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Review of studies on health related quality of life in patients with advanced chronic kidney disease in Spain

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ABSTRACT

Background: Advanced chronic kidney disease (ACKD) has a great impact on health-related quality of life (HRQL). The use of this variable in studies in our field is becoming more frequent, although there has been no comprehensive review of how Spaniards with ACKD are assessed. **Aims:** To offer a contrasted vision of the HRQL assessment tools that are most often used on Spanish ACKD population, also analysing how this population perceive their quality of life. **Method:** A review was carried out on literature published on studies undertaken in Spain that had used some kind of instrument, either generic or specific, in order to measure HRQL in patients with different stages of ACKD. Studies in kidney transplant patients were excluded when they were independently reviewed. The research was carried out in CINAHL, CUIDEN, DOCUMED, EMBASE, ERIC (USDE), IME, LILACS, MEDLINE, Nursin@ovid, PubMed, Scielo, Web of Science and TESEO. **Results:** 53 articles published between 1995 and May 2014 have been included in this review. Renal replacement therapy is the variable that is most often associated with the study of HRQL, with haemodialysis being the most studied. Most of the studies found are cross-sectional and the Short Form-36 Health Survey is the most used instrument. **Conclusions:** The majority of the studies show how HRQL is significantly affected in patients who receive renal replacement therapy. These results are independent from the instrument used to measure health-related quality of life and other associated variables throughout the various studies. HRQL has been particularly analysed in patients on haemodialysis, using mainly observational methods and the Short Form-36 Health Survey. There is a need for more studies that address aspects such as HRQL in the pre-dialysis phase, as well as studies with larger samples and longitudinal, analytical and experimental designs.

Keywords: Quality of life. Chronic kidney disease. Renal dialysis. End-stage renal disease.

Revisión de estudios sobre calidad de vida relacionada con la salud en la enfermedad renal crónica avanzada en España

RESUMEN

Antecedentes: *La enfermedad renal crónica avanzada (ERCA) tiene un gran impacto sobre la calidad de vida relacionada con la salud (CVRS). Cada vez es más frecuente el uso de esta variable en estudios en nuestro medio, aunque no se dispone de una revisión global sobre cómo se ha estudiado en población con ERCA española.* ***Objetivos:*** *Ofrecer una visión contrastada de los instrumentos de evaluación de la CVRS más usados en la población española con ERCA, analizando además la calidad de vida percibida por esta población.* ***Métodos:*** *Se llevó a cabo una revisión de la literatura publicada sobre estudios realizados en España que hubieran empleado algún instrumento para medir la CVRS, genérico o específico, en pacientes con diferentes estadios de ERCA. Se excluyeron estudios en pacientes trasplantados renales cuando eran estudiados de forma independiente. La búsqueda se realizó en CINAHL, CUIDEN, DOCUMED, EMBASE, ERIC (USDE), IME, LILACS, MEDLINE, Nursin@ovid, PubMed, Scielo, Web of Science y TESEO.* ***Resultados:*** *Se han incluido en esta revisión 53 artículos publicados entre el año 1995 y el mes de mayo de 2014. La terapia sustitutiva renal es la variable con mayor frecuencia asociada al estudio de la CVRS, siendo la hemodiálisis la más estudiada. La mayoría de los estudios encontrados son transversales y el Short Form-36 Health Survey es el instrumento más usado.* ***Conclusiones:*** *La mayoría de los estudios muestra cómo la CVRS se ve afectada de forma importante en pacientes que reciben terapia sustitutiva renal. Estos resultados se muestran independientes del instrumento usado para medir la calidad de vida relacionada con la salud y de otras variables asociadas a lo largo de los distintos estudios. La CVRS ha sido analizada especialmente en pacientes en hemodiálisis, con diseños fundamentalmente observacionales y con el Short Form-36 Health Survey. Se necesitan más estudios que aborden aspectos como la CVRS en la etapa prediálisis, así como estudios con muestras más grandes y diseños longitudinales, analíticos o experimentales.*

Palabras clave: *Calidad de vida. Insuficiencia renal crónica. Diálisis renal. Enfermedad renal crónica avanzada.*

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INTRODUCTION

Advanced chronic kidney disease (CKD) is a condition which by its nature has a great impact on health related

quality of life (HRQL). From the initial stages of the disease to its end stage, symptoms, restrictions (especially dietary) and its treatment affect the daily life of these patients.

The guidelines Kidney Disease Outcomes Quality Initiative (K/DOQI)[1] on chronic kidney disease state that in the course of this disease patient HRQL deteriorates, and that this is related to demographic factors (age, sex, education level, economic situation, etc.), with the complications of CKD (anaemia, malnutrition, etc.), with diseases that cause this disease (hypertension, diabetes, etc.) or with impaired renal function itself. Based on this, they advise that in all patients with a glomerular filtration rate below 60ml/min (stage III), HRQL is evaluated regularly in order to establish baseline function and monitor changes occurring over time as well as to evaluate the effects of various interventions on HRQL[1]. Baseline HRQL is of great importance to assess the results of interventions made during outpatient follow-up by doctors and nurses.

In 1994 the World *Health Organization Quality* of *Life Group* (WHOQOL)[2], was created, which defined quality of life as "an individual's perception of their position in life in the context of culture and value systems in which they live and in relation to their goals, expectations, standards and concerns."

It is difficult to find a consensus when defining HRQL. A currently accepted concept focuses on the subjective assessment by the person of how healthcare and health promotion influence their health status and their ability to achieve a performance level that allows them to continue performing those activities that are important to them and affect their welfare. Therefore, HRQL is a multidimensional concept based on the patient's subjective perception[3], in which "non-clinical" factors such as family, friends, religious beliefs, work, income and other life circumstances are also involved[4].

