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Magnetic Resonance Imaging in Preterm Infant: A Systematic Review on Clinical Procedure Safety

Raffaele Falsaperla, PhD,† Silvia Marino, MD,* Noemi Ganci, MD,‡ Guido Leone, MD,‡ Catia Romano, MD,* Angela Tropea, MD,§ Placido Romeo, MD,§ Janette Mailo, PhD,¶ and Martino Ruggieri, PhD‖*

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Background: Currently, there is no evidence that MRI produces harmful effects on premature newborns, as well as short-term and long-term safety issues regarding radiofrequency fields and loud acoustic environment, while the examination that is being performed has not been clearly investigated. MRI of the brain conducted on preterm infants should be part of the diagnostic workup, when necessary. This article is intended to evaluate the short-term safety of MRI performed in preterm infants, when required, by analyzing all vital parameters available before, during, and after the MRI procedures.

Methods: We conducted a systematic review of the literature on electronic medical databases (PubMed and ClinicalTrials.gov) following the Preferred Reported Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. We included all preterm infants who underwent MRI whose clinical, hemodynamic, and respiratory parameters were reported. The quality of the included articles was assessed using QUADAS-2 (Quality Assessment of Diagnostic Accuracy Studies) tool.

Results: Six studies were included with a total of 311 preterm infants. No severe adverse event, such as death, occurred during MRI procedures. Vital signs remained stable in about two-thirds of all patients.

Conclusions: Given the general clinical safety of MRI, we suggest it as a tool to be used in preterm infants in Neonatal Intensive Care Units, when necessary. We further suggest the development of standard protocols to guide the use of MRI in preterm infants to maximize the clinical safety of the procedure.

Keywords: MRI, neuroimaging, premature infants, safety, vital parameters

(*Top Magn Reson Imaging* 2024;33:1–5)

From the *Pediatric and Pediatric Emergency Department, University Hospital "Rodolico- San Marco," PO "San Marco", Catania, Italy; †Unit of Intensive Care and Neonatology, University Hospital "Rodolico- San Marco," PO "San Marco", Catania, Italy; ‡Department of Clinical and Experimental Medicine, Section of Pediatrics and Child Neuropsychiatry, University Hospital "Rodolico- San Marco", PO "Rodolico", Catania, Italy; §Unit of Radiology, University Hospital "Rodolico- San Marco," PO "San Marco", Catania, Italy; ¶Division of Pediatric Neurology, University of Alberta, Edmonton, Alberta, Canada;and ‖Unit of Rare Diseases of the Nervous System in Childhood, Department of Clinical and Experimental Medicine, Section of Pediatrics and Child Neuropsychiatry, University of Catania, Catania, Italy.

Received for publication August 21, 2023; accepted November 3, 2023.

Corresponding author. Address: Pediatric and Pediatric Emergency Department, University Hospital "Rodolico-San Marco," PO "San Marco", Via A. Ciampi, 2 Catania, 95100, Italy. E-mail address: silvia_marino86@hotmail.it (S. Marino).

The authors declare no conflict of interest

Author contributions: Conceptualization, R.F. and S.M.; methodology, R.F., M.R. S.M. and G.L.; software, N.G. and G. L.; validation, R.F., S.M. and M.R.; formal analysis, J.M.; investigation, A.T., P.R. and G.L.; resources, R.F. and S.M.; data curation, N.G. and G.L.; writing—original draft preparation, N.G. and G.L.; writing—review and editing, R.F., M.R. and G.L.; visualization, P.R.; supervision, R.F. and S.M.; project administration, R.F. All authors have read and agreed to the published version of the manuscript.

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Topics in Magnetic Resonance Imaging (2024) 33:e0310

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DOI: 10.1097/RMR.0000000000000310

In preterm infants, neuroimaging is not only primary importance for early diagnosis and subsequent treatment but also to identify those brain lesions that could be associated with neurodevelopment disability. Clinical evaluation of preterm infants is the cornerstone of diagnostic information and directs the instrumental diagnostic path.[1,2]

Cerebral ultrasonography (cUS) and magnetic resonance imaging (MRI) are the most widely used neuroimaging techniques in Neonatal Intensive Care Units (NICUs). cUS allows serial scan with low associated risk. It is used to detect germinal matrix hemorrhage, intraventricular hemorrhage (GMH-IVH), and periventricular leukomalacia (PVL).[3]

