Ventricular dilatation in relation to outcome at 2 years of age in very preterm infants: a prospective Finnish cohort study

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ABBREVIATIONS

BSID-II	Bayley Scales of Infant Development, 2nd edition
IVH	Intraventricular haemorrhage
MDI	Mental Developmental Index
NDI	Neurodevelopmental impairment
VLBW	Very low birthweight
VLGA	Very low gestational age

AIM The aim of this study was to analyse the relation between ventricular dilatation at term and neurodevelopmental outcome at 2 years corrected age in infants of very low birthweight (VLBW) or very low gestational age (VLGA).
METHOD A total of 225 VLBW or VLGA infants (121 males, 104 female; mean birthweight 1133g, SD 333g; mean gestational age 29wks, SD 2wks 5d) born in Turku University Hospital were included. Ventricular–brain ratio and the widths of each lateral ventricular horn were determined using ultrasonography, and the volume of the ventricles was measured by magnetic resonance imaging at term. The 2-year outcome measures included scores for the Hammersmith Infant Neurological Examination, the presence of cerebral palsy (CP), the Mental Developmental Index (MDI) of the Bayley Scales of Infant Development (2nd edition), and the presence of severe hearing or vision impairments or any neurodevelopmental impairment (NDI).
RESULTS CP was diagnosed in 15 participants (6.7%) and severe hearing deficit in 12 participants (5.3%). No severe vision impairment was found. Mild and severe cognitive delay was found in 24 (10.7%) and 8 (3.6%) of the VLBW or VLGA infants respectively. Isolated ventricular dilatation did not increase the risk for developmental impairments. However, ventricular dilatation with additional brain pathology was significantly associated with CP, MDI score below 70, and NDI. A ventricular–brain ratio above 0.35 was a sensitive measure of developmental impairment.
INTERPRETATION Ventricular dilatation at term increases the risk of poor developmental outcome only when associated with other brain pathology. The ventricular–brain ratio is a useful clinical tool for determining the prognosis in VLBW and VLGA infants.

Ventricular dilatation has been suggested to be an indicator of cortical and white matter injury,[1–5] which is known to be common in preterm infants. In a previous study, we found that ventricular dilatation was correlated with several brain lesions and small brain volumes in very-low-birthweight (VLBW) infants at term.[6] In addition, ventricular dilatation has frequently been associated with neurodevelopmental impairment (NDI) in preterm infants.[7–10] The clinical correlates vary from cerebral palsy (CP)[11] to difficulties in visuomotor performance[11,12] presenting as specific learning difficulties at school age (e.g. problems in carrying out geometric tasks).[11]

In contrast, other studies have found no association between isolated ventricular dilatation and poor outcome.[10,12] Furthermore, a recent study[13] found that cognitive outcome at 2 years of age in infants with intraventricular haemorrhage (IVH) grade III or IV combined with ventricular dilatation was better than reported in previous studies. In that study, only posthaemorrhagic ventricular dilatation necessitating lumbar puncture or a shunt was associated with poorer cognitive outcome at 2 years of age.

Because of these discrepant reports and variation in definitions of ventricular dilatation, we prospectively followed up a regional cohort of infants, using several reproducible measurements of ventricular dilatation by ultrasonography and magnetic resonance imaging (MRI). The aim of this study was to identify the relationship, if any, between ventricular dilatation at term and neurodevelopmental outcome at 2 years of age in VLBW infants or infants of very low gestational age (VLGA) with or without other brain pathology.

Participants

This prospective study is a part of the Development and Functioning of Very Low Birth Weight Infants from Infancy to School Age (PIPARI), a multidisciplinary follow-up study of VLBW and VLGA infants born in Turku University Hospital, Finland during 2001 to 2006.

