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Cerebellar injury in preterm infants: incidence and findings on ultrasound and MRI

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ABSTRACT

Purpose: To investigate the incidence and characteristics of cerebellar injury in a cohort of very preterm infants, using the mastoid fontanelle (MF) and posterior fontanelle (PF) approach in addition to routine cranial ultrasound (CUS) through the anterior fontanelle (AF), using MRI as the reference standard.

Materials and methods: The institutional review board approved this prospective study and informed consent was obtained. A cohort of 77 preterm infants (<32 weeks) was studied with serial CUS throughout the neonatal period, using the AF, PF, and MF MRI was performed around term equivalent age in 59/77 infants. Sensitivity, specificity, positive predictive value and negative predictive value of routine CUS and CUS with additional views were calculated.

Results: Seven of 77 infants (9%) were identified with posterior fossa hemorrhage, using the MF CUS approach. In only 2/7 infants the lesions were seen on routine AF views. The PF approach did not increase the detection rate of posterior fossa hemorrhage. MRI confirmed CUS findings in all cases. MRI showed punctate hemorrhages in the cerebellum in 6 infants with normal CUS findings. Among the 59 infants studied with both CUS and MRI, cerebellar injury was diagnosed in 11 (19%).

Conclusion: Cerebellar injury is a frequent finding in very preterm infants. CUS through the MF can demonstrate injury missed by the routine AF approach. Punctate hemorrhagic lesions may remain undetected even when the MF is used; the prognostic implications of these smaller lesions need further attention.
INTRODUCTION

Brain injury can be a major complication of preterm birth, posing survivors at risk for developmental disorders, cognitive dysfunction, and behavioral difficulties. Until recently, supratentorial brain injury, such as white matter injury and intraventricular hemorrhage (IVH), was considered to be responsible for the impaired neurological outcome of children born prematurely. More recently, injury to the developing cerebellum has been described as additional complication of prematurity, with major impact on neurodevelopmental outcome.1-3

The exact incidence of cerebellar injury related to preterm birth is unknown. Posterior fossa hemorrhages can occur in association with supratentorial hemorrhage, but they can also be an isolated finding and be clinically silent.4 Autopsy studies reported cerebellar hemorrhage in 10-25% of preterm infants.5-7 Ultrasound studies in surviving very preterm infants (gestational age <32 weeks and/or birth weight <1500g) have shown that, when imaging is specifically focused on the posterior fossa, cerebellar lesions are not rare and that the incidence may range from 2.3-3% in preterm infants <1500g up to 19% in infants <750 g.4,8,9 In addition, cerebellar growth and development can be impeded by preterm birth and both supra- and infratentorial brain injury.10-13

Cranial ultrasonography (CUS) is the best tool for serial imaging of the newborn brain. It is routinely performed through the anterior fontanelle (AF). This provides an excellent view of supratentorial structures, but visualization of infratentorial structures located further away from the transducer is less optimal.14 Decreasing transducer frequency and directing focus on the posterior fossa improves visualization, but the echoic tentorium and vermis still impede the detection of cerebellar injury. When using the mastoid fontanelles (MF) and the posterior fontanelle (PF) as additional windows, the transducer is closer to the posterior fossa structures and they are approached at a different angle. This provides a better detection of cerebellar injury.4,15-17 Despite the advantages of the MF and PF windows and the implications of cerebellar injury for neurodevelopmental outcome, these windows are generally not included in the ultrasound examination of the brain of preterm infants.

Magnetic Resonance Imaging (MRI) shows brain maturation in detail and demonstrates the size and extent of injury more precisely.18-24 The posterior fossa is well depicted by MRI. However, compared to CUS, MRI is a burdensome procedure for the very preterm infant. Therefore, unlike serial CUS examinations, serial MR examinations are undesirable and most neonatal centers only perform MRI to confirm CUS abnormalities and to demonstrate the localization and extent of lesions more precisely.14,25
To our knowledge, cerebellar injury has not been studied systematically by combining serial CUS (including scanning via MF and PF) and MRI in preterm infants.

