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Health-Related Quality of Life in People Across the Spectrum of CKD

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Introduction: People with chronic kidney disease (CKD) experience reduced quality of life (QoL) because of the high symptom and treatment burden. Limited data exist on the factors associated with overall and domain-specific QoL across all CKD stages.

Methods: Using data from a prospective, multinational study (Australia, New Zealand, Canada, and Spain) in 1696 participants with CKD, we measured overall and domain-specific QoL (pain, self-care, activity, mobility, anxiety/depression) using the EuroQoL, 5 dimension, 3 level. Multivariable linear regression and logistic modeling were used to determine factors associated with overall and domain-specific QoL.

Results: QoL for patients with CKD stages 3 to 5 (n = 787; mean, 0.81; SD, 0.20) was higher than in patients on dialysis (n = 415; mean, 0.76; SD, 0.24) but lower than in kidney transplant recipients (n = 494; mean, 0.84; SD, 0.21). Factors associated with reduced overall QoL (β [95% confidence intervals]) included being on dialysis (compared with CKD stages 3–5: –0.06 [–0.08 to –0.03]), female sex (–0.03 [–0.05 to –0.006]), lower educational attainment (– 0.04 [–0.06 to –0.02), lacking a partner (–0.04 [–0.06 to –0.02]), having diabetes (–0.05 [–0.07 to –0.02]), history of stroke (–0.09 [–0.13 to –0.05]), cardiovascular disease (–0.06 [–0.08 to –0.03]), and cancer (–0.03 [–0.06 to –0.009]). Pain (43%) and anxiety/depression (30%) were the most commonly affected domains, with dialysis patients reporting decrements in all 5 domains. Predictors for domain-specific QoL included being on dialysis, presence of comorbidities, lower education, female sex, and lack of a partner.

Conclusions: Being on dialysis, women with CKD, those with multiple comorbidities, lack of a partner, and lower educational attainment were associated with lower QoL across all stages of CKD.

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People with CKD have an increased risk of mortality. The excess risk extends from 1.2 times for patients with CKD not requiring kidney replacement therapy to over 100-fold among those with end-stage kidney disease compared with the general population.[1] The impact of impaired kidney function on overall QoL is also profound, particularly among those with advanced kidney disease.[1] Compared with other chronic conditions, utility-based QoL is lowest for patients with end-stage kidney disease, with estimates even lower than in patients with cancer or heart failure.[2–4]

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Although kidney transplant recipients may experience improved QoL compared with those on dialysis,[2] their overall QoL remains lower than the general population.[2,5]

Previous studies of QoL assessment in CKD have generally been small, and most have not provided details of domain-specific QoL data.[2] Few have examined the factors associated with domain-specific QoL in patients with CKD[6,7] and none across the entire spectrum of CKD. Knowledge of the contributing factors that negatively influence health-related QoL (HR-QoL) is important because those factors will inform the development and delivery of interventions targeting modifiable factors in patients with CKD. The purpose of this study was to compare the overall and domain-specific QoL in a large cohort of patients in different stages of CKD and to determine the factors associated with overall and domain-specific QoL in patients with CKD (stages 3–5), on dialysis and after kidney transplantation.

METHODS

Study Population

This is a substudy of the DETECT (Detecting Bowel Cancer in CKD) study. The DETECT study is a prospective, multicenter, cohort study of 1706 patients that aimed to determine the consequences of a 1-time screening for advanced colorectal neoplasia using fecal immunohistochemistry test across a broad spectrum of CKD stages.[8] We screened patients with CKD (stages 3–5 [not on kidney replacement therapy], dialysis and transplant recipients) aged between 35 and 74 years, for study eligibility and enrolled participants at 11 sites across Australia, New Zealand, Spain, and Canada including hospital, academic, and private practice clinics. The initial enrollment period for the cohort was from June 2010 to November 2015 with biennial follow-up for up to 4 years after the initial recruitment. QoL data were collected from all enrolled participants at baseline using the EuroQol 5 domain, 3 level (EQ-5D-3L) multiattribute utility measure before performing the fecal immunohistochemistry test.

The study protocol[9] was approved by the Human and Research Ethics Committee of all participating centers (Westmead, Gosford, Royal North Shore, Blacktown, Nepean, Sir Charles Gairdner, Concord, Royal Prince Alfred, Toronto General, Christchurch Hospitals, and the Hospital Clinic of Barcelona). All participants provided written informed consent.

