Intracranial volume-pressure relationship in man

Part 2: Clinical significance of the pressure-volume index

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Pressure-volume indices (PVI's) were determined for a heterogeneous group of 40 patients who underwent continuous monitoring of ventricular fluid pressure (VFP). The main purpose was to investigate the relationship between VFP and PVI and to establish the significance of the measured PVI values. Determinations of PVI appear to be useful only when baseline VFP is under 20 mm Hg, maximum VFP is under 30 mm Hg, A-waves are absent, and B-waves do not occur numerous. The authors advocate starting with 1-ml bolus infusions, and then, when the resulting pressure rise exceeds 4 mm Hg, additional bolus infusions can be omitted. Results indicate that 13 ml and 10 ml are the key values for the PVI. A PVI of less than 13 ml indicates the need for either reduction of VFP and improvement of compliance or intensive monitoring of both the VFP and the volume-pressure relationship; if the PVI is below 10 ml, anti-hypertensive treatment is almost always necessary. Values of PVI's between 13 and 18 ml, although pathological, usually have no therapeutic consequences.

KEY WORDS • pressure-volume index • pressure-volume relationship • intracranial pressure • ventricular fluid pressure • volume-pressure response

Since the original studies of Guillaume and Janny and Lundberg, many investigators have shown the usefulness of continuous monitoring of intracranial pressure (ICP) in the management of various disorders associated with intracranial hypertension. The first reports on the value of volume-pressure determinations were published in the early 1970's. Rapid administration of fluid into the craniospinal space and measurement of the resulting pressure changes was said to be useful for identification of patients at risk for a dangerous increase in ICP in the near future. The pressure-volume index (PVI), defined by Marmarou, et al., as the volume of a bolus infusion required to achieve a tenfold increase in the opening pressure, is the best known parameter for assessment of the volume-pressure relationship or compliance of the craniospinal space. The concept of Marmarou has been extensively tested by means of mathematical models and animal experiments and in some clinical studies. The existence of a monoexponential relationship between volume and pressure has been confirmed by most authors. Several of them have demonstrated that a better approximation of the PVI is obtained when the mathematical function describing the relationship between volume and pressure includes a constant term.

Taking into account the fact that Marmarou introduced the PVI in 1973, surprisingly few determinations of the PVI in patients have been reported. The present study was undertaken to investigate the diagnostic value of the PVI for a heterogeneous group of neurological and neurosurgical patients who underwent continuous monitoring of ventricular fluid pressure (VFP). By relating the data on the VFP recording to that of the bolus infusions, we attempted to establish when and how the PVI should be determined, as well as the significance of the measured PVI values.

Clinical Material and Methods

The VFP of 40 patients was monitored continuously for a mean period of 73.6 hours (Table 1). An intraventricular catheter was connected to an extracranial pressure transducer and an electromanometer.* A chart

*Extracranial pressure transducer and electromanometer manufactured by Hewlett-Packard Co., Palo Alto, California.
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TABLE 1
Diagnosis and age of 40 patients in this series

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No. of Cases</th>
<th>Age (yrs)</th>
<th>Mean</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>subarachnoid bleeding</td>
<td>12</td>
<td>52.7</td>
<td>26-76</td>
<td></td>
</tr>
<tr>
<td>space-occupying lesion</td>
<td>9</td>
<td>53.0</td>
<td>40-68</td>
<td></td>
</tr>
<tr>
<td>noncommunicating hydrocephalus</td>
<td>8</td>
<td>32.0</td>
<td>10-66</td>
<td></td>
</tr>
<tr>
<td>communicating hydrocephalus</td>
<td>6</td>
<td>53.2</td>
<td>11-72</td>
<td></td>
</tr>
<tr>
<td>head injury</td>
<td>3</td>
<td>37.7</td>
<td>22-64</td>
<td></td>
</tr>
<tr>
<td>benign intracranial hypertension</td>
<td>2</td>
<td>30.0</td>
<td>12-48</td>
<td></td>
</tr>
</tbody>
</table>

