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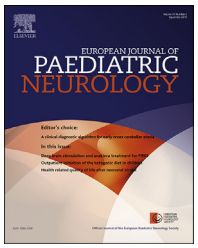

Original article

Health related quality of life and manual ability 5 years after neonatal ischemic stroke

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ABSTRACT

Aim: To investigate health-related quality of life (HRQOL) and manual ability five years after neonatal arterial ischemic stroke (NAIS).

Methods: Data was prospectively obtained by the Swiss Neuropaediatric Stroke Registry between 2000 and 2010. Two years after NAIS, cognitive and motor outcomes was assessed using the Bayley Scales of Infant Development (BSID-II). After 5 years, HRQOL was assessed with the KIDSCREEN-27 and manual ability with the ABILHAND-Kids. Manual ability and HRQOL were compared between children with and without cerebral palsy (CP) and HRQOL was correlated with manual ability.

Results: Seventy-four patients were examined at the age of 2 years, at the age of 5 years 61 patients underwent a follow-up examination. Two years after NAIS, 29 children (39.1%) were diagnosed with CP. HRQOL 5 years after NAIS was comparable to normative values. Children with CP had a significantly lower HRQOL-index ($p = 0.013$) and lower scores in the subscale psychological well-being ($p = 0.012$) and social support & peers ($p = 0.048$). The ABILHAND-Kids measure was significantly lower in children with CP compared to children without CP ($p < 0.001$). Manual ability correlated significantly with HRQOL.

Conclusion: Five years after NAIS, HRQOL is comparable to that of typically developing peers, but reduced in children with CP. Poorer manual ability is associated with lower HRQOL. Interventions improving hand function might influence HRQOL and should be considered early on.

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1. Introduction

Neonatal arterial ischemic stroke (NAIS) is defined as a focal disruption of the cerebral blood flow diagnosed between birth and the first 28 days of life.[1] NAIS is not rare; in Switzerland one in 7700 neonates is diagnosed with the condition.[2] Even though mortality is low, 30–60% of NAIS survivors show motor disabilities, 20–40% have cognitive impairments, and behavioral as well as attention problems are common.[3–5] These difficulties may considerably influence quality of life (QOL). A broad range of definitions and concepts for QOL research has been described. They usually include the subjective evaluation of multiple domains of a person's life. Health-related quality of life (HRQOL) specifically focuses on the aspects influenced by health.[6] Information regarding HRQOL after NAIS is scarce and results are contradictory.

A study measuring HRQOL in NAIS survivors and healthy controls found no difference between the two groups.[7] Other authors reported the same results when HRQOL measurement tools were addressed to the children themselves whereas the parents' perception was that their children's HRQOL differed significantly from that of healthy peers.[8] Authors seem to agree that HRQOL results in survivors of NAIS are better than for survivors of childhood ischemic stroke.[9,10] It has been shown, that neurological sequelae after childhood stroke are associated with poor HRQOL.[11–13] A study of both, childhood and neonatal stroke found that children with neurological impairments tended to have lower QOL compared to children with favorable neurodevelopmental outcome.[9] Two more recent studies contradict these results. A French multicenter prospective study found no association between functional independence, hemiparesis, epilepsy and HRQOL after NAIS.[7] Similarly, a smaller study of perinatal stroke survivors described no relation between HRQOL and neuromotor outcome.[8]

Although unilateral spastic cerebral palsy (CP) is diagnosed in about one-third of NAIS survivors,[3] it remains unclear whether motor performance after NAIS is associated with HRQOL.[14,15] The aim of the present study was to investigate HRQOL after NAIS. Based on previous literature we hypothesized that: (1) HRQOL after NAIS is similar to that observed in typically developing peers and (2) HRQOL after NAIS does not differ in children with and without CP and (3) manual ability after NAIS is not associated with poorer HRQOL.

2. Material and methods

2.1. Participants

Participants were registered between 2000 and 2010 in the Swiss Neuropediatric Stroke Registry (SNPSR) – a population-based registry including children aged 0–16 years diagnosed with arterial ischemic stroke or sinus venous thrombosis.[16] The SNPSR was approved by the Swiss Federal Ministry of Health and by the local ethics board. Details of the registration process, data collection and follow-up assessments have been published previously.[2] The present study focused on the two-year and the five-year follow up of NAIS survivors. Its assessments are part of the routine examinations carried out by the SNPSR. Inclusion criteria for the present study were: Term-born neonates with NAIS symptomatic at presentation, diagnosed during the first 28 days of life, ischemic insult located in an arterial territory confirmed by computed tomography or magnetic resonance imaging.

