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Original article

Early prediction of unilateral cerebral palsy in infants with asymmetric perinatal brain injury – Model development and internal validation

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ABSTRACT

Background: Early diagnosis of unilateral cerebral palsy is important after asymmetric perinatal brain injury (APBI). Our objective is to estimate the risk of unilateral cerebral palsy (UCP) in infants with APBI during the first months of life using neuroimaging and clinical assessment.

Patients and methods: Prognostic multivariable prediction modeling study including 52 infants (27 males), median gestational age 39.3 weeks with APBI from Sweden (n = 33) and the Netherlands (n = 19). Inclusion criteria: (1) neonatal MRI within one month after term equivalent age (TEA), (2) Hand Assessment for Infants (HAI) between 3.5 and 4.5 months of (corrected) age. UCP was diagnosed ≥24 months of age. Firth regression with cross-validation was used to construct and internally validate the model to estimate the risk for UCP based on the predictors corticospinal tract (CST) and basal ganglia/thalamus (BGT) involvement, contralesional HAI Each hand sum score (EaHS), gestational age and sex.

Results: UCP was diagnosed in 18 infants (35%). Infants who developed UCP more often had involvement of the CST and BGT on neonatal MRI and had lower contralesional HAI EaHS compared to those who did not develop UCP. The final model showed excellent accuracy for UCP prediction between 3.5 and 4.5 months (area under the curve, AUC = 0.980; 95% CI 0.95–1.00).

Conclusions: Combining neonatal MRI, the HAI, gestational age and sex accurately identify the prognostic risk of UCP at 3.5–4.5 months in infants with APBI.

Abbreviations: AI, Asymmetry index; APBI, asymmetric perinatal brain injury; BGT, basal ganglia and/or thalamus; BoHM, Both hands measure; CST, corticospinal tract; EaHS, Each hand sum score; HAI, Hand Assessment for Infants; PAIS, perinatal arterial ischemic stroke; PLIC, posterior limb of the internal capsule; PVHI, periventricular hemorrhagic infarction; TEA, term equivalent age; UCP, unilateral cerebral palsy.

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1. Introduction

Unilateral perinatal brain injury is commonly diagnosed in the neonatal intensive care unit. Most frequent forms of unilateral brain injury include perinatal arterial ischemic stroke (PAIS) in term born infants and periventricular hemorrhagic infarction (PVHI) in preterm infants. However, also other conditions such as white matter injury or parenchymal hemorrhages may lead to asymmetric brain injury in newborns. Infants with such asymmetric perinatal brain injury (APBI) are at high risk to develop unilateral cerebral palsy (UCP).[1–3]

UCP is usually diagnosed at the age of two to four years or even later in mildly affected children, while asymmetric hand use is typically reported much earlier by clinicians and parents.[4–6] Early diagnosis of UCP is important to adequately counsel families and to provide access to early interventions.[1,7,8] Increased knowledge about high plasticity in the young brain suggests that activity-based training should occur at an early age in order to be effective, in parallel with the development of the corticospinal tract.[9,10] New treatment strategies for neonatal brain injury, such as neuroprotective or neuroregenerative repair, have also become available and new motor assessment tools are needed to accurately and objectively study their effect.[11,12]

Magnetic resonance brain imaging (MRI) during the neonatal period is increasingly used as a predictive tool to identify infants at high risk for UCP.[13–15] Involvement of specific regions, such as the corticospinal tracts or the basal ganglia/thalamus, have been associated with adverse motor development and UCP.[14,16,17] To improve the prediction of UCP at an early age, a combination of MRI with standardized clinical assessments is recommended.[5] A promising clinical tool for prognosis of UCP is the newly developed Hand Assessment for Infants (HAI). The HAI is the first standardized assessment quantifying hand function in terms of asymmetry and measuring both hands use in infants at high risk for UCP from 3 to 12 month of age.[18] This makes the HAI especially suitable for infants with unilateral or asymmetric perinatal brain injury, in contrast to more commonly used motor assessment tools, which do not measure asymmetric hand use.[19]

The aim of this study is to develop and internally validate a multivariable prediction model to estimate the prognostic risk of UCP in infants with APBI following the recommendation of combining neuroimaging with a clinical assessment for the prediction of UCP as early as possible.[5,20,21] It is hypothesized that neonatal brain imaging in combination with an early assessment of hand asymmetry using the HAI and additional infant characteristics can predict UCP during the first months of life in infants with APBI. If so, this method may have the potential to predict the risk of UCP and facilitate individualized treatment that focuses on the infant's specific needs and prognosis.

