PROGNOSTIC VALUE OF CRANIAL ULTRASONOGRAPHY IN COMPARISON WITH MAGNETIC RESONANCE IMAGING IN CHILDREN WITH CEREBRAL PALSY: A POPULATION-BASED STUDY

Sanja Delin[1,2], Katarina Bošnjak Nađ[3], Sunčica Martinec[4], Dunja Čokolić Petrović[5], Andrea Šimic Klarić[2,6] and Vlatka Mejaški Bošnjak[7]

[1]Zadar General Hospital, Department of Pediatrics, Zadar, Croatia;
[2]School of Medicine, Josip Juraj Strossmayer University of Osijek, Osijek, Croatia;
[3]Special Hospital for Developmental Neurology and Rehabilitation, Zagreb, Croatia;
[4]Krapinske Toplice Special Hospital for Medical Rehabilitation, Krapinske Toplice, Croatia;
[5]Osijek University Hospital Centre, Department of Pediatrics, Osijek, Croatia;
[6]Požega General Hospital, Department of Pediatrics, Požega, Croatia;
[7]Zagreb Children's Hospital, School of Medicine, University of Zagreb, Zagreb, Croatia

SUMMARY – The aim of this population-based study was to evaluate the characteristics of cerebral palsy (CP) in relation to the predominant pattern of the Magnetic Resonance Imaging Classification System (MRICS) that was analogously applied to the neonatal/early infant cranial ultrasound (CUS). The study included children born during the 2004-2007 period from the Croatian part (C28 RCP-HR) of the Surveillance of Cerebral Palsy in Europe (SCPE) CP register. Motor functions, accompanying impairments and brain MRI were evaluated in 227 children, 185 of which also had CUS. Concerning CP types, 56% of children had bilateral spastic, 34% unilateral spastic, 9% dyskinetic and 1% ataxic CP type. Gross Motor Function Classification System (GMFCS) revealed that 62.05% had mild (GMFCS I-III) and 37.85% had severe motor impairment (GMFCS IV-V). CUS showed white matter injury in 60%, gray matter injury in 12%, maldevelopments in 8%, miscellaneous changes in 14%, while 6% were normal; MRI showed significant agreement ($\kappa=0.675$, $p<0.001$). Neuroimaging findings of maldevelopments and predominant gray matter injury were associated with more severe CP, but 7% of children with CP had normal MRI. As we found very good agreement between CUS and MRI findings, CUS is recommended in children at an increased risk of CP if MRI is not available.

Key words: *Cerebral palsy; Cranial ultrasonography; Functional classification; Magnetic resonance imaging; Surveillance of Cerebral Palsy in Europe*

Introduction

Cerebral palsy (CP) is the most common cause of severe neuromotor disability in children that affects 2-3/1000 live-born children[1,2]. According to a multi-center European study on CP, Surveillance of Cerebral Palsy in Europe (SCPE), CP is classified based on the predominant neurological symptoms as spastic (subtypes: bilateral and unilateral), dyskinetic (subtypes: choreo-athetotic and dystonic) and ataxic CP type[2,3]. The level of functional deficit is determined by standardized instruments, Gross Motor Function Classification System (GMFCS) and Bimanual Fine Motor Function (BFMF)[4-6]. The SCPE functional classifica-

Correspondence to: *Sanja Delin, MD*, Zadar General Hospital, Department of Pediatrics, Bože Peričića 5, HR-23000 Zadar, Croatia
E-mail: delinsanja@gmail.com

tion also includes accompanying neurodevelopmental impairments, i.e. epilepsy, speech difficulties, intellectual, visual and hearing impairment[3,6,7]. Although cranial ultrasound (CUS) and brain magnetic resonance imaging (MRI) are not part of CP definition, they show structural changes in more than 85% of CP children and reveal a pathogenic pattern that is responsible for CP[8,9]. Brain imaging can also help in understanding the relationship between structure and function[9,10]. Therefore, SCPE has proposed a classification system for MRI in children with CP, the Magnetic Resonance Imaging Classification System (MRICS), which can be used in CP registers. It is primarily a qualitative system based on pathogenic patterns associated with the time of lesion onset, but takes into account different pathologies within one timing period, which are partially also related to the extent of lesion[11].

The aim of this population-based study was to evaluate the level of functional deficit and accompanying impairments in children with CP in relation to the predominant pattern of MRICS that was analogously applied to the neonatal/early infant CUS. Additionally, the aim was to examine the correlation between MRI and CUS findings, as well as their prognostic value for type and accompanying impairments in children with CP.

Patients and Methods

This study was based on the data of children with the diagnosis of CP from the SCPE National Register C28, Registry of Cerebral Palsy in Croatia (RCP-HR), born between January 1, 2004 and December 31, 2007. During this period, a total of 130,249 children were live-born in the area covered by the register, of which 279 were diagnosed with CP. Data were collected on CP type and subtype, gross and fine motor functions, and accompanying impairments. The median age of the participants at the last assessment was 8.8 years (interquartile range 8.5-9.1 years), ranging from 6 to 10 years.

This study included 227 children with brain MRI, of which 185 also had neonatal/early infant CUS. Neuroimaging findings were divided, as proposed by SCPE, into 5 categories: (A) brain maldevelopments; (B) predominant white matter injury; (C) predominant gray matter injury; (D) miscellaneous changes; and (E) normal findings[11].