MRI is the most complete diagnostic tool, and its applications have increased enormously in recent years. MRI allows us to excellently observe white matter and to identify its lesions with more accuracy than cUS. Furthermore, early detection of newborns at risk of neurological impairment allows neonatologists to apply the most suitable therapy and the best measures to minimize the negative effects of brain injuries.[4]

Even if the environment in which the MRI is performed is particularly stressful for the premature, literature data have never described negative effects related to the MRI procedure, neither in acoustic noise nor heating and damage of exposed tissues. Therefore, MRI can be considered as a safe procedure.[5] However, preterm newborns are very susceptible to stress and hypothermia, so that they easily experience hemodynamic and respiratory instability and often require respiratory support. Consequently, it would be necessary to maintain intensive monitoring and safety of the environment during the patient transport and the scan with re-evaluation of the patient's clinical conditions after MRI execution.[6]

The aim of this systemic review was to evaluate the clinical safety of MRI performed in preterm infants, when required, analyzing all vital parameters before (i.e., during transportation), during, and after the performance of the examination. For clinical safety of MRI, we intend the physiological maintenance or with the help of intensivists of normal vital parameters before, during, and after the diagnostic technique. We wanted to study, by literature searching, whether vital parameters of premature infants undergoing MRI remained stable along all the duration of the examination as well as before and after it. Data on the clinical safety of MRI in preterm infants are critical to improve its use in this population and thus exploiting its benefits.

MATERIALS AND METHODS

We performed a systematic review of the literature on clinical safety of MRI performed in preterm infants following the Preferred Reporting Items for Systematic Review and Meta-Analyzes (PRISMA) guidelines (Fig. 1).[7]

Search strategy

An advanced search on PubMed and ClinicalTrials.gov was performed. The following keywords were included: "magnetic

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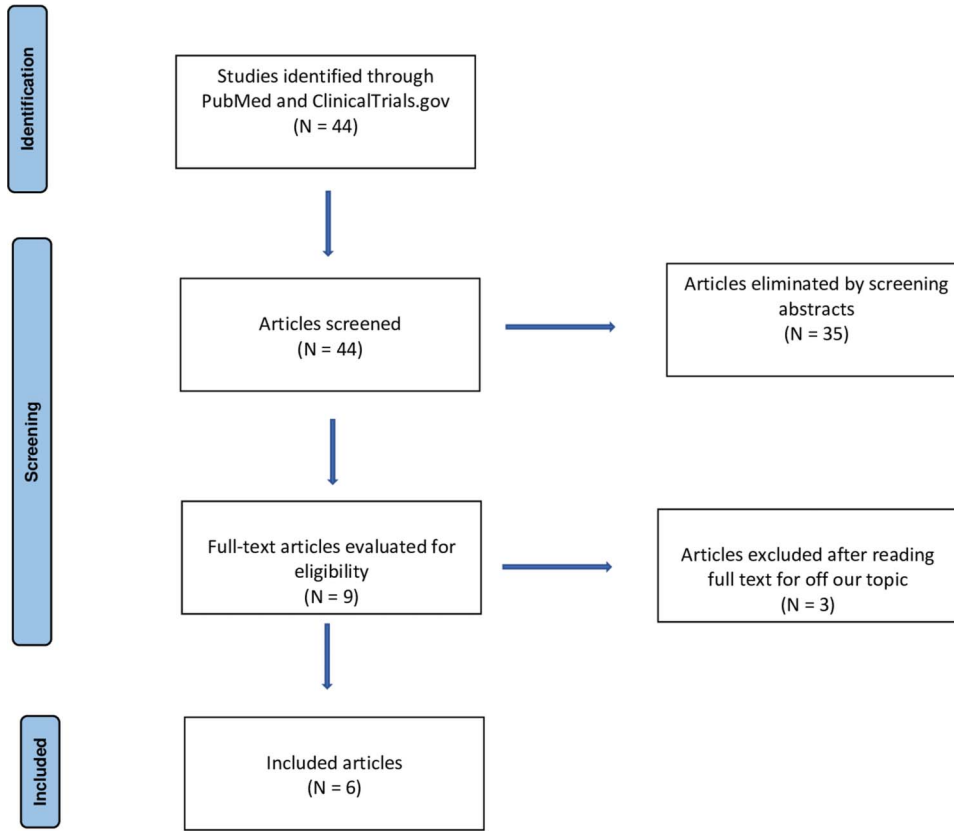

FIGURE 1. PRISMA flowchart.

resonance imaging" AND "safety" AND "preterm infant." We selected articles published from 2000 to 2021; the only filter applied concerned the English language.