2. Materials and methods

2.1. Participants

This prognostic multivariable prediction modeling study included a convenience sample of 52 infants with evidence of APBI from the Karolinska University Hospital and Södersjukhuset in Stockholm (n = 33), Sweden and the Wilhelmina Children's Hospital of the University Medical Center in Utrecht (UMCU), the Netherlands (n = 19), within April 2008 and May 2016. APBI was diagnosed after MR investigation in the neonatal unit during the first month after term equivalent age (TEA). In Stockholm, all infants were recruited from the national stroke follow-up program based on neurological signs and MRI evidence of APBI, and referred to the occupational therapy department for HAI assessments. In contrast, in Utrecht, only infants with high risk of UCP based on MRI findings were included and followed by HAI assessments. Inclusion criteria were: (1) an MRI within one month of TEA and (2) early assessment of hand function between 3.5 and 4.5 months of (corrected) age using HAI. Exclusion criteria were major congenital malformation or surgery before the first symptom was apparent. No children have been included in any specific training program prior to the investigation, five infants received erythropoietin as part of a safety and feasibility trial (Table 1).[12] UCP was diagnosed based on a clinical assessment by an experienced child neurologist or rehabilitation specialist at ≥24 months in compliance with international European guidelines.[22]

2.2. Ethical approval

Ethical approval was granted from the Regional Ethics Committee Stockholm (2008/148-31), and was applied for, but not required by the Medical Ethical Committee Utrecht (WAG/th/14/038370) because HAI assessment and MR imaging are considered standard medical care for infants with APBI who were considered at high risk of UCP.

2.3. Magnetic resonance imaging of the brain (MRI) and evaluation of MRI data

The MRI assessment was performed as part of the clinical examination of APBI. In the UMCU, MRI was performed on either a 3 T whole-body system (Philips Medical Systems, Best, the Netherlands), using a coronal or axial scanning protocol that consisted of at least a T1-weighed imaging (T1WI), T2WI and DWI. Infants at the UMCU were sedated for the MRI to

Table 1 – Descriptive data of participants.

	Total (n = 52)	Stockholm (n = 33)	Utrecht (n = 19)
Male	27 (52)	17 (52)	10 (53)
Gestational age at birth (in weeks)*	39.3 [33.5, 40.5]	40.3 [38.1, 40.5]	32.3 [26.1, 37.5]
Preterm (<37 weeks of gestation)*	19 (37)	6 (18)	13 (68)
Diagnosis			
Perinatal arterial ischemic stroke (PAIS)	26 (50)	19 (58)	7 (37)
Periventricular hemorrhagic infarction (PVHI)*	11 (21)	2 (6)	9 (47)
Other	15 (29)	12 (36)	3 (16)
Laterality of lesion			
Left	25 (48)	13 (40)	12 (63)
Right	24 (46)	17 (51)	7 (37)
Asymmetric bilateral	3 (6)	3 (9)	0 (0)
Erythropoietin	5 (10)	0 (0)	5 (26)[a]
UCP diagnosis*	18 (35)	6 (18)	12 (63)
Corrected age at HAI assessment			
15–16 weeks	18 (35)	12 (37)	6 (32)
16–17 weeks	9 (17)	5 (15)	4 (21)
17–18 weeks	9 (17)	5 (15)	4 (21)
18–19 weeks	5 (10)	2 (6)	3 (16)
19–20 weeks	11 (21)	9 (27)	2 (10)
Postnatal age at MRI scan (days)*	5.0 [3.0, 10.0]	5.0 [3.0, 6.8]	10.0 [5.0, 34.0]

Data presented as median [Interquartile Range] or number (percentage), where applicable. UCP – unilateral cerebral palsy, GA – gestational age.
*Differences between Stockholm and Utrecht group ($p < 0.05$).
[a] Two infants who received EPO did develop UCP.

avoid movement artefacts. MR imaging details for the Utrecht group have previously been described.[23] In the Karolinska University Hospital and Södersjukhuset, MRI was performed using a 1.5 T MRI system with protocols including T1WI and T2WI. Infants were not sedated, instead positioned in bean bags after being fed breastmilk or formula.