recorder was set at a scale of 1 mm Hg/mm with a paper speed of 1 mm/min. The following data were extracted from the pressure curve during each 24-hour period: 1) modal pressure (Pmod), being the baseline or most frequently occurring pressure during that 24-hour period; 2) maximum pressure (Pmax), defined as the highest pressure recorded for at least 10 minutes during that 24-hour period (all pressures were grouped into pressure classes of 5 mm Hg; a Pmod of 15 mm Hg or less, and a Pmax of 20 mm Hg or less were considered normal); 3) A-waves, spontaneous plateau-shaped pressure elevations with an amplitude of 20 mm Hg or more and a duration of more than 5 minutes; and 4) B-waves, rhythmic waves with a frequency of 0.5 to 2/min, an amplitude of 5 mm Hg or more, and a duration of longer than 10 minutes. During VFP recording, a series of five to 10 (mean 6.7) bolus infusions of 1 ml of saline was administered once a day, yielding a total of 114 series of infusions. During the infusion tests the paper speed was increased to 100 mm/min and the mean pressure was displayed. With a 5-ml syringe, a rapid bolus infusion of 1 ml was administered without interrupting the pressure recording, thus producing an artificial pressure peak within the first 10 seconds after injection. Therefore, we measured the pressure plateau or mean pressure between the 10th and 20th second after injection. Each time a new stable VFP level was reached this procedure was repeated. In order to avoid pressure waves, the increase in pressure was limited, when necessary, by withdrawing cerebrospinal fluid (CSF) in amounts of 1 ml. In a few patients with high baseline pressures, VFP had to be reduced before administering the bolus infusions. The mean difference between the resting pressure and the highest pressure level at which infusion was carried out amounted to 14.3 mm Hg (range 4 to 30 mm Hg). The time interval between two infusions was usually 1 to 2 minutes. For each series of 1-ml infusions we determined one volume-pressure response (VPR) and one PVI.

The VPR was obtained from the first 1-ml injection administered at baseline pressure. If more than one injection was administered at baseline pressure, the mean of the VPR’s was calculated. The PVI was calculated from a monoexponential relationship with a constant term and the maximum likelihood estimation of functional relationship.22 Shapiro, et al.,16 found PVI values of 17.9 to 30.5 ml for 23 normal patients aged 3 to 55 years. On the basis of their results we consider 18 ml to be the lower limit of a normal PVI.

For 25 days a number of patients underwent continuous CSF drainage so that no information on the actual VFP level or the occurrence of pressure waves was available. Therefore, analysis of the relationship between PVI and VFP was based on the remaining 89 24-hour epochs, for each of which we determined one Pmod, one Pmax, one VPR, and one PVI.

Results

The data from the VFP recordings of 40 patients taken during 89 24-hour epochs are summarized in Fig. 1. The baseline pressure varied from 6-10 to 36-40 mm Hg, the most frequently occurring Pmod being 11 to 15 mm Hg. The curve of Pmax showed a peak at 15 to 25 mm Hg and declined gradually to the highest Pmax of 86 to 90 mm Hg. Pmax values of greater than 40 mm Hg often originated from A-waves that occurred in 23 epochs with an increased Pmod. B-waves were seen during 55 epochs at normal as well as elevated Pmod levels.

VFP Related to PVI

The relationship between Pmod, Pmax, and the occurrence of pressure waves on the one hand and PVI on the other are shown in Figs. 2, 3, and 4. Regression analysis of Pmod and Pmax versus the PVI yielded low coefficients of correlation. The most conspicuous result was that a Pmod greater than 20 mm Hg, a Pmax greater than 30 mm Hg, and the presence of A-waves...
were invariably associated with a PVI of less than 13 ml. At normal baseline pressures a wide variation in PVI values was found: 57% were below 13 ml, 28% between 13 and 18 ml, and 15% above 18 ml. Contrary to expectations, the correlation between Pmax and PVI was even worse than that between Pmod and PVI. At maximum pressures below 30 mm Hg the PVI varied widely, between 30 and 50 mm Hg the PVI was smaller, and above 50 mm Hg the PVI was larger than predicted. A-waves were accompanied by low PVI values (mean 8.4 ± 2.6 ml) but the absence of A-waves had little predictive value regarding the PVI. B-waves were accompanied by a PVI of less than 18 ml in 100% and by a PVI of less than 13 ml in 93% of epochs, demonstrating that these waves are almost as good an indicator of low compliance as A-waves. The mean PVI during epochs without B-waves was comparatively high (15.2 ± 4.6 ml). Because B-waves occur much more frequently than A-waves at normal or mildly elevated pressures, their value for the assessment of the volume-pressure relationship is greater.