The aims of our study were to investigate the incidence and characteristics of cerebellar injury in a cohort of very preterm infants, using the MF and PF approach in addition to routine CUS through the AF, using MRI as the reference standard.

**Patients and Methods**

**Preterm infants**

Very preterm infants (gestational age [GA] <32 weeks), admitted to the neonatal unit of the Leiden University Medical Center (tertiary neonatal referral center) between April and October 2007, were eligible for participation in an ongoing neuro-imaging study, including serial CUS examinations throughout the neonatal period, and cerebral MRI examination around term equivalent age (TEA). The institutional review board approved this prospective study and parental consent was obtained. Exclusion criteria were congenital abnormalities of the central nervous system, chromosomal and metabolic disorders. Gestational age was estimated from the date of the mother’s last menstrual period and early prenatal ultrasound. Birthweight, gender and mode of delivery were recorded.

Patient characteristics are shown in Table 1. During the study period, 77 preterm infants <32 weeks were admitted to our neonatal unit and eligible for inclusion in the neuro-imaging study. All infants underwent serial CUS, including views through the MF and PF. CUS findings in all 77 infants were analyzed. Parental consent for performing MRI around TEA was obtained in 63/77 infants (82%). Four infants died during the neonatal period, after consent was obtained, but before MRI could be performed. Consequently, in 59/77 infants (77%) results of both serial CUS and MRI around TEA were available (Figure 1).

**Cranial ultrasound**

CUS was performed using an Aloka α10 ultrasound system with multifrequency (5–10 MHz) transducers (Biomedic Nederland B.V., Almere, The Netherlands). The standard CUS protocol in very preterm infants (<32 weeks) includes frequent examinations performed by the attending neonatologist, from the day of birth until discharge or transfer to another hospital. The AF is used as acoustic window and images are recorded in at least 6 coronal and 5 sagittal planes. Transducer frequency is set at 7.5 MHz. To assess deeper structures, including the posterior fossa, a frequency of 5 MHz can be applied.
Table 1. Patient characteristics.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>All infants</th>
<th>Infants with CUS and MRI data at TEA</th>
<th>Infants with consent died before MRI</th>
<th>Infants without consent for MRI (only CUS data)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>77</td>
<td>59</td>
<td>4</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>GA at birth, median (range), weeks + days</td>
<td>29 +1</td>
<td>(25-31+6)</td>
<td>27 +2</td>
<td>29 +5</td>
<td>0.85</td>
</tr>
<tr>
<td>Birth weight, median (range), grams</td>
<td>1214</td>
<td>(585-1960)</td>
<td>868</td>
<td>1235</td>
<td>0.12</td>
</tr>
<tr>
<td>Male, no. (%)</td>
<td>41 (53%)</td>
<td>33 (56%)</td>
<td>1 (25%)</td>
<td>7 (50%)</td>
<td>0.47</td>
</tr>
<tr>
<td>Grade II IVH, no. (%)</td>
<td>5 (6%)</td>
<td>5 (8%)</td>
<td>0</td>
<td>0</td>
<td>0.20</td>
</tr>
<tr>
<td>Grade III IVH, no. (%)</td>
<td>6 (8%)</td>
<td>5 (8%)</td>
<td>1 (25%)</td>
<td>0</td>
<td>0.55</td>
</tr>
<tr>
<td>PHVD, no. (%)</td>
<td>2 (3%)</td>
<td>2 (3%)</td>
<td>0</td>
<td>0</td>
<td>0.43</td>
</tr>
<tr>
<td>Cystic PVL, no. (%)</td>
<td>2 (3%)</td>
<td>2 (3%)</td>
<td>n.a.</td>
<td>0</td>
<td>0.43</td>
</tr>
</tbody>
</table>

Note: gestational age (GA), intraventricular hemorrhage (IVH), post hemorrhagic ventricular dilatation (PHVD), periventricular leukomalacia (PVL)

