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Title:

Relationships between appetite and quality of life in hemodialysis patients

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Abstract

The aim of this paper was to investigate the association between appetite and Kidney-Disease Specific Quality of Life in maintenance hemodialysis patients. Quality of Life (QoL) was measured using the Kidney Disease Quality Of Life survey. Appetite was measured using self-reported categories and a visual analog scale. Other nutritional parameters included Patient-Generated Subjective Global Assessment (PGSGA), dietary intake, body mass index and biochemical markers C-Reactive Protein and albumin. Even in this well nourished sample (n=62) of hemodialysis patients, PGSGA score (r=-0.629), subjective hunger sensations (r=0.420) and body mass index (r=-0.409) were all significantly associated with the Physical Health Domain of QoL. As self-reported appetite declined, QoL was significantly lower in nine domains which were mostly in the SF36 component and covered social functioning and physical domains. Appetite and other nutritional parameters were not as strongly associated with the Mental Health domain and Kidney Disease Component Summary Domains. Nutritional parameters, especially PGSGA score and appetite, appear to be important components of the physical health domain of QoL. As even small reductions in nutritional status were associated with significantly lower QoL scores, monitoring appetite and nutritional status is an important component of care for hemodialysis patients.

Keywords: Quality of Life – hemodialysis – nutritional status – appetite

Introduction

While maintenance hemodialysis can prolong the lives of patients with chronic kidney disease, maintaining quality of life (QoL) is an important consideration and is one indicator of the effectiveness of the medical care that patients receive (Valderrábano et al. 2001). QoL decreases with the progression of kidney disease and is significantly lower in hemodialysis patients than healthy controls ((Neto et al. 2000); (Gorodetskaya et al. 2005; (Loos-Ayav et al. 2008).

The Kidney Disease Quality of Life (KDQOL) survey has been widely used in this population (including in the international Dialysis Outcomes and Practice Patterns Study (Mapes et al. 2003) and is a valid method of measuring QoL in hemodialysis patients (Hays et al. 1994). It includes the SF-36 as the generic core, supplemented with additional items targeted at the specific concerns of dialysis patients. These include symptoms/problems, effects of kidney disease on daily life, burden of kidney disease, cognitive function, work status, quality of social interaction and sleep. No studies have reported the QoL of Australian hemodialysis patients using this kidney-disease specific approach.

A reduction in self-reported appetite has been closely linked with QoL in hemodialysis patients (Kalantar-Zadeh et al. 2001; (Carrero et al. 2007) although it is unknown whether this is related to the kidney-disease specific components of QoL. Visual Analog Scales (VAS) provide a more useful method of assessing appetite in research compared to categorical methods, as more moderate sample sizes are needed to show clinically meaningful and statistically significant effects. We have previously demonstrated that

VAS are sensitive to detect associations between subjective appetite ratings and a range of nutritional and inflammatory markers in hemodialysis patients (Zabel et al. 2009).

A strong relationship has been demonstrated between nutritional status and QoL in pre-dialysis patients and other populations (Gleason et al. 2002; (Kuehneman et al. 2002; (Davidson et al. 2004; (Hickman et al. 2004; (Isenring et al. 2004; (Wolf et al. 2004). Improvements in nutritional status correlate with improvements in quality of life, both in pre-dialysis chronic kidney disease (Campbell et al. 2008) and other populations (Hickman et al. 2004) (Davidson et al. 2004; (Isenring et al. 2004). Subjective Global Assessment (SGA) and the scored Patient-Generated Subjective Global Assessment (PGSGA) are widely used methods of measuring nutritional status in CKD in Australia (Campbell et al. 2009) as recommended in the Australian Evidence Based Practice Guidelines for the Nutritional Management of Chronic Kidney Disease (Ash et al. 2006), but there is minimal evidence from Australian hemodialysis patients on the relationship between nutritional status and QoL.

The aim of this study was to explore the association between appetite and Kidney-Disease Specific QoL in a sample of maintenance hemodialysis patients.

