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ORIGINAL ARTICLE

Development of disorder-specific normative data for growth in children with cerebral palsy

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Abstract

The purpose of this study was to create growth-percentiles for Caucasian children with cerebral palsy (CP). The studied parameters were height and age. In a retrospective analysis, we converted measurements collected in our center to create disorder-specific percentiles of normative data. Patients were stratified due to sex (male and female) and to mobility levels using the gross motor function classification system (GMFCS) (A = walking; GMFCS I–III, B = non walking; GMFCS IV–V) into four groups. In total, 2363 measurements in patients 0–18 years were collected. The mean age for group "Am" was 6.8 years (n = 862), group "Bm" 7.6 years (n = 563), group "Af" 7.7 years (n = 600), and group "Bf" 8.2 years (n = 366). The created percentiles for all groups were below the reference percentiles for healthy Caucasian children (KiGGS). The median curve for children with GMFCS levels I–III is slightly above the 3rd percentile, whereas the 50th percentile for GMFCS levels IV–V is mostly below the 3rd KiGGS centile.

Conclusion: In conclusion, children with cerebral palsy are smaller than healthy children. The difference between 50th percentile of CP patients compared to healthy children supports the need for the use of disorder-specific growth charts. Those charts can help clinicians differentiate growth disorders in patients with CP.

What is Known:

- *Children with cerebral palsy are shorter than healthy children and height is influenced by level of ambulation.*
- *Currently, only reference percentiles of American children with mixed ethical backgrounds are available to evaluate growth.*

What is New:

- *This paper presents disorder-specific reference percentiles for longitudinal growth of Caucasian children with cerebral palsy depending on motor function.*
- *These percentiles allow to asses longitudinal growth in children with cerebral palsy to detect other additional diseases impairing growth.*

Keywords Cerebral palsy · Growth retardation · Body height · Reference data

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Introduction

Cerebral palsy (CP) is defined as a syndrome comprising a wide spectrum of permanent developmental disorders affecting movement and posture due to non-progressive lesions of the developing brain [24]. In addition to the motor impairments, many patients present with further symptoms such as disturbances of sensation, perception, cognition, communication and behavior, mental retardation, epilepsy, secondary musculoskeletal problems, and swallowing disorders [24, 30]. Additionally, CP patients often show reduced body height. In general, body height results mainly from growth of the long bones. Longitudinal growth depends on processes in the epiphyseal plate, which are influenced by genetic and

environmental factors. Changes of these factors are likely to cause growth reduction of specific bones or result in small stature in general.

Genetic factors and endocrine disorders can cause short stature because growth depends on various hormonal interactions like, e.g., growth hormone [33], insulin-like growth factor (IGF-1) [22], and thyroidal hormones [21]. Despite the hormonal influence, bone growth depends on mechanical stimulation. Tension, induced by tendons during muscle activity, and compression via loading of the body weight are vital stimuli for physiological bone growth [9]. To provide the bone with sufficient supply, nutritional factors play a decisive role. Diet, malnutrition, and illness-specific nutritional deficiency result in reduced longitudinal growth [13, 23].

To assess health in pediatric patients, growth percentiles are a frequently used tool. Growth charts display predicted models for height development in comparison to sex and age in a general, healthy population. In Germany, the most frequently used growth references are the KiGGS percentiles [15]. If a child is below the third centile, it is considered to be too small, which indicates a reason for further investigation.

Using reference ranges and percentiles of healthy children, the majority of CP patients present with a reduced height. Their small shape is well-known and described, as well as their generally varying patterns of growth [7, 14, 27, 28, 31]. Krick et al. [14] were first to draw height versus age centiles. He found CP patients to be smaller than general children. Stevenson et al. [29] confirmed these findings with curves of their own. In addition, he found children's health to be negatively impacted depending on their deviation from age-specific references. The largest study was performed by Day et al. [7]. Their multicenter approach included measurements of more than 24,000 Californian children. While focusing on weight, they also created percentiles for height and BMI. The more that children differed from reference percentiles for American children, the greater their gross motor function impairment was. In a further approach, Brooks et al. were able to specify how much the reduced weight influenced morbidity and mortality. As a result of their large database, they were able to create growth percentiles for height, weight, and BMI which are publically accessible on the website of the "Life Expectancy Project (2011)" (LEP) [2]. These references include patients of varying ethnicities. Their use in assessing children with a Caucasian ethnicity is limited.

The fact that many children with CP are below the third percentile for healthy children might mislead physicians to the conclusion that all children with reduced body height are small due to the CP and thus other reasons for short stature may not be investigated in these children. Therefore, some other reasons for short stature in these children, unrelated to the CP, might be overlooked, such as hypothyroidism or celiac disease.

Additional reference curves allow better counseling of the families and can assist families and physicians in interpretation of growth in these children. Such disorder-specific reference curves are already established for some genetic disorders like Ullrich-Turner Syndrome [18] or Prader-Willi-Syndrome [4].

The aim of our study was to create height percentiles for CP patients depending on their motor impairments and to compare our centiles to the reference percentiles of the Life Expectancy Project as well as to German reference percentiles (KiGGS).

The percentiles could help identify CP children who are short of stature even for their disorder-specific reference curves. These children need further investigations to identify the underlying reason for the reduced body height (for instance endocrine or nutritional deficiencies), similar to the investigations done in short children without CP.

Methods

This is a monocentric, retrospective study. The measurements were performed by clinic staff at the Children's Hospital as part of clinical routine.

Participants and measurements

Eight hundred eighty-two patients with diagnosed CP received treatment at the University of Cologne, between January 2006 and June 2014. Participating patients were between 2 and 25 years of age. Five hundred sixteen were male, 366 were female. Eight hundred eighty-two patients with CP were identified in database. Thirty-two were excluded due to unknown gross motor function classification system (GMFCS) level. Nineteen patients were older 18 years of age. Twenty-five patients were recorded with implausible measurements.