HRQL is a concept constructed from many facets of life and patient situations, which are grouped around several dimensions: physical functioning, psychological wellbeing, emotional state, pain, social functioning, general perception of health and other factors, among which are included sexual function, life satisfaction, impact on labour productivity and activities of daily living. The number of visits to a doctor due to illness or medical problems and the need for drugs[5] are also frequently used as indicators of HRQL.

In 1995[6] the WHOLQOL group agreed on the following attributes of HRQL: subjective, multidimensional, including positive and negative feelings, and that it is variable over time.

Interest in the concept of HRQL began in the early seventies and has increased over the last twenty years, becoming a central goal of health care and an essential measurement performed by so called patient-reported outcome (PRO) instruments. PRO instruments are self-reports of Health-related quality of life by patients without mediation on the part of any professional[7] to capture concepts related to their experiences, how they feel or function in relation to their illness or treatment[8], and go beyond the classical evaluation of survival, traditional clinical efficacy or adverse events. The increasing use of PRO instruments in experimental studies is particularly marked in clinical drug trials, among which HRQL is the most used.

Given its ability to focus on the real needs perceived by the population, HRQL determination is considered a highly valuable discriminating tool for planning health policies or resource[9] distribution.

The importance of including HRQL indicators in the clinical management of patients with CKD stems from the close relationship between HRQL, morbidity and mortality, as many common factors[10,11] appear when analysing these three parameters. Therefore, in order to maintain an optimal HRQL in patients undergoing renal replacement therapy (RRT) is a key element that should guide decision-making in CKD treatment programmes.

Numerous published instruments are available to measure HRQL. Most are composed of a series of items or grouped questions in different dimensions that measure various aspects of health. Questionnaires measuring HRQL must meet the same criteria of validity, reliability and sensitivity, as required of any other measurement of health, and have a properly translated Spanish version validated for use in Spanish patients.

Before deciding on the choice of instrument for measuring HRQL, it is important to know how to use it correctly, apply scoring and carry out an analysis. For some instruments there are very useful reference population rules for comparison with a specific population. The choice of instrument depends on the intended purpose (monitoring the course of health care is different to assessing the impact of a clinical trial), the type of patients that provide data (with greater or less discriminatory power) and the mode of administration of the questionnaires. Most authors suggest the desirability of using different HRQL measurements to extend the range of the results obtained. The synergies or differences found among the results obtained should be explained in relation to the questionnaire used[12].

There are generic versions of instruments to measure HRQL in Spanish (Table 1) that can be used in patients with CKD and others that are specific to renal disease[12] (Table 2).

The Short Form-36 Health Survey (SF-36) is the most widely used in the national and international literature to measure HRQL. Despite being a generic questionnaire and the existence of specific questionnaires for these patients, it is also the most widely used to measure HRQL in patients with CKD. In our country many studies use it for measuring HRQL in relation to RRT techniques, sociodemographic variables anxiety, depression, coping strategies, etc. (Table 3).

If we compare, for example, studies examining HRQL in relation to the CKD and RRT based on the questionnaire used, we find that all show a poorer quality of life in these patients either using the specific questionnaire for renal disease Kidney Disease and Renal Patients Quality of Life-Short Form (SF-KDQOL)[75,76] or generic SF-36[77-80] and EUROQOL 5D (EQ-5D)[81].

In the literature there are two recent meta-analysis that include articles analysing quality of life in patients receiving RRT versus transplant patients, one including articles in which SF-36 questionnaire was used and one in which SF-36 and EQ-5D were used, both reviews reached the same conclusion: HRQL in patients who have received a kidney transplant is better than in those receiving RRT regardless of the questionnaire used[82,83].

HRQL measurement is common in patients with CKD, performed by both medical and nursing staff, since it makes it possible to evaluate patients continuously during prior follow-up before beginning RRT, helping to provide individualised care for each person according to their personal characteristics and life situations.

Furthermore, to assess HRQL it is important to adjust to cultural and population conditions defining this construct in each country and to specific situations, this applies to both the quality of the translations of the questionnaires as to the use of appropriate reference values.

HRQL is increasingly being used in more studies in our country, but there is no review available so far to evaluate articles published on the Spanish population. The purpose of this review is to provide a contrasted view of the instruments most commonly used in our environment when measuring HRQL in patients with CKD, assessing results according to the instrument used.

METHOD

A review was performed of the published literature on studies conducted in Spain that had used an instrument for measuring HRQL, validated in Spanish, whether generic or specific. Inclusion criteria were as follows: studies conducted on adult Spanish population, including different stages of CKD (pre-dialysis stage and dialysis, accepting studies of transplant patients when compared with patients in pre-dialysis or dialysis) with a sample size of at least ten patients per study group. All studies included in this review have used instruments that have been validated in Spanish, as shown in Table 1 and Table 2.

Table 1. Generic instruments used for assessing health related quality of life in patients with advanced chronic kidney disease in Spain

Instrument	Number of items/forms of administration	Subscales	Validation in Spanish/ Sample size	
Nottingham Health Profile	38 Self-administered	No	Yes[13,14] n = 1220	Cronbach's α : 0.58-0.85 C Correlation > 0.6 Criteria validity
Sickness Impact Profile	136 Self-administered and administered by others	No	Yes[15] n = 352	Cronbach's α: Not evaluated C Correlation: 0.84-0.96 Factorial analysis
SF-36 Health Survey	36 Self-administered and administered by others	Yes (SF-12/SF-8)	Yes[16] n = 47-46	Cronbach's α > 0.7 C Correlation: 0.58-0.99 Factorial analysis
EUROQOL 5D	15 + Visual analogic scale	No	Yes[17] n = 12 245	Cronbach's α: unknown C Determination R2: 0.45-0.81 Convergent criteria validity
COOP-WONCA Sheets	9 Self-administered and administered by others	No	Yes[18] n = 475	Cronbach's α > 0.7 C Correlation: 0.52-0.72 Factorial analysis

The search was conducted in the following databases: CINAHL, CUIDEN, DOCUMED, EMBASE, ERIC (USDE), IME, LILACS, MEDLINE, Nursin@ovid, PubMed, Scielo, Web of Science, Web of Knowledge and TESEO data base of PhD thesis. The words used during the search were "quality of life", "health-related quality of life", "chronic renal failure", "chronic kidney disease", "haemodialysis", "peritoneal dialysis", «predialysis», dial*, haemodial*.

