Longitudinal validation of a modified Edmonton symptom assessment system (ESAS) in haemodialysis patients

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Abstract

Background. Health-related quality of life (HRQL) is an important outcome in the treatment of end-stage renal disease (ESRD) and appears to be highly associated with patient self-report of symptom burden. This study examines the longitudinal validity of the modified Edmonton symptom assessment system (ESAS) to determine the impact of change in symptom burden on the change in HRQL of haemodialysis (HD) patients.

Methods. 261 haemodialysis patients completed the Kidney Disease Quality of Life-Short Form (KDQOL-SF) and the ESAS at baseline and at 6 months.

Results. The change in overall symptom distress score was strongly correlated with the change in KDQOL-SF subscales symptom/problem list (R = -0.73, P < 0.01), effects of kidney disease (R = -0.53, P < 0.01), and burden of kidney disease (R = -0.46, P < 0.01) as well as overall physical health composite (R = -0.58, P < 0.01) and overall mental health composite (R = -0.68, P < 0.01). The change in symptom burden, as described by the ESAS, accounted for 46% of the change in the mental HRQL and 34% of the change in the physical HRQL. There was no correlation between baseline demographics, comorbidity or changes in biochemical markers with changes in either the ESAS or HRQL scores.

Conclusion. The modified ESAS is a simple, valid tool for the longitudinal assessment of physical and psychological symptom burden in ESRD and is responsive to change in HD patients. The use of this symptom assessment scale and improved management of patient symptoms would be expected to positively impact HD patients’ HRQL.

Keywords: haemodialysis; health-related quality of life; pain, symptom assessment; symptom burden

Introduction

Health-related quality of life (HRQL) is an important outcome in the treatment of end-stage renal disease (ESRD) in that it is a critical aspect of health and predicts morbidity and mortality [1–4]. For these reasons, the treatment of patients with ESRD aims not only at prolong life, but also to achieve the greatest possible HRQL. Patients who reach ESRD are becoming older, have considerable comorbidity, and have a high symptom burden [5,6]. Recent research suggests that dialysis patients’ perception of symptom burden may be more important than objective clinical parameters in determining the HRQL in this patient population [7–13]. Symptom assessment, therefore, should be a fundamental component of quality care for patients with ESRD.

Although the most commonly used HRQL instruments in dialysis patients, the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) [14] and the Kidney Disease Quality of Life (KDQOL) [15] questionnaire have items pertaining to physical and psychological symptoms, they do not directly assess patient self-report of troublesome symptoms. In addition, these tools may be time-consuming and difficult for patients to complete. The tools used to evaluate that symptom burden must be simple, easily understood and should take little time to complete. They must be reliable, valid, sensitive, responsive to change and give useful information. The tools should also be a self-report since their outcomes are dependent on the perceptions and live experiences of individual patients.

The Edmonton symptom assessment system (ESAS) is a measurement tool that has been used extensively in palliative care settings [16] and more recently it has been used to assess physical and psychological symptom burden in patients with ESRD [5–9]. It is simple, short and self-completed, avoiding physician and nurse bias. The respondent burden is low, and the instrument can even be successfully completed by subjects close to death. We previously reported on the
reliability and construct validity for the cross-sectional assessment of peritoneal and haemodialysis (HD) patients [9]. This study examines the longitudinal validity of the modified ESAS to determine the impact of change in symptom burden on the change in HRQL of HD patients.

**Subjects and methods**

The Health Research Ethics Board of the University of Alberta approved all study procedures. Prevalent HD patients in the Northern Alberta Renal Program, a Canadian university-based renal programme, were surveyed in May 2004 and again 6 months later in November 2004. Participants included in-centre and satellite HD patients from eight HD units. Patients were excluded if they were <18 years of age, refused to complete the questionnaires or if they were unable to complete the questionnaires due to a language barrier. Patients completed the surveys while on dialysis during a mid-week treatment. The HD nurse administered the questionnaires to those patients who were unable to read or write while on dialysis.

**Measurement tools**

The modified ESAS consists of 10 visual analogue scales with a superimposed 0–10 scale for pain, activity, nausea, pruritus, depression, anxiety, drowsiness, appetite, well-being and shortness of breath. The scale for each symptom is anchored by the words ‘No’ and ‘Severe’ at 0 and 10, respectively (Table 5 as on-line content only). Moderate intensity of any symptom is defined as 4–6 and severe as 7–10 on the Likert scale. A total symptom distress score is calculated by summing of the scores for all 10 symptoms on the ESAS (ranges from 0 to 100).