Covariates of Interest

Demographic details were obtained from each patient at the time of enrollment, and prespecified clinical data were extracted from the healthcare records. Demographic data included age, gender, ethnicity, education level, and marital status. Higher education status was defined as those who attended college/university, whereas lower education status was defined as attending high school or below. Clinical information included CKD stage, comorbidities (diabetes mellitus, cardiovascular disease, and cerebrovascular disease), type of kidney replacement therapy, a personal or family history of cancer, and medications (including immunosuppressants, antiplatelets, anticoagulants, antihypertensives, hypoglycemics, antidepressants, iron replacement therapy, and erythropoiesis-stimulating agents). Glomerular filtration rate for stages 3 to 5 CKD patients and kidney transplant recipients was estimated using the Chronic Kidney Disease Epidemiology Collaboration formula.[10]

Outcomes of Interest

The EQ-5D-3L multiattribute utility instrument was used to assess the baseline QoL of all participants before bowel cancer screening with the fecal immunochemical test and was administered in English and Spanish. The validity and reliability of the EQ-5D instrument has been previously established in both general and disease-specific populations,[11] including adults with CKD.[2,6,12–14]

The EQ-5D-3L questionnaire assesses the 5 individual domains of mobility, self-care, usual activities, pain, and anxiety/depression at 3 response categories: no problems, some problems, and extreme problems.[15] For example, mobility (walking) may be described as having no problems, some problems, or a lot of problems walking. The combination of all possible levels and dimensions results in 243 unique health states. The EQ-5D levels are then converted into a single summary utility value by applying a formula that attaches the weights to each reported level in each domain. Scoring is based on an Australian value set, which results in utility values over the range of −0.217 (worse than dead) to 1.0 (perfect health).[16] Because it is a multiattribute utility measure, the EQ-5D-3L provides utility weights; however, we use the term "QoL score" throughout for simplicity. Domain levels were also dichotomized into those with "any problems" and those with "no problems" based on the response categories of the instrument.

Statistical Analysis

Baseline demographic data with continuous distributions were presented as means with SDs or medians with interquartile ranges (IQRs) for normally and non-normally distributed variables, respectively. Characteristics with binary distributions were reported as counts and percentages. QoL scores were expressed both as medians (IQRs) and means (SDs) to enable

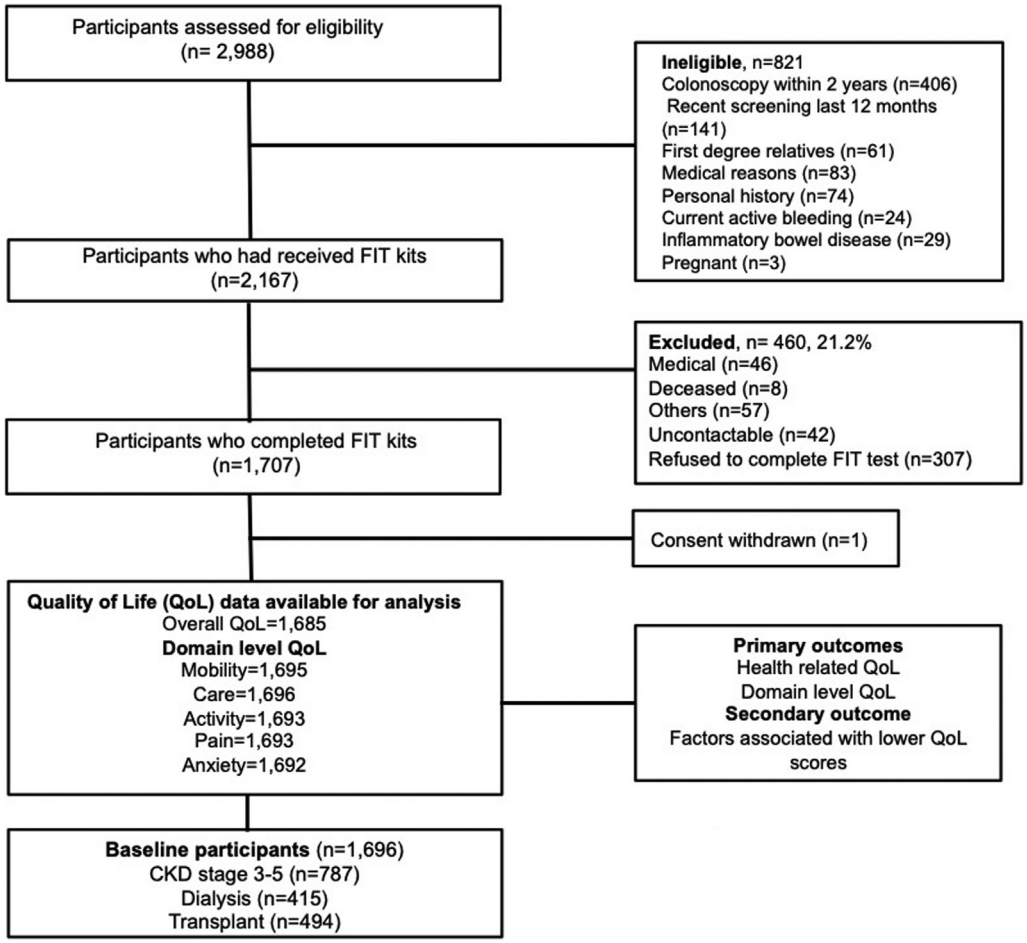

Figure 1. Participant flowchart. *Sites, 11 centers across Australia, New Zealand, Canada, and Spain. CKD, chronic kidney disease; FIT, fecal immunohistochemistry test.

comparison with other studies and for use in future health economic evaluations.

