



Topic Expert Group: Medical care and clinical practice

Neurological monitoring in the high-risk infant: ultrasound and MRI scanning

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Target group

- Term and preterm infants at risk for brain injury:
 - Infants with hypoxic-ischaemic encephalopathy (HIE)
 - Infants with encephalopathy for other causes (e.g. metabolic)
 - Infants with suspected or verified seizures
 - Infants requiring intensive care and/or surgery
 - Infants with suspected/confirmed congenital central nervous system (CNS) anomalies
- Parents

User group

Healthcare professionals, neonatal units, hospitals, and health services

Statement of standard

In order to improve evaluation and outcomes of newborn infants at risk of brain injury, management includes neurological monitoring using a structured, age-appropriate neurological assessment and a range of devices to evaluate brain haemodynamics, oxygen transport, brain function, and imaging, as required.

Rationale

Infants requiring neonatal intensive care constitute a high-risk population for developing brain injury, especially during the first days after birth due to respiratory, haemodynamic, infectious, or metabolic instability. Full term and preterm infants exposed to hypoxia-ischaemia or infections, or carrying conditions such as congenital malformations, antenatal (maternal) risk factors, neonatal diseases potentially involving CNS, or late prematurity, among others, are exposed to increased risk of brain injury. Early recognition of on-going disturbances of brain function or structural damage is important in implementing preventive or treatment strategies, and appropriate follow-up. Early detection of cerebral compromise, such as encephalopathy or seizures, is associated with better management of these conditions. High-risk infants should be identified as early as possible, the patient history together with a structured clinical examination and repeated clinical observations form the basis of the evaluation. The vulnerability of this population, the severity of underlying clinical conditions, and the complexity of care deserve preferably continuous, cot-side, and non-invasive monitoring tools. This can be accomplished from four perspectives: haemodynamics and oxygen transport, connectivity and function, structure, and clinical expression. The ultimate goal is to prevent or reduce risk for brain injury by early identification of high-risk infants and improved clinical management.



Benefits

Short-term benefits

- Reduced mortality and morbidity (i.e., detect sinovenous thrombosis, severe haemorrhages or post-haemorrhagic ventricular dilatation) (1–11)
- Direct feedback on neuroprotective interventions (i.e., low molecular weight heparin treatment for cerebral vein thrombosis, ventricular reservoir taps, ventriculo-peritoneal shunt treatment) (1–8)
- Improved assessment of severity of brain damage which might redirect care (i.e., in patients with hypoxic ischaemic encephalopathy (HIE), arterial stroke, venous infarction) (1–12)
- Provides proxy biomarker for outcome for evaluation in neuroprotective intervention trials (11–16)
- Informs prognosis for physicians and parents (11–16)

Long-term benefits

- More focused follow-up programmes (5,16–20)
- Improved understanding of brain injury pathophysiology (5,12,14,17–19)
- Improved assessment of neonatal brain development to guide future prevention and intervention strategies (5,16–19)

Components of the standard

Component	Grading of evidence	Indicator of meeting the standard
For parents and family		
1. Parents are informed by healthcare professionals about the role of brain imaging. (21)	A (Moderate quality) B (High quality)	Patient information sheet
For healthcare professionals		
2. A unit guideline on neurological monitoring including brain imaging is adhered to by all healthcare professionals, to include <ul style="list-style-type: none"> • term infants with suspected brain injury (1–5,9–13,15,16) • very preterm infants (1–5,12) 	A (High quality) B (High quality)	Audit report, guideline
3. Training on ultrasound and MRI procedures is attended by all responsible healthcare professionals.	B (High quality)	Training documentation
4. Teams with a focus of interest on neuroimaging (e.g. nurses, neonatologists, neurologists, neurophysiologists, radiologists, radiographers, and physicists) are	B (High quality)	Guideline



established. (18)

For neonatal unit

5. A unit guideline on neurological monitoring including brain imaging is available and regularly updated, to include standardised operational procedures for cranial ultrasound (CUS) (22–24) and magnetic resonance imaging (MRI). (20,21,25–27)	A (High quality) B (High quality)	Guideline
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For hospital