Classification of MRI was based on neuroimages (MRI power 1.5 or 3 Tesla) and/or written report. Neonatal/early infant CUS findings were classified analogously to MRICS. The most informative CUS was taken into consideration.

The CP type and subtype were classified according to SCPE recommendations. Functional grading of gross and fine motor functions was performed according to GMFCS and BFMF classification[4-6]. Data on the following accompanying impairments were collected: epilepsy, intellectual, visual and hearing impairments, and speech difficulties.

Epilepsy is defined as two or more unprovoked cerebral seizures, excluding neonatal or febrile seizures. Data on epileptic activity, i.e. anticonvulsive therapy, were collected.

Intellectual disability is classified into three categories based on IQ result, as follows: IQ ≥70 was classified as normal or borderline intellectual development, IQ 50-70 as mild intellectual impairment and IQ <50 as moderate-severe intellectual impairment as measured by Wechsler scale or clinically estimated[12].

Visual impairment according to SCPE is classified as normal or impaired vision, with a subcategory of severe visual impairment, defined as blindness or no useful vision after correction of the better eye, if visual acuity is <6/60 according to Snellen chart or <0.1 by decimal scale. Hearing impairment is classified as normal or impaired hearing, with a subcategory of severe hearing impairment defined as severe or profound hearing loss if the level of hearing loss is >70 dB prior to correction for the better ear[13]. Speech production difficulties were classified using the Viking Speech Scale into four levels, from normal to no understandable speech[13,14].

Like some other authors, on statistical analysis we divided our CP population into two groups based on GMFCS; in the text below, levels I, II and III are referred to as milder motor impairment, and levels IV and V as severe motor impairment[15].

Brain imaging techniques (MRI *vs.* CUS) were compared, as well as their prognostic value in predicting neurodevelopmental outcome.

Ethics

This study complied with ethical principles of the Declaration of Helsinki of 1975, as revised in 1983, and was approved by the Ethics Committee of the Za-

greb Children's Hospital in Zagreb and Ethics Committee of the School of Medicine, Josip Juraj Strossmayer University in Osijek.

Statistics

Category data were expressed as absolute and relative frequencies, and numerical data as arithmetic mean, standard deviation and median. Difference between category variables was tested by the χ^2-test, and if necessary, by the Fisher exact test. Distribution normality of numeric variables was tested by the Shapiro-Wilk test. As a measure of matching MRI and CUS findings, kappa (κ) coefficient was used. The level of significance was set at $p \leq 0.05$. On statistical analysis, statistical programs MedCalc Statistical Software version 17.8.2 and IBM SPSS Statistics version 17.0 were used.

Results

The study included 227 children, their median age at registration was 8 years (SD 0.5 years, range 6-9 years). According to CP type, 204 (89.9%) children had spastic, 76 (37.3%) unilateral and 128 (62.7%) bilateral CP. Twenty (8.8%) children had dyskinetic CP and three children (1.3%) ataxic CP.

Gross motor function accompanying impairments

According to GMFCS, 67 (29.52%) patients had level I, 58 (25.55%) level II, 16 (7.05%) level III, 21 (9.25%) level IV and 65 (28.63%) level V, which means that 141 (62.11%) children had milder motor impairment, while 86 (37.89%) children had severe motor impairment.

There were 90 (39.6%) children with normal or borderline, 53 (23.3%) with mild and 84 (37.0%) with moderate-severe intellectual impairment. In the group with severe intellectual impairment, there were significantly more children with severe motor impairment, 65/86 (75.6%) (χ^2-test, p<0.001). Epilepsy was found in 120 (52.9%) children, significantly more in those with severe motor impairment, 67/86 (78%) (χ^2-test, p<0.001). At the time of evaluation, 104 (86.67%) of these children had active epilepsy (receiving antiepileptic treatment at the last follow up).

Out of 144 (63.44%) children with visual impairment, severe impairment was present in 33 (22.92%)

patients. Visual impairment was significantly more common in patients with severe motor impairment, 68/86 (79%) (χ^2-test, p<0.001), of which 27 (39.7% of all with severe motor impairment and visual impairment) had severe visual impairment (χ^2-test, p<0.001). Hearing impairment was present in 15 (6.61%) children, significantly more (11/15) in those with severe motor impairment (Fisher exact test, p=0.005). In 6/15 children, hearing impairment was classified as severe.

Speech was affected in 116 (51%) children, significantly more in the group with severe motor impairment (χ^2-test, p<0.001), whereas 26% of children did not have understandable speech.

Neuroimaging (CUS and MRI)

The median age of children was 16 (range 1-40) weeks at the time of CUS and 48 (range 24-108) months at the time of brain MRI.

According to CUS findings, the majority of children had predominantly white matter injury, 111/185 (60%), of which significantly more children had milder motor impairment. In 22/185 (11.9%) children with predominantly gray matter injury, significantly more patients had severe motor impairment, 15 (19.5%) (χ^2-test, p<0.001). Out of 185 children examined with neonatal/early infant CUS, 77 (41.6%) had severe motor impairment and none of them had normal CUS finding (Table 1a).

