Title:
Symptoms and their recognition in adult haemodialysis patients: interactions with quality of life

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Short Running Title:
Symptoms and quality of life on dialysis
Abstract

**Aim:** We investigated the symptom burden in adults on haemodialysis; the recognition of symptoms by nurses and nephrologists; and the relationship between symptoms and quality of life.

**Methods:** In this cross-sectional observational study, symptoms and quality of life in hemodialysis patients were determined using validated surveys. Nurses and nephrologists independently estimated their patients’ symptoms, and these estimates were compared with patient responses (sensitivity; kappa values for inter-rater agreement). Associations between symptoms and quality of life were assessed using multi-level regression.

**Results:** 43 patients, 18 nurses and 3 nephrologists participated. The commonest symptoms (95%CI) reported by patients were: weakness, 69%(53 to 82); poor mobility, 44%(29 to 60); and drowsiness, 44%(29 to 60). Sensitivity less than 50% was seen towards 11 of 17 symptoms in nurse ratings compared to 15 of 17 in nephrologist ratings. Agreement with patient symptom ratings was mostly “fair” (0.21 - 0.4), with nurses’ scores showing greater agreement than nephrologists’. Physical, mental and kidney disease component summary scores of quality of life were negatively associated with total symptom score and the number of ‘major’ symptoms (r² values 0.3-0.36); while with multivariate regression, 50 to 60% of the variance in these scores was accounted for by parsimonious models containing symptoms such as pain and poor mobility.
Conclusion: Symptom burden worsened quality of life scores in hemodialysis patients. Clinician recognition of symptom burden was inaccurate, although nurses were more accurate than nephrologists. Using patient-completed surveys or including dialysis nurse feedback in routine outpatient settings may help improve symptom recognition by nephrologists.

Key Words
Nurse’s Role
Quality of Life
Renal dialysis
Surveys and Questionnaires
Symptom Assessment
Introduction

Adults on maintenance dialysis experience a poor quality of life (QOL) compared to their peers\(^1\), similar to those experiencing other chronic illnesses such as cancer\(^2,3\). Several studies of dialysis patients in the last three decades have demonstrated poor QOL outcomes, suggesting that despite advancements in renal replacement therapy, QOL has been difficult to improve\(^4-8\).

Patients undergoing maintenance dialysis experience a significant symptom burden, and this can directly influence their perceived QOL\(^6,10-12\). Heath-related quality of life (HRQOL), part of the larger canvas of overall QOL, is a particular area of interest for clinicians. HRQOL is influenced by illness, treatment, and its perceptions, and has been described as a composite of physical, psychological and social domains, each of which is composed of several contributing factors\(^11\). A comprehensive theoretical model detailing how various factors interact in affecting QOL was proposed by Ferrans and colleagues\(^13,14\). In this model, symptoms (physical, emotional and cognitive) have effects on QOL and are also influenced by other variables. Since several symptoms in dialysis patients are amenable to treatment, it can be postulated that reduction of the symptom burden could improve HRQOL. However, the identification and treatment of symptoms in dialysis patients are not straightforward. Suboptimal recognition of patients’ symptoms by their healthcare providers has been described in the dialysis population\(^15\).

We studied symptoms, their recognition and their interaction with QOL in an Australian dialysis population using validated symptom and QOL questionnaires. The purpose of this study was threefold: firstly, to obtain a cross-sectional snapshot of the symptoms and QOL, secondly, to study the recognition of symptoms by healthcare providers (nurses and
nephrologists) and finally, to document the interactions between symptoms, their recognition and QOL.

Methods

Study participants

A cross-sectional survey of maintenance haemodialysis patients, dialysis nurses and nephrologists was conducted at the satellite dialysis facility of a regional hospital in Tasmania, Australia (Australian Standard Geographical Classification Remoteness Area – RA2, Inner Regional)\(^1\). All adult (>18 years old) patients undergoing regular in-centre haemodialysis three times a week (for at least three months before enrolment) were eligible for inclusion. We excluded patients that had been hospitalised in the one month prior to data collection, since being in the hospital would mean greater interaction with the healthcare providers than the usual norm. Consecutive sampling was used, and all eligible patients were offered participation. Since this was an exploratory study within a small population (52 eligible patients in all), no sample size calculation was made. Participating healthcare providers consisted of each patient’s designated ‘primary dialysis nurse’ and treating nephrologist.