Given the skewed distribution of the QoL scores, comparisons by CKD stage were made using the Mann-Whitney U test. Comparisons between the EQ-5D-3L domain levels and CKD stages were performed using χ^2 tests.

Multiple linear regression models assessed the risk factors for changes in overall QoL scores, whereas logistic regression models examined the risk factors for reported problems in the individual domain levels. Covariates with $P < 0.25$ in the unadjusted association for QoL scores were included in the multivariable analyses. Several 2-way interactions between baseline characteristics and CKD stages were tested. The final model retained the covariates that remained significant after adjustment using a backward stepwise strategy. The same approach was undertaken for the logistic regression models. A random effects model was used to assess variation by country. Data were processed and scored using SPSS v25 (IBM North America, New York, NY). Data analyses were performed using SPSS v25, R, and SAS 9.4 (SAS Institute, Cary, NC), whereas Python was used to create graphs. $P < 0.05$ was considered statistically significant.

RESULTS

The inclusion criteria and screening protocol for this study have been described previously.[8] Of the 2988 patients with CKD who were screened, 2167 (72.5%) were eligible. The 460 (21.2%) who were ineligible did not undergo screening because of death, refusal, or medical reasons including hospitalization after screening kits were given. Overall, 1707 patients (78.8%) completed the fecal immunohistochemistry test. One withdrew consent after screening, and 21 participants had missing QoL data, leaving 1685 participants with overall QoL scores, whereas domain-level responses were available in up to 1696 participants (Figure 1).

Baseline Characteristics of the Study Cohort

Of the 1696 participants, 787 (46.4%) had CKD stages 3 to 5, 415 (24.5%) were on dialysis, and 494 (29.1%) were kidney transplant recipients. Overall, 1027

Table 1. Baseline characteristics

Characteristics	CKD 3–5 (n = 787, 46.4%)	Dialysis (n = 415, 24.4%)	Transplant (n = 494, 29.1%)	All (n = 1696)
Age, yr				
35–49	108 (13.7)	76 (18.3)	166 (33.6)	350 (20.6)
50–64	283 (36.0)	234 (56.4)	255 (51.6)	772 (45.5)
≥65	396 (50.3)	105 (25.3)	73 (14.8)	574 (33.8)
Sex				
Female	335 (42.6)	152 (36.6)	182 (37.0)	669 (39.4)
Male	452 (57.4)	263 (63.4)	312 (63.1)	1027 (60.5)
Race or ethnic groups				
White	543 (69.0)	275 (66.3)	389 (78.7)	1207 (71.2)
Asian	81 (10.3)	60 (14.5)	44 (8.9)	185 (10.9)
Middle eastern	30 (3.8)	16 (3.9)	18 (3.6)	64 (3.8)
Aboriginal/Torres Strait Islander/Maori/Pacific Islanders	18 (2.3)	21 (5.1)	13 (2.6)	52 (3.1)
Others	115 (14.6)	43 (10.1)	30 (6.1)	188 (11.1)
Education level				
High school graduate or less	316 (40.2)	159 (38.3)	249 (48.4)	724 (42.6)
College/university	457 (58.1)	244 (58.8)	239 (50.4)	940 (55.4)
Unknown	14 (1.8)	12 (2.9)	6 (1.2)	32 (1.9)
Marital status				
Married/partnered	560 (71.2)	276 (66.5)	370 (74.8)	1217 (71.8)
Single/divorced/widowed	225 (28.5)	136 (32.8)	121 (24.4)	471 (27.8)
Unknown	2 (0.3)	3 (0.7)	3 (0.8)	8 (0.4)
Smoking status				
Current	81 (10.3)	26 (6.2)	17 (3.4)	124 (7.3)
Ex-smoker	357 (45.4)	197 (47.5)	214 (43.3)	768 (45.2)
Never	339 (43.1)	185 (44.6)	255 (51.6)	779 (45.9)
Unknown	10 (1.3)	7 (1.7)	8 (1.6)	25 (1.5)
Diabetes mellitus				
Yes	317 (40.3)	149 (35.9)	109 (22.1)	575 (33.9)
No	470 (59.7)	266 (64.1)	385 (77.9)	1121 (66.0)
Cardiovascular disease				
Yes	207 (26.3)	112 (27.0)	72 (14.6)	391 (23.1)
No	580 (73.7)	303 (73.0)	422 (85.4)	1305 (76.9)
Cerebrovascular disease				
Yes	58 (7.3)	29 (7.0)	23 (4.7)	110 (6.4)
No	729 (92.6)	386 (93.0)	471 (95.3)	1586 (93.5)
Body mass index, kg/m^2				
<20	20 (2.5)	32 (7.7)	18 (3.6)	70 (4.1)
20.1–25	156 (19.8)	127 (30.6)	158 (32.0)	441 (26.0)
25.1–30	277 (35.2)	127 (30.6)	179 (36.2)	583 (34.4)
>30	301 (38.2)	108 (26.0)	123 (24.9)	532 (31.4)
Unknown	33 (4.2)	21 (5.1)	16 (3.2)	70 (4.1)
Prior cancer				
Yes	149 (18.9)	82 (20.0)	118 (23.9)	349 (20.5)
No	638 (81.1)	332 (80.0)	376 (76.1)	1346 (79.4)
Prior lower gastrointestinal endoscopy				
Yes	281 (35.7)	111 (26.7)	134 (27.1)	526 (31.0)
No	502 (63.8)	304 (73.3)	360 (72.9)	1166 (68.8)
Unknown	4 (0.5)	0	0	4 (0.2)
Daily use of antiplatelet agents				
Yes	239 (30.4)	147 (35.4)	138 (27.9)	524 (30.9)
No	548 (69.6)	268 (64.6)	356 (72.1)	1172 (69.1)
Daily use of anticoagulation				
Yes	67 (8.5)	65 (15.7)	26 (5.3)	158 (9.3)
No	720 (91.5)	350 (84.3)	468 (94.7)	1538 (90.7)
Types of dialysis				
Hemodialysis	NA	290 (69.9)	NA	290 (69.9)
Peritoneal dialysis	NA	125 (30.1)	NA	125 (30.1)

