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Magnetic resonance imaging for quantitative flow measurement in infants with hydrocephalus: a prospective study

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Object. Raised intracranial pressure (ICP) that is associated with hydrocephalus may lead to alterations in cerebral hemodynamics and ischemic changes in the brain. In infants with hydrocephalus, defining the right moment for surgical intervention based on clinical signs alone can sometimes be a difficult task. Clinical signs of raised ICP are known to be unreliable and sometimes even misleading. Furthermore, when sutures are closed, ICP does not always correlate with the size of the ventricles or with the clinical signs or symptoms. In this study the authors investigated whether cerebral blood flow (CBF) can be measured by using quantitative MR angiography in infants with progressive hydrocephalus. In addition, the authors investigated the relationship between CBF and ICP, before and after cerebrospinal fluid (CSF) diversion.

Methods. Fifteen infants with progressive hydrocephalus (age range 1 day–7 months) were examined. All patients underwent anterior fontanel pressure measurement, MR angiography, and mean arterial blood pressure measurements before and after CSF diversion. Brain volume was measured to compensate for the physiological increase in CBF during brain maturation in infants.

Results. The mean preoperative ICP was 19.1 ± 8.4 cm H_2O (± standard deviation). The mean postoperative ICP was 6.7 ± 4.0 cm H_2O ($p < 0.005$). The mean preoperative CBF was 25.7 ± 11.3 ml/100 cm^3 brain/min. After CSF diversion, CBF increased to 50.1 ± 12.1 ml/100 cm^3 brain/min ($p < 0.005$). The mean arterial blood pressure did not change after surgical intervention.

Conclusions. Magnetic resonance imaging can be used to measure CBF in infants with hydrocephalus. Raised ICP was related to a decrease in CBF. After CSF diversion, CBF and ICP improved to values within the normal range. *(DOI: 10.3171/PED/2008/2/9/163)*

Key Words • cerebral blood flow • hydrocephalus • infant • intracranial pressure • magnetic resonance angiography

Hydrocephalus is a common disorder that is encountered in pediatric neurological and neurosurgical practice. A distinction has to be made between spontaneously compensated hydrocephalus without signs of raised ICP and progressive hydrocephalus with raised ICP. In cases of raised ICP, CSF diversion is usually indicated to prevent damage to brain tissue given that elevated ICP is associated with worse neurodevelopmental outcome.[32]

Raised ICP in patients with hydrocephalus may also lead to alterations in cerebral hemodynamics.[34] A decrease in CBF to ischemic levels can lead to irreversible damage.[7,36] Decreased CBF has been observed in animal experiments and in adult patients with raised ICP due to trauma or hydrocephalus.[21,24,36,39,41,52,63,64] Compression of peripheral arterioles by raised ICP can influence CBF significantly.

The distinction between compensated and progressive hydrocephalus can be especially difficult[46] in infants because clinical signs and symptoms can be absent, nonspecific, or unreliable.[28,31,37] Moreover the size of the ventricles on CT scanning or MR imaging[4] does not always correlate with

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Abbreviations used in this paper: AFP = anterior fontanel pressure; BA = basilar artery; CBF = cerebral blood flow; CPP = cerebral perfusion pressure; CSF = cerebrospinal fluid; CVR = cerebral vascular resistance; ICA = internal carotid artery; ICP = intracranial pressure; MABP = mean arterial blood pressure; NPH = normal-pressure hydrocephalus; ROI = region of interest; RTT = Rotterdam Teletransducer.

ICP or neurodevelopmental outcome.[32] Hence there is a need for additional, preferably noninvasive, diagnostic techniques that can help to decide whether CSF diversion should be performed in infants with hydrocephalus. In the Dutch Hydrocephalus and Ischemia Research project, we investigate infants with progressive hydrocephalus by using MR imaging and MR angiography. The aim of this study was to determine whether the following occurs in infants with progressive hydrocephalus: 1) MR angiography can reliably measure CBF; 2) blood flow through the left ICA, the right ICA, and the BA is equally affected; 3) a significant decrease of CBF can be detected; 4) CBF increases after CSF diversion; and 5) whether there may be a relationship between CBF and ICP.

Methods

Patient Population

Fifteen patients with hydrocephalus whose ages ranged between 1 day and 7 months (mean 81 days) were included in the study. Hydrocephalus was diagnosed in these infants by using ultrasonography, CT scanning, or MR imaging. Only patients who underwent a CSF diversion intervention were included, and data were collected pre- and postoperatively. All patients had clinical signs of a progressive hydrocephalus such as progressive increase of head circumference, bulging of the fontanel, engorgement of scalp veins, downward gaze, or decreased level of consciousness. The decision to operate was made on clinical grounds, the presence of raised ICP, and neuroimaging findings. Patients with the combination of hydrocephalus and intraparenchymal lesions, such as an intracerebral tumor, were excluded. Patients with posthemorrhagic hydrocephalus were only included when there was no damage to brain parenchyma, that is, ventricular dilation after Grade II–III intraventricular hemorrhage according to Burstein et al.[14]

Hydrocephalus was diagnosed as communicating in 8 patients and noncommunicating or obstructive in 7 patients. Hydrocephalus was caused by spina bifida in 5 patients (Cases 1, 4, 5, 11, and 15), aqueductal stenosis in 4 patients (Cases 2, 3, 8, and 12), an arachnoidal cyst in 3 patients (Cases 6, 9, and 14), posthemorrhagic ventricular dilation after intraventricular hemorrhage Grade III in 2 patients (Cases 7 and 10), and mucopolysaccharidosis in 1 patient (Cases 13). Descriptive data of the patients are listed in Table 1.

In 12 patients (Cases 1, 3–5, 7, and 9–15) a shunt was inserted, and in 3 patients (Cases 2, 6, and 8) a third ventriculocisternostomy was performed. In case of a third ventriculocisternostomy, flow through the stoma was assessed postoperatively by using MR imaging and was adequate in all 3 patients. No patient had clinical signs of raised ICP postoperatively, which was confirmed by ICP measurement.

