

# Health-Related Quality of Life in Children and Adolescents with Stroke, Self-Reports, and Parent/Proxies Reports: Cross-Sectional Investigation

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**Objective:** Limited data are available on health-related quality of life (HR-QoL) in pediatric stroke survivors. The aim of the present study was to assess HR-QoL by self-assessment and parent/proxy-assessment in children and adolescents who survived a first stroke episode.

**Methods:** We investigated HR-QoL in pediatric stroke survivors (71 preschool children [G1] and 62 school children/adolescents [G2]) and in 169 healthy controls. HR-QoL was assessed in patients and parents/proxies with the generic KINDL-R questionnaire exploring overall well-being and 6 well-being subdimensions (physical, psychological, self-esteem, family-related, friend-related, and school-related). In pediatric stroke survivors the neurological long-term outcome was measured with the standardized Pediatric Stroke Outcome Measure.

**Results:** Of stroke survivors, 65% exhibited at least 1 neurologic disability. Pediatric stroke survivors reported lower overall well-being compared with healthy controls. In G2 stroke patients, friend-related well-being respectively emotional well-being was significantly reduced compared with healthy controls (73.0 vs 85.0 points;  $p < 0.001$  respectively 80.2 vs 84.5 points;  $p = 0.049$ ). Parents/proxies of both stroke survivors rated the overall well-being and all subdimensions (except family-related and school-related well-being in G1 and G2 stroke survivors and physical functioning in G2 stroke survivors) lower compared with parents/proxies of healthy children/adolescents. Overall well-being was significantly reduced in children with moderate/severe neurological deficits compared with normal/mildly affected patients (75.5 vs 83.3 points,  $p = 0.01$ ). Neonatal stroke survivors reported a significantly better neurological long-term outcome compared to childhood stroke survivors (82.0 vs 75.0 points;  $p = 0.005$ ).

**Interpretation:** Pediatric stroke survivors compared with healthy controls are strongly affected regarding their overall well-being and older children/adolescents regarding their well-being with peers.

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The incidence of stroke in neonates and children is estimated at between 2.6 to 6.4 per 100,000 per year.<sup>1–4</sup> Stroke in neonates and children is associated with significant morbidity and mortality, leading to a common cause of acquired disability in childhood. Although survival is a key outcome indicator for this population, health-related quality of life (HR-QoL) is an

important outcome in survivors and provides information about how the disease and its complications and treatment affects the child and his/her ability to function within the home, school, and community environment.

In 1947, the World Health Organization defined health as a state of complete physical, mental, and social well-being of a human being and not merely the absence

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Additional Supporting Information can be found in the online version of this article.

of disease or infirmity.<sup>5</sup> Measurement of HR-QoL started in the 1970s as a complement to traditional clinical outcome indicators, recognizing that self-reports on subjective states captures essential information which was not captured by traditional outcome indicators.<sup>6</sup> Subsequently, the multidimensional construct HR-QoL combines different domains such as physical, emotional, mental, social, and behavioral well-being of subjects assessed by the patients themselves as well as by different observers.<sup>7</sup> During the last decade HR-QoL was increasingly included in outcome research on patients with cerebrovascular disease.<sup>8–16</sup>

HR-QoL assessment plays an equally important role in evaluating the effectiveness of therapeutic interventions in children and adolescents.<sup>17,18</sup> HR-QoL instruments used with children and adolescents evaluate the physical, emotional, social, and behavioral dimensions of well-being.<sup>5</sup> These instruments have 3 features that distinguish them from other types of health outcome indicators. They typically include: (1) multidimensional factors, (2) measure children's and adolescents' health in terms that are important to the child/adolescent and his/her family, and (3) measure the child/adolescent and parent/proxy perspective.

Although numerous HR-QoL questionnaires have been developed, few investigators have used these instruments to assess children's outcomes after stroke.<sup>19,20</sup> Therefore, the present study evaluated HR-QoL, concomitant with neurologic long-term outcome, in a German pediatric cohort of stroke survivors.