* P-values calculated for differences between infants with MRI around TEA and those without MRI, level of significance < 0.05

Figure 1. Flow diagram showing the number infants eligible for inclusion, the number of infants with serial CUS and the final number of included infants with both serial CUS and MRI around TEA.
During the study period, the CUS examinations with additional MF and PF views were performed biweekly, starting between the 3\textsuperscript{rd} and 7\textsuperscript{th} day of life. When abnormalities were suspected, these additional views were performed more frequently. All CUS scans that included MF and PF views were performed by SJS, having five years of experience in CUS imaging. CUS was repeated (by SJS) around TEA, on the same day as the MRI, including images obtained through the AF, PF, and MF. The mean number of CUS with additional MF and PF views was 2.7/ patient (range 1-6).

Scanning through the PF included 5 sagittal and 3 coronal views, as described by
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Correa et al.\textsuperscript{16} Scanning through the MF was performed as described by van Wezel-Meijler\textsuperscript{14} and Enriquez et al.\textsuperscript{17} Scans were performed in axial and coronal planes with views of the ventricular system, brain stem, cerebellar peduncles, vermis, and hemispheres (Figure 2).

All CUS scans were reviewed by at least two investigators (GvWM, SJS and LML with 20, 5 and 4 years of experience in CUS imaging, respectively) for abnormalities of the posterior fossa, including echogenicity changes in the cerebellar parenchyma (hemispheres and/or vermis), abnormalities in echogenicity, size and shape of the 4\textsuperscript{th} ventricle, and abnormalities of the structures surrounding the cerebellum. In addition, the cerebellum was evaluated for signs of abnormal development or atrophy. This was done at least 3 months after the scans were performed. The investigators, who were blinded to the patient names, reviewed the scans together and any discrepancies in interpretation were solved by means of consensus. While evaluating CUS scans, the presence of major supratentorial injury such as cystic periventricular leukomalacia (PVL), periventricular hemorrhagic infarction (PVHI), post hemorrhagic ventricular dilatation (PHVD), and supratentorial hemorrhage (i.e. germinal matrix/ intraventricular hemorrhage, [GMH/IVH]) was also recorded. GMH/IVH was classified according to Volpe.\textsuperscript{26} PHVD was defined according to Levene.\textsuperscript{27} PVL was classified according to de Vries et al.\textsuperscript{28}

MRI

MRI examination of the brain was performed around TEA, using a 3 Tesla MRI system (Philips Achieva 3T, Philips Medical Systems, Best, The Netherlands). Infants were sedated with chloral hydrate (50 mg/kg) 30–45 minutes prior to the procedure and ear protection (Natus MiniMuffs, Natus Medical Inc, San Carlos, CA) was applied. The MRI protocol included T\textsubscript{2} turbo spin echo (TSE), T\textsubscript{1}3D turbo field echo (TFE), T\textsubscript{2}* fast field echo (FFE), diffusion-weighted spin echo (DwSE) and diffusion-tensor imaging (DTI) sequences in transverse planes. Slice thickness was 1-4 mm without interslice gap and field of view 180-230 mm. All scans were reviewed, by at least 2 experienced investigators (FTdB and GvWM, having 15 years, and SJS and LML having 4 years experience in neonatal MR imaging). To avoid recall bias this was done at least 6 weeks after reviewing the CUS scans. The investigators reviewed the scans together and any discrepancies in interpretation were solved by means of consensus. The pediatric neuroradiologist (FTdB), who was unaware of the CUS findings, was always present. The other investigators (GvWM, SJS, and LML), who were involved in patient care during admission, were blinded to the patient names. Scans were reviewed for presence of posterior fossa hemorrhage, and the cerebellar parenchyma was examined for signs of disruption, in-
farction, or atrophy. If lesions were present, the location, extent, and laterality were noted and whether the lesions were visible on the $T_1$- and/or $T_2$-weighted images or only on the susceptibility scan.

