Health-Related Quality of Life in Children on Dialysis

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Introduction

Kidney dialysis remains a life-sustaining treatment for youth who have kidney failure. Optimum renal replacement therapy (RRT) results require strict adherence to dialysis prescription, to diet requirements/restrictions, and close follow-up with medical providers. While clinical markers of dialysis patient's health status (e.g., growth, infection rates, hospitalization, and survival) are necessary indicators of health outcomes, health care providers have become increasingly interested in patient and family perception of quality of life (QOL) as an adjunctive measure of treatment efficacy.

Many QOL experts point to the World Health Organization's 1958 definition of health as being an early catalyst for the expansion of the focus on mortality and morbidity to broader considerations of quality of life [1–3]. In the 6 decades since WHO distinctively defined health "as a state of complete physical, mental and social well-being and not merely the absence of disease and infirmity" [4], data has been accumulated about the importance of patient perception of illness and health. Nevertheless, there still is not a unanimous acceptance in healthcare environments of the utility of systematic assessment of patient and family perception of quality of life. Unfortunately, in the case of youth with chronic kidney disease (CKD), even when there is acceptance of the multidimensional nature of health and illness and the value of assessing quality of life, limited health care resources prohibit widespread routine assessment.

In this chapter, we will describe the constructs of quality of life and health-related quality of life, review quality of life instruments that have been validated for use in pediatric dialysis populations, and summarize published literature on the impact of dialysis on the quality of life in children with kidney disease. Our aim is twofold. First, we hope to provide a foundation for clinicians and researchers to appreciate the utility and importance of health-related quality of life (HRQOL) assessment. Secondly, we hope to provide an up-to-date resource for choosing evaluation tools for use in research.

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Definition and Utility of Quality of Life and Health-Related Quality of Life

In a general sense, quality of life refers to one's sense of well-being and functional outcome within various domains of life. Over the past decade, the recognition that chronic health problems impact QOL and that both illness severity and treatment interventions may alter psychological, social, physical, and educational outcomes have lead to development of the construct of health-related quality of life (HRQOL) [5, 6]. Health-related quality of life refers to one's sense of well-being and functional outcome within various domains of life assuming that a disease and its treatment have impacted aspects of psychological, social, physical, educational, and/or vocational functioning. Measurement of health-related quality of life has been described as an attempt to quantify, in scientifically analyzable terms, the net consequence of a disease and its treatment on the patient's perception of his/her ability to live a useful and fulfilling life [7]. In a practical sense therefore, the measurement of QOL in children with medical problems results in an assessment of their HRQOL. The term HRQOL will be used throughout the remainder of this chapter to refer to the assessment of QOL of children with kidney disease.

By definition, HRQOL is something that must include assessment through direct inquiry. However, until recently, direct assessment of children's perceptions of their HRQOL has been hindered by the belief that children could not accurately report on their own well-being. This belief in turn, stalled the development of reliable pediatric assessment tools. Fortunately, in the past decade, several instruments that allow for the direct evaluation of children's HRQOL have been developed. These tools demonstrate that children do indeed have the ability to accurately report on their psychological, social, physical, and educational status [8, 9]. Discrepancies between caregiver and child perceptions within domains of HRQOL have lead to the recognition that differences in parent–child perceptions of well-being are as worthy of more in-depth assessment as are agreements of problem areas [6, 10, 11].

HRQOL is a multifaceted/multidimensional phenomenon and generally includes the following domains and components: (1) physical status and physical functioning, (2) psychological status and emotional functioning, (3) social interactions and social functioning, and (4) educational/vocational status and functioning. A growing number of HRQOL researchers also endorse the assessment of religious and/or spiritual status given the growing body of research that links spirituality to self-perceptions of well-being [2, 12, 13].

Health-related quality of life data has many potential uses. For example, it can be used to evaluate the impact of individual treatments or programs on individual patients or groups of patients. This type of application is sometimes referred to as a cost/utility analysis [14–16]. In addition, HRQOL data can be used to inform health policy [16–18]. Perhaps the most ambitious use of HRQOL data occurs when it is used to predict the future functional outcomes of people with an illness or condition [19, 20].