Inclusion and exclusion criteria

All articles reporting information on safety along transportation to MRI scanner, during MRI procedure and after its end in preterm infants, which was configured in the assessment of their vital parameters (heart rate, oxygen saturation, and body temperature), were included.

Articles that did not report data related to the clinical conditions and vital signs of newborns undergoing MRI, as well as articles which did not include preterm infants, and only describing anesthetic periprocedural interventions or physical characteristics of the MRI were excluded.

Study selection

One author consulted all the cited databases according to the search strategies and then removed duplicate studies. Then, 2 authors, who perfectly agreed on studies elimination at the final confrontation, independently screened titles and abstracts from PubMed and ClinicalTrials.gov searches. Selected full-text articles were read by all the authors. Complete consensus was found about the articles to be included in this study. Each researcher followed the inclusion criteria unanimously decided in the preselection phase.

Risk of bias and quality assessment

All included studies were assessed using QUADAS-2 (Quality Assessment of Diagnostic Accuracy Studies), a tool to assess the quality of primary diagnostic accuracy studies included in systematic reviews focused on risk of bias and applicability in the study. Judgment regarding risk of bias is to be based on the predefined signaling questions regarding the following 4 domains: patient selection, index test, reference standard, and flow timing. Judgment regarding applicability is based on the extent to which bias is likely to affect the question in the review in any domain. The risks of bias and the applicability concerns were rated as "low," "high," or "unclear" and are summarized for each study in Table 1. Moreover, according to AMSTAR 2 (A MeaSurement Tool to Assess systematic Reviews 2) score, "moderate quality review" evaluation was obtained for this work.

Definition of entity of the adverse events

To better standardize the adverse events occurred throughout the MRI procedures, here we provide some definitions: minor adverse event was considered as an episode of hemodynamic or respiratory instability lasting less than 20 seconds and not requiring medical intervention; major adverse event was defined as an analog episode whose duration was more than 20 seconds or requiring immediate intervention; and severe adverse event coincided with death. Hypothermia was accounted as a minor adverse event.

RESULTS

Forty-three articles were identified on PubMed by searching the predetermined keywords. One more article by Benavente-Fernández et al. was extracted during cross reference step of the analysis because it fulfilled our inclusion criteria. Thirty-five articles were

TABLE 1. Assessment of Risk of Bias and Applicability Concerns

ASSESSMENT OF RISK OF BIAS				
	Patients selection	Index test	Reference standard	Flow and timing
Plaiser et al.[5]	Low	Low	Low	Low
M. Battin et al.[12]	Low	Low	Low	Low
Benavente-Fernández et al.[6]	Low	Low	Low	Low
Sirin et al.[9]	Low	High	Low	High
Fumagalli et al.[10]	High	High	Low	Low
Merchant et al.[11]	Low	High	Low	Low

ASSESSMENT OF APPLICABILITY OF CONCERNS				
	Patients selection	Index test	Reference standard	Flow and timing
Plaiser et al.[5]	Low	Low	Low	Low
M. Battin et al.[12]	Low	Low	Low	Low
Benavente-Fernández et al.[6]	Low	Low	Low	Low
Sirin et al.[9]	Low	Low	Low	Low
Fumagalli et al.[10]	Low	Low	Low	Low
Merchant et al.[11]	Low	Low	Low	Low

Low | High | Unclear

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excluded based on the title and abstract. Of the 9 included articles, 3 were further excluded after full text reading as the content was not considered relevant to our review. Finally, 6 full-text articles were evaluated for eligibility, including 4 prospective and 2 retrospective studies (Fig. 1).[5,6,8–11] No further articles were found by searching ClinicalTrials.gov. Three hundred eleven preterm infants were evaluated. It was not possible to standardize the mean age at scan, baseline oxygen saturation, and body temperature.

