

# Health-Related Quality of Life in End-Stage Renal Disease Patients: How Often Should We Ask and What Do We Do with the Answer?

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## Key Words

Quality of life · End-stage renal disease · Frequency of assessment

## Abstract

**Background:** End-stage renal disease (ESRD) patients have poor health-related quality of life (HRQOL) comparing to general population and comparable HRQOL to patients with other major chronic diseases. Poor HRQOL is associated with shorter survival. There is a limited threshold to which dialysis dose and parameters management can improve HRQOL in ESRD patients. Numerous studies have sought to find interventions to improve HRQOL. This article is to review the symptoms associated with poor HRQOL and how frequent the quality of life (QOL) should be evaluated to improve the outcome. **Summary:** It is required by the Center for Medicare and Medicaid Services to evaluate HRQOL of dialysis patients annually. KDIGO recommends the symptoms to be assessed regularly and the treatment is redirected toward a patient-centered care model. Studies have shown that measuring patient-reported outcomes frequently, from 4 times a day to every 3–6 months, without intervention did not improve the HRQOL significantly. Appropriate intervention of the symptoms may improve the quality of life (QOL). Studies

in oncology have also showed a similar result. The commonly used tools to evaluate the HRQOL in dialysis patients take up to 30 min for completion. Therefore, frequent assessment of all the symptoms can provide more burden than benefit to the patients. In addition to the annual HRQOL measurements, more frequent evaluation of targeted symptoms can be helpful. For appropriate intervention of the symptoms, effective communication between providers, as well as a multidisciplinary approach, is essential to improve HRQOL and outcomes in dialysis patients. **Key Messages:** Measurement of patient-reported outcomes may provide an opportunity to improve outcomes in ESRD. The frequent measurement of symptoms and QOL may be burdensome. Consider targeted measurement of symptoms to complement HRQOL measurement. Improved communication and the use of a multidisciplinary team provide mechanisms to improve HRQOL in ESRD.

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## Introduction

Health-related quality of life (HRQOL) is multi-dimensional and focuses on the effects of the health status of patients on their quality of life (QOL). Poor HRQOL is

associated with increased risk of mortality and hospitalization in patients with end-stage renal disease (ESRD) [1]. Dialysis patients have compromised HRQOL [1] when compared to the general population and have decrements comparable to patients with other chronic diseases including cancer and heart failure [2].

HRQOL is required by the Center for Medicare and Medicaid Services to be incorporated annually in the care of ESRD patients. Despite improvements in process of care outcomes such as hemoglobin levels, Kt/V and phosphorous control, HRQOL among incident dialysis patients has not substantially improved over the past decade [3] [4]. Numerous studies have sought to identify the interventions that will improve the HRQOL in dialysis population [5, 6]. A key KDIGO Controversies Conference has recommended the need for symptoms assessment and management in dialysis patients [7].

Incorporating HRQOL assessment in the care of ESRD is indeed an essential intervention. The HRQOL assessment in ESRD patients can inform the medical personnel of the effectiveness of treatment interventions such as more or less frequent dialysis or anemia correction. It also plays an important role in improving patient's care, assessing patient's needs, setting treatment goals and monitoring disease progression. However, the lack of improvement in overall HRQOL among dialysis patients over the past decade makes us face some serious questions. Is it because yearly evaluation of symptoms may not be enough to improve the HRQOL? In that case, how frequently should we assess the symptoms? Can evaluation of symptoms on every dialysis session be beneficial toward improving the treatment outcome? This review aims to highlight the most common symptoms attributing to the poor HRQOL and the role of frequent assessment of those symptoms in improving the HRQOL in dialysis population.