Brain MRI findings most often showed white matter injury, recorded in 130/227 (57.3%) children, significantly more often in children with milder motor impairment, whereas in children with severe motor impairment brain maldevelopments and gray matter injuries were reported more frequently, in 18 (20.9%) and 17 (19.8%) children, respectively. There were 16/227 (7%) patients with normal brain MRI, significantly more in the group with milder motor impairment, 14/141 (9.9%) children (χ^2-test, p=0.002). Severe motor impairment was present in two (2.3%) children with normal MRI (Table 1a).

Out of a total of 138 (80%) children with bilateral brain injury according to CUS findings, there were significantly more children with severe motor impairment, and similar results were obtained with MRI (χ^2-test, p<0.001) (Table 1b).

By CUS findings, significantly more children with severe motor impairment had brain maldevelopments

Table 1a. Cranial ultrasonography (CUS) and magnetic resonance imaging (MRI) findings according to the Gross Motor Function Classification System (GMFCS)

	Number (%) of children with GMFCS level			p^*
	GMFCS I, II, III	GMFCS IV, V	Total	
CUS				
A. Maldevelopments	5 (4.6)	10 (13.0)	15 (8.1)	
B. Predominant white matter injury	67 (62.0)	44 (57.1)	111 (60.0)	
C. Predominant gray matter injury	7 (6.5)	15 (19.5)	22 (11.9)	**<0.001**
D. Miscellaneous	17 (15.7)	8 (10.4)	25 (13.5)	
E. Normal	12 (11.1)	0	12 (6.5)	
Total	108 (100)	77 (100)	185 (100)	
MRI				
A. Maldevelopments	13 (9.2)	18 (20.9)	31 (13.7)	
B. Predominant white matter injury	84 (59.6)	46 (53.5)	130 (57.3)	
C. Predominant gray matter injury	15 (10.6)	17 (19.8)	32 (14.1)	**0.002**
D. Miscellaneous	15 (10.6)	3 (3.5)	18 (7.9)	
E. Normal	14 (9.9)	2 (2.3)	16 (7.0)	
Total	141 (100)	86 (100)	227 (100)	

$^*\chi^2$-test

Table 1b. Lateralization of brain damage according to the Gross Motor Function Classification System (GMFCS)

	Number (%) of children with GMFCS level			p^*
	GMFCS I, II, III	GMFCS IV, V	Total	
CUS finding				
Right	14 (15)	3 (4)	17 (10)	
Left	17 (18)	1 (1)	18 (10)	**<0.001**
Bilateral	65 (68)	73 (95)	138 (80)	
Total	96 (100)	77 (100)	173 (100)	
MRI finding				
Right	22 (17)	3 (4)	25 (12)	
Left	33 (26)	1 (1)	34 (16)	**<0.001**
Bilateral	72 (57)	80 (95)	152 (72)	
Total	127 (100)	84 (100)	211 (100)	

$^*\chi^2$-test

and severe lesions of white matter, i.e. severe periventricular leukomalacia (PVL) (B1.2). In children with milder motor impairment, mild white matter injury, i.e. mild PVL (B1.1) was significantly more common (χ^2-test, p<0.001).

Mild PVL (B1.1) was present in 42 children, 35 (83.3%) of them also with milder motor impairment; post-hemorrhagic infarction (B2) in 18 children, 12 (66.7%) of them also with milder motor impairment; and a combination of PVL and intraventricular hemorrhage (IVH) sequels (B3) in 11, seven (63.6%) of them with milder motor impairment. Conversely, of 40 children with extensive white matter injury (B1.2), 27 (67.5%) belonged to the group with severe motor impairment (Table 2).
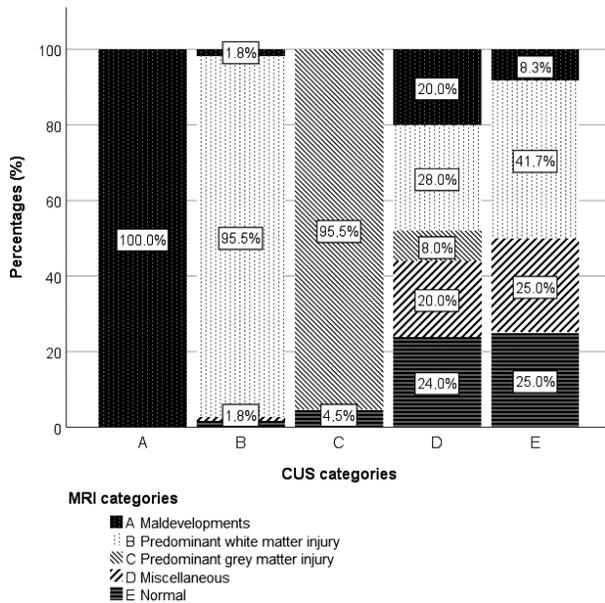
Predominant gray matter injury (C1.1, C1.2) was present in 12/22 children, significantly more in those with severe motor impairment (Fisher exact test, p=0.02). Cortico-subcortical (C2) lesions were observed in only 8/22 subjects, all with severe CP. Infarction of the middle cerebral artery (C3) was recorded in 2/22 children with milder motor impairment.

