Original article

Congenital Hemiplegia: Morphology of Cerebral Lesions and Pathogenetic Aspects from MRI

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Abstract

We have analyzed the MRI findings from the brains of 33 children with congenital hemiplegia. Referral of these children to our hospital was either because of neurological problems or a history of complicated birth. According to maturation-dependent pathophysiological mechanisms we have classified the lesions into the following five groups: 1. malformations/prenatal encephalo-clastic lesions, 2. periventricular leukomalacia or atrophy, 3. diencephalic lesions, 4. subcortical and cortical lesions, and 5. normal findings. Combination of lesions was not uncommon. The neuroradiologically most prominent and most expanded lesions determined the classification to the different groups. We detected malformations/encephalo-clastic lesions (Group 1) in 5 children; one of these children also presented additional lesions of Groups 2 and 3. Six children displayed periventricular leukomalacia (Group 2), and in one child in combination with diencephalic and subcortical lesions. Ten children exhibited diencephalic lesions (Group 3), in one case combined with periventricular leukomalacia. The MRI of seven children showed subcortical/cortical lesions (Group 4), in four cases extending into diencephalic structures. Two children had a combination of evenly matched periventricular, diencephalic and subcortical/cortical lesions, where it was impossible to define a principal lesion. Three children had normal MRI findings. Significantly, 8 of 33 children had bilateral lesions although presenting with hemiplegia. The large proportion of diencephalic lesions, not described in similar CT studies, and the small number of normal MRI findings show the value of MRI in evaluation of congenital hemiplegia. The ability to correlate, to some extent, neuroradiological findings of damage to developmental stage affords the conclusion that at least a third of the children in our series with congenital hemiplegia suffered prenatal damage.

Key words

Magnetic resonance imaging – Cerebral palsy – Congenital hemiplegia

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Introduction

The prevalence and panorama of cerebral palsy (CP) has changed during the last decades (5, 6, 14, 15, 17). Congenital hemiplegia is the most common form of CP among children born at term and second only to diplegia among preterms.

In our study we defined CP as a non-progressive motor disability of cerebral origin, and congenital hemiplegia (a form of CP with unilateral motor disability) where a postnatal event could not be detected. The etiology and pathophysiology of congenital hemiplegia are very different, however, recently there have been several attempts to allocate different cerebral lesions to defined periods during brain maturation (1, 18, 20, 21).

Various CT studies (3, 4, 9, 21) have addressed the etiological and temporal relationship of cerebral lesions leading to congenital hemiplegia. Studies discussing the value of MRI in detecting the neuropathophysiology of cerebral palsy, particularly spastic diplegia (8, 10, 11, 18, 19, 22), have been reported. However, we are not aware of any study contributing to the same questions in congenital hemiplegia.

This paper describes and classifies the findings in cerebral MRI from a hospital-based group of 33 children with congenital hemiplegia. Following an approach similar to a previous CT study by *Wiklund* et al (21) we have tried to classify the cerebral lesions to reflect pathophysiological mechanisms of the damaging event thought to be responsible for motor disability.

Material and methods

This study included thirty-three children (23 boys and 10 girls) with congenital hemiplegia referred to our hospital because of neurological and/or developmental problems or followed because of perinatal asphyxia. (For definition of asphyxia see legend to Table 1 or *Steinlin* et al [16].) The cohort contained 26 term (21 boys and 5 girls) and 7 preterm (2 boys and 5 girls) infants (Patients 2, 3, 11, 13, 18, 21, 25). Only one child (Patient 10) was clearly small for gestational age.

All children were examined neurologically at least twice, and 29 underwent developmental testing. The results of neurological and neurodevelopmental outcome in relation to the neuroradiological findings are being analysed. Since 28 of 33 children were 3 years or younger at their initial evaluation, we cannot exclude the possibility that some patients with diencephalic lesions will later develop additional dyskinetic symptoms, nor can we assure that the assumption of hemiplegic

Table 1 Anamnestic data and neuroradiological findings in 33 children with congenital hemiplegia.

