

# Predictors of health-related quality of life perceived by end-stage renal disease patients under online-hemodiafiltration

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## Introduction

Patients' perception of health quality of life (HRQOL) is a consistent and powerful predictor that affects the outcome of end-stage renal disease (ESRD) patients under dialysis.

Patients with ESRD have a high mortality rate that far exceeds the mortality rate for the non-ESRD population. Our present knowledge of the mechanisms leading to increased death in this context is incomplete. In the last years, this medical field has known significant technological and pharmacological improvements. Although some evidence may suggest that mortality rate among dialysis patients have decreased over the last few years, actually, patient's survival is still low. Cardiovascular disease (CVD) has been considered the most common cause of death in these patients.

In recent years, in addition to mortality and morbidity, health-related quality of life (HRQOL) in ESRD patients has become a focus of interest in the evaluation of the individual strategy of treatment, to determine the efficacy of medical intervention, and to evaluate the quality of medical care. Some reports have showed that questionnaire-derived assessment of HRQOL is a strong and independent predictor of mortality and morbidity in ESRD patients

This study aims to identify factors that could predict the HRQOL among ESRD patients under online-hemodiafiltration (OL-HDF).

## Material and Methods

### Patients and study design

In this transversal study, we evaluated 322 ESRD patients (59.63% males; 64.9 ± 14.3 years old) under online hemodiafiltration (OL-HDF), from five dialysis units in the north of Portugal. Socio-demographic data, comorbidities, hematological data, iron status, dialysis adequacy, nutritional and inflammatory markers were collected from patients records. Furthermore, patient's reported HRQOL score, by using the Kidney Disease Quality of Life-Short Form (KDQOL-SF) was assessed. The study was conducted to assess the predictors of quality of life among sociodemographic, laboratorial and clinical variables, in ESRD patients divided into quartiles based on their HRQOL perception, first quartile (n = 80), the second quartile (n = 81), the third quartile (n = 81), and the last quartile (n = 80). The main causes of renal failure, in our group of patients, were diabetic nephropathy (n=116), hypertensive nephrosclerosis (n=45), other diseases and/or uncertain etiology (n=136). Patients were under therapeutic dialysis three times per week for the duration of 3-5 hours each session.

For OL-HDF procedure, Fresenius Medical Care dialysis machines (model 5008) and synthetic high-flux polysulfone dialyzers (Fresenius Medical Care, Bad Hamburg, Germany) were used. Patients were excluded if they: (1) do not accept to participate in the study; (2) under 18 years old; (3) were cognitively impaired; (4) had a severe speech or hearing impairment; (5) in the dialysis program for less than three month; (6) patients with malignancy, autoimmune disease, and with inflammatory or infectious diseases. At starting the study, the patients were clinically evaluated and blood samples were collected for biannual analytical evaluation; KDQOL-SF questionnaire was self-administered to all patients. This survey collects data on age, gender, time under dialysis, etiology of kidney disease, hematological data, iron status, and dialysis, inflammatory and nutritional markers. Laboratory data were obtained by using standard techniques.

### Kidney Disease Quality of Life Questionnaire-Short Form

HRQOL was assessed with the validated instrument KDQOL-SF version 1.3 for Portuguese population, which has been distributed in the beginning of dialysis session, and the patients were helped to fill out the forms, if necessary. The KDQOL-SF can be divided in a generic part and in a disease-specific part. The generic part is formed by the Short Form with 35 questions (SF-36) version 2. The SF-36 can be divided in 8 domains: the patient's physical functioning (10 items); role physical (4 items); pain (2 items); general health (5 items), emotional well-being (5 items); role-emotional (3 items); social functioning (2 items); and energy and fatigue (4 items). The questions used for the kidney disease component summary are not part of the SF-36 (18). They are included in the KDQOL-SF to take into account particular health-related concerns of individuals with kidney diseases and ESRD patients treated by dialysis. The disease-specific part of the KDQOL-SF consists of 43 kidney disease-targeted questions. The responses to these items are condensed in 11 domains: symptom/problems (12 items), effects of kidney disease (8 items), burden of kidney disease (4 items), work status (2 items), cognitive function (3 items), quality of social interaction (3 items), sexual function (2 items), sleep (4 items), social support (2 items), staff encouragement (2 items) and patient satisfaction (1 item). The scores of the mental component summary (MCS) and the physical component summary (PCS) were derived from the eight different domains, originally developed for the SF-36 Short-Form Health Survey (SF-36). The domains included in PCS are physical functioning, role-physical, pain and general health, and in MCS are vitality, social functioning, role-emotional, and mental health.