The protocol was approved by the Dutch central committee for human research and the medical ethical committee of the University Medical Center Utrecht the Netherlands. Informed consent was given by the children's parents.

TABLE 1

Descriptive data of 15 infants with hydrocephalus

Case No.	Age (wks), Sex*	Cause of Hydrocephalus	Clinical Signs†
1	1, M	spina bifida	1, 2
2	1, F	aqueductal stenosis	1, 2, 3, 4
3	1, F	aqueductal stenosis	1, 2
4	2, M	spina bifida	2, 4
5	2, F	spina bifida	1, 2
6	4, F	arachnoidal cyst	1, 2, 3
7	5, M	posthemorrhagic Grade III	1, 2, 3, 4
8	5, F	aqueductal stenosis	1, 2, 3
9	6, M	arachnoidal cyst	1, 2, 3, 4
10	13, F	posthemorrhagic Grade III	1, 2, 3, 4
11	17, M	spina bifida	1, 2, 4
12	21, M	aqueductal stenosis	1, 2
13	27, F	mucopolysaccharidosis	1, 2, 3
14	31, M	arachnoidal cyst	1, 2, 4, 5
15	33, F	spina bifida	1, 4, 5

* Patient age is noted for the time of inclusion in the study.

† Clinical signs are as follows: 1, progressive increase in skull circumference; 2, bulging of the fontanel; 3, engorgement of scalp veins; 4, setting sun sign; and 5, decreased level of consciousness.

Measurement of ICP

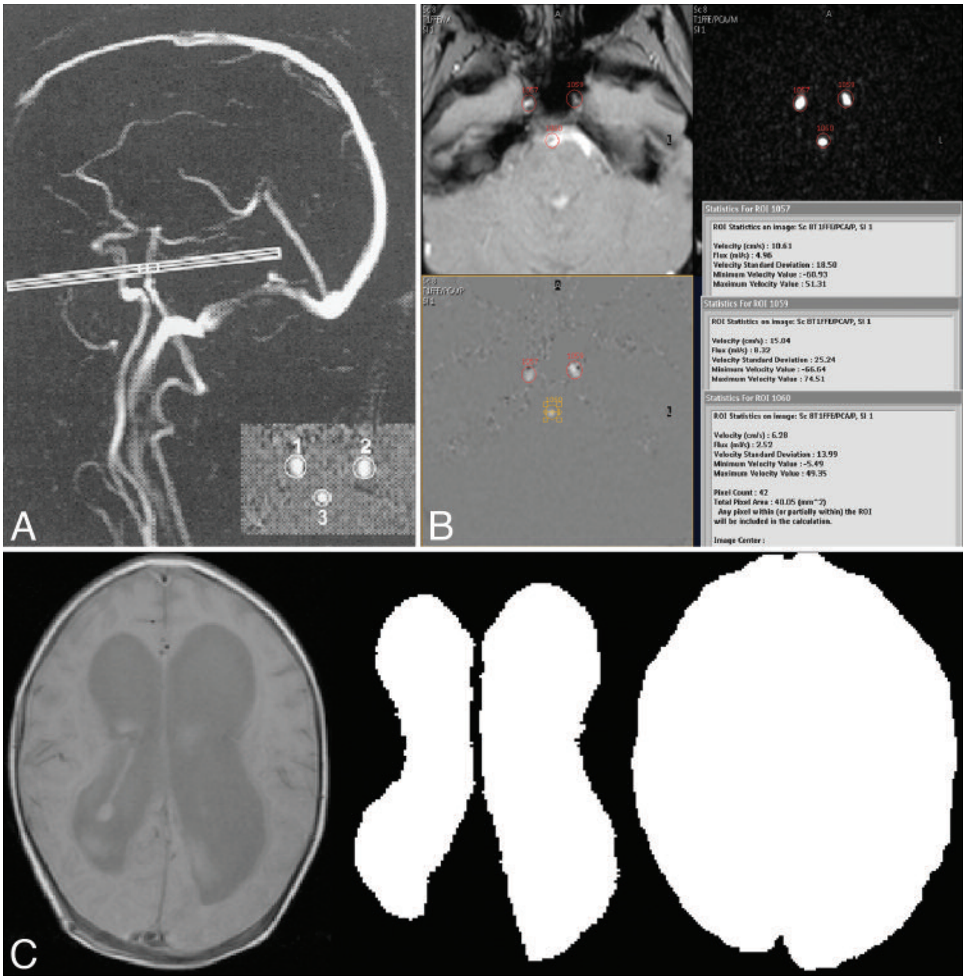
All patients had their AFP measured pre- and postoperatively on the day of MR angiography. The AFP was measured using the RTT, which is known to be a reliable technique with a good correlation (r = 0.96–0.98) to the intraventricular pressure.[55] This transducer, its principles, and the technical details are well described.[17–19] The transducer consists of a passive coil capacitor circuit, inductively energized by an externally located sweep frequency oscillator. The pressure sensor consists of a metal diaphragm that is effectively stretched by moving up the ceramic bearing of the capacitor plate. Therefore, the resistance to deformation is increased and the dynamic range of the diaphragm is augmented. Thus for small deflections a linear relationship between pressure differential load on the diaphragm and the resonance frequency of the transducer circuit can be approximated. The resonance frequency is detected by a monitor that consists of a calibrator circuit and a buffered oscillator continuously sweeping over a narrow band of frequencies. The oscillator signal is then conducted to the detector coil, which is loosely mounted over the adaptor containing the RTT. Transfer of energy to the transducer is established electromagnetically.[56] All patients were asleep (State 1, according to Beintema and Prechtl criteria[8]) without sedation during the measurement. Measurements were performed for at least 60 minutes. The mean value of the AFP was calculated over this period. If the fontanel was already closed or too small for the measurement, ICP was measured directly in the ventricle. Intraventricular ICP measurement was obtained in 4 patients (Cases 3, 8, 10, and 13) on the day of postoperative MR imaging. The AFP and ICP are expressed in cm H_2O. Because the values of AFP are slightly higher than those of ICP,[34,55,58,64,65] AFP values > 20 cm H_2O were reduced by 3 cm H_2O, values between 10 and 20 cm H_2O were reduced by 2 cm H_2O, and values between 5 and 10 cm H_2O were reduced by 1 cm H_2O. The obtained ICP values were compared with normal values[1,3,24,25,30,35,50,56,69–71] both pre- and postoperatively.