All images were re-evaluated by two experts in the field of neonatal neurology (LdV, NW) through visual inspection of specific regions that are known to be predictive of adverse motor outcome: the corticospinal tract (CST), basal ganglia and thalamus (BGT).[14,24] The assessors were unaware of the clinical diagnosis and functional outcome. Visual inspection of the DWI was done when the MRI was performed during the first week after symptom onset or of the T1-and T2-weighted images when the MRI was acquired later. Involvement of the CSTs was determined at the level of the posterior limb of the internal capsule (PLIC) and the cerebral peduncle as described previously.[17,25] Involvement of the BGT was noted when there was involvement of the basal ganglia and/or the thalamus.

2.4. *Hand Assessment for Infants (HAI)*

The HAI is a newly developed standardized observation-based assessment for infants 3–12 months of age at risk of developing UCP.[18] It assesses the degree and quality of goal-directed manual actions performed with each hand separately as well as both hands together.

In a semi-structured, video-recorded 10–15 min play session 12 unimanual and 5 bimanual items are tested and scored on a 3-point rating scale.[18] The sum score is Rasch-transformed into an interval level logit-based Both hands measure, BoHM (0–100 HAI-units) with higher scores indicating better performance. For unimanual items, each hand is scored separately resulting in the Each hand sum score, EaHS (0–24 points). Based on the EaHS an asymmetry index, AI, (0–100 percentage difference) is calculated.[18] The HAI showed excellent validity and reliability of scores for the evaluation of bilateral hand use in infants from 3 to 12 months of age at risk of UCP, and showed very good predictive validity for UCP in infants at risk.[18]

HAI data was collected at 3.5–4.5 months of (corrected) age. The time of the initial assessment varied depending on different clinical routines. HAI assessments were video-recorded and subsequently scored by experienced assessors from Utrecht and Stockholm, who were unaware of the clinical diagnosis.

2.5. *Statistical analysis*

Descriptive summary measures were reported either as mean with standard deviation (SD) or median with interquartile ranges [IQR] depending on their distribution.

To investigate the predictive validity of the qualitative evaluation of involvement of the CST and BGT on neonatal MRI, predictive values, accuracy, and likelihood ratios were calculated from contingency tables.

Firth penalized regression was applied to construct a multivariable prediction model to estimate the prognostic risk of UCP at ≥24 months and at the same time consider the quasi-complete separation in the predictor CST involvement, i.e. all infants that did not show CST involvement on the MRI, did not develop UCP. As Firth penalized regression does not allow for variable selection, the model was based on all available and relevant clinical predictors (CST, BGT, HAI, gestational age, sex). A single model constructed from the sample data may be overly optimistic in predicting UCP. To limit overfitting, we applied tenfold cross-validation, i.e. dividing the sample data in ten subsets, where nine serve to

construct the model and the tenth is used to evaluate its accuracy; this procedure is repeated for each subset and results in reduced model coefficients. Receiver operating characteristics (ROC) curve analysis was performed and the area under the curve (AUC) calculated to evaluate the model accuracy. Statistical analysis was performed in Stata IC 15.

3. Results

3.1. Participants

Baseline characteristics of all 52 infants are summarized in Table 1. PAIS and PVHI were the most common forms of ABPI in our cohort with 26 and 11 infants (50% and 21%) affected respectively. Other diagnoses (n = 15) included parenchymal hemorrhage (n = 5), white matter injury (n = 3), watershed injury (n = 2), subdural hemorrhage (n = 2), antenatal PVHI leading to porencephalic cyst (n = 1) and thalamic hemorrhage (n = 1). At the age of 24 months 18 infants (35%) had developed UCP. More preterm infants (61%, n = 11) than term infants (39%, n = 7) developed UCP ($p < 0.01$), and more males than females (66% vs. 33%) developed UCP, but this difference did not reach statistical significance ($p > 0.05$). The HAI was collected across the whole age range of 3.5–4.5 months with the majority of assessments at lower age (Table 1). Median [IQR] scores of the HAI (contralesional EaHS, AI and BoHM) at 3.5–4.5 months of age were lower in infants who developed UCP compared to those who did not develop UCP (all $p < 0.002$) (Table 2).