Methods

This study was granted approval by the hospital (approval numbers 200643 and 2008093) and university (approval number 0800000367) ethics committees and informed consent was obtained from all participants. This was a cross-sectional design where QoL was measured in combination with appetite and a range of other nutritional parameters. Figure 1 details the study design. Data collection occurred in the dialysis unit of two hospitals in Brisbane, Australia. Exclusion criteria were having been on hemodialysis for less than three months or unable to give informed consent due to intellectual impairment or mental illness impairing the ability to follow instructions (this was decided by the medical and nursing staff). Eligible patients were approached for recruitment and 62 agreed to participate. These patients completed the KDQOL survey and were assessed for appetite and other nutritional parameters as described below. Patients were receiving hemodialysis on average three times per week. Demographic information (age, gender, dialysis vintage) and results for blood albumin and C-Reactive Protein (CRP) levels were obtained from the medical records.

Measurement of quality of life

Quality of life was measured using the Kidney Disease Quality of Life (KDQOL) questionnaire which contains the SF-36 as the generic core, supplemented with additional items targeted at the specific concerns of dialysis patients. The reliability and validity of the tool has been demonstrated previously (Hays et al. 1994). The questionnaire was administered during a routine hemodialysis session and patients were encouraged to complete the form independently but were offered assistance if requested. The raw scores were converted to the domains of quality of life using the Kidney

Disease Quality of Life Short Form software version 1.3 (KDQOL-SF™ v1.3 © RAND University). Due to the large number of individual domains (21 domains of QoL compared to a sample size of 62 patients), only the three summary scores (SF12 Physical Health, SF12 Mental Health and the Kidney Disease Component Summary) were used in the analysis for correlation with nutritional parameters.

Measurement of appetite

Sensations of appetite were measured using a Visual Analog Scale (VAS) with the following retrospective question: "Over the past week, in general how hungry have you been feeling?". The VAS is weighted with the extremes at each end (0=Not at all and 100=Extremely) of a 100mm line. This method has previously been shown to be associated with a range of nutritional and inflammatory markers in dialysis patients (Zabel et al. 2009). Appetite was also measured on a categorical scale using the retrospective question developed by Burrowes et al 1996) , which asks patients to record their appetite over the past week using the question "During the past week, how would you rate your appetite?". Response options are very good, good, fair, poor or very poor.

Other nutritional parameters

All nutritional parameters were measured during a routine hemodialysis session. All patients were receiving standardised nutrition care in line with evidence based guidelines (Ash et al. 2006) which included 6 monthly follow-up and adjustment of nutritional care if nutritional recommendations were not met. Nutritional status was assessed using subjective global assessment (SGA) (Detsky et al. 1987) and the scored

137 Patient-Generated Subjective Global Assessment (PG-SGA), both of which have been
138 validated in dialysis patients (Steiber et al. 2004; (Desbrow et al. 2005). The SGA
139 includes a medical history (covering weight change, dietary intake, gastrointestinal
140 symptoms and changes in functional capacity) and physical examination (assessment of
141 muscle stores, ascites and oedema) (Detsky et al. 1987). Patients are assigned to a rating
142 of well-nourished (A), moderately malnourished (B) or severely malnourished (C). The
143 PG-SGA provides a score for each section, and incorporates additional nutrition impact
144 symptoms and presence of metabolic stress. All of the component scores are added (0-
145 35) with the higher the score, the greater risk of malnutrition. Dietary intake was
146 measured for three consecutive days using a self-report food diary. All entries were
147 verified with the patient by the dietitian using food models and the data analysed using
148 the Australian nutrient analysis software Foodworks (Xyris ver 4, Australia). The
149 procedure recommended in the evidence-based guidelines for nutritional management
150 of chronic kidney disease (Ash et al. 2006) was used to calculate energy and protein
151 intake in kJ/kg ideal body weight/day and g/kg ideal body weight/day.
152
153 *Statistical analysis*
154 Data was analysed using SPSS for Windows ver 15.0 (SPSS Inc, Chicago IL, USA).
155 Correlation coefficients (Pearson normal/Spearman not normal) and associated
156 significance level were used to assess the relationship between nutritional parameters
157 and the three summary domains of quality of life. The effect sizes suggested by Cohen
158 (Cohen 1988) were used for interpretation of r-values: 0.1-0.29 small; 0.3-0.49 medium;
159 0.5-1.0 large. ANOVA was used to test for statistically significant differences between
160 QoL for appetite response categories. Due to the amount of missing data (final n=45)

161 for the main summary scores of the SF36 (SF12 Physical Health and SF12 Mental
162 Health) the statistical power was reduced to a level where multivariate analysis was no
163 longer appropriate. Statistical significance was set at $p<0.05$.
164

Results

Most of this sample were well nourished (97% SGA A; PGSGA score 2(0-9)) and the average rating of subjective hunger was in the middle of the VAS at 49mm (scale 0-100mm) (Table 1).