**Data analysis**

The incidence of cerebellar injury was calculated. Infants with and without MRI around TEA were compared for general characteristics and supratentorial CUS findings, using a t-test for numerical data and a Pearson Chi-Square or Fisher’s Exact Test where appropriate for categorical data. P values less than .05 were considered to indicate a significant difference. The diagnostic competence of serial CUS throughout the neonatal period until TEA, using additional windows for the detection of cerebellar injury, and the diagnostic competence of the AF view alone were compared with the results of MRI, which was used as the reference standard. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated.

**RESULTS**

**Preterm infants**

We found no significant differences in general characteristics and supratentorial CUS findings between patients with and without MRI (Table 1).

**CUS**

Among the total group of 77 very preterm infants, seven (9%) had abnormalities in the infratentorial region detected by CUS (Table 2). In 5/7 infants, these occurred in combination with supratentorial hemorrhage, whereas hemorrhage was isolated to the cerebellum in two infants. Two of the seven infants with cerebellar lesions died during the neonatal period. Of the five surviving infants, two developed cerebellar atrophy on follow up CUS scans.

In 5/7 infants (71%), the abnormalities in the posterior fossa were only detected using the MF, but not on AF or PF views. Unilateral focal echogenic areas in one of the cerebellar hemispheres were seen in three infants. Two of these infants also showed echodensities in the 4th ventricle (probably presenting a hemorrhagic clot) and in one infant the cerebellar vermis was also involved (Figure 3). Two other infants showed echodensities in the 4th ventricle (probably presenting a hemorrhagic clot), co-existing with infratentorial extra-axial hemorrhage. On follow up ultrasound scans both infants
**Table 2. Imaging findings in infants with infratentorial CUS and/or MRI abnormalities.**

<table>
<thead>
<tr>
<th>Infant no.</th>
<th>GA weeks</th>
<th>*Age at CUS (CUS)</th>
<th>Cranial ultrasonography, mastoid fontanelle</th>
<th>MRI</th>
<th>Supratentorial hemorrhage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>26</td>
<td>Day 3</td>
<td>Lentiform shaped echodense lesion right cerebellar hemisphere</td>
<td>Died, no MRI</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>26</td>
<td>Day 4</td>
<td>Circular echodense lesion right cerebellar hemisphere</td>
<td>Died, no MRI</td>
<td>IVH grade 3</td>
</tr>
<tr>
<td>3</td>
<td>26</td>
<td>Day 3</td>
<td>Bilateral hemorrhages cerebellar hemispheres. Day 14</td>
<td>Hemorrhage both cerebellar hemispheres, severe atrophy</td>
<td>None</td>
</tr>
<tr>
<td>4</td>
<td>26</td>
<td>Day 3</td>
<td>Echodense lesion in 4th ventricle, vermis, and left cerebellar hemisphere</td>
<td>Hemosiderin residue in 4th ventricle and vermis, small hemorrhagic lesion left hemisphere</td>
<td>IVH grade 3, PHVD</td>
</tr>
<tr>
<td>5</td>
<td>27</td>
<td>Day 3</td>
<td>Echodense lesion 4th ventricle and left hemisphere</td>
<td>Hemosiderin residue in 4th ventricle, small hemorrhagic lesion left hemisphere</td>
<td>IVH grade 2, PVHI</td>
</tr>
<tr>
<td>6</td>
<td>26</td>
<td>Day 5</td>
<td>Echodense lesion 4th ventricle and surrounding cerebellar parenchyma. Dilatation 4th ventricle</td>
<td>Hemosiderin residue in 4th ventricle and subarachnoid space surrounding cerebellum</td>
<td>IVH grade 3</td>
</tr>
<tr>
<td>7</td>
<td>30</td>
<td>Day 4</td>
<td>Echodense lesion 4th ventricle and around cerebellum, dilatation 4th ventricle. Day 14</td>
<td>Hemorrhage and dilatation of 4th ventricle, arachnoid cyst posterior fossa, atrophy left hemisphere</td>
<td>IVH grade 3, PHVD, PVHI</td>
</tr>
<tr>
<td>8</td>
<td>27</td>
<td>Normal</td>
<td>Single small hemorrhagic lesion vermis</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>9</td>
<td>29</td>
<td>Normal</td>
<td>Single punctate hemorrhage hemisphere</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>10</td>
<td>27</td>
<td>Normal</td>
<td>Multiple punctate hemorrhages both hemispheres</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>11</td>
<td>29</td>
<td>Normal</td>
<td>Single punctate hemorrhage hemisphere</td>
<td>None</td>
<td>IVH grade 2</td>
</tr>
<tr>
<td>12</td>
<td>28</td>
<td>Normal</td>
<td>Multiple punctate hemorrhages left hemisphere</td>
<td>None</td>
<td>IVH grade 2</td>
</tr>
<tr>
<td>13</td>
<td>26</td>
<td>Normal</td>
<td>Punctate hemorrhage and hemosiderin in 4th ventricle</td>
<td>None</td>
<td>IVH grade 3</td>
</tr>
</tbody>
</table>