Magnetic Resonance Angiography

All infants underwent pre- and postoperative MR imaging. The MR imaging examinations were performed using a 1.5-T imaging unit (Philips Gyroscan NT-Intera Best). On the basis of 2 localizer MR angiograms in the coronal and sagittal planes, a 2D slice was positioned at the level of the skull base to measure the volume flow in the ICAs and the BA (nontriggered; TR 16 msec; echo time 9 msec; flip angle 7.5°; section thickness 5 mm; field of view 250 × 250 mm; matrix size 256 × 256; 8 averages; velocity sensitivity 100 cm/second).[5,6] Figure 1A illustrates the positioning of a 2D phase-contrast slice through the ICAs and the BA. Several studies have shown that phase-contrast MR angiography is a reliable method to quantify volume flow[15,26–28,40,54,57,62] and provides a useful, noninvasive technique to investigate flow changes in patients.[9,12,13,44,66–68] On an independent workstation, quantitative flow values were calculated from the phase-contrast images by using interactive data language-based custom software (Cinetool version 4, General Electric Healthcare). Circular to elliptical ROIs were drawn manually around both ICAs and the BA on the phase-contrast images (Fig. 1A and B). These ROIs encompassed the entire lumen of the vessel. The value of mean signal intensity in each ROI reflected the flow velocity in the vessel (cm/second). Flow (in ml/second) was calculated by multiplying the average velocity with the cross-sectional area of the vessel. To calculate CBF (in ml/minute), flow rates for the ICAs and the BA were added. This method is similar to flow measurement methods described previously.[11,13,24,29,49,61,68,73] Postoperative CBF values were compared with preoperative values and with normal CBF values.[10,16,43]

Mean Arterial Blood Pressure

The MABP (calculated as MABP = diastolic blood pressure + 1/3 × (systolic − diastolic blood pressure)) was calculated pre- and postoperatively from the manually measured systemic blood pressure. The MABP was compared with normal values of infants corrected for age, sex, and height, to investigate whether blood pressure changes account for possible changes in CBF.



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Statistics For ROI 1057
ROI Statistics on image: Sc 8T1FFE/PCA/P, SI 1

Velocity (cm/s) : 10.61
Flux (ml/s) : 4.96
Velocity Standard Deviation : 18.50
Minimum Velocity Value : -60.93
Maximum Velocity Value : 51.31

Statistics For ROI 1059
ROI Statistics on image: Sc 8T1FFE/PCA/P, SI 1

Velocity (cm/s) : 15.04
Flux (ml/s) : 8.32
Velocity Standard Deviation : 25.24
Minimum Velocity Value : -66.64
Maximum Velocity Value : 74.51

Statistics For ROI 1060
ROI Statistics on image: Sc 8T1FFE/PCA/P, SI 1

Velocity (cm/s) : 6.28
Flux (ml/s) : 2.52
Velocity Standard Deviation : 13.99
Minimum Velocity Value : -5.49
Maximum Velocity Value : 49.35

Pixel Count : 42
Total Pixel Area : 40.05 (mm^2)
  Any pixel within (or partially within) the ROI
will be included in the calculation.

Image Center :
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FIG. 1. Images detailing the CBF and volumetric measurements. A: Sagittal localizing MR angiogram illustrating the positioning of a 2D phase-contrast MR angiography section to measure the volume through the ICAs and BA. *Inset:* The 1 indicates the right ICA; 2, the left ICA; and 3, the BA. B: An MR image in which the quantitative flow values are obtained by integrating across manually drawn ROIs that enclose both ICAs and the BA. The CBF is calculated by adding flow values of 1, 2, and 3. C: Brain volume measurement using dedicated in-house-developed image processing software running under imageXplorer; semiautomatic segmentation of the different tissue types is based on the intensities of the different voxels in each image.

Brain Volume

Volume of the ventricles[72] and volume of the brain tissue were measured with dedicated in-house-developed image processing software running under imageXplorer based on region growing[2] (Fig. 1C). The software allows for quantitative volumetric measurement by semiautomatic segmentation of the different tissue types based on the intensities of the different voxels in each image. To define a proper ROI for the brain segmentation process, a preprocessing step (the Brain Extraction Tool) was used to extract the cranium in the different MR images.[60] Volumetric measurements were obtained to express CBF in ml/100 cm^3 brain tissue/min, thus compensating for physiological growth of the brain when comparing MR images from an infant before and after surgery. This is necessary because of the time interval between the pre- and postoperative MR imaging (mean 90 days).

Statistical Analysis

Preoperative and postoperative values were compared using paired t-tests. To analyze associations between CBF values, ICP, and age, paired samples t-tests were used as well as logistic regression analysis. Pearson correlation analysis was used to identify linear relations between ICP, CPP, and CBF.

Results

Mean values are expressed as the means ± standard deviations. In all patients preoperative ICP was increased (mean 19.1 ± 8.4 cm H_2O). After the operation, ICP significantly ($p < 0.005$) decreased to values within the normal range (mean 6.7 ± 4.0 cm H_2O)[1,2,33,50] (Fig. 2 and Table 2). Postoperative intraventricular ICP measurements obtained in 4 patients who had been sedated did not differ significantly from those in the 11 patients in whom ICP was measured using the RTT while patients were asleep (7.0 cm vs 6.5 cm H_2O, respectively). Moreover, the MABP did not differ significantly (69 vs 60 mm Hg, respectively).

The mean preoperative CBF was 25.7 ± 11.3 ml/100 cm^3 brain/min. After CSF diversion, the mean CBF increased significantly ($p < 0.005$) to 50.1 ± 12.1 ml/100 cm^3 brain/min (Fig. 3 and Table 3). The postoperative mean CBF values were within the normal range.[10,16,43]

As a group, the infants with raised ICP had a significantly lower CBF than the infants with postoperatively lower ICP. The relationship between CBF and ICP is more or less linear, showing an ~ 10 ml/100 cm^3 brain/min decrease in CBF with every 10 cm H_2O ICP increase (Fig. 4). The correlation coefficient between CBF and ICP was −0.55 ($p < 0.01$).