When several parameters of the VFP recording were combined, the differentiation between high and low compliance barely improved (Table 2). For instance, patients exhibiting a Pmod of 15 mm Hg or less without B-waves had a mean PVI of 15.3 ± 4.64 ml compared with a mean PVI of 13.6 ± 4.72 ml for a Pmod of 15 mm Hg or less alone, and a mean PVI of 15.2 ± 4.56 ml when only B-waves were absent. The highest mean PVI (16.5 ± 5.21 ml) was calculated for 19 epochs featuring a Pmod of 15 mm Hg or less, a Pmax of 20 mm Hg or less, and no A- or B-waves; in other words

**FIG. 2.** Plot of modal pressure (Pmod, all pressures grouped into pressure classes of 5 mm Hg) against the pressure-volume index (PVI). n = 89. Regression equation: \( y = -0.18x + 14.9; r = -0.39; p < 0.01. \)

**FIG. 3.** Plot of maximum pressure (Pmax, all pressures grouped into pressure classes of 5 mm Hg) against the pressure-volume index (PVI). n = 89. Regression equation: \( y = -0.17x + 18; r = 0.27; p < 0.01. \)

**FIG. 4.** Distribution of pressure-volume index (PVI) values recorded during 66 epochs without A-waves, 23 epochs with A-waves, 34 epochs without B-waves, and 55 epochs with B-waves. The mean values and standard deviations of the PVI are indicated in the figure.
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TABLE 2
Mean PVI at different values of Pmod, Pmax, and Evans index with or without pressure waves*

<table>
<thead>
<tr>
<th>Parameters</th>
<th>No. of Epochs</th>
<th>PVI (ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pmod ≤ 15 mm Hg</td>
<td>46</td>
<td>13.6</td>
</tr>
<tr>
<td>Pmod &gt; 15 mm Hg</td>
<td>43</td>
<td>9.4</td>
</tr>
<tr>
<td>Pmax ≤ 20 mm Hg</td>
<td>24</td>
<td>14.9</td>
</tr>
<tr>
<td>Pmax &gt; 20 mm Hg</td>
<td>65</td>
<td>10.3</td>
</tr>
<tr>
<td>no A-waves</td>
<td>66</td>
<td>12.7</td>
</tr>
<tr>
<td>A-waves present</td>
<td>23</td>
<td>8.4</td>
</tr>
<tr>
<td>no B-waves</td>
<td>34</td>
<td>15.2</td>
</tr>
<tr>
<td>B-waves present</td>
<td>55</td>
<td>9.4</td>
</tr>
<tr>
<td>Pmod ≤ 15 mm Hg, no B-waves</td>
<td>30</td>
<td>15.3</td>
</tr>
<tr>
<td>Pmod &gt; 15 mm Hg, B-waves present</td>
<td>39</td>
<td>9.0</td>
</tr>
<tr>
<td>Pmax ≤ 20 mm Hg, no B-waves</td>
<td>20</td>
<td>15.9</td>
</tr>
<tr>
<td>Pmax &gt; 20 mm Hg, B-waves present</td>
<td>51</td>
<td>9.3</td>
</tr>
<tr>
<td>no A-waves or B-waves</td>
<td>33</td>
<td>15.4</td>
</tr>
<tr>
<td>A-waves &amp; B-waves present</td>
<td>22</td>
<td>8.4</td>
</tr>
<tr>
<td>Pmod ≤ 15 mm Hg, Pmax ≤ 20 mm Hg, no A-waves or B-waves</td>
<td>19</td>
<td>16.5</td>
</tr>
<tr>
<td>Pmod &gt; 15 mm Hg, Pmax &gt; 20 mm Hg, A-waves &amp; B-waves present</td>
<td>22</td>
<td>8.4</td>
</tr>
<tr>
<td>Evans index ≤ 0.30</td>
<td>31</td>
<td>12.3</td>
</tr>
<tr>
<td>Evans index &gt; 0.30</td>
<td>58</td>
<td>11.2</td>
</tr>
</tbody>
</table>