Note: intraventricular hemorrhage (IVH), post hemorrhagic ventricular dilatation (PHVD), periventricular hemorrhagic infarction (PHVI)

* indicates the postnatal age at which the abnormalities in the posterior fossa were detected
developed dilatation and deformity of the 4th ventricle, in one of them combined with a cystic abnormality in the posterior fossa (Figure 4).

In 2/7 infants cerebellar injury was seen on the AF, PF and MF views. AF sonography showed an echogenic area in the right cerebellar hemisphere in one infant and bilateral echodensities in the cerebellum in the other, probably presenting hemorrhages. MF imaging improved visualization of these lesions in both infants (Figure 5). There were no patients in whom addition of PF views increased the detection rate of cerebellar injury.

**MRI**

Forty-eight/fifty-nine infants (81%) had normal findings of the infratentorial region. In 11 infants (19%) MRI showed hemorrhagic injury of the cerebellum (Table 2).

**MRI in infants with infratentorial CUS abnormalities**

In all five surviving infants with abnormalities on CUS in the infratentorial region, these lesions were confirmed by MRI. These five infants had hemorrhagic lesions in the cerebellar hemispheres and/or the vermis, and/or the 4th ventricle (Figure 5). In the infant with a cystic abnormality in the posterior fossa on CUS, a fluid collection thought to be an arachnoid or leptomeningeal cyst was diagnosed by MRI (Figure 4).
Figure 4. Ultrasound scan in preterm infant (male, GA 30 weeks, with bilateral IVH grade 3, first seen on 3rd day of life)

A: Coronal view using the MF as acoustic window, shows extension of hemorrhage in the 4th ventricle (arrowhead) and possible extension in the vermis (arrow). The 3rd ventricle is mildly dilated (asterisk). Note the normal shape of the vermis and cisterna magna (bold arrow).

B: Two weeks after birth CUS shows deformity and dilatation of the 4th ventricle (arrowhead) and cystic dilatation of the cisterna magna (arrow). There is post hemorrhagic dilatation of the 3rd ventricle (asterisk) and temporal horns of the lateral ventricles.

C: T2-weighted image performed on day of life 81, illustrating fluid collection in posterior fossa (black arrow) and small hemosiderin deposits in left cerebellar hemisphere (white arrows).
Figure 5. CUS scan in preterm neonate (male, GA 26 weeks), on 3\textsuperscript{rd} day of life.

A: Coronal view through the cerebellum using the AF as acoustic window and transducer frequency set at 5 MHz, showing a suspect echogenic area in both cerebellar hemispheres (arrows). No signs of supratentorial hemorrhage.

B: (left) Axial and C: Coronal views through the cerebellum, using the left MF as acoustic window, clearly demonstrating the hemorrhage in both hemispheres (arrows).

D: (left) T1-weighted image performed on day of life 109 illustrates destructive lesions in both cerebellar hemispheres.