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The study population consisted of VLBW or VLGA infants (birthweight ≤1500g) from Finnish- or Swedish-speaking families (Finnish and Swedish being official languages in Finland) who were living within the hospital catchment area. The inclusion criteria were modified during the PIPARI study period so that full gestational cohorts up to 31 gestational weeks (regardless of birthweight) were included from the beginning of 2004. Between January 2001 and December 2006, 296 infants of VLBW or VLGA were born preterm in Turku University Hospital. Forty-two (14.1%) died before discharge, most during the first week of life. Sixteen infants were excluded: seven because their families did not speak Finnish or Swedish, seven because the family lived outside the hospital catchment area, one infant who suffered from Bloom syndrome, and one who was diagnosed with osteogenesis imperfecta. A total of 238 infants remained eligible for the study, the families of 10 of whom refused to participate. Two infants were withdrawn from the study during follow-up and brain imaging studies were not obtained for one infant, resulting in a final total of 225 VLBW or VLGA infants included in the study.

METHOD

Ventricular dilatation in cranial ultrasound examination

At term, a paediatric radiologist (HR) used cranial ultrasonography to measure the ventricular–brain ratio and the widths of the ventricular horns. The radiologist was blind to the infants' clinical data. The instrument used was a 7.5MHz vector transducer (Aloka SSD 2000; Aloka Co. Ltd, Tokyo, Japan) from January 2001 to August 2002, and an 8MHz vector transducer (General Electric Logic 9; Waukesha, WI, USA) from September 2002 to March 2007.

The ventricular–brain ratio was defined as the ratio of the added widths of both ventricular midbodies at the border of the frontal horns and the midbodies to the width of both brain hemispheres as determined on a coronal ultrasound at the level of the foramen of Monro (Fig. S1, published online only). In our study population, neither number of brain lesions nor brain volumes differed between infants with a ventricular–brain ratio of 0.35 (accurate to within 0.01) and infants with a ventricular–brain ratio of no greater than 0.34.[6] However, infants with a ventricular–brain ratio greater than 0.35 had more brain lesions and smaller brain tissue volumes than infants with a ventricular–brain ratio of 0.35.[6] Thus, in this study, we defined a ventricular–brain ratio of greater than 0.35 as abnormal. We performed reliability measurements for 10% of the ultrasound examinations with regard to ventricular–brain ratio. We assessed interobserver reliability using the intraclass correlation coefficient (ICC). The ICC of ventricular–brain ratio was 0.97.

The oblique widths of the frontal horns of the lateral ventricles were measured in the coronal plane at the level of the foramen of Monro (Fig. S2, published online only). In the parasagittal view, the widest sagittal measure of both lateral ventricles was measured at the trigonum of the occipital horns (Fig. S3, published online only). The anatomical landmarks of the measurements of the ventricular widths have been described previously.[6] The reference values for ventricular horns determined by Virkola[14] were used to define ventricular dilatation in VLBW or VLGA infants at term. The cut-off value used for a dilated frontal horn was 0.3cm (1.0SD above the mean for the VLBW population). The same cut-off value has been used in previous studies.[15–17] The cut-off value used for a dilated occipital horn was 1.15cm (1.0SD above the mean for the VLBW population). The number of dilated ventricular horns was used as an independent variable.

What this paper adds

- Ventricular dilatation is associated with developmental impairments in VLBW and VLGA infants only when associated with other brain pathology.
- A ventricular–brain ratio of 0.35 is a useful cut-off value in clinical work to define ventricular dilatation.
- VLBW or VLGA infants with ventricular dilatation would benefit from MRI to identify possible additional brain lesions commonly associated with ventricular dilatation.

Ventricular dilatation in MRI of the brain

MRI of the brain was performed at term on the same day as the ultrasound examination. Imaging was conducted during postprandial sleep without any pharmacological sedation. The infants were swaddled to calm them and to reduce movement artefacts. The infants were fitted with pulse oximeter during the MRI examinations. A physician attended the examination if monitoring of the infant was considered necessary. The MRI equipment was an open 0.23-tesla Outlook GP (Philips Medical Inc., Vantaa, Finland), equipped with a multipurpose flexible coil fitting the head of the infant. The open MRI equipment permitted good visual control and easy access to the infant. A total of 125 infants were examined by 0.23T MRI until it was upgraded to a 1.5T Philips Intera (Philips Medical Systems, Best, the Netherlands), which was used to image the remainder of the study infants (n=100).