Strategies of previous searches were supplemented by manual review of bibliographies of identified articles and review articles.

In the case of papers from the same research team, same school or same sample, after checking that it was the same study, we included those containing a larger sample and most recent studies, rejecting others.

The search began in October 2012 and ended in May 2014, and all articles published both in Spanish and in other languages between 1995 and May 2014 that were carried out on Spanish populations were included.

RESULTS

A total of 377 articles were found. The title and abstract of 135 of them were reviewed and finally the full text of 88 was evaluated. The full selection process is detailed in Figure 1.

Of the articles found, 53 met the criteria for inclusion in this review. Publication dates were from 1995 to May 2014. One of the studies was a doctoral thesis.

Table 3 summarises the characteristics of the studies analysed.

Types of patients in which health related quality of life was studied

In general, when studying HRQL in renal disease, it is on patients on haemodialysis (HD) where we find the greatest number of studies, either alone or in combination with other stages/treatments. Consequently, in 49 of the articles found (92.45%) HRQL is analysed in patients on HD, compared with 26.41% (n = 14) in patients undergoing peritoneal dialysis (PD) and 5.66% (n = 3) in patients in the pre-dialysis stage, this group is the least studied over the last twenty years. It must be noted that HRQL in patients receiving PD without being compared to other stages or treatments is only studied in three articles, the first from 2008, with no studies until that moment focusing exclusively on this type of RRT. PD appears in eleven more articles compared to other stages/ treatments.

The number of patients included in the articles varies considerably, as we established a minimum of ten to be included in this review. The average sample size is 143.32 (SD 180.170) patients, although there is great variability in these figures, from a maximum of 1013 patients to a minimum of 10 patients, with a median of 75 years of age.

HRQL results obtained were independent of the type of instrument used. We found that patients who had received a renal transplant had a better HRQL than those on RRT (HD/PD).

Types of instruments used to assess health related quality of life

Of the studies reviewed, only eleven (20.75%) use two instruments together to measure HRQL, the remainder used only one.

Table 2. Specific instruments used for evaluating health related quality of life in patients with advanced chronic kidney disease in Spain

Instrument	Number of items/form of administration	Subscales	Validation in Spanish/Sample size	
Kidney Disease Questionnarie	26 Administered by others	No	Yes[19] n = 35	Cronbach's α: 0.93 C Correlation: 0.62-0.77 Criteria validity
Kidney Transplant Questionnarie	25 Self-administered	No	Yes[20] n = 31	Cronbach's α : 0.8-0.9 C Correlation: 0.6-0.85 Criteria validity
Kidney Disease and Quality of Life-Short Form	43 Self-administered	Subscale of KDQOL TM (97 items)	Yes[21] n = 240	Cronbach's α : C Correlation: unknown Factorial analysis

