Relationships between intracranial pressure, ventricular size, and resistance to CSF outflow

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In 230 patients with normal-pressure hydrocephalus, high-pressure hydrocephalus, or benign intracranial hypertension, measurements of the intracranial pressure (ICP), ventricular size, and cerebrospinal fluid (CSF) outflow resistance (R,) have revealed a linear relationship between ICP and R,. It is shown that on average the CSF formation rate tends to decrease with increasing ICP. It is also shown that the size of the ventricles increases as the ICP levels off toward normal values. The clinical implication of this is that a small or normal ventricular size in acute or subacute phases does not preclude defective CSF resorption.

KEY WORDS • intracranial pressure • hydrocephalus • cerebrospinal fluid • ventricular size

The indication for treatment of clinical conditions caused by impaired cerebrospinal fluid (CSF) outflow is often based on computerized tomography (CT) findings, especially of dilatation of the ventricular system. This is particularly the case in patients with normal-pressure hydrocephalus, a diagnosis that is partially based on CT findings. However, the only two studies on the CT findings and CSF dynamics in patients with hydrocephalus failed to demonstrate any relationship between resistance to outflow of CSF (R,) and the ventricular size as measured by the Evans ratio. This lack of correlation may be explained by either the small clinical samples, samples restricted to patients with normal-pressure hydrocephalus, or an actual absence. In clinical practice the size of the ventricular system is often also used to decide whether the condition (for example, following subarachnoid hemorrhage (SAH) or head injury) is the result of impaired CSF outflow, and the demonstration of a normal ventricular system is thought to exclude the possibility of a defect in CSF resorption. However, studies on CSF dynamics compared to ventricular size in humans are few and have mainly focused on volume-pressure relationships.

Some investigators have shown a clear relationship in animal experiments between the intracranial pressure (ICP), CSF formation rate (CSF), R,, and ventricular size, while others have shown that the relationship between ICP and ventricular size seems to be entirely random.

The purposes of the present study were: 1) to evaluate the relationship between ICP and the size of the ventricles; 2) to establish the relationship between R, and ICP; and 3) to estimate the CSF and its relationship to increased ICP. The study is based on measurements of these parameters in 230 patients with a diagnosis of high-pressure hydrocephalus, benign intracranial hypertension, or normal-pressure hydrocephalus.

Clinical Material and Methods

A total of 230 patients were included in this study (Table 1). The patients were divided into two groups: one group of 168 patients had a mean ICP of 12 mm Hg or below, the other group of 62 patients had a mean ICP above this level. Table 1 summarizes the possible etiology for the disorder, which included normal-pressure hydrocephalus in 168 patients, benign intracranial hypertension in 23, and the acute or subacute state following SAH, meningitis, operation for intracranial tumor, and the like in the remaining 39.

The size of the ventricles was measured on CT scans and expressed as an Evans ratio (width of frontal horns divided by internal skull diameter). In each patient the ICP was measured continuously via an intraventricular catheter, and recorded on a paper-strip recorder.
for at least 24 hours. In 12 patients with benign intracranial hypertension, an epidural pressure transducer was used. The pressure recordings were analyzed for the mean ICP level by measuring diastolic and systolic blood pressure and by calculating mean ICP as diastolic pressure plus one-third of the pulse pressure amplitude.

The \( R_o \) was measured by the perfusion method described by Børgesen, et al.\(^4\) Briefly, the method involves infusion of lactated Ringer's solution through a lumbar cannula or ventricular catheter at a known constant rate at a constant intraventricular pressure level. The absorbed volume is measured at several pressure levels. The correlation between ICP and absorbed volumes is a straight line. The regression coefficient is an expression of the \( R_o \). In the 12 cases where an intraventricular catheter was not inserted, the procedure was modified so that the solution was infused through a lumbar cannula in a similar system.\(^10\)

The statistics were computed using the SPSS software package on a personal computer.\(^*\) Analysis employed cross-tabulation, multiple-regression, and Pearson correlation techniques.