Patients	GA (weeks)	BW (g)	Age (months)	MRI* primary lesion	secondary lesion	Side of MRI lesion	Risk factors prenatal	perinatal
1	42 2/7	3840	2	1		left	–	–
2	36 3/7	2950	20	1		both	–	–
3	36 4/7	3890	1	1		left	–	–
4	t	3500	5	1		both	–	–
5	40 4/7	4000	24	1	2+3	right	–	–
6	41 1/7	2560	11	2		left	–	–
7	40 4/7	3420	31	2		both	–	–
8	39 5/7	4040	3	2		both	–	+
9	39 0/7	2840	6	2		left	+	+
10	38 6/7	1810	2	2		left	+	+
11	35 3/7	2200	10	2	3+4	right	+	–
12	38 4/7	2450	22	2+3		both	–	+
13	34 6/7	2440	60	2+3+4		right	+	–
14	39 5/7	3650	24	3	2	both	–	–
15	41 4/7	3230	3	3		right	–	–
16	38 0/7	3620	3	3		right	–	+
17	38 4/7	2910	13	3		left	–	+
18	33 1/7	2100	12	3		left	+	+
19	37 6/7	2640	9	3		left	+	+
20	41 0/7	3500	8	3		left	+	+
21	33 4/7	2000	39	3		right	–	–
22	t	rec. lost	18	3		both	–	+
23	38 4/7	3300	41	3		left	+	+
24	40 2/7	3700	7	4	3	left	+	+
25	32 2/7	1450	18	4	3	left	–	+
26	t	rec. lost	11	4	3	left	–	+
27	t	3260	36	4		both	–	+
28	t	2610	48	4	3	left	+	+
29	40 0/7	3400	6	4		left	+	+
30	40 0/7	2770	18	4		left	–	+
31	38 3/7	2480	3	5			–	–
32	40 1/7	4160	9	5			–	+
33	40 4/7	3600	6	5			–	+

* The numbers correspond to the classification as defined in Material and methods. GA = gestational age; BW = birth weight; t = term (no more details available) Age: refers to last MRI examination

Risk factors
Prenatal: bleeding, imminent abortion, meconium stained amniotic fluid, placental insufficiency, gestosis
Perinatal: evidence of asphyxia, (Apgar score $\leq$ 5 at 5 min and $\leq$ 8 at 10 min, umbilical artery pH $\leq$ 7.1, base excess $\leq$ – 10 mmol/l), delivery by caesarian section/vacuum/forceps because of fetal symptoms, reanimation, mechanical ventilation or respiratory distress after birth

CP, currently based on neurological findings, will remain the definite diagnosis at long-term follow-up.

With informed consent by the parents, all children underwent one or more MRI of the brain. The mean age at last MRI examination was 16 months, ranging from 1 month to 60 months of age (children with postnatally changing character of MRI findings were at least aged 3 months at the time of last examination). The children were sedated for the examination by mild drugs such as chloralhydrate and/or flunitrazepam. T1-(SE 500/30 msec) and T2-(3000/120 msec) weighted images were performed on a 2.35 Tesla superconducting MR system using a 256 × 256 imaging matrix.

Classification of MRI findings

1. Malformation of cerebral tissue (evidence of defective organogenesis or histogenesis) and prenatal encephaloclastic lesions. Examples: complex cystic malformations, schizencephaly, hemi-hydranencephaly (Fig. 1). This group represents, by definition, prenatal encephalopathies.

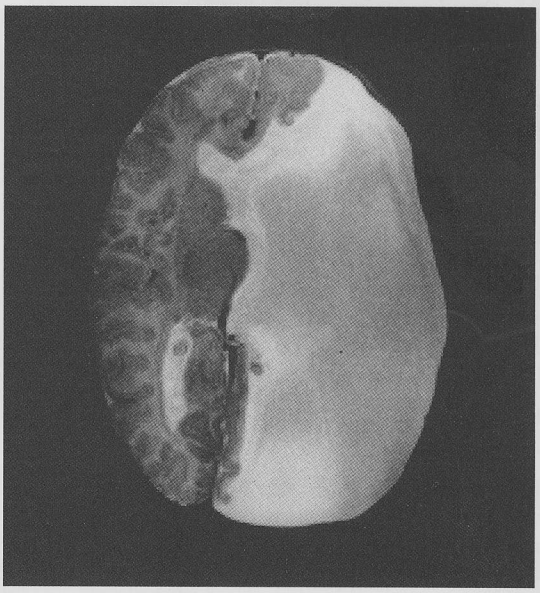

Fig. 1 Hemihydranencephaly, examined at 2 months, Patient 1. Axial view (TR 2940/TE 120).