(Continued on following page)

Table 1. (Continued) Baseline characteristics

Characteristics	CKD 3–5 (n = 787, 46.4%)	Dialysis (n = 415, 24.4%)	Transplant (n = 494, 29.1%)	All (n = 1696)
Donor types				
Deceased	NA	NA	308 (62.3)	308 (62.3)
Living	NA	NA	186 (37.7)	186 (37.7)
Daily immunosuppression use				
Prednisone	40 (5.1)	29 (7.0)	448 (90.7)	517 (30.5)
Azathioprine	9 (1.1)	4 (1.0)	52 (10.5)	65 (3.8)
Mycophenolate mofetil	9 (1.1)	3 (0.7)	381 (77.1)	393 (23.2)
Tacrolimus	1 (0.1)	3 (0.7)	303 (61.3)	3097(18.1)
Cyclosporine	5 (0.6)	1 (0.2)	104 (21.1)	110 (6.5)
Regular use of erythropoiesis-stimulating agents				
Yes	38 (4.8)	201 (48.4)	31 (6.3)	270 (15.9)
No	749 (95.2)	214 (51.6)	463 (93.7)	1426 (84.1)

CKD, chronic kidney disease; NA, not applicable.
Values are n (%).

(60.5%) were men, with a median age of 59.9 years. Most were white (n = 1208, 71.2%), and most (n = 1,523, 89.8%) had at least 1 comorbidity (diabetes mellitus, cardiovascular, or cerebrovascular disease). Three hundred fifty patients (20.6%) had a history of prior cancer (skin and nonskin cancers), and 892 (52.6%) were either ex- or current smokers. Of the 415 patients receiving dialysis, 69.9% were maintained on hemodialysis and 30.1% were maintained on peritoneal dialysis; 62.2% of all kidney transplant recipients received deceased donor kidneys. Seven hundred fourteen participants (42.1%) had a higher education, and 1217 (71.8%) were married or partnered (Table 1).

Overall HR-QoL Score by CKD Stage

Most of the cohort (n = 987, 58.2%) reported decrements in QoL (EQ-5D-3L overall score < 1). The overall mean QoL score was 0.80 (SD, 0.22), and the median QoL score was 0.83 (IQR, 0.70–1.00). QoL scores for participants on dialysis (median, 0.79; IQR, 0.68–1.00; mean [SD], 0.76 [0.20]) were lower compared with kidney transplant recipients (median, 1.00; IQR, 0.73–1.00; $P < 0.001$; mean [SD], 0.84 [0.21]) and participants with CKD stages 3 to 5 (median, 0.83; IQR, 0.71–1.00; $P < 0.001$; mean [SD], 0.81 [0.20]) (Figure 2, Table 2). Compared with those with CKD stages 3 to 5, a greater proportion of participants on dialysis experienced any decrement from perfect health (CKD stages 3–5 vs. dialysis: 59.5% vs. 67.7%, $P = 0.005$), whereas a lower proportion of transplant recipients experienced a decrement from perfect heath (CKD stages 3–5 vs. transplant: 59.5% vs. 49.4%, $P < 0.001$). A sensitivity analysis comparing the QoL of the Spanish participants using normative Spanish EQ-5D data was conducted