### **Frequent Measures of Patient-Reported Outcomes in ESRD**

The literature that evaluates the outcome of HRQOL in dialysis population by frequent assessment is sparse. The frequency of the assessment of patient-reported outcomes in those studies varies from several times a day to every 3–6 months. Bakewell et al. [8] evaluated 88 peritoneal dialysis patients in the United Kingdom every 6 months for 2 years. In the study, the QOL declined over time. Self-assessing QOL every 3 months over a period of 2 years demonstrated that it declined in the initial months

but it remained stable over time in dialysis population [2]. In the study by Gabbay et al. [3], the HRQOL scores of 11,079 hemodialysis patients was evaluated by using SF-36 for 2–4 times per year over a decade. There was no substantial improvement in HRQOL despite improvements in outcomes such as hemoglobin levels, Kt/V and phosphorous control. In the Netherlands Cooperative Study on the Adequacy of Dialysis study, QOL was assessed by SF-36 form at 3, 6, 12 and 18 months after the start of dialysis treatment. The study showed that parameters of adequacy of dialysis were not associated with improved QOL over time [9].

The studies using frequent measurements have demonstrated marked variability in day-to-day scores and across the day among patients with ESRD. Roumelioti et al. [10] evaluated the sleep quality, mood and alertness of patients with kidney diseases daily for 14 consecutive days by using visual analogue scales of the Pittsburgh Sleep Diary and then compared them with those of healthy control subjects. In the study, ESRD patients had worse sleep quality, mood and alertness than control subjects and the symptoms varied day-to-day. In the study by Abdel-Kader et al. [11], the symptoms (subjective vitality, mood and alertness) of 55 hemodialysis patients were assessed 4 times a day for 7 consecutive days by using Day-time Insomnia Symptom Scale. This study found these symptoms were related to both the day of dialysis and the time of day. Fatigue, sleepiness and exhaustion were worsened later in the day and on the dialysis days. These observational studies measuring patient-reported outcomes without targeted interventions have not been associated with improvements in QOL. This variability in scores among patients with ESRD suggests that frequent assessment of symptoms may be problematic given the underlying variability in scores.

### **Use of HRQOL to Inform Patient Care**

There are many studies examining the effects on patient well-being and outcome by evaluating HRQOL [12–15]. The results of using HRQOL to inform patient care have been mixed. Velikova et al. [13] did a randomized controlled trial involving 28 oncologists and 286 cancer patients. The patients were assigned to (a) interventional group in which patients were to complete the QOL questionnaire at regular periods and feedback was provided to physicians, (b) attention-control group where patients were to complete the questionnaires but no feedback was resulted to providers and (c) control group in which no

HRQOL was measured. In the interventional group and the attention-control group, HRQOL was assessed regularly at baseline, third visit (2–3 months), 4 and 6 months. Patients in the intervention and attention-control groups had better QOL compared to those in the control group. The physician–patient communication as well as emotional functioning was improved by routine assessment of HRQOL. Rosenbloom et al. [15] performed a similar study using 213 patients with metastatic breast, lung or colorectal cancer who were randomly assigned to 1 of 3 groups. This study examined a usual care (control group), the HRQOL assessment group (assessment control condition) and the HRQOL assessment followed by structured interview group (structured interview and discussion condition). In this study, there were no statistically significant differences found in HRQOL across the 3 groups. The authors suggested that the routine HRQOL assessments without appropriate intervention are not enough to improve HRQOL. In another randomized controlled trial with 115 inoperable lung cancer patients, the weekly assessment with patient-held QOL diary for 16 weeks without appropriate feedback to healthcare professionals and without the provision of appropriate support had no significant improvement in QOL over time comparing to the standard care group when assessed at baseline and at 2 and 4 months after baseline [14].

### **Symptoms Associated with Poor HRQOL**

ESRD patients have a high burden of physical and emotional symptoms that were associated with impaired HRQOL [16]. Weisbord et al. [16] assessed physical and emotional symptoms in 162 dialysis patients with Dialysis Symptom Index. Among them, more than 50% of patients reported to have dry skin, fatigue, itchiness or bone/joint pain. These physical and emotional symptoms were associated with impaired QOL and depression.