6. Training on ultrasound and MRI procedures is ensured. (20,21,25–27)	A (High quality) B (High quality)	Training documentation
7. An interdisciplinary team for neurological evaluation of high-risk infants in the NICU is supported.	B (Moderate quality)	Audit report
8. Facilities for brain imaging (CUS and MRI) are provided.	B (High quality)	Audit report

For health service

9. High-risk infants are transferred to NICUs with appropriate neuro-monitoring systems and expertise. (17,28)	A (High quality)	Audit report, guideline
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Where to go – further development of care

Further development	Grading of evidence
For parents and family N/A	
For healthcare professionals N/A	
For neonatal unit	
<ul style="list-style-type: none"> Develop a full neonatal neuro-critical care concept, including guidelines and close collaboration with neurologists. 	B (Moderate quality)
For hospital N/A	
For health service	
<ul style="list-style-type: none"> Monitor incidence, treatment and long-term outcomes after neonatal brain injury such as intra-ventricular haemorrhage. (18) 	A (High quality)



- Develop multi-centre expertise by sharing imaging databases.

B (Moderate quality)

Getting started

Initial steps

For parents and family

- Parents are verbally informed by healthcare professionals about the role of brain imaging.

For healthcare professionals

- Attend training on ultrasound and magnetic resonance imaging (MRI) procedures.
- Identify leading healthcare professionals with a focus of interest on neonatal neurological monitoring.

For neonatal unit

- Develop and implement a unit guideline on neurological monitoring including brain imaging.
- Develop parental information material about brain imaging, also including parental perspectives.
- Provide resources for specific training on brain imaging tools.

For hospital

- Support healthcare professionals to participate in training on ultrasound and MRI procedures.

For health service

- Create systems to effectively transfer high-risk infants to NICUs with appropriate neuro-monitoring systems and expertise.

Description

Despite several major advances in fetal and neonatal care, the frequency of neurodevelopmental disability among the survivors of neonatal intensive care remains high. Although mortality for both, preterm infants and severely compromised term infants has decreased, the population of newborn infants at risk for neurological disability is still increasing. (29,30) Neuroimaging is a critical investigation in the provision of adequate diagnostic or prognostic information for parents. (1–5) Neuroimaging in newborn infants at risk of brain damage is oriented to:

- a. Diagnosing brain injury to provide the most appropriate medical management.
- b. Early detection of lesions associated with long-term neurodevelopmental disabilities.

Early diagnosis of structural brain damage can steer neuroprotective and/or neurorehabilitation treatment strategies, and guide appropriate follow up. It can also give us an understanding of the pathophysiology. (1–5)

Neonatal neuroimaging techniques such as CUS, MRI and CT scanning have been used for many decades and have proven to be extremely helpful assessing brain



maturation and injury. However, there are still several challenges associated with neonatal neuroimaging, which will be highlighted below. (5,11,13,25)

Proper assessment of neonatal brain images requires extensive knowledge about neonatal brain injury (aetiology, pathophysiology, prognosis), developmental neuro-anatomy (neuro-embryology), the advantages and disadvantages of the different imaging techniques, pitfalls and optimal timing. (5,11,13,25) Furthermore, the transport and sedation of critically ill neonates for both MRI and CT scanning often represents a major challenge. (25–27) Proper scanning requires a dedicated team. The most common used neonatal neuroimaging modalities are: CUS and MRI. The use of CT is very limited and because of radiation should be avoided. All these factors have to be taken into account when choosing timing and modality to image the neonatal brain.

There are advantages and disadvantages for each of the modalities: (5,11,13,25–27)

<i>Cerebral Ultrasound</i>	
Advantages	Disadvantages
<ul style="list-style-type: none"> • Bedside, patient friendly, save • Reliable for detection of severe haemorrhagic lesions (e.g. peri-intraventricular haemorrhage-P/IVH- in preterms) and severe white matter damage • Doppler technique (detection of thrombosis) • Specific lesions: germinolytic cysts, calcifications, lenticulo-strtriate vasculopathy -LSV • Repeated assessments (i.e., measurements such as the Levene index in posthaemorrhagic ventricle dilatation –PHVD patients) 	<ul style="list-style-type: none"> • Difficult to detect cortical abnormalities • Difficult to detect posterior fossa abnormalities (the use of posterior fontanel and mastoid fontanel can be of help) • Less reliable in detecting small lesions and subtle white matter damage • Difficult to assess myelinisation
<i>MRI</i>	
Advantages	Disadvantages
<ul style="list-style-type: none"> • Relatively safe (no radiation) • Good assessment of whole brain (including cortex and posterior fossa) • Detailed information about brain development (including myelination) • Reliable information about localisation and extent of brain damage • Reliable for detection of small lesions and subtle white matter damage • Special sequences for different 	<ul style="list-style-type: none"> • More burden/distress for (often unstable) infants and medical team: transport issues, sedation, time consuming • High costs (depending on hospital) • Some lesions more difficult to assess (LSV, calcifications, germinolytic cysts)