**Results**

Figure 1 displays the distribution of \( R_o \) for the whole series. As can be seen, it varies considerably from normal values (<10 mm Hg/ml/min) to very high values (>100 mm Hg/ml/min). The ICP is plotted against \( R_o \) in Fig. 2, showing that the ICP increases with \( R_o \). Regarded as a linear function, the correlation coefficient is 0.72 (p < 0.001). The slope of the line is 0.3 and the y intercept is 3.9. In Fig. 2, the best-fit curve is shown, calculated by:

\[
\text{ICP} = 3.9 + 0.30 \times R_o. \quad (1)
\]

If the cases with ICP greater than 12 mm Hg are selected, the equation is:

\[
\text{ICP}_{>12} = 19 + 0.14 \times R_o. \quad (2)
\]

The correlation coefficient for this equation is 0.54 (p < 0.001), which indicates that the CSFFR decreases in the higher ICP ranges (mean = 0.14 ml/min in the present series).

In Fig. 3, the ICP is compared to the size of the

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**TABLE 1**

Clinical data in two intracranial pressure (ICP) groups

<table>
<thead>
<tr>
<th>Parameter</th>
<th>ICP ( \leq 12 ) mm Hg</th>
<th>ICP &gt; 12 mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>no. of cases</td>
<td>168</td>
<td>62</td>
</tr>
<tr>
<td>sex (M:F)</td>
<td>98:70</td>
<td>24:38</td>
</tr>
<tr>
<td>age (yrs)</td>
<td>59</td>
<td>46</td>
</tr>
<tr>
<td>mean</td>
<td>61</td>
<td>53</td>
</tr>
<tr>
<td>median</td>
<td>12-87</td>
<td>12-78</td>
</tr>
<tr>
<td>type of CSF disturbance</td>
<td>NPH of unknown cause</td>
<td>109</td>
</tr>
<tr>
<td>trauma</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>subarachnoid</td>
<td>27</td>
<td>19</td>
</tr>
<tr>
<td>hemorrhage</td>
<td>other causes</td>
<td>28</td>
</tr>
<tr>
<td>benign intracranial hypertension</td>
<td></td>
<td>23</td>
</tr>
</tbody>
</table>

*Abbreviations: CSF = cerebrospinal fluid; NPH = normal-pressure hydrocephalus.*

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* Software obtained from SPSS Inc., Chicago, Illinois.
ICP, ventricular size, and resistance to CSF outflow

ventricles expressed as an Evans ratio. Although the plot shows many scattered measurements, it is clear that a relationship between ICP and Evans ratio does in fact exist. The Evans ratio is higher in patients with low or normal ICP (the correlation coefficient is 0.64, p < 0.001). Conversely, small ventricular systems are predominantly seen in patients with increased ICP levels.

In Table 2, the ICP is cross tabulated with the duration of the symptoms. There is a slight tendency toward a short history in patients with high ICP (contingency coefficient = 0.58, chi-square = 80, p < 0.001). The duration of symptoms has a slight influence on R_o (Table 3). The contingency coefficient was 0.51 (chi-square = 68, p < 0.001). Table 4 compares the duration of symptoms with the Evans ratio, divided into four groups. No correlation between the length of the history and large ventricular size could be found.

Discussion

The resistance to outflow of CSF may be increased in a variety of clinical conditions, including normal-pressure hydrocephalus, high-pressure hydrocephalus, benign intracranial hypertension, and protein-producing tumors. These conditions may be distinguished from each other by ICP level, the degree of hydrocephalus, the etiology, and the CT findings. The R_o is increased to some degree in all of them, so these disorders may be considered as “diseases of impaired CSF resorption.” Both the ICP and the R_o may be regarded as representing a continuum from normal values to very high values seen in patients in severe clinical conditions. This present study has shown that the ICP increases with increasing R_o but, interestingly, this correlation was not found to be absolutely linear.

It is commonly accepted that the relationship between ICP, outflow pressure in the sagittal sinus (P_s), CSF_FR, and R_o may be expressed as: ICP = P_s + CSF_FR \times R_o. This equation assumes a linear relationship between ICP and CSF_FR, based on a constant production rate of CSF.13 If this equation is applied to the present series (Equation 1), the opening pressure in the sagittal sinus was 3.9 mm Hg (y intercept) and the CSF_FR was 0.3 ml/min (slope). The correlation coefficient for the curve is satisfyingly high (0.72) and statistically significant (p < 0.001).

