Pressure-volume index as a function of cerebral perfusion pressure

Part 2: The effects of low cerebral perfusion pressure and autoregulation

W. JOHN GRAY, F.R.C.S., AND MICHAEL J. ROSNER, M.D.

Division of Neurosurgery, University of Alabama, Birmingham, Alabama

The pressure-volume index (PVI) was measured in six adult cats while cerebral perfusion pressure (CPP) was reduced from normal levels to below the autoregulatory range by a continuous infusion of adenosine triphosphate. Anesthesia was induced with methohexital and maintained with an N₂O:O₂ (70%:30%) mixture. Body temperature, hematocrit, and PaCO₂ were held constant throughout each experiment. Cerebral blood flow (CBF) was measured by the hydrogen clearance method. At CPP levels over 50 mm Hg, CBF remained relatively constant despite changes in CPP. Within this range, the PVI varied directly with CPP (PVI = 0.24 ml + 0.0013 mm Hg CPP). Below the autoregulatory range, CBF fell progressively with further decreases in CPP; in this range, PVI was found to increase as CPP fell (PVI = 0.84 ml - 0.0071 mm Hg CPP). These results indicate that the PVI is a complex function of CPP, varying directly with CPP within the autoregulatory range and indirectly with CPP below the autoregulatory range.

KEY WORDS pressure-volume index • cerebral perfusion pressure • cerebral blood flow • autoregulation • intracranial pressure

Previous studies of the relationship of cerebral perfusion pressure (CPP) changes to "brain stiffness," whether measured by compliance, elastance, volume pressure response, or pressure-volume index (PVI), have suggested that at normal levels of intracranial pressure (ICP), "brain stiffness" does not change significantly when CPP is changed within the 50- to 160-mm Hg range. Recent work by us in cats has shown that deep barbiturate anesthesia nearly obliterates the relationship between PVI and CPP, but under light anesthesia cats showed a significant positive relationship between PVI and CPP, with the PVI varying directly with CPP in the 50- to 160-mm Hg range.

Most authors believe that the PVI is a measure of the intracranial vascular response to an induced volume change. A suggested explanation for the discrepancy of results between deep and light anesthesia is that under deep barbiturate anesthesia the cerebrovascular resistance (CVR) is held relatively constant despite CPP changes, while under light anesthesia a more normal physiological response is seen with vessels changing in diameter as CPP is changed within the autoregulatory range. At low CPP, when vessel diameter and intracranial blood volume are presumably maximal, the ability to accommodate a volume load is at its minimum, and this is reflected by a low PVI. The present study was undertaken to test the hypothesis that the PVI will be at its lowest at the lower limit of autoregulation, and will increase at CPP values below the autoregulatory range, when cerebral blood flow (CBF) diminishes.

Materials and Methods

Six adult cats of either sex, each weighing 2.5 to 4.5 kg, were used in this study. Anesthesia was induced in each animal with intravenous methohexital sodium (10 mg/kg). The animals were then paralyzed with pancuronium bromide (0.2 mg/kg), intubated endotracheally, and ventilated with a 70% N₂O:30% O₂ mixture. Details of the surgical preparation, placement of catheters, and monitoring of ICP, PaCO₂, body temperature, and hematocrit have been given previously. Cerebral perfusion pressure was reduced in all animals by means of a continuous infusion of a fresh solution containing 5
mg/ml adenosine triphosphate (ATP) in 0.9% NaCl at rates of 0.2 to 3.0 mg/min.

Cerebral blood flow was measured by the hydrogen clearance method. Insulated platinum electrodes were constructed using a platinum (90%)-iridium (10%) wire, diameter 0.007 in., and a bare tip of 2 mm. An electrode was placed in each caudate nucleus, and in the deep frontal white matter bilaterally. The electrodes were polarized to +450 mV. A stainless steel reference electrode was positioned in the posterior cervical muscles. The electrodes were sealed in position with quick-setting cyanoacrylic glue. Ten percent hydrogen gas was introduced into the inspired gas mixture until the electrode currents were stable, and the ensuing washout curves were recorded.* The regional CBF for each electrode was then calculated from the equation: CBF (ml/100 gm/min) = 69.3/Tₜ, where Tₜ = the time in minutes required for the electrode current (representing H₂ concentration) to fall to half of its original value. Cerebrovascular resistance was calculated from the formula: CVR (mm Hg/ml/100 gm/min) = CPP (mm Hg)/CBF (ml/100 gm/min).

The PVI was calculated from the ICP response to a bolus of 0.1 ml of 0.9% NaCl solution injected over a period of 1 second into the lateral ventricle, by the equation:

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PVI_{(ml)} = \frac{V}{P_P - P_o} \log_{P_P}
\]

where \(V\) = volume injected (ml), \(P_P\) = peak ICP after injection (mm Hg), and \(P_o\) = baseline ICP before injection (mm Hg).