Materials & Procedures

The Palliative Outcome Score-Renal (POS-Renal) questionnaire, validated for use in patients with advanced kidney disease, and recommended by recent guidelines, was used to survey symptoms\(^{17-20}\). The POS-Renal lists the same 17 symptoms (e.g., pain, shortness of breath, itching) on both patient-completed and staff-completed forms. Symptoms are rated on a 5-point Likert scale (see below). Healthcare providers independently rated the severity of each symptom in their patients, without seeing the results of patient – completed surveys.
Self-reported QOL scores were collected from patients using the Kidney Diseases Quality of Life-Short Form 1.3 (KDQOL-SF 1.3). Responses to this 80-item questionnaire are used to calculate scores for multiple subscales of QOL, as well as three overall composite scores - the SF-12 Physical Composite [PCS], and SF-12 Mental Composite [MCS]) and the Kidney Disease Component Score (KDCS).

Data collection

The study protocol was approved by the Tasmanian Health and Medical Human Research Ethics Committee (H0013482). Data collection from consenting patients (and their dialysis nurses) occurred during the week prior to their scheduled outpatient visit to their nephrologist. Patients completed the POS-Renal and the KDQOL-SF 1.3 forms.

Nephrologists completed the symptom surveys within 48 hours of seeing the patient in the outpatient clinic. Data was collected from December 2013 to March 2014.

Demographic data collected from the dialysis and hospital records included age, gender, years on dialysis and the presence of comorbidities. Comorbidities and functional status were ascribed as per the treating nephrologist. The Charlson’s Comorbidity Index and the Karnofsky Functional Index were calculated for each patient. Biochemical parameters reported within one month of the data collection week were collected - including haemoglobin, albumin, phosphate and dialysis Kt/V (measured with Diascan© realtime monitoring system, Gambro AB/Baxter International Inc., USA).
Data analysis

Symptom Burden, Sensitivity and Inter-rater Agreement

The total symptom score was used to reflect symptom burden. Symptom scores were converted into categorical variables for sensitivity analysis, with two categories possible; ‘minor’ or ‘major’. Scores of 0 (not at all) and 1 (slightly, but not bothered to be rid of it) were categorised as ‘minor’, while scores of 2 (limits some activity or concentration), 3 (activities/concentration markedly affected), and 4 (unable to think of anything else) were categorised as ‘major’. The number of symptoms reported as major was calculated.

We calculated the sensitivity of symptom recognition using the patients’ reports as the gold standard, shown in Table 1 (as previously described by Weisbord et al)\textsuperscript{15}. Sensitivity \[ \text{sensitivity} = \frac{TP}{TP+FN} \times 100\% \] of recognition – which was the probability of identifying a symptom as ‘major’ when the patient also identifies it as being ‘major’ - was calculated for all the symptoms for both nurses and nephrologists.

A rating for a symptom by patient and by a healthcare provider was considered to be in agreement if both scored it either ‘minor’ or ‘major’. We used the Cohen’s kappa statistic to determine inter-rater ‘agreement’. The kappa statistic is standardised so that a value of zero is ‘exactly that expected by mere chance’ while a value of 1 denotes ‘perfect agreement’\textsuperscript{24}.

Quality of Life

The KDQOL-SF 1.3 was scored using the Microsoft Excel-based KDQOL-SF 1.3 Scoring Program (v2.0)\textsuperscript{26}. This program generates scores for each patient for each of the sub-scales listed above, as well as descriptive statistics and summary scores across all patients.
Relationship between Quality of Life and Symptom Burden

Univariate regression was used to analyse relationships between total symptom score and the number of symptoms reported as ‘major’ with the summary scores of quality of life – Kidney Disease Component Summary (KDCS), Physical Component Summary (PCS) and Mental Component Summary (MCS). We also constructed mixed-effects linear regression models for KDCS, PCS and MCS, using the five most common symptoms in our population. Observations that had missing data for a particular component were excluded from the related analysis. Data analysis was performed using Microsoft Excel and Stata v 12.1 (Stata Corp, USA).