A conceptual definition of HRQOL is illustrated schematically in Fig. 34.1. The illustration highlights the interdependent nature of the domains, the importance of multidimensional assessment in understanding the full range of manifestations of health and illness, and the influences of variables that have been shown to mediate HRQOL.

Assessment of HRQOL in Patients with End-Stage Renal Disease

The charge by Medicare to assess the cost–utility of the various dialysis treatments provided for in the Medicare End-Stage Renal Disease program has led to the inclusion of an assessment of HRQOL in dialysis patients of age 18 years and older [21, 22]. This mandate appears to have been strongly influenced by the National Kidney Foundation's Clinical Practice Guidelines and Clinical Practice Recommendations for Hemodialysis (HD) and PERITONEAL DIALYSIS (PD) Adequacy originally published in 1997 and revised in 2006 [22].

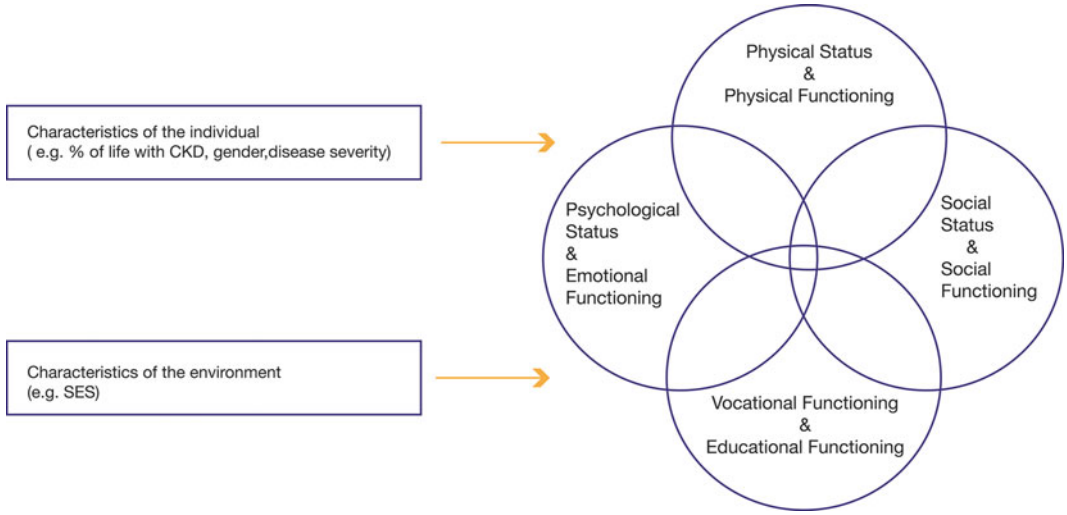

Fig. 34.1 Schematic definition of domains of health-related quality of life

Given improvements in dialysis treatment and decreased mortality, the 1997 NKF-DOQI guidelines recommended an expansion of the assessment of clinical outcomes to include both generic and disease- /treatment-specific measures of HRQOL [23]. Unfortunately, in 1997, none of the available survey instruments had been established as having the necessary reliability and validity in the ESRD population; so the DOQI work group advised that each dialysis facility serially evaluate HRQOL in patients over the age of 18 years using the tool of their choice. The workgroup further recommended that outcomes research using promising instruments be completed in order to establish a standardized HRQOL assessment that could be integrated into the routine care and evaluation of patients with ESRD [23].

The 1997 DOQI guidelines did not provide any recommendations for the assessment of HRQOL in children who were receiving dialysis. Similar to the situation for adults with ESRD, no instruments with sufficient psychometric authority were available to assess the HRQOL of youth with ESRD in 1997. Fortunately, the recognition of the value of assessing HRQOL in youth with chronic medical conditions has been a catalyst over the past decade for the development of reliable and valid tools to monitor the impact of disease and its treatment in children with CKD [24, 25].