3.2. Predictive validity of CST and BGT involvement on neonatal MRI

All infants who developed UCP showed CST involvement, while infants who did not develop UCP predominantly showed no CST involvement (71%, n = 24) (Table 2). CST involvement on neonatal MRI had excellent sensitivity (100%), but only moderate specificity (71%) and likewise an excellent NPV (100%), but moderate PPV (64%) to predict the presence of UCP at ≥24 months of (corrected) age with an accuracy of 81% (Table 3). MRI performance increases the likelihood to identify UCP in infants that later developed UCP to a minor extent (LR+ 3.4). In infants who developed UCP, 78% (n = 14) showed BGT involvement, while in infants who did not develop UCP, 32% (n = 11) showed BGT involvement. BGT involvement showed somewhat lower values with 78% sensitivity and 68% specificity, 56% PPV and 85% NPV with 71% accuracy (Table 3).

3.3. Prognostic risk of developing UCP

The final model included all available predictors, including gestational age (in weeks), male sex, CST and BGT involvement observed from neonatal MRI, and the contralesional HAI EaHS between 3.5 and 4.5 months. ROC analysis for this model yielded an AUC of 0.980 (95% CI 0.953–1.00, Fig. 1). The equation of the final model to estimate the prognostic risk of developing UCP between 3.5 and 4.5 months of (corrected) age is: $invlogit = 2.19 + 3.49^{*}CST + 1.85^{*}\ BGT - 0.51^{*}contralesional\ HAI\ EaHS - 0.04\ gestational\ age + 1.81^{*}sex$.

A nomogram based on the final model presented in the equation above serves to estimate the prognostic risk or probability of an individual infant (Fig. 2). For further explanation of the nomogram, see also Appendix 1. The sensitivity and specificity at various thresholds of the prognostic risk of UCP at ≥24 months is displayed in Fig. 3.

An alternative to the final model with all available data at one month of term equivalent age (thereby excluding HAI) yielded an AUC of 0.842 (95% CI 0.733–0.950). In contrast, another variant of the model excluding the MRI evaluation of CST and BGT still including HAI EaHS between 3.5 and 4.5 months, gestational age and sex resulted in a similar performance as the complete final model, but with wider confidence intervals (AUC of 0.930, 95% CI 0.859–1.00).

4. Discussion

A multivariable prediction model, that was developed and internally cross-validated, was able to calculate with high accuracy the risk of UCP already from 3.5 months of age based on CST and BGT involvement observed from neonatal MRI, a contralesional HAI EaHS between 3.5 and 4.5 months, and the infant's gestational age and sex. However, external validation

Table 2 – Descriptive data from neonatal MRI and HAI.

	Total (n = 52)	No UCP (n = 34)	UCP (n = 18)
No CST involvement*	24 (46)	24 (71)	0 (0)
CST involvement	28 (54)	10 (29)	18 (100)
PLIC alone	12 (23)	4 (12)	8 (44)
PLIC and cerebral peduncles	16 (31)	6 (18)	10 (56)
No BGT involvement*	27 (52)	23 (68)	4 (22)
BGT involvement	25 (48)	11 (32)	14 (78)
HAI contralesional EaHS*	15 [9–18]	17 [15–19]	7 [5–10]
HAI ipsilesional EaHS	17 [15–19]	18 [15–19]	17 [13–19]
HAI asymmetry index*	12 [5–47]	6 [0–15]	59 [46–71]
HAI BoHM*	51 [40–59]	57 [51–61]	38 [35–48]

Data presented as median [Interquartile Range] or number (percentage), where applicable.
*Signifcant difference between infants with and without UCP, $p < 0.01$.
UCP – unilateral cerebral palsy, GA – gestational age, CST – corticospinal tract, BGT – basal ganglia/thalamus, PLIC – posterior limb of internal capsule, HAI – Hand Assessment for Infants, EaHS – Each hand sum score, BoHM – Both hands measure.