Results

Of 52 patients invited, 43 (82.6%) consented to participate in the study (Table 2). All healthcare providers approached consented to participate, including 3 nephrologists and 18 hemodialysis nurses. The study population was predominantly Caucasian (Caucasian 41, Torres Straits Islander 1, Filipino 1).

Frequency of Symptoms

The mean total symptom score per patient (possible range: 0 to 68) was 16.8 (SD=11.3). On average, patients scored 5 symptoms out of 17 as ‘major’ (range: 1 to 9 symptoms). Among symptoms reported as major by patients, the most common were weakness or lack of energy (in 69%), followed by poor mobility, drowsiness, difficulty sleeping, and shortness of breath (Table 3).

Nurse / Nephrologist Sensitivity and Inter-Rater Agreement

The mean (SD) total symptom score assigned by nurses to their patients was 14 (8.93), and the average (SD) number of symptoms which they recorded as ‘major’ for their patients was 4(4). For nephrologists, the mean (SD) total score was only 5 (6) and the average (SD)
number of symptoms per patient reported as ‘major’ was 1.5 (2).

Sensitivity was less than 50% for nurses in 11 out of 17 symptoms. Among nephrologists, sensitivity was less than 50% in 15 out of 17 symptoms (Table 3). The symptoms that were identified with the highest sensitivity scores were similar for both nurses and nephrologists - poor mobility (reported as major by 41% of patients), feeling depressed (seen in 15% of patients), weakness/lack of energy (seen in 66% of patients) and pain (seen in 27% of patients).

Table 3 lists the values of the kappa statistic of inter-rater agreement. Agreement between nurses and patients was ‘fair’ for 10 symptoms, ‘moderate’ for two and ‘substantial’ for one (poor mobility). For comparisons between doctors and patients, the statistic was reported as ‘fair’ agreement for four symptoms, and ‘moderate’ for two.

Symptoms and effect on QOL

Of the 43 patients in the study, 27 also completed the KDQOL-SF v1.3. There were no significant differences in the demographic characteristics and symptom scores between patients that completed the QOL questionnaires and those that did not. The common symptoms in the two groups were mostly similar.

On univariate analysis, QOL summary scores were negatively correlated with total number of symptoms as follows (Coefficient; 95%CI): KDCS (-0.96; -1.5 to -0.4); PCS (-0.57; -0.94 to -0.2) and MCS (-0.59; -0.98 to -0.2); all p values < 0.005. Similar negative correlation was seen with the number of ‘major’ symptoms as follows (Coefficient; 95%CI): KDCS (-2.5; -4 to -0.98); PCS (-1.56; -2.54 to -0.58) and MCS (-1.72; -2.74 to -0.7); all p values < 0.003.

Using mixed-effects multi-linear regression, we created parsimonious models for the
summary scores of KDCS, PCS and MCS, initially using the most common symptoms along with variables such as age, gender, dialysis vintage, Charlson’s Comorbidity Score and Karnofsky Performance Index (see Table 4). We used a p-value of 0.2 as initial cut-off. After stepwise regression, the model for KDCS (adjusted $r^2 = 0.52$) included the symptom of poor mobility. For the PCS, the model (adjusted $r^2 = 0.5$) included poor mobility and pain. Similarly, the model for MCS (adjusted $r^2 = 0.6$) also included poor mobility and pain.

Symptom recognition and quality of life

Patients’ healthcare providers, as a whole, under-estimated symptom burden (reflected in the total symptom score in the POS-Renal) and severity (estimated as the number of symptoms scored as major). Despite this, on univariate analysis, higher total symptom scores and number of major symptoms recorded by nurses and by nephrologists were correlated with lower QOL summary scores (similar to patient-reported scores). The absolute difference per patient in the total symptom score or the number of major symptoms recorded, compared to their healthcare providers, did not influence QOL scores.

Discussion

A significant burden of symptoms was observed in the haemodialysis patients participating in the study. The most common symptoms were weakness, poor mobility and drowsiness, similar to findings from other studies\textsuperscript{5,6,12,27}. Healthcare providers did not perform well in recognizing the presence or the severity of symptoms, exhibiting low sensitivity rates and poor agreement with patient estimates.