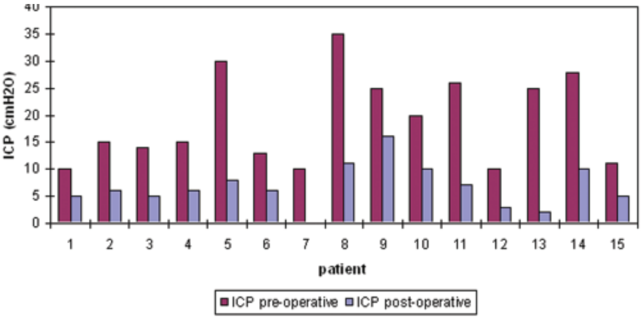

FIG. 2. Bar graph showing pre- and postoperative ICP values.

TABLE 2

Measurement data obtained pre- and postoperatively in 15 patients with hydrocephalus

	Measurement		
Case No.	CBF (ml/min)	ICP (cm H_2O)	MABP (mm Hg)
1			
preop	154	10	58
postop	390	5	63
2			
preop	101	15	58
postop	226	6	57
3			
preop	62	14	54
postop	317	5	64
4			
preop	59	15	56
postop	262	6	63
5			
preop	74	30	58
postop	253	8	63
6			
preop	49	13	57
postop	323	6	60
7			
preop	276	10	64
postop	541	0	62
8			
preop	111	35	68
postop	701	11	78
9			
preop	84	25	62
postop	255	16	63
10			
preop	129	20	75
postop	419	10	67
11			
preop	264	26	52
postop	503	7	50
12			
preop	377	10	77
postop	519	3	73
13			
preop	398	25	60
postop	599	2	67
14			
preop	408	28	67
postop	533	10	53
15			
preop	271	11	63
postop	649	5	48

The CPP was derived from the ICP and MABP and then compared with the CBF. The Pearson correlation coefficient was 0.548 and was significant at the 0.01 level. Their relationship is shown in Fig. 5.

The contribution of the blood flow through the right and left ICAs to the CBF was 34 and 38% preoperatively and 31 and 41% postoperatively, respectively. For the BA the contribution of blood flow was 27% preoperatively and 29% postoperatively. The mean differences were not significant, meaning that raised ICP in hydrocephalic infants affects both left and right as well as anterior and posterior circulation equally.

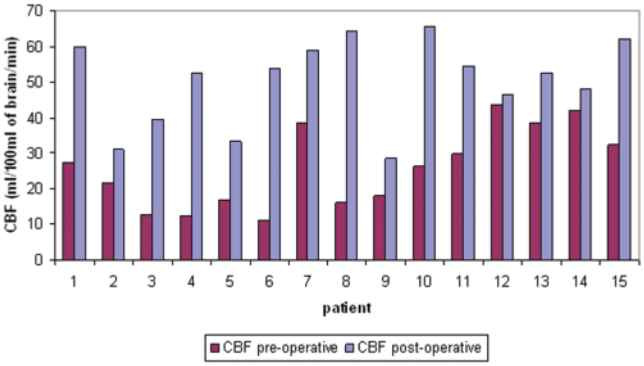

FIG. 3. Bar graph showing pre- and postoperative CBF values.

In all patients the MABP was within physiological limits pre- and postoperatively (mean 61.9 ± 7.3 and 62.1 ± 7.9 mm Hg, respectively)[53] (Table 4).

Discussion

Measurement of CBF with the aid of MR angiography is feasible in infants with hydrocephalus. The technique is noninvasive and can be performed during MR imaging that is indicated for the clinical workup. The quantitative flow measurement by MR angiography through the ICAs and the BA reflects CBF well.[61] To the best of our knowledge this is the first study in which a significant decrease in CBF due to progressive hydrocephalus is found in infants by measuring CBF by using MR angiography. The CBF may improve to values within the normal range after successful CSF diversion.

Several studies have shown a low CBF in patients with hydrocephalus.[39,41,47,65] These studies were performed in adult patients with NPH or chronic hydrocephalus.[33,38,51] The low CBF was explained by a disturbed cerebral autoregulation.[65] Other explanations were distortion of the periventricular vessels caused by ventricular dilation and an increase in blood flow resistance caused by compression of arterioles and veins.[22,51,59]

In patients with hydrocephalus, disturbance of autoregulatory vasomotor capacity also may reduce the CPP, which may lead to CBF reduction.[45] Low CBF may also be caused by a reduction in the number and caliber of capillaries as observed in periventricular regions and cortical regions of patients and animals with hydrocephalus.[17,22,48] In animal experiments reduction of CBF to the 40% threshold is usually well tolerated, and the affected tissue is not at risk of ischemia under uncomplicated conditions.[7] If CBF decreases further, brain parenchyma can become irreversibly damaged and will progress to infarction depending on the duration of ischemia. Selective neuronal death may also occur, even with only mildly reduced CBF values.[7,36]

The increase of CBF after CSF diversion found in adult patients with idiopathic chronic hydrocephalus was ~ 50%,[39] whereas this increase was not significant in patients with NPH.[42,45] According to our study, progressive hydrocephalus in infants leads to greater reduction in CBF than it does in adults with idiopathic chronic hydrocephalus. This may be caused by the shorter existence of the hydrocephalus, the different consistency of the developing parenchyma in infants, and the higher vulnerability of the maturing periventricular white matter in infants.

