, it may depend on the integral of the waveform over the selected time window, and the value of this integral is determined by overall waveform shape. As a result, the mean ICP might change independently of the ICP waveform if the shape of the waveform changes. Waveforms with identical amplitudes can have different means and waveforms with identical means can have different amplitudes, so that the degree to which waveform shape can be physiologically altered might reflect the degree of decorrelation between mean ICP and ICP wave amplitude. Waveform shape analysis performed in real time by monitoring pulsatility parameters can explain, in principle, why it is possible to observe ICP waves with high amplitude and low mean ICP and vice versa. In the present study, we did observe considerable variability in waveform shape both within and across patients. However, as indicated by the results of our multivariate regression studies, such changes were not the dominant reason for the reported long-term decorrelation between mean ICP and ICP wave amplitude.

While we are unaware of any correlation between clinical events and the shift and drift phenomena we describe, one possible partial explanatory mechanism relates to postural changes. Such changes are known to redistribute CSF in fluid compartments, resulting in abrupt changes in the mean ICP with no corresponding changes in the ICP wave amplitude. Still, it should be noted that the parameters mean ICP and mean ICP wave amplitude referred to here were determined simultaneously during the same 6-second time windows (observations). Hence, these pressure parameters were not differently affected by activities taking place within the intensive care unit, such as manipulation of the patient, medication, or type of respiratory support. Moreover, the 6-second time windows used for analysis were

accepted according to the algorithm for automatic single wave identification.⁹ The 6-second time windows containing signals corrupted by unacceptable levels of noise were not included for analysis to ensure that only the cardiac-beat-induced pressure waves (and not pressure waveform artifacts) were considered.

It is important to note that measurement of ICP pulsatility parameters does not preclude simultaneous monitoring of the mean ICP. As in the present study, a single transducer can be used to monitor static ICP and pulsatile ICP parameters. Real-time analysis of a single pressure signal from a standard ICP transducer can convert that signal into a mean ICP trace and a train of pulsatility parameter values. Thus, ICP pulse amplitude need not encode the same physiological information as the mean ICP to prove useful as a clinical indicator, as modern clinical systems are capable of monitoring static and pulsatile ICP parameters simultaneously, and even of generating plots such as those shown in Figs. 4 and 5 in real time.

Abrupt Shifts and Gradual Drifts as Main Source to Decorrelation

We have investigated the source of the long-term decorrelation between static and pulsatile ICPs and found that it is due primarily to abrupt shifts and gradual drifts in ICP parameters.

The shift and drift phenomena reflect noise processes of physiological origin as well as sensor-associated measurement noise. In mathematical terms, noise refers to the variance of measured quantities. Because noise processes can affect the measurement of static and pulsatile ICPs independently, noise-related events can cause the short-term linear relationship between these parameters to vary over time. The overall average frequency with which we observed significant perturbations to the short-term linear relationship between static and pulsatile ICPs (major shifts as defined in *Results* as either a change in static ICP of > 2.5 mm Hg or a change in pulsatile ICP of > 2 mm Hg over successive 6-second observation windows) was approximately once per 55 minutes. Thus, observations over periods shorter than ~ 55 minutes are likely to show strong correlation between static and pulsatile ICPs, whereas the linear relationship between these parameters will be observed to change over longer time scales. While the relatively low prevalence of the data acquisition systems required to compute, monitor, and store ICP-derived parameters may have precluded studies over such long time scales in the past, clinical use of multichannel data acquisition systems with massive storage capacity is becoming more widespread. Importantly, it was only through the use of such a system, unavailable to many research teams until recent years, that we were able to make the observations reported here.

Our analysis of random variation in ICP parameters indicates that measurements of pulsatile ICP are more robust to noise than traditional measurements of mean ICP, and for this reason might serve as useful adjunct measurements in the clinical interpretation of mean ICP. The increased robustness of pulsatile relative to static ICP measurements may arise from the inherently differential nature of ICP wave amplitude. Static measurements of ICP are comparisons of a measured pressure to a baseline reference pressure, and as a result they are subject to fluctuations associated with perturbations in the pressure reference. Waveform amplitude measurements are immune to such common-mode perturbations because waveform amplitude measurements do not rely on an external reference pressure but rather

compute a differential-mode quantity. As indicated in Fig. 1, the dP is defined as a difference between pressure measurements at 2 time points spaced sufficiently close together that significant reference point variation does not have time to occur.

