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Relation of health-related quality of life to near final height and body composition in adolescents with chronic endocrinopathies during transition period

Janna Mittnacht | Daniela Choukair | Thomas Breil | Daniela Klose | Ioana Inta | Markus Bettendorf

Division of Paediatric Endocrinology and Diabetes, Department of Paediatrics, University Hospital Heidelberg, Heidelberg, Germany

Correspondence
Janna Mittnacht, MD, Division of Paediatric Endocrinology and Diabetes, Department of Paediatrics, University Hospital Heidelberg, Im Neuenheimer Feld 430, Heidelberg D-69120, Germany.
Email: janna.mittnacht@uni-heidelberg.de

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Abstract

Introduction: We evaluated sequelae of disease and therapy in adolescents with chronic endocrinopathies using a medical and psychological workup to record health-related quality of life (HRQoL), near final height (NFH) and body compositions during the transition period from paediatric to adult care.

Methods: Near final height, weight, body mass index (BMI), grip strength (GS), hip and waist circumference (HC; WC), skin folds (SF) and HRQoL T-scores by KIDSCREEN and DISABKIDS were assessed in 134 patients (70 females and 64 males) from May 2010 to March 2016 diagnosed with congenital adrenal hyperplasia (CAH; n = 22), multiple pituitary hormone deficiency (MPHD; n = 17), growth hormone deficiency (GHD; n = 37), Turner syndrome (TS; n = 27), SGA-short stature (SGA; n = 20) and Klinefelter syndrome (KS; n = 11).

Results: Median HRQoL T-scores for KIDSCREEN (50.6-56.5) and DISABKIDS (52.7-58.9) ranged within references with considerable variations but without significant deficit in any diagnosis. Median-corrected height SDS (CoH-SDS: NFH-SDS–TH [target height]-SDS) was >−1, except in KS (SDS + 1.3) and in TS (SDS − 1.9; $P < .0001$) without correlations with HRQoL. Median BMI was below 25 kg/m^2 in all patients except MPHD (26.5 kg/m^2; SDS 1.5; $P = .006$). BMI correlated negatively in CAH females with self-perception ($r_s = -.64$, $P = .0338$), physical well-being ($r_s = -.8$; $P = .0086$), social exclusion $r_s = -.65$; $P = .031$) and emotions ($r_s = -.7$; $P = .0169$).

Conclusion: Health-related quality of life and body compositions were similar to those of healthy adolescents. Lower scores in HRQoL dimensions as self-perception, physical well-being, social exclusion and emotions were detected and correlated negatively with BMI. Treatment strategies and psychological support should consider HRQoL and adapted in specific treatment guidelines.

KEYWORDS

anthropometry, chronic endocrinopathies, health-related quality of life, transition

1 | INTRODUCTION

Chronic endocrinopathies may be detected early postnatally in newborn screening assuring treatment start before irreversible symptoms occur.[1,2] After reaching the goals of paediatric hormone treatment according to national and international treatment guidelines such as normal height, body composition, psychosocial development and timely physical development, other objectives become relevant to the patients' future life. The adolescent patient has to deal with disease-specific morbidity and sequelae such as altered body composition, reduced fertility and potential limitations in their quality of life (QoL).[3] Adolescence is also characterized by distinct psychosocial changes including the transfer from familial protection to autonomy and self-responsibility. Additionally, the transition from paediatric to adult medical care is planned in this period. Therefore, the transition period of adolescent patients from paediatric to adult care is an appropriate time to investigate individual sequelae of chronic disease and therapy. To comprehend disease-specific limitations, we established a standardized medical and psychological workup and assessed health-related quality of life (HRQoL) and auxological measures as near final height (NFH), body mass index (BMI), hip and waist circumference (HC; WC), grip strength (GS) and skin folds (SF). The aim of this explorative study was to evaluate the coherence between stature, body composition and HRQoL in childhood-onset endocrinopathies of adolescents at the time of transition.

2 | PATIENTS AND METHODS

2.1 | Patients

The study was prospectively planned as a single-centre, explorative, descriptive, open, noncontrolled study. The Ethics Committee of Heidelberg University Clinic approved the study (S-019/2011). Written informed consent was obtained from mature patients and parents of the remaining participants. Consecutive 134 patients treated in the Paediatric Endocrinology Outpatient Clinic at the University Hospital Heidelberg Department of Paediatrics were included after achieving the primary paediatric treatment goals (girls: bone age ≥14 years and menarche and boys: bone age ≥16 years and adult voice) between May 2010 and March 2016. Their diagnoses were as follows: congenital adrenal hyperplasia (CAH; n = 22), multiple pituitary hormone deficiency (MPHD; n = 17), isolated growth hormone deficiency (GHD; n = 37), Turner syndrome (TS; n = 27), isolated short stature after born small for gestational age (SGA; n = 20) and hypergonadotropic hypogonadism (HH) caused by the Klinefelter syndrome (KS; n = 11) (Table 1). Patient's care was conducted according to German national or international standards.[4-8]