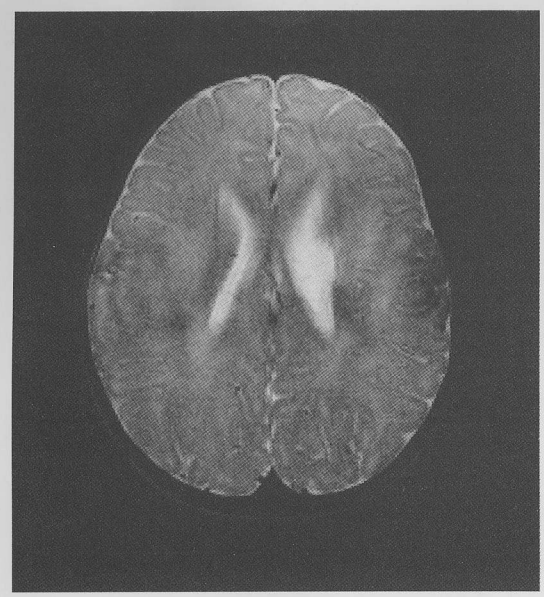

Fig. 2 Unilateral ventricular enlargement with irregular outline of the lateral wall and reduced white matter. Patient 19, aged 9 months (TR 2940/TE 120).

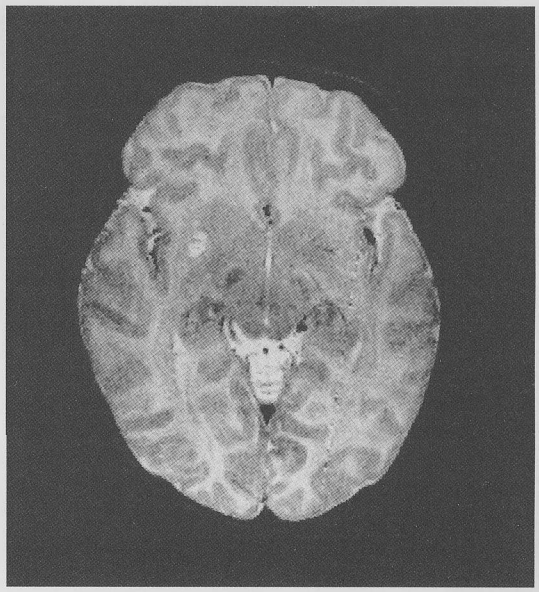

Fig. 4 Isolated focal lesion in the putamen, Patient 15; MRI at 4 weeks (TR 3000/TE 120).

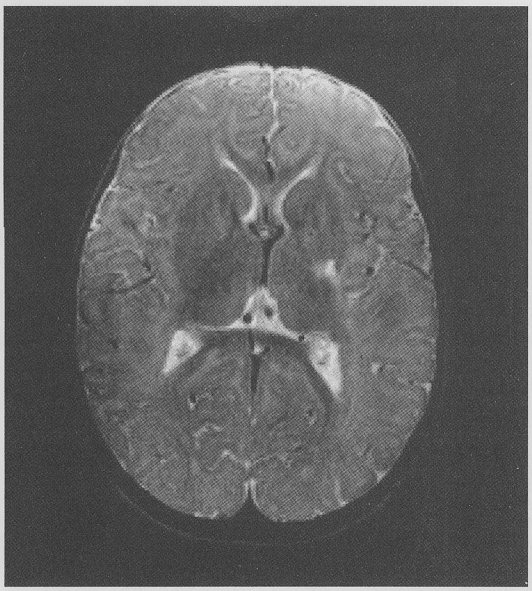

Fig. 3 Circumscribed lesion in the putamen, lateral to the internal capsule, Patient 19, at 9 months (TR 2940/TE 120).