For the final analysis, measurements of 806 discrete patients with a total of 2363 measurements (mean measurements of 1 patient was 2.9) were used to create the height percentiles. Measurements were excluded for being implausible when patients' height decreased over the observed 1-year period. We concluded that one of the measurements had to be false. We were unable to retrospectively identify the false measurement, which is why all data of the patient was excluded from analysis. All patients were from Caucasian ethnicity and were part of the germane health insurance system.

Patients' heights were measured at first presentation, after 6 months and after 12 months. Of these patients, additional data about growth development were collected from their treating pediatrician and their preventive medical check-ups, which are part of the germane healthcare system. Patients who were able to stand were measured using a wall-mounted stadiometer Seca 213 (SECA GmbH, Hamburg, Germany),

whereas the other patients were measured by using a tape measure. This was performed in patients not able to stand. They were lying on their back on a flat bed with the head positioned at a fixed point. Then, the patient was placed as straight as contractures and "scoliosis allowed" and the most distant heel was used to measure length, ignoring deformities of the feet. By using this method, we assessed "functional length" of the patients.

Stratification by GMFCS level

The gross motor function classification system (GMFCS) was used to assess the functional status of the patients. The GMFCS is a standardized and validated 5-level system to describe the gross motor function in patients with CP [17]. The GMFCS-assessment was performed by experienced doctors specialized in CP and movement disorders.

We combined GMFCS levels I to III to create group A and level IV to V to create group B. Patients in group A could walk with or without assisting devices whereas patients in group B depended on help from others for their mobility or were unable to walk. Stratifying patients into "walking" and "non-walking" for the purposes of an analysis was also used by other authors before [8].

Group Am: walking, GMFCS I–III, male, age 0 to 18:
n(GMFCS I) = 103, n(GMFCS II) = 272, n(GMFCS III) = 487.
Group Af: walking, GMFCS I–III, female, age 0 to 18:
n(GMFCS I) = 68, n(GMFCS II) = 186, n(GMFCS III) = 346.
Group Bm: non-walking, GMFCS IV–V, male, age 0 to 18:
n(GMFCS IV) = 441, n(GMFCS V) = 122.
Group Bf: non-walking, GMFCS IV–V, female, age 0 to 18:
n(GMFCS IV) = 296, n(GMFCS V) = 70.

To enlarge the database, we sent questionnaires to all families of the 882 participating children asking for documented height measurements from external pediatricians, e.g., from their infancy examinations. We received answer from 92 patients. The additional data was included as long as they contained a month-specific date of measurement. In these cases, we standardly set the 15th of the month. If the reported measurements were in between a 6-month time span, only the first of them was used to create the percentiles. Hereby, 397 additional measurements of 77 patients were collected in total.

Percentiles

Percentiles for height depending on age were created for these four groups. As statistical software we used "R" (version 3.2.1). The additional GAMLSS package (version 3.3-7) was necessary to apply the LMS method [6, 11, 20]. The LMS method uses the Box-Cox-transformation to calculate normally distributed Z values, which depend on the factors L, M, and S. The formula to calculate the Z values is as follows:

$$Z_{\mathrm{LMS}} = \frac{1}{S \times L} \times \left[\left(\frac{x}{M} \right)^{L} - 1 \right] \text{ for } S, L, \text{and } M \neq 0$$

M stands for the median, S symbolizes the standard deviation, while L corrects the unproportional skewness. Each parameter gets adjusted by individual degrees of freedom. The higher the degrees are, the better is the fit of the parameter. We identified the best model for the data through worm plots [32], Q tests [26], and their general appearance. The created percentile curves were compared to German reference growth charts (KiGGS). For reasons of clarity and comprehensibility, we only show the 3rd, 50th, and 97th percentiles.

Comparison to Life Expectancy Project graphs

Neither Day [7] nor Brooks [3] published data to recreate their graphs. The growth percentiles divided by GMFCS level are available via the website of the Life Expectancy Project [2]. To compare their results to ours, we manually transferred the graphs. The Life Expectancy Project presents different percentiles for GMFCS level V depending on the need of a tube for feeding. We chose the graph for orally fed patients, because most of our collective is independent of artificial feeding. As a matter of clarity, we only compared the 50th percentiles (median) of each graph.

Results

Figure 1 contains the height percentiles of male patients. The left graph shows the percentiles for walking male patients (GMFCS levels I to III) in comparison to KiGGS reference curves. Eight hundred sixty-two measurements in 271 patients were included in calculating the model. The 50th CP percentile (cP50) starts covering the 3rd reference percentile. Between the age of 3 and 15 years, the created percentile runs above the 3rd KiGGS percentile and below its 50th percentile. cP50 and the third KiGGS percentile cross two times afterwards. cP50 finishes on top of the third KiGGs percentile. cP97 is permanently located between the 50th and 97th reference percentile.

The right graph of Fig. 1 shows the percentiles for non-walking male patients (GMFCS levels IV to V) in comparison to KiGGS reference curves. Five hundred sixty in 202 patient measurements were included in calculating the model. The 50th CP percentile covers the 3rd KiGGS-percentile until the age of 12 years. The absence of growth acceleration during puberty leads to the drop of the percentiles. The 97th CP percentiles covers the 50th KiGGS percentile during all ages. The detailed data are presented in Table 1 for males able to walk and in Table 2 for the non-walkers.

The groups Am and Bm showed no statistical difference regarding age between Am and Bm (p value = 0.6339).