Calculation of CSF_FR in the patients with increased ICP (ICP > 12 mm Hg) shows that the formation rate decreases to a mean value of 0.14 ml/min (Equation 2). This result confirms the assumption of decreasing CSF_FR with increasing ICP, proposed by Gjerris, et al.10

![Graph](image-url)

**FIG. 3.** Plot of Evans ratio correlated with intracranial pressure (ICP). The ICP is highest in patients with small ventricles (p < 0.001).
when reporting on a small series of patients with high-pressure hydrocephalus.

A linear relationship between ICP and \( R_o \) is a prerequisite for the determination of \( R_o \) either by bolus-injection methods or perfusion methods. Børgesen and Gjerris, Ekstedt, and Kosteljanetz found the relationship between CSF absorption and pressure to be linear, indicating constant CSF\( \text{FR} \) during the measurements. The decrease in CSF\( \text{FR} \) with increasing ICP in the present study can only be explained by the time factor involved. We “compared” the CSF\( \text{FR} \) between patients with different pressure levels and \( R_o \), but the CSF\( \text{FR} \) remained constant in each individual patient, at least during the time it took to perform a perfusion test.

Most CSF is produced by a filtration process in the choroid plexus, and it is difficult to explain why CSF production decreases with increasing ICP. It may be postulated, however, that the decrease is mainly of the fraction of CSF that originates from the ventricular walls, the brain surface, and perhaps the surface of the spinal cord. It is readily understandable that this excretion of fluid can be hindered by increased ICP.

In the present study the size of the ventricles was inversely correlated to ICP. In the acute phase following SAH or head trauma, for example, an increase in \( R_o \) may result in elevation of the mean ICP, while an increase in ventricular size may take some time to develop. This time factor may be a part of the explanation of the seemingly paradoxical ICP/Evans ratio correlation. If the condition remains untreated, the CSF resorption may improve and the elevated ICP subside to normal levels. The ICP may also decrease as the ventricles grow in size, according to the law of Laplace. This mathematical law states that the pressure decreases with the square of the radius of the cavity and, while the “radius of the ventricles” is a somewhat imaginary concept, it does not hinder application of the law of Laplace to the system.

A number of the cases in this series presented with increased ICP and normal or small ventricular systems. This has been observed in other series of patients with benign intracranial hypertension and in children with small ventricles who have been treated for hydrocephalus and whose shunt malfunctioned. While there may be some reduction in the CSF formation, as shown in the present study, the observation of small ventricles indicates that the absorption of CSF may take place at a high ICP and that this increased ICP does not necessarily lead to dilatation of the ventricles. However, the force on the ventricular walls, calculated according to the law of Laplace, must in these cases be higher than in the cases where the ventricles have dilated. Sklar, et al., proposed that in cases where the ventricles do not dilate, an absorptive reserve exists that enables the ventricular volume to stabilize. Shapiro, et al., explained this absorptive reserve by arguing that a variety of mechanisms of CSF resorption exists, and that each of these mechanisms can be involved separately. In agreement, Page convincingly demonstrated increasing transepidermal resorption with increasing ICP in dogs. The decrease in CSF\( \text{FR} \) in patients with high ICP levels contributes to the understanding of this condition. An equilibrium between small ventricular size and increased ICP may be maintained only because the CSF\( \text{FR} \) is so low that it does not initiate ventricular dilatation.

Conclusions

A linear relationship exists between ICP and \( R_o \), which indicates that increased \( R_o \) is a major factor responsible for increased ICP in the patients comprising the present series. The size of the ventricles, as estimated by the Evans ratio on CT scans, does not give reliable information about the resorptive capacity for CSF. If a clinical condition raises a suspicion of “CSF resorption disease,” this should be investigated by other means (for example, by ICP monitoring or by measurement of \( R_o \)).

The CSF\( \text{FR} \) tends to decrease with increasing ICP. The reduction may amount to more than 50% of baseline formation. This decrease probably plays an important role in the apparent paradox between increased ICP and increased \( R_o \) in patients who exhibit small or normal ventricles on CT scans.

References

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Manuscript received August 19, 1986.
Accepted in final form March 6, 1987.
This work was supported by the Research Foundation of Lundbeck and Eskofot A/S.
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