Diagnostic Accuracy of Magnetic Resonance Imaging for Nerve Injury in Obstetric Brachial Plexus Injury: Protocol for Systematic Review and Meta-analysis

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Protocol

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Abstract

Background

Obstetric brachial plexus injury (OBPI) is typically caused by excessive traction to the neck during delivery and can cause permanent dysfunction of the upper limb. Surgical exploration is typically performed at 3 months of age if insufficient signs of spontaneous functional recovery are demonstrated, and nerve reconstruction is performed at this point if indicated. Magnetic resonance imaging (MRI) offers a non-invasive alternative in detecting nerve injury, however the reported diagnostic accuracy in existing literature is conflicting. A systematic review is therefore required to clarify the accuracy of MRI and help define its role clinically. The primary objective is to determine the diagnostic accuracy of MRI for detecting root avulsion in obstetric brachial plexus injuries. The secondary objectives are to determine the diagnostic accuracy of MRI for detecting any nerve abnormality (including post-ganglionic injury) and to determine the diagnostic accuracy of MRI for detecting pseudomeningocele(s) as a surrogate marker of root avulsion.

Methods

Electronic databases will be searched systematically for studies reporting the accuracy of MRI (index test) compared to surgical exploration (reference standard) in detecting root avulsions, other nerve abnormalities and pseudomeningocele in children with OBPI. A revised QUADAS-2 tool will be used to assess methodological quality of included studies. If appropriate, summary sensitivities and specificities for target conditions (root avulsion, abnormal nerve and pseudomeningocele) will be obtained via meta-analyses using a bivariate model.

Discussion

This study will aim to clarify the current diagnostic accuracy of MRI for detecting nerve injury and define its clinical role.

Systematic review registration

PROSPERO registration CRD42021267629.

Background

Obstetric brachial plexus injury

Obstetric brachial plexus injury (OBPI) is defined as flaccid paralysis of the upper limb at birth (1) and is typically caused by excessive traction applied to the neck during delivery. OBPI affects 0.4 to 2 children per 1000 births (2). Risk factors include fetal macrosomia, shoulder dystocia, humeral fracture and vacuum or forceps evacuation (3, 4). Fracture of the clavicle during a dystocic delivery is often considered to be protective as the space between the clavicle and first rib is increased leading to reduced

force on the brachial plexus as it leaves the thorax (5). However, some studies argue that a clavicle fracture is indicative of birth trauma and therefore the risk of OBPI is increased (6). All roots from C5-T1 can be damaged however C5 and C6 involvement (Erb's palsy) is most frequent (7, 8).

Spontaneous recovery is common within the first 3 months of life, however this recovery is incomplete in 10–30% of cases (9). Muscle changes in infants with permanent brachial plexus injuries can result in shoulder and elbow contractures (tightening of the muscles and tendons) which can lead to long term pain and loss of function (10). Joint deformity, weakness and limited movement at the wrist and hand may also occur with permanent OPBI (11, 12). An increased risk of psychological effects has been reported for affected infants and their mothers (13) as well as disruption to overall family functioning (14). In terms of hospital finances, the cost of babies born with OPBI is roughly twice as high (15). The lifetime costs are also significant when accounting for the cost of treatment, disability costs and loss of income.

The strongest prognostic factor that determines outcome is the extent of the primary plexus injury (16). Neuropraxia (stretching of the nerves) confers the best prognosis, nerve rupture more severe, and root avulsion (nerve roots pulled away from the spinal cord) the worst (17). The Sunderland classification can be used to define the severity of the injury, ranging from first degree (loss of axon conduction) to fifth degree (loss of continuity of the entire nerve trunk) (18). Hardly any functional recovery is observed with fourth and fifth degree injury (19).

Infants and children with limited to no functional recovery can benefit from surgical intervention with nerve grafting or transfers. Nerve transfer is used in cases of pre-ganglionic injury (root avulsion) which involves redirecting functioning nerves in the neck to supply the arm (20). Post-ganglionic injuries are managed with nerve grafts which involve harvesting less important nerves (e.g. the sural nerve) and using them to restore continuity in the ruptured nerve. In both cases early reconstructive nerve surgery is associated with better functional recovery (21).