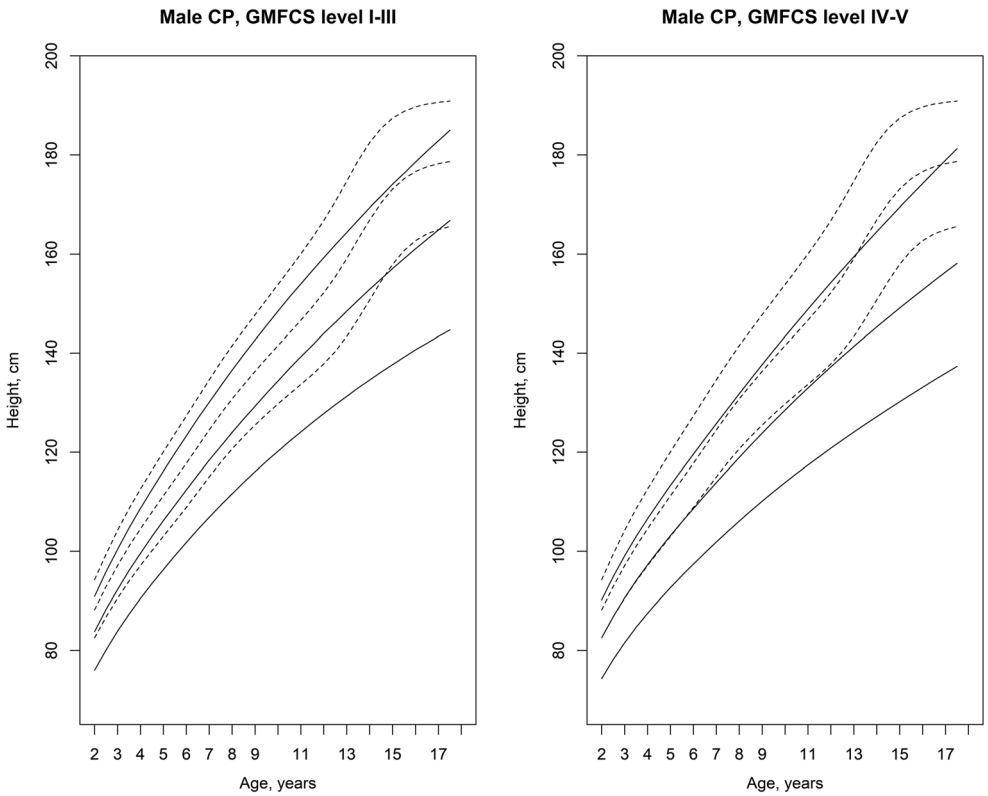

Fig. 1 Disorder-specific growth charts for male patients with CP. Black lines indicate percentiles of patients with CP (cP3, cP50, and cP97) for body height of male walking patient (group Am/left side) and male non-walking patients (group Bm/right side). Dotted lines (P3, P50, P97) indicate KiGGS reference percentiles

Regarding height, there was a significant difference between Am (mean height 120.7 cm) and Bm (mean height 116.7 cm) (p value = 0.002092) showing that males with GMFCS III–V are significantly shorter than males GMFCS I–II.

Figure 2 contains the height percentiles of female patients. The left graph shows the percentiles for walking female patients (GMFCS levels I to III) in comparison to KiGGS reference curves. Six hundred measurements in 200 patients were included in calculating the model. The 50th CP percentile starts almost identical to the 3rd KiGGS percentile. Between the age of 4 and 13 years, it is above the 3rd KiGGS-percentile. The 97th CP percentile is placed between the 50th and 97th KiGGS percentile approaching the 50th percentile at the end of growth.

The right graph of Fig. 2 shows the percentiles for non-walking female patients (GMFCS levels IV to V) in comparison to KiGGS reference curves. Three hundred forty-one measurements in 132 patients were included in calculating the model. The 50th CP percentile is parallel to the 3rd KiGGS percentile and slightly below. The curves separate around the age of 11. The 50th CP percentile reaches the plateau of the 3rd KiGGS percentile with the 18th birthday.

Group Bf's 97th CP percentile is slightly below 97th percentile of healthy children at the age of 1 year and drops afterwards to P50, crossing 50th percentile of KIGGS data at the age of 13 years. Raw data for walkers and non-walkers are presented in Tables 3 and 4.

As in males, there was no statistical difference regarding age between Af and Bf (p value = 0.3211). Regarding height, there was a significant difference between Af (mean height 122.6 cm) and Bf (mean height 119.5 cm) (p value = 0.02565) showing that females with GMFCS III–V are significantly shorter than females GMFCS I–II.

In general, the created growth percentiles for height are below the standard KiGGS centiles. The median disorder-specific centile (cP50) for children able to walk is slightly above or identical to the third KiGGS percentile, whereas the median centile of CP patients of group B is below the third KiGGS centile. The 97th CP percentile is generally located between P97 and P50, while group A's 97th CP percentile is closer to the 97th KiGGS percentile than group B's. The third CP percentile never touches, crosses, or comes close to the third KiGGS percentile in any group. Although the general appeal of both percentile curves is similar, CP percentiles for patients in group B and for male patients in group A appear to reach a maximum height at a younger age than healthy children. We identified a significant distance between the third KiGGS percentile and the third percentile of CP-curves.

In Figs. 3 and 4, the median percentile of our created disorder-specific growth percentiles are shown in comparison with the median percentile of every GMFCS level for patients of the same sex as published by the "Life Expectancy Project" (LEP) divided into our groups A and B.