### Statistical analysis

All variables are reported as mean ± standard deviation or as proportions. Data were analyzed using the program SPSS 21.0 for Windows (SPSS, Inc., Chicago, IL). The Normality of data was tested using the Kolmogorov-Smirnov test. Multiple comparisons between groups were performed by one-way ANOVA supplemented with Tukey's HSD Post Hoc test. Differences between groups were analyzed by using Student t-test or Mann-Whitney test, according to the results obtained in the Kolmogorov-Smirnov test. The association between categorical variables was analyzed using the chi-squared test or Fisher's exact test. Pearson's rank correlation coefficient was used to evaluate relationships between sets of data. P<0.05 was accepted as statistically significant. Mental and physical components summary of SF-36 were calculated. It included a Z-score transformation for each dimension, followed by an arithmetic component (\*10+50), added after the sum of the Z-transformed corresponding dimensions of each component summary. The raw and adjusted analyses of the SF-36 scores were performed using multiple linear regression. KDQOL-SF total score, SF-36 physical and mental component summaries were used as dependent variables and the socio-demographic, laboratorial and clinical variables were used as independent variables. The adjustment model for linear regression was of backwards type, i.e. all the variables were included in the initial model and, through successive exclusions, only the variables that showed a value of p < 0.05 were kept in the model.

## Results

Patients with higher total score of HRQOL showed a significant increased age, mean cell volume (MCV), mean cell hemoglobin concentration (MCHC), urea and creatinine serum levels, and a decrease in RDW. A trend (p=0.1) for higher hemoglobin concentration was found in patients with higher total score of HRQOL. Moreover, the highest total score of HRQOL was associated with a higher proportion of males, and with a lower proportion of diabetic patients and central venous catheter use. For multiple linear regression analysis, we included variables presenting a p value less than 0.1 in the ANOVA analysis. The model included the following independent variables: age, home-clinic distance, gender (male), type of vascular access (arteriovenous fistula), presence of diabetes, body mass index, hemoglobin concentration, MCV, MCHC, RDW and serum levels of potassium, creatinine, urea and total proteins. Our results showed three significant predictors of HRQOL: RDW, gender (male) and diabetes. Linear regression equation can be written as: HRQOL = 62.66 - 2.32 X RDW + 6.37 X gender (male) - 6.46 X diabetes (yes). The final model explained 12.1% of the variation of total score of HRQOL.

Table I – HRQOL results based on the KDQOL-SF instrument for ESRD patients on OL-HDF patients.

	ESRD patients total Score of HRQL (n = 322)
<b>ESRD-targeted Areas</b>	
Symptoms/problem list	76.10 (16.46)
Effects of kidney disease	66.52 (21.05)
Burden of kidney disease	25.14 (24.49)
Work status	12.54 (28.38)
Cognitive function	77.77 (20.04)
Quality of social interaction	81.36 (19.43)
Sexual function	78.03 (26.78)
Sleep	40.06 (15.31)
Social support	81.23 (28.51)
<b>Dialysis care</b>	
Staff encouragement	89.46 (20.78)
Patient satisfaction	59.35 (23.21)
<b>36-item health survey (SF-36)</b>	
Physical functioning	44.41 (30.76)
Role-physical	26.89 (32.67)
Pain	63.14 (29.75)
General health	35.12 (21.87)
Emotional well-being	61.45 (24.91)
Role-emotional	45.27 (31.71)
Energy/ Fatigue	48.33 (19.77)
Social function	68.19 (34.50)
<b>Total score, physical and mental components summary</b>	
PCS	49.75 (9.44)
MCS	50.17 (9.51)
Score Total	53.17 (15.31)

Results are presented as median (SD). PCS: physical component summary; MCS: mental component summary.

Table II – Clinical data, hematological and biochemical data, nutritional markers and dialysis adequacy for ESRD patients on OL-HDF, according to HRQOL (quartiles).