## Patients and Methods

### Ethics

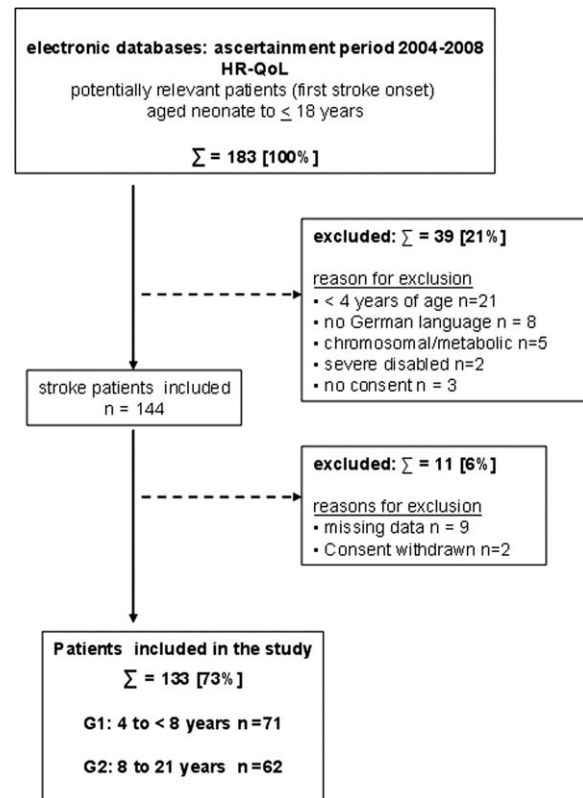
The present study was performed in accordance with the ethical standards laid down in the updated version of the 1964 Declaration of Helsinki and was approved by the medical ethics committee of the University of Münster, Germany.

### Inclusion Criteria

German speaking pediatric patients, aged 4 to 21 years, admitted to the Münster stroke treatment center for diagnosis, treatment, and neurological follow-up following a first stroke onset (age at first stroke onset 0.1 to 17.6 years, median 6.3 years) were included.

### Exclusion Criteria

Patients aged less than 4 years at the time of completion of the questionnaire (n = 21), non-German-speaking families (n = 8), childhood stroke patients with chromosomal aberrations or metabolic diseases (n = 5), children who were unable to answer the questions due to severe disabilities (n = 2), and families without written consent (n = 3). In addition, patients/parents who did not complete the questionnaire within 6 months of their last neurological examination were excluded (n = 1).



**FIGURE 1: Flowchart study cohort: inclusion and exclusion criteria and final study cohort is depicted.**

### Study Population

In January 2010, 144 stroke survivors (74 preschool children aged 4 to <8 years, median 4.1 years after stroke onset [G1] and 70 school children/adolescents aged 8.0 to 21 years, median 7.6 years after stroke onset [G2]), were enrolled in the Münster stroke treatment center based on age at assessment. Sixty-four out of 74 children in G1 and 16 out of 70 children in G2 had suffered from acute stroke during infancy. Patients and their parents were evaluated on HR-QoL, concomitant with neurologic long-term outcome. Figure 1 depicts the final study population with respect to inclusion and exclusion criteria.

Child self-report and parent/proxy versions of the HR-QoL assessment were administered. Participants completed the questionnaires during a routine ambulatory follow-up visit (1) by themselves or (2) if unable to read and write, with the help of a study nurse. Proxy versions were completed by mothers, fathers, or both parents together.

### Control Population

Data were collected from 169 population-based healthy controls, recruited from kindergarten/school mates or friends from the same catchments areas as the patients. In addition, controls were matched for age and socioeconomic background.