18 patients (29%) self-reported their appetite as very good, 29 patients (47%) as good and 15 patients (24%) as poor or very poor (Table 2). Patients who self-reported a poor or very poor appetite had significantly lower scores in nine domains of QoL including seven in the SF36 component and two in the kidney-disease specific module. There were seven domains of QoL with below average scores (<50; scale 0-100): burden of kidney disease, work status, SF-12 physical and mental health, role limitations-physical, general health and energy/fatigue. The highest score of 90 was for dialysis staff encouragement.

The PGSGA score was associated with all three summary scores of QoL. The strongest correlation was with SF12 Physical Health ($r=-.629$, $p<0.05$) (Table 3). This negative association demonstrates that greater malnutrition via a higher PG-SGA score is associated with a lower quality of life. Hunger ratings were significantly associated with the SF12 Physical Health summary score ($r=0.420$, $p<0.05$). There were statistically significant correlations between protein intake and the SF12 Mental Health. A higher BMI was associated with a lower SF12 Physical Health Domain score ($r=-0.409$, $p<0.05$).

Discussion

This study investigated the link between Kidney Disease-Specific QoL, appetite and other nutritional parameters in a sample of Australian hemodialysis patients. Patients who self-reported a poor or very poor appetite had significantly lower scores in nine domains of QoL and seven of these were in the generic SF36 component of the tool. PGSGA score, BMI and hunger ratings were significantly associated with the SF12 Physical Health Domain of QoL.

Self-reported appetite had a relationship with a range of domains of QoL, both physical (such as SF12 Physical health, pain, general health) and mental/social (social functioning, cognitive function) (Table 2). This suggests that a reduction in appetite has a significant impact on patients' lives (such as in the social aspects of life and enjoyment of food), that goes beyond the impact on food intake and nutritional status. Other studies have also found relationships between appetite and the generic SF36 domains of QoL (Dwyer et al. 2002; (Kalantar-Zadeh et al. 2004; (Carrero et al. 2007) although we could not find any other studies that examined the relationship with kidney disease-specific QoL.

Recent evidence suggests that possible causes of poor appetite in hemodialysis patients include the presence of inflammation and alterations in peptide hormones such as leptin, obestatin and ghrelin (Oner-Iyidogan et al. 2011). We have previously demonstrated that subjective hunger ratings are associated with a range of inflammatory and nutritional parameters in hemodialysis patients (Zabel et al. 2009) and now show an association with QoL as well. The advantage of using a VAS for research purposes is

211 that it is on a continuous scale and therefore allows one to detect clinically meaningful
212 changes with more moderate sample sizes than categorical scales. These results
213 therefore reinforce the importance of a decline in appetite in hemodialysis patients, and
214 assist in describing a quantitative method of measuring appetite which is useful in
215 research.
216
217 One of the advantages of using the scored PGSGA over SGA alone is its ability to
218 detect clinically meaningful changes that may not be obvious when relying solely on the
219 broad categories in the SGA. This became evident in this study where even in this well-
220 nourished sample (97% SGA A, PGSGA 2(0-9)) there were significant associations
221 between nutritional status and QoL. Australian Evidence Based Practice Guidelines for
222 the Nutritional Management of Chronic Kidney Disease (Ash et al. 2006) recommend
223 the use of SGA and PGSGA to measure nutritional status. The SGA has previously been
224 shown to be associated with QoL, with a recent study linking the SGA with the physical
225 summary of SF36 and three kidney-disease specific components of QoL (Mazairac et al.
226 2011). We did not find any previous studies that linked the PGSGA with QoL in
227 hemodialysis patients. This study adds to the evidence by demonstrating that even a
228 small decline in nutritional status may be associated with significant reductions in QoL.
229 This highlights the usefulness of the PGSGA assessment tool in hemodialysis patients.
230
231 A strength of this study was the use of the validated assessment tools SGA and PGSGA
232 to measure nutritional status. Many previous studies have only used single biological
233 markers such as albumin or creatinine to examine the relationship between nutritional
234 status and quality of life. A systematic review and meta-analysis (Spiegel et al. 2008)