All CAH patients were diagnosed before the introduction of the newborn screening in 1999 in Germany. Nine patients were diagnosed in the newborn period, four patients in the first year of life and nine patients in childhood before the onset of puberty. Fifteen patients were classified as salt wasting (SW), two as simple virilizing (SV) and five as nonclassical CAH. Female newborns with virilization were classified according to Prader scales, and five girls with Prader stages II to IV underwent feminizing genitoplasty. At transition, 10 patients were treated with dexamethasone (0.25-0.75 mg/d once daily) and fludrocortisone (0.05 mg twice daily), four patients received a combination of hydrocortisone (15 mg/m^2/d in 3 SD) and fludrocortisone (0.05 mg twice daily), and one patient received hydrocortisone 20 mg, prednisolone in the evening 3 mg and fludrocortisone 0.05 mg twice daily. Seven patients received just hydrocortisone n = 2; 15 mg/m^2/d in three doses or dexamethasone n = 5; 0.25-0.75 mg in one dose/d.

Two patients with GHD or MPHD were not treated with growth hormone (GH). Fifty two patients were treated with GH (0.025 mg/kg/d in one dose subcutaneously) after diagnosis was confirmed in childhood by standard arginine and insulin tolerance tests. At the time of transition, five patients with MPHD and two with GHD were still treated with GH. The aetiologies of MPHD are given in Table 2. Therapies comprised L-thyroxine (25-200 μg once daily, n = 23) in central hypothyroidism, hydrocortisone (5-20 mg three times daily; n = 13) in central adrenal insufficiency and estradiol valerate (2 mg in one dose every day) + chlormadinonacetate CMA (n = 5; from day 1 to day 12 every month) or testosterone undecanoate (250 mg/mo or 1000 mg/3 mo im; n = 6) or human chorionic gonadotropin (500-1500 IU s.c. twice a week) in HH.

Three patients with TS were diagnosed before birth. Eleven patients with TS were identified before the age of 8 years, and 13 patients were diagnosed between 9.25 and 15.67 years of age (Table 1). 25/27 patients (92.6%) were treated with GH (0.045-0.05 mg/kg/d

TABLE 1 Chronological age (CA; years) of patients (n = 134) at time of diagnosis and at time of transition (median, minimum and maximum) grouped by individual diagnoses

	Age diagnosis (years)	Age transition (years)
Total cohort (n = 134)	5.9 0.0-16.5	17.6 14.0-30.6
CAH (n = 22)	0.3 0.0-10.5	18.2 14.2-30.6
MPHD (n = 17)	6.6 0.2-16.5	20.9 15.3-29.6
GHD (n = 37)	6.1 2.4-16.1	17.1 14.1-24.1
TS (n = 27)	7.6 0.0-15.7	17.7 14.3-24.4
SGA (n = 20)	7.4 2.2-12.0	15.8 14.0-18.3
KS (n = 11)	0.0 0.0-12.3	18.3 15.2-20.8

Abbreviations: CAH, congenital adrenal hyperplasia; GHD, isolated growth hormone deficiency; KS, Klinefelter syndrome; MPHD, multiple pituitary hormone deficiency; SGA, small for gestation age; TS, Turner syndrome.

TABLE 2 Aetiology of MPHD acquired versus congenital

	Female	Male
Acquired (n = 11)		
Craniopharyngioma	3	2
Pilocytic astrocytoma	1	0
Intracerebral germinoma	1	0
Orbital embryonic rhabdomyosarcoma	0	1
Pituitary adenoma	0	2
Traumatic brain injury	0	1
Congenital (n = 6)		
Septo-optic dysplasia	1	0
Congenital MPHD	1	4
Total	7	10

subcutaneously), while two patients remained untreated as their epiphyses were already fused at diagnoses. Estradiol valerate (2 mg in one dose) and cyclic CMA (2 mg; day 1-day 12 every month) were given in 20 patients. Six girls with TS (X mosaicism 3:45 X0/46 XX and 3:45 X0/47 XXX) showed spontaneous regular menses without treatment. Hashimoto's thyroiditis and hypothyroidism were diagnosed in six patients and treated with L-thyroxine (25-125 μg once daily).

Seven patients with KS were diagnosed prenatally, two were diagnosed before the age of 10 years and the remaining two were diagnosed before the age of 13 years. Seven of them were treated with testosterone undecanoate 1000 mg/every 3 months im, one with transdermal testosterone 2.5 g/daily and two with testosterone undecanoate 250 mg/mo im. One patient remained untreated because of adequate endogenous testosterone production.

2.2 | Patients' characteristics

We analysed the following patients' characteristics at the time of transition: chronological age (CA, years), near final height (NFH, cm), weight (kg), body mass index (BMI, kg/m^2), waist circumference (WC, cm) and hip circumference (HC, cm), skin folds (SF, (biceps, triceps, subscapular and suprailiacal, mm) and grip strength (GS, newton).[9] NFH was measured to the nearest 0.1 cm in a standing position using a Holtain audiometer (Holtain; Crymych). Weight was measured to the nearest 0.1 kg using a standard medical electronic scale (Seca, Germany). Target height (TH) was calculated according to the method of Tanner (maternal height [cm] + paternal height [cm] + 13 (males)/−13 (females)/2).[10] Corrected height (CoH) SDS was calculated by subtracting TH-SDS from NFH-SDS. GS was measured three times for the nondominate hand with a handheld Jamar dynamometer. The mean of the three measurements was calculated. The scale of the dynamometer indicated the result in kg which was multiplied by 9.81 to yield Newton.[11] SF was measured on the left side using a Holtain skinfold calliper. WC and HC were measured to the nearest 0.1 cm in accordance with the World Health Organization (WHO) recommendations. We transformed anthropometric data to standard deviation score (SDS) using appropriate German references when available or international reference data.[9,12-14]