E: Susceptibility scan, showing bilateral extensive cerebellar hemorrhages.
Two infants with cerebellar injury developed cerebellar atrophy as shown by the MRI around TEA, confirming CUS findings.

**MRI in infants without infratentorial CUS abnormalities.**
In six out of 54 infants who underwent MRI and had normal CUS findings of the infratentorial region on both AF and MF views, MRI showed punctate hemorrhages in the cerebellar hemispheres and/or vermis (Figure 6). These small hemorrhagic lesions were most prominently seen on the susceptibility scan, but were also detected on T1- or T2-weighted images in all infants. Three infants had a single, unilateral punctate hemorrhage; the other three had multiple small hemorrhagic lesions. In three infants these lesions were associated with supratentorial IVH. None of these six infants developed cerebellar atrophy.

The sensitivity and specificity of routine CUS for detection of posterior fossa abnormalities as seen on MRI, were 18% and 100%, and of additional CUS 45% and 100%, respectively. The PPV and NPV of routine CUS were 100% and 84%, and of additional CUS 100% and 89%, respectively.

**Discussion**

The developing cerebellum is extremely vulnerable to injury. Several factors can lead to destruction of immature cerebellar structures and developmental arrest. This may have great impact on neurological development. Therefore, detection of cerebellar...
injury is of importance in high-risk preterm infants. Among a group of 59 very preterm infants, studied with both CUS and MRI, we found an incidence of hemorrhage in the cerebellum and/or 4th ventricle of 19%.

Of the total group of 77 infants, seven (9%) had abnormalities in the infratentorial region that were detected by CUS. This percentage is high compared to previous literature reports that describe an overall incidence of 2.3-3% in preterm infants <1500g \(^4\) and is probably related to the fact that we performed serial CUS, including the MF approach, and paid special attention to cerebellar injury. In a recent study, Müller \(^9\) et al. reported cerebellar hemorrhage in six out of 260 (2.3%) very preterm infants (GA <32 weeks), using AF sonography, focusing on the cerebellum. The detection rate in their study-population would probably have been higher if the MF had also been used. In our study cerebellar injury was missed using only the AF in 5/7 (71%) infants with abnormalities in the posterior fossa, despite adapting transducer frequency and focusing on the fossa posterior. In these infants cerebellar injury was only detected using the MF. Merill \(^4\) et al. also showed a better detection of posterior fossa hemorrhage by using the MF. In a prospective study over a 2-year period, they identified 13/525 (3%) infants (including 250 infants weighing <1500 g) with posterior fossa hemorrhage, whereas only two cases were identified over a retrospective 3-year period, using only AF views. The lower incidence they found may be related to the fact that they only reported large cerebellar hemispheric hemorrhages, whereas we also included other types and localizations of posterior fossa hemorrhage. Apart from the five infants with echogenic areas in the cerebellar hemispheres, we found two infants with 4th ventricular hemorrhage who, on follow up CUS, developed obvious abnormalities in the cerebellar region. In one of these infants a retrocerebellar fluid collection, thought to be an arachnoid or leptomeningeal cyst, was seen by US and MRI. Most arachnoid cysts are congenital, developmental abnormalities. However, a small number are acquired due to adhesions following hemorrhage, meningitis, or surgery. In this patient the fluid collection in the cisterna magna was only visualized on late CUS scans and MRI around term. This has been described before in a patient with intraventricular hemorrhage. We hypothesize that entrapment of spinal fluid within arachnoid adhesions, following hemorrhage may be the cause of the cyst formation.