According to MRI findings, there was a significant difference in motor impairment according to white matter injury; among 53 (41%) children with mild PVL (B1.1) there were significantly more children with milder motor impairment, while severe PVL (B1.2) was significantly more prevalent in children with severe motor impairment (χ^2-test, p<0.001) (Table 2).

Table 2. Cranial ultrasonography (CUS) and magnetic resonance imaging (MRI) findings according to the level of gross motor function

	Number (%) of children			p*
	GMFCS I, II, III	GMFCS IV, V	Total	
CUS				
A. Maldevelopments				
A 1.1. Disorders of cortical formation (proliferation /migration/ organization)	4/5	2/10	6/15	0.09†
A 1.2. Other maldevelopments (holoprosencephaly, Dandy Walker malformation, corpus callosum agenesis, cerebellar hypoplasia)	1/5	8/10	9/15	
B. Predominant white matter injury				
B 1.1. Mild periventricular leukomalacia (PVL)	35 (52)	7 (16)	42 (38)	<0.001
B 1.2. Severe periventricular leukomalacia (PVL)	13 (19)	27 (61)	40 (36)	
B 2. Sequels of intraventricular hemorrhage (IVH) or periventricular hemorrhagic infarction	12 (18)	6 (14)	18 (16)	
B 3. Combination of PVL and IVH sequels	7 (10)	4 (9)	11 (10)	
C. Predominant gray matter injury				
C 1.1. Mild (basal ganglia/thalamus lesions)	4/7	5/15	9/22	0.02†
C 1.2. Severe (basal ganglia/thalamus lesions + cortical gray matter and/or hippocampus)	1/7	2/15	3/22	
C 2. Cortico-subcortical lesions only (watershed lesions in parasagittal distribution/multicystic encephalomalacia)	0	8/15	8/22	
C 3. Arterial infarctions (middle cerebral artery/other)	2/7	0	2/22	
D. Miscellaneous				
D. (cerebellar atrophy, cerebral atrophy, delayed myelination, ventriculomegaly not covered by B, hemorrhage not covered by B, brainstem lesions, calcifications)	17/17	8/8	25/25	-
E. Normal	12/12	0	12/12	-
MRI				
A. Maldevelopments				
A 1.1. Disorders of cortical formation (proliferation/migration/ organization)	10/13	8/18	18/31	0.14†
A 1.2. Other maldevelopments (holoprosencephaly, Dandy Walker malformation, corpus callosum agenesis, cerebellar hypoplasia)	3/13	10/18	13/31	
B. Predominant white matter injury				
B 1.1. Mild periventricular leukomalacia (PVL)	48 (57)	5 (11)	53 (41)	<0.001
B 1.2. Severe periventricular leukomalacia (PVL)	15 (18)	32 (70)	47 (36)	
B 2. Sequels of intraventricular hemorrhage (IVH) or periventricular hemorrhagic infarction	11 (13)	3 (7)	14 (11)	
B 3. Combination of PVL and IVH sequels	10 (12)	6 (13)	16 (12)	
C. Predominant gray matter injury				
C 1.1. Mild (basal ganglia/thalamus lesions)	3/15	5/17	8 (25)	0.17†
C 1.2. Severe (basal ganglia/thalamus lesions + cortical gray matter and/or hippocampus)	2/15	4/17	6 (19)	
C 2. Cortico-subcortical lesions only (watershed lesions in parasagittal distribution/multicystic encephalomalacia)	4/15	7/17	11 (34)	
C 3. Arterial infarctions (middle cerebral artery/other)	6/15	1/17	7 (22)	
D. Miscellaneous				
D. (cerebellar atrophy, cerebral atrophy, delayed myelination, ventriculomegaly not covered by B, hemorrhage not covered by B, brainstem lesions, calcifications)	15/15	3/3	18/18	-
E. Normal	14/14	2/2	16/16	-

*χ^2-test; †Fisher exact test; GMFCS = Gross Motor Function Classification System

MRI categories
- A Maldevelopments
- B Predominant white matter injury
- C Predominant grey matter injury
- D Miscellaneous
- E Normal

Neonatal/early infant CUS findings in our children were in good correlation with MRI findings, especially in the category of maldevelopments (A) with 100% concordance. In predominant white (B) and gray (C) matter injury, concordance was also very high, 95.5% for each category. Conversely, among children with miscellaneous findings (D) on CUS, MRI showed predominant white matter injury (B) in 28%, maldevelopments (A) in 20%, predominant gray matter injury (C) in 8%, while 20% had normal finding (E). In children with normal CUS (E), predominant white matter injury (B) was highly represented on MRI with 41.7%, miscellaneous (D) and normal (E) findings were present in one-quarter of children each, and 8.3% had maldevelopments (D).

Fig. 1. Cranial ultrasonography (CUS) classification compared to Magnetic Resonance Imaging Classification System (MRICS).

Comparing the CUS and brain MRI according to MRICS, we observed significant agreement in the results (κ=0.675, p<0.001), most evident in brain maldevelopments and predominant white and gray matter lesions (Fig. 1).

Multiple severe accompanying impairments were most commonly reported in children with brain maldevelopments and gray matter injury. Figure 2a presents percentage of associated impairments in five main MRICS categories while Figure 2b presents CUS findings. The results we obtained were mostly matching again in the first three MRICS categories. Mismatch was noted in the category of normal CUS compared to normal brain MRI with a significantly lower percentage of active epilepsy (16.7 *vs.* 43.8%) and severe intellectual disability (8.3 *vs.* 31.3%).