<p>purposes: e.g., diffusion-weighted imaging (DWI) (cytotoxic oedema), diffusion tensor imaging (DTI) (quantitative white matter tract analysis), magnetic resonance venography (MRV) (venous system), susceptibility weighted imaging (SWI) (haemorrhages), contrast (tumour, abscess), magnetic resonance angiography (MRA) (arterial vessels)</p>	
<p>CT</p>	
<p>Advantages</p>	<p>Disadvantages</p>
<ul style="list-style-type: none"> • Good visualisation of bone structures • Often wider availability than MRI 	<ul style="list-style-type: none"> • Relatively unsafe (radiation) • Poor tissue contrast (low resolution) • To detect haemorrhages beyond one week can be difficult

Disease states and recommended neuroimaging technique:*

*Based on several factors, including local availability, expertise, and protocols.

Cerebral Ultrasound (examples)

- High-risk neonatal conditions: e.g. preterms (gestational age (GA) less than 32 weeks), intrauterine growth restriction, congenital abnormalities (syndromes), post-resuscitation, HIE, meningitis/encephalitis, metabolic diseases, symptomatic hypoglycaemia, hyperbilirubinemia (above exchange transfusion threshold), sudden severe anaemia, congenital heart defects, post-surgery, pre-extracorporeal membrane oxygenation (ECMO), post-ECMO, sudden clinical deterioration.
- Newborn infants with neurological symptoms/signs: e.g. seizures, hyper- or hypotonia, abnormal movements, abnormal consciousness, unexplained central apneas, unexplained irritability and restlessness, micro- or macrocephaly.

MRI (examples)

- Neurological symptoms not explained by other diagnoses
- Convulsions
- Symptomatic hypoglycaemia
- Severe hyperbilirubinemia and neurological symptoms or abnormal ultrasound
- HIE grade II or III
- P/IVH with PHVD or periventricular haemorrhagic infarction (PVHI)
- (Suspected) congenital CNS abnormalities
- (Suspected) sinovenous thrombosis
- Abnormalities in posterior fossa
- Parenchymal injury (periventricular leukomalacia -PVL>II, intraparenchymal haemorrhage, stroke, inhomogeneous periventricular echogenicity -PVE)
- Symptomatic extra-cerebral haemorrhage



Suggested timing of neuroimaging:

Cerebral Ultrasound

Term infants:

- Neurological symptoms suggesting brain injury: as soon as possible (to exclude acute conditions that need intervention)
- Suspected congenital CNS abnormalities: 1st day after birth

Preterm infants:

- GA >28 weeks: scan on day 1-3-7-14,21,28, at 6 weeks and at term equivalent age (TEA)
- GA < 28 weeks: scan on day 1-3-7-14-21-28- than every two weeks until 34 weeks GA and at term equivalent age (TEA)
- Intensify CUS in case of abnormalities or after episode of clinical deterioration (e.g. unexplained anaemia, neurological symptoms, P/IVH, PHVD, inhomogeneous PVE, cerebellar haemorrhage, surgery, HIE, CNS infection, metabolic disease, etc.)

MRI

Term infants (examples):

- Neurological symptoms of unknown origin: as soon as possible
- Hypoxic Ischemic Encephalopathy: between day 4-7
- Suspected parenchymal damage (e.g. stroke): between 3-7 days after insult

Preterm infants (examples):

- Neurological symptoms of unknown origin: as soon as possible
- Routine neuroimaging in extreme preterm infants: preferred timing around TEA

Source

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Lifecycle

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