Table 1 Data of CP specific growth percentiles for male walking patients GMFCS I–III (group Am)

Centiles - male GMFCS I–III									
C3	C10	C25	C50 = *M*	C75	C90	C97	*S*	*L*	Measurements per age group
76.0	78.6	81.1	83.8	86.4	88.7	90.9	0.047	2.156	27
80.1	82.8	85.4	88.3	91.1	93.5	95.9	0.047	1.801	
83.9	86.6	89.4	92.3	95.3	97.9	100.4	0.048	1.514	55
87.3	90.1	93.0	96.1	99.2	102.0	104.7	0.048	1.284	
90.5	93.4	96.3	99.6	102.9	105.8	108.7	0.049	1.101	104
93.5	96.5	99.6	103.0	106.4	109.5	112.5	0.049	0.962	
96.3	99.5	102.7	106.2	109.8	113.0	116.2	0.050	0.861	107
99.1	102.3	105.7	109.3	113.1	116.4	119.8	0.050	0.793	
101.8	105.1	108.6	112.4	116.3	119.8	123.3	0.051	0.755	87
104.4	107.9	111.4	115.4	119.5	123.1	126.8	0.052	0.743	
106.9	110.5	114.2	118.4	122.5	126.3	130.1	0.052	0.753	65
109.3	113.1	116.9	121.2	125.5	129.5	133.4	0.053	0.782	
111.6	115.6	119.5	124.0	128.5	132.5	136.6	0.053	0.826	60
113.9	118.0	122.1	126.7	131.3	135.5	139.7	0.054	0.883	
116.1	120.3	124.6	129.3	134.1	138.4	142.7	0.055	0.950	60
118.2	122.6	127.0	131.9	136.8	141.3	145.6	0.055	1.026	
120.2	124.8	129.4	134.4	139.5	144.0	148.5	0.056	1.108	57
122.2	126.9	131.6	136.9	142.1	146.7	151.3	0.056	1.195	
124.1	129.0	133.9	139.3	144.6	149.3	154.0	0.057	1.286	45
126.0	131.0	136.1	141.6	147.1	151.9	156.7	0.058	1.379	
127.8	133.0	138.3	144.0	149.5	154.5	159.3	0.058	1.474	40
129.6	135.0	140.4	146.2	152.0	157.0	161.9	0.059	1.571	
131.3	136.9	142.5	148.5	154.3	159.5	164.4	0.059	1.670	33
133.0	138.8	144.5	150.7	156.7	161.9	166.9	0.060	1.771	
134.6	140.7	146.6	152.9	159.0	164.3	169.4	0.060	1.873	32
136.2	142.5	148.5	155.0	161.2	166.6	171.7	0.061	1.978	
137.7	144.2	150.4	157.1	163.4	168.9	174.1	0.061	2.083	24
139.2	145.9	152.3	159.1	165.5	171.1	176.3	0.061	2.189	
140.7	147.6	154.1	161.1	167.6	173.2	178.6	0.062	2.296	19
142.0	149.2	155.9	163.0	169.7	175.4	180.8	0.062	2.401	
143.4	150.8	157.7	164.9	171.7	177.5	182.9	0.063	2.505	12
144.7	152.3	159.5	166.8	173.7	179.5	185.0	0.063	2.609	

The left graph shows the median percentile of groups Am and Af in comparison with the LEP's graphs of GMFCS levels I–III. During childhood, the curves for Caucasian patients with CP with mobility levels I–III are even above the LEP curves for GMFCS I. When reaching puberty, our curve crosses 97th LEP percentile.

Ending above the 50th percentile. The right graphs of Fig. 3 and for compare our median curve for male and female patients of group B compared to the LEP percentiles for GMFCS IV and V. In this comparison, Caucasian children are taller during whole adulthood compared to the US data.

Discussion

The created growth charts show a significant difference in body height between CP and general children. These findings confirm previous studies [7, 14, 29]. On average, our CP patients are smaller than general children resulting in a shorter final height. The higher the motor impairment, the more likely the patients are short of stature. Therefore, common growth percentiles are not entirely suitable to evaluate health in CP patients.

The strengths of our study are the large amount of measurements and patients that are included and who are all of Caucasian ethnicity. To our knowledge, there are no

Table 2 Data of CP-specific growth percentiles for male non-walking patients GMFCS IV–V (group Bm)

	Centiles - male GMFCS IV and V									
Age	C3	C10	C25	C50	C75	C90	C97	*S*	*L*	Measurements per age group
2	74.3	77.0	79.7	82.6	85.4	87.8	90.2	0.051	1.794	15
2.5	78.1	81.0	83.8	86.8	89.8	92.4	94.9	0.051	1.714	
3	81.6	84.5	87.4	90.6	93.7	96.5	99.1	0.051	1.635	32
3.5	84.6	87.7	90.8	94.1	97.3	100.2	103.0	0.052	1.560	
4	87.5	90.7	93.8	97.3	100.7	103.7	106.6	0.052	1.491	63
4.5	90.2	93.4	96.7	100.3	103.8	107.0	110.0	0.053	1.424	
5	92.7	96.1	99.5	103.2	106.9	110.1	113.3	0.053	1.356	82
5.5	95.1	98.6	102.1	106.0	109.8	113.2	116.5	0.054	1.288	
6	97.4	101.0	104.7	108.7	112.6	116.2	119.6	0.054	1.221	65
6.5	99.7	103.4	107.2	111.3	115.4	119.1	122.7	0.055	1.159	
7	101.9	105.7	109.6	113.9	118.2	122.0	125.8	0.056	1.099	54
7.5	104.0	108.0	112.0	116.4	120.9	124.9	128.8	0.057	1.044	
8	106.1	110.2	114.4	119.0	123.6	127.7	131.8	0.057	0.994	30
8.5	108.2	112.4	116.7	121.4	126.2	130.5	134.8	0.058	0.951	
9	110.1	114.5	118.9	123.9	128.8	133.3	137.7	0.059	0.915	24
9.5	112.0	116.5	121.1	126.2	131.3	136.0	140.6	0.060	0.883	
10	113.9	118.5	123.2	128.5	133.8	138.6	143.4	0.061	0.854	40
10.5	115.7	120.5	125.3	130.8	136.3	141.2	146.2	0.062	0.824	
11	117.4	122.3	127.4	133.0	138.6	143.8	148.9	0.063	0.793	32
11.5	119.2	124.2	129.4	135.1	141.0	146.3	151.6	0.064	0.759	
12	120.8	126.0	131.3	137.3	143.3	148.8	154.3	0.065	0.721	32
12.5	122.5	127.8	133.2	139.3	145.6	151.2	156.9	0.066	0.680	
13	124.1	129.5	135.1	141.4	147.8	153.6	159.5	0.067	0.636	27
13.5	125.6	131.2	136.9	143.4	149.9	156.0	162.0	0.067	0.592	
14	127.2	132.8	138.7	145.3	152.1	158.3	164.5	0.068	0.547	16
14.5	128.7	134.5	140.4	147.2	154.2	160.6	167.0	0.069	0.502	
15	130.2	136.1	142.2	149.1	156.3	162.8	169.5	0.070	0.456	10
15.5	131.7	137.7	143.9	151.0	158.3	165.0	171.9	0.071	0.410	
16	133.1	139.2	145.5	152.8	160.3	167.2	174.3	0.072	0.363	6
16.5	134.6	140.7	147.2	154.6	162.3	169.4	176.6	0.072	0.317	
17	136.0	142.2	148.8	156.4	164.2	171.5	179.0	0.073	0.272	7
17.5	137.4	143.7	150.4	158.1	166.2	173.6	181.3	0.074	0.227	