Axial T2 weighted images, coronal 3D T1 weighted images, and coronal T2 weighted images of the entire brain were obtained. All sequences were optimized for the imaging of the term infant brain. The total imaging time was approximately 25 minutes. One neuroradiologist (RP) manually measured the ventricular volumes from all the MRI images. Ventricular volume was defined as the sum of the volumes of the lateral ventricles, the third ventricle, and the fourth ventricle but excluding the choroid plexus. The neuroradiologist was blind to both clinical information and the results of ultrasound examinations.

The reproducibility of ventricular volume measurements was assessed by having another neuroradiologist, blind to the first measurements, carrying out repeated volume measurements in 20 children. The ICC of ventricular volume measurements was 0.99.

Brain pathology

Brain pathology in this study included all grades of IVH or cystic periventricular leukomalacia detected by ultrasonography during the infants' stay in the neonatal intensive care unit and/or at term, and/or IVH, white matter injury, ventriculitis, hypoplastic corpus callosum, cortical injury, basal

ganglia or thalamus injury, abnormal signal in the posterior limb of the internal capsule, width of the frontal extracerebral space more than 4mm, or anomaly/haemorrhage in the posterior fossa structures detected by MRI at term. Brain pathology findings on MRI are described in more detail in the Appendix S1 (published online only).

Neurodevelopmental outcome measures

A diagnosis of CP was determined during systematic follow-up to 2 years corrected age. Severe visual impairment was categorized as visual acuity below 0.3 or blindness. Severe hearing impairment was defined as hearing loss requiring amplification in at least one ear or a hearing impairment with a cut-off of 40dB.

The children were examined at 2 years corrected age using the Hammersmith Infant Neurological Examination (conducted by JM and a physiotherapist KS), which has been standardized for term infants at 12 to 18 months.[18] It has also been shown to be a reliable prognostic assessment tool in a preterm cohort.[19] The optimal score for the scale in term infants at 18 months of age is between 74 and 78. Because the optimal scores for preterm infants at 2 years of age are not available, we used the total scores as a continuous variable in this study.

The Mental Developmental Index (MDI) of the Bayley Scales of Infant Development, second edition (BSID-II),[20] was used to assess cognitive development. BSID-II is a standardized instrument and widely used to evaluate cognitive outcome in preterm infants. The assessment was conducted by a psychologist (primarily PM). The MDI had a mean value of 100 (SD 15); MDI scores below 85 (−1SD) and below 70 (−2SD) were used as definitions of mild and severe cognitive delay respectively at 2 years corrected age.

An examination by an ophthalmologist was included in the routine clinical follow-up at 2 to 3 years of age. Hearing was screened by brainstem auditory evoked potential during early infancy in addition to later clinical follow-up. NDI included at least one of the following findings at 2 years corrected age: CP, MDI score below 70, or severe hearing or visual impairment.

The PIPARI Study protocol was approved by the ethics review committee of the Hospital District of South-West Finland in December 2000. All parents provided written consent after receiving oral and written information.

Statistical analysis

The data in the tables are shown as number (percentage) or mean (SD) and as minimum and maximum values. The measurements of the frontal and occipital horns were dichotomized as normal or abnormal (defined in the Method section). A ventricular–brain ratio greater than 0.35 was considered abnormal.

Associations between perinatal characteristics and ventricular dilatation were studied using the following methods. Comparisons between two nominal variables were completed using the χ^2 test or Fisher's exact test, as appropriate. Associations between ordinal and categorical variables were studied using χ^2 tests for trend. Logistic regression was used to test univariate associations between the dependent variable, ventricular–brain ratio classification (>0.35 and ≤0.35), and continuous independent variables.

Ventricular dilatation (separated into ventricular–brain ratio classification, the number of dilated ventricular horns, and ventricular volumes) and brain pathology were used as predictors of categorical outcome variables (CP, hearing impairment, categorized BSID-II [MDI <85/≥85, and <70/≥70] and NDI) using logistic regression analyses.

Preliminary analysis indicated that the effect of ventricular dilatation on continuous outcome variables depended on brain pathology; thus, continuous outcome variables were studied separately in infants with and without additional brain pathology. Associations between ventricular–brain ratio classification (≤0.35 and >0.35) and continuous outcome variables were analysed using the Mann–Whitney *U*-test. Associations between ventricular dilatation (the number of dilated ventricular horns or ventricular volumes) and continuous outcome variables were analysed using Spearman's correlation coefficient.