2.3 | Health-related quality of life

We evaluated the HRQoL with KIDSCREEN-52 and DISABKIDS DCGM-37 questionnaires.[15,16] The generic KIDSCREEN-52 questionnaire is a multidimensional, standardized instrument to assess HRQoL. The questionnaire includes 52 items regarding physical well-being, psychological well-being, moods and emotions, self-perception, autonomy, parent relations and home life, financial resources, social support and peers, school environment and social acceptance. The intensity and frequency of a certain feeling or behaviour within a period of one week is evaluated on a five-point Likert scale. The outcome measure was the T-score in each dimension (mean = 50; SD = 10) with higher scores indicating better quality of life. T-scores below 40 (1 SD below the mean) were considered as revealing low HRQoL. This generic instrument allows comparison of HRQoL in healthy references and adolescents with chronic endocrinopathies. In addition, a comparison of HRQoL among the different endocrinopathies was made.

The DISABKIDS DCGM-37 is a chronic generic module that estimates the HRQoL in children and adolescents with different health conditions. The chronic generic module of the DISABKIDS DCGM-37 consists of 37 Likert-scale items regarding independence, emotions, social inclusion, social exclusion, limitation and treatment. The intensity and frequency of a certain feeling or behaviour is evaluated within the last 4 weeks. Scale score can range from 6 to 30 except the subscale emotion ranges from 7 to 35. The subscales can be added to a total score. The outcome measure was the T-score in each dimension (mean = 50; SD = 10) with higher scores indicating better HRQoL. T-scores below 40 (1 SD below the mean) were considered as revealing low HRQoL. The HRQoL DISABKIDS evaluates directly the HRQoL circumstance of children with chronic health conditions.

2.4 | Statistics

Statistical analyses were performed using SAS® STATVIEW® Software Version 5.0. Results are presented as median and minimum and maximum for all variables or frequencies and graphed in box plots indicating 10th, 25th, 50th, 75th and 90th percentiles. Group comparisons were based on nonparametric Kruskal–Wallis test. Correlations were calculated with nonparametric Spearman's coefficient. The results were considered significant at $P < .05$.

3 | RESULTS

We included 134 patients (70 females and 64 males) patients in this study. The CA of all patients at transition ranged from 14.0 to 30.6 years (median: 17.7 years; Table 1).

3.1 | Anthropometry

Near final height of all patients was 162.4 cm (SDS −1.3; male 173.5 cm, SDS −0.81 and female 156.3 cm, SDS −1.9) (Table 3). NFHs were significantly different in the different patient's groups ($P = .0001$); median CoH (NFH-SDS - TH-SDS) SDS was −0.5 (male −0.3 and female −0.8, Table 3; Figure 1A) being highest in KS and lowest in TS while comparable in females and males in the other patient's groups.

Median BMI was 21.8 kg/m^2 (n = 134, SDS 0.26; male 21.7 kg/m^2; SDS 0.16; female 21.9 kg/m^2; SDS 0.32) and was significantly different between all groups of patients ($P = .0003$; Table 3, Figure 1B), similar in males and females but highest in MPHD (26.5 kg/m^2; SDS 1.5; $P = .006$). SF biceps ($P = .0024$), SF triceps ($P = .0061$), SF subscapular ($P = .0017$) and SF suprailiacal ($P = .0041$) were significantly different in all patient's groups and again highest in MPHP (Table 4). Median WC and HC were also within SDS −2 – SDS + 2 (Table 3). These circumferences were significantly different in all the groups of patients (HC $P = .0009$ and WC $P = .0005$) and highest in MPHP (n.s., Table 4). Median GS ranged between −2 and + 2 SDS for all patient's groups and were not significantly different (Table 3; n.s.). For all patients, there was a positive correlation between BMI and SF and HC and WC. For NFH and GS, we found a weak positive correlation ($P = .0242$; $r_s = .2$).

CAH: NFH, CoH and BMI of male adolescent patients with CAH were >−2 SDS and <2 SDS (n = 10). All anthropometric measures of girls with CAH (n = 12) were above −2 SDS and below + 2 SDS.