comparable growth percentiles for CP patients living in Europe with a Caucasian ethnicity. Our study allows to compare growth charts of healthy children with newly created percentiles for children with CP [7, 14, 29]. We can confirm that CP is accompanied with small stature for age. Furthermore higher impairments of motor function cause shorter stature.

Due to the fact, that the 50th percentile is comparable to the 3rd reference percentile (KiGGS), up to 50% of CP patients are likely to be considered pathologically short and would need further diagnostic workup using non disorder-specific reference charts which is not done in routine.

Nevertheless, compared by the median percentiles, our percentiles show taller stature than suggested by the CP growth charts by Brooks and Day which included a heterogeneous population. This might be due to differences in longitudinal growth, which has already been shown to vary in different ethnicities [1, 5]. The normal growth curves for healthy children used in the reference percentiles by Day at al. are slightly shorter than those for Caucasian children. A 15-year-old healthy boy is

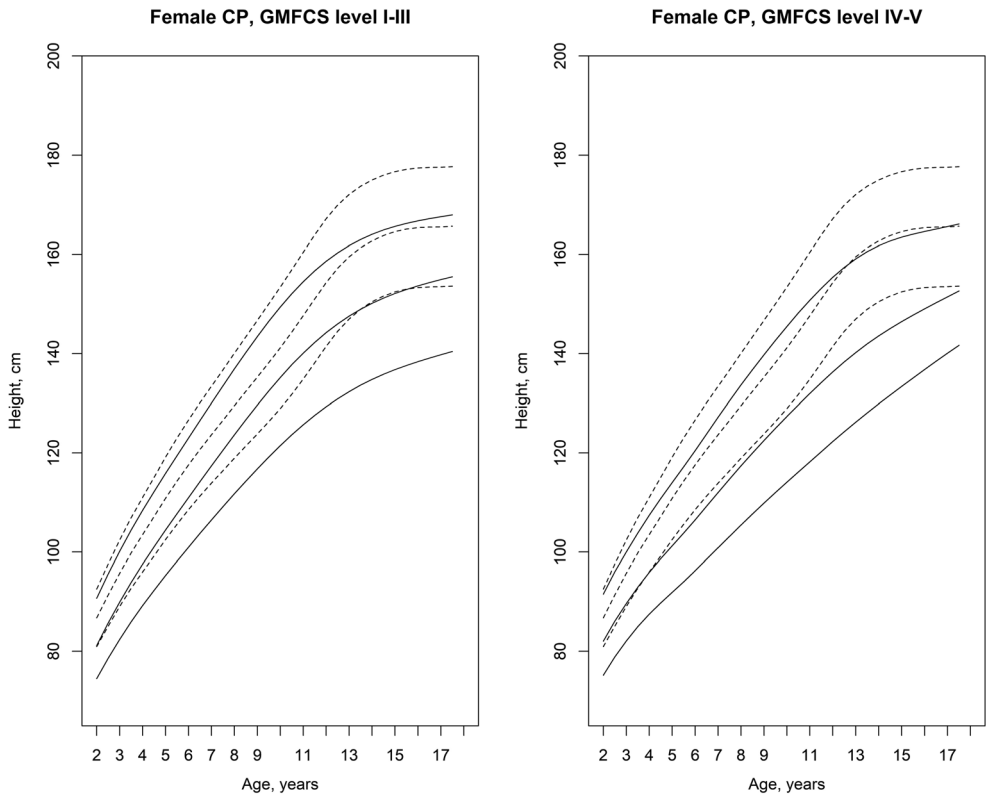

Fig. 2 Disorder-specific growth charts for female patients with CP. Black lines indicate percentiles of patients with CP (cP3, cP50, and cP97) for body height of female walking patients (group Af/left side) and female non-walking patients (group Bf/right side). Dotted lines (P3, P50, P97) indicate KiGGS reference percentiles

approximately 2 cm taller in Germany than in the USA. The distribution of different GMFCS levels is nearly similar between our group of patients and that of Day et al.; level IV and V = 39% of patients compared to 44% in the population investigated by Day et al. Therefore, we do not assume that our results reflect an underrepresentation of severely impaired children. The patients from Day et al. were assessed 1987–2002 while our children were measured 15–20 years later. Therefore, we can not totally exclude that improvements in standard of care influenced our results.