TABLE 3

Volumetric measurement leading to CBF

Case No.	Ventricle Vol (cm^3)	Brain Vol (cm^3)	CBF (ml/min)	CBF (ml/100 cm^3 brain/min)
1				
preop	180.20	566.16	154	27.20
postop	22.13	652.01	390	59.83
2				
preop	480.02	467.63	101	21.60
postop	79.81	729.67	226	30.97
3				
preop	155.22	486.31	62	12.76
postop	256.63	803.45	317	39.45
4				
preop	583.66	472.37	59	12.49
postop	535.52	498.61	262	52.55
5				
preop	90.13	439.18	74	16.85
postop	17.32	762.75	253	33.17
6				
preop	610.49	439.66	49	11.14
postop	713.90	601.15	323	53.73
7				
preop	88.12	716.71	276	38.51
postop	81.34	1004.17	541	58.88
8				
preop	890.01	681.49	111	16.29
postop	1144.53	1090.25	701	64.30
9				
preop	819.66	467.39	84	17.97
postop	953.34	891.34	255	28.61
10				
preop	685.56	489.47	129	26.36
postop	1056.12	639.13	419	65.56
11				
preop	976.12	886.73	264	29.77
postop	990.82	924.82	503	54.39
12				
preop	149.44	865.42	377	43.56
postop	88.42	1112.60	519	46.65
13				
preop	504.68	1028.09	398	38.71
postop	291.41	1137.16	599	52.68
14				
preop	1222.13	971.25	408	42.01
postop	1255.69	1105.55	533	48.21
15				
preop	275.54	839.60	271	32.27
postop	104.15	1045.29	649	62.09

The CBF is the quotient of CPP × (MABP − ICP) and the CVR.[29] The CVR is probably higher in the presence of raised ICP due to arteriolar and venular compression. The MABP did not alter postoperatively in our study. This is in accordance with the relationship we found between ICP and CBF (Fig. 4).

The CBF is known to increase from birth to a maximum at 5 years and to decrease afterward to adult values. In a SPECT study, CBF increased from 50 to 70 ml/min/100 g brain (a 40% change) during the first 5 years of life.[16] In our patients CBF increased from 25.7 ml/100 cm^3 brain/min to 50.1 ml/100 cm^3 brain/min after correction of the pathophysiological state of progressive hydrocephalus. Moreover, postoperative CBF values were within the normal

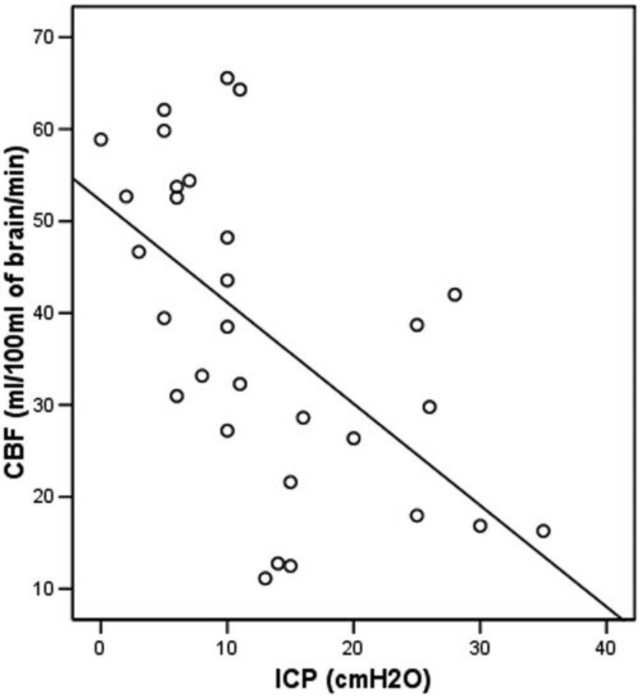

FIG. 4. Scatterplot showing the linear relation between ICP and CBF.

range.[10,20,43] This illustrates that the increase in CBF is probably not caused by aging.

In NPH a loss of vascular response is observed, whereas it is well known that the CBF remains constant over a wide range of ICP values, usually ranging between 0 and 50 mm Hg because of CBF-CSF autoregulation.[65] Thus, an increase in CBF resulting from relief of CSF pressure is considered to indicate impaired autoregulation of the cerebral microcirculation.[65] The impairment may be caused by an increased tissue pressure in the periventricular white matter, due to diffusion of the CSF from the ventricles. Impairment of the cerebral microcirculation was also substantiated by a study in which the capillaries collapsed and ultimately decreased in number in the periventricular tissue of experimental hydrocephalus in animals.[23] The experiment also found that CSF shunting rapidly reverses the capillary collapse. Therefore, the results in our study, such as the postoperative normalization of CBF, may indicate that the preoperative CBF reduction in the white matter was related to ischemia. The CBF normalization in parallel with clinical improvement suggests that CSF drainage relieved CSF diffusion and the resulting ischemia from the periventricular white matter. Further investigation is necessary to gain better insights in this pathological mechanism.

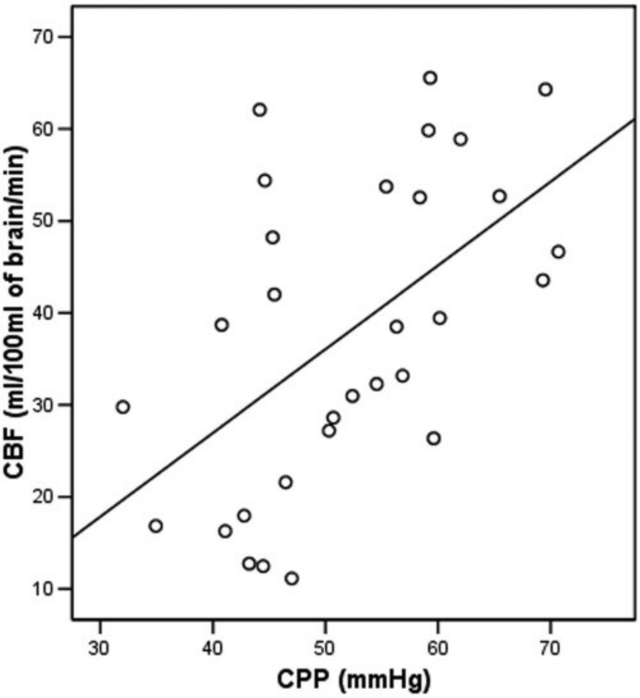

FIG. 5. Scatterplot showing the linear correlation between CBF and CPP.