Pruritus is one of the most common symptoms in ESRD patients. According to the DOPPS study, 42% of prevalent dialysis patients experienced moderate to severe pruritus that was associated with poor sleep quality, physician-diagnosed depression and poor HRQOL [17]. In the study by Mathur et al. [18], the worsening of itchiness by 20% or greater in patients with moderate to severe pruritus was associated with significant reduction in HRQOL measures.

Depressive symptoms and pain are commonly reported by patients undergoing dialysis [19–21]. The international, prospective, observational study with more than

10,000 patients demonstrated that nearly 20% of the cohort had depression [20] while in study by Weisbord et al. [21], pain is present in about 50% of the dialysis patients. Belayev et al. [19] also showed that pain and depressive symptoms are independently associated with HRQOL after assessing the pain and depressive symptoms monthly and HRQOL quarterly for 24 months. Both DOPPS [20] and the study by Weisbord et al. [21] demonstrated that depression is associated with increased hospitalization and mortality. HEMO Study had similar results with decrease in survival time from all-cause mortality in patients with low mental health scores [22].

Sleep is also one of the factors related to QOL. The data from CHOICE study showed that approximately 75% of dialysis patients had impaired sleep quality, and 14% of them had a decline in sleep quality in the first year of treatment. Decline in sleep quality was associated with decreased HRQOL and shorter survival [23]. Moreover, many of these symptoms were interconnected and affected by each other [16, 23–25].

The family and health of the patients themselves were also important domains for most of the ESRD patients. It was shown in the study by Abdel-Kader et al. [26] where 151 ESRD and advanced chronic kidney disease patients were evaluated by an instrument that assessed individualized QOL on the basis of patient-identified domains. More than two-thirds of ESRD patients nominated family and health as their important domains.

This underlines the importance of all of these symptoms in the improvement of HRQOL in ESRD patients. Despite the importance of these symptoms on the HRQOL of ESRD patients, treatable symptoms such as pain, pruritus, sexual dysfunction, sleep problems and psychological distress were under-recognized and its severity was underestimated by the renal providers [27]. This strong correlation between symptom burden and HRQOL suggests that interventions to alleviate these symptoms may provide a potential opportunity to improve HRQOL.

### **How to Improve HRQOL in Dialysis Population?**

For our ESRD patients, assessing HRQOL alone may not be enough to improve HRQOL. This position was supported by a recent study of nearly 11,000 patients undergoing hemodialysis in the US showing that there has been no substantial change in mental and physical well-being with the implantation of routine measures of HRQOL [3].

The data for how frequently we should evaluate the HRQOL to improve the outcome are lacking. The most commonly used tools to evaluate the HRQOL, KDQOL and SF-36 require up to 30 min for completion. Therefore, it can be a challenge for the patients to answer these questions very frequently such as daily or every dialysis session or weekly. This can lead to significant missing data and incomplete information [28]. The burden to the patients will be more than the benefit in this scenario.

More recently, the KDIGO Controversies Conference had recommended assessing symptoms regularly and directing treatment toward a patient-centered care model. This model will emphasize the treatment of symptoms that matter to the patients and align the care to the patients' values, preferences and goals [7]. KDIGO also recommended stepwise approach to manage the symptoms with non-pharmacological interventions as first-line and then pharmacological treatments as second-line therapy (table 1) [7].

Assessment and treatment of symptoms is an important opportunity to improve HRQOL in ESRD patients. Weisbord et al. [6] did a randomized trial (SMILE study) in 220 dialysis patients to compare 2 management strategies for pain, erectile dysfunction and depression. In the study, the patients were in observation phase for 2–12 months and then randomized to 12 months participation in 2 arms: (1) feedback intervention in which the symptoms were assessed monthly, renal providers were informed of patients' symptoms, and treatment was dependent upon the providers and (2) management intervention in which symptoms were assessed monthly and trained nurses were used to evaluate patients and facilitate the implementation of treatment recommendations. In this study, both approaches had improvements in symptoms comparing to usual care as shown in figure 1. Evaluation and treatment of depression with sertraline in peritoneal dialysis population improved the HRQOL and symptoms related to depression. In the study, 124 peritoneal dialysis patients were involved and depression as screened by Beck Depression Inventory and HRQOL was evaluated by SF-36. The depressed patients were treated with sertraline for 12 weeks. The side effect of the medication on treatment arm was evaluated biweekly, and the HRQOL and depression were evaluated again after 12 weeks of treatment with sertraline [29]. World Health Organization 3-step analgesic ladder is useful for treating the pain of dialysis population especially for the individuals younger than 65 years of age. In the study by Barakzoy et al. [30], the severity of pain of 45 hemodialysis patients were evaluated by SF McGill Pain Questionnaire and then