Over the past 10 years, a number of HRQOL instruments have been validated for use in adults and children with ESRD and evidence has mounted regarding the association between HRQOL and both morbidity and mortality. The 2006 KDOQI update acknowledged the accumulation of valuable information regarding HRQOL outcomes and recommends that increased resources be allocated to incorporate the assessment of HRQOL into ongoing quality improvement efforts [26]. Moreover, the 2006 KDOQI Clinical Practice Update added a pediatric clinical practice guideline that echoed the adult recommendation for monitoring HRQOL as an important health outcome and referenced two instruments that have been validated for use in children on dialysis. Notwithstanding the 2006 KDOQI recommendation regarding the importance of evaluating HRQOL in pediatric ESRD patients, CMS did require its assessment in children in the 2008 Clinical Performance Measures Project, as it did in dialysis patients over the age of 18 years [22].

Quality of Life Studies in Children on Dialysis

Much of the early research assessing HRQOL in children on dialysis did not include validated multidimensional measures, but rather

used qualitative methods such as telephone interviews, investigator-designed questionnaires, and instruments that measure a single domain of HRQOL [25].

For example, in 1991, Roscoe et al. used a structured telephone interview to evaluate HRQOL. This study reported on the functional outcomes (defined by educational level, ability to care for oneself, employment, marital status, achievement of parenthood, and opinion of the caregiver on general adjustment) in 118 adolescents who were 11–19 years old when therapy for ESRD was initiated between 1966 and 1986 [27]. With a mean age of 22 years and a mean follow-up of 8 years, the authors found that almost 70% of patients were living with family members, and only 28.9% were living on their own or with a spouse. Thirteen percent of patients were neither enrolled in an educational program nor were employed. Furthermore, in over 73% of transplant recipients, functional outcome was defined subjectively by the caregiver as good or excellent. However, caregivers described good or excellent functional outcomes in only 45% of patients on dialysis. When the type of dialysis was considered, 25% of hemodialysis patients had good or excellent functional outcomes, compared to 75% of peritoneal dialysis patients.

The European Dialysis and Transplant Association registry reported similar results regarding HRQOL and functional health status assessment of individuals with a history of dialysis during childhood [28]. Of 617 patients who started RRT as children and were 21–35 years of age in 1986, 56% had completed secondary school and 16% were in a school for the handicapped. Also, 56% were employed but most (61%) lived with their parents. In comparison to the "healthy" population of the same age, employment was somewhat lower, and one third or more had some disability. Further information on the employment status of dialysis patients was presented in the single-center experience of 150 children transplanted between 1970 and 1993, as reported by Offner et al. [29]. Notably, 29% of patients on dialysis after graft failure were unemployed compared to 9% with functioning grafts.

Rosenkranz et al.'s large multicenter study (n = 479) published in 1992 comprising five pediatric nephrology centers in Germany reported similarly disappointing outcomes with regard to educational attainment and age-appropriate independence of adults with childhood onset kidney disease [30]. In 2005, Rosenkranz et al. used a HRQOL questionnaire validated for use in Germany to determine if their center's efforts over the previous two decades to improve HRQOL and functional outcomes of their patients had been successful. The study authors concluded that while some improvements could be attributed to their center's efforts, patients were still at a disadvantage compared to the general population with regard to educational attainment and vocational attainment [30].

In 1994, Morton et al. reported on the functional and psychological health of patients with onset of renal disease in childhood (mean age of renal disease onset was 8 years, range 0–16) and who had received RRT for an average duration of 10 years in the United Kingdom. Functional status and responses on several psychiatric inventories were compared in this group of 45 young adult survivors of ESRD (mean age at time of study was 24.8 years) to those of healthy age-matched controls of comparable socioeconomic status [31]. More of the renal patients were unemployed (31%) than were the healthy subjects (12%). Living with parents, lack of experience of close relationships, lack of educational qualifications, and unemployment were more common in the renal groups [31]. Interestingly, although the renal group described more psychological problems when they were less than 17 years old, they did not have evidence of significantly higher rates of psychiatric disorders in adulthood; they also had lower rates of use of drugs and alcohol compared to the age-matched controls [31].