The different character of static and pulsatile ICP measurements also explains the partial independence of the noise associated with these 2 quantities. This independence in turn implies that pulsatile ICP measurements, as adjunct indicators, could help validate clinical measurements of mean ICP when fluctuations in static and pulsatile ICPs are strongly correlated, while cautioning against the use of less reliable fluctuations in mean ICP when such changes do not correlate with variations in pulsatile ICP. Clinical decisions involving ICP need not be based solely on isolated values of mean ICP relative to a fixed threshold. More detailed impressions of intracranial physiology may be inferred by tracking the recent history of static and pulsatile ICP.

To investigate a mechanistic cause of the nonlinear relationship between mean ICP and ICP pulse amplitude, further systematic assessment of alterations of intracranial characteristics may be considered. In experimental data analysis in animals, the canine intracranial system changes under normal and elevated ICP have been characterized using transfer function analysis²³ and time-varying transfer function analysis applied to the arterial blood pressure waveform as the input signal and the ICP waveform as the output signal.²³ The results suggest that free movement of CSF may play an important role in absorbing strong arterial pulsations under normal conditions. It can be speculated that a pathological disease state might cause a dysfunction of the pulsation absorber mechanism. Based on the results from the experimental data analysis in animals²³ and the present studies, we conjecture that further studies may reveal that the elevated ICP pulse amplitudes observed in pathological states may be a result of dysfunction or reduced function of the pulsation absorber mechanism.

Conclusions

The prevailing model of ICP physiology suggests that mean ICP should be understood as an indicator of the intracranial compliance. The same model predicts a stable, linear relationship between mean ICP and ICP waveform pulse amplitude, whereas the observations we present here indicate that the relationship between mean and pulsatile ICPs is more complicated than predicted by the prevailing model. In particular, the relationship between the static and pulsatile components of ICP is not fixed in time, but evolves, even in individual patients, over several hours. Major causes of decorrelation between static ICP (mean ICP) and pulsatile ICP (ICP wave amplitude) during long-term monitoring are abrupt shifts and gradual drifts of the static and pulsatile ICP parameters. These phenomena may contribute to the presence of high pulsatile ICP, indicative of reduced intracranial compliance, despite normal mean ICP in some patients with SAH. Further research is therefore needed to understand intracranial fluid dynamics completely, to determine how to assess intracranial compliance most accurately during continuous monitoring of ICP, and to determine the most effective indicators to use in guiding decisions on patient management.

Video 1. Animated time-dependent scatter plots of static and pulsatile ICP in a multihour recordings from 4 patients, corresponding to Fig. 4. The animated data exhibit behavior typically observed in long-term ICP recordings and illustrate the tendency of short-term linear trends to shift and drift over time in ways that weaken the overall linear correlation between static and pulsatile ICPs. [Click here to view with Windows Media Player.](#)

Video 2. Time-dependent scatter plot from 24 hours of simultaneous paired recordings using identical ICP sensors placed in the right and left frontal lobe parenchyma of a single patient, corresponding to the data presented in Fig. 5. Red and blue points correspond to data from the right and left hemispheres, respectively. Recent data points and their best-fit trend lines are plotted in intense hues, while data farther into the past become fainter with time. The animated data demonstrate that even within an individual patient the short-term linear relationship between static and pulsatile ICPs undergoes abrupt shifts and gradual drifts. The shift phenomenon is evident from the relative movement of the right- and left-hemisphere trend lines over time, while the drift phenomenon is illustrated by the movement of recent data points relative to the background of past data. [Click here to view with Windows Media Player.](#)

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Abbreviations used in this paper

dP	pulse amplitude
dT	rise time
dP/dT	rise time coefficient
ICP	intracranial pressure
SAH	subarachnoid hemorrhage

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Fig. 1.