Categorical outcome variables were also studied separately in infants with and without additional brain pathology. Associations between ventricular–brain ratio classification (≤0.35 and >0.35) and categorical outcome variables were studied using the χ^2 test or Fisher's exact test. Logistic regression was used to test associations between categorical dependent variables and ventricular volumes. Associations between the number of dilated horns and categorical outcome variables were studied using χ^2 tests to identify trends.

A receiver operating characteristic (ROC) curve was drawn to illustrate the sensitivity and specificity of the ventricular–brain ratio for CP, MDI score below 70, and NDI.

A p value of 0.05 was considered as the cut-off for statistical significance. Data analysis was performed using SAS for Windows, version 9.2 (SAS Institute Inc., Cary, NC, USA).

RESULTS

The characteristics of the study infants according to ventricular dilatation classification as determined by ultrasonography are shown in Table I. The infants underwent MRI and ultrasound scanning on the same day in 97% of cases. The elapsed time between MRI and ultrasound imaging was at most 8 days (median 0d; range 0–8d). Ultrasound and MRI were performed at term (SD 5d) in 93% of infants. The time between term age and imaging day was at most 29 days (in one infant). One or more ventricular measurements were obtained in all of the 225 infants. The ventricular–brain ratio was measured in 221 infants, the widths of the ventricular horns in 220, and ventricular volume in 205 infants. The Hammersmith Infant Neurological Examination was carried out in 215 (96%) infants and the MDI in 206 (92%) VLBW or VLGA infants at 2 years corrected age. CP was diagnosed in 15 (6.7%) and severe hearing deficit in 12 (5.3%) participants, but none developed a severe vision impairment. Mild or severe cognitive delay was detected in respectively, 24 (10.7%) and eight (3.6%) participants.

Table I: Perinatal and parental characteristics of the very-low-birthweight or very low gestational age infants