### Neurological Outcome

Apart from the main study goal, ie, the assessment of HR-QoL outcome in children with stroke, on an explorative basis the neurological

TABLE 1: Neurologic Outcome Classification According to the PSOM Questionnaire

Outcome Classification	Outcome Definition by Score and Category <sup>a</sup>
Good	
Normal	0 in all 5 categories
Mild deficit	0.5 in only 1 category
Poor	
Moderate deficit	0.5 in 2, 3, or 4 categories; or 1 in 1 category; or 1 in 1 category plus 0.5 in 1 category
Severe deficit	0.5 in all 5 categories; or 1 in 2 categories; or 1 in 1 category plus 0.5 in 2 categories; or 2 in 1 category

<sup>a</sup>Categories are defined as follows: sensory or motor; language expressive and comprehensive; and cognitive and behavior. Scores are defined as follows: 0 = no impairment; 0.5 = minimal/mild impairment: normal function; 1 = moderate impairment: decreased function; 2 = severe impairment: loss of function. PSOM = Pediatric Stroke Outcome Measurement.

deficits were measured within 3 months using the standardized Canadian Pediatric Stroke Outcome Measure (PSOM) (Table 1).<sup>21</sup> The most severe neurological outcome, represented as the most severe summary score of the PSOMs performed by 2 independent neuropediatric investigators within a 3-month period, was included as primary type of neurological outcome in the statistical analysis.

### HR-QoL Outcome

HR-QoL was assessed with the generic KINDL-R questionnaire.<sup>22</sup> Because most of the HR-QoL instruments for children are developed in English and only afterward translated into new target languages such as German, we decided to use the KINDL-R questionnaire, which was originally developed in the German language. The KINDL-R instrument is a standardized outcome measure developed and validated for use in healthy children and pediatric patients aged 4 to 16 years. The questionnaire has been translated into 23 languages (www.kindl.org) and normative data are available from the mental health module (BELLA Study)<sup>23</sup> within the German Health Interview and Examination Survey for Children and Adolescents (KiGGS). The KiGGS was conducted between May 2003 and May 2006 by the Robert-Koch-Institute in a nationwide representative German population sample with overall 17,641 families with children and adolescents.<sup>24</sup> We used the results of the BELLA Study to compare our study results with German population norms. Separate versions of the KINDL-R questionnaire are available for age groups 4 to 7, 8 to 12 and 13 to 16 years.<sup>22</sup> The KINDL-R questionnaire is a self-report assessment of HR-QoL consisting of 24 items generating a total well-being score and 6 subscores (physical well-being, psychological well-being, self-esteem, family-related well-being, friend-related well-being, and school-related well-being), each with values between 0 and 100 points. Items are positive statements of HR-QoL aspects, eg, "I am easily able to make friends," and higher values indicate better HR-QoL. The self-report for age 4 to 7 years is simplified to include a total of only 12 items pertaining to the 6 dimensions with 3 categorical responses (never, sometimes, always) generating 1 total score (overall well-being), which summarizes all 12 items for this age group.

In agreement with common practice, the KINDL-R questionnaires for age group 8 to 12 years were combined with the version for age group 13 to 16 years. The latter was also distributed to two 21-year-old patients, who suffered stroke before the age of 18 years. Data on socioeconomic parameters (education, income, occupation [parental reports]) were also requested. Subsequently, households' socioeconomic situations were classified as low, middle, or high.<sup>26</sup>