In each animal, a baseline CBF was identified and a series of three PVI estimations were made. The CPP was then reduced by ATP infusion. Measurements of PVI and CBF were recorded at steady-state CPP levels in the midpoint of the autoregulatory range (100 to 110 mm Hg), at the lower limit of the autoregulatory range (50 to 60 mm Hg), and below the autoregulatory range (< 50 mm Hg). Blood gas levels and hematocrit were measured at each new level of CPP, and adjusted as required to maintain constant values.

**Results**

A total of 76 PVI estimations were made in the six animals. These were divided into two groups, depending upon the autoregulatory range of the animal at the time of the PVI measurement. When CBF remained constant (flow changing by less than 15% from the baseline measurement while CPP was reduced) the PVI measurement was considered to have been made within the autoregulatory range. Forty-one PVI measurements fell into this category. The lower limit of autoregulation was considered to have been reached or exceeded when CBF decreased quickly (more than 15% reduction) with further reductions in CPP. Thirty-five PVI measurements were made in this range (that is, below the lower limit of autoregulation).

Within the autoregulatory range, a relationship was found between PVI and CPP similar to that described in our previous study using methohexital anesthesia.†

The PVI decreased as CPP was decreased (PVI = 0.24 ml + 0.0013 mm Hg CPP) (Fig. 1 left). In contrast, once the lower limit of autoregulation had been exceeded, the relationship between PVI and CPP reversed: as CPP was reduced further, the PVI increased; in effect, the PVI varied indirectly with CPP (PVI = 0.84 ml - 0.0071 mm Hg CPP) (Fig. 1 right). The lowest values of PVI were found at the lower limit of autoregulation. Both of these relationships were statistically significant (p < 0.001).

The exact point at which the lower limit of autoregulation was breached varied with individual animals from 40 to 60 mm Hg, with the mean lower limit being 50 mm Hg. Within the autoregulatory range, CBF fell slightly as CPP was decreased (CBF = 31.0 ml/100 gm/min + 0.079 mm Hg CPP), while below the lower limit of autoregulation, there was a marked decrease in CBF as CPP fell (CBF = 7.0 ml/100 gm/min + 0.527 mm Hg CPP). Upon examining the relationship between PVI and CVR, we found that, within the autoregulatory range, when CVR varied directly with the CPP, PVI was estimated at 0.35 ml + 0.007 mm Hg/ml/100 gm/min CVR. In contrast, below the autoregulatory range, PVI values rose as CVR was reduced (PVI = 0.69 ml - 0.127 mm Hg/ml/100 gm/min CVR); thus, PVI varied directly with CVR.

Comparison of the baseline ICP levels before each PVI measurement and hematocrit levels within and below the autoregulatory range did not reveal any significant differences. There was a small difference in the PaCO₂ levels between the two ranges (1.3 mm Hg), but it was concluded that this had no influence on the results. These findings are summarized in Table 1 and show the following: 1) Within the autoregulatory range, PVI decreased as CPP was decreased; PVI varied directly with CPP and CVR when measured below the lower limit of autoregulation. 2) Below the lower limit of autoregulation, PVI increased as CPP was decreased. Within this range, PVI also increased as CVR was reduced; thus, PVI varied indirectly with CPP and CVR when measured below the lower limits of autoregulation. 3) The PVI was minimal (volume tolerance was lowest) at the lower limit of autoregulation, with the best values of PVI being found at the very highest and lowest CBF values.

**Discussion**

In a previous publication on the effects of CPP changes on PVI,† it was established that, under light methohexital anesthesia, there was a direct relationship between PVI and CPP; PVI increased in a linear fashion with increasing CPP within the 50- to 160-mm Hg range. Although we did not measure CBF in these animals, the relationship between PVI and CPP was very similar to that found within the autoregulatory range in the present study. Our results are similar to

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* Polygraph, Model 7D, manufactured by Grass Instrument Co., Quincy, Massachusetts.
Effects of low CCP and autoregulation on pressure-volume index

FIG. 1. Scattergrams showing the pressure-volume index (PVI) versus cerebral perfusion pressure (CPP). The linear regression equation for the group is given. Each point represents the average of three PVI determinations. Left: Values within the autoregulatory range showing a positive relationship between PVI and CPP. Note the positive slope. These determinations were considered as falling within an intact autoregulatory range if they varied no more than 15% from baseline blood flows. Right: Values below the autoregulatory range. If blood flow was more than 15% below the baseline flow, values were judged to be outside the autoregulatory range. Note the markedly negative slope which represents a reversal of the relationships shown left. basically, when the experimental conditions were such that the animal was below the lower limits of autoregulation the PVI appears to “improve” as CPP is reduced further.