MPHD: NFH-SDS and CoH-SDS of all female and male adolescents with MPHD were > −2 SDS and < +2 SDS. All measures of

TABLE 3 Target height (cm, SDS; TH), near final height (cm, SDS; NFH), corrected height SDS (TH-SDS – NFH-SDS), body mass index (SDS; BMI), grip strength (SDS) as median, minimum and maximum grouped by individual diagnoses

	TH (cm)	TH (SDS)	NFH (cm)	NFH* (SDS)	CoH (SDS)	Grip strength (SDS)	BMI* (SDS)
Total cohort (n = 134)	168.5 150.0-187.5	−0.7 −3.3-1.5	162.4 146.0-197.3	−1.3 −4.4-2.7	−0.5 −4.9-2.3	−0.9 −6.1-7.6	0.2 −4.2-5.0
CAH (n = 22)	168.2 154.5-187.5	−0.6 −2.4-1.2	166.3 153.4-185.0	−0.9 −2.8-0.8	−0.3 −2.3-1.3	−0.2 −5.4-7.6	0.4 −1.7-5.0
CAH female (n = 12)	162.0 154.5-169.0	−1.0 −2.4-0.5	161.4 153.4-179.2	−1.1 −2.7.2.5	−0.1 −1.7-3.5	0.1 −2.0-7.6	0.1 −1.3-5.0
CAH male (n = 10)	178.5 169.5-187.5	−0.2 −1.6-1.2	174.3 161.0-185.0	−0.8 −2.8-0.8	−0.4 −2.3-0.8	−1.1 −5.4-1.9	0.7 −2.5-3.2
MPHD (n = 17)	171.0 160.0-187.0	−0.4 −2.6-1.1	168.7 153.3-185.2	−0.6 −3.9-2.4	−0.5 −2.9-1.9	−1.1 −6.1-6.1	1.5 −0.7-3.1
MPHD female (n = 7)	166.0 160.0-171.0	−0.2 −1.4-0.8	163.8 153.3-179.2	−0.6 −2.7-2.4	−0.2 −2.5-1.9	−0.3 −3.2-6.1	2.3 0.2-3.1
MPHD male (n = 10)	175.0 163.0-187.0	−0.8 −2.6-1.1	176.9 154.6-185.2	−0.4 −3.9-0.9	−0.6 −2.9-1.6	−1.1 −6.1- −0.2	0.5 −0.7-3.0
GHD (n = 37)	170.0 153.0-187.0	−0.8 −2.7-1.1	166.0 152.0-184.2	−1.3 −4.4-1.0	−0.2 −3.1-0.8	−1.0 −4.1-1.7	−0.1 −4.2-2.2
GHD female (n = 14)	161.2 153.0-169.0	−1.1 −2.7-0.4	158.5 152.8-169.3	−1.2 −2.8-0.4	−0.1 −1.5-0.8	−1.3 −1.9-1.7	−0.2 −2.2-1.4
GHD male (n = 23)	175.5 163.4-187.0	−0.7 −2.6-1.1	169.5 152.0-184.2	−1.3 −4.4-1.0	−0.3 −3.1-0.8	−0.9 −4.1-1.0	0.1 −4.2-2.2
TS (n = 27)	163.0 156.0-174.5	−0.8 −2.2-1.5	152.6 147.7-162.3	−2.7 −3.8-−0.9	−1.9 −4.9-0.0	−1.2 −5.1-2.9	0.6 −1.8-2.9
SGA (n = 20)	167.7 150.0-185.0	−1.0 −3.3-0.8	160.2 146.0-174.3	−1.9 −3.6-−0.8	−0.6 −3.3-1.3	−0.5 −3.3-2.9	−0.3 −2.1-2.5
SGA female (n = 10)	158.2 150.0-168.5	−1.7 −3.3-0.3	153.0 146.0-161.9	−1.7 −3.6-−0.8	−0.4 −1.2-1.3	−0.9 −3.3-2.3	−0.6 −1.4-2.5
SGA male (n = 10)	175.0 167.5-185.0	−0.8 −1.9-0.8	163.1 159.5-174.3	−1.9 −2.9-−0.8	−0.7 −3.3-0.1	−0.3 −2.4-2.9	0.3 −2.1-1.9
KS (n = 11)	177.5 171.5-184.5	−0.4 −1.3-0.7	183.8 175.4-197.3	0.6 −0.7-2.7	1.3 −0.3-2.3	−0.6 −3.9-0.4	0.3 −2.8-1.4

Abbreviations: CAH, congenital adrenal hyperplasia; GHD, growth hormone deficiency; KS, Klinefelter syndrome; MPHD, multiple pituitary hormone deficiency; SGA, small for gestation age; TS, Turner syndrome.

*$P < .05$.

