Associations between lower urinary tract dysfunction and health-related quality of life in children with chronic kidney disease

Helena Öborn (helena.oborn@karolinska.se)[1], Lena Wettergren[2], Maria Herthelius[1]*, Ulla Forinder[3,4]*

1.Department of Clinical Science, Technology and Intervention, Division of Pediatrics, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden
2.Department of Neurobiology, Care Sciences and Society, Division of Nursing, Karolinska Institutet, Stockholm, Sweden
3.Department of Neurobiology, Care Sciences and Society, Division of Social Work, Karolinska Institutet, Stockholm, Sweden
4.Department of Health and Working Life, Division of Social Work and Psychology, University of Gävle, Gävle, Sweden

ABSTRACT

Aim: Little is known about the health-related quality of life (HRQoL) of children with lower urinary tract dysfunction (LUTD) and chronic kidney disease (CKD). We investigated LUTD and other possible predictors of impaired HRQoL in children with conservatively treated moderate-to-severe CKD or with a kidney transplant.

Methods: All 64 children with CKD or a kidney transplant treated at Karolinska University Hospital, Stockholm, Sweden, between June 2011 and December 2012 were approached and 59 children aged 8–18 were enrolled in the study. Lower urinary tract function was evaluated with voiding history, frequency and volume chart, uroflowmetry and postvoid ultrasound measurements. Self-reported HRQoL was assessed with validated generic instruments.

Results: The HRQoL of the study cohort was as good as the general paediatric population, apart from the physical and psychological well-being dimensions, and was no different to children with other chronic conditions. Urinary incontinence, but not LUTD in general, was associated with impaired HRQoL, as was having a kidney transplant and being female in some dimensions.

Conclusion: LUTD was common in children with CKD or a kidney transplant but did not affect their general HRQoL. Predictors of impaired HRQoL included incontinence, having had a kidney transplant and being female.

INTRODUCTION

Living with paediatric chronic kidney disease (CKD) is still associated with risks for complications requiring lifelong management (1). Optimal care to prevent or delay the progress of CKD places demands on medical staff and on the psychosocial management of the everyday lives of these children and their families (2,3).

Approximately one-third of paediatric CKD cases are caused by urological abnormalities and are often associated with lower urinary tract dysfunction (LUTD) (4). Early attention and better understanding of LUTD, together with improvements in surgical interventions, have improved graft survival after renal transplantation in this subgroup of patients (5). However, signs and symptoms consistent with LUTD, such as large maximum voided volumes, postvoid residual urine and incontinence, are also common in children with CKD without urological abnormalities (6). The underlying mechanisms in these patients are unknown, but possible reasons could be long-standing effects of oliguria or polyuria. Incontinence, which might be an explicit sign of LUTD, is known to be associated with an impaired HRQoL and lower self-esteem in healthy children (7). Both children with conservatively treated CKD and paediatric renal transplant recipients with signs of LUTD are routinely prescribed bladder training regimens in order

Abbreviations
CKD, Chronic kidney disease; DCGM-37, DISABKIDS Chronic Generic Module-37; ESRD, End-stage renal disease; GFR, Glomerular filtration rate; HRQoL, Health-related quality of life; LUT, Lower urinary tract; LUTD, Lower urinary tract dysfunction; QoL, Quality of life.

Key Notes
- Little is known about health-related quality of life (HRQoL) in children with lower urinary tract dysfunction (LUTD) and chronic kidney disease (CKD).
- Our Swedish study of 57 children aged 8–18 showed impaired physical and psychological well-being in children with CKD or a kidney transplant compared to the general paediatric population.
- Predictors of impaired HRQoL included incontinence, having had a kidney transplant and being female.

to prevent bladder distension, urinary tract infections, urinary incontinence and, in the long term, to delay the deterioration of their kidney function (4).

Health professionals currently agree that children and young people should be asked how their everyday life with a chronic illness is perceived, to get a better understanding of the need for supportive measures (8). Accordingly, health-related quality of life (HRQoL) has become an important health indicator for evaluating treatment-associated interventions and for displaying patient-oriented outcomes related to the constraints of the disease and its treatment (9).

A number of HRQoL studies in children and adolescents with CKD have focused on living with end-stage renal disease (ESRD), which requires dialysis or a kidney transplant. Most of these studies have reported a lower HRQoL in children undergoing dialysis compared to children with a kidney transplant (2,10). In earlier CKD stages, anaemia and poor growth have been identified as factors associated with impaired HRQoL outcomes (1,11). Little is known, however, about the impact of LUTD on the HRQoL of children with CKD and in paediatric renal transplant recipients (12) and more knowledge is needed to understand how to support them in the best way possible.