Whilst scoring systems such as the Active Movement Scale (22) can be used to aid in assessment, it is still difficult to clinically determine the extent of the injury.

Diagnostic modalities of interest

Imaging can be used to support decision making in obstetric brachial plexus surgery. Clinical practice has moved away from computed tomography myelography in the evaluation of OBPI and towards magnetic resonance imaging (MRI) (23) which has clear advantages when it comes to imaging children such as the absence of ionising radiation and intrathecal contrast agent. Enhanced soft tissue visualisation and multiplanar reconstructions also make MRI a suitable modality. MRI is currently thought to be the best non-invasive test for imaging the brachial plexus and detecting nerve root avulsion (24), but has been demonstrated to have variable sensitivity (63%-88%) and specificity (89%-100%) for detecting pre-ganglionic injury and sensitivity 60-75% and specificity 89-100% for post-ganglionic injury (23, 25–28) when compared to surgical exploration. Pseudomeningoceles from leakage of cerebrospinal fluid can

additionally be used as a surrogate marker of nerve root avulsion on MRI scans but again the reported accuracy of this is variable (29).

Due to the only moderate sensitivity of MRI to detect pre and post-ganglionic injuries this cannot be relied on to fully inform clinical decisions. It is critical to differentiate between pre-ganglionic and post-ganglionic injuries due to the differing prognosis and surgical approaches for these injuries. There is a pressing need to define the characteristics of the nerve injury that has potential to recover with reconstructive surgery. Post-ganglionic injuries are associated with better outcomes because the anterior horn cells are unaffected, meaning that motor function can be recovered if nerve continuity is restored (30, 31). Pre-ganglionic injuries confer the worst prognosis and require nerve transfer rather than grafting because the native motor neurons recede (32). Currently the only way to be certain of the extent of injury is to perform a surgical exploration at which point nerve reconstruction can be performed if necessary. Surgical exploration is typically indicated if there is no or limited improvement in biceps or deltoid function at 3 months of age (33).

1. Surgical exploration of the brachial plexus

   Involves an incision in the supraclavicular fossa which enables direct visualisation of the roots C5-T1 (under general anaesthetic).
2. MRI

   Produces detailed images of the brachial plexus (also performed under general anaesthetic due to the young age of patients)

Clinical pathway

Diagnosis of OPBI is usually made at birth or soon after. Once diagnosed, a referral to physiotherapy for stretching and exercises is advised. The physiotherapist will manage the child for several weeks, looking for signs of functional recovery. If spontaneous recovery occurs then the child will be discharged. However, a referral to specialist services is required if the limb remains flaccid before the infant is 12 weeks of age. A specialist assessment involves performing a detailed history and examination, noting factors such as birth weight, shoulder dystocia, assisted delivery, Apgar scores (heart rate, respiratory effort, muscle tone, reflex and colour), presence of Horner’s sign, hemi-diaphragm paralysis, presence of fractures and post-natal recovery of the affected arm. Scoring systems such as the Toronto score (34) are also used to classify functional status. Surgical exploration of the brachial plexus is indicated in children who fall into moderate or severe injury categories, and MRI can be performed to provide information prior to this.

Prior tests

Some babies will have had X-Rays performed of the upper limbs to examine for fractures and some may not have. Other tests for example ultrasound of the shoulders or blood tests may have also been

performed.

Importance of this review

A highly sensitive and specific imaging modality that could clearly define the extent of the brachial plexus injury would enable earlier surgical intervention in those that require it, as well as limiting numbers of unnecessary surgical explorations. The reliability of MRI in detecting root avulsion and other nerve abnormalities is uncertain, therefore assessing the current accuracy of MRI for obstetric brachial plexus injuries will help define its role clinically and suggest areas for development. In existing literature, the reported diagnostic accuracy of MRI for obstetric brachial plexus injuries is variable and is often based on clinical follow-up (23) or electrophysiology (35). This review aims to clarify the overall diagnostic accuracy by comparing MRI to surgical exploration as a reference standard.