found the weighted mean correlation of these markers with SF36 scores was r=0.15 (95%CI: 0.05 to 0.25; 16 studies) for albumin and r=0.29 (95%CI: 0.21 to 0.37; 6 studies) for creatinine. These correlation coefficients from the literature are considerably lower than those found in this study for the PGSGA (r=-0.629, $p<0.05$). This may be explained by the fact that both the quality of life assessment (KDQOL) and the PGSGA are subjective measures while albumin and creatinine are biochemical markers that are not solely related to the nutritional status but may be affected by non-nutritional factors. The PGSGA includes a physical examination of fat, muscle and fluid status and therefore would be expected to relate to an assessment of physical health as measured by the physical health component of the KDQOL. This highlights the importance of using validated nutrition assessment tool such as the PGSGA rather than single biological parameters to measure nutritional status.

In this study, a higher BMI tended to be associated with lower QoL. This result has also been reported in other studies (Kalantar-Zadeh et al. 2006; (Hsieh et al. 2007; (Bossola et al. 2009). Several possible explanations exist for this relationship. Firstly, it reflects that having a high BMI does not necessarily mean a patient is well nourished. In fact, malnutrition is often present and under-diagnosed in overweight patients (Markovic et al. 2009). A higher fat mass has been associated with raised levels of inflammatory cytokines such as IL-6 and TNF-α (Bastard et al. 2006). This may lead to a higher risk of malnutrition via a range of mechanisms including suppression of appetite (Kalantar-Zadeh et al. 2003; (Yao et al. 2004) and protein depletion (Mitch 1998). The higher fat mass combined with the significant fluid shifts that can occur in dialysis patients may mask the loss of lean body mass and decline in nutritional status (sarcopenic obesity).

Another potential explanation is that a higher overall body mass may make activities of daily living more difficult which may reflect in a lower score in the physical health component of quality of life. Further, this reinforces the importance of using validated, multi-component nutrition assessment tools such as the PGSGA to measure nutritional status.

We did not find a relationship between CRP and quality of life. Of three previous studies, none found a significant relationship with CRP (Fujisawa et al. 2000; (Kalantar-Zadeh et al. 2001); (Hung et al. 2002), TNF or IL-1 (Hung et al. 2002). This may be due to these relationships being a comparison between biological markers with the subjective measure of QoL. While recent studies have increasingly found associations between bio-markers of inflammation and appetite (peptides such as leptin and ghrelin) (Mafra et al. 2011), other studies have not found associations when comparing appetite peptides and inflammatory markers to subjective methods of measuring appetite (Zabel et al. 2009). Control over biological markers is complex and may be altered by the disease process and progression and this may explain the lack of relationships.

While the nutritional parameters measured had a strong relationship with the SF12 Physical Health domain, the relationship with the other summary scores (SF12 Mental Health and Kidney Disease Component Summary) was lower. Only the PGSGA and protein intake were moderately associated with these components. Therefore while nutrition is an important consideration for the Physical Health component of QoL, there

282 are likely to be other factors that impact more on the mental health and kidney-disease
283 specific components.
284
285 There are a number of limitations to this study. There was a significant amount of
286 missing data in the summary components of SF12 Physical Health and SF12 Mental
287 Health. This is due to the summary components of the survey being reliant on a
288 complete dataset for each individual component for each patient. Therefore if a patient
289 did not fully complete even one individual question, the entire summary component
290 cannot be calculated. This is a significant limitation of the KDQOL-SF survey tool and
291 accompanying software. The survey was mostly self-administered then analysed later,
292 with assistance being offered if requested. In future it may be helpful to provide more
293 one-on-one assistance and checking at the time of survey completion to ensure a
294 complete dataset. The overall sample size was relatively small and the low rates of
295 malnutrition mean the results may not be generalizable to malnourished hemodialysis
296 patients.
297
298 Nutritional parameters including appetite appear to have an important impact on the
299 QoL of hemodialysis patients, and this covered both physical functioning and social
300 wellbeing domains. It appears that there are minimal relationships between appetite and
301 the kidney-disease specific components of QoL. Even in a well-nourished sample, there
302 were strong relationships between nutritional parameters and QoL. This highlights the
303 need to monitor nutritional status and appetite as even small reductions were strongly
304 associated with a decline in QoL.