Illustration of the ICP-volume curve and its relationship to the intracranial pulsatility parameters. Under normal physiological conditions with high intracranial compliance, the ICP wave amplitude is correspondingly small. As intracranial compliance decreases (steep part of the pressure-volume curve), the brain behaves increasingly like a linear elastance and so variations in intracranial volume correlate increasingly well with changes in mean ICP, the steepness of the pressure-volume curve also accounts for large-amplitude ICP waveforms.

Fig. 2.

Graphs. The mean ICP wave amplitude was regressed against the mean ICP for each of the 39 patients. **A:** The resulting best-fit lines are plotted together, illustrating the variability of best-fit parameters across patients. **B:** A histogram of the Pearson correlation coefficients (R values) for the set of linear regressions, indicating the highly variable and overall poor correlation between mean ICP and ICP wave amplitude.

Fig. 3.

A density plot presenting the tabulated data shown in Table 1 binned at a finer resolution, using color intensity to represent relative frequency within the data set of 1,998,944 6-second time windows. The plot shows bimodal behavior of ICP pulse amplitude with respect to mean ICP for mean ICP > 12 mm Hg, demonstrating that in practice there is not a functional (one-to-one) relationship between static and pulsatile ICPs.

Fig. 4.

Scatter plots of mean ICP and ICP wave amplitude in long-term recordings from 4 different patients. These scatter plots exhibit several classes of behavior observed in long-term ICP recordings and illustrate the tendency of short-term linear trends to shift and drift over time in ways that weaken the overall linear correlation between static and pulsatile ICPs.

Fig. 5.

Scatter plots from 24 hours of simultaneous paired recordings using identical sensors placed in the left and right frontal lobe parenchyma of a patient. Each subfigure corresponds to a time point as indicated by the plot label. Recent data points are plotted in color against a background of past data (*red* and *blue* points correspond to data from the right and left hemispheres, respectively), with past data plotted in *gray* (darker shades indicate later data points). The data shown in this figure indicate that even within an individual patient the short-term linear relationship between static and pulsatile ICPs undergoes abrupt shifts and gradual drifts. The shift phenomenon is evident from the relative movement of the right- and

left-hemisphere trend lines from one frame to the next, while the drift phenomenon is illustrated by the movement of recent data points relative to the background of past data.

TABLE 1

Summary frequencies binned according to clinically useful parameter thresholds *

ICP Pulsatility Parameters	Mean ICP [†]		p Value [‡]
	<15 mm Hg	15 mm Hg	
mean dP			
1.0 dP<5.0	784,251 (39.2)	198,328 (9.9)	
dP 5.0	553,551 (27.7)	462,814 (23.2)	<0.001
mean dT			
0.1 dT<0.20	314,497 (15.7)	182,954 (9.2)	
dT 0.2	1,023,305 (51.2)	478,188 (23.9)	<0.001
mean dP/dT			
0.0 dP/dT<20	692,189 (34.6)	211,547 (10.6)	
dP/dT 20	645,613 (32.3)	449,595 (22.5)	<0.001

* The numbers include 1,998,944 observations of mean ICP wave amplitude, latency, and rise-time coefficient.

[†] Numbers in columns represent the number of observations with the percentages in parentheses.[‡] Significance was assessed using the Fisher exact test (2-sided p value).

TABLE 2

Numbers (and percentages) of 6-second time windows with combinations of mean ICP and mean ICP wave amplitude categories*

Mean dP	Mean ICP (mm Hg)									
	-10.0	Mean ICP<0	0	Mean ICP<15.0	15.0	Mean ICP<20.0	20.0	Mean ICP<30.0	Mean ICP	30.0
1.0 dP<4.0	23,264 (1.2)		516,671 (25.8)		84,273 (4.2)		12,530 (0.6)		1,122 (0.1)	
4.0 dP<5.0	3,285 (0.2)		241,031 (12.1)		49,792 (2.5)		49,554 (2.5)		1,057 (0.1)	
5.0 dP<7.0	1,493 (0.1)		371,425 (18.6)		84,749 (4.2)		94,595 (4.7)		9,966 (0.5)	
7.0 dP<10.0	246		159,571 (8.0)		72,756 (3.6)		56,023 (2.8)		12,933 (0.6)	
dP 10.0	10		20,806 (1.0)		22,084 (1.1)		46,919 (2.3)		62,789 (3.1)	

* Percentages are in parentheses.