Similar findings were reported by Weisbord and colleagues\textsuperscript{15}, who performed an observational study of 75 patients on hemodialysis and 18 renal providers (nephrologists,
nurse practitioners and nurse managers), with the aim of studying the recognition of symptoms and their severity, using the 30-item Dialysis Symptom Index\textsuperscript{15}. They estimated that providers underreported the presence of 29 of 30 symptoms, underestimated severity in 19 of 30 symptoms and demonstrated a sensitivity rate of <50% in 27 of 30 symptoms. Differences between nephrologists and other types of providers were not reported. Though the study was conducted in a different country and healthcare system compared to our study, the similarities in the findings are clear.

Our study extended the findings of Weisbord and colleagues by comparing nurses and nephrologists, and also by exploring the impact of symptom burden on patients’ QOL. Within our healthcare setting, nephrologists are primarily responsible for symptom management, and we felt it was important to compare their recognition of symptoms with that of nurses. Additionally, we demonstrated an important consequence of persistent symptoms by showing their impact on quality of life scores.

Mean summary scores (for PCS, MCS and KDCS) in our population were similar to the mean scores reported in other studies within Australia and internationally\textsuperscript{28,29}. Higher values for “total symptom score” or “number of major symptoms” were both associated with a lower self-reported QOL, whether scoring was completed by patients, nurses or nephrologists. This underscores the influence of perceived and recognized symptoms on QOL in this population. Our findings are similar to those of a recent study of 893 subjects, where the presence of symptoms such as pain and poor mobility had detrimental effects on health-related QOL\textsuperscript{12}.

Nurses performed better than nephrologists in terms of sensitivity to symptoms and inter-rater agreement with patient estimates. This should be interpreted with caution, however, since we
did not adjust for potential confounders in the patient interaction, such as the influence of gender, or the differences in duration and setting of patient contact (regular, 4-hour dialysis unit interactions for nurses versus the hurried, 20-minute outpatient clinic visit with nephrologists, which occurs once in 6 to 8 weeks in our model). Future research could consider further investigation of the suggestion that different healthcare providers vary in their sensitivity to their patients’ symptom burden.

Additionally, we studied the associations between symptom recognition and QOL scores. Within the limitations placed by the small numbers of healthcare providers and patients, it is worthwhile to note that nephrologists did not perform well in recognizing the symptoms that were significantly associated with summary scores of QOL (sensitivity for poor mobility = 54%, and for pain = 29%). We could not show direct correlations between underestimation of symptoms by healthcare providers (i.e., difference between patient and nephrologist ratings) and QOL scores—this reflects the complexity of the interaction. One can anticipate that symptom amelioration is more likely to affect QOL than mere recognition.

Our study had limitations. The dialysis population studied was almost entirely Caucasian, and results may be different in other areas where linguistic or cultural barriers coexist. Nephrologists' responses could only be collected 24 to 72 hours after a clinic visit. This could have contributed to underreporting of symptoms (compared to nurses) since we relied on the nephrologists’ recall of patient encounters. Nephrologists spent much shorter periods of time with patients compared to nurses. However, this is a realistic representation of current models of care, mirroring how much (or little) time nephrologists have to elicit symptoms or understand QOL experiences.
An important factor limiting the generalizability of our findings and the robustness of the regression is the small sample size. These numbers are indicative of the size of our dialysis facility – in fact, over 80% of the patients consented to participate, as did 100% of the nurses and nephrologists. Additionally, only 65% of patients with recorded symptom burden could comply with the request to return the completed 81-item QOL surveys within one week of the symptom survey, perhaps suggesting that more time ought to have been allotted for submitting QOL data.

Despite these limitations, our study reflects actual clinical practice in a regional Australian dialysis centre, with its limited numbers of patients and healthcare personnel. Therefore, our study has important clinical implications for our current models of care, and we believe these findings need further exploration in a larger sample of patients, clinicians and participating centres. It remains to be seen if similar findings will be obtained in more urban or rural areas, which can differ widely from us in terms of the proportions of nurses and doctors to patients and the models of care employed.