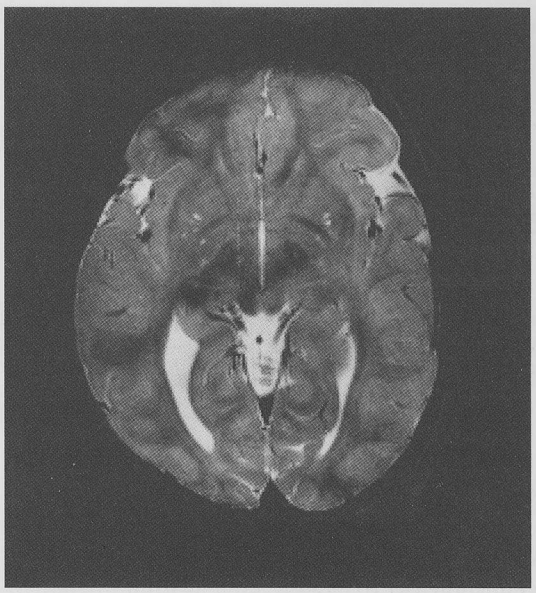

Fig. 5 Multiple small bilateral lesions in the basal ganglia, Patient 14. MRI at 1 month (TR 3000/TE 120).

2. Periventricular leukomalacia (PVL) or atrophy: presence of periventricular signal alterations (T2 hyperintensities) or ventricular enlargement with irregular outline of the lateral wall and/or reduced white matter (Fig. 2).

   Note: These are descriptive terms not implying a particular pathogenetic mechanism.

3. Diencephalic lesions: signal alterations localized in the diencephalon, including thalamus, basal ganglia, caudate nucleus as well as the internal capsule (Figs. 3–5).
4. Cortical or subcortical lesions: identification of subcortical signal alterations with or without associated cortical damage. Lesions in cortical areas but considered to have been caused by malformation (Group 1) were not included in this group (Figs. 6–7).
5. Normal MRI findings.

As a rule lesions in Group 1 and 3 were evident in both T1- and T2-weighted images while findings in Group 2 and 4 were better seen in T2 MRI.

Results

The results from evaluating the MRI of the 33 children with congenital hemiplegia are presented in Tables 1 and 2. Table 2 shows the results classified according to the prin-

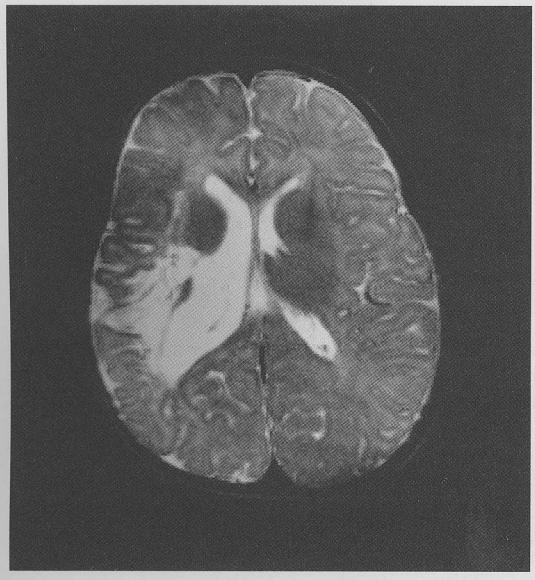

Fig. 6 Cortical and subcortical changes, in combination with ventricular enlargement and reduction of white matter as well as with a defect in the posterior putamen, Patient 11. Examination at 11 months (TR 3000/TE 120).

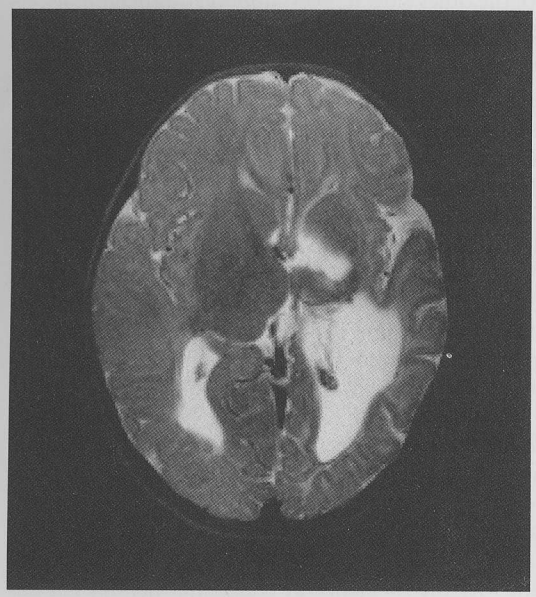

Fig. 7 Combination of diencephalic, periventricular and subcortical lesions in an infant (Patient 12) aged 11 months (TR 2940/TE 120).