* PVI = pressure-volume index; Pmod = modal pressure; Pmax = maximum pressure; SD = standard deviation.

a normal VFP recording. Yet the PVI was less than 18 ml in 63% and less than 13 ml in 37% of these epochs, demonstrating that compliance may be low even if VFP is completely normal for 24 hours.

The mean PVI found for 31 epochs with an Evans index of 0.30 or less was not appreciably different from that found for 58 epochs with an Evans index greater than 0.30, showing that the volume of the CSF compartment had little influence on the PVI in these adult patients.

PVI Related to VFP

The distribution of Pmod and Pmax at four levels of the PVI is depicted in Fig. 5. A PVI of less than 10 ml was virtually always associated with an increased baseline pressure and/or maximum pressure. At PVI values below 10 ml we encountered the highest pressures, which included 74% of the A-waves and 58% of the B-waves. A PVI between 10 and 13 ml was accompanied by a normal Pmod in 60% and a normal Pmax in almost 40% of epochs. The lower limit of a normal PVI was defined as 18 ml. Patients exhibiting a PVI between 13 and 18 ml appeared to have abnormal VFP recordings in 63% of epochs; however, baseline pressure was mostly normal, A-waves were absent, and the maximum pressure did not exceed 30 mm Hg.

VPR Related to PVI

The magnitude of the VPR depends on the level of VFP, and therefore only volume-pressure responses evaluated at baseline pressure can be used to compare compliance among patients. Like Miller, et al., we consider a VPR of 2 mm Hg or less to be normal and a VPR greater than 4 mm Hg to be definitely pathological. Indeed, only PVI values of 12 ml or less were found when the initial VPR was over 4 mm Hg (Fig. 6), indicating that further bolus infusions can be omitted. On the other hand, a VPR of 2 mm Hg or less certainly was not always associated with a normal PVI. Since the correlation coefficient calculated from regression analysis of VPR and PVI was as low as −0.33, we conclude that the VPR does not provide reliable information about the volume-pressure relationship. Particularly when the VPR is 4 mm Hg or less, additional bolus infusions should be administered in order to be able to determine the PVI.

It is concluded that a PVI of less than 13 ml indicates a pathologically decreased compliance. When the PVI

Fig. 5. Distribution of modal pressures (Pmod) and maximum pressures (Pmax) (all pressures grouped into pressure classes of 5 mm Hg) at four levels of the pressure-volume index (PVI). A signifies a PVI of greater than 18 ml, B a PVI of 13.1 to 18 ml, C a PVI of 10 to 13 ml, and D a PVI of less than 10 ml. The solid and dashed lines represent the number of epochs during which the relevant values of Pmod and Pmax, respectively, were recorded. VFP = ventricular fluid pressure.

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The PVI is a measure of compliance or distensibility of the CSF compartment, but it refers only to the pressure changes caused by uncompensated rapid volume changes. However, pathological volume changes of the intracranial contents do not occur rapidly, and the PVI provides little information about the capacity to accommodate an additional volume.\textsuperscript{18,19} This capacity for spatial compensation depends mainly on the functioning of the CSF absorption system. Marmarou, et al.,\textsuperscript{6} demonstrated how the resistance to outflow of CSF can be calculated from the pressure decay after a single bolus injection. Although theoretically attractive, we find this method to be inaccurate for patients. Particularly in the event of high resistance or low compliance, it is difficult to obtain a pressure decay measurement undisturbed by artifacts, and resistance values tend to vary considerably. We prefer a constant infusion or constant pressure infusion test to determine CSF outflow resistance, certainly under conditions of relatively stable hydrodynamics. In patients with head injuries, the intracranial hydrodynamics may change rather frequently. Since for practical reasons it is almost impossible to perform repeated steady-state infusion tests, bolus infusions are more suitable for identifying those patients who may develop a dangerously elevated ICP.