	ESRD patients 1st quartile total score of HROQL (n = 80)	ESRD patients 2nd quartile total score of HROQL (n = 81)	ESRD patients 3rd quartile total score of HROQL (n = 81)	ESRD patients 4th quartile total score of HROQL (n = 80)	P-value ANOVA
<b>Clinical data and dialysis adequacy markers</b>					
CVC use, n (%)	26 (32.5)	15 (18.7)	17 (21.0)	12 (15.0)	0.04#
AVF use, n (%)	54 (67.5)	65 (81.3)	64 (79.0)	68 (85.0)	p<0.005#
Diabetic patients, n (%)	28 (39.4)	40 (51.9)	29 (38.2)	19 (23.8)	0.01#
Hypertensive patients, n (%)	10 (12.5)	11 (13.6)	12 (14.8)	13 (16.3)	0.92#
Previous time on dialysis, months	76.85 (160.92)	58.20 (100.9)	66.26 (146.70)	52.54 (56.3)	0.62
URR, %	1.67 (0.52)	1.68 (0.35)	1.68 (0.48)	1.84 (1.61)	0.91
KT/Ve	125.80 (35.81)	136.88 (39.63)	136.84 (38.82)	148.11 (38.32)	0.82
Creatinine, mg/dL	6.53 (3.11)	7.66 (2.83)	8.05 (2.76)a	8.14 (3.00) a,b	p<0.001
Darbeopoeitin, µg/kg/week	0.48 (0.48)	0.50 (0.48)	0.48 (0.71)	0.46 (0.38)	0.91
<b>Hematological data</b>					
Hemoglobin, g/dL	11.41 (1.23)	11.49 (1.30)	11.88 (1.64)	11.74 (1.25)	0.10
Hematocrit, %	35.66 (3.87)	35.50 (4.22)	36.40 (4.96)	36.02 (3.77)	0.54
Erythrocytes, x10 <sup>12</sup> /L	3.75 (0.43)	3.80 (0.52)	3.82 (0.58)	3.74 (0.48)	0.70
MCV, fl	95.75 (5.74)	93.74 (5.79)	95.63 (5.92)	96.60 (5.79)b	0.02
MCH, pg	30.22 (4.00)	30.40 (2.09)	30.76 (4.01)	31.09 (4.10)	0.44
MCHC, g/dL	31.05 (1.01)	32.42 (1.11) a	32.57 (1.12) a	32.59 (1.02) a	p<0.001
RDW, %	15.35 (1.77)	14.76 (1.50)	14.38 (1.23) a	14.25 (0.95) a	p<0.001
White blood cells, x10 <sup>9</sup> /L	6.77 (2.03)	6.73 (2.45)	2.72 (2.88)	6.48 (1.99)	0.86
Neutrophil/Lymphocyte ratio	2.93 (1.23)	2.76 (1.45)	2.93 (1.63)	2.76 (1.30)	0.77
<b>Iron status</b>					
Iron, mg/dL	64.81 (32.04)	66.15 (24.63)	72.37 (33.02)	72.57 (27.02)	0.22
Transferrin, mg/dL	208.43 (122.94)	193.83 (69.74)	198.43 (71.70)	195.57 (67.30)	0.72
Transferrin saturation, %	25.42 (13.09)	26.59 (11.80)	27.84 (12.11)	29.13 (14.83)	0.31
Ferritin, ng/mL	415.30 (283.04)	396.77 (234.39)	384.09 (257.90)	403.17 (184.24)	0.88
<b>Inflammatory markers</b>					
CRP, mg/dL	10.52 (13.27)	10.52 (21.16)	10.11 (15.89)	7.54 (11.76)	0.73
<b>Nutritional markers</b>					
Albumin, g/dL	41.02 (11.42)	43.21 (12.38)	42.19 (9.15)	43.81 (9.14)	0.38
BMI, Kg/m <sup>2</sup>	25.91 (5.35)	26.50 (4.82)	25.06 (3.82)	25.05 (3.69)	0.11
nPCR, g/kg/day	1.34 (0.62)	1.38 (0.64)	1.32 (0.56)	1.42 (0.61)	0.74

Results are presented as median (SD). # chi-squared test or Fisher's exact test. a) p< 0.05 vs. 1st quartile total score of HROQL; b) p< 0.05 vs. 2nd quartile total score of HROQL. CVC: central venous catheter; AVF: arteriovenous fistula; URR: urea reduction ratio; MCV: mean cell volume; MCH: mean cell hemoglobin; MCHC: mean cell hemoglobin concentration; RDW: red blood cell distribution width; CRP: C-reactive protein; BMI: body mass index; nPCR: normalized protein catabolic rate.

Table III- Multivariate linear regression models for total score

Final models	β	S.E.	R <sup>2</sup>	95% CI	p-value
<b>Total Score</b>					
Constant (β0)	80.46	16.42		(55.89 ; 105.02)	p<0.001
RDW	-2.15	0.83		(-3.78 ; -.51)	p<0.01
Gender (male)	6.39	2.52	0.12	(1.40 ; 11.37)	p<0.05
Diabetes (yes)	-6.02	2.53		(-11.04 ; -1.00)	p<0.05

## Conclusion

Our results showed that associated morbidities, specially diabetes, gender and erythropoietic disturbances are independent predictors of HRQOL in patients under OL-HDF.

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