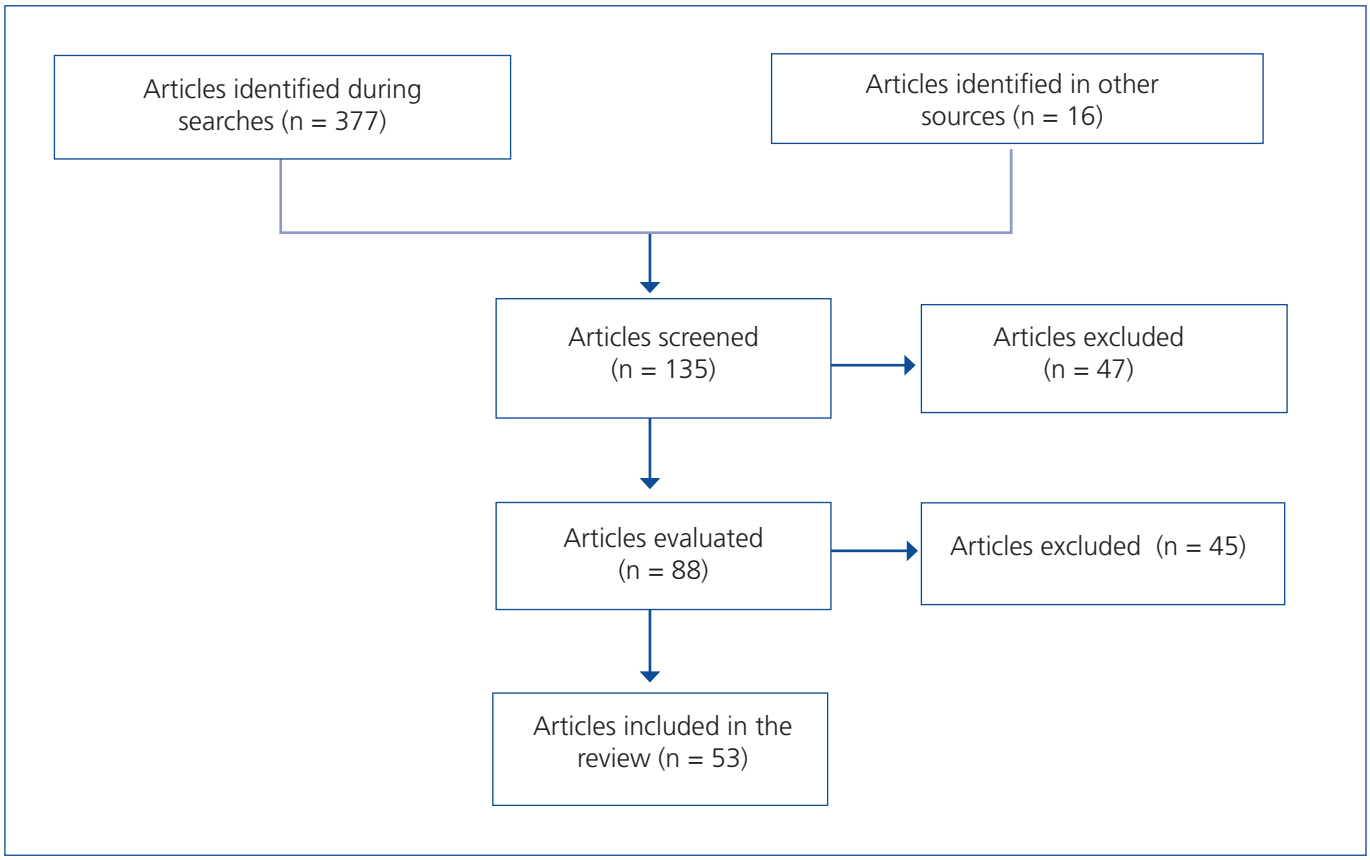

Figure 1. Process of articles selections.

The instrument mainly chosen (52.83%, n =28) by the authors in our country to measure HRQL is SF-36 (generic instrument). This instrument is followed by KDQOL-SF, used in 13.2% (n = 7) of cases, also the Sickness Impact Profile, with 13.2% (n = 7), and COOP-WONCA Charts, with 13.2% (n = 7). Fewer studies used the Nottingham Health Profile, with 11.32% (n = 6) and the Kidney Disease questionnaire was only used in a study of Spanish population (1.88%).

Types of studies most often used to measure health-related quality of life

Most of the studies included in this review are observational and cross sectional: 84.9 % (n = 45). 7.5% (n = 4) are quasi-experimental studies, 3.8% (n = 2) experimental, as also longitudinal observational studies: 3.8% (n = 2).

Impact and evolution of health-related quality of life in different studies

Since the first HRQL studies in our country to this day, RRT itself, either HD or PD, is the variable most commonly associated with HRQL studies in patients with CKD.

Most of the studies show how HRQL is significantly affected in patients receiving RRT. These results are independent of the instrument used to measure HRQL and other associated variables.

Many studies in this review show association between the presence of anxiety and depressive symptoms and the perception of a poorer HRQL. Anxiety and depression are present in varying degrees in all people with CKD, in which the presence of any of these symptoms is analysed in relation to perceived HRQL[31,38,40,41,43,44,46,50,55,56,58,59,65,69,71,73].

Comorbidity associated with CKD also appears in the studies analysed as a highly influential variable on HRQL[28,29,32,33,42,47,56,57].

In reviewing the association between patient age and perceived HRQL, there are differences in the results obtained, with studies in which there is a positive association between age and HRQL[33,35,36,39], and others in which there is a negative association, although we must

Table 3. Summary of studies analysed on chronic studies on health related quality of life in advanced chronic kidney disease

Study	Type/sample	Stage/ treatment	Instrument	Study variables	Conclusions
EXPERIMENTAL DESIGNS					
1. Moreno F et al. (1995)[22]	Quasi-experimental study n = 57 MA: 50 56 % M, 44 % F	HD	SIP	Treatment with EPO	Treatment of anaemia with EPO significantly improves HRQL in patients with HD.
2. Moreno F et al. (2000)[23]	Quasi-experimental study n = 156 MA: 44 60 % M, 40 % F	HD	SIP	Haematocrit/ haemoglobin Functional state	Normalising haematocrit in patients undergoing HD increases HRQL and decreases mortality without significant adverse effects
3. Segura-Ortí E et al. (2009)[24]	Randomised experimental study n = 27 Group 1: MA: 53,5 64.7 % M, 35.3 % F Group 2: MA: 60,1 87.5 % M, 12.5 % F	HD	SF-36	Effect of an intra-dialysis resistance exercise programme on the exercise capacity of patients, their muscular strength and physical functioning and HRQL.	Statistically significant improvement of physical functioning in patients participating in the exercise programme during HD, without significantly affecting patient HRQL.
4. Sánchez E et al. (2010)[25]	Quasi-experimental study n = 25 MA: 66 68 % M, 32 % F	PD	EUROQOL 5D SF-36	Cost of treatment PD	PD is a good option for managing patients with refractory heart failure it improves functional grade and quality of life, and reduces hospitalisation and health costs.
5. Contreras GM et al. (2011)[26]	Quantitative experimental pre and post-treatment study n = 10 MA: 66.6	HD	KDQOL-SF	Force-resistance training programme combined with electrotherapy during HD sessions.	An intra-dialysis force-resistance work programme increased functional capacity and improved the physical component of HRQL in patients.
6. Tomás E et al. (2013)[27]	Quasi-experimental study n = 23 MA: 71.2 56 % M, 44 % F	HD	EuroQol-5D	Intra-dialysis physical exercise programme.	The group undergoing intervention globally presented significant improvement in tests performed. EuroQol-5D (58.7 ± 13.6 vs. 63.7 ± 17.7) We should consider physical exercise during dialysis as part of the integral care of renal patients on HD.
OBSERVATIONAL DESIGNS					
7. Álvarez-U de F et al. (1995)[28]	Observational cross-sectional study n = 45 MA: 64 62 % M, 38 % F	HD CAPD	NottinghamHealthProfile SIP	Sociodemographic and clinical factors Compares results of both HRQL measurement profiles	Advanced age, greater rate of comorbidity, presence of diabetes and lower haematocrit values correlate with a worse HRQL. SIP can be more useful for HRQL measurement in patients on dialysis.