The aim of this study was to evaluate HRQoL in children with CKD or a kidney transplant, with or without LUTD. As we found it difficult to motivate children with CKD or a kidney transplant to adhere to bladder training regimens, we hypothesised that LUTD was not a priority for these patients, as they had many other problems, and therefore, it would have little or no influence on HRQoL. We also searched for other potential predictors of impaired HRQoL, such as sex, age and CKD status, using children in the general paediatric population and children with other chronic conditions as control groups.

MATERIALS AND METHODS

Design

This cross-sectional, single-centre study was conducted between June 2011 and December 2012 at the Astrid Lindgren Children's Hospital in Stockholm, a referral centre treating approximately two-thirds of children with CKD or a kidney transplant in Sweden. The study inclusion criteria were being between eight and 18 years of age, having CKD stages 3–5 or having had a kidney transplant and possessing sufficient cognitive abilities and Swedish language skills to respond to the questionnaires. We consecutively approached all patients who met these criteria.

Participants

A total of 62 of the 64 eligible patients, 33 boys and 29 girls, agreed to participate and were enrolled in the study. One boy with a kidney transplant later dropped out and two boys with CKD were excluded because of incomplete questionnaire responses, leaving a total of 59 participants, which was a response rate of 92%. One of the patients was 18 years old when he was asked to participate and had turned 19 when he answered the questionnaires, but was still enrolled. Another patient with CKD was included despite being in stage two, because at the time of inclusion she was in stage three. The sample comprised 23 children (39%) with stages 3–5 CKD and 36 children (61%) who had received a kidney transplant at least one year before entering the study. None of the participants were on dialysis. The causes of CKD were classified as nonglomerular in 19 children (32%) and as glomerular in 40 children (68%). Nonglomerular disorders were posterior urethral valves, VUR/hydronephrosis with or without multicystic dysplasia, other urinary tract anomalies and a neurogenic bladder.

Evaluation of kidney and bladder function

Glomerular filtration rate (GFR) was assessed by clearance of iohexol or estimated by cystatin C and LUT function with voiding history, frequency and volume chart, uroflowmetry and postvoid ultrasound measurements to detect residual urine. The evaluation was performed according to the local pre- and post-transplant programmes and has been described elsewhere (6). To ensure adequate data concerning LUT function, the Swedish version of the International Consultation on Incontinence Questionnaire-Female Lower Urinary Tract Symptoms inventory (13) was used as a complement to the comprehensive history mentioned above. The inventory is a psychometrically validated instrument for assessing LUT symptoms in females of all ages and was chosen for this study due to the lack of appropriate questionnaires regarding LUT symptoms in children. Signs of LUTD were regarded as the presence of daytime intermittent incontinence with or without concomitant enuresis, referred to as incontinence in this paper, an abnormal maximum voided volume for age, a staccato, an interrupted or a plateau flow pattern and, or, residual urine amounting to 20 mL or more (6). The terminology and definitions used here are in accordance with the International Children's Continence Society guidelines (14). None of the patients had continuous urinary incontinence.

Assessment of HRQoL

HRQoL was assessed with two self-reported generic instruments, the KIDSCREEN-27 and the DISABKIDS Chronic Generic Module-37 (DCGM-37). Both instruments are also available as proxy versions and were developed in close cooperation using the same methodology. The aim of the instruments was to survey subjective HRQoL in healthy, chronically ill and disabled paediatric populations (15).

The KIDSCREEN-27 was developed cross-culturally in Europe with 13 cooperating countries and designed to survey generic HRQoL in healthy and chronically ill children and adolescents aged 8–18. The questionnaire consists of 27 items covering five dimensions: physical well-being, psychological well-being, autonomy and parent relations, social support and peer relations and school environment. All items are scored on a five-point Likert

scale ranging from one for poor, not at all or never to five for excellent, extremely or always, with reference to the preceding week (16). The DCGM-37, which was designed to measure generic HRQoL in children and adolescents with chronic conditions (15), was included with the intention of increasing the sensitivity for condition-specific aspects. It consists of six dimensions: independence, emotion, social inclusion, social exclusion, physical limitation and treatment, representing the physical, mental and social well-being life domains. All items refer to the preceding four weeks and use a Likert scale ranging from one for never to five for always (17). The sum scores for each item of the instruments were transformed following the standard scoring algorithms according to the KIDSCREEN and DISABKIDS manuals (16,17). The transformed summary data were used in our analyses, with a higher score indicating a better HRQoL.