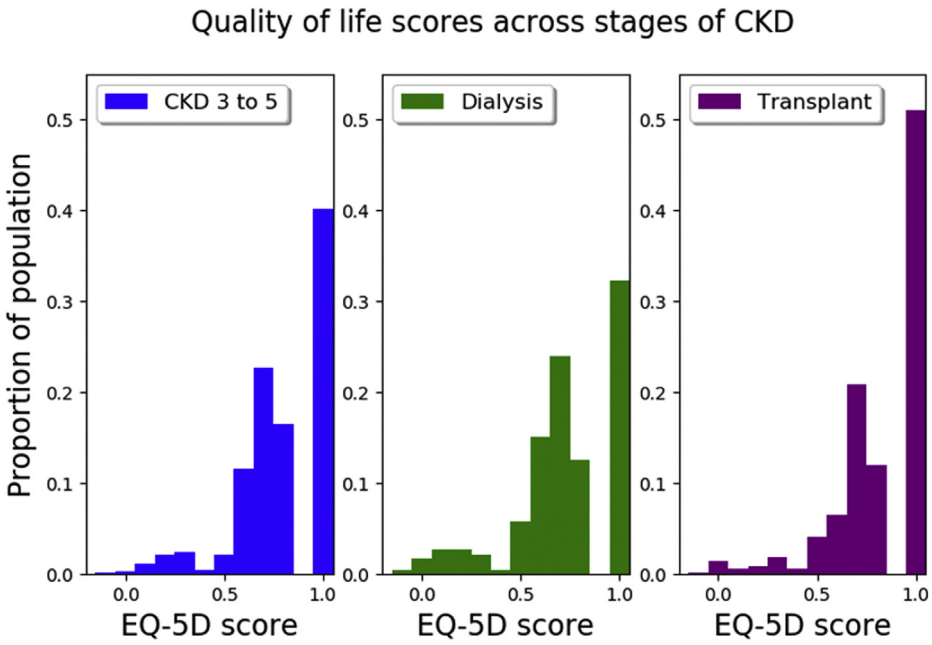

Figure 2. Quality of life in participants with chronic kidney disease (CKD), stratified by stage. EQ-5D, EuroQoL, 5 dimension.

Table 2. Summary quality of life scores

Summary statistics	CKD stages 3–5 (n = 787)	Dialysis (n = 415)	Transplant (n = 494)
Median (interquartile range)	0.83 (0.71–1.00)	0.79 (0.68–1.00)	1.00 (0.73–1.00)
Mean (SD)	0.81 (0.20)	0.76 (0.24)	0.84 (0.21)
P value[a]		<0.001	0.001

CKD, chronic kidney disease.
[a]Compared with CKD stages 3–5 by the Mann-Whitney U test.
Data are missing for 21 participants.

and found similar results to the Australian set (Supplementary Sensitivity Analysis).

Domain-Specific QoL by CKD Stage

A large proportion of participants experienced pain (43%), 29% experienced anxiety/depression, 29% reported decreased mobility, and 28% reported problems with performing daily activity (Table 3). Only 9% of the participants reported any deficit in the domain of self-care. Compared with participants with CKD stages 3 to 5, a greater proportion of participants receiving dialysis reported any problems with self-care (7% vs. 17%, $P < 0.001$), usual activities (26% vs. 40%, $P < 0.001$), and anxiety/depression (27% vs. 39%, $P < 0.001$). Transplant recipients were less likely to experience pain (36% vs. 45%, $P = 0.002$) or impairments in mobility (22% vs. 31%, $P = 0.001$) and usual activities (21% vs. 26%, $P = 0.05$) compared with those with CKD stages 3 to 5, but there were no differences in the domains of self-care ($P = 0.99$) and anxiety/depression ($P = 0.65$) (Supplementary Figure S1). Compared with kidney transplant recipients, a greater proportion of participants receiving dialysis reported problems in all 5 domains: mobility (35% vs. 22%, $P < 0.001$), self-care (17% vs. 7%, $P < 0.001$), activity (40% vs. 21%, $P < 0.001$), pain (48% vs. 36%, $P < 0.001$), and anxiety/depression (39% vs. 26%, $P < 0.001$).

Factors Associated With Overall HR-QoL Across All CKD Stages

The adjusted risk factors associated with reduced overall HR-QoL (β [95% confidence interval]) included being on dialysis (compared with CKD stages 3–5: −0.06 [−0.08 to −0.03]), female sex (−0.03 [−0.05, −0.006]), lower educational attainment (−0.04 [−0.06, −0.02]), and lack of a partner (compared with having a spouse/partner: −0.04 [−0.06, −0.02]). Comorbidities were also associated with lower QoL: diabetes (−0.05 [−0.07, −0.02]), stroke (− 0.09 [−0.13, −0.05]), cardiovascular disease (− 0.06 [−0.08, −0.03]), and history of prior cancer (− 0.03 [−0.06, −0.009]) (Figure 3). Univariate analysis of the predictors of QoL are shown in Supplementary Table 1. There was no interaction between CKD stages and other factors including sex and marital and education status.

Factors Associated With Reduced HR-QoL Stratified by CKD Stage

The presence of coexisting comorbidities was the key predictor for reduced QoL across all CKD stages. Although lack of a partner was associated with worse QoL in those with CKD stages 3 to 5 and on dialysis, lower education attainment was associated with worse QoL in transplant recipients. Dialysis participants on the transplant waitlist experienced better QoL compared with unlisted participants. Additionally, for patients with CKD stages 3 to 5, the use of erythropoiesis-stimulating agents was associated with better QoL but was associated with worse QoL in kidney transplant recipients (Figure 3).