2.2. Two-year follow up

The *two-year follow-up* included a neurologic and developmental assessment performed by a research pediatrician associated with the SNPSR. In some cases, the neurodevelopmental unit of the hospital where the child was transferred to initially performed the examination.

A. To measure physical, mental, social and emotional development, the Bayley Scales of Infant Development II (BSID-II) was used.[17] The BSID II includes two subscales, a mental developmental index (MDI) and a psychomotor index (PDI) with a mean score of 100 and a standard deviation (SD) of 15. Mental and motor outcome were classified as normal (mental developmental index [MDI] respectively psychomotor developmental index [PDI] 85–114), mildly delayed (MDI respectively PDI 70–84) or severely delayed (MDI respectively PDI<70). In some cases, a BSID-II testing could not be assessed, e.g. due to lack of cooperation or due to severe impairment. In these cases, the development of the children was classified according to the neurological examination.
B. Motor performance at the 2-year follow-up was assessed by the research pediatrician associated with the SNPSR or by the treating pediatric neurologist. CP was diagnosed according to the definition of Rosenbaum et al.,[18] CP subtypes were classified according to the guidelines of the Surveillance of Cerebral Palsy in Europe network.[19]

2.3. Five-year follow up

Five years after NAIS, participating families were contacted by mail about the *five-year follow-up* and received standardized questionnaires regarding HRQOL and manual ability. Non-respondents were sent a reminder letter and contacted by phone. The required time for the parents to fill in both questionnaires was about 20–25 min. The questionnaires included the following measures:

A. To assess HRQOL we used the parent/proxy version of the KIDSCREEN-27 – a questionnaire intended for healthy and chronically ill children and adolescents. It is a shorter version of the KIDSCREEN-52 and has previously been used to assess HRQOL after childhood stroke.[13] The questionnaire includes 27 questions to be scored according to a five-point scale subdivided into the dimensions physical well-being, psychological well-being, parent relations and autonomy, social support and peers, and school. An overall HRQOL-index can be calculated. Rasch-scores can be computed for all dimensions with a mean (M) of 50 and a standard deviation (SD) of 10.[20]

B. Manual ability was evaluated using the ABILHAND-Kids questionnaire, which was developed to measure manual ability of children with CP. It is a unidimensional measure for 21 mostly bimanual activities of varying difficulty. Parents rate the 21 items as impossible (0), difficult (1) or easy (2). The score of the ABILHAND-Kids questionnaire was transformed into an ABILHAND-Kids measure ranging from +6.68 (all 21 bimanual activities are rated as easy to perform) to −6.75 (none of the activities is rated as possible) using a Rasch analysis.[21]

2.4. Statistical analyses

We used the Statistical Package for Social Sciences for Windows, version 25 (IBM SPSS Statistics). To test for normality a Shapiro–Wilk Test was performed. Since the outcome data of the two and five-year follow-up were mostly not normally distributed, we used nonparametric statistical tests for further statistical analyses. In order to compare the Kidscreen-27 results of the study population with those of the Swiss norm, a Wilcoxon-test was performed. A Chi-squared test was used to calculate differences in distribution between groups. To determine group differences within the study population, we performed a Mann-Whitney-U test. Correlations between manual ability and HRQOL measures were calculated with a Spearman correlation. The level of significance was set at 0.05.

3. Results

3.1. Participants

Between 2000 and 2010, 100 neonates with NAIS were registered in the SNPSR (67 boys, mean gestational age 39.8 weeks). The demographic results of this original cohort including the two-year follow-up were published previously.[2] Of these 100 patients, 74 completed a 2-year follow-up examination. A 5-year follow-up was performed on a total of 61 children, of whom 54 completed both the 2-year and the 5-year follow-up. There was no relevant difference in sex distribution, gestational age, birth weight and age at stroke manifestation between the original population and patients who underwent a 2-year, 5-year, and a 2-year and 5-year follow-up respectively. The demographic data of the study population at different follow-up times can be found in Supplement 1.