TABLE 4

*Mean CBF, ICP, and MABP values in 15 infants with hydrocephalus**

Value	Preop	Postop
mean CBF (ml/100 cm^3 brain/min)	25.7 ± 11.3	50.1 ± 12.1
mean ICP (cm H_2O)	19.1 ± 8.4	6.7 ± 4.0
MABP (mm Hg)	61.9 ± 7.3	62.1 ± 7.9

* Values are recorded as the mean ± standard deviation.

This study demonstrates that CBF measurement by MR angiography can noninvasively contribute to the detection of risk factors in progressive hydrocephalus in infants, thus contributing to the detection of patients at risk of cerebral damage due to ischemia. Our data suggest that CBF increases to normal values after CSF diversion.

Conclusions

Quantitative measurement of CBF with MR angiography is a useful noninvasive method in infants with progressive hydrocephalus and can detect a decrease in CBF that ultimately can cause ischemia of the brain resulting in cerebral damage. Diversion of CSF leads to a significant increase in CBF, restoring the pathophysiological situation. This increase is probably not only caused by a decrease in ICP, but also by reduction of CVR. The CVR reduction can be explained by vasogenic, interstitial, or cytotoxic edema. Further investigation will be necessary to distinguish between the different types of brain edema, thus classifying the risk or degree of brain ischemia.

Disclaimer

This study is part of the Hydrocephalus and Ischemia Research Project of the Rudolf Magnus Institute of Neuroscience of the University Medical Center Utrecht and is approved by the Central Committee on Research involving Human Subjects in the Hague.

Acknowledgment

With great regret we announce the death of coauthor Pediatric Neurosurgeon Dr. Patrick Hanlo. He died April 12, 2008, due to a tragic sailing accident.