	V/B ratio ≤0.35 (*n*=189)	V/B ratio >0.35 (*n*=32)	All horns normal (*n*=106)	One horn dilated (*n*=44)	Two horns dilated (*n*=31)	Three horns dilated (*n*=16)	Four horns dilated (*n*=23)	*p* value
Gestational age at birth, wk + d	29 + 2 (2 + 5) [23 + 0, 35 + 6][c]	27 + 0 (2 + 3) [23 + 3, 33 + 0][c]	29 + 5 (2 + 3) [23 + 0, 35 + 6]	28 + 4 (2 + 6) [23 + 5, 34 + 6]	28 + 2 (2 + 5) [24 + 2, 35 + 1]	27 + 5 (2 + 3) [23 + 3, 31 + 5]	27 + 6 (2 + 5) [23 + 2, 33 + 0]	<0.001
Nr of males (%)	101 (53.4)	20 (62.5)	52 (49.1)	24 (54.6)	18 (58.1)	12 (75.0)	15 (65.2)	ns
Nr of females (%)	88 (46.6)	12 (37.5)	54 (50.9)	20 (45.4)	13 (41.9)	4 (25.0)	8 (34.8)	ns
Birthweight (g)	1149 (324)[b] [400, 2120]	959 (288)[b] [570, 1730]	1201 (324) [400, 2120]	1091 (318) [590, 1970]	1030 (319) [565, 1570]	1036 (364) [570, 1670]	1001 (252) [520, 1500]	
Small for gestational age, *n* (%)	78 (41.3)[a]	6 (18.8)[a]	40 (37.7)	16 (36.4)	12 (38.7)	7 (43.8)	8 (34.8)	
Head circumference at birth (cm)	26.7 (2.7) [20.0, 39.9]	25.0 (2.8) [20.5, 30.4]	27.2 (2.7) [20.0, 39.9]	26.0 (2.6) [20.8, 30.0]	25.6 (2.5) [20.7, 29.5]	26.0 (3.1) [20.5, 30.4]	25.5 (2.5) [20.0, 31.0]	0.001
Low Apgar score (<6) at 5min, *n* (%)	34 (18.4)[b]	13 (41.9)[b]	20 (19.4)	10 (22.7)	5 (16.1)	4 (26.7)	7 (31.8)	0.04
Ventriculoperitoneal shunt, *n* (%)	1 (0.5)[c]	5 (15.6)[c]	0	0	0	1 (6.3)	5 (21.7)	<0.001
Postnatal steroids (dexamethasone), *n* (%)	23 (12.2)	7 (21.9)	12 (11.3)	5 (11.6)	5 (16.1)	3 (18.8)	5 (21.7)	ns
Chronic lung disease, *n* (%)	23 (12.3)	8 (25.0)	10 (9.5)	5 (11.6)	6 (19.4)	3 (18.8)	7 (30.4)	0.006
Operated necrotizing enterocolitis, *n* (%)	9 (4.8)	4 (12.5)	4 (3.8)	5 (11.4)	0	1 (6.3)	3 (13.0)	ns
No IVH, *n* (%)	148 (78.7)[c]	14 (43.8)[c]	89 (84.0)	35(79.6)	19 (61.3)	10 (62.5)	9 (40.9)	<0.001
IVH grade 1 or 2, *n* (%)	36 (19.1)	6 (18.7)	16 (15.1)	7 (15.9)	10 (32.1)	2 (12.5)	7 (21.8)	for IVH
IVH grade 3 or 4, *n* (%)	4 (2.1)[c]	12 (37.4)[c]	1 (0.9)	2 (4.5)	2 (6.5)	4 (25.0)	6 (27.2)	
Cystic PVL	1 (0.5)	2 (6.3)	0	0	1 (3.2)	1 (6.3)	1 (4.8)	0.01
White matter abnormalities in MRI, *n* (%)	17 (9.5)[c]	16 (50.0)[c]	1 (2.9)	4 (9.5)	7 (26.9)	6 (37.5)	12 (54.6)	<0.001
Ventriculitis, *n* (%)	11 (6.0)[c]	11 (34.4)[c]	3 (2.9)	1 (2.3)	8 (27.6)	5 (31.3)	4 (17.4)	<0.001
Corpus callosum hypoplasia, *n* (%)	2 (1.1)[c]	7 (21.9)[c]	0	1 (2.3)	1 (3.5)	2 (12.5)	4 (17.4)	<0.001
Cortical injury, *n* (%)	2 (1.1)	3 (9.3)	0	0	0	0	4 (17.4)	0.001
PLIC injury	8 (4.2)[c]	14 (43.7)[c]	1 (1.0)	2 (4.6)	4 (13.7)	5 (31.3)	9 (39.1)	<0.001
Width of extracerebral space, >4mm	14 (7.6)	6 (18.8)	9 (8.7)	6 (13.6)	1 (3.5)	2 (12.5)	2 (18.7)	ns
Anomaly or haemorrhage in posterior fossa structures	9 (4.8)	1 (3.3)	3 (2.8)	1 (2.3)	2 (7.1)	1 (6.3)	2 (9.1)	ns
Age of the mother at child's birth	31.6 (5.0) [19, 43]	29.8 (6.0) [17, 39]	31.4 (4.8) [22, 42]	32.6 (5.2) [21, 43]	31.3 (5.7) [19, 39]	28.3 (6.0) [17, 39]	31.6 (4.9) [24, 41]	ns
Maternal education (y)								
≤9	22 (11.9)	5 (16.1)	13 (12.6)	4 (9.5)	7 (22.6)	3 (18.8)	0	ns
9–12	47 (25.5)	11 (35.5)	28 (27.5)	14 (33.3)	6 (19.4)	5 (31.3)	5 (21.7)	
>12	115 (62.5)	15 (48.4)	61 (59.8)	24 (57.1)	18 (58.1)	8 (50.0)	18 (78.3)	
Paternal education (y)								
≤9	19 (10.4)	2 (6.9)	12 (11.9)	3 (5.4)	3 (10.0)	2 (13.3)	1 (4.6)	ns
9–12	104 (57.1)	19 (65.5)	59 (58.4)	23 (54.8)	19 (63.3)	10 (66.7)	11 (50.0)	
>12	59 (32.4)	8 (27.6)	30 (29.7)	16 (38.1)	8 (26.7)	3 (20.0)	10 (45.5)	