A psychometric evaluation suggested that both the KIDSCREEN-27 and the DCGM-37 satisfied the requirements for validity and reliability (15–17). In this study, both instruments indicated good internal consistency for all dimensions, with Cronbach's alpha values from 0.70 to 0.93.

Comparison groups

The KIDSCREEN-27 Swedish normative data did not cover the entire age span in our study, so instead we compared the study results with KIDSCREEN-27 data from the Swedish general population, collected in cooperation with Jervaeus et al. (18). We randomly selected 500 children and young adults from the Swedish Population and Address Register and 257 subjects (54%) who had completed the KIDSCREEN-27 at a median age of 16 years (range 11–23 years) agreed to take part (18). The 203 participants who were aged 19 years or younger were included as controls in the present study, to match our age group. In comparisons using the DCGM-37, norm data from field studies of 1152 chronically ill European children and adolescents aged 8–16 were used (17). These norm children suffered from asthma, arthritis, atopic dermatitis, diabetes, cerebral palsy, cystic fibrosis or epilepsy.

Procedure

Children and their parents were contacted at their routine outpatient three-month, six-month or annual visit and were given verbal information and written information addressed to them. If they agreed to participate, we scheduled a time to respond to the questionnaires. The children completed the questionnaires on the outpatient ward without any help from their parents, but they could ask one of the investigators to clarify the questions if they needed to. The time required to answer the questionnaires was approximately 30 minutes.

Statistical analysis

Subgroup comparisons regarding HRQoL, as well as comparisons with control groups, were analysed using independent-samples *t*-tests. As the multiple subgroup comparisons could increase the risk of type I errors, all

conclusions were carefully drawn in cases where isolated, unexpected significant differences could not be explained logically and, or, by earlier research. All potential outcome predictors were also evaluated with ANOVA to correct for possible confounding factors. These results are not presented in the Results section, but they are commented on in the Discussion. A statistical significance level of $p < 0.05$ was applied to all the analyses. The statistical analyses were performed using IBM SPSS Statistics version 20 for Windows (IBM Corp, Armonk, NY, USA).

RESULTS

Demographics and clinical characteristics are presented in Table 1. At least one sign of LUTD was reported by 32 children (58%) and the most frequent was postvoid residual urine, followed by an abnormal maximum voided volume for age and incontinence.

HRQoL in certain subgroups of patients was analysed to detect possible associations with an impaired HRQoL (Table 2). Children with one or more signs of LUTD did not rate their HRQoL differently than children with a normal LUT function. The children with incontinence gave lower ratings on the physical limitation and treatment dimensions, but not on the other DCGM-37 dimensions compared with those who were continent. Furthermore, children with nonglomerular disorders reported significantly more physical limitations than those with glomerular disorders.

Boys and girls, younger and older children, as well as different CKD statuses, were compared (Table 3). Girls rated significantly lower on the total score and on three of the six DCGM-37 dimensions (independence, emotion and social inclusion), as well as on two of the five KIDSCREEN-27 dimensions (physical and psychological well-being). Children aged 15–19 rated their HRQoL worse compared with those aged 8–14 on three of the KIDSCREEN-27 dimensions (physical and psychological well-being and social support and peers), as well as on three of the DCGM-37 dimensions (independence, emotion and social inclusion). Children with a kidney transplant scored significantly lower than children with CKD stages 3–5 on the physical well-being and independence dimensions, according to the KIDSCREEN-27 and DCGM-37, respectively.

Comparisons between the study and control groups are presented in Table 4. The study children rated HRQoL lower on two of the KIDSCREEN-27 dimensions (physical and psychological well-being) compared to those in the general population. No statistically significant differences in HRQoL were detected between the study group and the field study results based on children with chronic conditions other than CKD, as measured with the DCGM-37.

DISCUSSION

The present study is, to the best of our knowledge, the first one with a main focus on HRQoL in children and adolescents with LUTD of glomerular and nonglomerular