References

1. Adelson PD, Clyde B, Kochanek PM, Wisniewski SR, Marion DW, Yonas H: Cerebrovascular response in infants and young children following severe traumatic brain injury: a preliminary report. **Pediatr Neurosurg 26:**200–207, 1997
2. Anbeek P, Vincken KL, van Bochove GS, van Osch MJ, van der Grond J: Probabilistic segmentation of brain tissue in MR imaging. **Neuroimage 27:**795–804, 2005
3. Anegawa S, Hayashi T, Torigoe R: Clinical significance of ICP measurement in infants. Part I: Normal intracranial pressure, in Matsumoto S, Tamaki N (eds): **Hydrocephalus: Pathogenesis and Treatment.** New York: Springer-Verlag, 1991, pp 248–256
4. Ashley WW Jr, McKinstry RC, Leonard JR, Smyth MD, Lee BC, Park TS: Use of rapid-sequence magnetic resonance imaging for evaluation of hydrocephalus in children. **J Neurosurg 103 (2 Suppl):**124–130, 2005
5. Bakker CJ, Hartkamp MJ, Mali WP: Measuring blood flow by nontriggered 2D phase-contrast MR angiography. **Magn Reson Imaging 14:**609–614, 1996
6. Bakker CJ, Kouwenhoven M, Hartkamp MJ, Hoogeveen RM, Mali WP: Accuracy and precision of time-averaged flow as measured by nontriggered 2D phase-contrast MR angiography, a phantom evaluation. **Magn Reson Imaging 13:**959–965, 1995
7. Baron JC: Perfusion thresholds in human cerebral ischemia: historical perspective and therapeutic implications. **Cerebrovasc Dis 11 (1 Suppl):**2–8, 2001
8. Beintema DJ: State of the infant. **Clin Dev Med 28:**28–41, 1968
9. Bendel P, Buonocore E, Bockisch A, Besozzi MC: Blood flow in the carotid arteries: quantification by using phase-sensitive MR imaging. **AJR Am J Roentgenol 152:**1307–1310, 1989
10. Biagi L, Abbruzzese A, Bianchi MC, Alsop DC, Del Guerra A, Tosetti M: Age dependence of cerebral perfusion assessed by magnetic resonance continuous arterial spin labeling. **J Magn Reson Imaging 25:**696–702, 2007
11. Bisschops RH, Kappelle LJ, Mali WP, van der Grond J: Hemodynamic and metabolic changes in transient ischemic attack patients: a magnetic resonance angiography and (1)H-magnetic resonance spectroscopy study performed within 3 days of onset of a transient ischemic attack. **Stroke 33:**110–115, 2002
12. Blankensteijn JD, Van der Grond J, Mali WP, Eikelboom BC: Flow volume changes in the major cerebral arteries before and after carotid endarterectomy: an MR angiography study. **Eur J Vasc Endovasc Surg 14:**446–450, 1997
13. Buijs PC, Krabbe-Hartkamp MJ, Bakker CJ, de Lange EE, Ramos LM, Breteler MM: Effect of age on cerebral blood flow: measurement with ungated two-dimensional phase-contrast MR angiography in 250 adults. **Radiology 209:**667–674, 1998
14. Burstein J, Papile LA, Burstein R: Intraventricular hemorrhage and hydrocephalus in premature newborns: a prospective study with CT. **AJR Am J Roentgenol 132:**631–635, 1979
15. Caputo GR, Kondo C, Masui T, Geraci SJ, Foster E, O'Sullivan MM: Right and left lung perfusion: in vitro and in vivo validation with oblique-angle, velocity-encoded cine MR imaging. **Radiology 180:**693–698, 1991
16. Chiron C, Raynaud C, Maziere B, Zilbovicius M, Laflamme L, Masure MC: Changes in regional cerebral blood flow during brain maturation in children and adolescents. **J Nucl Med 33:**696–703, 1992
17. de Jong DA, Maas AI, Berfelo MW, den Ouden AH, de Lange SA: The Rotterdam teletransducer. A telemetric device for measuring epidural pressure. **Biotelem Patient Monit 9:**154–165, 1982
18. de Jong DA, Maas AI, den Ouden AH, de Lange SA: Long-term intracranial pressure monitoring. **Med Prog Technol 10:**89–96, 1983
19. de Jong DA, Ouden AH, van de Boon TA, Yeskoot F, Maas A: Telemetered epidural pressure. **Biotelemetry 2:**257–264, 1975
20. Dekaban AS: Changes in brain weights during the span of human life: relation of brain weights to body heights and body weights. **Ann Neurol 4:**345–356, 1978
21. Del Bigio MR: Neuropathological changes caused by hydrocephalus. **Acta Neuropathol 85:**573–585, 1993
22. Del Bigio MR, Bruni JE: Changes in periventricular vasculature of rabbit brain following induction of hydrocephalus and after shunting. **J Neurosurg 69:**115–120, 1988
23. Del Bigio MR, Bruni JE: Periventricular pathology in hydrocephalic rabbits before and after shunting. **Acta Neuropathol 77:** 186–195, 1988
24. Dombrowski SM, Schenk S, Leichliter A, Leibson Z, Fukamachi K, Luciano MG: Chronic hydrocephalus-induced changes in cerebral blood flow: mediation through cardiac effects. **J Cereb Blood Flow Metab 26:**1298–1310, 2006
25. Easa D, Tran A, Bingham W: Noninvasive intracranial pressure measurement in the newborn. **Am J Dis Child 137:**332–335, 1983
26. Enzmann DR, Marks MP, Pelc NJ: Comparison of cerebral artery blood flow measurements with gated cine and ungated phase-contrast techniques. **J Magn Reson Imaging 3:**705–712, 1993
27. Evans AJ, Iwai F, Grist TA, Sostman HD, Hedlund LW, Spritzer CE: Magnetic resonance imaging of blood flow with a phase subtraction technique: in vitro and in vivo validation. **Invest Radiol 28:**109–115, 1993
28. Firmin DN, Nayler GL, Klipstein RH, Underwood SR, Rees RS, Longmore DB: In vivo validation of MR velocity imaging. **J Comput Assist Tomogr 11:**751–756, 1987
29. Goh D, Minns RA, Hendry GM, Thambyayah M, Steers AJ: Cerebrovascular resistive index assessed by duplex Doppler sonography and its relationship to intracranial pressure in infantile hydrocephalus. **Pediatr Radiol 22:**246–250, 1992
30. Hanlo PW, Gooskens RH, Faber JA, Peters RJ, Hermsen AA, Nijhuis IJ: Relationship between anterior fontanelle pressure measurements and clinical signs in infantile hydrocephalus. **Childs Nerv Syst 12:**200–209, 1996
31. Hanlo PW, Gooskens RH, Nijhuis IJ, Faber JA, Peters RJ, van Huffelen AC: Value of transcranial Doppler indices in predicting raised ICP in infantile hydrocephalus. A study with review of the literature. **Childs Nerv Syst 11:**595–603, 1995
32. Hanlo PW, Gooskens RJ, van Schooneveld M, Tulleken CA, van der Knaap MS, Faber JA: The effect of intracranial pressure on myelination and the relationship with neurodevelopment in infantile hydrocephalus. **Dev Med Child Neurol 39:**286–291, 1997
33. Iacopino DG, Zaccone C, Molina D, Todaro C, Tomasello F, Cardia E: Intraoperative monitoring of cerebral blood flow during ventricular shunting in hydrocephalic pediatric patients. **Childs Nerv Syst 11:**483–486, 1995
34. Jorgensen PB, Riishede J: Comparative clinical studies of epidural and ventricular pressure, in Brock M, Dietz H (eds): **Intracranial Pressure I.** Berlin: Springer-Verlag, 1972, pp 41–45
35. Kaiser AM, Whitelaw AG: Normal cerebrospinal fluid pressure in the newborn. **Neuropediatrics 17:**100–102, 1986
36. Kirkness CJ: Cerebral blood flow monitoring in clinical practice. **AACN Clin Issues 16:**476–487, 2005
37. Kirkpatrick M, Engleman H, Minns RA: Symptoms and signs of progressive hydrocephalus. **Arch Dis Child 64:**124–128, 1989
38. Klinge P, Rückert N, Schuhmann M, Berding G, Brinker T, Knapp WH, et al: Neuropsychological sequels to changes in global cerebral blood flow and cerebrovascular reserve capacity after shunt treatment in chronic hydrocephalus—a quantitative PET-study. **Acta Neurochir Suppl 81:**55–57, 2002
39. Klinge PM, Berding G, Brinker T, Knapp WH, Samii M: A positron emission tomography study of cerebrovascular reserve before and after shunt surgery in patients with idiopathic chronic hydrocephalus. **J Neurosurg 91:**605–609, 1999
40. Kondo C, Caputo GR, Semelka R, Foster E, Shimakawa A, Higgins CB: Right and left ventricular stroke volume measurements with velocity-encoded cine MR imaging: in vitro and in vivo validation. **AJR Am J Roentgenol 157:**9–16, 1991
41. Kristensen B, Malm J, Fagerland M, Hietala SO, Johansson B, Ekstedt J: Regional cerebral blood flow, white matter abnormali-

ties, and cerebrospinal fluid hydrodynamics in patients with idiopathic adult hydrocephalus syndrome. **J Neurol Neurosurg Psychiatry 60:**282–288, 1996