Table 2 Classification of the principal MRI findings.

	n	Preterm/term
Malformation/encephalo-clastic lesion	5	2/3
PVL	6	1/5
PVL/diencephalic lesion	2	1/1
Diencephalic lesion	10	2/8
Subcortical/cortical	7	1/6
Normal	3	0/3
Total	33	7/26

PVL = periventricular leukomalacia

cipal pathological findings, defined as the most prominent and most expanded morphological cerebral lesion. Children with unilateral lesions all showed hemiplegia corresponding to the affected side, except one child with asymmetric ventricular enlargement. However, eight children with hemiplegia had lesions detected by MRI in both hemispheres. There was no obvious difference in the proportion of children born preterm in all our groups.

A cerebral malformation/encephalo-clastic lesion (Group 1) was seen in 5 children (Patients 1–5). Two had schizencephaly, one child bilaterally (Patient 4). The other child had unilateral schizencephaly, but additional ischemic lesions were found in the internal capsule of the same side and occipital PVL on both sides (Patient 5). One child showed hemihydranencephaly (Patient 1). Two children showed a complex cystic malformation; one associated with cerebral hemihypotrophy, absent corpus callosum and basal ganglia (Patient 2), and the other combined with hypoplasia of cerebellum and brainstem (Patient 3).

PVL was seen in 10 children (Patients 5–14). In 5 infants PVL was the only lesion detected (Patients 6–10). Occipital PVL was the most prominent finding in one child, extending into the crus posterior of the internal capsule, putamen and thalamus, and reaching the subcortical regions (Patient 11). In two children PVL and diencephalic lesions could be detected evenly matched, but with independent localization from each other (Patients 5, 12). In another child there was severe normal pressure ventricular dilatation reaching the subcortical area and destroying the thalamus and crus posterior of the internal capsule (Patient 13). Another child had diencephalic lesions and less pronounced PVL (Patient 14).

The most common finding was diencephalic lesions, presented by 18 children (Patients 5, 11–26, 28). Nine of this group displayed isolated diencephalic lesions affecting basal ganglia, crus posterior of the internal capsule, thalamus, and only in one case also the caudate nucleus (Patients 15–23). One child had principal diencephalic and less pronounced periventricular lesions (Patient 14). Another child had a combination with PVL (Patient 12). Also, one child had PVL and subcortical lesions (Patient 13), but without any clear predominance of one kind of lesion. Four children suffered infarction in the territory of the medial cerebral artery reaching deep into the diencephalon (Patients 24–26, 28).

There were 9 children with subcortical/cortical lesions (Patients 11, 13, 24–30). Five had an infarction in the territory of the medial cerebral artery (Patients 24–28), 3 times reaching into the diencephalon and once with additional cystic lesion in the crus posterior of the internal capsule. In one child we could detect a watershed infarction between the medial and anterior cerebral arteries (Patient 29). In one child the lesion was consecutive to occipital intraparenchymatous hemorrhage because of immune thrombocytopenia (Patient 30). In two children there was diffuse severe damage also reaching the subcortical areas (Patients 11, 13).

Finally, three children showed normal MRI results (Patients 31–33).

Discussion

Out of 33 children with congenital hemiplegia we detected MRI abnormalities in 30. This is a considerably greater proportion than could be detected in similar CT studies (3, 4, 9, 21) and supports the conclusion that MRI is more sensitive than CT to detect abnormalities in CP (19). In our view, this discrepancy in favour of MRI is not sufficiently explained by our patient selection.

Although MRI is also more sensitive in detecting migration disorders we observed a similar percentage of malformations/encephalo-clastic lesions to that found by *Wiklund* et al in a CT study (21). Malformation of the brain is a consequence of damage to the developing brain in early gestation, between the 2nd and 5th month. In one child (Patient 5), schizencephaly, which is related to damage between the 2nd and 4th month of gestation, was combined with PVL and diencephalic lesions, suggesting a second adverse event in the third trimester.