Table 1 Patient characteristics. Signs and symptoms of LUTD

	All participants n = 59	CKD stages 3–5 n = 23	Kidney transplant n = 36
Males (%)	30 (51)	13 (57)	17 (47)
Age, years, mean (SD)	14.1 (3.3)	13.2 (2.9)	14.6 (3.4)
Range	8.0−19.1	8.0−18.0	8.3−19.1
Aged 8–14 years	30	16	14
Aged 15–19 years	29	7	22
GFR mL/min/1.73 m^2, mean (SD)	45.3 (21.4)	29.5 (16.1)	55.4 (17.9)
Range	10−89	10−63	21−89
CKD duration, years, mean (SD)	11.1 (4.6)	9.4 (4.1)	12.2 (4.6)
Range	1.5−18.8	1.5−15.3	2.4−18.8
Years since transplantation, mean (SD)			7.2 (4.7)
Range			1.0−17.5
CKD stage			
2	16	1[†]	15
3	27	9	18
4	11	8	3
5	5	5	0
Urological disorders (%)	19 (32)	10 (43)	9 (25)
Bladder dysfunction/LUTD (%)	32/55[‡] (58)	15/22[‡] (68)	17/33[‡] (52)
Daytime incontinence ± enuresis	15/59 (25)	6/23 (26)	9/36 (25)
Abnormal maximum voided volume	14/53[‡] (26)	7/22[‡] (32)	7/31[‡] (23)
Postvoid residual urine	21/57[‡] (37)	10/22[‡] (45)	11/35[‡] (31)

CKD = chronic kidney disease; LUT = lower urinary tract; LUTD = lower urinary tract dysfunction; GFR = glomerular filtration rate; SD = standard deviation.
[†]CKD stage 2, previously 3.
[‡]Measurements not available for all patients.

Table 2 Comparisons of self-reported HRQoL between groups with and without LUTD, urinary incontinence and urological disorders. Mean[†,‡] SD and p values

	LUTD			Incontinence			Urological disorders		
	No	Yes	p[§]	No	Yes	p[§]	No	Yes	p[§]
n	23	32		44	15		39	20	
KIDSCREEN-27[†]									
Physical well-being	44.6 ± 9.1	46.5 ± 7.8	0.414	45.5 ± 8.6	44.7 ± 7.8	0.757	44.6 ± 8.9	46.8 ± 7.1	0.360
Psychological well-being	49.4 ± 12.3	50.3 ± 9.1	0.750	50.1 ± 11.0	47.9 ± 7.8	0.484	50.3 ± 10.8	47.9 ± 9.1	0.407
Autonomy and parent relationship	53.9 ± 9.7	51.0 ± 8.0	0.227	53.1 ± 8.8	48.5 ± 7.5	0.079	53.0 ± 8.2	49.7 ± 9.3	0.169
Social support and peers	54.9 ± 10.3	53.3 ± 6.8	0.504	52.7 ± 11.3	54.4 ± 7.3	0.595	52.6 ± 11.8	54.3 ± 6.7	0.572
School	54.3 ± 11.8	53.4 ± 6.9	0.727	53.9 ± 9.5	53.1 ± 6.6	0.781	54.2 ± 9.2	52.6 ± 8.2	0.531
DISABKIDS-37[‡]									
Independence	78.8 ± 18.1	80.7 ± 1.4	0.673	81.1 ± 15.7	75.8 ± 16.8	0.279	80.3 ± 15.7	78.5 ± 17.1	0.690
Physical limitation	73.4 ± 16.6	76.3 ± 18.3	0.544	77.7 ± 17.0	66.9 ± 16.0	**0.035**	78.6 ± 16.2	67.3 ± 17.3	**0.017**
Emotion	74.8 ± 21.0	74.3 ± 23.5	0.934	77.3 ± 19.6	65.0 ± 25.7	0.057	76.3 ± 20.5	69.9 ± 24.4	0.302
Social exclusion	84.8 ± 14.1	82.2 ± 17.7	0.559	84.7 ± 15.7	76.4 ± 18.7	0.100	84.8 ± 16.1	77.9 ± 17.7	0.139
Social inclusion	76.2 ± 19.0	75.3 ± 15.0	0.858	75.0 ± 17.3	74.2 ± 17.3	0.873	75.6 ± 18.1	73.2 ± 15.4	0.619
Treatment	80.2 ± 19.4	69.0 ± 25.0	0.078	78.9 ± 20.5	57.5 ± 25.0	**0.002**	71.9 ± 23.8	76.2 ± 23.0	0.481
Total DCGM-37	78.0 ± 14.2	76.3 ± 14.8	0.685	79.1 ± 13.0	69.2 ± 16.1	**0.020**	77.9 ± 14.4	73.9 ± 14.4	0.322

LUTD = lower urinary tract dysfunction = abnormal maximum voided volume, postvoid residual urine and/or incontinence.
[†]T-scores, higher scores indicating better HRQoL.
[‡]Transformed summary scores, possible range 0–100, higher scores indicating better HRQoL.
[§]Group mean differences tested by independent-samples t-test.
Values in bold indicate significance.

origin and with moderate-to-severe CKD or following a kidney transplant. Our main finding was that the children with symptoms consistent with LUTD generally experienced as good a HRQoL as those with normal LUT

function. However, the children with incontinence reported impaired physical functioning.