Values are mean (SD) [minimum, maximum] unless otherwise indicated. [a]$p \leq 0.05$ compared with V/B ≤0.35; [b]$p \leq 0.01$ compared with V/B ≤0.35; [c]$p \leq 0.001$ compared with V/B ≤0.35. Ventricular dilatation was determined by ventricular–brain (V/B) ratio and by the number of dilated ventricular horns on ultrasound examination at term. Chronic lung disease was defined as the need for supplemental oxygen at 36 weeks. Cystic periventricular leukomalacia (PVL) was defined as multiple cysts with typical location in posterior periventricular white matter adjacent to the lateral ventricle and in the white matter adjacent to the foramina of Monro. Posterior limb of the internal capsule (PLIC) injury was defined as abnormal sign with magnetic resonance imaging in the PLIC. *p* values for the associations between number of dilated horns and background variables are presented in the last column. Small for gestational age $p=0.02$. IVH, intraventricular haemorrhage; ns, not significant.

Table II: Two-year outcome measures in very-low-birthweight (VLBW) or very low gestational age (VLGA) infants with ventricular dilatation as determined by ultrasonography and with or without other brain pathology as determined by ultrasonography and/or MRI at term

	VLBW/VLGA infants without other brain pathology		VLBW/VLGA infants with other brain pathology	
	V/B ≤0.35 (*n*=122)	V/B >0.35 (*n*=8)	V/B ≤0.35 (*n*=67)	V/B >0.35 (*n*=24)
Infant scale scores (*n*=215)	74 (3)	74 (2)	72 (5)	66 (12)
CP, *n* (%)	1 (0.8)	0	4 (6.0)	10 (42)
MDI total scores (*n*=206)	105 (12)	109 (19)	98 (16)	89 (19)
MDI <70 (<–2.0SD), *n* (%)	1 (0.8)	0	3 (5.0)	4 (19)
Hearing impairment, *n* (%)	4 (3.3)	1 (13)	4 (6.0)	3 (13)
NDI, *n* (%)	6 (5.2)	1 (13)	10 (17)	13 (59)

Values are presented as mean (SD) unless otherwise indicated. V/B ratio is the widths of both ventricular midbodies in relation to the width of both brain hemispheres from the coronal ultrasound. V/B ratio ≤0.35 was defined as normal and V/B ratio >0.35 as abnormal. CP, cerebral palsy; MDI, mental development index; NDI, neurodevelopmental impairment (includes CP, MDI <70, severe hearing impairment, or severe visual impairment). Ventricular dilatation in ultrasound was determined by ventricular-brain ratio (V/B ratio) at term age.

In infants without other brain pathology, abnormal ventricular–brain ratios were not associated with adverse outcome. However, in infants with other brain pathology, an abnormal ventricular–brain ratio was associated with CP (p<0.001), MDI below 70 (p=0.05), MDI score (p=0.04), and NDI (p=0.002) When the effect of brain pathology was controlled for, the associations with abnormal ventricular–brain ratio and CP (p=0.003), MDI score below 70 (p=0.04), and NDI (p=0.002) remained significant (Table II). In further analyses, we evaluated the sensitivity and specificity of the association between ventricular–brain ratio and CP, MDI score below 70, and development of NDI. The sensitivity (67%) and specificity (89%) for CP were good at a ventricular–brain ratio of 0.36 (Fig. 1).

An increase in the number of dilated ventricular horns in the absence of other brain pathology was not associated with an increased risk for adverse outcome. Among infants with other brain pathology, an increased number of dilated ventricular horns was significantly associated with development of CP (p<0.001), MDI score below 70 (p=0.05), and NDI (p<0.001). When the effect of brain pathology was controlled for, only the associations with CP (p<0.001) and NDI (p=0.002) remained significant (Table III).

In infants without other brain pathology, high ventricular volumes were not associated with any adverse outcome. Larger ventricular volumes in infants with other brain pathology were significantly associated with a diagnosis of CP (p=0.009), MDI score below 70 (p=0.03), and NDI (p<0.05). When the effect of brain pathology was controlled for, the association with CP (p=0.006), MDI score below 70 (p=0.04), and NDI (p=0.04) remained significant.