The first published study to evaluate the health status of pediatric dialysis patients using a multidimensional, standardized, HRQOL questionnaire was published in 1994 by Kurtin et al. In this pilot study, a modified version of the parent-completed questionnaire, developed and validated in the Children's Health and Quality of Life Project,

was used with 20 English-reading adolescents maintained on chronic HEMODIALYSIS at the Children's Hospital of Los Angeles between April and June of 1992 [32]. The authors tested the discriminant validity of the items in the questionnaire and the association between health and family scale scores and compliance. Less-compliant adolescents consistently reported more pain and poorer general and mental health than more compliant adolescents, as well as lower family involvement. Data presented in Kurtin's report supported the use of a standardized questionnaire to evaluate HRQOL in children on dialysis [32].

In 1999, the first US multicenter longitudinal study of quality of life in children and adolescents with CKD was initiated by Furth et al. The study sought to expand on Kurtin's pilot research and validate two multidimensional generic quality of life measures (Child Health Questionnaire-Parent Form, CHQ-PF50, Child Health and Illness Profile-Adolescent Edition, CHIP-AE) for use in youth with various stages of kidney disease severity.

One of the published reports from this study demonstrated an association between anemia, defined by level of hematocrit, and HRQOL in pediatric patients with CKD [33]. The report was a cross-sectional analysis and included CHQ-PF50 surveys completed by parents of 113 CKD patients (mean age 14.4 ± 1.9 years) requiring dialysis (D), with a functioning kidney transplant (TX) or with advanced stage 2 or stage 3–5 CRI (chronic renal insufficiency) as defined by the NKF KDOQI. Seventy-five patients were found to be anemic as defined by a hematocrit ≤36%. In the domains of physical discomfort, limitations of activity, and overall satisfaction with health, patients with a lower hematocrit scored significantly lower than CKD patients with a hematocrit >36% [33].

Further cross-sectional analysis of data from Furth's study, this time looking at adolescent self-perceptions of HRQOL, revealed that the CHIP-AE distinguished between adolescents with kidney disease and healthy adolescents in a number of domains [34]. Using a case control design, analysis of study patients with kidney disease (mean age = 14; 39 CRI, 21 D and 53 TX) compared with two control groups of age: socioeconomic and sex-matched peers without kidney disease, and youth with CKD had lower overall satisfaction with health and more restriction in activity. Moreover, study patients receiving dialysis were less physically active and experienced more physical discomfort and limitations in activities than did study patients who had received a kidney transplant or study patients whose kidney disease had not advanced to ESRD [34].

A 4-year longitudinal analysis of the Furth et al. data using serially completed parent CHQ questionnaires of 78 youth with CKD found that height gain was associated with parent perceptions of improved physical and psychosocial functioning of their children and GFR decline was associated with parent perceptions of worse physical functioning [35].

The first studies to simultaneously evaluate both parent and youth perceptions of HRQOL were published in 2006 by Goldstein et al. and McKenna et al. using the Pediatric Quality of Life Inventory (PedsQL). Goldstein and his research team used a matched control design to evaluate 85 pediatric patients and 96 parents of children with ESRD receiving HD, PD, or TX to a matched group of healthy children [36]. The HRQOL of children with ESRD within the domains of physical, emotional, social, and school functioning were significantly lower compared to the healthy controls. Furthermore, the data suggested that dialysis patients had worse physical health than transplant patients [36]. McKenna et al.'s study population consisted of 64 pediatric patients with CKD (20 CRI, 17 D, 27 TX) [37]. Self-report HRQOL data of study participants and caregiver proxy HRQOL data was compared to published norms. Youth receiving dialysis had lower physical and school functioning scores in comparison to their healthy peers but similar emotional and social functioning scores [37]. In contrast, parent proxy HRQOL scores of youth receiving dialysis were lower than the normative group in all PedsQL domains [37].