42. Lee EJ, Hung YC, Chang CH, Pai MC, Chen HH: Cerebral blood flow velocity and vasomotor reactivity before and after shunting surgery in patients with normal pressure hydrocephalus. **Acta Neurochir (Wien) 140:**599–605, 1998
43. Leenders KL, Perani D, Lammertsma AA, Heather JD, Buckingham P, Healy MJ: Cerebral blood flow, blood volume and oxygen utilization. Normal values and effect of age. **Brain 113:**27–47, 1990
44. Levine RL, Turski PA, Holmes KA, Grist TM: Comparison of magnetic resonance volume flow rates, angiography, and carotid Dopplers: preliminary results. **Stroke 25:**413–417, 1994
45. Mamo HL, Meric PC, Ponsin JC, Rey AC, Luft AG, Seylaz JA: Cerebral blood flow in normal pressure hydrocephalus. **Stroke 18:**1074–1080, 1987
46. Marmarou A, Young HF, Aygok GA, Sawauchi S, Tsuji O, Yamamoto T: Diagnosis and management of idiopathic normal-pressure hydrocephalus: a prospective study in 151 patients. **J Neurosurg 102:**987–997, 2005
47. Mataró M, Poca MA, Salgado-Pineda P, Castell-Conesa J, Sahuquillo J, Díez-Castro MJ: Postsurgical cerebral perfusion changes in idiopathic normal pressure hydrocephalus: a statistical parametric mapping study of SPECT images. **J Nucl Med 44:**1884–1889, 2003
48. McAllister JP II, Chovan P: Neonatal hydrocephalus. Mechanisms and consequences. **Neurosurg Clin N Am 9:**73–93, 1998
49. Mikulis DJ: Functional cerebrovascular imaging in brain ischemia: permeability, reactivity, and functional MR imaging. **Neuroimaging Clin N Am 15:**667–680, 2005
50. Minns RA, Engleman HM, Stirling H: Cerebrospinal fluid pressure in pyogenic meningitis. **Arch Dis Child 64:**814–820, 1989
51. Mori K, Maeda M, Asegawa S, Iwata J: Quantitative local cerebral blood flow change after cerebrospinal fluid removal in patients with normal pressure hydrocephalus measured by a double injection method with N-isopropyl-p-[(123)I] iodoamphetamine. **Acta Neurochir (Wien) 144:**255–263, 2002
52. Owler BK, Momjian S, Czosnyka Z, Czosnyka M, Péna A, Harris NG: Normal pressure hydrocephalus and cerebral blood flow: a PET study of baseline values. **J Cereb Blood Flow Metab 24:**17–23, 2004
53. Park MK: Blood pressure tables. **Pediatrics 114 (2 Suppl):**555–576, 2004
54. Pelc LR, Pelc NJ, Rayhill SC, Castro LJ, Glover GH, Herfkens RJ: Arterial and venous blood flow: noninvasive quantitation with MR imaging. **Radiology 185:**809–812, 1992
55. Peters RJ, Hanlo PW, Gooskens RH, Braun KP, Tulleken CA, Willemse J: Non-invasive ICP monitoring in infants: the Rotterdam Teletransducer revisited. **Childs Nerv Syst 11:**207–213, 1995
56. Plandsoen WC, de Jong DA, Maas AI, Stroink H, Avezaat CJ: Fontanelle pressure monitoring in infants with the Rotterdam Teletransducer: a reliable technique. **Med Prog Technol 13:**21–27, 1987
57. Rutgers DR, Blankensteijn JD, van der Grond J: Preoperative MRA flow quantification in CEA patients: flow differences between patients who develop cerebral ischemia and patients who do not develop cerebral ischemia during cross-clamping of the carotid artery. **Stroke 31:**3021–3028, 2000
58. Schettini A, McKay L, Majors R, Mahig J, Nevis AH: Experimental approach for monitoring surface brain pressure. **J Neurosurg 34:**38–47, 1971
59. Shapiro K, Fried A, Marmarou A: Biomechanical and hydrodynamic characterization of the hydrocephalic infant. **J Neurosurg 63:**69–75, 1985
60. Smith SM: Fast robust automated brain extraction. **Human Brain Mapp 17:**143–155, 2002
61. Spilt A, Box FM, van der Geest RJ, Reiber JH, Kunz P, Kamper AM, et al: Reproducibility of total cerebral blood flow measurements using phase contrast magnetic resonance imaging. **J Magn Reson Imaging 16:**1–5, 2002
62. Spritzer CE, Pelc NJ, Lee JN, Evans AJ, Sostman HD, Riederer SJ: Rapid MR imaging of blood flow with a phase-sensitive, limited-flip-angle, gradient recalled pulse sequence: preliminary experience. **Radiology 176:**255–262, 1990
63. Steiner LA, Andrews PJ: Monitoring the injured brain: ICP and CBF. **Br J Anaesth 97:**26–38, 2006
64. Sundbärg G, Nornes H: Simultaneous recording of the epidural and ventricular fluid pressure, in Brock M, Dietz H (eds): **Intracranial Pressure I.** Berlin: Springer-Verlag, 1972, pp 46–50
65. Tanaka A, Kimura M, Nakayama Y, Yoshinaga S, Tomonaga M: Cerebral blood flow and autoregulation in normal pressure hydrocephalus. **Neurosurgery 40:**1161–1167, 1997
66. Vanninen R, Koivisto K, Tulla H, Manninen H, Partanen K: Hemodynamic effects of carotid endarterectomy by magnetic resonance flow quantification. **Stroke 26:**84–89, 1995
67. Vanninen RL, Manninen HI, Partanen PLK, Vainio PA, Soimakallio S: Carotid artery stenosis: clinical efficacy of MR phase-contrast flow quantification as an adjunct to MR angiography. **Radiology 194:**459–467, 1995
68. Vernooij MW, van der Lugt A, Ikram MA, Wielopolski PA, Vrooman HA, Hofman A: Total cerebral blood flow and total brain perfusion in the general population: the Rotterdam Scan Study. **J Cereb Blood Flow Metab 28:**412–419, 2008
69. Volpe JJ: Intracranial hemorrhage: germinal matrix-intraventricular hemorrhage of the premature infant, in **Neurology of the Newborn, ed 4.** Philadelphia: WB Saunders, 2001, pp 457–462
70. Volpe JJ: Intracranial hemorrhage in the newborn: current understanding and dilemmas. **Neurology 29:**632–635, 1979
71. Yordy M, Hanigan WC: Cerebral perfusion pressure in the high-risk premature infant. **Pediatr Neurosci 12:**226–231, 1985
72. Xenos C, Sgouros S, Natarajan K: Ventricular volume change in childhood. **J Neurosurg 97:**584–590, 2002
73. Zhao M, Amin-Hanjani S, Ruland S, Curcio AP, Ostergren L, Charbel FT: Regional cerebral blood flow using quantitative MR angiography. **AJNR Am J Neuroradiol 28:**1470–1473, 2007

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