Factors Associated With Decrements in Domain-Specific QoL

Being on dialysis was associated with reduced mobility (adjusted odds ratio [95% confidence interval]): 1.36 [1.02–1.78]), problems with self-care (2.98 [2.00–4.46]), problems with usual activities (2.02 [1.54–2.63]), and worse anxiety/depression (1.62 [1.24–2.10]) when compared with CKD stages 3 to 5 (Figure 4). Similar to overall QoL, the key determinants associated with the QoL domains of reduced mobility, problems with self-

Table 3. Proportion of participants reporting decrements in each domain-specific area, stratified by chronic kidney disease stage

Domain	CKD stages 3–5 (n = 787)	Dialysis (n = 415)	*P*[a]	Transplant (n = 494)	*P*[a]	All (n = 1696)
Mobility	243 (31)	146 (35)	0.13	109 (22)	0.001	498 (29)
Self-care	54 (7)	69 (17)	<0.001	34 (7)	0.99	157 (9)
Activity	207 (26)	165 (40)	<0.001	106 (21)	0.05	478 (28)
Pain	354 (45)	198 (48)	0.33	179 (36)	0.002	731 (43)
Anxiety/depression	214 (27)	160 (39)	<0.001	129 (26)	0.65	503 (29)

CKD, chronic kidney disease.
Values are n (%). Number of missing data: overall health-related quality of life = 21, mobility = 11, self-care = 10, activity = 13, pain = 13, anxiety/depression = 14.
[a]Compared with CKD stages 3–5 using the χ^2 test.

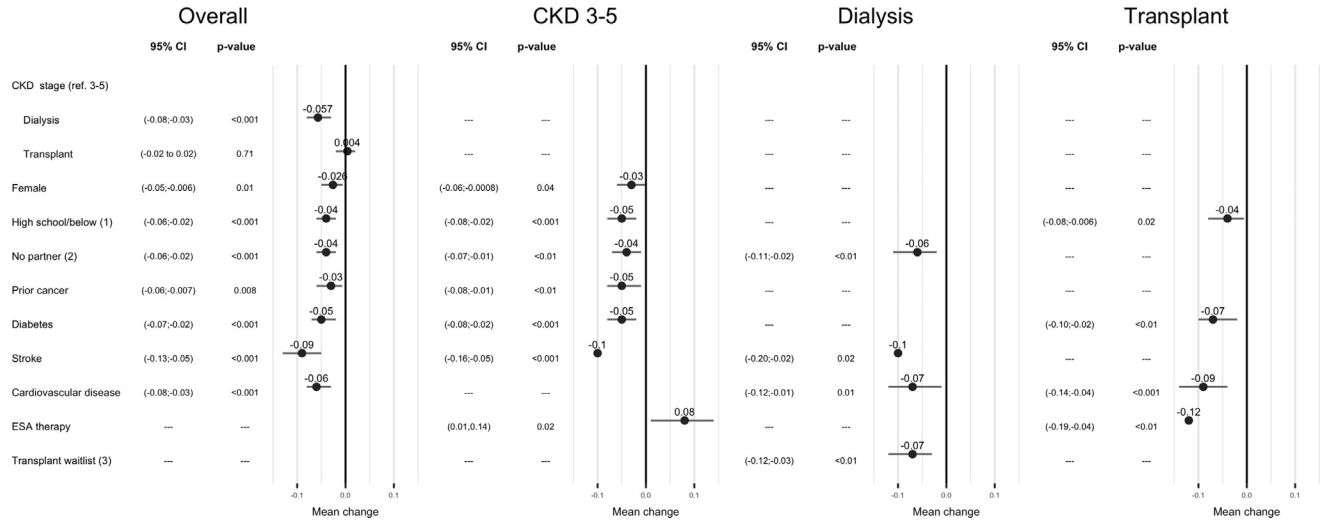

Figure 3. Forest plot of overall quality of life (QoL) and QoL by chronic kidney disease (CKD) stage. *Multivariate-adjusted model; 1, compared with college/university; 2, compared with married/partnered; 3, compared with waitlisted; CI, confidence interval; ESA, erythropoiesis-stimulating agent.

care, and usual activities were a lower education attainment, lack of a partner, or comorbid conditions such as diabetes, stroke, or cardiovascular disease. Women were also more likely to experience pain than men. Although advancing age was associated with poor mobility, it was inversely associated with anxiety/depression.

DISCUSSION

In this large study of 1696 participants from 4 countries and 11 centers and across the spectrum of CKD from stages 3 to 5 and dialysis and transplant recipients, overall, we found a considerable decrement in QoL. Consistent with previous studies,[2] being on dialysis has the greatest impact on overall QoL. The 3 key domains that were commonly affected were pain, anxiety/depression, and mobility, with dialysis patients reporting more problems in almost all domains compared with other CKD stages. The most striking finding was that the relative decrements in the utility-based QoL were similar across patients of female sex, lower education status, lacking a partner, and with comorbidities such as diabetes, stroke, and cardiovascular disease.