Discussion

Cranial ultrasonography and MRI are the main techniques of brain imaging in diagnosing perinatal brain injury[16,17]. CUS is a low-cost, widely available and noninvasive technique, particularly useful for detection and follow-up of IVH and cystic PVL (cPVL)[16]. However, CUS is not reliable in detecting mild or diffuse lesions of white and gray matter[18]. The disadvantage of CUS also refers to limited visualization of parietal brain cortex and posterior fossa[18]. A superior method that can help in prognostic evaluation of perinatal damage is brain MRI, while it provides a more detailed view of brain structure[17]. Brain MRI is the gold standard for the diagnosis of diffuse abnormality of white matter, optimally performed after the 2nd year of life when myelination is mainly completed[20,21]. This allows precise differentiation of gray and white matter, which is important for the detection and accurate classification of malformations and brain injuries (discrete lesions of white matter or basal ganglia/thalamus lesions)[11].

In our study, according to CUS and MRI findings, there were significantly more maldevelopments and predominant gray matter injuries in the group of children with severe motor impairment. Our results were similar to the west-Swedish population study by Himmelmann and Uvebrant from 2011, despite the fact that these authors did not base their research on MRICS but used the MRI/CT techniques[10].

We found significant differences on CUS in the subcategories of predominant white matter (B) and predominant gray matter injury (C) between the groups with milder and severe motor impairment. Our results were similar to the results of the west-Swedish cohort and also a meta-analysis by Australian authors, which included 1630 patients from 34 studies[10,22]. On MRI findings of our subjects, significant differences were found between the groups with milder and severe motor impairment only for the subcategories of predominant white matter lesions.

Cranial ultrasonography has been proven to be an excellent method for monitoring the evolution of IVH and cPVL, which corresponds to the results reported by Horsch *et al.*[23]. In our study, CUS findings in the early diagnosis of perinatal brain injury of CP children were well-matched with MRI findings (kappa coefficient 0.675, p<0.001). This compatibility was most evident in
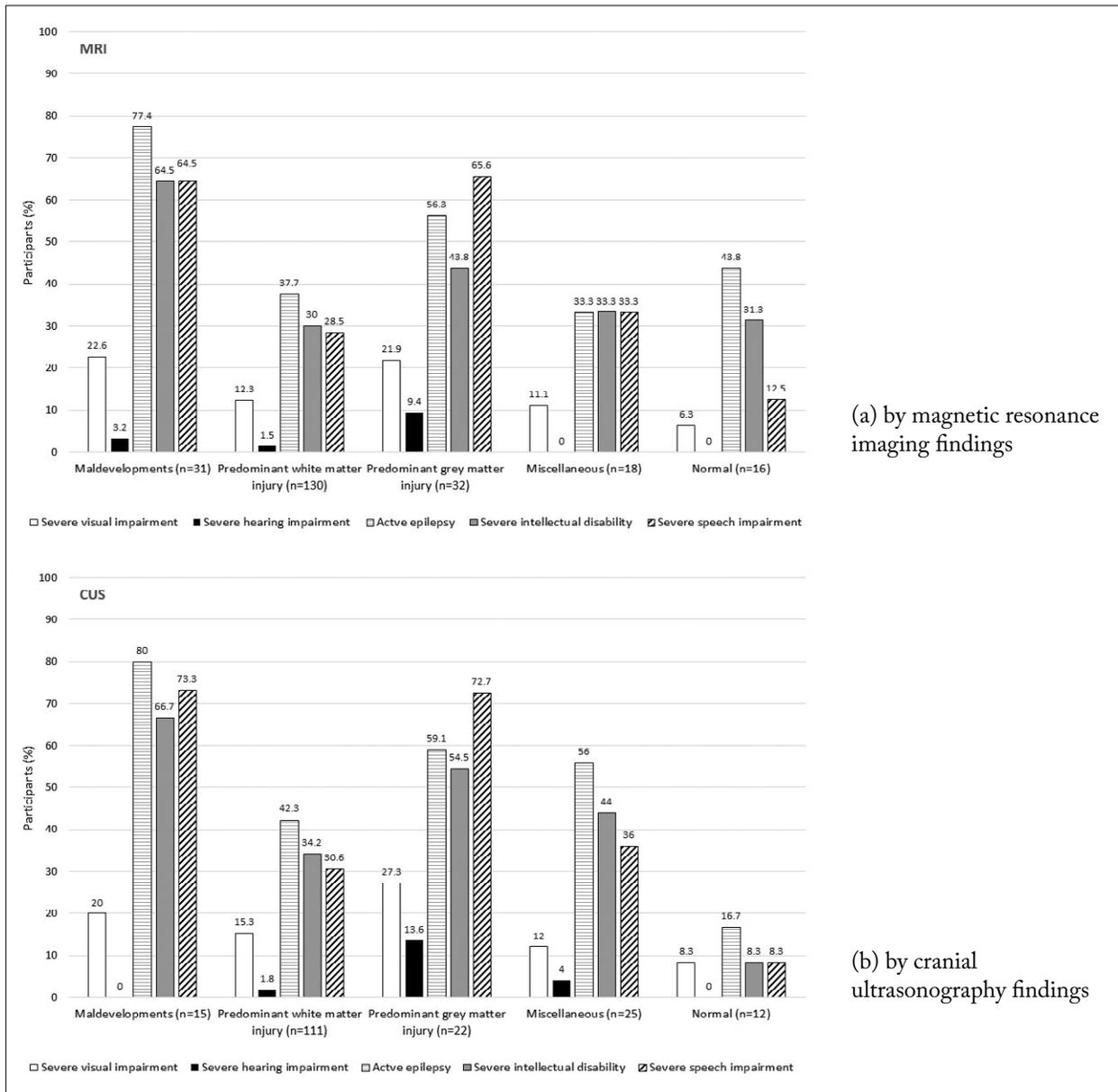
Fig. 2. Accompanying severe impairments.