This study confirms our prior findings of a high prevalence of LUTD in children with CKD or a kidney transplant

Table 3 Comparisons of self-reported HRQoL within the study group regarding sex, age and CKD/kidney transplant. Mean[†,‡] SD and p values

	Boys	Girls	p[§]	8–14 years	15–19 years	p[§]	CKD 3–5	Kidney transplant	p[§]
n	30	29		30	29		23	36	
KIDSCREEN-27[†]									
Physical well-being	47.4 ± 8.4	43.1 ± 7.9	**0.047**	48.5 ± 8.4	42.1 ± 7.0	**0.002**	48.9 ± 8.4	43.0 ± 7.6	**0.007**
Psychological well-being	52.6 ± 9.8	46.3 ± 9.9	**0.017**	52.4 ± 11.5	46.5 ± 8.0	**0.026**	51.3 ± 9.4	48.4 ± 10.8	0.283
Autonomy and parent relation-ship	52.0 ± 8.1	51.8 ± 9.4	0.905	51.5 ± 8.4	52.4 ± 9.0	0.678	51.6 ± 6.7	52.1 ± 9.7	0.815
Social support and peers	55.7 ± 8.7	50.6 ± 11.5	0.060	56.0 ± 8.6	50.2 ± 11.4	**0.029**	54.2 ± 12.5	52.5 ± 9.0	0.529
School	54.7 ± 7.8	52.7 ± 9.8	0.386	55.3 ± 9.4	52.1 ± 8.1	0.165	54.6 ± 7.5	53.1 ± 9.6	0.533
DISABKIDS-37[‡]									
Independence	84.0 ± 13.5	75.3 ± 17.4	**0.035**	83.9 ± 13.4	75.4 ± 17.6	**0.042**	85.1 ± 12.7	76.3 ± 17.1	**0.037**
Physical limitation	78.5 ± 17.0	71.4 ± 17.1	0.117	75.8 ± 17.5	74.1 ± 17.3	0.710	74.3 ± 19.0	75.5 ± 16.3	0.799
Emotion	81.4 ± 18.3	66.7 ± 22.9	**0.008**	79.9 ± 16.8	68.4 ± 24.9	**0.041**	78.4 ± 17.5	71.5 ± 24.0	0.269
Social exclusion	85.0 ± 15.4	80.0 ± 18.0	0.259	84.3 ± 15.3	80.7 ± 18.3	0.420	86.1 ± 15.4	80.3 ± 17.4	0.204
Social inclusion	79.3 ± 13.9	70.1 ± 19.1	**0.037**	80.4 ± 14.0	69.0 ± 18.4	**0.010**	79.6 ± 13.3	71.7 ± 18.8	0.088
Treatment	77.6 ± 20.0	69.1 ± 26.2	0.172	76.4 ± 20.0	70.3 ± 26.6	0.321	72.7 ± 17.6	73.7 ± 26.7	0.864
Total DCGM-37	81.0 ± 11.4	72.0 ± 15.8	**0.015**	80.2 ± 11.8	72.9 ± 16.1	0.051	79.4 ± 11.3	74.8 ± 16.0	0.230

CKD = chronic kidney disease.
[†]T-scores, higher scores indicating better HRQoL.
[‡]Transformed summary scores, possible range 0–100, higher scores indicating better HRQoL.
[§]Group mean differences tested by independent-samples *t*-test.
Values in bold indicate significance.

Table 4 Comparisons of self-reported HRQoL between the study population and comparison groups. Mean[†,‡] SD and p values

KIDSCREEN-27[†]	Patients vs. population-based Swedish comparison group		
	Patient (n = 47)[§]	Comparison group (n = 203)[§]	p[¶]
Physical well-being	44.7 ± 8.4	47.7 ± 8.9	**0.037**
Psychological well-being	49.1 ± 9.9	52.1 ± 9.2	**0.047**
Autonomy and parent relationship	52.0 ± 8.4	52.4 ± 8.3	0.761
Social support and peers	52.0 ± 10.6	52.2 ± 7.9	0.867
School	53.4 ± 8.2	52.3 ± 7.8	0.429
DISABKIDS-37[‡]	Patients vs. European children with chronic conditions		
	Patient (n = 59)	Comparison group (n = 1152)	p[¶]
Independence	79.7 ± 15.9	76.9 ± 18.3	0.204
Physical limitation	75.0 ± 17.1	73.9 ± 18.2	0.764
Emotion	74.2 ± 21.6	76.7 ± 20.6	0.386
Social exclusion	82.6 ± 16.4	85.2 ± 15.6	0.230
Social inclusion	74.8 ± 17.0	75.3 ± 17.8	0.902
Treatment	73.4 ± 23.3	72.3 ± 22.7	0.689
Total DCGM-37	76.6 ± 14.3	77.0 ± 14.2	0.802