The height development of our groups Am and Af is most comparable to GMFCS level I's median percentile, created by Brooks et al. [2]. Due to the fact that our graphs consist of a heterogeneous collective of patients with GMFCS levels I to III, we expected groups Am's and Af's 50th percentile to roughly cover the median percentile of GMFCS level II by Brooks et al. [2].

Groups Bm and Bf are not only taller than expected but also they never cross the graphs of GMFCS IV or V from Brooks at al. Overall, the median percentiles of group B deviate more from GMFCS levels IV and V, than do group A's median percentile from GMFCS I to III.

We conclude three statements from this study:

1. Average CP patients are smaller than general children of the same age.
2. High motor impairment (stratified by GMFCS) is accompanied with a high likelihood of growth deficiency.
3. Caucasian CP patients are taller than CP-specific growth percentiles by Day and Brooks [2, 3, 7]. These findings especially apply for GMFCS levels IV and V.

For the normal pediatric practitioner, these percentiles will ease the evaluation of growth patterns of children with cerebral palsy. They will make it easier to decide if further investigations are necessary to exclude other reasons for small statue (e.g., endocrine disorders, malnutrition, chronic diseases) or if growth is adequate for the underlying disorder.

Our study does not emphasize the causes of reduced height. The main goal was to display the growth deficiency separated by clinical parameters in order to identify those who are short of stature even compared to disorder-specific reference curves.

Of all the factors causing limited body height, there are two most important for CP. These two are the oral motor dysfunction [10, 12, 19] and the limited capability of physiological movement [34]. The significant difference in height between walkers and non-walkers support the

Table 3 Data of CP-specific growth percentiles for female walking patients GMFCS I–III (group Af)

Age	Centiles - female GMFCS I–III									Measurements per age group
	C3	C10	C25	C50	C75	C90	C97	*S*	*L*	
2	74.5	76.4	78.5	81.1	84.1	87.2	90.7	0.051	−2.627	15
2.5	78.6	80.6	82.9	85.7	88.8	92.0	95.6	0.051	−2.379	
3	82.4	84.6	87.0	89.9	93.2	96.5	100.2	0.051	−2.142	25
3.5	85.9	88.2	90.8	93.9	97.3	100.7	104.4	0.051	−1.913	
4	89.2	91.7	94.3	97.6	101.1	104.6	108.4	0.051	−1.691	59
4.5	92.3	94.9	97.7	101.1	104.7	108.3	112.2	0.051	−1.476	
5	95.3	98.0	100.9	104.4	108.2	111.9	115.8	0.052	−1.265	74
5.5	98.1	101.0	104.1	107.7	111.6	115.4	119.4	0.052	−1.059	
6	101.0	104.0	107.2	111.0	115.0	118.9	123.0	0.052	−0.857	63
6.5	103.7	106.9	110.3	114.2	118.4	122.4	126.5	0.053	−0.658	
7	106.5	109.8	113.3	117.4	121.7	125.8	130.0	0.053	−0.463	37
7.5	109.1	112.6	116.3	120.5	125.0	129.2	133.5	0.054	−0.271	
8	111.7	115.4	119.2	123.6	128.2	132.5	136.9	0.054	−0.081	45
8.5	114.3	118.1	122.1	126.7	131.4	135.8	140.2	0.054	0.106	
9	116.8	120.8	124.9	129.6	134.5	138.9	143.4	0.055	0.291	48
9.5	119.2	123.3	127.6	132.5	137.4	142.0	146.5	0.055	0.474	
10	121.5	125.8	130.2	135.2	140.2	144.8	149.4	0.055	0.654	38
10.5	123.6	128.1	132.6	137.7	142.8	147.5	152.1	0.055	0.833	
11	125.7	130.3	134.9	140.1	145.3	149.9	154.5	0.055	1.010	30
11.5	127.6	132.3	137.0	142.3	147.5	152.1	156.7	0.054	1.185	
12	129.3	134.1	138.9	144.2	149.4	154.1	158.6	0.054	1.359	29
12.5	130.9	135.8	140.7	146.0	151.2	155.8	160.3	0.053	1.531	
13	132.3	137.3	142.2	147.6	152.8	157.3	161.8	0.053	1.701	32
13.5	133.6	138.7	143.6	149.0	154.1	158.6	163.0	0.052	1.871	
14	134.8	139.9	144.8	150.2	155.3	159.8	164.1	0.052	2.038	23
14.5	135.8	141.0	145.9	151.2	156.3	160.7	164.9	0.051	2.205	
15	136.8	141.9	146.9	152.1	157.2	161.5	165.6	0.050	2.370	18
15.5	137.6	142.8	147.7	152.9	157.9	162.2	166.2	0.049	2.534	
16	138.4	143.5	148.5	153.7	158.6	162.8	166.7	0.049	2.697	14
16.5	139.1	144.3	149.2	154.3	159.2	163.3	167.2	0.048	2.858	
17	139.8	144.9	149.8	154.9	159.7	163.8	167.6	0.047	3.019	14
17.5	140.4	145.6	150.5	155.5	160.2	164.2	168.0	0.046	3.179	

theory of the functional muscle-unit describing muscles forces as a strong osteoanabolic and growth stimulation factor.

Both are linked to an increase in severity depending on the GMFCS level. Therefore, both theories could explain the reduced height in CP compared to healthy children but they do not explain the differences from the percentiles published by Day et al.