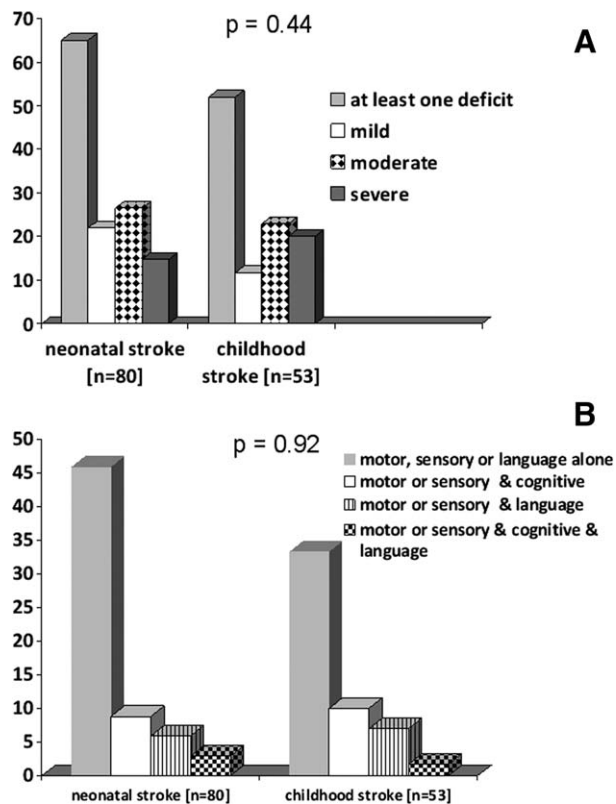
### Statistics

All statistical analyses were performed using SPSS software (version 17.0; SPSS, Inc., Chicago, IL) and StatView (version 4.0; SAS Institute, Inc., Cary, NC). Metric variables were presented as mean (standard deviation), and the *t* test was used to compare differences between 2 independent groups. Internal consistency of the KINDL-R-questionnaire was examined by Cronbach's alpha ( $\alpha$ ). The Pearson's correlation coefficient was used to measure pairwise correlation between patient self-report and parent/proxy report, respectively, control self-report, and control parent/proxy report. Correlation was designated as follows: poor to fair correlation ( $\leq 0.40$ ); moderate correlation (0.41–0.60); good correlation (0.61–0.80), and excellent correlation (0.81–1.00). In addition, interrater reliability was calculated with intraclass correlation coefficients (ICC1; see Supporting Information Table 1). Associations between neurological outcome and HR-QoL total scores were analyzed by linear regression analysis: neurological outcome was classified as dichotomous variable (normal-mild deficit vs moderate-severe deficit) and adjusted for age at stroke onset and vascular territory involved (left-sided vs right-sided circulation). In addition, HR-QoL total scores were compared between patients with neonatal stroke ( $n = 80$ ) and patients with childhood stroke ( $n = 53$ ). A *p* value  $< 0.05$  was considered statistically significant.

### Results

#### Study Population

Of the 144 patients enrolled in the study, 133 were included in the final sample (see Fig 1). The pediatric stroke population consisted of 60 girls (45%) and



**FIGURE 2:** (A) Proportion of leading neurologic long-term outcome in study participants with neonatal stroke and childhood stroke. Columns 2 to 4 sum up to column 1 ( $n = 133$ ). (B) Proportions of neurologic outcomes according to the most frequently observed deficits investigated with the PSOM in study participants with neonatal and childhood stroke. Columns 1 to 4 add up to 100% ( $n = 133$ ). PSOM = Pediatric Stroke Outcome Measurement.

73 boys (55%), with a median age of 6.3 years (minimum–maximum: term neonate to 17.6 years) at diagnosis of stroke. Brain lesions at stroke onset were found in the left anterior circulatory ( $n = 58$ ), the right anterior circulatory ( $n = 46$ ), bilateral anterior circulatory ( $n = 13$ ), or vertebrobasilar circulatory ( $n = 16$ ) systems. No statistically significant differences could be detected with respect to socioeconomic status between younger (G1) and older (G2) patients and between patients and controls.

### Neurological Long-Term Follow-Up

After a median (minimum–maximum) period of 4.1 years (2.0–7.1: G1 cohort) and 7.6 years (2.0–16.0: G2 cohort), 65% in the younger age group and 52% in children and adolescents with stroke exhibited at least 1 leading motor, sensory, language, or cognitive disability. The severity of the leading neurological symptoms on the PSOM for groups G1 and G2 at time of evaluation of the HR-QoL assessment are shown in Figure 2A. No differences were found between the 2 age groups on severity of neurological outcome (neonatal stroke vs childhood

stroke:  $p = 0.44$ ). Figure 2B depicts the type of single or combined major neurological deficits within the neurological domains of PSOM. The most often detected major deficits in order of frequency included: motor, sensory, or language deficit alone; motor or sensory deficit combined with cognitive or language deficit; motor or sensory deficit combined with cognitive and language deficit; and motor or sensory/cognitive/language deficits combined with visual deficit or hearing loss. There were no statistically significant differences in the distributions of the major neurological deficits between children in the neonatal stroke and childhood stroke groups ( $p = 0.92$ ). It has to be emphasized that neurological outcomes described in this survey on an explorative basis represent major leading neurological deficits only.