The KDQOL-SF [15] was constructed for use in the Renal Outcomes Study and is a self-report measure of HRQL developed for individuals with kidney disease that incorporates kidney-disease targeted items as well as a generic core, which was scored using the recommended methods for the RAND-12 [14]. The RAND-12 measures physical and mental dimensions of health and contains the same 12 items as the SF-12, taken from the eight scales of the SF-36/ RAND-36. Six of the 12 items create the physical health composite (PHC) and the remaining six items create the mental health composite (MHC). The derivation of these summary scores is based on item response theory and oblique (correlated) factor rotations. The RAND method of scoring offers several theoretical advantages over the standard SF-12 scoring which is based on the principle component factor analysis with orthogonal factor rotations [17]. The RAND scoring approach better discriminates between known groups and appears more responsive to change [18–21].

The Charlson comorbidity index (CCI) [22] was used to quantify comorbidity. It is commonly used in research with ESRD patients and has been validated specifically for studies on HRQL [23]. The CCI is based on weights for each comorbidity and age class. The weights express the associated risk of mortality and are summed to obtain a final score [24]. Comorbidity was defined in terms of presence or absence of disease at the onset of chronic dialysis treatment. The sample was characterized in terms of demographic variables including age, sex, cause of ESRD, comorbidity and duration of therapy for ESRD. Data on the following clinical parameters: Kt/V, dialysis modality, haemoglobin, calcium, phosphorus and serum albumin concentrations, were also collected.

**Statistical analysis**

SPSS 13.0 for windows was used to perform statistical analyses. A $P < 0.05$ was considered for statistical significance. Patient characteristics were described as frequencies and percentages or as a mean±SD. Descriptive statistics were obtained for the change in ESAS total symptom distress score, PHC, MHC and the KDQOL-SF summary scores: symptom/problem list, effects of kidney disease and burden of kidney disease. We calculated Pearson’s correlation coefficients between change in ESAS and change in the KDQOL-SF summary, PHC and MHC, as well as the change in clinical parameters. We hypothesized that the change in ESAS total symptom distress score would be consistent (i.e. strongly correlated) with the changes in the other patient-reported outcome measures, but only weakly or negligibly associated with various clinical parameters.

Regression analysis was conducted to find the variables associated with change in HRQL (MHC and PHC). In univariate and multivariate regression analysis, the primary outcomes were the change in HRQL and change in ESAS as the independent variable. We adjusted for covariates which might influence the change in HRQL, including age, gender, Caucasian $\text{vs}$ others, diabetic status, modality of dialysis, years on dialysis, CCI and change in clinical parameters. Independent variables significant at $P < 0.2$ in univariate analyses were selected and fit into a multivariate model. Variables found to be statistically significant in the multivariate model ($P < 0.05$) were kept in the final model. As an observational cohort study, we assessed the power of our analyses retrospectively, given the available sample size, to detect an association between the change in clinical parameters and the change in HRQL.

**Results**

Out of 478 eligible HD patients, 456 patients (95%) completed the surveys at baseline. There were no differences in age, gender, cause of ESRD, time on dialysis, or biochemical parameters between the non-responders and the responders. At 6 months, 135 patients were censored for follow-up: 70 patients had died, 15 were acutely ill and physically unable to complete the questionnaire, 35 had been transplanted, 14 had moved to other dialysis units or had been switched to peritoneal dialysis, and one had recovered renal function. Of the remaining 321 patients, 261 (81%) completed both the ESAS and the KQQL-SF at the 6 month follow-up. Patients were elderly (64.1±15.9 years), 57% were male, mostly Caucasian (75.5%) and 43% were diabetic. The CCI was 7.2±2.7 (Table 1). The majority of patients completed the surveys themselves (80.8% at baseline and
multivariate analysis with borderline significance when haemoglobin was added to the model in the change in MHC (Table 4). This only increased to 47% change in symptom burden, as described by the ESAS chemical markers and changes in the ESAS (Table 3). Correlations were negligible between changes in bio-

disease (Figure 1). Also consistent with our hypotheses, (disease (20.2–90.9)