Vital parameters (hear rate, oxygen saturation, body temperature)

Heart rate, oxygen saturation, and body temperature remained generally stable during and after MRI scan procedures in two-thirds of all patients.

In 311 preterm infants, some minor adverse events were recorded, including hypothermia and brief hemodynamic and respiratory instability episodes. Hypothermia was described in only 10/311 patients (3%) and was not considered clinically relevant by the authors of the included studies (Table 2). A total of 106/311 infants (34%) had minor adverse events, that is, one or more short desaturations that did not require any intervention. Only 20/311 premature newborns (6.4%) experienced major respiratory instability so that MRI was stopped to prevent a further deterioration of the clinical conditions. Major hemodynamic instability was observed in 14/311 infants (4.2%) within 24 hours after scan. Generally, adverse events were not described before MRI procedures, including along the transportation (in this case, vital parameters were reported only for the 69 newborns of the studies of Benavente-Fernàndez et al.[6] and Fumagalli et al.[9]).

No severe adverse event, such as death, occurred throughout the procedures.

DISCUSSION

The aim of this systematic review was to evaluate the clinical safety of MRI in preterm infants by collecting all the clinical evidence present in the literature. Preterm neonates enrolled in the studies included in our review presented abnormal cUS findings, highly suspicious for brain injury.

Nowadays, we do not know how dangerous both transportation to and execution of MRI are for the preterm newborn. MRI could potentially create different concerns regarding safety, consisting in

TABLE 2. Results of Included Studies

Author (Study Type)	Plaiser et al.[5] (Retrospective Study)	Battin et al.[11] (Prospective Study)	Benavente-Fernández et al.[6] (Prospective Study)	Sirin et al.[8] (Retrospective Study)	Fumagalli et al.[9] (Prospective Study)	Merchant et al.[10] (Prospective Study)
Preterm infants (n)	52	23*	33†	84 (with incubator)‡ 13 (without incubator)‡	36	70§
Gestational age or postmenstrual age or term equivalent age at scan	30 wk (mean) of GA	27 wk (median) of GA	Early scan: 29.5 wk (mean) of PMA Late scan: 38–42 wk (mean) of TEA	With incubator: 40.6 wk (mean) of PMA Without incubator 47.8 wk (mean) of PMA	43.8 wk (mean) of TEA	30 wk (median) of PMA
Acquisition scan time	30 min (mean)	53.5 min (mean)	Early scan: 26.8 min (mean) Late scan: 22.5 min (mean)	34 min (mean)	35 min (mean)	55 min (median)
Heart rate (bpm)	N/A‖	159 (median)	Previous 144 (mean) Transporting 148 (mean) MRI 151 (mean) Posterior 196 (mean)	With incubator 152 (mean) at start 152.6 (mean) at end	Before MRI 136 (mean) After MRI 137 (mean)	N/A¶
$SatO_2$ (%)	N/A¶	736/2087 > 97 42/2087 < 90 8/2087 < 85 3/2087 < 80	Previous 97 (mean) Transporting 96.87 (mean) MR 96.83 (mean) Posterior 97 (mean)	Whit incubator 97.2 (mean) at start 96.1 (mean) at end	Before MRI 97.5 (mean) After MRI 97.2 (mean)	N/A¶
Axillary temperature (Ta, °C) Rectal temperature (Tr, °C) Skin temperature (Ts, °C)	N/A#	Ta 36.9 (median)	Previous Ta 36.78 (mean) Posterior Ta 36.74 (mean)	Tr previous transporting 37.2 (mean) Tr posterior scan 37.1 (mean)	Before MRI Tr 37 (mean) After MRI Tr 37 (mean) Before MRI Ts 35 (mean) After MRI Ts 36.1 (mean)	Ta: 64 preterm infants > 36 4 preterm infants < 36

*39 MRIs in total; 2087 minutes of physiological data.
†46 MRIs in total.
‡117 MRIs in total.
§2 deferred MRIs.
‖Reported as stable, increased hemodynamic instability in 14 infants.
¶Reported as stable.
#Reported as stable, 9 presented hypothermia (Ta < 36°C).

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hemodynamic, respiratory, and temperature stability of the preterm infant before (i.e., along transportation), during and after the MRI scan.