Approximately two thirds of our patients on dialysis (68%) reported reduced QoL, compared with 60% of those with CKD stages 3 to 5 and 49% with kidney

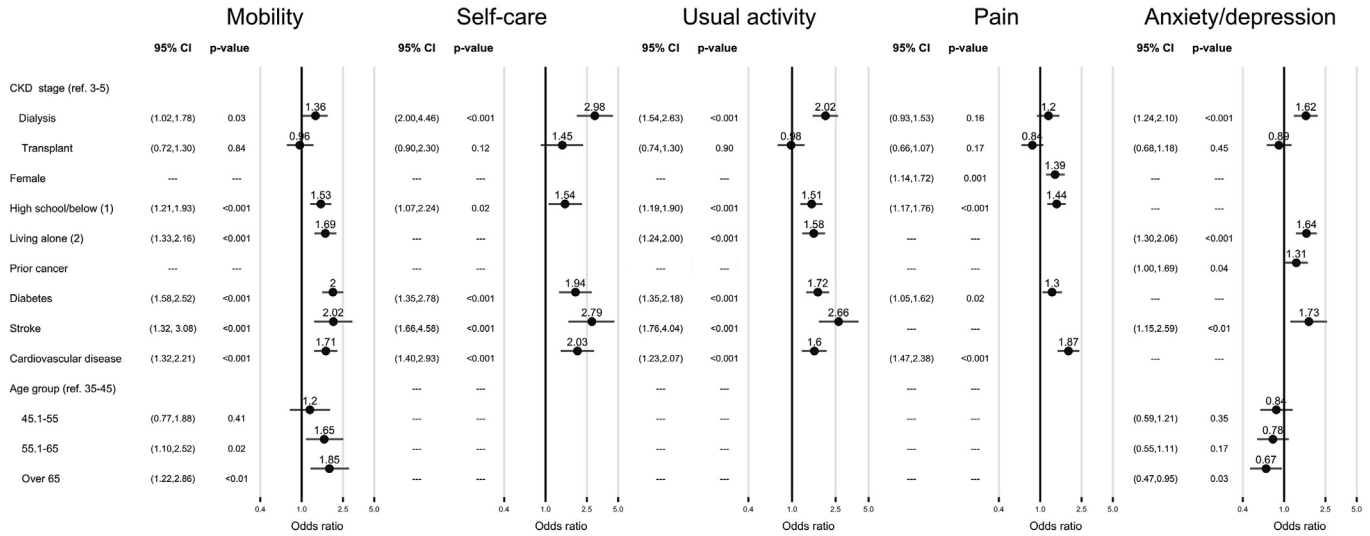

Figure 4. Forest plot of domain-level quality of life. *Multivariate-adjusted model; 1, compared with college/university; 2, compared with married/partnered; CI, confidence interval; CKD, chronic kidney disease.

transplants. On average, patients on dialysis experienced larger mean decrements of 0.24 in the overall QoL score (from a score of 1.0 representing full health) compared with decrements of 0.16 and 0.19 among those with kidney transplants and with CKD stages 3 to 5, respectively. Changes in QoL are important when they reflect a meaningful alteration in a patient's experience of an illness, and this important difference was found to be 0.06 to 0.08 in EQ-5D measurements, particularly in patients with malignancy.[17,18] These differences could be extrapolated in patients with CKD because those with CKD, particularly advanced-stage kidney disease, may experience comparable decrement in QoL as in patients with cancer.[4] Although kidney transplant recipients had higher mean QoL scores (by 0.08) compared with those on dialysis, this was still inferior when compared with the general Australian or American population.[19–21] Although offering improved survival and freedom from dialysis, transplant recipients still live with the affliction of chronic disease, with the need to comply with a strict medication regimen that is typically associated with multiple adverse effects and the requirement of ongoing medical care and support.

Deficits in mobility, usual activities, and anxiety/depression were reported in one third of our cohort regardless of CKD stage. Pain was pervasive across the cohort, with nearly 50% of those with CKD stages 3 to 5 and on dialysis reporting moderate to severe pain compared with 36% of kidney transplant recipients. Although prior studies using the EQ-5D-3L have reported substantial problems in these domains,[6,7] we also demonstrated that a large proportion of this cohort had concerns with anxiety/depression, with nearly 40% of dialysis patients reporting moderate to severe problems.

Identifying and understanding the key factors that may impact on the overall and domain-specific QoL are crucial because targeted treatments and interventions could be implemented to reduce risk and increase protective factors for this vulnerable group of patients with CKD. Additionally, worse QoL may be associated with increased mortality.[22]

Living alone without a spouse or partner is becoming more prevalent in today's societies, although this is not necessarily associated with loneliness.[23,24] People living alone may also be at different stages of their lives, and conflicting findings between the relationship between living alone and overall QoL have been observed in the general population. Although prior work has suggested that married persons experience better QoL,[25] more recent work in a Korean cohort[26] has noted that this differed by age and gender. Although older married men and women reported higher QoL as compared with younger single men who reported the lowest QoL, interestingly younger single women reported the highest QoL in the general population.[25,26] Additionally, being alone could be considered a surrogate for social isolation, especially in older individuals. Patients with CKD, particularly dialysis, are at a greater risk of social isolation, occurring possibly from a loss of independence, financial stress from early retirement, and a lack of control over daily activities.[27] Social isolation may be associated with higher mortality, higher rates of depression, poor self-rated health, and unfavorable health behaviors such as poor diet and noncompliance with treatment,[23,28,29] likely because of the lack of social support that facilitates health-promoting behaviors.