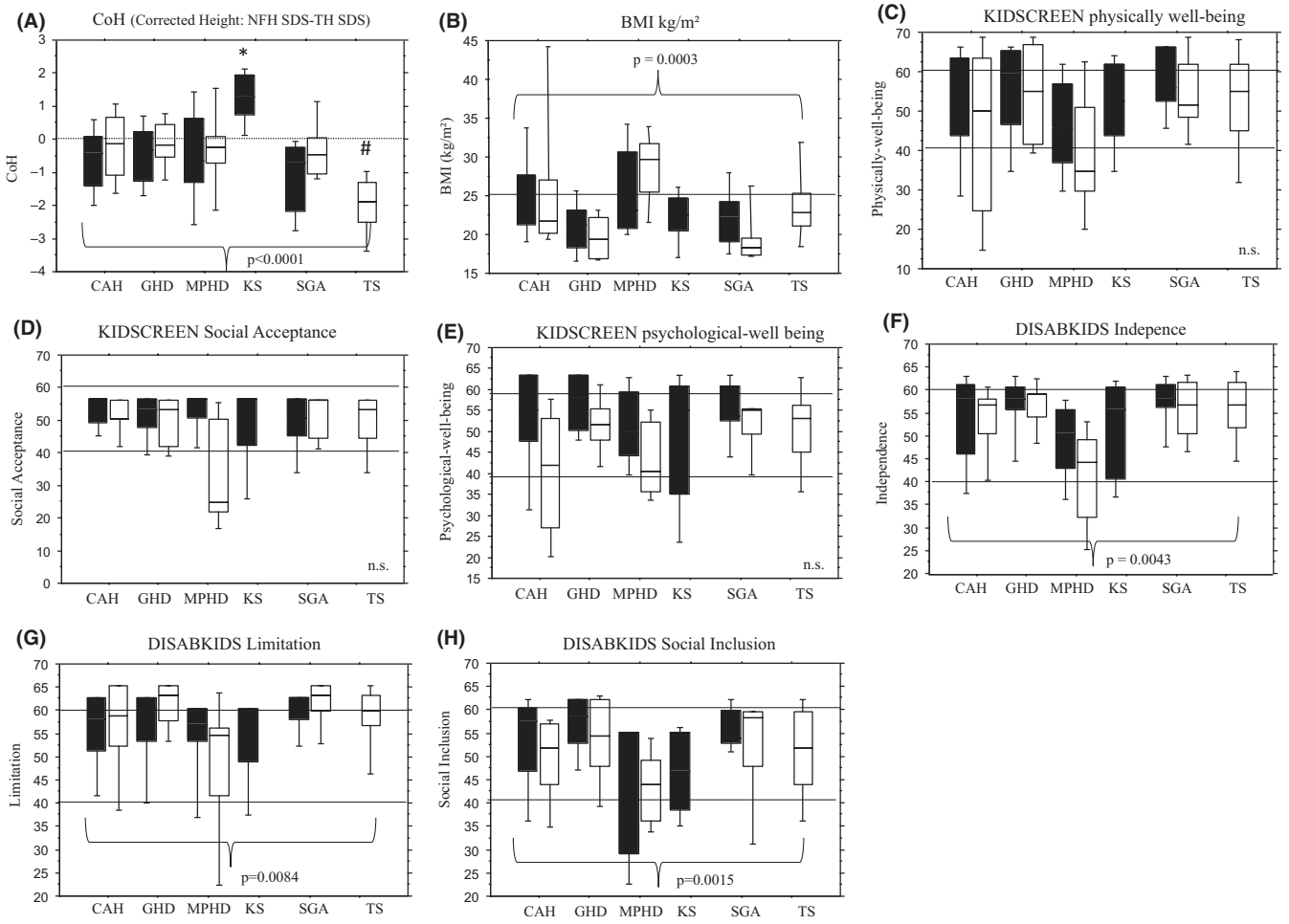

FIGURE 1 (A) CoH-SDS, (B) BMI kg/m², (C) health-related quality of life (HRQoL) scores for KIDSCREEN physical well-being, (D) KIDSCREEN social acceptance, (E) KIDSCREEN psychological well-being, (F) DISABKIDS independence, (G) DISABKIDS limitation, (H) DISABKIDS social inclusion in 6 patients groups by diagnoses. CAH: n = 22 (congenital adrenal hyperplasia), GHD: n = 37 (growth hormone deficiency), MPHD: n = 17 (multiple pituitary hormone deficiency), KS: n = 11 (Klinefelter syndrome), SGA: n = 20 (small for gestational age) and TS n = 27 (Turner syndrome). Box plots indicate 10th, 25th, 50th, 75th and 90th percentiles. T-score (mean 50 SD ± 10). Group comparisons were done with nonparametric Kruskal–Wallis test; results were considered significant at $P < .05$: *taller than other patient groups; # shorter than other patient groups □, Female; ■, Male

body composition in adolescents with GHD (n = 37) range above SDS −2 and below SDS + 2.

TS: Girls with TS (n = 27) were shorter than all other patients. Median CoH-SDS of all patients was −0.5 but lower in TS (TS −1.9; $P = .0001$) (Table 3, Figure 1A).

SGA: NFH-SDS was −1.9 in SGA, but CoH-SDS was above SDS −1 (SDS female CoH −0.4 and male −0.7). Median of BMI-SDS and SF-SDS was within −2 and + 2 SDS (Table 3 and Figure 1A,B).

KS: Boys with KS (n = 11) were taller than all other patients (median CoH-SDS + 1.3; $P = .0001$; NFH-SDS + 0.6; $P = .0001$; Table 3, Figure 1A).

3.2 | Quality of life

One hundred and twenty four of 134 patients returned the HRQoL KIDSCREEN, and 119 of 134 patients returned the HRQoL DISABKIDS questionnaire, representing an overall response rate of 90.25% (92.5 and 88.8%). Seven KIDSCREEN questionnaires and six DISABKIDS questionnaires were not returned from patients with GHD. Median T-score for each dimension in the KIDSCREEN ranged from 50.6 to 56.5 in the study cohort, indicating a HRQoL above 40 indicating medium HRQoL. The generic HRQoL questionnaire KIDSCREEN revealed no significant differences between the different patient groups (P = ns; Figure 1C-E).