To the best of our knowledge, this is the first systematic review that collects all the evidence of the literature on the clinical safety of MRI in preterm infants. There are safety guidelines on the physical properties of the MRI, while there are still very few data concerning clinical stability and safety during the procedure. The 6 studies we included in this article report 311 preterm infants. These studies evaluated the safety of MRI in clinical stability during the procedure, and some of them also evaluated before the procedure, including along transportation, and after it. The clinical stability is certainly a good safety index because it is one of the most important critical issues in preterm infants.[2] From the data extrapolated from these studies, it can be stated that the clinical parameters measured ($SatO_2$, heart rate, temperature) remained stable in about two-thirds of cases. In only 1 study,[5] it was found an increased hemodynamic instability in 26.9% (14 infants) within 24 hours after scan, which however did not translate into serious clinical events.

In 3 of the examined studies, MRI with a 3-Tesla state magnetic field was performed. 3-Tesla MRI allows a better resolution and quality of the images to the detriment, however, of the increase in acoustic noise and specific absorption rate (SAR), the latter indicating the degree of absorption of radiofrequency radiation by exposed tissues and their consequent heating. In all 3 studies with 3-Tesla MRI mentioned above on 203 children and with an acquisition time range of 34–55 minutes, the temperature remained stable and did not undergo clinically relevant changes. In general, all the studies show that the scan time (ranging from 22.5 minutes to 55 minutes) is not a parameter that affects clinical stability.

Many data also state that a magnetic field of 3-Tesla has no deleterious effects on human tissues; the Food and Drug Administration (FDA) ensures that for magnetic fields up to 8-Tesla, there is no significant risk to patients regardless of age.

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Another parameter to consider is noise: The FDA recommends hearing protection for exposures greater than 99 dB. Therefore, different measures are used to attenuate the acoustic noise, such as neonatal ear muffs. In regards, the use of the right MRI compatible equipment is essential to ensure monitoring of vital sign by avoiding burns or image alterations due to interference with the magnetic field. In some centers, the MRI scanner is located inside the NICU. This makes easier to monitor vital signs and maintain intensive care, while others have MR compatible incubators. The use of a MR compatible incubators was evaluated in the study of Sirin et al.,[8] finding an improvement in safety, handling, and quality of the scan images obtained even in unstable patients. However, from various studies examined and especially from those ones of Benavente-Fernández et al.[6] and Fumagalli et al.,[9] which evaluated vital parameters before and after MRI scan, significant changes in vital parameters and clinical stability were not found. Therefore, MRI can be considered safe even in the absence of a compatible incubator or when it is placed outside the NICU. Nevertheless, it would be useful to perform more studies to collect as much data as possible and to establish a standard protocol, ranging from preparation to transport and scanning of the newborn, to be ideally performed in the same way in all centers.

Based on the data about safety regarding clinical stability collected in this review, it would be reasonable to implement the use of MRI, when necessary, in the management of preterm newborns in Neonatal Intensive Care Units. Owing to the paucity of available evidence in the literature about this topic, it is important to conduct new studies and collect more data on the safety and management of the preterm infants with the aim to obtain a standard safety protocol to be applied equally in all centers.

Limitations of the study

To the best of our knowledge, literature data on this topic are very limited. Therefore, the main limitation of this systematic review is the low number of relevant articles identified due to the paucity of the available evidence in the literature regarding this topic. Another important limitation is the absent standardization of the population, especially in age at the moment of the examination, baseline oxygen saturation, and body temperature.

CONCLUSION

From the analysis of the studies included in our systematic review, which accounts for 311 preterm infants, it is evident that the vital parameters remain generally stable during the MRI procedure and they do not undergo significant changes. Vital parameters are indicators of clinical safety of the procedure, and this is a very important issue considering that hemodynamic and respiratory instability is one of the main problems in preterm infants. As mentioned above, given the general clinical safety of MRI, we suggest it as a tool to be used in preterm infants in Neonatal Intensive Care Units, when necessary.

MRI seems to be a safe instrumental investigation, especially with the help of a multidisciplinary coordination and of an intensive monitoring. We further suggest the development of standard protocols to guide the use of MRI in preterm infants to maximize the clinical safety of the procedure.

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