The third percentile is the lower limit of regular growth. Patients with CP crossing this line in our disorder-specific growth charts should undergo further investigation for additional causes for their small stature. Depending on the results of the assessments, medical treatment for the limited growth needs to be considered. Our growth charts should help clinicians to identify those patients with CP who have an elevated risk of an additional disease affecting their growth.

Limitations of the study

Unlike Day [7] or Brooks [2, 3], we did not create percentiles for each GMFCS level. Due to our study mainly relying on the

Table 4 Data of CP-specific growth percentiles for female non-walking patients GMFCS IV–V (group Bf)

Age	Centiles - female GMFCS IV and V									Measurements per age group
	C3	C10	C25	C50	C75	C90	C97	*S*	*L*	
2	75.1	77.1	79.3	82.0	85.0	88.1	91.5	0.052	−2.292	7
2.5	78.9	80.9	83.3	86.1	89.3	92.5	96.0	0.052	−2.245	
3	82.1	84.3	86.7	89.6	93.0	96.3	100.0	0.052	−2.184	21
3.5	84.9	87.2	89.8	92.9	96.4	99.9	103.8	0.053	−2.114	
4	87.5	89.9	92.6	95.9	99.6	103.3	107.4	0.054	−2.040	38
4.5	89.8	92.3	95.2	98.7	102.5	106.5	110.8	0.055	−1.965	
5	91.9	94.6	97.6	101.2	105.3	109.4	114.0	0.057	−1.891	39
5.5	94.0	96.8	100.0	103.8	108.1	112.4	117.2	0.058	−1.824	
6	96.2	99.2	102.5	106.5	111.0	115.5	120.5	0.059	−1.766	33
6.5	98.5	101.6	105.1	109.2	113.9	118.6	123.8	0.060	−1.716	
7	100.9	104.1	107.6	112.0	116.9	121.8	127.2	0.061	−1.675	26
7.5	103.1	106.5	110.2	114.7	119.8	124.9	130.5	0.062	−1.643	
8	105.4	108.9	112.7	117.4	122.6	127.9	133.7	0.062	−1.619	42
8.5	107.7	111.2	115.2	120.0	125.4	130.8	136.8	0.063	−1.603	
9	109.9	113.5	117.6	122.5	128.0	133.6	139.8	0.063	−1.593	30
9.5	112.0	115.7	119.9	125.0	130.6	136.3	142.7	0.064	−1.587	
10	114.1	117.9	122.1	127.3	133.1	139.0	145.5	0.064	−1.583	15
10.5	116.1	120.0	124.4	129.7	135.6	141.6	148.2	0.064	−1.581	
11	118.2	122.2	126.6	132.0	138.0	144.1	150.8	0.064	−1.581	12
11.5	120.2	124.3	128.7	134.2	140.3	146.4	153.2	0.064	−1.582	
12	122.3	126.3	130.8	136.3	142.4	148.6	155.4	0.063	−1.583	15
12.5	124.3	128.3	132.8	138.3	144.4	150.6	157.4	0.062	−1.584	
13	126.2	130.3	134.7	140.2	146.3	152.4	159.1	0.061	−1.585	9
13.5	128.1	132.1	136.5	142.0	148.0	154.0	160.6	0.059	−1.586	
14	129.9	133.9	138.2	143.6	149.5	155.3	161.8	0.058	−1.586	24
14.5	131.6	135.6	139.9	145.1	150.8	156.5	162.7	0.056	−1.586	
15	133.4	137.2	141.4	146.5	152.0	157.5	163.5	0.054	−1.585	19
15.5	135.1	138.8	142.9	147.8	153.1	158.4	164.1	0.051	−1.585	
16	136.8	140.4	144.3	149.0	154.2	159.2	164.6	0.049	−1.584	17
16.5	138.4	141.9	145.7	150.3	155.2	160.0	165.1	0.047	−1.583	
17	140.1	143.5	147.1	151.5	156.2	160.7	165.6	0.044	−1.583	9
17.5	141.7	144.9	148.5	152.6	157.1	161.5	166.1	0.042	−1.582	

connection of the GMFCS levels, we only conclude tendencies. In our cohort, the number of data available in the older age groups to create the percentiles is small and therefore final height should be interpreted with caution. The calculation of the upper and lower limits (3rd and 97th percentile) are also affected by the sample size but according to Royston et al. the standard error is only 5–9% of the SD [25]. In addition, we were not able to present data about onset of puberty in our children; however, the lack of a pubertal growth spurt in children with CP has been reported before and is consistent with the findings by Brooks et al.

Conclusion

Our created disorder-specific growth charts show significantly different growth patterns compared to charts of healthy children (KiGGS). We showed an influence of GMFCS level on the difference from normal growth percentiles. We conclude that longitudinal growth of CP patients depends on their motor development.

The divergence from normal growth percentiles varies during childhood with a tendency to lose height the older the patients get. Similar conclusions were made by Oftedal [16].

