A New Method of Estimating Intracranial Elastance

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Abstract

Objective: Current methods of calculating Intracranial Elastance Index (IEI) depend from CSF pulse-wave, whose shape may deeply change during ICP rising. The main aim of this study was to evaluate the reliability and specificity of a novel method to calculate IEI (method C), based on the integral of the CSF pulse-wave area.

Method: Twenty ventricular infusion-tests of patients with idiopathic NPH were re-evaluated. We have compared method C with the most widely used methods to calculate IEI: a modified Szewczykowski method (diastolic ICP against CSF pulse-wave amplitude-method A) and a modified Czosnyka method (diastolic ICP against the fundamental harmonic-method B). R-squared (R²) was calculated for each test. Means were compared through ANOVA and t-test.

Results: Mean R² values for methods A, B and C were 0.91 ± 0.06, 0.9 ± 0.06 and 0.96 ± 0.03, respectively. Mean R² values obtained through method A vs C and through method B vs C were significantly different (p = .006 and p = .001, respectively), while values obtained through method A vs B were not (p = 1). Analysis of ICP tracks demonstrated that 9 patients showed no different shape of the ICP wave during the infusion test, while the remaining 11 did. The mean R² values obtained through method A vs C and through method B vs C were significantly different (p < .001 for both) for patients showing a different shape of the ICP wave during the infusion test.

Conclusions: Method C seems to be the most reliable method to calculate IEI, as it is independent from CSF pulse wave modifications.

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Introduction

The intracranial pressure (ICP) waveform analysis is a method to assess the so called intracranial system compliance. Several clinical conditions can be accompanied by a modification of the intracranial system compliance, including head trauma and normal pressure hydrocephalus. Nonetheless, despite the several preclinical and clinical studies on this subject, the clinical value of ICP waveform analysis is still a matter of debate [1–5]. The main reason is that all the method used to assess compliance reflect intracranial system compliance but do not describe brain compliance directly [3]. Intracranial Elastance (IE) is a measure of the pressure/volume response of the intracranial system at a given level of ICP, i.e. the reciprocal of intracranial compliance. With each heartbeat, there is a pulsatile increase in cerebral blood volume, and the amplitude of cerebrospinal fluid (CSF) pressure pulsations (CSFPPAmp) is the response of the ICP to that increment of volume [6]. Szewczykowski et al. postulated that, in a patient at rest, with constant blood pressure and cardiac stroke volume, CSFPPAmp is directly proportional to IE [7]. Therefore, the relationship for each single ICP pulse wave between CSFPPAmp and its correspondent mean value provides a valid estimation of IE [8,9]. The same authors observed that the slope of the linear regression of the CSFPPAmp/IEC curve can be considered as a reliable index of IE (IEI) [9–11].

In healthy subjects, an ICP increase is accompanied by an elevation of the CSF pulse wave components P2 and P3. The CSF pulse wave initially becomes rounded and then, at higher ICP values, acquires a pyramidal shape [12,13]. If the CSF pulse wave changes its shape, the point where to measure its amplitude also changes, Czosnyka et al. proposed to calculate IEI as the slope of the linear regression between ICP and the amplitude of the fundamental (first) harmonic component, as obtained through the Fourier's spectral analysis, of 6–12 CSF pulse waves included in a given period [14]. That method was based on the assumption that the fundamental harmonic of the pulse waves accurately reflects the CSFPPAmp variations. As the authors themselves observed, the
slope of the fundamental harmonic/pressure curve may differ from the slope of the CSFPPAmp/pressure curve, depending on the shape of each individual pulse wave. [14] Moreover, Anile et al. performed a Fourier’s spectral analysis of CSF pulse wave morphology and found out that the change in the shape of the CSF pulse wave induced by ICP rising was associated with a negative phase shift of the fundamental harmonic in respect to the second harmonic [7,15]. This phase shift could be responsible for inaccuracies in estimating IEI, potentially reducing the reliability for clinical purpose of the infusion test.

Therefore, none of the above mentioned methods of estimating IEI seemed to guarantee that its results were not altered by changes in CSF pulse wave morphology.

Indeed, Foltz hypothesized that a progressively higher CSF pulse pressure could be considered as an index of intracranial compliance loss and that CSF pulsatility could be related to the mathematical formula of power [16]. This formula calculates the power involved in bringing a volume of moving fluid of known mass, travelling at a known velocity to a condition of rest and can be applied on CSF pulse pressure waves. The wave power can be approximated as the integral of the surface delimited by the wave itself. This method considers the single CSF wave as a whole, whatever its shape. This means that it should be far less sensitive to the changes of CSF pulse wave morphology (induced by ICP rising). On this basis, we have tried to use the integral of each single CSF pulse wave surface as a parameter to estimate the IEI and have compared this method with the most widely used methods to calculate IEI. The main potential clinical benefit of our study could be the evaluation of patients with suspected normal pressure hydrocephalus, in order to better understand the relationship between intracranial system compliance and shunt responsiveness.

**Materials and methods**

This study includes 20 ventricular infusion tests we had performed on patients with idiopathic normal pressure hydrocephalus between December 2005 and December 2006 (Table 1).
The tests were carried out by means of an intraventricular infusion of lactate Ringer’s solution at a constant rate of 1 ml/minute for 30 minutes through a 21-gauge needle inserted in a subcutaneous previously positioned large Rickham reservoir (Codman) connected to an intraventricular catheter inserted in the right frontal horn. These tests have been re-evaluated with a software which is able to analyze CSP pulse waves by elaborating every single wave with a 128-bit waveform analysis of the ICP recording [17].