**Table 1.** Symptom assessment and management recommendations by KDIGO Controversies Conference [7]

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Symptom assessment and management is an integral component of quality care for patients with advanced chronic kidney disease. Regular global symptom screening using validated tools should be incorporated into routine clinical practice

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Symptom management requires a stepwise approach. First-line treatment includes non-pharmacological interventions and then advancing to more complex therapies. Second-line treatment is pharmacologic therapy. Consideration should be given to low-dose pharmacological therapy that may have efficacy across several symptoms

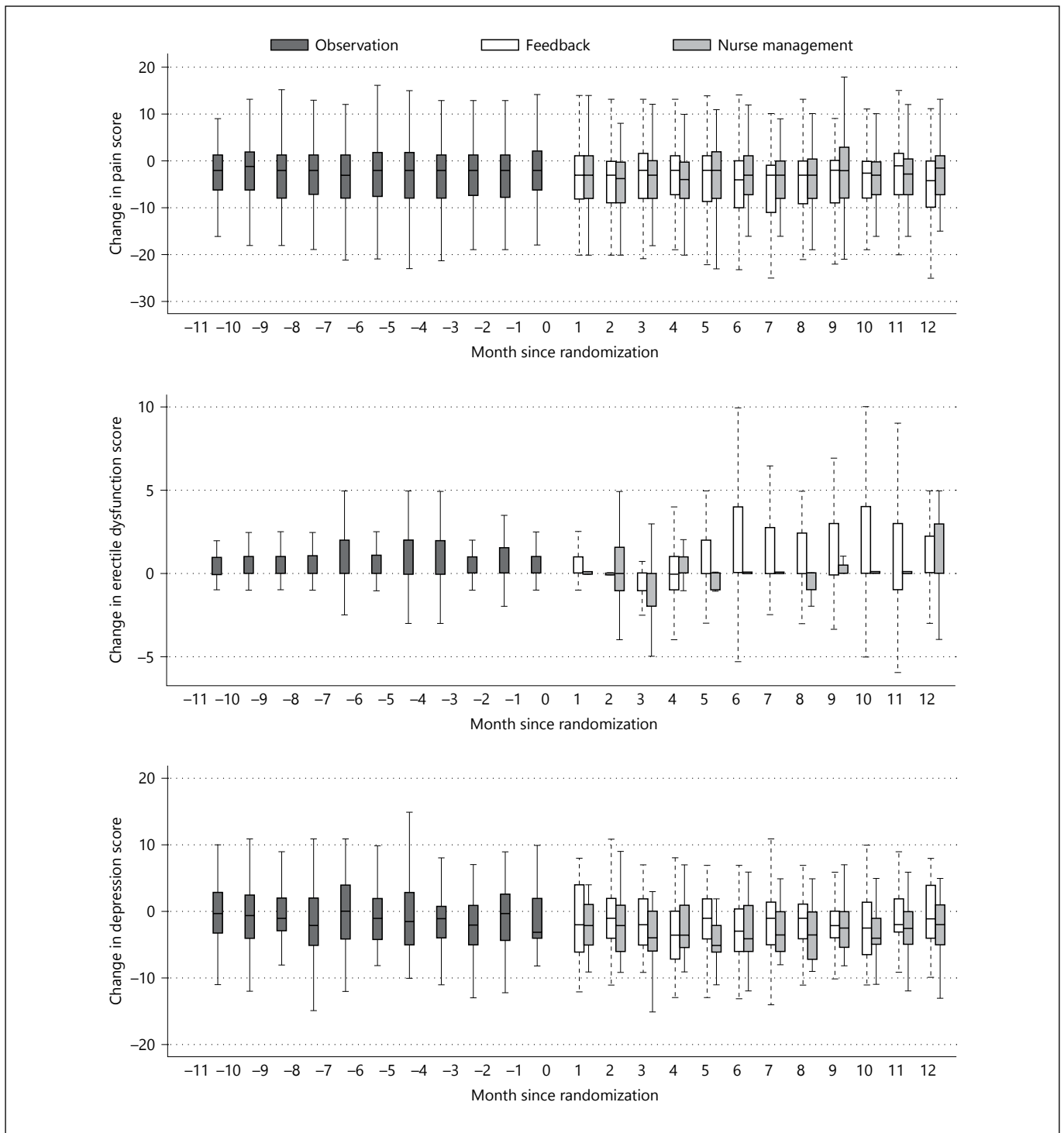
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Symptom management is a research priority in chronic kidney disease. Particular attention is required on the relative effectiveness of management strategies, including the impact on outcomes most relevant to patients such as overall symptom burden, physical function and HRQOL