3.2. Two-year follow up

Details regarding the two-year follow-up are provided in Table 1. Twenty-nine of the 74 children (39.2%) were diagnosed with CP (28 with spastic CP and one child (2.0%) with ataxic CP). Of the 74 included participants a BSID-II assessment was performed in 56 children (76%) (PDI in 54 children [73%], MDI in 56 children [76%]). The results of the PDI were significantly worse in patients with CP, but there was no significant group difference regarding the MDI. The frequency of delayed cognitive and motor development was considerably higher in children with CP. In 18 children (24%) a neurological examination, but no BSID-II assessment was performed (due to poor compliance or because development testing was not possible due to severe disability). The severity of the developmental delay - estimated by the clinical examination - was significantly more pronounced in children with cerebral palsy (see Table 1). Seven children, all diagnosed with CP, received antiepileptic medication.

3.3. Five-year follow up

The results of the 5-year follow-up are summarized in Table 2. All parents involved completed the questionnaires. There was no statistically significant difference in HRQOL between our sample and the normative Swiss population (*M* 50; *SD* 10), neither in any of the five dimensions nor in the overall HRQOL-index (overall HRQOL-Index [*M* 50.59, *SD* 12.8, $z = -0.740$, $p = 0.46$, $n = 59$], physical well-being [*M* 51.0, *SD* 12.4, $z = -0.870$, $p = 0.39$, $n = 60$], psychological well-being [*M* 50.63, *SD* 12.3, $z = -0.120$, $p = 0.94$, $n = 58$], parent relations and autonomy [*M* 51.84, *SD* 13.6, $z = -0.023$, $p = 0.98$, $n = 37$], social support and peers [*M* 48.28, *SD* 13.9, $z = -1.176$, $p = 0.24$, $n = 54$] and school [*M* 51.20, *SD* 10.2, $z = -0.855$, $p = 0.43$, $n = 60$]). HRQOL (HRQOL-index and all domains) did not differ between boys and girls.

The results of the Kidscreen-27 in patients diagnosed with CP during the 2-year follow-up and in children without motor abnormalities are illustrated in Fig. 1. There were significant differences between patients with and without CP in the Kidscreen-27 dimensions psychological well-being ($p = 0.012$) and social support & peers ($p = 0.048$), as well as in the Kidscreen-27 HRQOL index ($p = 0.013$). The results of the ABILHAND-Kids questionnaire were significantly worse in children with CP ($p < 0.001$).

3.4. Correlations between HRQOL and manual ability

The results of the correlations HRQOL and manual ability are summarized in Table 3. All subscales and the overall HRQOL-index of the KIDSCREEN-27 were significantly correlated with manual ability.

4. Discussion

Supporting our first hypothesis and in agreement with others,[7] HRQOL five years after NAIS did not differ from the normative population. Although not statistically significant, parents rated the overall HRQOL-index of the KIDSCREEN-27 even slightly higher than the normative sample. This counterintuitive finding could be interpreted using the concept of the "disability paradox". This concept suggests that life satisfaction depends on a person's ability to achieve a balance between body, mind and spirit, rather than the degree of impairment itself. Thus a patient's objective health and disability does not necessarily correspond with his or her self-reported well-being.[22] In addition to the child's HRQOL, intra-family factors also play a major role in the child's well-being. How a child's parents deal with the disease and the health system has an impact on the child's HRQOL. Other authors who focused on the care-givers well-being and family

Table 1 – Description of study population at two year follow up.

	All participants ($n = 74$)	Patients without motor impairment ($n = 45$)	Patients with CP ($n = 29$)	P-Value
Sex	46 boys (62.2%) 28 girls (37.8%)	26 boys (57.8%) 19 girls (42.2%)	20 boys (69.0%) 9 girls (31.0%)	$p = 0.333$*
Birth weight (g)	3410.56 (404.7)	3484.86 (339.9)	3304.81 (469.0)	$p = 0.104$**
Gestational Age (weeks)	39.75 (1.4)	39.98 (1.3)	39.41 (1.5)	$p = 0.114$**
Age at manifestation (days)	2.99 (4.0)	2.96 (3.1)	3.04 (5.1)	$p = 0.202$**
BSID-II MDI ($n = 56$)	96.04 (13.1) MDI >85: 43 (76.8%) MDI 70–85: 13 (23.2%)	97.47 (12.4) MDI >85: 30 (83.3%) MDI 70–85: 6 (16.7%)	93.45 (12.3) MDI >85: 13 (65.0%) MDI 70–85: 7 (35.0%)	$p = 0.397$** $p = 0.119$*
BSID-II PDI ($n = 54$)	92.59 (13.6) PDI >85: 39 (72.2%) PDI 70–85: 11 (20.4%) PDI <70: 4 (7.4%)	95.18 (13.1) PDI >85: 29 (85.3%) PDI 70–85: 3 (8.8%) PDI <70: 2 (5.9%)	88.20 (13.6) PDI >85: 10 (50%) PDI 70–85: 8 (40%) PDI <70: 2 (10%)	$p = 0.031$** $p = 0.014$*
BSID-II not performed Severely handicapped	6	0	6	
BSID-II not performed Developmental delay	3	0	3	
BSID-II not performed Normal development	9	9	0	
Antiepileptic medication	7 (%)	0	7 (%)	$p = 0.001$*