brain maldevelopments and predominant white or gray matter injury, where the correlation was 95.5%. The biggest differences were recorded in the interpretation of miscellaneous changes and normal CUS finding. This could be explained by the limitation of CUS in the diagnosis of perinatal brain injury. Conversely, low grade IVH (1/2) shown by CUS and categorized as miscellaneous changes (D) is usually not reported on postneonatal MRI and is classified as normal (E).

Major brain maldevelopments can be diagnosed with CUS, but it is not a suitable method for the detection of mild disorders such as polymicrogyria and gray matter heterotopia, or developmental disorders of the posterior fossa. However, brain maldevelopments in our sample made only a small part of causes of cerebral palsy (8.1% based on CUS and 13.7% based on brain MRI), which is in accordance with the data reported by other authors[9,10,24].

Cranial ultrasonography is not appropriate method for diffuse white matter injury, according to previous literature reports[17]. Therefore, it is not surprising that a large proportion (69.7%) of white matter injuries described on MRI findings are described on CUS as miscellaneous changes or normal findings. In our patients, miscellaneous changes, especially abnormalities of the posterior cranial fossa, such as cerebellar injury, brain stem infarctions and sinus thrombosis, were difficult to diagnose with CUS. In 25% of normal CUS findings, MRI found unspecific changes. However, CUS should remain a standardized routine method of examination in newborns and young infants at risk of long-term neurodevelopmental disorders since it can exclude severe abnormalities in more than 90% of cases[23,25,26].

In our study, considering the CUS findings, major differences between children with milder and severe motor impairment were found in the groups of brain maldevelopments and gray matter injury, whereas according to MRI findings this difference was most obvious in the group of brain maldevelopments (9.2% *vs.* 20.9%), which is consistent with previous literature data[9,10,27].

In our children with brain maldevelopments and gray matter injury detected by both CUS and MRI, multiple severe accompanying impairments were most commonly reported. Predominant white matter injury also detected by both techniques had a significantly lower percentage of accompanying multiple severe impairments. In miscellaneous MRI, multiple neurodevelopmental impairments (active epilepsy, severe intellectual disability and severe speech difficulties) were represented by a significant percentage (33.3% each), but the same was present within CUS findings (56%, 44% and 36%, respectively). In the group of children with normal MRI findings, 43% had active epilepsy and 31.3% had moderate-severe intellectual disability. The fact that normal MRI finding was present in 16 (7%) children that also had multiple severe accompanying impairments indicates the need for advanced quantitative MRI techniques to clarify structural lesions causing CP and accompanying impairments[28,29].

A limitation of this study was a relatively small number of children in contrast to the large number of MRI and CUS categories and subcategories compared with gross motor function and accompanying impairments. CUS was not performed in 42/227 (18.5%)

children and MRI findings were not available in 54/279 (19.3%) CP children in our register, which may also have affected the results. Another remark would refer to the routine use of the anterior fontanelle as an acoustic window. Access through the mastoid fontanelle and posterior fontanelle would provide better visualization of the posterior fossa.

In conclusion, comparing the findings of CUS and brain MRI in the evaluation of children with CP, we obtained similar results. Although MRI offers a more complete visualization of brain damage and is more informative about the pathogenic pattern of brain damage, brain MRI and CUS are complementary methods. Therefore, CUS as a widely available method for detection and follow up of perinatal brain injury should remain a standardized routine method for examination of children at risk of long-term neurodevelopmental disorders. By implementing neonatal/early infant CUS in the SCPE classification system, more data would be available in children with CP who did not undergo brain MRI for any reason. Since brain imaging can predict the type and level of gross motor impairment, as well as the association of multiple severe neurodevelopmental impairments, this information could help optimize the type and range of habilitation procedures and finally improve the outcome.

References

1. Surveillance of cerebral palsy in Europe. A collaboration of cerebral palsy surveys and registers. Dev Med Child Neurol. 2000;42:816-24.

2. Surveillance of Cerebral Palsy in Europe. Prevalence and characteristic of children with cerebral palsy in Europe. Dev Med Child Neurol. 2002;44:633-40.

3. Cans C, Dolk H, Platt MJ, Colver A, Prasaukiene A, Krägeloh-Mann I; on behalf of SCPE collaborative group. Recommendations from the SCPE collaborative group for defining and

classifying cerebral palsy. Dev Med Child Neurol Suppl. 2007; 109:35-8.