IEI was therefore evaluated by measuring the slope of the linear regression between diastolic ICP (dICP) and the corresponding: 1) CSFPPAmp for each wave (method A)—i.e. a modified method from Szewczykowski et al.; 2) fundamental CSF pulse wave harmonic calculated for each wave (method B)—i.e. a modified method from Czosnyka et al.; 3) integral of each CSF pulse wave area (method C). The integral of each CSF pulse wave area was calculated by means of a self-developed computer program [2]. The selection of a single CSF pulse wave occurs through the identification of 2 consecutive minimum points from an interval of points, called a window [2]. We modified the original method of evaluating IE using the diastolic ICP values on the x axis instead of the mean ICP values. In our opinion, indeed, the diastolic pressure level represents the true pressure value during a single cardiac cycle, while the mean pressure value is an artificial variable, mathematically calculated, without a true physiological meaning [18].

In order to evaluate the morphological changes in CSF pulse waveform during the infusion test, we identified the three peaks as described by Gega et al. [19] and Cardoso et al. [12], namely the systolic peak (P1), the tidal peak (P2) and the dicrotic peak (P3). While in normal condition the systolic peak (P1) is higher than the other two and the dicrotic notch is well evident, in pathological situations, as during an infusion test, P2 and P3 exceed P1 and the dicrotic notch disappears so producing a modification in the shape of the CSF pulse wave morphology which progressively assumes a sinusoidal morphology (Figs. 1-2) [12].

Statistical analysis

The statistical analyses were carried out using SPSS version 11.0.1. Methods A and B were used as gold standard and were compared with method C. R² was used to evaluate the reliability of each test.

IEI and R² (mean and standard deviation) obtained by the aforementioned three methods were then compared. An analysis of variance (ANOVA) was performed to determine significant differences of the three methods. A t-test with Bonferroni correction was used to evaluate between-group differences.

Results

Analysis of ICP tracks demonstrated that 9 patients showed no different shape of the ICP curve during the infusion test (Fig. 1), while the remaining 11 did (Fig. 2). IEI obviously presented different values according to the method of calculation (Table 1): the lowest values were obtained through method B, the highest through method C.

When IEI was calculated using the integral of ICP wave area (method C), R² values were very high, nearest to 1 (Table 1).
R² values for method A, method B and method C were 0.91 ± 0.06SD, 0.9 ± 0.06SD and 0.96 ± 0.03SD, respectively.

An analysis of variance showed mean R² values obtained through method A and method C and through method B and method C were significantly different (p = .006 and p = .001, respectively), while mean R² values obtained through method A and method B were not significantly different (p = 1).

The t-test with Bonferroni correction showed R² values calculated using method A and method B were not significantly different (p = .12). Instead, R² values calculated using method C, when plotted against the other two methods, showed a significant difference (p < .001).

When comparing R² values, we observed that for patients whose ICP shape did not change during the infusion test, the mean values obtained through method A vs method B, method A vs method C and method B vs method C were not significantly different (p = .15, p = .53 and p = .13, respectively). For the 11 patients whose ICP shape changed during the infusion test, the mean R² values obtained through method A vs method C and method B vs method C were significantly different (p < .001 for both), while mean R² values obtained through method A vs method B were not significantly different (p = .3)-Fig. 3.

Discussion

Current methods of estimating IEI derive from the original method described by A. Marmarou and later modifications by Szewczykowski et al. and by Czosnyka et al. [9,10,14,17,20,21] Despite these original methods and their derived methods are fast and practical, question remains on their reliability and accuracy. The main limitation of these methods is that CSFPPAmp can widely vary during the infusion test. In fact, the shape of the ICP waveform can deeply vary during the infusion test (Fig. 2) and the P2 component can become much higher than the P1 component of the waveform (as in patients belonging to group 2). Therefore, the point where to measure each single wave amplitude also changes, from wave to wave. Czosnyka et al., whose method was based on the assumption that the fundamental harmonic of the pulse waves reflects the CSFPPAmp variations, also confirmed that the slope of the fundamental harmonic/pressure curve and the slope of the CSFPPAmp/pressure curve may be different, depending on the shape of each single pulse wave. Moreover, the analysis of 6-12 CSF pulse waves (instead of the analysis of each single wave) may constitute a further limitation of these methods based on the analysis of clusters of waves [21].

Our method (method C) was compared with the previously described, gold standard methods (methods A and B). The only way to compare these methods and to establish which one was the most reliable (from a theoretical-mathematical point of view) was to evaluate and compare the R-squared for each method. The higher the R-squared, the more statistically significant the linear relationship between the two variables.

Our study showed that R² rates obtained with method C were significantly higher than those obtained with the other methods and were very high, nearest to 1 (that is maximum, ideal, statistical significance) (Table 1).

Another important finding of this study was that when the CSF pulse wave presented few or no changes in its shape due to ICP rising, R² rates of the three methods were very high (all near to 1) and there was no difference among the R² mean values. Instead, for patients whose baseline CSF pulse wave shape progressively changed during the infusion test, there was a remarkable difference.
among the mean $R^2$ values, being $R^2$ obtained through method C the highest (near to 1), and mean $R^2$ obtained through the other two methods strikingly and significantly lower.

These results seem to demonstrate that CSF pulse wave integral is completely insensitive to changes in the CSF pulse wave morphology. This novel technique may improve the clinical relevance of ICP waveform analysis, but prospective clinical studies are warranted to substantiate this suggestion.

Disclosure

The authors report no conflict of interest concerning the methods and the results of this study.

References