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Conflict of interest statement

The funding bodies had no involvement in the study design, collection, analysis and interpretation of data, writing of the manuscript or decision to submit the manuscript for publication. There are no conflicts of interest to declare.

Statement of authorship

RZ designed the study, collected and analysed the data and wrote the manuscript. SA, NK, PJ and JB also designed the study and provided critical review of the data and manuscript. All authors read and approved the final manuscript.

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448 Table 1: Characteristics of 62 hemodialysis patients

	Mean (SD)
Age, years	63 (16)
Gender, % male	40%
Dialysis vintage, months	23 (3-207)†
SGA rating, %	97% SGA A
PGSGA score	2 (0-9)†
Protein intake (g/kg IBW/d)	1.2 (0.5)
Energy intake (kJ/kg IBW/d)	101 (35)
Body Mass Index (kg/m^2)	27 (6.9)
Hunger, mm	49 (26)
CRP, mg/L	4 (0-76)†
Albumin, g/L	37 (5)

449 † median (range)

450

451 Table 2: Relationship between quality of life and self-reported appetite (overall n=62)

	Mean (SD) QoL score according to self-reported appetite			**Overall average score for each domain of quality of life**	
	Very good N=18	Good N=29	Fair/Poor N=15	Mean(SD)	Number of complete and valid responses
SF-12 Physical health	43 (11)	39 (9)	28 (12)*	38 (11)	45
SF-12 Mental health	50 (11)	48 (12)	43 (14)	48 (12)	45
Cognitive function	86 (18)	85 (21)	64 (24)*	80 (22)	52
Overall health	62 (20)	61 (23)	46 (18)	58 (22)	60
Physical functioning	57 (32)	52 (28)	22 (23)*	46 (31)	61
Role limitations-physical	51 (45)	38 (43)	21 (36)	39 (43)	59
Pain	74 (25)	76 (24)	44 (33)*	68 (29)	61
General health	52 (27)	49 (22)	31 (21)*	46 (24)	61
Emotional wellbeing	80 (20)	80 (20)	64 (21)	76 (21)	61
Role limitations-emotional	76 (37)	58 (47)	58 (45)	63 (44)	57
Social functioning	72 (25)	66 (33)	36 (30)*	60 (33)	61

Energy/fatigue	52 (20)	52 (24)	25 (26)*	46 (26)	59
Symptom/problem list	78 (16)	82 (15)	64 (13)*	77 (16)	57
Effects of kidney disease	65 (30)	66 (29)	45 (25)	60 (29)	56
Burden of kidney disease	45 (35)	50 (30)	17 (21)*	41 (32)	61
Work status	35 (42)	31 (39)	32 (37)	33 (39)	60
Quality of social interaction	81 (16)	81 (16)	72 (23)	79 (18)	52
Sleep	71 (19)	62 (22)	54 (21)	63 (22)	60
Social support	81 (30)	72 (26)	74 (21)	75 (26)	59
Dialysis staff encouragement	90 (22)	78 (21)	87 (17)	84 (21)	58
Patient satisfaction	80 (27)	72 (24)	70 (22)	74 (24)	59

*P<0.05 [Indicates average QoL scores are significantly different in each appetite category, analysed using ANOVA]

457 Table 3: Association between nutritional parameters and summary scores of quality of
458 life (n=45 complete and valid responses out of the total sample of 62 patients)

	SF12 Physical Health	SF-12 Mental Health	Kidney Disease Component Summary
	Pearson's Correlation co-efficient (r-value)		
Age	-0.324*	0.112	0.112
Dialysis vintage	0.140†	0.041†	-0.008†
PGSGA	-0.629*†	-0.323*†	-0.313*†
Hunger ratings	0.420*	-0.079	-0.079
Energy intake	0.040	-0.202	0.013
Protein intake	-0.104	-0.354*	-0.332*
C-Reactive Protein	-0.122†	0.067†	0.060†
Albumin	0.254	0.116	0.092
Body Mass Index	-0.409*	0.100	-0.167

459 † Spearman's correlation co-efficient (r-value)

460 * $p<0.05$

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