[†]T-scores, higher scores indicating better HRQoL.
[‡]Transformed summary scores, possible range 0–100, higher scores indicating better HRQoL.
[§]Patient group age and control group age adjusted to match one another.
[¶]Group mean differences tested by independent-samples *t*-test.
Values in bold indicate significance.

regardless of the underlying cause of the disease (6,19). Postvoid residual urine and abnormal maximum voided volumes were the most frequent signs of LUTD, but, as hypothesised, these had no impact on HRQoL. Despite routinely given advice regarding bladder training regimens, it is possible that these abnormalities are not perceived as bothersome by the child, which may explain why they had no impact on HRQoL. However, in this population, there might be additional reasons why postvoid residual urine and abnormal maximum voided volumes did not appear to have a negative influence on HRQoL. As children and adolescents have a strong desire to be like their peers, they may deny their bladder problems. Another possible explanation is that, as LUT anomalies are usually diagnosed early in life (20), LUTD may have become a natural part of everyday life for the children and therefore they did not warrant special attention from their point of view. Furthermore, these children also have to pay considerable attention to their medical management (1,11) and other areas, such as developing autonomy, physical capacity, self-esteem, body image, relationships and school functioning (11,21). We believe, however, that the most plausible explanation is that the children were simply not aware of their large capacity bladder or the postvoid residual urine. Incontinence, which is known to be a stressful life event in healthy children (7), as well as in children with CKD (12,22), was less frequently observed than postvoid residual urine and abnormal maximum voided volumes, but was associated with lower HRQoL in the physical and treatment domains.

Differences in HRQoL between boys and girls in the study group emerged and were more of a problem for girls with regard to physical and emotional functioning and

independence. This finding was in line with those from other studies on children with CKD or other chronic conditions (22–24), as well as in healthy children in the general population (25). They may reflect more drastic developmental processes in girls requiring adjustment to bodily changes and the development of identity (26). Emotional concerns among the girls in our cohort may possibly have been attributed to physical appearance, which is known to be affected by advanced CKD stages, leading to body image concerns and impaired HRQoL (21,23). Impaired growth and weight gain are some of the common adverse effects of CKD and its treatment, leading to a changed body image, which may bother children more with increasing age (1,11).

Older age was also associated with a lower HRQoL in the univariate analysis and this finding was comparable with that in the general population (25). However, although the age groups were similar regarding the number of participants in our study, there was a bias regarding sex distribution across the groups. The majority in the younger group consisted of boys and two-thirds of older participants were girls, which may have distorted the results, as the girls rated their HRQoL lower. Furthermore, transplanted children were older than nontransplanted children. Consequently, when age was adjusted for sex and CKD status in the multivariate analysis, it no longer remained a significant predictor of impaired HRQoL.

Despite a higher mean GFR, children with a kidney transplant did not, as one might have assumed, report a better HRQoL than children and adolescents in CKD stages 3–5. On the contrary, they reported significantly lower mental and physical well-being, but this finding may have been influenced by the fact that none of the CKD patients were on dialysis. The result persisted after controlling for sex and age in the multivariate analysis. Renal transplantation is the preferred therapy for children with advanced CKD and is generally expected to improve health and HRQoL (2,27). Nevertheless, there are still treatment-related demands following renal transplantation that limit the child's everyday life in different areas, such as the need for lifelong immunosuppressive therapy, the side effects of the medication and the fear of a kidney rejection, to name just a few (21,28). In addition, the child's diminished independence may reflect overprotection by parents and health professionals and lead to a lower HRQoL. Similar findings were reported in the study by McKenna et al. (29), which revealed an equal or lower HRQoL in children with a kidney transplant than children receiving dialysis.

Based on our results, children with CKD or a kidney transplant were generally satisfied in the majority of HRQoL areas, such as autonomy and interactions with family and friends, as well as with school, compared with the sample drawn from the general Swedish population (18). Lower HRQoL levels in the areas of physical and psychological well-being may have reflected the impact of a chronic illness on everyday life. Similar findings have been demonstrated in comparisons between children with CKD, regardless of treatment modality, and healthy children (11,28). However, HRQoL was found to be

equal to that in children with other chronic conditions than CKD.