### HR-QoL Assessment

Results on the HR-QoL self-reports and parent/proxy reports for the patients and healthy controls are summarized in Tables 2, 3, and 4. Whereas in the younger age group proxy versions were completed by mothers in 95.1% of cases and by fathers in 4.9%, in the older age group proxy forms were completed by mothers in 76%, fathers in 12%, and by both parents in 12%. Table 2 shows self-reports and parent/proxy reports in children with stroke aged 4 to <8 years (first stroke onset: 93% neonatal stroke with 11% delayed or perinatal stroke, 7% childhood stroke) compared to healthy population-based controls. Tables 3 (self-reports) and 4 (parent/proxy reports) show data for children aged 8.0 to 21 years (11% neonatal stroke; 9% stroke during infancy; 80% childhood stroke).

In both stroke survivor groups self-reports were scored lower compared to healthy controls. Stroke survivors in the G2 group additionally rated their friend-related well-being 12.0 points lower than their healthy counterparts ( $p < 0.001$ ). The difference in emotional well-being in the G2 group reached statistical significance either but was less expressive: 4.3 points lower in cases compared with controls. Except for family-related well-being and school-related well-being in both groups and for physical well-being in G2, both G1 and G2 parents/proxies rated HR-QoL in their children/adolescents lower than parents/proxies with healthy children/adolescents.

When comparing overall well-being scores in children with neonatal stroke with those of patients with childhood stroke, neonatal stroke patients reported a significantly better overall well-being score (82.0 vs 75.0 points;  $p = 0.005$ ).

In addition to our population-based control population Tables 2 through 4 display German population norms for both self-reports and parent/proxy reports

**TABLE 2: Health-Related Quality of Life Scores for G1 Children (4–7 years old) with Stroke (n = 71); Healthy Population-Based Children 4–7 Years Old (n = 98), Self-Reports and Parent/Proxy Reports, and Norm Data for Children 3–6 Years Old from the KiGGS Study (n = 3,875)**

KINDL-R-Scores	Self-Reports			Parent/Proxy Reports				
	Children with Stroke (n = 71)	Healthy Children (n = 98)	KiGGS Participants	Parents of Children with Stroke (n = 69)	Parents of Healthy Children (n = 96)	KiGGS Participants (n = 3875) <sup>a</sup>		
	Mean (SD)	Mean (SD)	<i>p</i> <sup>b</sup>	Mean (SD)	Mean (SD)	Mean (SD)	<i>p</i> <sup>b</sup>	Mean
Overall well-being	81.3 (12.3)	85.3 (9.1)	0.017	Not available	72.0 (9.2)	78.1 (9.0)	<0.001	80.0
Physical well-being					76.0 (21.3)	82.5 (14.1)	0.038	80.2
Emotional well-being					80.0 (12.6)	85.2 (10.7)	0.005	83.0
Self-esteem					72.0 (13.1)	76.7 (10.7)	0.013	73.6
Family-related well-being					76.9 (11.0)	80.2 (12.2)	0.084	80.7
Friend-related well-being					69.2 (16.6)	80.3 (11.2)	<0.001	79.7
School-related well-being					77.3 (11.6)	78.8 (14.6)	0.517	83.3

<sup>a</sup>Ravens-Sieberer and colleagues.<sup>24</sup>  
<sup>b</sup>*t* test for 2 independent subgroups.  
G1 = 4–7 years old; KINDL-R = revised KINDer Lebensqualitätsfragebogen; SD = standard deviation; KiGGS = German National Health Interview and Examination Survey for Children and Adolescents.

deriving from the KiGGS (4 to 7 years old) and the BELLA Study (8 to 16 years old).<sup>23,24</sup>

Psychometric testing of the KINDL-R in terms of internal consistency measured by Cronbach's  $\alpha$ , are shown in Supporting Information Tables 1 and 2. Patients self-reported overall well-being showed an internal consistency of 0.62 (G1 patients) and 0.80 (G2 patients), respectively. In the healthy population-based controls internal consistency equaled 0.51 (G1) and 0.83 (G2), respectively. In G2 patients internal consistency varied between 0.50 (school-related well-being) and 0.80 (overall well-being) and in G2 healthy population-based children/adolescents between 0.25 (friend-related well-being) and 0.83 (overall well-being). Parent/proxy reports showed an internal consistency between 0.20 (school-related well-being in parent/proxy reports of G1 controls) and 0.93 (overall well-being in parent/proxy reports of G1 patients). In G2 parent/proxy reports internal consistency reached from 0.60 (family and school-related well-being in parent/proxy

reports of patients and friend-related well-being in parent/proxy reports of healthy population-based children) to 0.89 in overall well-being in parent/proxy reports of healthy population-based children.