In this cohort of patients with CKD, we have shown that the lack of a spouse or partner (single, widowed, or divorced) is associated with worse overall QoL as well as problems in mobility, daily activity, and anxiety/depression, suggesting that social support (including virtual or online support, focus groups, patient/community navigators) may have beneficial effects on QoL and the management of serious illnesses.[30,31] Although social contact is difficult to prescribe, recognizing isolation itself and putting in place measures to support these individuals may benefit them. Further work quantifying social isolation and evaluation of measures against perceived social isolation may be a useful health promotion strategy in these patients. Interestingly, there was no evidence of interaction between living alone without a partner or spouse and age or gender, suggesting that living alone has a similar effect on QoL in both genders.

Similarly, lower education status was associated with worse overall QoL and domain-level QoL. The chronic nature of kidney disease requires a sufficient amount of understanding by patients to enable them to actively participate in the management of their health. Limited health literacy may result in patients becoming overwhelmed, resulting in decreased compliance and poorer health outcomes.[32] Although certain social structures cannot be changed without enormous political action, health literacy is susceptible to social environments and could be improved by targeted health education.[33,34] These socioeconomic measures such as education and marital status may influence life opportunities such as access to health care and the individual's perception of his or her QoL.[35,36] Additionally, we have shown that female sex was associated with worse QOL,[18,37,38] reflecting the vulnerability of women with chronic disease as well as their different psychosocial perspective on life (such as experiencing more psychological distress, stigmatization, having family roles that compete for time and resources, and a

feeling of disempowerment in their interactions with health professionals) when compared with men.[39–41] Although the use of erythropoiesis-stimulating agents was associated with better QoL in CKD stages 3 to 5, it was associated with worse QoL in transplant recipients, suggesting this may be a surrogate for declining allograft function along with the additional burden of needing subcutaneous injections.

Pain is common in CKD, with nearly 50% of this population reporting moderate to severe pain, regardless of being on dialysis or managed conservatively.[42] Women seemed to experience more pain compared with men, and this is in keeping with the population prevalence of chronic pain conditions that seem to more frequently affect women. This is likely because of a complex interplay of biologic (effect of sex hormones and endogenous opioids) and psychosocial (pain coping techniques, gender roles) mechanisms.[43] Chronic pain is associated with poor QoL, depression, and missed medical treatment. This symptom is often underrecognized and poorly managed by physicians because chronic pain is a multidimensional phenomenon with both physical and psychosocial components. Identifying pain and focusing therapy in a multimodal manner (physical, behavioral, and pharmacotherapy) is vital in managing this issue.[44] Similarly, the burden of a chronic illness and the rigors associated with dialysis treatment and its intrusiveness into social life domains can result in higher rates of anxiety/depression in patients with kidney disease. Assessments need to extend beyond simply questioning a patient regarding his or her mood. If an anxiety/depressive disorder is suspected, formal assessment should be considered along with psychotherapy and pharmacotherapy.[45]

Our study has several strengths. Because it is a prospective, multicenter study conducted across 11 centers in 4 countries in a routine screening setting, the study population is likely to be representative of the general CKD population. Although most other studies focused on moderate to severe CKD and/or dialysis populations, our study investigated QoL across moderate CKD, end-stage kidney disease, and transplant recipients. Our response rate was high with almost all participants (99.4%) completing the QoL questionnaire. Additionally, we assessed both QoL data and domain-specific data.

Our study also has a number of potential limitations. First, this was a cross-sectional study without serial measurements. As such, we were unable to compare the changes in QoL scores over time, particularly in relation to events related to life-changing events such as change in dialysis modalities or transition between dialysis and transplantation across the lifespan of a person with CKD. Second, there is a possibility of selection or volunteer bias, leading to recruitment of a relatively healthier patient population. Third, for the purposes of this study, the Australian scoring system of the Euro-QoL was used for all participants, although the sensitivity analyses conducted using the Spanish version of the Euro-QoL were aligned with the findings observed using the Australian version of the Euro-QoL.

In conclusion, in this multicenter cohort of adults with CKD stages 3 to 5, on dialysis and with kidney transplants, there were widespread deficits of QoL. Being on dialysis was associated with poor overall QoL as well as pervasive deficits in domain-specific scores. In addition, a lower educational status, concurrent comorbidities, and lack of a partner were associated with reduced QoL in almost all dimensions. Knowledge of this triad of factors will provide valuable means of identifying those who are most at risk of poor QoL and defining novel social and medical interventions and the resources to support them, which are of benefit to this group of individuals.

DISCLOSURE

All the authors declared no competing interests.

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SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Figure S1. Domain-specific quality of life by chronic kidney disease stage.

Table S1. Univariate analysis of the predictors of quality of life.

Supplementary Sensitivity Analysis.

Strobe Statement.

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