Differences in distribution were determined using the Chi-square test*. The group differences were determined using the Mann–Whitney test**. If not indicated otherwise results are Mean (SD). Abbreviations: BSID-II-MDI = Bayley Scales of Infant Development II Mental Developmental Index, BSID-II-PDI = Bayley Scales of Infant Development II Psychomotor Developmental Index.

Table 2 – Description of study population at five year follow up.

	All participants	Boys: n = 37 (61%)	Girls: n = 24 (39%)	P-Value
Antiepileptic Medication	1 (2%)	1	0	$p = 0.417$*
Kidscreen-27 HRQOL index	50.59 (12.8)	50.46 (13.0)	50.78 (12.8)	$p = 0.823$**
Kidscreen-27 physical well-being	51.0 (12.4)	52.01 (12.7)	49.47 (12.0)	$p = 0.722$**
Kidscreen-27 psychological well-being	50.63 (12.3)	50.49 (13.1)	50.82 (11.3)	$p = 0.580$**
Kidscreen-27 parents & autonomy	51.84 (13.6)	51.17 (13.1)	52.93 (14.8)	$p = 0.925$**
Kidscreen-27 social support & peers	48.28 (13.9)	47.68 (11.9)	49.21 (17.0)	$p = 0.528$**
Kidscreen-27 school	51.20 (10.2)	51.00 (11.2)	51.54 (8.5)	$p = 0.623$**
ABILHAND-Kids	3.97 (2.5)	3.71 (2.6)	4.38 (2.4)	$p = 0.374$**

Differences in distribution were determined using the Chi-square test*. The group differences were determined using the Mann–Whitney test**. If not indicated otherwise results are Mean (SD).

perception, and not on the patients HRQOL, found an association between perceived severity of their child's illness and caregiver depression.[24] A Canadian study showed high satisfaction with health care services.[25]

Contrary to the previously published French study including a similar population,[7] HRQOL was rated worse by parents with children with CP than by parents of children without CP. The parents of children with a CP also rated the domain psychological well-being worse. We consider these differences between the two subpopulations to be clinically relevant. These differences between studies may be explained by the nature of the questionnaires being used to assess HRQOL. Whereas we used the KIDSCREEN-27 (which focuses on HRQOL during school age), the French group used the QUALIN, a questionnaire which was designed to determine HRQOL in infancy and preschool age. The QUALIN questionnaire does not contain specific questions on participation, aspects that are better captured by the Kindscreen-27. Social difficulties experienced by children after childhood and perinatal stroke have been reported previously – even in the absence of behavioral and cognitive difficulties.[23] This indicates that parents of children diagnosed with ischemic stroke are particularly concerned about their child's participation. Future studies should investigate social participation in children diagnosed with ischemic stroke in more detail.

There was no statistically significant difference regarding physical well-being between children with and without CP, but parents of children diagnosed with CP perceived the domain psychological well-being less good. This finding might indicate that not the perception of the physical impairment itself, but mainly the psychological burden attributed to the stigma of looking and functioning differently that affects the HRQOL.