Isolated ventricular dilatation (n=130) did not increase the risk of adverse outcome. Among infants with no brain pathology other than ventricular dilatation, only 1 out of 130 (1%) developed CP. This infant had one dilated ventricular horn and a ventricular–brain ratio of 0.34. In addition, one (1%) infant with isolated ventricular dilatation developed a hearing impairment. In this infant, all ventricular horns were dilated and the ventricular–brain ratio was 0.36. In no infant with isolated ventricular dilatation alone was the MDI score below 70. Ventricular dilatation was not associated with mild cognitive delay.

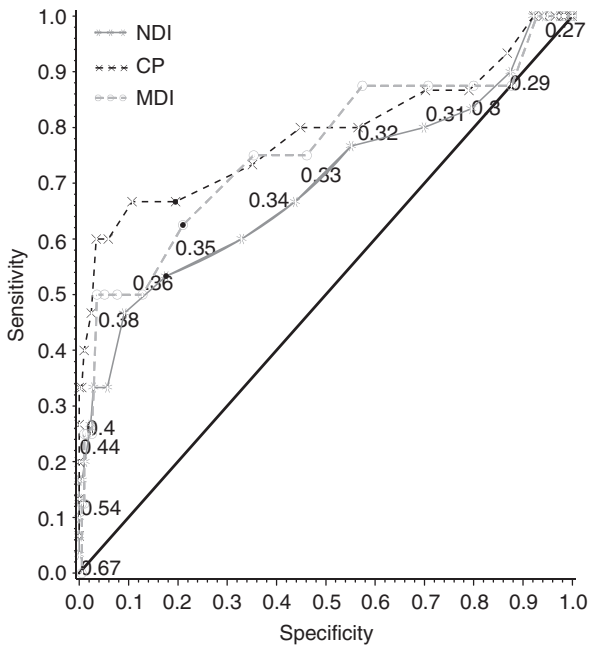

Figure 1: Ventricular measurements used to define ventricular dilatation at term by ultrasound. NDI, neurodevelopmental impairment; CP, cerebral palsy; MDI, Mental Developmental Index.

DISCUSSION

In our study population, the incidence of ventricular dilatation varied significantly depending on the definition, from 15% when ventricular dilatation was defined as a ventricular–brain ratio greater than 0.35, to 52% when defined as dilatation of one or more ventricular horns. Isolated ventricular dilatation at term (i.e. in the absence of other brain pathology) was not associated with the risk of later developmental impairments in VLBW or VLGA infants. However, ventricular dilatation in

Table III: Two-year outcome measures in very low-birthweight infants (VLBW) or very low gestational age (VLGA) with ventricular dilatation as determined by ultrasonography and with or without other brain pathology as determined by ultrasonography and/or MRI at term. Ventricular dilatation at term was grouped into five categories: normal or one to four dilated horns

	All horns normal	One horn dilated	Two horns dilated	Three horns dilated	Four horns dilated
VLBW/VLGA infants without other brain pathology (*n*=130)					
n	75	27	13	9	6
Infant scale scores	74 (3)	74 (3)	75 (2)	75 (2)	74 (3)
CP, *n* (%)	0	1 (3.7)	0	0	0
MDI total scores	105 (12)	103 (12)	107 (14)	101 (14)	111 (14)
MDI <70 (<–2.0SD), *n* (%)	1 (1.4)	0	0	0	0
Hearing impairment, *n* (%)	4 (5.3)	0	0	0	1 (17)
NDI, *n* (%)	5 (6.9)	1 (3.9)	0	0	1 (17)
VLBW/VLGA infants with other brain pathology (*n*=90)					
n	31	17	18	7	17
Infant scale scores	73 (4)	73 (3)	73 (4)	67 (14)	65 (12)
CP, *n* (%)	1 (3.2)	0	2 (11)	4 (57)	7 (41)
MDI total scores	99 (16)	96 (12)	98 (13)	88 (14)	89 (25)
MDI <70, (<–2.0SD), *n* (%)	2 (7.1)	0	0	1 (25)	4 (24)
Hearing impairment, *n* (%)	1 (3.2)	1 (5.9)	2 (11)	0	3 (18)
NDI, *n* (%)	4 (14)	1 (7.7)	4 (22)	5 (100)	9 (53)

Values are means (SD) unless otherwise indicated. CP, cerebral palsy; MDI, mental developmental index; NDI, neurodevelopmental impairment (includes CP, MDI <70, severe hearing impairment, or severe vision impairment).

infants with other brain pathology was an additional risk for developmental impairments.