Table 3 – Predictive value of MRI parameters for UCP.

	Sen (%)	Spec (%)	PPV (%)	NPV (%)	Acc (%)	LR +	LR –
CST involvement	100	71	64	100	81	3.4	0.0
BGT involvement	78	68	56	85	71	2.4	0.3

MRI – magnetic resonance imaging, UCP – unilateral cerebral palsy, CST – corticospinal tract, BGT – basal ganglia and/or thalamus, Sen – sensitivity, Spec – specificity, PPV – positive predictive value, NPV – negative predictive value, Acc – accuracy, LR +/– – positive/negative likelihood ratio.

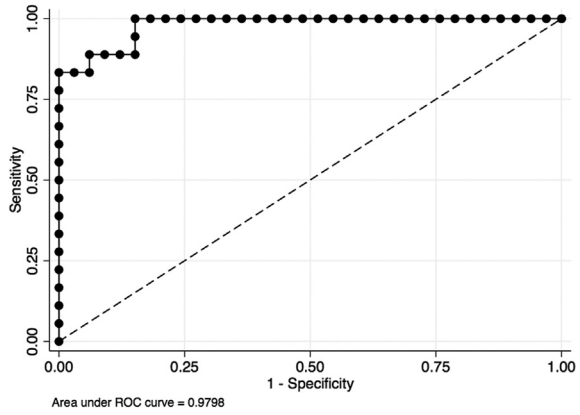

Fig. 1 – Receiver operating characteristics (ROC) curve displaying sensitivity and 1-specificity of the final prediction model for UCP at 3.5–4.5 months.

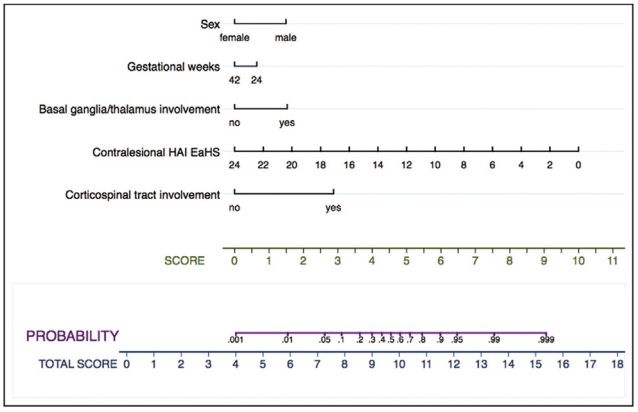

Fig. 2 – Nomogram relating potential predictors (sex, gestational weeks at birth, basal ganglia/thalamus involvement on neonatal MRI, contralesional HAI Each hand sum score (EaHS) between 3.5 and 4.5 months (corrected) age, corticospinal tract involvement) to the prognostic risk score of UCP. For each predictor, read the points assigned on the 0–11 'Score' scale (green) and then sum these points. Find the sum score on the 0–18 'Total score' (blue) scale and then read the corresponding 'Probability' (prognostic risk, purple) of UCP above it. Application of the nomogram is explained in a practice example displayed in the appendix. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

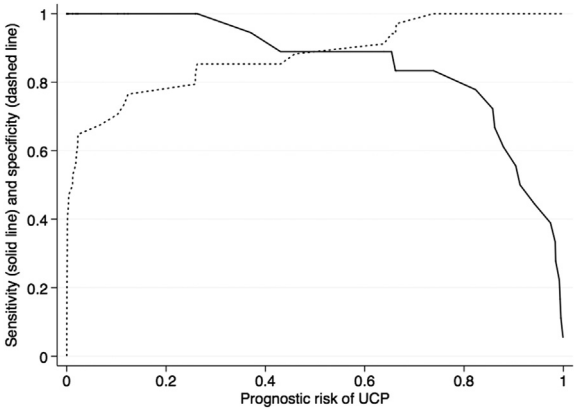

Fig. 3 – Graph displaying the sensitivity and specificity of the prognostic risk (probability) of UCP.

is required before implementation of this model and its accompanying nomogram in clinical practice.