The median T-scores in the HRQoL questionnaire DISABKIDS for all included patients (n = 119) ranged from 52.7 to 58.9 and thus above the lower normal limit of 40. Significant differences were detected between the patient groups in the dimensions independence ($P = .0043$), limitation ($P = .0084$), social inclusion ($P = .0015$) and total score ($P = .0213$; Figure 1F-H). Female patients with MPHD achieved lower median scores in the dimensions independence (44.2), limitation (54.5), social inclusion (43.9) and total score (47.3), but all median scores were still above 40. Male patients with MPHD

TABLE 4 Waist circumference (SDS; WC), hip circumference (SDS; HC) and skinfolds (SF) biceps, triceps, subscapular and suprailiacal grouped by individual diagnoses (median, minimum and maximum)

	WC* (SDS)	HC* (SDS)	SF* biceps (SDS)	SF* triceps (SDS)	SF* subscapular (SDS)	SF* suprailiacal (SDS)
Total cohort (n = 134)	0.7 −1.8-5.1	−1.43 −4.4-4.1	0.8 −3.6-31.5	0.7 −2.0-9.5	1.4 −4.2-19.6	1.1 −2.4-9.7
CAH (n = 22)	0.6 −0.7-5.1	−1.7 −3.5-3.5	0.3 −1.5-8.0	0.0 −2.0-9.5	1.2 −2.4-13.3	1.5 −1.7-4.3
CAH female (n = 12)	0.4 −0.7-5.1	−1.7 −3.5-1.6	0.4 −0.0-3.9	−0.5 −1.5-1.3	1.2 −1.1-5.2	0.4 −1.7-2.1
CAH male (n = 10)	0.6 −0.7-3.8	−0.7 −2.5-3.5	−0.3 −1.5-8.0	3.3 −2.0-9.5	1.0 −2.4-13.3	2.6 1.5-4.3
MPHD (n = 17)	2.3 −1.8-3.5	1.3 −1.9-4.1	2.2 −0.2-31.5	3.8 −0.5-10.9	5.7 0.1-19.5	3.0 0.1-7.9
MPHD female (n = 7)	3.2 0.8-3.5	0.2 −1.9-4.1	3.5 0.7-6.3	3.5 −0.5-4.5	5.0 0.1-9.4	2.4 0.1-3.1
MPHD male (n = 10)	2.0 −1.8-3.4	1.4 −0.1-3.4	1.7 −0.2-31.5	5.9 0.4-10.9	6.3 1.4-19.6	4.4 1.5-7.9
GHD (n = 37)	0.1 −1.2-2.4	−1.8 −4.0-0.5	0.2 −1.5-8.6	0.2 −2.4-9.3	1.0 −1.6-9.8	0.7 −1.8-8.2
GHD female (n = 14)	0.4 −0.7-2.4	−1.9 −3.2-0.5	0.3 −1.4-8.5	0.2 −2.4-5.0	0.7 −1.6-9.4	0.3 −1.8-3.0
GHD male (n = 23)	−0.1 −1.2-1.9	−1.7 −4.0-0.1	−0.1 −1.5-6.1	0.3 −2.4-9.3	1.2 −0.8-9.8	1.3 −0.8-8.2
TS (n = 27)	1.1 −0.9-3.2	−1.5 −4.4-2.1	2.8 −2.6-10.0	0.9 −2.8-6.7	1.2 −3.1-10.0	1.4 −2.3-3.8
SGA (n = 20)	0.1 −1.8-3.8	−1.8 −2.9−0.8	0.5 −3.6-8.0	0.1 −3.3-7.9	1.4 −4.2-6.3	−0.2 −2.4-4.4
SGA female (n = 10)	−0.0 −1.7-3.8	−1.9 −2.6-0.1	−0.2 −1.4-1.5	−0.1 −1.6-7.9	3.3 −4.2-6.3	−0.1 −1.5-3.1
SGA male (n = 10)	0.5 −1.8-1.7	−1.5 −4.4-2.1	1.7 −3.6-8.0	1.0 −3.3-2.9	1.3 −1.5-5.4	−0.8 −2.4-4.4
KS (n = 11)	0.8 −0.1-2.8	−0.3 −1.7-1.5	3.9 −0.5-13.4	0.8 −1.2-7.4	2.8 −0.2-10.5	1.0 0.3-9.7

Abbreviations: CAH, congenital adrenal hyperplasia; GHD, growth hormone deficiency; KS, Klinefelter syndrome; MPHD, multiple pituitary hormone deficiency; SGA, small for gestation age; TS, Turner syndrome.

*$P < .05$.

exhibited even lower median scores than the female group (38.6) in the dimension social inclusion indicating low quality of life in social inclusion.

3.3 | Correlations HRQoL and anthropometric measures

No correlations were detected between HRQoL dimensions and BMI for female patients with MPHD. But there was a negative correlation in female patients with CAH for BMI and self-perception ($r_s = -.64$, $P = .0338$), BMI and physical well-being ($r_s = -.8$; $P = .0086$), BMI and social exclusion ($r_s = -.65$; $P = .031$) and BMI and emotions ($r_s = -.7$; $P = .0169$). BMI of female patients with SGA correlated negatively with emotions ($r_s = -.71$; $P = .0464$). NFH of male patients with GHD correlated positively with social acceptance ($r_s = -.46$; $P = .037$). There were no more correlations between other anthropometric measures and HRQoL in all patient's groups.