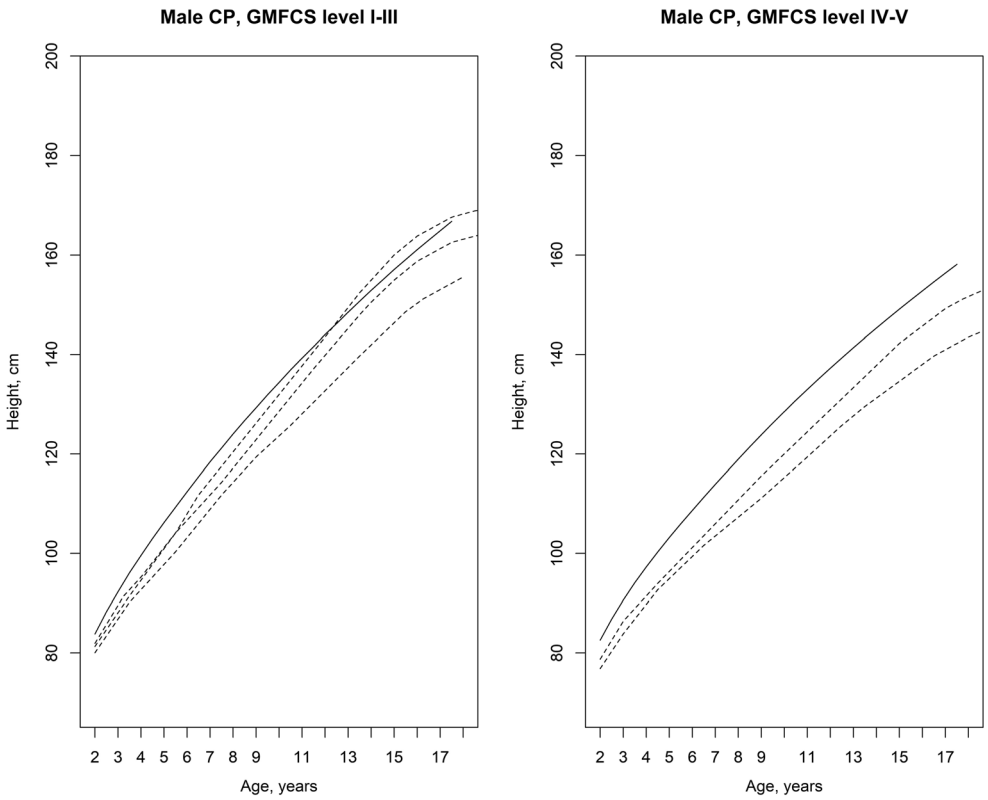

Fig. 3 The 50th percentile of disorder-specific growth curve for male patients with CP compared to the curves presented by Day et al. Left side walking children (group A) (solid black line) compared to data for GMFCS levels I–III by Day (dotted lines). On the right side, comparison of group B with references for GMFCS IV and V by Day (dotted lines)

This demonstrates the need for disorder-specific "height-for-age" charts. Compared with regular growth charts, the patients present with an increasing lack of growth, which might be misinterpreted as a sign of an additional illness. The comparison with American CP percentiles shows the need for national percentiles.

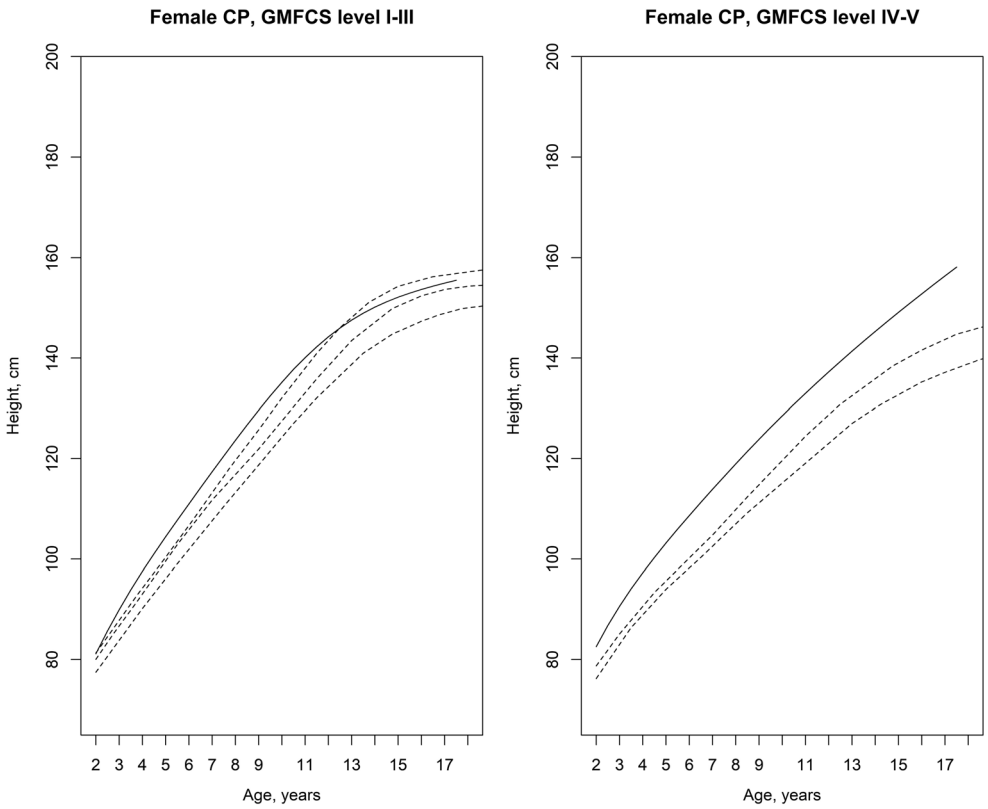

Fig. 4 The 50th percentile of disorder-specific growth curve for female patients with CP compared to the curves presented by Day et al. Left side walking children (group A) (solid black line) compared to data for GMFCS levels I–III by Day et al. (dotted lines). On the right side, comparison of group B with references for GMFCS IV–V by Day (dotted lines)

Authors' Contributions PE, OS and ES designed the research project. PE KM, CS, ID and OS collected the data and OS, SH and ID performed the statistical analysis. ID, CS, KM ES and OS cared for the patients. EP, SH and OS drafted the manuscript. All authors approved the final version of the manuscript.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This study was approved by the ethics committee of the University of Cologne (15-241).

Abbreviations *CP,* Cerebral palsy; *IGF-1,* Insulin-like growth factor; *LEP,* Life Expectancy Project; *GMFCS,* Gross motor function classification system

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