We used two HRQoL instruments, the KIDSCREEN-27 and the DCGM-37, in our study to capture generic as well as chronic condition-related information about HRQoL. The available disease-specific HRQoL instruments for paediatric renal populations are designed for children with ESRD on dialysis or with a kidney transplant (23). Because none of the participants had yet developed ESRD, such a disease-specific instrument was not chosen for this study. As shown in the Result section, the impact of incontinence and a nonglomerular background was captured by the DCGM-37, but not by KIDSCREEN-27, which may indicate that the DCGM-37 was more sensitive in capturing information on condition-specific aspects (15).

This study has some limitations that should be mentioned. Our Swedish reference material did not cover the youngest children aged eight to 10 in the sample and therefore the youngest children were left out in comparison with the controls. The results of the HRQoL questionnaires were based solely on child reports. Indeed, children's opinions are highly desirable, but parental ratings, although they are known to differ slightly from children's ratings, could provide an important complement by providing information from an additional perspective and should be addressed in future studies. Everyday life in paediatric renal patients is assumed to be affected in different ways across CKD stages and treatment modalities. Even though it was useful to combine the two instruments, the KIDSCREEN-27 and the DCGM-37, the assessment may not have been sensitive enough to capture important specific information on various aspects of the disease, including signs and symptoms of LUTD, as well as specific treatments, frequent check-ups at the hospital and fear of graft loss, among other things. Thus, in the future, we will be looking forward to generic HRQoL instruments with a disease-specific module for paediatric renal patients with questions covering different CKD stages, associated symptoms and treatment-related issues. Furthermore, we cannot completely rule out that the results were influenced by unmeasured confounding factors, such as possible cognitive impairments, personality and the child's socio-demographic setting.

Causal connections and further conclusions cannot be drawn from this cross-sectional study. Longitudinal data, including information on somatic symptoms and parental emotional functioning, are needed, to understand factors that may influence HRQoL in different CKD stages and treatment modalities (21,23,28).

CONCLUSION

Common signs of LUTD, such as abnormal maximum voided volume and postvoid residual urine, did not seem to affect the HRQoL of children and adolescents with CKD or a kidney transplant, with the exception of incontinence. Thus, incontinence should be recognised and treated as previously demonstrated. Consistent with previous findings, female sex was associated with a lower HRQoL, which

should raise concern in clinical practice. An unexpected finding was that children with a kidney transplant reported lower physical well-being and independence than those with moderate-to-severe CKD. This finding points to the need for more support for paediatric renal transplant recipients. Continued research is recommended, to expand our understanding of the everyday life of paediatric renal patients and identify their support needs.

CONFLICT OF INTERESTS
The authors have no conflict of interests to declare.

ETHICAL APPROVAL
The study was approved by the Regional Ethical Review Board in Stockholm. The informed consent of all participants and their parents was obtained before inclusion in the study.