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Continues table 3. Summary of studies analysed on chronic studies on health related quality of life in advanced chronic kidney disease

Study	Type/sample	Stage/ treatment	Instrument	Study variables	Conclusions
8. Moreno F et al. (1996)[29]	Observational cross-sectional study n = 1013 MA: 56 56 % M, 44 % F	HD PD	SIP	Age, comorbidities, anaemia correction with EPO, techniques for use of and use of bicarbonate in HD solution	25% of patients show a significant disease impact on HRQL. Increase of haemoglobin improves HRQL. Advanced age and comorbidities impact negatively on HRQL.
9. García MP et al. (1996)[30]	Observational cross-sectional study n = 143 MA: 42.66 53 % M, 47 % F	HD/Renal Tx	Nottingham HealthProfile		Transplanted patients have better indicators of quality of life than those undergoing HD on the waiting list.
10. Miguel I et al. (1998)[31]	Observational cross-sectional study n = 50 MA: 60.7 60 % M, 40 % F	HD PD	SF-36	Type of dialysis (HD/PD) Anxiety/depression	Patients on dialysis have a HRQL below "good", with both types of dialysis. Level of depression compatible with subclinical situational depression. Degree of anxiety is at mean level with regards to reference group.
11. Rebollo P et al. (1998)[32]	Observational cross-sectional study n = 124 MA: 71 53.6 % M, 43.7 % F	HD Renal Tx	SIP SF-36	Sociodemographic and clinical variables HD vs. Renal Tx	Transplanted patients have a better HRQL than patients on HD. Economic and educational level, functional state and comorbidity influence HRQL.
12. Rebollo P et al. (1999)[33]	Observational cross-sectional study n = 562 Tx: MA: 51 66.8 % M, 33.2 % F HD: MA: 65 54.5 % M, 45.5 % F PD: MA: 67 58.4 % M, 41.6 % F	HD PD Renal Tx	SF-36 SIP	Survival and HRQL in elderly patients on RRT. Sociodemographic, clinical analytical or RRT dependent factors. Karnofsky scale Comorbidities	Quality of life in elderly patients is better than in younger ones, even transplanted patients have a better HRQL than the same age group in the general population. The most important variables determining a poor HRQL were Karnofsky scale and comorbidity.
13. Álvarez U de F et al. (1999)[34]	Observational cross-sectional study n = 60 MA: 66 55 % M, 45 % F	HD	NottinghamHealthProfile	Sleep disorders Sociodemographic and clinical factors	Half the patients evaluated presented sleep disorders and a quarter restless limb syndrome. Variables associated with sleep disorders are: Comorbidities, restless limbs and civil status. Sleep disorders are significantly and independently associated with global score of the perceived health questionnaire.

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Continues table 3. Summary of studies analysed on chronic studies on health related quality of life in advanced chronic kidney disease

Study	Type/sample	Stage/ treatment	Instrument	Study variables	Conclusions
14. Rebollo P et al. (2000)[35]	Observational cross-sectional study n = 506 Tx: MA: 51 66.7 % M, 33.3 % F HD: MA: 67 51.2 % M, 48.8 % F	HD Renal Tx	SF-36 SIP	Sociodemographic and clinical factors	In general, HRQL is better in transplanted patients than in those on HD. In both groups HRQL increases with age. In patients on HD days of hospitalisation increase during the last year when HRQL is worst. A better functional state is associated with a better HRQL.
15. Rebollo P (2000)[36]	Observational cross-sectional study HD: n = 170 MA: 51,61 52.1 % M, 47.9 % F Tx: n = 210 MA: 47,29 65.6 % M, 34.4 % F	HD Renal Tx	SF-36	Age < or ≥ 65 years	Patients with renal transplants have lower SF-36 scores, although sometimes near to or even higher than general population. HRQL in elderly patients on HD is not much worse than the HRQL of the general population of their age and sex, and is better than that of young patients on HD.
16. González VC et al. (2000)[37]	Observational cross-sectional study n = 27 59.3 % M, 40.7 % F	HD	NottinghamHealthProfile	HD	The most affected areas are physical and psychological (energy, sleep and mobility). Deterioration of health state proportional to time of treatment on HD, which does not correlate with the degree of health perceived by the patient.
17. Álvarez-U de F et al. (2001)[38]	Observational cross-sectional study n = 58 MA: 68,5 48 % M, 52 % F	HD	KDQ NottinghamHealthProfile	Frequency and severity of physical symptoms and emotional disturbances (anxiety and depression).	Patients on HD frequently suffer emotional disorders that seem to be associated with non-specific physical symptoms, which significantly affect their wellbeing. Perceived health questionnaires contribute to the diagnosis of these disorders.
18. Rebollo P et al. (2001)[39]	Observational cross-sectional study n = 485 Mean age < 65 years: 49 65.7 % M, 34.3 % F Mean age > 65 years: 66 75 % M, 25 % F	HD Renal Tx	SF-36	HD/Renal Tx Age	Both with HD and renal transplant older patients show a better quality of life than younger ones. In the case of transplanted patients they even have a better HRQL than the general population of the same age and sex.
19. Vázquez I et al. (2003)[40]	Observational cross-sectional study n = 117 MA: 41,68 46.2 % M, 53.8 % F	HD	KDQOL-SF	Demographic, clinical and psycho-social characteristics.	In non-diabetic patients on HD ≤ 65 years of age with low comorbidity, psychological factors such as anxiety and depression are crucial for the determination of HRQL.