Table 1. Patient characteristics

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>n = 261</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years, mean ± SD (range)</td>
<td>64.1 ± 15.9</td>
<td>(20.2–90.9)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>114</td>
<td>43.7</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>197</td>
<td>75.5</td>
</tr>
<tr>
<td>Aboriginal</td>
<td>23</td>
<td>8.8</td>
</tr>
<tr>
<td>Asian</td>
<td>13</td>
<td>5.0</td>
</tr>
<tr>
<td>Pacific Islander</td>
<td>11</td>
<td>4.2</td>
</tr>
<tr>
<td>Indian Sub-continent</td>
<td>8</td>
<td>3.1</td>
</tr>
<tr>
<td>Black</td>
<td>6</td>
<td>2.3</td>
</tr>
<tr>
<td>Mid-East/Arabian</td>
<td>3</td>
<td>1.1</td>
</tr>
<tr>
<td>Cause of ESRD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>112</td>
<td>42.9</td>
</tr>
<tr>
<td>No</td>
<td>149</td>
<td>57.1</td>
</tr>
<tr>
<td>Years on dialysis</td>
<td>3.8 ± 3.2</td>
<td></td>
</tr>
<tr>
<td>Charlson comorbidity index</td>
<td>7.2 ± 2.7</td>
<td></td>
</tr>
<tr>
<td>Biochemical markers, mean ± SD (range)</td>
<td>Baseline</td>
<td></td>
</tr>
<tr>
<td>Kt/V</td>
<td>1.6 ± 0.3 (0.8–2.8)</td>
<td></td>
</tr>
<tr>
<td>Calcium, mmol/l</td>
<td>2.3 ± 0.2 (1.8–2.9)</td>
<td></td>
</tr>
<tr>
<td>Serum albumin, g/l</td>
<td>37.0 ± 4.0 (21–46)</td>
<td></td>
</tr>
<tr>
<td>Haemoglobin, g/l</td>
<td>113 ± 14 (66–155)</td>
<td></td>
</tr>
<tr>
<td>Phosphorous, mmol/l</td>
<td>1.7 ± 0.6 (0.5–4.7)</td>
<td></td>
</tr>
</tbody>
</table>

82.4% at 6 months). The remaining patients were assisted by their dialysis nurse.

Tiredness, decreased well-being, pruritus and pain were the most common symptoms (Table 2). On an average patients had 7.1 of the 10 symptoms and 4.2–4.5 moderate-to-severe symptoms. About 42–47% of the patients reported moderate or severe pain and 34–39% of them reported moderate or severe anxiety and depression.

Consistent with our hypotheses, changes in ESAS scores were significantly associated with changes in all the measured HRQL scores. The change in overall symptom distress score was strongly correlated with changes in the KDQOL-SF subscales symptom/problem list \( (R = -0.73, P < 0.01) \), effects of kidney disease \( (R = -0.53, P < 0.01) \) and burden of kidney disease \( (R = -0.46, P < 0.01) \) (Table 3) as well as PHC \( (R = -0.58, P < 0.01) \) and MHC \( (R = -0.68, P < 0.01) \) (Figure 1). Also consistent with our hypotheses, correlations were negligible between changes in biochemical markers and changes in the ESAS (Table 3).

The univariate regression analysis indicates that change in symptom burden, as described by the ESAS symptom distress score, accounted for 46% of the change in MHC (Table 4). This only increased to 47% when haemoglobin was added to the model in the multivariate analysis with borderline significance \( (P = 0.07) \). Similarly, only 34% of the change in PHC is explained by the change in the ESAS score. The explained variability in PHC increased only slightly to 38% when the statistically significant variables Kt/V and calcium were included in the multivariate model. Although serum albumin was statistically significantly associated with PHC in the univariate analysis (Table 4), it was not an independent predictor of change in PHC in the multivariate analysis. Only 2–3% variability of the change in PHC is explained in the univariate model by the change in biochemical indices Kt/V (2.2%), serum albumin (2.0%) or calcium (2.7%) (Table 4). Our sample size of 261 patients provided 81% power to detect a minimum change in \( R^2 \) of 0.02 attributed to one or more of these biochemical indices over and above the initial \( R^2 \) of 34% for the PHC.

Discussion

When there is no cure for a chronic illness such as ESRD, an essential healthcare goal must be to maximize HRQL. Unfortunately, HRQL remains much lower for the ESRD population than for the general population [13]. The identification of effective interventions to improve HRQL for ESRD patients is an important clinical objective. In order to address this, the Kidney Dialysis Outcomes Quality Initiative Clinical Practice Guidelines recommend regular assessment of HRQL for all patients with chronic kidney disease [25].