In a large retrospective ultrasound study, Limperopoulos \(^8\) et al. detected cerebellar injury in 35/1242 (3%) infants weighing <1500 grams. During the last part of their study they found cerebellar hemorrhage in 19% of infants <750 gram. An increasing expertise with the MF approach and a decrease in mortality may have played a role in the increased detection of cerebellar lesions. In our study population, the majority of infants with cerebellar injury had a GA <28 weeks.
In our study, MRI confirmed presence and location of lesions in the five infants with infratentorial abnormalities on CUS. MRI demonstrated small hemorrhagic lesions in the cerebellar region in six additional infants without CUS abnormalities. Dyet et al.\textsuperscript{3} performed serial MRI in preterm infants born between 23-30 weeks gestation and found cerebellar hemorrhagic lesions on early MRI scans in 8/119 preterm infants (7%). They used a 1.0 T MRI system in the majority of infants and assessed T\textsubscript{1} - and T\textsubscript{2} -weighted images. For our study, a 3.0 T system was used, slice thickness 1-2 mm for T\textsubscript{1} - and T\textsubscript{2} -weighted images, without interslice gap, allowing detailed imaging. This may have been an advantage for the detection of small lesions. Furthermore, we performed susceptibility-weighted imaging, being more sensitive for small hemorrhagic foci than conventional T\textsubscript{1} - and T\textsubscript{2} -weighted imaging.\textsuperscript{32} Although small hemorrhagic lesions were detected on T\textsubscript{1} - and/or T\textsubscript{2} -weighted images, they were most prominently seen on the susceptibility-weighted images. The long-term consequences of small hemorrhagic lesions remain unclear and need further investigation. Hemosiderin deposits on the cerebellar surface can cause damage to underlying structures and may impair further growth and development. In infants and children with superficial cerebellar siderosis, subsequent cerebellar atrophy has been described.\textsuperscript{33-35} The toxic effects of hemosiderin may especially be pronounced in the immature and rapidly developing cerebellum. In a large group of preterm infants with different patterns of cerebellar atrophy on MRI, performed at 2 months to 6 years of life, Messerschmidt et al.\textsuperscript{11} found hemosiderin deposits in the majority of infants, even in the absence of primary cerebellar hemorrhage. We detected cerebellar atrophy in 2/7 infants with overt cerebellar hemorrhage, but did not see cerebellar atrophy in the six infants with only punctate cerebellar lesions. As these were early MRI examinations, performed around TEA, atrophy may still develop. In addition, we did not perform volumetric analysis, so small alterations in cerebellar volumes may have been overlooked. The effect of small punctate hemorrhages and hemosiderin deposits on cerebellar volume and on neurodevelopmental outcome should be the subject of further study.

Our study had limitations. For several reasons, including early neonatal death and lack of parental consent for MRI, we did not perform MRI in all infants. However, as there were no significant differences between the infants with and without MRI for GA at birth, birth weight, male gender, and supratentorial abnormalities, this probably did not cause a bias in our study population. Another limitation is that some of the investigators were involved in patient care and interpreted CUS examinations during admission, may have recalled CUS images when reviewing the MRI scans. However, there was a 6 week interval between reviewing the CUS examinations and the MRI scans.
Combining the results of high-quality CUS, including the use of supplemental acoustic windows and MRI, we found cerebellar lesions in 11/59 (19%) of very preterm infants. CUS, focusing on the posterior fossa and including MF views detected most lesions, but small punctate hemorrhages remained beyond the scope of CUS. The PF approach did not contribute to detection of cerebellar injury. The high incidence of cerebellar injury warrants routine CUS examinations including MF views in very preterm infants. Perinatal risk factors, the effect of cerebellar hemorrhage on neurological outcome, and the prognostic implications of punctate lesions need further investigation.

**ADVANCES IN KNOWLEDGE**

1) Cerebellar injury occurs frequently in very preterm infants.
2) Addition of mastoid fontanelle views in cranial ultrasonography leads to improved detection of cerebellar injury compared with anterior fontanelle sonography alone.
3) Small hemorrhagic cerebellar lesions remain beyond the scope of sonography and can only be detected with MRI.

**IMPLICATIONS FOR PATIENT CARE**

The high incidence of cerebellar injury warrants serial cranial ultrasound examinations, including mastoid fontanelle views, in very preterm infants (<32 weeks gestation).
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REFERENCES