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Continues table 3. Summary of studies analysed on chronic studies on health related quality of life in advanced chronic kidney disease

Study	Type/sample	Stage/ treatment	Instrument	Study variables	Conclusions
20. Gil JM et al. (2003)[41]	Observational cross-sectional study n = 51 MA: 79,5 32 % M, 68 % F	HD	KDQOL-SF	Age ≥ 75 years Sociodemographic and analytical factors, functional capacity and self-sufficiency, depression and cognitive deterioration	Women have a worse HRQL than men. HRQL in elderly patients on HD is lower than that of the general population of the same sex and was not modified by factors related to the disease or its treatment. Cognitive deterioration or depression were important.
21. Ruiz MJ et al. (2003)[42]	Observational cross-sectional study n = 446 55.7 % M, 44.3 % F	Pre-dialysis HD PD Renal Tx	Nottingham Health Profile KDQOL-SF	Clinical, analytic and sociodemographic parameters.	Advanced age, female sex, presence of associated diseases and a low socio-economic and educational level are associated with a worse HRQL.
22. Oto A et al. (2003)[43]	Observational cross-sectional study n = 77 MA: 59 45.45 % M, 54.54 % F	HD	SF-36	HD Anxiety/depression Comorbidities	HRQL in patients on HD is clearly reduced with regards to the general healthy population. HD per se determines a lower HRQL and an increase of anxiety and depression scales.
23. Moreno E et al. (2004)[44]	Observational cross-sectional study n = 57 MA: Unknown 66.66 % M, 33.33 % F	HD	COOP-WONCA Sheets	Affective and anxious disorders.	There is an elevated prevalence of anxiety and depression symptoms in patients on HD associated to factors related to HRQL and their functional capacity.
24. Gómez MI et al. (2004)[45]	Observational cross-sectional study n = 285 MA: 47 63.5 % M, 36.5 % F	HD Renal Tx	SF-36	HD/Renal Tx	The SF-36 questionnaire is a reliable and valid tool to measure quality of life in patients on RRT.
25. Vázquez I et al. (2004)[46]	Observational cross-sectional study n = 152 Mean age in males: 43,38 Mean age in females: 42,9, 45.39 % M, 54.6 % F	HD	KDQOL-SF	Sex and socio-demographic, medical and psycho-social variables.	The worst HRQL of women on HD is a reflexion of the differences between sexes also seen in the general population and related to a greater prevalence of anxiety and depressive symptoms.
26. Arenas MD et al. (2004)[47]	Observational cross-sectional study n = 163 MA: 62,5 65.06 % M, 34.96 % F	HD	COOP-WONCA Sheets	HD Functional capacity	COOP-WONCA sheets could be a good instrument to measure HRQL in patients on HD Patients who have been longer on HD have worse general functions. Older patients only had worse HRQL's for the "physical state" dimension. Other factors related to a perceived worse state of health were sex (women), comorbidities, work situation, civil status and means of transport.

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Continues table 3. Summary of studies analysed on chronic studies on health related quality of life in advanced chronic kidney disease

Study	Type/sample	Stage/ treatment	Instrument	Study variables	Conclusions
27. Martin F et al. (2004)[48]	Observational cross-sectional study n = 60 MA: Unknown Unknown % M/F	HD	COOP-WONCA Sheets SF-36	HD	Validity of COOP-WONCA sheets for the determination of HRQL in patients on dialysis, providing information similar to that provided by more complex instruments without losing psychometric quality. Quick and easy to fill in.
28. Rebollo P et al. (2004)[49]	Observational cross-sectional study n = 221 MA: 60,4 67.9 % M, 32.1 % F	HD PD	EUROQOL 5D SF-36	HRQL perceived by carers of patients on HD or PD.	Carers of patients on dialysis (family and health carers) are aware of the wellbeing and functional state of these patients and are a source of information on HRQL.
29. Vázquez I et al. (2005)[50]	Observational cross-sectional study n = 194 MA: 48,55 43.29 % M, 56.7 % F	HD	KDQOL-SF	Anxiety/depression Social support	Anxiety and depressive symptoms are strongly associated with HRQL evaluation in patients on HD.
30. Alfaro A et al. (2006)[51]	Longitudinal observational study n = 11 MA: 56 54.54 % M, 45.45 % F	HD HDF	SF-36	Conventional HD/HDF Functional capacity	The group of patients that went from conventional HD to HDF underwent a significant improvement of their HRQL and functional capacity.
31. Martín F et al. (2006)[52]	Observational cross-sectional study n = 103 MA: 61,3 100 % M	HD	COOP-WONCA Sheets	Activity and sexual function	Sexual dysfunction is a highly prevalent problem in men on HD, but this is not necessarily associated with severe deterioration of HRQL.
32. Martín F et al. (2006)[53]	Observational cross-sectional study n = 60 MA: 60,32 57.1 % M, 42.9 % F	HD	COOP-WONCA Sheets SF-36	HD	The process of psycho-social adaptation to problems caused by dialysis is satisfactory. COOP-WOONCA sheets are a useful instrument to determine HRQL in patients on HD without losing psychometric quality.
33. Sanz-Guajardo D et al. (2006)[54]	Observational cross-sectional study n = 171 MA: 62,2 60.8 % M, 39.2 % F	Pre-dialysis	SF-36	Influence of early intervention by a nephrologist and their present during pre-dialysis consultation.	No significant differences have been found between HRQL measured between early and late referral to nephrologist groups, except in the "general health" dimension, which is higher in those referred late to a nephrologist. Quality of life of patients during the phase prior to dialysis is much lower than in the reference population, even after adjusting for age and sex.

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Continues table 3. Summary of studies analysed on chronic studies on health related quality of life in advanced chronic kidney disease