4. Palisano R, Rosenbaum P, Walter S, Russell D, Wood E, Galuppi B. Development and reliability of a system to classify gross motor function in children with cerebral palsy. Dev Med Child Neurol. 1997;39:214-23.

5. Elvrum AK, Andersen GL, Himmelmann K, Beckung E, Ohrvall AM, Lydersen S, *et al.* Bimanual fine motor function (BFMF) classification in children with cerebral palsy: aspects of construct and content validity. Phys Occup Ther Pediatr. 2016;36:1-16. doi: 10.3109/01942638.2014.975314. Epub 2014 Nov 6.

6. Beckung E, Hagberg G. Neuroimpairments, activity limitations and participation restrictions in children with cerebral palsy. Dev Med Child Neurol. 2002;44:309-16.

7. Himmelmann K, Backung E, Hagberg G, Uvebrant P. Gross and fine motor function and accompanying impairments in cerebral palsy. Dev Med Child Neurol. 2006;48:417-23. doi: 10.1017/S0012162206000922.

8. Krägeloh-Mann I, Helber A, Mader I, Staudt M, Wolff M, Groenendaal F, *et al.* Bilateral lesions of thalamus and basal ganglia: origin and outcome. Dev Med Child Neurol. 2002; 44:477–84.

9. Krägeloh-Mann I, Horber V. The role of MRI imaging in elucidating pathogenesis of cerebral palsy – a systematic review. Dev Med Child Neurol. 2007;40:144-51. doi: 10.1111/j.1469-8749.2007.00144.x

10. Himmelmann K, Uvebrant P. Function and neuroimaging in cerebral palsy: a population-based study. Dev Med Child Neurol. 2011;53:516-21. doi: 10.1111/j.1469-8749.2011.03932.x

11. Himmelmann K, Horber V, De la Cruz J, Horridge K, Mejaski-Bosnjak V, Hollody K, Krägeloh-Mann I; SCPE Working Group. MRI Classification System (MRICS) for children with cerebral palsy: development, reliability and recommendations. Dev Med Child Neurol. 2017;59:57-64. doi: 10.1111/dmcn.13166. Epub 2016 Jun 21

12. Wechsler D. Wechsler Intelligence Scale for Children Manual. 4th edn. San Antonio, TX: The Psychological Corporation, 2003.

13. http://www.scpenetwork.eu/en/my-scpe/rtm/functional-grading/cognitive-communication-visual-hearing-epilepsy/ last accessed 28 of February 2018.

14. Pennington L, Virella D, Mjøen T, da Graça Andrada M, Murray J, Clover A, *et al.* Development of the Viking Speech Scale to classify the speech of children with cerebral palsy. Res Dev Disabil. 2013;34:3202-10. doi: 10.1016/j.ridd.2013.06.035. Epub 2013 Jul 24

15. Glinac A, Matović L, Delalić A, Mešalić L. Quality of life in mothers of children with cerebral palsy. Acta Clin Croat. 2017;56:299-307. doi: 10.20471/acc.2017.56.02.14

16. Hintz SR, Barnes PD, Bulas D, Slovis TL, Finer NN, Wrage LA, Das A, Tyson JE, Stevenson DK, Carlo WA, Walsh MC, Laptook AR, Yoder BA, Van Meurs KP, Faix RG, Rich W,

Newman NS, Cheng H, Heyne RJ, Vohr BR, Acarregui MJ, Vaucher YE, Pappas A, Peralta-Carcelen M, Wilson-Costello DE, Evans PW, Goldstein RF, Myers GJ, Poindexter BB, McGowan EC, Adams-Chapman I, Fuller J, Higgins RD; SUPPORT Study Group of the Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network. Neuroimaging and neurodevelopmental outcome in extremely preterm infants. Pediatrics. 2015;135:e32-42. doi: 10.1542/peds.2014-0898. Epub 2014 Dec 1

17. Hinojosa-Rodríguez M, Harmony T, Carrillo-Prado C, Van Horn JD, Irimia A, Torgerson C, *et al.* Clinical neuroimaging in the preterm infant: diagnosis and prognosis. Neuroimage Clin. 2017;16:355-68. doi: 10.1016/j.nicl.2017.08.015. eCollection 2017.

18. Parodi A, Morana G, Severino MS, Malova M, Natalizia AR, Sannia A, *et al.* Low-grade intraventricular hemorrhage: is ultrasound good enough? J Matern Fetal Neonatal Med. 2013; 28(Suppl 1):2261-4. doi: 10.3109/14767058.2013.796162. Epub 2013 Aug 23

19. Govaert P, de Vries LS. An Atlas of Neonatal Brain Ultrasound. Clinics in Developmental Medicine. London: Mac Keith Press, 2010.