Contrary to our third hypothesis, we found a significant association between HRQOL and manual ability. Previous studies could not demonstrate a relation between HRQOL and

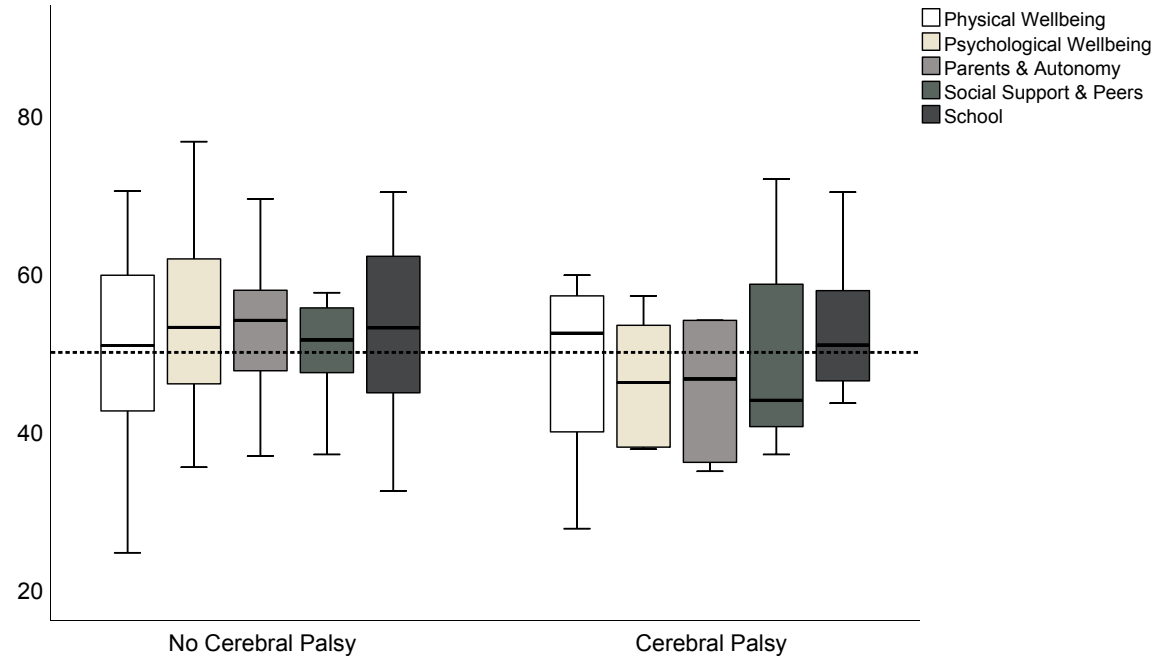

Fig. 1 – Boxplot Results KIDSCREEN-27 for children with and without cerebral palsy. Boxplot showing the results regarding the Kidscreen-27 subscales in children with and without CP at the age of 2 years. There was a significant difference between the two groups in the subscales psychological well-being ($p = 0.012$) and social support & peers ($p = 0.048$). No significant differences were found in the subscales physical well-being ($p = 0.078$), parents & autonomy ($p = 0.081$) and school ($p = 0.051$) [group differences were analyzed with the Mann–Whitney test].

Table 3 – Correlations between HRQOL and manual ability.

	KS-27 physical well-being	KS-27 psychological well-being	KS-27 parent relations and autonomy	KS-27 social support and peers	KS-27 school	HRQOL-Index	ABILHAND-Kids
KS-27 physical well-being		r = 0.452 p < 0.001	r = 0.203 p = 0.235	r = 0.332 p = 0.015	r = 0.255 p = 0.051	r = 0.574 p < 0.001	r = 0.520 p < 0.001
KS-27 psychological well-being	r = 0.452 p < 0.001		r = 0.659 p < 0.001	r = 0.473 p < 0.001	r = 0.434 p = 0.001	r = 0.846 p < 0.001	r = 0.497 p < 0.001
KS-27 parents & autonomy	r = 0.203 p = 0.235	r = 0.659 p < 0.001		r = 0.642 p < 0.001	r = 0.368 p = 0.025	r = 0.786 p < 0.001	r = 0.610 p < 0.001
KS-27 social sup & peers	r = 0.332 p = 0.015	r = 0.473 p < 0.001	r = 0.642 p < 0.001		r = 0.577 p < 0.001	r = 0.683 p < 0.001	r = 0.426 p = 0.002
KS-27 school	r = 0.255 p = 0.051	r = 0.434 p = 0.001	r = 0.368 p = 0.025	r = 0.577 p < 0.001		r = 0.583 p < 0.001	r = 0.413 p = 0.001
HRQOL-Index	r = 0.574 p < 0.001	r = 0.846 p < 0.001	r = 0.786 p < 0.001	r = 0.683 p < 0.001	r = 0.583 p < 0.001		r = 0.573 p < 0.001
ABILHAND-Kids	r = 0.520 p < 0.001	r = 0.497 p < 0.001	r = 0.610 p < 0.001	r = 0.426 p = 0.002	r = 0.413 p = 0.001	r = 0.573 p < 0.001	