4 | DISCUSSION

Here, we investigated HRQoL and body composition of adolescents with growth disorders and different chronic endocrinopathies in the period of transition. The overall HRQoL scores for all studied adolescent patients were within references range without perceptible disease inherent impacts. Furthermore, NFH, as well as body composition measured as BMI, SF, and GS, and WC, and HC were above −2 SDS and below + 2 SDS with distinct variability, indicating appropriate somatic growth and body composition after adequate

TABLE 5 Waist circumference (SDS; WC), hip circumference (SDS; HC) and skinfolds (SF) biceps, triceps, subscapular and suprailiacal grouped by individual diagnoses (median, minimum and maximum)

	Age* at diagnosis	WC (SDS)	HC (SDS)	SF biceps (SDS)	SF triceps (SDS)	SF subscapular (SDS)	SF suprailiacal (SDS)	BMI (SDS)
MPHD female acquired (n = 5)	12.7 1.1-14.7	3.3 1.8-3.5	0.2 −1.2-3.4	2.2 −0.2-31.5	3.5 −0.5-4.5	5.0 3.6-9.4	2.4 0.1-3.1	2.3 1.1-3.1
MPHD female congenital (n = 2)	2.3 2.2-2.4	1.9 0.8-3.0	1.1 −1.9-4.1	5.4 2.2-8.6	3.4 2.4-4.5	4.8 0.1-9.4	2.3 1.6-3.0	1.4 0.2-2.6
MPHD male acquired (n = 6)	12,7 6.8-16.5	2.2 −1.0-3.4	2.3 1.4-3.4	0.8 −0.2-31.5	6.2 0.4-10.9	6.0 1.4-19.6	4.3 1.5-7.9	1.1 −0.7-3.0
MPHD male congenital (n = 4)	4.0 0.2-6.6	1.8 −1.8-2.3	0.2 −1.1-0.5	6.9 1.7-12.1	4.8 1.3-8.2	7.9	3.7 2.7-4.6	0.5 −0.3-1.5

Abbreviation: MPHD, multiple pituitary hormone deficiency.

*$P < .05$.

long-term hormone treatment. For further analysis, patients were grouped according to individual diagnoses.

It is well established that one long-term consequences of adrenal replacement with corticoids in patients with CAH are obesity and a higher risk to develop metabolic syndrome.[17] Interestingly, in our cohort markers of body compositions were between −2 SDS and + 2 SDS for female and male patients with CAH, but SF-SDS triceps and suprailiacal in the male adolescents were above + 2 SDS. BMI for female and male patients previously published was higher than in our groups of patients with CAH.[18] Further, correlations of higher BMI and lower scores in the dimensions self-perception, physical well-being, social exclusion and emotions of CAH girls were detected. Thus, the prevention of overweight should be considered in long-term CAH therapy. Another consequence of long-term replacement with glucocorticoids may be final height (FH) below average.[17] Han et al[17] reported FH as a surrogate marker for childhood disease control. CoH of our patient groups was comparable to those in other investigations or even above.[18,19] Bouvattier et al[18] evaluated the outcome of 219 adult men with CAH who achieved a mean NFH of 167.8 ± 8.36 cm. Parental height in the Bouvattier study was only available for 61 patients, and the mean difference between TH and near NFH was 8.7 cm and was compared to our study higher (our difference TH and NFH: 1.9 cm). Hence, satisfactory disease control may be assumed in our adolescent CAH group and substantiate the general good HRQoL of the patients with CAH reported here. As Bennecke et al[19] concluded, one reason for the overall good HRQoL of CAH patients represents a tight endocrine control starting in early childhood. Nevertheless, our female patients had lower scores in the dimension psychological well-being than the other groups of patients, but median scores were still in normal range. Females with CAH often report about psychological problems after genital surgery,[20] but in our cohort only 5 out of 12 females underwent feminizing genitoplasty without detectable impact on HRQoL.

Growth hormone deficiency patients showed normal body composition and HRQoL, and a positive correlation between NFH and social acceptance was detected. Attanasio et al[21] found similar to our findings no significant impairment of HRQoL in the transition period of patients with GHD. Our results are in line with those reported by Maghnie et al.[22] These authors concluded that adult heights in patients with permanent idiopathic GHD and spontaneous puberty were similar to adult heights of patients with MPHD and induced puberty. In contrast, we found lower scores in the dimensions independence, limitation, social inclusion, psychological well-being, physical well-being, autonomy and social acceptance in the HRQoL questionnaires of females with MPHD. Furthermore, male patients with MPHD had even lower median scores than the MPHD females in the dimension social inclusion. Female MPHD patients had also a significantly higher BMI, and in accordance, their SF and WC were also higher than in the other patient groups. In males, MPHD patient's SF-SDS of triceps, subscapular and HC was higher although BMI was <2 SDS. MPHD ensues often craniopharyngioma or antineoplastic therapy of malignant brain tumours. Childhood-onset craniopharyngioma often affects hypothalamic or pituitary regions as well as the optic chiasm,[23] and postoperative obesity occurs in up to 52% of patients with craniopharyngioma.[24] In our MPHD cohort, six patients had congenital MPHD and the aetiology varied in 11 patients (Table 2). Five patients actually had a craniopharyngioma, and three suffered from a malignant brain tumour. In our study, there was no significant difference in the body composition of congenital or acquired MPHD only a tendency that of lower BMI and SF in congenital MPHD. In other studies, investigating HRQoL patients had lower scores when they suffered from obesity following craniopharyngioma and hypothalamic involvement[25] which could not be confirmed in our study (Table 5).