Unfortunately, the role of pain and other physical and psychological symptoms in dialysis patients’ perception of their HRQL appears to have been greatly underappreciated. The ESAS has been shown to be a reliable symptom assessment tool in HD patients with an intraclass correlation coefficient in a 1-week test–retest of 0.70, \( P < 0.01 \), similar to that in cancer patients [9]. Cross sectional validity of the ESAS in HD has been established: total ESAS scores correlate highly with both mental (slope = −0.82 ± 0.07, \( P < 0.01 \)) and physical HRQL (slope = −0.48 ± 0.07, \( P < 0.01 \)) after controlling for potential confounding variables including comorbidity [9]. The ESAS symptom distress score accounted for 29% of the impairment in PHC and 39% of the impairment in MHC. This study demonstrates that the changes in symptom burden using the ESAS are strongly predictive of the changes in KDQOL-SF, a well-recognized HRQL measure for this patient population. In fact, worsening of symptom burden explained 46% and 34% of the deterioration in perceived mental and physical HRQL, respectively, for these HD patients. Our results support the notion that clinical interventions aimed at improving subjective assessment of both physical and mental symptoms would have a tremendously positive impact in HRQL for HD patients [26].

It should be noted, however, that while the correlation between the ESAS and the KDQOL-SF scores were strong (i.e. >0.5), there remained a substantial
In fact, the ESAS is routinely and successfully required for data collection, analysis and reporting are limited patient or staff burden, and the resources be a tool that can be routinely administered with in the dialysis unit. The ESAS, on the other hand, may be cumbersome and impractical for routine assessment way as the ESAS can. HRQL measurement tools can do not guide clinical decision-making in the same KDQOL-SF are not easy to interpret and therefore KDQOL-SF in this sample. HRQL tools such as the captures unique information which complemented the patient-reported measures, indicating that the ESAS proportion of ESAS variance unexplained by the other
distressing symptoms to their assessment of HRQL. This is consistent with a growing body of literature in ESRD, where various demographic and biochemical variables have not demonstrated clinically meaningful associations between either symptom burden [27–29] or HRQL [7,8,10–13]. It is therefore essential to systematically gather patient-reported outcomes to fully evaluate our interventions.

Although studies in ESRD patients have shown that the CCI is significantly associated with HRQL, the variability in comorbidity in these patients could not predict the change in their HRQL. Likewise, anaemia has been associated with reduced HRQL in ESRD [30] and improving anaemia with erythropoietin has been linked to improvements in functioning and well-being [30–36]. However, changes in haemoglobin within the range experienced by these patients could not predict changes in HRQL.

There are limitations to this study. Patients were primarily Caucasian and were recruited from a single programme thus potentially limiting the generalizability of the results. However, other patient demographics are similar to the general Canadian and US dialysis population [37,38]. The ESAS is a non-disease-specific tool, and is therefore not inclusive of the entire repertoire of symptoms experienced by HD patients. However, there are no additional symptoms,
with the exception of insomnia, that have been shown to independently impact HRQL. The addition of insomnia to this tool would likely be beneficial and may further explain the variation seen in both physical and mental HRQL. The simplicity and brevity of this scale is central to its clinical utility. The absence of a correlation between the changes in biochemical parameters and HRQL may reflect too little or too much variation in the biochemical parameters and therefore may not represent a true lack of relationship between the study variables. In this study, however, there was sufficient variability in the biochemical parameters to detect correlations with the ESAS or HRQL scores if a relationship existed. We computed a coefficient of variation (CV) to compare the variability in biochemical parameters relative to the variability seen with the ESAS. The CVs were as follows: ESAS (28.4), Kt/V (4.6), serum albumin (8.3), haemoglobin (22.5), calcium (38.9) and phosphorous (60.9). In addition, as per the sample size calculation, the sample size was sufficient to detect a relationship ($R^2 = 0.02$) between biochemical parameters and HRQL given the variability of the data indicating the variability was not too great. On the other hand, strong and significant correlations were observed between the patient-reported ESAS and HRQL, further emphasizing the disconnection between biochemical parameters and how the patients actually feel, particularly with regards to mental health issues.

Research with the modified ESAS is ongoing to determine its utility in predicting survival and other outcome measures.

The modified ESAS is a simple, valid tool for the longitudinal assessment of physical and psychological

![Fig. 1. Correlation between total symptom burden (ESAS score) and physical (PHC) and mental health composite (MHC) scores.](image-url)

![Table 4. Predictors of change in HRQL variables](table-url)
symptom burden in ESRD and is responsive to change in HD patients. The simplicity of the ESAS allows for its relative easy integration into routine clinical practice. The use of well-validated symptom assessment scales such as this modified ESAS and improved management of patient symptoms appear to be important in the evaluation and clinical care of HD patients and would be expected to positively impact their HRQL.

Acknowledgements. This research was partially funded by the Institute of Health Economics.

Conflict of interest statement. None declared.

References


Received for publication: 4.5.06
Accepted in revised form: 6.6.06