Objectives

1. To determine the diagnostic accuracy of MRI for detecting root avulsion in obstetric brachial plexus injuries
2. To determine the diagnostic accuracy of MRI for detecting abnormal nerves in obstetric brachial plexus injuries
3. To determine the diagnostic accuracy of MRI for detecting pseudomeningocele(s) as a surrogate marker of root avulsion in obstetric brachial plexus injuries

Methods/ Design

The Cochrane Handbook for Reviews of Diagnostic Test accuracy was used as guidance to write the methods (36) and the preferred reporting items for systematic reviews and meta-analyses (PRISMA) (37) guidelines were followed.

Types of studies

Studies involving infants with obstetric brachial plexus injuries that report the findings of preoperative MRI in comparison to surgical exploration of the brachial plexus roots will be included. Case reports will be excluded.

Participants

This review will include studies involving children under five years old with obstetric brachial plexus injuries. All injuries to the brachial plexus that occur during delivery will be included, irrelevant of the aetiology (e.g. shoulder dystocia, forceps delivery etc.) Bilateral injuries will also be included.

Index Test

The role of MRI will be to detect root avulsions, other nerve abnormalities and pseudomeningoceles. In OBPI MRI is typically performed at 3 months in infants with persistent upper limb functional limitations. The MRI acquisition will vary in terms of the physical scanner used (manufacturer and model), field strength, pulse sequences, coil arrangement, gradients, postprocessing techniques and other factors – all of which will impact upon image quality and hence diagnostic accuracy. Variations will also arise due to the subjective nature of image interpretation. A radiologist will review the images and either confirm or exclude the presence of avulsion, other nerve abnormality or pseudomeningocele. Positive findings for avulsion are detected by a lack of continuity or absence of the nerve root between the spinal cord and exit foramen (29). Other nerve abnormalities than may be detected include nerve scarring, neuroma or rupture, and these can also be referred to as post-ganglionic nerve injuries (25, 27). An abnormal contour of the dura and collection of dorsal extraspinous fluid is indicative of pseuomeningocele (38) and is considered a surrogate marker of root avulsion given that rupture of the dura mater suggests that the nerve root is also ruptured, although this has been disputed in some literature (39, 40). The presence of one suspected avulsion is of equal importance to that of any number of avulsions, given that any avulsion would warrant nerve transfer surgery. Due to the lower energy stretching forces that typically cause OBPI other types of severe nerve injury apart from avulsion may also be present and can also require surgery e.g. nerve grafting. Avulsions, other nerve injury and pseudomeningoceles can occur at any spinal level from C4 to T2 and may, in rare cases, occur bilaterally. The ability of MRI to identify patients with no root avulsion is vital as surgical exploration could potentially be avoided.

Target condition

Avulsion of the roots of the brachial plexus is the target condition. The ability of MRI to differentiate between any number of root avulsions and no avulsions will be examined. The secondary target conditions are an abnormal nerve and pseudomeningocele.

Reference standard

Surgical exploration of the brachial plexus is the reference standard for detecting root avulsion and other nerve abnormalities. The operation is performed under general anaesthesia and involves an incision in the supraclavicular fossa which extends towards the deltopectoral groove (29). The operation allows direct inspection of the spinal nerve roots C4-T1. Additional intraoperative tests such as somatosensory evoked potentials (SEPs) and bipolar motor nerve stimulation are included as part of the reference standard. SEPs involve measuring cortical activity induced by applying pulses of varying frequency to the nerve roots. Avulsed nerves will not transmit signals to the brain meaning no activity is detected on an encephalogram. Bipolar nerve stimulation involves applying a current across the nerve which would normally cause the corresponding muscle to contract, however in the case of avulsion, no muscle contraction is observed. These intraoperative tests aid surgeons in the diagnosis of root avulsion.

Search strategy

Electronic searches

EMBASE, PubMed and CENTRAL electronic databases will be searched from inception to present date with no restrictions. The medRxiv and bioRxiv preprint archives will also be searched using medrixr (41). GScraper will be used to further increase coverage by pulling hits from Google Scholar (42). The planned EMBASE and PubMed search strategy was formulated with a search strategist and is presented in appendix 1.

References from published studies

Citations will be imported and de-duplicated using EndNote. References will then will be screened using CitationChaser (43).