MRI is recognized as the most reliable neuroimaging method to predict CP and several distinct MRI parameters have been associated with CP in later life. For example, brain injury with involvement of the CSTs at the level of the PLIC and/or cerebral peduncles is associated with CP.[6,14,26] In our study, no UCP was seen in the absence of CST involvement (100% NPV). However, involvement of the CST resulted in 10 infants who did not develop UCP, and therefore a low specificity (71%) and PPV, leading to considerable overdiagnosis of UCP. These findings are similar to other research reporting that absence of CST involvement resulted in typical motor development in 94% of infants, while CST involvement had lower sensitivity (67%) and associated PPV.[17] BGT involvement is another MRI parameter that has been associated with adverse motor outcome in neonatal brain injury,[16,17,26] but was much less predictive in our cohort. This may be due to a heterogeneous group of infants, including a large number of preterm infants with PVHI in our cohort, for whom the predictive value of BGT involvement has not yet been established. Additionally, in our cohort CST and BGT involvement was perhaps low due to timing of the MRI. The MRI was not always performed in the acute phase after injury, when predictive ability of MRI (including DWI) is highest, but sometimes >7 days in term infants or around TEA in preterm infants. By dichotomizing the evaluation of brain structures (CST, BGT) additional information on the location and size of the lesion, which are also assumed to be predictive for the extent of UCP, could not be taken into account.

Although MRI is a good predictor, a prediction model for UCP based on neonatal MRI combined only with gestational

age and sex, can indeed within one month of TEA predict UCP with good accuracy, but with less confidence. This seems helpful for very early preliminary risk estimation, as the MRI is performed much earlier than the assessment of hand function. Prediction performance increases further at 3.5–4.5 months in the same model using HAI instead of MRI. However, when information about CST and BGT involvement from neonatal MRI and asymmetric hand function measured by HAI are combined in a final model the prediction performance becomes excellent. Such a combination of imaging and standard assessment has also been recommended in recent guidelines.[5] It needs to be noted though that this prediction model is valid only for the predictors measured at specific time-points, i.e. MRI within one month of TEA and the contralesional HAI EaHS between 3.5 and 4.5 months of (corrected) age. An earlier model including HAI prior to 3.5 month of age shows insufficient predictive ability due to large variations of voluntary upper limb actions at this early age.

Asymmetric hand function has been described as one of the earliest clinical manifestations of UCP.[27] The HAI enables us to measure this asymmetric hand function in infants as early as three months of age.[18] Indeed, our results show that of all three HAI scales (contralesional EaHS, BoHM and the AI) were significantly different between infants who developed UCP and those who did not. The contralesional EaHS was the most predictive HAI scale for infants with risk for UCP when investigating the statistical model. Due to large variations of voluntary upper limb actions before 3.5 month of age, this study only included HAI scores from 3.5 months onwards. HAI values typically increase by age and asymmetric hand function may also become more obvious, thereby changing the predictive ability of the model at other ages. This will be elaborated upon in future studies of our own group (personal communication). Recently, we have described three distinct developmental trajectories of hand function in infants with UCP over the first year of life (3–12 month). Although, the future severity level of UCP could not yet be detected at 3–4 months of age due to large variation and overlap between curves, at six months of age the trajectories were clearly delineated.[28] Additionally, normative values of different HAI scores are established and can be used to further compare the development of infants at risk of UCP and typical developing infants.[29] In future, HAI may not only serve as a predictive tool, but also as an outcome measure of early intervention. It has already been used in a study demonstrating improvement of manual ability after constraint induced movement therapy in infants younger than 12 months of age.[7] Overall, accumulating results of these studies will increase our knowledge about the development of upper limb function in children with UCP.

A limitation of this study is that the cohort consisted of infants with different diagnoses of APBI, and consequences of these types of injury on motor behavior differ. Around 30–50% of children who suffer from PAIS develop UCP.[16,17,30] Unilateral PVHI in preterm infants leads to UCP in 50–70% of children.[31–33] Other diagnoses, such as white matter injury, are less likely to lead to UCP, depending on site and extent of the injury. To account for these differences, we focused on MRI parameters that can be applied to various forms of brain injury such as involvement of the CST and BGT. Differences in recruitment might have caused selection bias, though combining of infants from two sites had the advantage to increase variation and to identify various prediction factors in order to build a more clinically relevant model. To address potential selection bias, the model was tested separately in both groups in a pos hoc analysis and showed very similar performance (AUC for Utrecht 0.97, 95% CI 0.920–1.00; AUC for Stockholm 0.96, 95% CI 0.901–1.00).