There is no general agreement on how to administer the bolus infusions. Miller, et al.,\textsuperscript{11} performed multiple 1-ml infusions at different times and at different levels of resting pressure. Shapiro, et al.,\textsuperscript{16} first removed 2 ml of CSF and used the PVI calculated from this maneuver to determine a safe volume for subsequent infusions. Sullivan and co-workers\textsuperscript{21} calculated a safe injection volume from three volume-pressure responses while requiring that the cerebral perfusion pressure never drop below 40 mm Hg. The maximum infused volume for their six patients varied from 5 to 7 ml. We agree that the best method is to start with a few 1-ml infusions in steps of 1 ml while never exceeding a VFP of 50 mm Hg. After each infusion, VFP should be allowed to return to baseline level. We do not recommend giving the 1-ml infusions at increasing VFP levels, as in this study, because 1) this procedure is time-consuming, 2) VFP is insufficiently raised for determination of the PVI in some patients with a high compliance, 3) the error in evaluating the pressure difference is larger, and 4) calculation of the resistance to outflow of CSF be-
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comes very complicated. During infusion, the VFP recording should not be interrupted and the injection of saline into the CSF space should preferably occur via a different channel from that used to monitor the pressure. In this way, the true peak of the pressure response is recorded. To circumvent the problem of measuring the pressures in the same phase of the cardiac and respiratory cycles, computer analysis of the pressure signal is recommended. In a previous publication, we demonstrated that a monoexponential function with a constant term provides the best approximation of the PVI.

When is it useful to determine the volume-pressure relationship? We studied the relationship between VFP and PVI irrespective of the nature of the intracranial disorder. This heterogeneous group contained patients with mass lesions as well as diffuse brain damage or a disturbed CSF outflow. Patients showing a baseline pressure of greater than 20 mm Hg or a maximum pressure of greater than 30 mm Hg are on or very near the steep vertical part of the volume-pressure curve. Volume-pressure determinations in these cases are both superfluous and not without danger. The same holds true for the presence of A-waves. B-waves were also almost invariably associated with a small PVI and, certainly if they are numerous, volume-pressure tests can be omitted. For patients exhibiting a normal or mildly elevated VFP without pressure waves, determination of the PVI may provide valuable information. The frequency of PVI determinations depends on the changes in VFP in the course of time, the neurological status, and the computerized tomography findings. The time required to complete the bolus infusions, together with the associated risks of infection and induced pressure rises, restrict the number of measurements considerably.

The PVI is a measure of compliance, but its magnitude depends on many other factors such as neural axis volume, CSF outflow resistance, systemic arterial pressure, and arterial pCO2. It has been suggested that the PVI is suitable for comparison of the compliance at different times in one patient but not for comparison among patients. Our results, however, indicate that a number of limits of the PVI are applicable to all conditions associated with intracranial hypertension in adult patients. Although a PVI of less than 18 ml has to be considered pathological, we have found that 13 and 10 ml are the key PVI values. A PVI of less than 10 ml points to a dangerously tight brain that requires treatment at short notice, even in the rare event of a normal VFP. A PVI of 10 to 13 ml will be accompanied more often by a normal or mildly elevated VFP, indicating that the patient is on the horizontal part of the volume-pressure curve but close to the vertical part. In patients showing neurological deterioration, an increasing shift of midline structures, or discrete signs of a rising VFP, a PVI of 10 to 13 ml should encourage the initiation of vigorous medical or surgical therapy to reduce VFP and improve compliance. Such therapy will rarely be needed for patients with PVI values between 13 and 18 ml, and the bolus infusions have to be repeated less frequently. It is concluded that volume-pressure determinations are useful, but only for a limited number of patients; namely, those with head injuries who have a normal or mildly elevated VFP without pressure waves. For the interpretation of the results of these tests, 13 and 10 ml should be characterized as the critical PVI values.

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