20. de Vries LS, Benders MJNL, Groenendaal F. Progress in neonatal neurology with a focus on neuroimaging in the preterm infant. Neuropediatrics. 2015;46:234-41. doi: 10.1055/s-0035-1554102. Epub 2015 Jun 29

21. Kostović I, Kostović-Srzentić M, Benjak V, Jovanov-Milošević N, Radoš M. Developmental dynamics of radial vulnerability in the cerebral compartments in preterm infants and neonates. Front Neurol. 2014;5:139. doi: 10.3389/fneur.2014.00139. eCollection 2014

22. Arnfield E, Guzzetta A, Boyd R. Relationship between brain structure on magnetic resonance imaging and motor outcomes in children with cerebral palsy: a systematic review. Res Dev Disabil. 2013;34:2234-50. doi: 10.1016/j.ridd.2013.03.031. Epub 2013 May 1

23. Horsch S, Skiöld B, Hallberg B, Nordell B, Nordell A, Mosskin M, *et al.* Cranial ultrasound and MRI at term age in extremely preterm infants. Arch Dis Child Fetal Neonatal Ed. 2010; 95:F310-4. doi: 10.1136/adc.2009.161547. Epub 2009 Oct 19

24. Reid SM, Dagia CD, Ditchfield MR, Carlin JB, Reddihough DS. Population-based studies of brain imaging patterns in cerebral palsy. Dev Med Child Neurol. 2014;56:222-32. doi: 10.1111/dmcn.12228. Epub 2013 Nov 8

25. Rademaker KJ, Uiterwaal CS, Beek FJ, van Haastert IC, Lieftink AF, Groenendaal F, *et al.* Neonatal cranial ultrasound *versus* MRI and neurodevelopmental outcome at school age in children born preterm. Arch Dis Child Fetal Neonatal Ed. 2005; 90:489-93. Epub 2005 Jun 14.

26. De Vries LS, Van Haastert IL, Rademaker KJ, Koopman C, Groenendaal F. Ultrasound abnormalities preceding cerebral palsy in high-risk preterm infants. J Pediatr. 2004;144:815-20.

27. Himmelmann K, Hagberg G, Beckung E, Hagberg B, Uvebrant P. The changing panorama of cerebral palsy in Sweden.

IX. Prevalence and origin in the birth-year period 1995-1998. Acta Paediatr. 2005;94:287-94.

28. Fiori S, Cioni G, Klingels K, Ortibus E, Van Gestel L, Rose S, *et al.* Reliability of a novel semi-quantitative scale for classification of structural brain magnetic resonance imaging in children with cerebral palsy. Dev Med Child Neurol. 2014;56:839-45. doi: 10.1111/dmcn.12457. Epub 2014 Apr 19

29. Vollmer B, Lundequist A, Mårtensson G, Nagy Z, Lagercrantz H, Smedler AC, *et al.* Correlation between white matter microstructure and executive functions suggests early developmental influence on long fibre tracts in preterm born adolescents. PLoSOne. 2017;12:e0178893. doi:10.1371/journal.pone.0178893. eCollection 2017

Sažetak

PROGNOSTIČKA VRIJEDNOST INTRAKRANIJSKOG ULTRAZVUKA U USPOREDBI S MAGNETSKOM REZONANCIJOM MOZGA U DJECE S CEREBRALNOM PARALIZOM: POPULACIJSKA STUDIJA

S. Delin, K. Bošnjak Nađ, S. Martinec, D. Čokolić Petrović, A. Šimic Klarić i V. Mejaški Bošnjak

Cilj ove populacijske studije bio je procijeniti karakteristike cerebralne paralize (CP) u odnosu na predominantni uzorak na magnetskoj rezonanciji mozga prema klasifikacijskom sustavu *Magnetic Resonance Imaging Classification System* (MRICS) koji je analogno primijenjen i na novorođenački/rani dojenački intrakranijski ultrazvuk (UZV). Istraživanje je uključivalo djecu rođenu od 2004. do 2007. godine iz hrvatskog dijela (C28 RCP-HR) Registra Europskog projekta nadzora cerebralne paralize (*Surveillance of Cerebral Palsy in Europe*, SCPE). Ispitivane su grube i fine motoričke funkcije, pridružena odstupanja i slikovni prikazi mozga u 227 djece s MRI mozga od kojih je 185 imalo i neonatalni/rani dojenački UZV. U odnosu na tip CP, 56% djece imalo je bilateralno spastičnu, 34% jednostrano spastičnu, 9% diskinetsku i 1% ataktičku CP. Prema funkcionalnoj klasifikaciji grubih motoričkih funkcija *Gross Motor Function Classification System* (GMFCS), 62,05% djece imalo je blaže motoričko oštećenje (GMFCS I-III), a 37,85% teško motoričko oštećenje (GMFCS IV-V). Intrakranijski UZV pokazao je oštećenje bijele tvari mozga u 60%, ozljedu sive tvari u 12%, poremećaj razvoja mozga u 8%, razne promjene u 14% ispitanika, dok ih je 6% imalo normalan nalaz; MRI je pokazala značajnu podudarnost (κ=0,675, p<0,001). Poremećaji razvoja mozga i predominantne ozljede sive tvari mozga bile su povezane s težim stupnjem CP, no 7% djece s CP imalo je normalnu MRI mozga. Zbog vrlo dobre podudarnosti UZV i MRI nalaza u našem istraživanju UZV se preporučuje kod djece s povećanim rizikom od CP ako MRI nije dostupna.

Ključne riječi: *Cerebralna paraliza; Intrakranijski ultrazvuk; Funkcionalna klasifikacija; Magnetska rezonancija; Europski projekt nadzora cerebralne paralize*