Study	Type/sample	Stage/ treatment	Instrument	Study variables	Conclusions
34. Sánchez JM et al. (2006)[55]	Observational cross-sectional study n = 45 53.33 % M, 46.66 % F	HD	SF-36	State of health, degree of depression, personality factors. HD	The state of health of patients on HD in this study is generally poor. Personality profile shows a patter with introversion characteristics.
35. Muñoz R et al. (2006)[56]	Longitudinal observational study n = 52 Mean age of patients who died: 70 Mean age of patients who lived: 57 57.7 % M, 42.3 % F	HD	SF-36	Demographic, anxiety/ depression, changes in morbidity determinants. HD	The value of quality of life is significantly determined by state of depression, age and degree of comorbidity
36. Rodríguez MA et al. (2007)[57]	Observational cross-sectional study n = 36 MA: 65,83 50 % M, 50 % F	HD	SF-36	HDHRQL associated variables. Cooperation problems	Patients studied reported HRQL similar to that described for other groups on HD. The scales for anxiety and depression were high and greatly influenced HRQL. The incidence of cooperation problems detected may be related to the patients perceived HRQL.
37. Arenas MD et al. (2007)[58]	Observational cross-sectional study n = 75 MA: 49,2 66.66 % M, 33.33 % F	HD	COOP-WONCA Sheets	Anxiety/depression HD	A high percentage of patients on HD suffered emotional disorders (anxiety and depression). A good correlation was seen between HRQL and levels of anxiety and depression. Measurement of HRQL using COOP-WONCA sheets may help to diagnose these problems.
38. Luque E et al. (2007)[59]	Observational cross-sectional study n = 50 MA: 57 64 % M, 36 % F	HD PD	EUROQOL 5D	Nurses HRQL perception of autonomous patients	There is a great difference with regards to quality of life perceived by patients and by nurses, due possibly that when considering an autonomous patient the professional believes they do not require special care.
39. Cirera F et al. (2007)[60]	Observational cross-sectional study n = 306 MA: 62,55 52 % M, 48 % F	Pre-dialysis PD HD	SF-36	Treatment for chronic renal failure. Demographic data.	No significant differences are found when evaluating HRQL depending on RRT used. Female sex and > age have been shown to be indicators of worse HRQL in this simple. SF-36 is a useful instrument for nurses, since it allows nurses to diagnose both health and real risks.

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Continues table 3. Summary of studies analysed on chronic studies on health related quality of life in advanced chronic kidney disease

Study	Type/sample	Stage/ treatment	Instrument	Study variables	Conclusions
40. Barrena E et al. (2008)[61]	Observational cross-sectional study n = 98 MA: 69,3 61 % M, 38.9 % F	HD	SF-36 KDQOL-SF	HD Age Bio-psycho-social needs and degree of satisfaction. Dialysis technique.	The HD technique employed significantly influences perception of quality of life. Also perceived quality of life is influenced by > comorbidities and > age.
41. Reina M et al (2008)[62]	Observational cross-sectional study n = 89 MA: 60,31 45 % M, 55 % F	PD	SF-36	PD modality Demographic data.	Women have lower scores. The patient age group 25-34 had higher scores. There do not seem to be significant differences between CAPD and APD.
42. Ruiz de Alegría B et al. (2008)[63]	Observational cross-sectional study n = 93 MA: 53,67 64.5 % M, 35.4 % F	HDH CAPD	SF-36	Coping strategies	Patients on dialysis with worse mental health face disease using non-adaptive avoidance techniques. Life satisfaction (subjective wellbeing) is related to providing a meaning for experience (subjective wellbeing) and social support.
43. Miguel M et al. (2009)[64]	Observational cross-sectional study n = 50 MA: 64,84	HD	EUROQOL 5D	Patient satisfaction in a dialysis unit.	Identifying the factors that modulate satisfaction is as important as evaluating it. Furthermore, it is necessary to take into account individual variables of each patient which condition perceived satisfaction.
44. Ruiz de Alegría B et al. (2009)[65]	Observational cross-sectional study n = 93 MA: 54 64.5 % M, 35.5 % F	HD CAPD	SF-36	Hospital HD vs. CAPD Coping strategies	Between these two types of dialysis there are no differences in perception of quality of life. Patients on CAPD tend to greater satisfaction with life and have more adaptive coping strategies, which suggests they may have a greater acknowledgment and control of their disease.
45. Del Campo MC et al. (2009)[66]	Observational cross-sectional study n = 30 MA: 63 56.66 % M, 43.33 % F	HD olHDF	SF-36	Conventional HD vs.olHDF	The SF-36 questionnaire is useful and easy to use in patients on dialysis. HRQL according to measured parameters improves in olHDF in comparison with HD.
46. Seguí A et al. (2010)[67]	Observational cross-sectional study n = 96 MA: 62,12 53.1 % M, 46.9 % F	HD	SF-36	HD	HRQL in patients with TCKD is worse than in the reference population for all dimensions.

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Continues table 3. Summary of studies analysed on chronic studies on health related quality of life in advanced chronic kidney disease

Study	Type/sample	Stage/ treatment	Instrument	Study variables	Conclusions
47. Valdés C et al. (2010)[68]	Observational cross-sectional study n = 50 MA: 64,84 58 % M, 42 % F	HD	EUROQOL 5D	Assessment of HRQL in patients on dialysis carried out by nursing staff. Coincides with assessment by patients themselves.	Nurses seem to coincide more with assessments carried out by patients of their own HRQL when more observable aspects are evaluated and when the patients are in more favourable health conditions.
48. Cobo JL et al. (2011)[69]	Observational cross-sectional study n = 47 MA: 62 67 % M, 33 % F	HD	EUROQOL 5D	Sociological factors.	Almost 70% of patients present pain/discomfort and almost half are anxious or depressed. The sociological variables that most influence HRQL are age, civil status, persons cohabiting and income level.
49. Pelayo R et al. (2011)[70]	Observational cross-sectional study n = 38 MA: 65 66 % M, 34 % F	HD	EUROQOL 5D	Patient vascular access during HD	There is no significant influence of vascular access on quality of life perceived by patients. The greatest inconveniences and discomforts are caused by patients with central venous catheters who have been on HD for over one year.
50. Varela L et al. (2011)[71]	Observational cross-sectional study n = 53 MA: 49,54 45.3 % M, 54.7 % F	PD	KDQOL-SF	Psychological variables that control the effect of clinical variables, age and sex.	In patients on PD, anxiety, depression and alexitimia are important determinants of HRQL, and should therefore be considered both during evaluation and treatment of these patients.
51. Morales AI et al. (2011)[72]	Observational cross-sectional study n = 239 MA: 64,8 62.5 % M, 37.5 % F	HD	COOP-WONCA Sheets	Optimism, optimistic personality, hospital admittances over one year.	Pessimistic personality characteristics are associated with hospital admittances independent of age, length of dialysis and degree of comorbidities of the patient. Optimistic patients have better perceived health.
52. Perales CM et al. (2012)[73]	Observational cross-sectional study n = 39 69.23 % M, 30.76 % F	HD	SF-36	Psycho-social variables (anxiety, depression, self-sufficiency, optimistic disposition, social support and coping strategies).	Patients had HRQL values lower than standard. Depression is the main predictor of HRQL negatively associated with all its dimensions.
53. Ruiz de Alegría-Fernández de Retana B et al. (2013)[74]	Longitudinal observational study n = 98 MA: 51 ± 13,16 56.6 % M, 43.4 % F	HD PD Renal Tx	SF-36	Positive and negative affect scale (PNA), Ways of coping scale-25	The types of coping strategies most used were search for information, problem resolution, cognitive restructuring, delegation and regulated expression of emotions. Avoidance at the beginning was a predictor of greater negative affectivity and worse mental component of SF-36 after one year.