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treated with World Health Organization analgesic ladder. They were evaluated every week for 4 weeks. At the end of the study, the mean pain score was significantly declined. The formal assessment of pain treatment on the QOL of the patients was not conducted but about half of the patients made comments that treatment of pain provided more restful sleep, better functional status as well as better ability to tolerate dialysis.

In addition to assessing and treating symptoms, there are approaches to improving HRQOL measurement, which may positively influence patient outcomes. With the advancement in technology, assessing symptoms and HRQOL electronically has been an increasing interest. Patient-reported outcomes are captured electronically and then integrated with electronic medical records. It is shown to be an effective way in integrating into existing care pathways and getting timely manner intervention. Some studies showed that it improves HRQOL and is beneficial to the patients [11, 28]. We believe that incorporating technology to HRQOL assessment will increase the patient–doctor communication, lead to more accurate HRQOL and symptoms assessments and decrease the patients' burden of responding to the conventional HRQOL instruments, which are prone to recall bias. This will also provide a practical ground for more frequent HRQOL assessment studies. It is also important to give an adequate social support to ESRD patients. Social functioning is a main component of HRQOL measures. ESRD patients who have more social support were found to have better HRQOL and fewer hospitalizations than those with poor social support [31].



**Fig. 1.** Longitudinal change in symptom score by study phase and intervention arm for patients with pain, erectile dysfunction and depression. The figure adopted from the study by Weisbord et al. [6] with the permission of authors. Pain (change in symptom score):  $p < 0.01$  for feedback vs. observation; erectile dysfunction (change in

symptom score):  $p < 0.01$  for feedback vs. observation,  $p < 0.05$  for nurse management vs. observation; depression (change in symptom score):  $p < 0.01$  for feedback vs. observation,  $p < 0.05$  for nurse management vs. observation.

## Conclusion

We recommend the evaluation of HRQOL on a regular basis. The data for optimal frequency of assessment are lacking, and more studies are necessary for further evaluation. The administrative and patient burden can outweigh the benefits for patients in frequently measuring patient-reported outcomes. We should focus on the patient-centered therapy and treat the symptoms accordingly to improve the overall HRQOL and patients' outcome. During the treatment for symptoms, targeted measurement of symptoms should be considered.

As studies have shown that most renal providers believed non-renal providers are responsible for treatment of these symptoms [32] and pharmacologic therapy was

more commonly prescribed by the primary care physicians [33], communication between the healthcare providers is important. A multidisciplinary team approach to treat the symptoms will be beneficial to improve the QOL and overall care of the dialysis patients.

## Conflicts of Interest

The authors have no financial conflicts of interest or grant support to declare. This Mini-Review has not been previously published or submitted to another journal.

## Disclosure Statement

The authors have nothing to disclose.

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