The recognition of symptoms by the treating nephrologists is the first step to providing symptom relief, and there is clearly room for improvement here. We suggest that the clinical review of dialysis patients should deliberately include input from dialysis nurses. Additionally, we recommend the use of a short patient-completed symptom survey, such as the POS-Renal, during the routine outpatient review of dialysis patients. This will enable the comprehensive documentation of patients’ symptoms, and direct the attention of healthcare providers towards troubling symptoms more accurately.
It remains to be seen if more accurate symptom documentation will then lead to appropriate treatment, a reduced symptom burden and subsequently, improvements in health-related QOL. Along this pathway, there are barriers to symptom recognition and to their management, and insufficient evidence that patient-reported symptom documentation improves management or reduces the symptoms themselves. More likely, considering that the symptom burden is but one of the many contributors to health-related QOL, easing the symptom burden may produce only modest benefits. However, patients on dialysis already experience multiple impediments to regaining a satisfactory QOL, and any amelioration of this burden will be meaningful to the individual patient.

Acknowledgements

Mrs. Bridget Brown MSc, CKD Educator, Division of Nephrology, Launceston General Hospital, Tasmania, Australia 7250.
References


19. Murphy EL, Murtagh FEM, Carey I, Sheerin NS. Understanding Symptoms in


Table 1: Symptom classification for estimating the sensitivity of recognition

<table>
<thead>
<tr>
<th>Description</th>
<th>Patient scored as</th>
<th>Staff scored as</th>
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<tbody>
<tr>
<td>True positive (TP)</td>
<td>2, 3 or 4 [Major]</td>
<td>2, 3 or 4 [Major]</td>
</tr>
<tr>
<td>True negative (TN)</td>
<td>0 or 1 [Minor]</td>
<td>0 or 1 [Minor]</td>
</tr>
<tr>
<td>False positive (FP)</td>
<td>0 or 1 [Minor]</td>
<td>2, 3 or 4 [Major]</td>
</tr>
<tr>
<td>False negative (FN)</td>
<td>2, 3 or 4 [Major]</td>
<td>0 or 1 [Minor]</td>
</tr>
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</table>
### Table 2: Characteristics of the Study Population

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patient Data (n=43)</th>
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</thead>
<tbody>
<tr>
<td>Mean Age (SD)</td>
<td>63.9(±15.7)</td>
</tr>
<tr>
<td>Male / Female Gender (%)</td>
<td>63/37</td>
</tr>
<tr>
<td>Mean years on Dialysis (SD)</td>
<td>5.2 (±4.2)</td>
</tr>
<tr>
<td>Mean Charlson's Comorbidity Score (SD)</td>
<td>6.5 (±3.2)</td>
</tr>
<tr>
<td>Mean Karnofsky Score (SD)</td>
<td>70 (±10)</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>40</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>91</td>
</tr>
<tr>
<td>Ischaemic Heart Disease (%)</td>
<td>42</td>
</tr>
<tr>
<td>Peripheral Vascular Disease (%)</td>
<td>33</td>
</tr>
<tr>
<td><strong>Mean Biochemical parameters (SD)</strong></td>
<td></td>
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<tr>
<td>Haemoglobin g/L</td>
<td>113.3 (±13.5)</td>
</tr>
<tr>
<td>Albumin g/L</td>
<td>33 (±3.8)</td>
</tr>
<tr>
<td>Phosphate mmol/L</td>
<td>1.7 (±0.6)</td>
</tr>
<tr>
<td>Kt/V Urea</td>
<td>1.4 (±0.2)</td>
</tr>
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</table>
Table 3: Frequency of Symptoms Reported as “Major”, Sensitivity of Recognition and Agreement with patient reports