References

1. Wong CJ, Moxey-Mims M, Jerry-Fluker J, Warady BA, Furth SL. CKiD (CKD in children) prospective cohort study: a review of current findings. *Am J Kidney Dis* 2012; 60: 1002–11.
2. Goldstein SL, Gerson AC, Furth S. Health-related quality of life for children with chronic kidney disease. *Adv Chronic Kidney Dis* 2007; 14: 364–9.
3. Aldridge MD. How do families adjust to having a child with chronic kidney failure? A systematic review *Nephrol Nurs J* 2008; 35: 157–62.
4. Penna FJ, Elder JS. CKD and bladder problems in children. *Adv Chronic Kidney Dis* 2011; 18: 362–9.
5. Nahas WC, Antonopoulos IM, Piovesan AC, Pereira LM, Kanashiro H, David-Neto E, et al. Comparison of renal transplantation outcomes in children with and without bladder dysfunction. A customized approach equals the difference. *J Urol* 2008; 179: 712–6.
6. Oborn H, Herthelius M. Lower urinary tract symptoms in children and adolescents with chronic renal failure. *J Urol* 2010; 183: 312–6.
7. Gladh G, Eldh M, Mattsson S. Quality of life in neurologically healthy children with urinary incontinence. *Acta Paediatr* 2006; 95: 1648–52.
8. Heath J, Mackinlay D, Watson AR, Hames A, Wirz L, Scott S, et al. Self-reported quality of life in children and young people with chronic kidney disease. *Pediatr Nephrol* 2011; 26: 767–73.
9. Taylor RM, Wray J, Gibson F. Measuring quality of life in children and young people after transplantation: methodological considerations. *Pediatr Transplant* 2010; 14: 445–58.
10. Lopes M, Ferraro A, Koch VH. Health-related quality of life of children and adolescents with CKD stages 4-5 and their caregivers. *Pediatr Nephrol* 2014; 29: 1239–47.
11. Gerson AC, Wentz A, Abraham AG, Mendley SR, Hooper SR, Butler RW, et al. Health-related quality of life of children with mild to moderate chronic kidney disease. *Pediatrics* 2010; 125: e349–57.
12. Dodson JL, Cohn SE, Cox C, Hmiel PS, Wood E, Mattoo TK, et al. Urinary incontinence in the CKiD cohort and health related quality of life. *J Urol* 2009; 182: 2007–14.
13. Abrams P, Avery K, Gardener N, Donovan J, Board IA. The International Consultation on Incontinence Modular Questionnaire: www.iciq.net. *J Urol* 2006; 175: 1063–6; discussion 6.
14. Austin PF, Bauer SB, Bower W, Chase J, Franco I, Hoebeke P, et al. The standardization of terminology of lower urinary tract function in children and adolescents: update report from the standardization committee of the International Children's Continence Society. *Neurourol Urodyn* 2016; 35: 471–81.
15. Ravens-Sieberer U, Erhart M, Wille N, Wetzel R, Nickel J, Bullinger M. Generic health-related quality-of-life assessment in children and adolescents: Methodological considerations. *Pharmacoeconomics* 2006; 24: 1199–220.
16. The KIDSCREEN Group Europe. *The KIDSCREEN questionnaires Quality of life questionnaires for children and adolescents Handbook*. Lengerich, Germany: Pabst Science Publishers, 2006.
17. Schmidt S, The European DISABKIDS Group. *The DISABKIDS questionnaires; Quality of life questionnaires for children with chronic conditions; Handbook*. Lengerich, Germany: Pabst Science Publishers, 2006.
18. Jervaeus A, Kottorp A, Wettergren L. Psychometric properties of KIDSCREEN-27 among childhood cancer survivors and age matched peers: a Rasch analysis. *Health Qual Life Outcomes* 2013; 11: 96.
19. Herthelius M, Oborn H. Bladder dysfunction in children and adolescents after renal transplantation. *Pediatr Nephrol* 2006; 21: 725–8.
20. Esbjorner E, Berg U, Hansson S. Epidemiology of chronic renal failure in children: a report from Sweden 1986–1994. Swedish Pediatric Nephrology Association. *Pediatr Nephrol* 1997; 11: 438–42.
21. Anthony SJ, Hebert D, Todd L, Korus M, Langlois V, Pool R, et al. Child and parental perspectives of multidimensional quality of life outcomes after kidney transplantation. *Pediatr Transplant* 2010; 14: 249–56.
22. Deshpande AV, Craig JC, Smith GH, Caldwell PH. Factors influencing quality of life in children with urinary incontinence. *J Urol* 2011; 186: 1048–52.
23. Neul SK, Minard CG, Currier H, Goldstein SL. Health-related quality of life functioning over a 2-year period in children with end-stage renal disease. *Pediatr Nephrol* 2013; 28: 285–93.
24. Nordlund B, Konradsen JR, Pedroletti C, Kull I, Hedlin G. The clinical benefit of evaluating health-related quality-of-life in children with problematic severe asthma. *Acta Paediatr* 2011; 100: 1454–60.
25. Svedberg P, Eriksson M, Boman E. Associations between scores of psychosomatic health symptoms and health-related quality of life in children and adolescents. *Health Qual Life Outcomes* 2013; 11: 176.

26. Michel G, Bisegger C, Fuhr DC, Abel T. Age and gender differences in health-related quality of life of children and adolescents in Europe: a multilevel analysis. *Qual Life Res* 2009; 18: 1147–57.

27. Giessing M, Muller D, Winkelmann B, Roigas J, Loening SA. Kidney transplantation in children and adolescents. *Transplant Proc* 2007; 39: 2197–201.

28. Diseth TH, Tangeraas T, Reinfjell T, Bjerre A. Kidney transplantation in childhood: mental health and quality of life of children and caregivers. *Pediatr Nephrol* 2011; 26: 1881–92.

29. McKenna AM, Keating LE, Vigneux A, Stevens S, Williams A, Geary DF. Quality of life in children with chronic kidney disease-patient and caregiver assessments. *Nephrol Dial Transplant* 2006; 21: 1899–905.