KS-27 = KIDSCREEN-27, HRQOL = Health Related Quality of Live, Social sup. = social support.

day-to-day activities after NAIS. In the study by Darteye et al.[7] everyday activity was measured with the Functional Independence Measure for Children (WeeFIM), an instrument that measures the functional independence in the domains self-care, mobility, and cognition. The ABILHAND-Kids questionnaire in contrast specifically assesses a person's ability to manage daily activities requiring the use of the upper limbs regardless of the strategy involved. The reported association between manual ability and HRQOL is of considerable clinical importance. Early recognition of manual impairment and timely interventions to improve hand function may not only improve motor skills, but also positively influence HRQOL during later development. We strongly recommend early assessment of hand function in all children diagnosed with NAIS. A recent study with similar study population has shown a clear relation between manual dexterity and cognitive function, but not HRQOL.[26] In the present study a definite conclusion with respect to the relation of cognition and manual dexterity is not possible due to the different time points of cognitive assessment and manual ability.

5. Conclusion

Five years after neonatal stroke HRQOL is comparable to that of typically developing peers, but CP is associated with poorer HRQOL. Manual ability 5 years after NAIS correlates with HRQOL. Assessments focused on manual ability are indicated to identify children at risk for impairment at an early stage.

6. Limitations

We used the parent/proxy version of the KIDSCREEN-27 because no other HRQOL questionnaires for younger children with Swiss control data are available. As the KIDSCREEN-27 is not validated for children below 8 years, we chose only to use the parent ratings of HRQOL. Our results therefore do not reflect HRQOL perceived by the children themselves. The ABILHAND-Kids is validated for children from 6–15 years. Although our population was only slightly younger, some tasks included in the ABILHAND-Kids might have been be too difficult to perform for the participants. An assessment of manual ability at later age may therefore be preferable. Cognitive and motor assessments took place during the two-year follow up. As cognitive function and motor performance may change during development and children may grow into their deficits, we chose not to correlate the results of the two-year follow-up and those of the five-year follow up. No information regarding socioeconomic status has been gathered and therefore its effect on HRQOL could not be assessed. Despite manual ability, various other factors (such as socioeconomic status) may influence HRQOL after early brain injury and associations between manual ability and HRQOL may be influenced by other co-variates. Future studies assessing HRQOL after NAIS should therefore consider this. Another limitation of the present study is the incomplete follow-up of children at the age of 5 years. There was no relevant difference in gender distribution, age at stroke manifestation, gestational age and birth weight between the original study population and patients who participated in the 2 and 5-year follow-up (see supplement 1). Patients may drop out of a study because they are doing well - or the opposite may be the case. Diagnosis of CP at 5 years was similar to that of the original sample at 2 years (39%). However, 8 patients with CP from the original sample were not recorded at 5 years. This may bias our results as these children may either be severly impaired and therefore have dropped out or be doing so well, that further study participation seems unnecessary for the caregivers.

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Conflict of interest

None declared.

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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.2019.08.002.