Pediatric HRQOL Measures

As interest in assessing HRQOL has increased in the past decade, many research groups have become involved in efforts to develop tools to

evaluate this construct objectively and systematically. Two types of HRQOL measures have been developed: generic and condition-specific instruments. Generic instruments provide summary ratings of functioning within multiple life domains and allow for comparison of HRQOL across different patient groups. Condition-specific measures of HRQOL assess challenges associated with a particular illness and allow for a more specific assessment of the impact of a particular disease and its treatment on QOL. A number of excellent review articles are available that discuss the relative merits of generic and condition-specific HRQOL instruments [1, 38–42]. Table 34.1 lists a selection of generic HRQOL instruments that have been validated for use with pediatric dialysis patients. Also included in Table 34.1 is a description of a condition-specific instrument that has specifically been developed for children who have ESRD.

Below is a brief description of the purpose and content of the HRQOL survey tools listed in the aforementioned table. The reliability and validity evidence that exists to support clinical and research application of each tool is also presented. The development of clinically useful measurement tools is an iterative process. Clinicians and researchers must work together to determine how best to integrate the assessment of HRQOL into clinical practice and how best to use the information obtained to improve functional outcomes of children with ESRD.

Child Health and Illness Profile-Adolescent Edition

The Child Health and Illness Profile-Adolescent Edition (CHIP-AE) is a 153-item self-report instrument that assesses 6 domains of health status (discomfort, satisfaction, disorders, achievements, resilience, and risks) and takes about 20 min to complete [43, 44]. Reliability (test-retest and internal) and validity (criterion and construct) studies support its use as a generic health status assessment for youth aged 11–17 years [45]. In addition to the CHIP's usefulness in discriminating between healthy and ill adolescents [46], it has also been sensitive to age, gender, and socioeconomic influences [47, 48]. Use of the CHIP-AE was evaluated in a multicenter cross-sectional study in adolescents with CRI, on dialysis and post-transplant [34].

The Children's Health Questionnaire

The Children's Health Questionnaire (CHQ) is a generic HRQOL instrument that has both parent and child versions [49]. The child version is appropriate for administration to children aged 10–18 years and takes about 20 min to complete. The proxy version is appropriate for children aged 5–18 years. The CHQ measures 12 domains of health status (physical functioning, limitations in schoolwork and activities with friends, general health, bodily pain and discomfort, limitations in family activities, emotional/time impact on the parent, impact of emotional or behavior problems on school work and other daily activities, self-esteem, mental health, behavior, family cohesion, and change in health). Internal consistency and concurrent validity have been demonstrated [49]. One advantage of this instrument is that the availability of both parent and youth forms allows for direct and simultaneous comparison of health status perceptions for parents and children. The child-completed CHQ has previously been used in a single-center study with children who have kidney disease and who were maintained on HD [32]. Use of the CHQ-PF50, a parent proxy of HRQOL, has also been evaluated in a multicenter cross-sectional study of health status in adolescents with CRI, on dialysis and post-transplant [33] as well as in a longitudinal study of adolescents with CKD [35].

The Pediatric Quality of Life Inventory

The Pediatric Quality of Life Inventory (PedsQL) is a 23-item generic HRQOL instrument that assesses 5 domains of health (Physical Functioning, Emotional Functioning, Psychosocial Functioning, Social Functioning, and School Functioning) in children and adolescents aged 2–25 years [50]. Internal reliability as well as construct and clinical validity have been demonstrated [51–53]. Parent and youth forms are available.