The interrater correlation between patient self-reports and parent/proxy reports as well as control self-reports and control parent/proxy reports are shown in Supporting Information Tables 1 and 2 either. In G1 study participants interrater correlation equaled 0.60 in patients and 0.41 in healthy population-based children. In G2 study participants, the best interrater correlation was found for physical well-being in patients (0.75) and for overall well-being in healthy population-based children (0.79). By contrast, the poorest interrater correlations were detected for family-related well-being in patients (0.47) and friend-related well-being in healthy population-based children (0.17).

Overall well-being in patients with moderate-severe neurological deficit was significantly reduced compared to patients with normal-mild deficit (75.5 vs 83.3 points;

**TABLE 3: Self-Reported Health-Related Quality of Life in G2 (8–21 Years Old) Children/Adolescents with Stroke (n = 62) and in 8–16-Year-Old Healthy Population-Based Children (n = 71), and Self-Report Data from the Mental Health Module (BELLA Study) of the KiGGS Study for 11–17-Year-Old Children and Adolescents (n = 1,895)**

KINDL-R Scores (Self-Reports)	Children with Stroke (n = 62)	Healthy Population-Based Children (n = 71)	<i>p</i> <sup>a</sup>	BELLA Participants (n = 1,895) <sup>b,c</sup>
Overall well-being, mean (SD)	75.2 (10.1)	79.4 (9.5)	0.030	73.0 (10.2)
Physical well-being, mean (SD)	73.4 (16.4)	78.4 (17.3)	0.136	70.7 (16.8)
Emotional well-being, mean (SD)	80.2 (13.7)	84.5 (8.9)	0.049	81.6 (12.6)
Self-esteem, mean (SD)	67.0 (16.8)	65.6 (16.1)	0.671	58.4 (18.3)
Family-related well-being, mean (SD)	81.3 (15.3)	85.6 (12.1)	0.131	82.5 (15.3)
Friend-related well-being, mean (SD)	73.0 (17.1)	85.0 (11.0)	<0.001	77.5 (14.6)
School-related well-being, mean (SD)	76.0 (16.8)	77.3 (16.9)	0.694	67.2 (16.9)

<sup>a</sup>*t* test for 2 independent subgroups.<sup>b</sup>Ravens-Sieberer and colleagues.<sup>23</sup><sup>c</sup>Data solely for the age group 11–17 years.

BELLA = mental health module within the KiGGS; KiGGS = German Health Interview and Examination Survey for Children and Adolescents; KINDL-R = revised KINDer Lebensqualitätsfragebogen; SD = standard deviation.

*p* = 0.01). Multivariate analysis (linear regression) adjusted for age at stroke onset and vascular territory showed a significant association between neurologic outcome and overall well-being (moderate-severe vs normal-

mild deficit: –8.2 [95% confidence interval [CI], –12.3 to –3.6] points, *p* = 0.031). Neither age at onset nor vascular stroke territory itself, were significantly related with poorer neurological outcome in the children investigated.