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Patients (%) reporting symptom as ‘major’ (n = 43)</th>
<th>Sensitivity – Nurses (%) (95%CI)</th>
<th>Sensitivity – Nephrologists (%)</th>
<th>Kappa statistic†: Nurses</th>
<th>Kappa statistic†: Nephrologists</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weakness/Lack of energy</td>
<td>69 (53-82)</td>
<td>69</td>
<td>54</td>
<td>0.32*</td>
<td>0.23*</td>
</tr>
<tr>
<td>Poor mobility</td>
<td>44 (29-60)</td>
<td>68</td>
<td>58</td>
<td>0.62*</td>
<td>0.51*</td>
</tr>
<tr>
<td>Drowsiness</td>
<td>44 (29-60)</td>
<td>37</td>
<td>11</td>
<td>0.28*</td>
<td>0.11*</td>
</tr>
<tr>
<td>Difficulty sleeping</td>
<td>40 (24-55)</td>
<td>59</td>
<td>6</td>
<td>0.17</td>
<td>0.03</td>
</tr>
<tr>
<td>Shortness of breath</td>
<td>38 (22-52)</td>
<td>31</td>
<td>7</td>
<td>0.37*</td>
<td>0.07*</td>
</tr>
<tr>
<td>Pain</td>
<td>35 (20-49)</td>
<td>64</td>
<td>29</td>
<td>0.48*</td>
<td>0.21*</td>
</tr>
<tr>
<td>Poor appetite</td>
<td>30 (16-45)</td>
<td>38</td>
<td>36</td>
<td>0.14</td>
<td>0.23</td>
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<tr>
<td>Changes in skin</td>
<td>29 (14-42)</td>
<td>42</td>
<td>18</td>
<td>0.37*</td>
<td>0.22*</td>
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<tr>
<td>Nausea</td>
<td>28 (14-42)</td>
<td>38</td>
<td>0</td>
<td>0.37*</td>
<td>0.00</td>
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<tr>
<td>Itching</td>
<td>21 (8-34)</td>
<td>22</td>
<td>13</td>
<td>0.21</td>
<td>0.19*</td>
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<tr>
<td>Restless legs</td>
<td>21 (8-34)</td>
<td>44</td>
<td>0</td>
<td>0.29</td>
<td>0.00</td>
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<tr>
<td>Feeling anxious</td>
<td>19 (6-31)</td>
<td>63</td>
<td>14</td>
<td>0.32*</td>
<td>0.01</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>19 (6-31)</td>
<td>38</td>
<td>14</td>
<td>0.43*</td>
<td>0.22*</td>
</tr>
<tr>
<td>Vomiting</td>
<td>17 (5-28)</td>
<td>29</td>
<td>14</td>
<td>0.23*</td>
<td>0.22*</td>
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<tr>
<td>Feeling depressed</td>
<td>17 (5-28)</td>
<td>67</td>
<td>67</td>
<td>0.39*</td>
<td>0.55*</td>
</tr>
<tr>
<td>Mouth Problems</td>
<td>12 (6-22)</td>
<td>20</td>
<td>0</td>
<td>0.13</td>
<td>-0.02</td>
</tr>
<tr>
<td>Constipation</td>
<td>10 (0-18)</td>
<td>0</td>
<td>0</td>
<td>-0.08</td>
<td>0.00</td>
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</table>

* p Value < 0.05

† Interpretation of kappa statistic of agreement: <0 - Less than chance; 0.01 - 0.2 - Slight; 0.21 - 0.4 – Fair; 0.41 - 0.6 – Moderate; 0.61 - 0.8 – Substantial; 0.81 - 0.99 - Almost Perfect
<table>
<thead>
<tr>
<th>Summary Score</th>
<th>Symptoms correlated†</th>
<th>Coefficient (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>KDCS ($r^2 = 0.52$)</td>
<td>Poor mobility</td>
<td>-21.68 (-31.2 to -12.2)</td>
</tr>
<tr>
<td>PCS ($r^2 = 0.50$)</td>
<td>Poor mobility</td>
<td>-11.98 (-16.91 to -7.05)</td>
</tr>
<tr>
<td>PCS</td>
<td>Poor mobility</td>
<td>-11.61 (-16.91 to -6.3)</td>
</tr>
<tr>
<td>PCS</td>
<td>Pain</td>
<td>-8.98 (-14.2 to -3.8)</td>
</tr>
<tr>
<td>MCS ($r^2 = 0.60$)</td>
<td>Pain</td>
<td>-7.71 (-12.67 to -2.77)</td>
</tr>
</tbody>
</table>

†Adjusted for age, gender, years on dialysis, Karnofsky’s score & Charlson’s comorbidity index