Appendix. Names of the Members of the Swiss Neuropediatric Stroke Registry

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REFERENCES

1. Raju T, Nelson K, Ferriero D, Lynch J. Ischemic perinatal stroke: summary of a workshop sponsored by the national institute of child health and human development and the national institute of neurological disorders and stroke. *Pediatrics* 2007;**120**:609–16.
2. Grunt S, Mazenauer L, Buerki S, et al. Incidence and outcomes of symptomatic neonatal arterial ischemic stroke. *Pediatrics* 2015;**135**:1120–8.
3. deVeber G, MacGregor D, Curtis R, Mayank S. Neurologic outcome in survivors of childhood arterial ischemic stroke and sinovenous thrombosis. *J Child Neurol* 2000;**15**:316–24.
4. Sreenan C, Bhargava R, Robertson C. Cerebral infarction in the term newborn: clinical presentation and long-term outcome. *J Pediatr* 2000;**137**:351–5.
5. Laucht M, Esser G, Baving L, et al. Behavioral sequelae of perinatal insults and early family adversity at 8 years of age. *J Am Acad Child Adolesc Psychiatry* 2000;**39**:1229–37.
6. The WHOQOL Group. The World Health Organization quality of life assessment (WHOQOL): development and general psychometric properties. *Soc Sci Med* 1998;**46**:1569–85.
7. Darteyre S, Renaud C, Vuillerot C, et al. Quality of life and functional outcome in early school-aged children after neonatal stroke: a prospective cohort study. *Eur J Paediatr Neurol* 2014;**18**:347–53.
8. Suppiej A, Traverso A, Baggio L, et al. Long-term neuropsychological outcome and quality of life in perinatal ischemic stroke. *J Pediatr Neurol Med* 2016;**1**:104.
9. Neuner B, von Mackensen S, Krümpel A, et al. Health-related quality of life in children and adolescents with stroke, self-reports, and parent/proxies reports: cross-sectional investigation. *Ann Neurol* 2011;**70**:70–8.
10. Ghotra SK, Johnsan JA, Qiu W, Newton A, Rasmussen C, Yager JY. Age at stroke onset influences the clinical outcome and health-related quality of life in pediatric ischemic stroke survivors. *Dev Med Child Neurol* 2015;**57**:1027–34.
11. Gordon A, Ganesan V, Towell A, Kirkham F. Functional outcome following stroke in children. *J Child Neurol* 2002;**17**:429–34.
12. Friefeld S, Yeboah O, Jones J, deVeber G. Health-related quality of life and its relationship to neurological outcome in child survivors of stroke. *CNS Spectr* 2004;**9**:465–75.
13. Kornfeld S, Studer M, Winkelbeiner S, Regényi M, Boltshauser E, Steinlin M. Quality of life after paediatric ischaemic stroke. *Dev Med Child Neurol* 2017;**59**:45–51.
14. Jemta L, Dahl M, Fugl-Meyer KS, Stensman R. Well-being among children and adolescents with mobility impairment in relation to demographic data and disability characteristics. *Acta Paediatr* 2005;**94**:616–23.
15. Vargus-Adams J. Health-related quality of life in childhood cerebral palsy. *Arch Phys Med Rehabil* 2005;**86**:940–5.
16. Steinlin M, Roellin K, Schroth G. Long-term follow-up after stroke in childhood. *Eur J Pediatr* 2004;**163**:245–50.
17. Bayley N. *Bayley scale for infant development (BSID-II)*. 2nd ed. San Antonio: The Psychological Corporation; 1993.
18. Rosenbaum P, Paneth N, Leviton A, et al. A report: the definition and classification of cerebral palsy April 2006. *Dev Med Child Neurol* 2007;**109**(Suppl.):8–14.
19. Surveillance of cerebral palsy in Europe: a collaboration of cerebral palsy surveys and registers. Surveillance of cerebral palsy in Europe (SCPE). *Dev Med Child Neurol* 2001;**42**:816–24.
20. Ravens-Sieber U, Gosch A, Abel T, et al. Quality of Life in Children and adolescents: a European public health perspective. *Sozial- Präventivmed* 2001;**46**:294–302.
21. Arnould C, Penta M, Renders A, Thonnard JL. ABILHAND-Kids: a measure of manual ability in children with cerebral palsy. *Neurology* 2004;**63**:1045–52.
22. Albrecht G, Devlieger P. The disability paradox: high quality of life against all odds. *Soc Sci Med* 1999;**48**:977–88.
23. Lo W, Gordon A, Hajek C, et al. Social competence following neonatal and childhood stroke. *Int J Stroke* 2013;**9**:1037–44.
24. Bemister TB, Brooks BL, Dyck RH, Kirton A. Predictors of caregiver depression and family functioning after perinatal stroke. *BMC Pediatr* 2015;**15**:75.
25. Shevell M, Oskoui M, Wood E, et al. Family-centred health care for children with cerebral palsy. *Dev Med Child Neurol* 2019;**61**:62–8.
26. Thébault G, Martin S, Brouillet D, Brunel L, Dinomais M, Presles É, et al. Manual dexterity, but not cerebral palsy, predicts cognitive functioning after neonatal stroke. *Dev Med Child Neurol* 2018;**60**:1045–105.