**TABLE 4: Parent/Proxy Reported Health-Related Quality of Life in G2 (8–21 Years Old) Children/Adolescents with Stroke (n = 39) and in 8–16-Year-Old Healthy Population-Based Children (n = 66), and Parents/Proxies Reports from the Mental Health Module of the KiGGS Study (BELLA Study) for 7–17-Year-Old Children and Adolescents (n = 2,863)**

KINDL-R Scores (Parents/Proxies Reports)	Parents/Proxies of Children with Stroke (n = 39)	Parents/Proxies of Healthy Population-Based Children (n = 66)	<i>p</i> <sup>a</sup>	BELLA Participants (n = 2,863) <sup>b</sup>
Overall well-being, mean (SD)	72.3 (12.4)	80.0 (9.9)	0.001	76.3 (10.1)
Physical well-being, mean (SD)	70.4 (19.7)	77.8 (17.3)	0.053	76.5 (17.3)
Emotional well-being, mean (SD)	77.6 (16.0)	84.0 (13.1)	0.036	80.8 (12.8)
Self-esteem, mean (SD)	68.1 (16.3)	74.7 (14.3)	0.039	68.8 (14.2)
Family-related well-being, mean (SD)	77.0 (12.7)	79.5 (14.5)	0.359	77.7 (14.3)
Friend-related well-being, mean (SD)	67.1 (20.9)	85.7 (10.3)	<0.001	78.0 (13.4)
School-related well-being, mean (SD)	74.5 (17.4)	78.9 (16.9)	0.225	76.0 (16.0)

<sup>a</sup>*t* test for 2 independent subgroups.<sup>b</sup>Ravens-Sieberer and colleagues.<sup>23</sup>

BELLA = mental health module within the KiGGS; KiGGS = German Health Interview and Examination Survey for Children and Adolescents; KINDL-R = revised KINDer Lebensqualitätsfragebogen; SD = standard deviation.

## Discussion

The present study evaluated HR-QoL including self-reports and parent/proxy reports in 133 children and adolescents following a first stroke onset compared to 169 healthy controls. Additionally, the leading neurological long-term sequelae were assessed in the patient population on an explorative basis. Compared to healthy population-based controls, HR-QoL was significantly reduced in overall well-being in both younger and older stroke survivors. The older stroke survivors additionally showed impaired emotional well-being and impaired friend-related well-being compared to healthy population-based controls. Lower scores for physical well-being, self-esteem, family-related as well as school-related well-being in older stroke survivors compared with healthy population-based controls did not reach statistical significance. In addition, we could demonstrate that survivors after neonatal stroke reached a significant better overall well-being compared with survivors of childhood stroke. Our results also showed that the degree of neurological deficit was a significant predictor of poorer overall well-being, with scores for patients with moderate-severe neurological deficits significantly reduced compared to patients with normal neurological outcomes or mild dysfunctions. Apart from these leading neurologic symptoms, further comprehensive neurophysiologic diagnostic investigations within our study population detected more behavioral problems, such as an increase of social and attention deficiencies and school-based problems.<sup>27</sup>

Although in almost 50% of older childhood stroke survivors neurological impairment and functional deficits persist,<sup>21,28,29</sup> only few studies have investigated quality of life in children with stroke.<sup>19,20,30,31</sup> In 2002, Gordon and colleagues<sup>30</sup> reported a decreased quality of life in 17 children and adolescents with arterial ischemic stroke from the United Kingdom. In their study population physical health was the most affected category, and severity of stroke was positively correlated with a reduced HR-QoL.<sup>30</sup> Two years later, in 2004, Han and colleagues<sup>31</sup> described similar findings of decreased well-being in the physical health of 84 children with stroke from the United States. In the same year a Canadian group published HR-QoL data obtained from 100 children with stroke (84 with arterial ischemic stroke and 16 patients with cerebral sinovenous thrombosis) assessed from both self-questionnaires and parent/proxy questionnaires.<sup>19</sup> The authors found significantly reduced overall HR-QoL in their patients, particularly within the school, emotional, and social domains. Comparison of child self-reports and parent/proxy reports showed a lack of concordance in data.<sup>19</sup> Very recently, in 2010, Cnossen and

colleagues<sup>20</sup> from Rotterdam described the functional outcome and HR-QoL in 76 children with stroke from the Netherlands. In their study population all children had reduced HR-QoL depending on age at stroke onset, fever at presentation, and infarction located in the territory of the right middle cerebral artery.<sup>20</sup>