In 10 children we detected PVL. This hypoxic-ischemic damage of brain tissue occurs in the third trimester of gestation, between 28 and 34 weeks of gestation. At this stage of brain development the periventricular white matter is a vascular border zone. The white matter is also a region of relatively active anaerobic glycolysis and shows high vulnerability of actively differentiating periventricular glial cells (1, 20). Both vascular factors and intrinsic metabolic properties are thought to be responsible for the localization of PVL (20). The typical clinical pattern of PVL is spastic diplegia, but several CT studies (3, 4, 9, 21) showed that unilateral PVL can be found in spastic hemiplegia. Note that in the study of *Wiklund* et al (21) PVL was the most frequent lesion in congenital hemiplegia.

However, in this work the largest patient group presented diencephalic lesions. Diencephalic lesions are not described in CT studies of congenital hemiplegia, most probably because of technical limitations. They were also a rare finding in CP patients in the MRI study of *Truwit* et al (18), and were not discussed in several MRI studies of children with spastic diplegia (8, 10, 11, 22). The developmental stage associated with damage causing diencephalic lesion is not known. Considering that six of our children had multilocular diencephalic lesions, in two of them combined with separate PVL, the observation by *Keeney* et al (7) of diencephalic predisposition to hemorrhage during the third trimester and the results of *Barks* et al (2) showing high concentration of glutamate receptors in basal ganglia and thalamus in the fetal brain, suggest that the diencephalon is an area of minor resistance to ischemic events during the third trimester of gestation. Diencephalic lesions in the thalamus and basal ganglia have been proposed to result in choreoathetosis (20). In the study of *Truwitt* et al (18) the seven cases showed quadriplegia or diplegia. All our children showed hemiplegia at the time of evaluation, even without evident lesion in the internal capsule. No member of our cohort has to date displayed symptoms of ataxia or choreoathetosis, although many children were probably too young to assign a definitive diagnosis.

We detected subcortical and cortical lesions in nine children. Two of them (both preterm babies of the 35 and 36 week of gestation, respectively) (Patients 11, 13) also showed pronounced PVL and diencephalic lesions reaching to the subcortical areas. These lesions have to be interpreted as subcortical leukomalacia. Depending upon the stage of vascular maturation of the brain, subcortical areas are the most vulnerable region between 34th and 38th week of gestation (1). In five children the MRI was interpreted as an infarction in the territory of the middle cerebral artery. In another child the MRI indicated an infarction in the border zone of the medial and anterior cerebral arteries. Cortical lesions are due to infarction of one or more vessels and show the same neuropathology as in the mature brain. Five children were born at term, the one born preterm had severe neonatal complications, and thus the exact time of infarction remains unknown.

A normal MRI was found in only three children. One boy had severe microcephaly (Patient 31), and therefore his inclusion in the Group 1 category is arguable. Thus, we conclude that MRI is more sensitive than CT for the evaluation of different kinds of CP, as well as the assessment of congenital hemiplegia.

Bilateral involvement of the brain was found in 8 of these 33 children (24 %). These findings confirm the observation of *Wiklund* et al (21) that bilateral brain damage is occasionally evident in infants with "pure" hemiplegia. The lower percentage in their series (12 %) is probably a further indication of the superior value of MRI for evaluation of congenital hemiplegia. Note, however, that it is not always possible to detect mild impairment of one side in the presence of dominant hemiplegia of the other side; it is certainly very difficult to ascertain this in small children.

Eleven children here had prenatal, and 20 had perinatal risk factors, while eleven had none. Both pre- and perinatal risk factors existed for nine children, and this allows dicussion of whether prenatal damage (with consequent movement disorder of the fetus) contribute to perinatal problems. Interestingly in our Group 1 with prenatal encephalopathies, no prenatal or perinatal risk factors were recorded. The analysis of the risk factors has not allowed us to draw firm conclusions about the time/period and pathogenesis responsible for the cerebral lesions found. Malformations and intrauterine proven prenatal damage was found in 7 children here. Six subjects showed PVL after fullterm gestation, indicating a prenatal third trimenon fetal compromise. These data suggest a prenatal origin of congenital hemiplegia in 20 to 40 percent of this series. Timing the damaging events of the six multilocular diencephalic lesions during the third trimenon even up to 60 percent of all our children had prenatal origin of hemiplegia. These data agree with a growing consensus (12, 13, 18, 21) and could explain why the incidence of congenital hemiplegia has not decreased during the last decades, despite advances in peri- and neonatal care.

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