A ventricular–brain ratio greater than 0.35 was a specific and sensitive measure of severe cognitive delay and any NDI, but especially CP. McArdle et al.,[21] based on a study of 51 neonates, proposed a cut-off value close to ours for ventricular–brain ratio. Clinical use of the ventricular–brain ratio is supported by the fact that it is easily obtainable and reliable.

Measuring the size of individual ventricular horns using ultrasonography is an alternative method of defining ventricular dilatation, and the findings have previously been shown to correlate well with ventricular volumes measured using MRI.[6,17] However, although we found that dilatation of one or more ventricular horns was associated with adverse outcome, this method proved not to be superior to ventricular–brain ratio in predicting adverse outcome in VLBW or VLGA infants. In addition, this technique is more time-consuming to perform than ventricular–brain ratio measurement.

Ventricular volumes can be measured exactly using MRI. We found that increased ventricular volume was associated with the same adverse outcomes as an abnormal ventricular–brain ratio. However, ventricular volume as a predictor of adverse outcome was also not superior to ventricular–brain ratio, perhaps because we included the volumes of the third and fourth ventricles in the total whereas ultrasound methods measure the volume of only the lateral ventricles. Ventricular volume was used as a continuous variable because normative values for the VLBW or VLGA infants were not available. Furthermore, the clinical use of ventricular volumes is limited because volumetric MRI is not universally available. According to our previous study, MRI is not necessary for diagnosis of ventricular dilatation.[6]

The important point for clinicians to note is that a ventricular–brain ratio above 0.35 together with other brain pathology indicates a significant risk for adverse outcome in VLBW and VLGA infants. This group also includes infants with ventricular shunts, who are also known to be at increased risk of an adverse outcome.[14] However, in our study, only a minority of the 13 children who developed an NDI had had a shunt (*n*=4).

Our data support previous findings that ventricular dilatation is associated with CP[11] and with poorer neurodevelopmental outcome.[7–12] Although a correlation between ventricular dilatation and CP has been identified previously, the definition of ventricular dilatation has been inconsistent, making the results difficult to compare. In some previous studies, the identification of ventricular dilatation has been based on clinical judgement rather than on exact values that can be measured reliably and reproducibly.

In our previous study,[6] we demonstrated that ventricular dilatation indicates a group of VLBW or VLGA infants with other brain pathology. This study shows that information regarding other brain pathology is important for prognosis. Therefore, our results support the use of brain MRI to identify the presence of other brain pathology than ventricular dilatation in VLBW or VLGA infants.

Although none of the infants in our study developed a major visual impairment, we cannot exclude the existence of milder visuomotor difficulties or visual field defects. In addition, the assessment of cognition at 2 years corrected age has well-known limitations. Thus, our report is limited to severe developmental impairments that can be diagnosed at 2 years corrected age. We did not correct for multiple testing to avoid type II errors, and it is, therefore, possible that some of the reported significant findings are false positives.

In conclusion, ventricular dilatation at term in VLBW or VLGA infants with other brain pathology was associated with an increased risk for poor neurodevelopmental outcome at 2 years corrected age. Accordingly, VLBW or VLGA infants with ventricular dilatation would benefit from MRI to identify possible additional brain lesions commonly associated with ventricular dilatation but not readily apparent on ultrasound scans. A ventricular–brain ratio above 0.35 predicted abnormal

neurological outcome at 2 years corrected age. Thus, all infants with ventricular dilatation should be followed up carefully.

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ONLINE MATERIAL/SUPPORTING INFORMATION

Additional material and supporting information may be found in the online version of this article.

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