Self-report questionnaires are regarded as the primary method for assessing HR-QoL in adults as well as in children once they have reached a certain age and level of cognitive development.<sup>32,33</sup> However, apart from the fact that self-reports and parent/proxy reports in childhood constitute complementary sources of information reflecting the perspective of both,<sup>34,35</sup> parent/proxy questionnaires are the gold standard methods when assessing well-being in children who are too young to respond themselves or who have cognitive deficits.<sup>36</sup> In the pediatric stroke literature, parent/proxy questionnaires alone have been used in the United Kingdom and the United States,<sup>30,31</sup> whereas in the study by Friefeld and colleagues,<sup>19</sup> Cnossen and colleagues,<sup>21</sup> and in our study population, both patient and parent/proxy assessment forms were used. In line with the Canadian findings we could also demonstrate that HR-QoL assessment scores (proxy versions) were reduced in 2 of 6 domains in the younger cohort and in 3 of 6 domains in older children but not always in a concordant manner. It is highly relevant to note that in our results self-reported HR-QoL in older stroke survivors differed from healthy population-based controls in only 2 out of 6 subdimensions. This has to be interpreted in the context of either (1) a partially successful adaptation to the clinical situation during the long-term clinical course of the disease, or (2) to a measurable consequence of an increased medical and psychosocial patient-family support (no differences in family-related well-being in patients and healthy population-based adolescents). Furthermore, (3) results may have been influenced by the comparator chosen (the individual population-based control group), and finally, (4) results may be influenced by the use of a generic rather than a disease-specific questionnaire. Interestingly, as in our study, all studies on HR-QoL in children with stroke used generic instruments, such as the Child Health Questionnaire (UK),<sup>30</sup> the Pediatric Quality of Life 4.0 Generic Inventory Scale (PedsQL; Canada),<sup>19</sup> the Preschool and Children's Adolescents' Quality of Life Questionnaires of the Netherlands Organization for Applied Scientific Research Academic Medical Center Leiden (TAPQOL, TACQOL, TAAQOL; The Netherlands)<sup>20</sup> and compared the HR-QoL of children with stroke to population-based controls. The identification of valid

indicators of HR-QoL from the patients perspective remains an open question in the pediatric age group.<sup>13,14,37</sup> Our findings highlight the importance of healthy control data in any study of pediatric stroke, and possibly in pediatric disease studies in general.

Internal consistency measured with Cronbach's  $\alpha$  is a statistical tool calculated from the pairwise correlations between items. It ranges between 0 and 1. A commonly-accepted rule of thumb is that an  $\alpha$  of 0.6 to 0.7 indicates acceptable reliability, and 0.8 or higher indicates good reliability. Our study determined that the HR-QoL total score internal consistency is adequate ranging from 0.51 to 0.93 across parent, proxy, healthy, and patient groups at both age distributions. In addition, all patient subscales are at or above 0.5 for G2, and for G1. These findings are similar to those reported from the German HR-QoL study in children with chronic conditions and the representative BELLA Study (see Supporting Information Table 3).<sup>38,39</sup>

For diseases like stroke that have the potential to result in mortality and disability, however with low rates (5–10%), mortality measured alone is an incomplete outcome measure. To establish best practice clinical guidelines for treatment and rehabilitation of child survivors of stroke, standardized functional neurological outcome measures such as the Canadian PSOM instrument developed for children as well as age-dependent quality of life outcome metrics are required to achieve high standards of excellence in comparison of treatment/rehabilitation benefits across disease states. Thus, we conclude that (1) generic quality of life instruments such as the KINDL-R questionnaire concomitantly used with standardized physician-based clinical/neurological outcome measures, such as the PSOM, are essential tools for assessing outcome and quality of life in children with stroke. In addition, when using generic HR-QoL instruments (2) both assessment variants, ie, self-reports and parent/proxy reports, should be included to gain as much information as possible and to identify the factors that influence quality of life in survivors of first episode stroke. Moreover, use of (3) control pediatric data are important in interpreting stroke-related HR-QoL. Finally, for future studies in the field (4) a disease-specific stroke questionnaire, which allows a deeper insight in the specific problems related to this disease, should be developed and validated to be compared with the pediatric generic HR-QoL instruments available so far.

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## Potential Conflict of Interest

Nothing to report.

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