TABLE 1
Experimental group variables in and below autoregulatory range

<table>
<thead>
<tr>
<th>Variable</th>
<th>Autoregulatory Range</th>
<th>Below Autoregulatory Range</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean &amp; SD</td>
<td>No. of Tests</td>
</tr>
<tr>
<td>CPP (mm Hg)</td>
<td>107 ± 21</td>
<td>41</td>
</tr>
<tr>
<td>ICPo (mm Hg)</td>
<td>7.5 ± 3.1</td>
<td>41</td>
</tr>
<tr>
<td>pCO2 (mm Hg)</td>
<td>29.5 ± 1.6</td>
<td>25</td>
</tr>
<tr>
<td>hematocrit (%)</td>
<td>30.6 ± 4.3</td>
<td>18</td>
</tr>
<tr>
<td>PVI (ml)</td>
<td>0.38 ± 0.05</td>
<td>41</td>
</tr>
<tr>
<td>CVR</td>
<td>2.7 ± 0.8</td>
<td>39</td>
</tr>
<tr>
<td>CBF</td>
<td>38.9 ± 9.8</td>
<td>39</td>
</tr>
</tbody>
</table>

* Abbreviations: CPP = cerebral perfusion pressure; ICPo = baseline intracranial pressure; PVI = pressure-volume index; CVR = cerebrovascular resistance (in mm Hg/ml/100 gm/min); CBF = cerebral blood flow (in ml/100 gm/min); SD = standard deviation.

those reported by Schettini and Walsh in hypotensive dogs using methohexital anesthesia. They found that compliance decreased as systemic arterial blood pressure was decreased within the autoregulatory range.

We propose that the decrease in PVI that occurs when CPP is reduced within the autoregulatory range is due to the fact that the cerebral blood volume (CBV) increases as CPP is decreased. It has been well established that the cerebral arterial tree dilates progressively as CPP is reduced in the autoregulatory range. A consequence of this vasodilatation is an increase in CBV, as has been demonstrated in the cat by Risberg, et al., who showed a linear correlation between CBF and CBV. At the lower limit of the autoregulatory range, maximum vessel dilatation will occur and CBV will be at its maximum. At this point, the PVI reaches its minimum values.

Below the lower limit autoregulation, an opposite relationship between PVI and CPP was found. As CPP fell within this range (< 50 mm Hg), the PVI started to increase again and continued to increase in a linear relationship but indirectly with CPP reduction. In this range of CPP, the vessels have reached a stage of maximal dilatation, so that reduction of CPP is accompanied by a reduction in CBF, and also by a reduction in CBV. This falling CBV is reflected by a rise in PVI within this range. Using the regression equation for this portion of the curve, we calculated that the PVI would reach a maximum value of 0.69 ml at zero CPP. This is close to the PVI measurements that we derived from postmortem animals.

Although we believe, as others do, that the vascular component is one of the most important determinants of the PVI, other factors besides the CBV may play a part. Within the autoregulatory range, changes in CVR caused minimal although significant change in the PVI. The mean CVR in this range of CPP was 2.7 mm Hg/ml/100 gm/min. However, below the autoregulatory range, the PVI was found to increase as CVR fell. The mean CVR below the autoregulatory limit was 1.9 mm Hg/ml/100 gm/min. The CVR measurements are based on calculations from CPP and CBF measurements. While most of the CVR change is arterial, it is not known how much of this decreased resistance may occur on the venous side of the intracranial vasculature, and in fact, little is known about changes in the venous blood volume during changes in CPP. Shapiro, et al., have suggested that differences in the size of the intracranial venous pool may be one of the main reasons

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for different PVI responses between individuals of the same species and for differences in PVI between different species. The ratio between arterial:venous volumes or either volume to the total CBV may be important. It may be possible that at very low levels of CVR, the ease of egress of blood from the intracranial cavity is improved, and so the pressure response to a volume load is decreased, giving a high PVI value.

In the amounts used in our study, ATP does not appear to have any direct effect on the intracranial vessels. It acts by causing a fall in systemic arterial blood pressure secondary to peripheral vasodilatation, and does not directly alter the CVR.2,3,9

Two other factors that could have influenced CBF directly, and therefore CBV and CVR indirectly, are $\text{PaCO}_2$, and hematocrit. These variables were held constant throughout each study. There was no significant difference between hematocrit levels in each experiment and, although the $\text{PaCO}_2$ levels happened to be slightly lower within the autoregulatory range compared to those below the autoregulatory range, this small difference (1.2 mm Hg) should not have had any great influence on the results.

Conclusions

1. These results support our previous findings that PVI varies directly with CPP within the autoregulatory range,2 and interpretations of PVI must take account of CPP changes. They also establish that great care must be exercised when interpreting PVI measurements below the autoregulatory range.

2. Traditionally, high PVI measurements have been interpreted as indicating a well compensated craniospinal axis. The studies have shown that high PVI measurements will be found below the autoregulatory range when CBF is low and, although this suggests a good tolerance to a volume load, it clearly does not directly alter the CVR.2,3,9

3. These experiments have been conducted in otherwise healthy animals and with presumably normal brains. These conclusions are best applied to similarly normal individuals; it is suspected and preliminary observations support the fact that the discrepancy between PVI and CPP will be more pronounced under conditions where autoregulation is impaired.

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References


Address reprint requests to: Michael J. Rosner, M.D., Division of Neurosurgery, MEB 516, University Station, University of Alabama, Birmingham, Alabama 35294.