Table 34.1 Domains of multidimensional pediatric HRQOL measurement instruments

	CHQ-PF 50	CHQ-CF 87	CHIP-AE	PEDS-QL	PEDS-QL ESRD
Number of domains	13	13	6	4	7
Title of domains	Physical functioning, emotional/behavioral role functioning, physical role functioning, bodily pain, general behavior, mental health, self-esteem, general health perceptions, parental impact (emotional), parental impact (time), family activities, family cohesion	Physical functioning, emotional/behavioral role functioning, physical role functioning, bodily pain, general behavior, mental health, self-esteem, general health perceptions, parental impact (emotional), parental impact (time), family activities, family cohesion	Discomfort, disorders, satisfaction with health, achievement, risks, resilience	Physical functioning, emotional functioning, social functioning, school functioning	General fatigue, side effects of kidney disease, treatment problems, family and peer interactions, worry, perceived physical appearance, communication
Age range	5–18	10–18	11–17	2–25	5–25
Rating scale	4–6 point Likert scale	4–6 point Likert scale	3–5 point Likert scale	3–5 point Likert scale	3–5 point Likert scale
Number of items	50	87	107	23	34
Average completion time	20	20	30	10	10
Respondent	Proxy	Patient	Patient	Proxy or patient	Patient

CHQ-PF50 Child Health Questionnaire Parent Version
CHQ-CF87 Child Health Questionnaire Youth Version
CHIP-AE Child Health and Illness Profile-Adolescent Edition
PEDS-QL Pediatric Quality of Life Inventory, Core Scales
PEDS-QL ESRD Pediatric Quality of Life Inventory, End-Stage Renal Disease Module

The inventory takes approximately 5 min to complete. One of the most significant advantages of this instrument is its short length that allows for quick completion by patients and caregivers. Use of the PedsQL has been evaluated in a single-center study and multicenter study of QOL in children with CRI, on dialysis and post-transplant [36, 37]. The PedsQL has also been evaluated in a large multicenter study of children with mild to moderate CKD [54].

PedsQL ESRD Module

The 34-item PedsQL 3.0 ESRD Module developed by Goldstein et al. includes seven scales: (1) general fatigue, (2) side effects of kidney disease, (3) treatment problems, (4) family and peer interactions, (5) worry, (6) perceived physical appearance, and (7) communication. Parallel forms are available for parents of children between the ages of 2 and 18 years and for youth between the ages of 5 and 18 years. The format, instructions, Likert response scale and scoring method are similar to the PedsQL 4.0 Generic Core Scales with higher scores reflecting better HRQOL (fewer symptoms or problems) [55, 56]

Measuring HRQOL in Outpatient Nephrology Clinics

A variety of influences have increased interest in the potential utility of assessing health-related quality of life in pediatric nephrology clinical practices including: (1) pediatric research studies demonstrating the relationship between kidney disease severity and quality of life [33–35, 37, 55, 56], (2) the recent American Academy of Pediatrics recommendation that psychosocial assessments be performed at every well-child visit [57], (3) the belief that assessment of HRQOL could facilitate communication, uncovering patient problems and monitoring response to treatment [3], and (4) the recent CMS mandate to monitor HRQOL in adult patients with ESRD [22].

In spite of the fact that several HRQOL measures have received initial validation for use with pediatric patients with CKD, a number of questions about their use in clinical practice remain unanswered. For example, little research has been done to directly establish clinically meaningful cutoff scores in children with pre end-stage and end-stage kidney disease and to demonstrate test-retest reliability or responsiveness to change [20, 58, 59]. Given the status of current research in this field, there is little evidence base on which to recommend at what intervals these instruments should be administered in the outpatient setting, or what interventions can be made to improve HRQOL if scores are low. To this end, several multicenter research studies are currently underway which will begin to provide the necessary data for allowing the integration of HRQOL assessment into clinical practice [60].

Summary

Recent emphasis on patient-centered assessment of quality of life has been the result of an understanding that patients and their families can best assess the global effects that chronic disease and its medical management have on health. In this chapter, we have reviewed existing generic health status measures for children and adolescents, and summarized current studies evaluating their use in pediatric dialysis patients. Clinically, these tools can be used to assess patient health status over time in response to therapy. In research, these instruments can be used to measure the effectiveness of different medical practices on the health outcomes of children and adolescents with kidney disease. Future research encompassing measures of quality of life in pediatric dialysis is needed to assist health professionals in making more informed clinical decisions, using patient-centered assessments in conjunction with traditional medical and clinical endpoints to judge the “success” of therapy.

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