Study selection

JB will apply the eligibility criteria to screen titles and abstracts for relevance. Two authors (JB and CH) will independently screen identified citations using Rayyan REF. Disagreements will be resolved by discussion with a third author (GB). Full text of eligible studies will then be screened and subsequently labelled as included or excluded. Reasons for exclusion will be noted.

Data Extraction

For included studies the following data will be extracted using an excel spreadsheet. This will be done independently in duplicate by JB and CH: study identifier; number of participants; sex; participants age at diagnosis, MRI scan and surgery; country of origin; time from birth to imaging and surgery; presence of clavicular/humeral fracture; type of MRI scanner used (including brand, model and field strength); pulse sequence; number of true positives, false positives, true negatives and false negatives relating to the detection of root avulsion, abnormal nerve or pseudomeningocele using MRI. The priority outcome is the detection of root avulsion at the brachial plexus as this is the is most important clinically. Detection of abnormal nerves and pseudomeningocele are secondary outcomes. We will contact authors of studies by email if data is missing or unclear.

Methodological quality assessment

An adapted version of the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) (44) tool (Appendix 2) will be used to assess the risk of bias and strength of evidence of the eligible studies respectively at the study level. Two authors (JB and CH) will independently complete the assessment. Disagreements will be resolved by discussion with a third author (GB).

Data synthesis

Analysis will be performed separately for each target condition (root avulsion, abnormal nerve and pseudomeningocele) with the patient and then the nerves being the unit of analysis. Forest plots and receiver operating characteristic plots will be used to display estimates of sensitivity and specificity of the included studies as part of the preliminary analysis. These plots will be generated using MetaDTA (45).

Summary sensitivities and specificities will be obtained using a bivariate model for meta-analyses, providing data is sufficient (46). Meta-analyses will be performed using Stata version 15 (47).

Investigations of heterogeneity

Heterogeneity in the diagnostic accuracy of MRI will be examined using meta-regression or subgroup analyses if data permits. Variations in field strength is likely to be a source of heterogeneity (29) and will be investigated. Babies with OPBI who have not undergone surgical exploration (e.g. they are too unwell) may result in underestimation of the number false negatives which in turn could upwardly bias the sensitivity of MRI. Furthermore, the diagnostic accuracy of MRI could be biased by retrospective studies which have recruited an unrepresentable sample of patients.

Sensitivity analysis

The impact of bias will be evaluated via sensitivity analyses. Studies with a high or unclear risk of bias as identified by the tailored QUADAS-2 tool will be excluded.

Assessment of reporting bias

Reporting bias will not be assessed given the lack of sensitive statistical methods (36). Data will be made available on the Open Science Framework.

Discussion

OBPI can lead to significant morbidity both in terms of the physical implications (e.g. loss of function) and psychological impact (13, 48). MRI offers a non-invasive method of visualising the brachial plexus which could potentially reduce the number of infants undergoing surgery and facilitate earlier treatment in those that require it. However, the reported sensitivity and specificity of MRI in detecting root avulsion and other nerve injuries is variable. A systematic review is required to determine the diagnostic accuracy of MRI in detecting nerve injury in infants with OBPI and define its role clinically. We anticipate variability in scanning techniques, scan reporting as well as surgical techniques and reporting of findings. There is likely to also be a mix of prospective and retrospective studies. We also anticipate possible presence of bias in included studies, for example non-consecutive recruiting or reporting only of positive findings MRI findings. The quality and variability of the included studies will be carefully evaluated using the methods described and results interpreted appropriately.

List Of Abbreviations

OBPI Obstetric Brachial Plexu Injury

MRI Magnetic Resonance Imaging

QUADAS-2 Quality Assessment of Diagnostic Accuracy Studies

Declarations

Ethics approval and consent to particiate

Not applicable

Consent for publication

Not applicable

Availability of data and materials

Data sharing is not applicable to this article as no datasets were generated or analysised. Materials (Search strategy and QUADAS-2 tool) are available in Appendix 1 and Appendix 2.

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Competing interests

The authors declare they have no competing interests.

Authors Contributions

CH, JB and GB conceived the study. CH and JB drafted and revised the protocol, designed data collection tools and the statistical analysis plan with input from GB, RW and IT. CH is the guarantor of the review.

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Not applicable.

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