Turner syndrome may be characterized by short stature, high BMI and absence of spontaneous puberty.[26,27] These days most girls with TS are treated with GH to improve growth in childhood and final height.[27] In our study, 25 of 27 TS patients were treated with GH (92.3%) and NFH improved similarly as reported previously.[27] Bannink et al[27] could demonstrate that higher HRQoL scores of TS significantly correlated with individual content of NFH. As TS tend to higher BMI leading to obesity-related

problems in adult life,[4] GH treatment can improve BMI by reducing total body fat and abdominal fat.[26] However, we observed lower BMI in our study than reported elsewhere.[28] Another consistent feature of TS is absence of puberty, which can cause psychological problems in young females. In our cohort, six girls (23.1%) with X mosaicism (3:45 X0/46 XX and 3 45 X0/47 XXX) experienced spontaneous puberty. All other girls had induced puberty according to the guidelines and received estradiol valerate and cyclic CMA supplementation at time of transition.[4] The overall HRQoL in our TS population was good. Other investigations reported impaired self-esteem, social isolation, anxiety, immaturity and stigmatization and lower occupational status.[29] Many studies investigating adolescents with TS emphasize the deleterious effects of short stature and delayed sexual development on body image, sense of identity and social integration with peers.[30] The overall good HRQoL in our study may already reflect the adherence to current treatment guidelines.[4]

Children born SGA suffer from restricted foetal growth. 10%-20% of these children have no spontaneous catch-up growth. Various studies have shown that long-term continuous GH therapy can significantly increase FH within normal range.[31] Median CoH of our cohort was within reference range, and NFH height was in line with Dahlgren et al[8] within 1 SD of target height. HRQoL was also not impaired similar to the study from Bannink et al,[32] who reported better QoL in SGA children after GH therapy.

Klinefelter syndrome may be associated with tall stature, and most males with KS are infertile due to azoospermia and develop hypergonadotropic hypogonadism. Furthermore, nonfamilial obesity is another stigma of KS as is poor muscular bulk.[33] CoH of KS was higher than those of the other patient groups. In our study, BMI was similar in all groups of patients, but SF of the biceps was above + 2 SDS. All KS patients received testosterone treatment except one boy at time of transition. According to the literature, HRQoL of patients with KS is reduced, especially the measures of psychological well-being, self-esteem and general health compared with reference population.[34] We could not observe an overall reduction in HRQoL in our cohort. Almost all boys in our group of patients were diagnosed with KS before onset of puberty; only one boy was diagnosed at the age of 12 years at the beginning of puberty. Accordingly, all patients received expert care in paediatric endocrinology before developing clinical signs of testicular failure. As reported previously, early diagnosis and start of care of KS lead to more favourable outcome.[34]

4.1 | Strength and limitations of this study

Several limitations of this study should be pointed out. One major limitation of this study is the small sample size of individual patient's subgroups and the explorative, descriptive study design. All anthropometric measurements were performed by several paediatricians during routine care in a single centre contributing to a distinct variance in the reported results which may mitigate the significance and conclusions of our findings. As controls, we used the reference population for the DISABKIDS and KIDSCREEN as well as anthropometric measures.

Despite these limitations, we identified disease-specific morbidity as higher BMI of patients with MPHD and negative correlations of HRQoL dimensions and BMI in girls with CAH. Overall, primary paediatric therapy goals after standard hormone therapy as NFH comparable to TH and adequate body composition were achieved and the overall level of QoL in these patients with various diagnoses is adequate.

5 | CONCLUSIONS

The levels of HRQoL of most adolescents in the period of transition from paediatric to adult care with growth disorders and chronic endocrinopathies were within normal reference ranges indicating compensation of growth disorders and endocrinopathies by adequate hormone supplementation and treatment during childhood. Further, body compositions and NFH were within above −2 SDS and below + 2 SDS in TS, KS, SGA and GHD indicating regular somatic development. However, we found higher BMI and lower scores in the HRQoL dimensions in patients with MPHD without correlation between HRQoL dimensions and BMI. Furthermore, we detected correlations in female patients with CAH with higher BMI having lower scores in the HRQoL dimensions self-perception, physical well-being, social exclusion and emotions. Treatment strategies and psychological support of patients with MPHD and female CAH should consider growth and body composition as well as HRQoL to ensure adequate psychosomatic development. All patients with chronic endocrine diseases still need to be sensitized for their specific morbidity and individual need for specialty care in adulthood.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

ETHICAL APPROVAL

The Ethics Committee of Heidelberg University Clinic approved execution of the study (S-019/2011). Written informed consent was obtained from parents for each participant in this study. All procedures performed were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Janna Mittnacht https://orcid.org/0000-0001-6106-2959

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