Erythropoietin is another factor that might be assumed to influence the outcome, but in this study treatment with erythropoietin did not add to the prediction model. It would also be of interest to investigate General Movements (GMs) assessment or Hammersmith Infant Neurological Examination (HINE) as they are currently the most predictive tools of CP.[5] Unfortunately, this data was inconsistently collected in our clinical cohort and could not be included in this study. It has to be noted that this is a convenience, hospital-based cohort including high risk infants. Infants without a neonatal event would most likely have been referred to other health care services at later age and are not the target group for this model. An important next step in this research is to externally validate the model in a similar population before implementation in clinical practice.

4.1. *Clinical implication*

In general, the diagnosis of UCP is based on clinical signs from neurological examination and medical history in accordance with national guidelines. This first explorative study strengthens the interpretation of the signs, showing that neonatal MRI gives good information about UCP development already at one month TEA, but prediction performance increases considerably with complementary information about hand asymmetry between 3.5 and 4.5 months of age measured by HAI.

A clinically relevant threshold for sensitivity and specificity of the prognostic risk of UCP depends on the context and the actions that follow. For early treatment, one wants to choose a lower threshold at higher sensitivity to not miss any infant that could benefit from early intervention that does not harm the infant. If on the other hand one would like to inform the parents, one would like to choose a higher threshold at higher specificity in order to minimize the number of false-positives and thus not unnecessarily worry parents.

As a next step, this model needs to be externally validated and possibly refined in a larger sample with similar participants in order to implement the nomogram into clinical practice, to enable clinicians to early inform families about their infant's risk to develop UCP, and refer those with a high probability to early intervention programs. The case in Appendix 1 may help to illustrate the further use of the nomogram in clinical practice.

5. Conclusions

A combination of a qualitative evaluation of the CST and BGT from neonatal MRI, a contralesional HAI Each hand sum score, gestational age and sex of the infant can already between 3.5 and 4.5 months of (corrected) age predict the prognostic risk of UCP in infants with APBI.

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The authors have no financial relationships relevant to this article to disclose.

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Conflict of interest

The authors have no conflicts of interest relevant to this article to disclose.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejpn.2019.04.004.

Appendix

Clinical Case explaining the use of the Nomogram

A baby **girl** was born at **25 + 3** weeks of gestation. She was born after an emergency caesarean section due to decelerations on cardiotocography. Her birth weight was 900 g and her Apgar scores were 4/7/9 after 1/5/10 min. She had her MRI around term equivalent age that showed clear **asymmetry of the corticospinal tracts (CST)** at the level of the PLIC (A). The **basal ganglia and thalamus (BGT) were also affected**, as they showed clear asymmetry. She was discharged and returned for follow-up at 17 weeks of corrected age, when the HAI was performed. The **HAI Each hand sum score (EaHS)** of the left **(contralesional) hand was 7**.

Read from the nomogram (B) by drawing a vertical line (arrow) from each predictor scale to the 0–11 'Score' scale and read:

- For sex, 'Score' scale for being female (purple) is **0**
- For gestational age 'Score' scale for 25 gestational weeks (yellow) is **0.6**
- For basal ganglia involvement (yes/no) 'Score' scale for yes (turquoise) is **1.5**
- For HAI contralesional Each hand sum score (EaHS) 'Score' scale (pink) for the 7 EaHS is **7.1**
- For corticospinal tract involvement (yes/no) 'Score' scale for yes (orange) is **2.8.**
- Sum these scores: **0 + 0.6 + 1.5 + 7.1 + 2.8 = 12.**
- Find the sum score of 12 points on the 0–18 'Total score' (bottom line).
- Read the assigned prognostic risk of developing UCP from the 'Probability' scale by drawing an orthogonal line (red arrow) from 12 'Total score' scale to the 'Probability' scale: **0.94.**

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