HRQL: Health Related Quality of Life; PD: Peritoneal Dialysis; APD: Automated Peritoneal Dialysis; CAPD: Continuous Ambulatory Peritoneal Dialysis; MA: Mean Age; EPO: Erythropoietin; EUROQOL 5D: 5 Dimensional EuroQol; HD: Haemodialysis; HDF: Haemodiafiltration; OLHDF: On-Line Haemodiafiltration; HHD: Hospital Haemodialysis; ESCRF: End-stage Chronic Renal Failure; KDQ: Kidney Disease Questionnaire; KDQOL-SF: Kidney Disease and Quality of Life-Short Form; W: Woman; SF-36: Short Form-36 Item Health Survey; SIP: Sickness Impact Profile; RRT: Renal Replacement Therapy; Tx: Transplant; M: Man.

say that comorbidity appears as an age and HRQL[28,29,42,56,57] related variable.

Only three studies[31,61,65] compare HRQL (SF-36) according to whether the patient is receiving HD or PD, and found no significant differences in HRQL according to type of treatment chosen in our country. Furthermore, Ruiz de Alegría et al. (2008) note that continuous outpatient PD patients have a higher life satisfaction and cope better with life than those on HD (n = 93).

In over 77% of the articles included in this review, the male population is larger than the female. 100% of the studies using sex as a study variable showed a poorer HRQL perceived by women, compared with men. So far it has not been determined whether this is because there is a greater impact of the disease and its treatment on them or if, on the other hand, this reflects sex differences that also occur in the general population. A study was performed in Spain, using the SF-36[84] questionnaire, on 9151 subjects where the effect of sex on HRQL in the general population is clear.

DISCUSSION

From the early stages of kidney disease, the symptoms that accompany it are reflected in patients' daily life. RRT only partially corrects uraemic symptoms, but creates substantial changes in the daily life of these patients, caused by having to go to hospital three times a week in the case of HD, daily peritoneal fluid refills in the case of PD, major dietary restrictions in all cases, etc. All these circumstances significantly decrease quality of life in patients in the last stages of CKD.

HD is still the most used RRT technique in Spain. Consequently, for example, we found that in Andalusia in 2013 it was the method of choice for new incidents in 81.4% of cases, followed by the PD in 15% and advance renal transplantation in 3.6%[85]. Therefore, it is not surprising, given the high number of patients who choose this form of treatment, that most of the studies on CKD Spanish populations in which HRQL is measured have focused on HD.

The stage prior to the start of the RRT is little studied, despite its importance and the high number of patients currently attending medical and nursing consultations during this period. There are also few studies on PD, a treatment that is increasing, which more people are choosing in Spain, as also more extensive studies with a higher number of patients comparing the difference in perceived quality of life among Spanish PD and HD populations.

We did not find significant differences when analysing HRQL in different RRT treatments in Spain. This finding is partly consistent with the overall results seen in the literature, although there are a few more physical components of HRQL in patients undergoing HD[86]. The few studies carried out in Spain make it impossible to study this issue in greater depth and this is an area that urgently requires further investigation.

SF-36, despite being a generic questionnaire, is most often used when assessing HRQL in patients with renal disease, both in our country and internationally[82]. So far there are no studies using its reduced form (SF-12).

The number of patients included in these studies is often low, with the consequent losses in possibilities of generalisation and statistical power, demonstrating a clear need for new multicentre studies with larger and more diverse samples, in order to better assess the external validity of results and also include patients in pre-dialysis.

The small number of studies with strong designs (longitudinal, analytical, experimental) is remarkable, although there are published clinical practice guidelines[1,87] on the usefulness of HRQL evaluation in cohorts of patients in pre-dialysis or RRT to assess the impact of disease or treatment over time.

The patient's psycho-emotional state is another aspect that should be taken into account when assessing a person with CKD. Because HRQL is a multidimensional concept, in which the psychological state of the individual plays an important role, problems such as depression or anxiety have a big impact on HRQL. It was found that the psychosocial constructs that are more closely associated with HRQL are stress, affection and cognitive evaluation[88]. Therefore, it is very important to identify these states of anxiety and depression in patients with CKD to make it possible to treat them appropriately and systematically and thorough evaluation of the psycho-emotional state is recommended as an integral part of the treatment offered to optimise quality of life[89]. Studies would be necessary to assess HRQL in the presence of affective disorders such as anxiety or depression.

The results of this review show CKD has a significant impact on patient's quality of life.

We conclude that measurement of HRQL should be part of professionals' routine and systematic practice when treating renal patients. This measurement can provide very valuable and important information, allowing us to act on the most affected dimensions, thus achieving the best possible state of well-being for these patients.

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Conflicts of interest

The authors declare that they have no conflicts of interest related to the contents of this article.

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