Quality of life in advanced renal disease managed either by haemodialysis or conservative care in older patients

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Quality of life in advanced renal disease managed either by haemodialysis or conservative care in older patients.

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Abstract:

Objective: Consideration of quality of life (QoL) in people with end-stage renal disease (ESRD) has become an important part of treatment decision-making. The aim of this study was to report on QoL and other functional outcomes in patients with advanced chronic kidney disease (CKD). Method: This was a cross-sectional study. Two samples of older patients (>60 years old) either conservatively managed (CM) or receiving hospital-based haemodialysis (HD), compared kidney disease quality of life (KDQoL-36) outcomes. Results: Data from 263 CM patients (CKD 4 n=188, mean age 73.6 years, 48 females; CKD 5 n=75, mean age 74.4 years, 26 female) and 74 patients on HD (mean age 73.8 years, 24 female) were analysed. Significant group differences were identified for two subscales of KDQoL-36. Symptoms/Problems List subscale was significantly better for those receiving HD compared to those CM with CKD 5 (p=<.001). Symptom/Problem List scores of CM CKD stage 4 patients were not significantly different compared to HD patients but were significantly better than CM CKD stage 5 patients (p<.001). Burden of Kidney Disease subscale was significantly better for both CKD 4 (p<.001) and CKD 5 (p<.001) CM patients when compared to those receiving HD. Conclusion: Symptoms of advanced CKD significantly impact QoL for patients CM with CKD stage 5. Conversely, QoL is significantly impacted for those in receipt of haemodialysis due to the burden of treatment. These findings provide evidence for the use of QoL tools to help with clinical prognostication in advanced CKD. Utilising QoL tools will ensure specialist support is available for appropriate management of patients with CKD.

Key words: End-stage renal disease, conservative care, haemodialysis, quality of life

Introduction

End-stage renal disease (ESRD) is increasingly common, in part due to a rapid expansion in the numbers of older people, but also due to advances in the management of comorbidities (particularly cardiovascular disease) associated with chronic kidney disease (CKD). (1) Although renal replacement therapy (dialysis or renal transplantation) are well established interventions for ESRD, these treatments carry significant risks and impose a substantial burden of care on patients. These burdens may outweigh the benefits in some groups of patients with ESRD, particularly those with multi-morbidity due to advancing age. (2)

A rapidly ageing and multi-morbid patient population has led to the default clinical practice of dialyzing older and sicker patients. There is a growing need to find non-dialytic alternatives for ESRD. (1, 3) Conservative management (CM) is considered an alternative choice to dialysis for ESRD (2) and is provided by a multidisciplinary team often in liaison with the community team and general practitioner. Although only limited epidemiologic evidence exists, it has been suggested that as many as one in seven ESRD patients may opt not to dialyze. (4) Addressing these end-of-life issues is an important component of caring for persons with ESRD but there is still limited agreement on the optimal clinical tools for prognostication. (4, 5)

To date, research suggests there is no survival advantage among patients aged >80 years choosing dialysis over conservative management (6), particularly for those with higher levels of comorbidities and poorer functional status. (7) A study conducted in the United States reported >75-year olds will account for over 25% of ESRD patients (8), which will carry increased morbidity and mortality issues (9) whereby dialysis may not be suitable in all cases. Quality of life is an important domain consideration by health care professionals in such circumstances. Patients with ESRD commonly experience a compromised QoL and severe symptom burden (10) which can be amplified in older patient populations. It is reported that ESRD patients suffer significantly and have similar, if not greater, symptom severity than cancer populations. (11) Accurate projections about survival and expected QoL would help to guide appropriate patient decision-making in ESRD, where balancing the impact of therapies on lifespan, symptoms and quality of life is crucial. However, there continues to be limited evidence within renal disease.

A systematic review (12) examining quality of life of older patients with ESRD undergoing conservative management found three studies directly comparing CM and HD (13, 14, 15). Only one study used KDQoL-SF with CKD stage 5 patients receiving conservative management (n=101) compared to those who commenced dialysis (n=38). QoL was similar between both groups after two years (13) however, patients were all >75 years and/or had high comorbidity burden (Charlson Comorbidity Index score of >8). The SF-36 was used in the two remaining studies with mixed findings. De Biase et al. (14) reported similar quality of physical and mental outcomes for age-matched CKD stage 5 CM and HD patients. Da Silva-Gane et al. (15) reported poorer quality of physical health for the CM group whereas quality of mental health was similar

between CM and those that transited to HD. Interestingly, life satisfaction reduced significantly for those that initiated dialysis; which did improve at follow up. A recent cross-sectional study (16) also conducted in the United States, used the KDQoL-36 reporting significant levels in Burden and Effect of Kidney Disease subscales in HD patients compared to those CM. However, the authors highlight heterogeneity between the groups concerning co-morbid conditions. Overall, the current evidence base is limited and there is a need for further studies. (12, 16)

Materials & Methods:

Aim

The primary objective of this paper was to explore QoL findings in two contrasting studies of older patients with advanced CKD. Study one included a group of CKD stage 5 patients receiving HD. Study two included a group of patients with advanced CKD (stage 4 & stage 5) managed conservatively. Protocols for these studies are published elsewhere. (17, 18) Cross-sectional QoL findings and functional outcomes were compared for HD and CM patients.

Study population

Study 1: Adult haemodialysis (HD) patients

Patients were recruited during haemodialysis (17). HD patients >60 years (n=74) who attended two haemodialysis units within the United Kingdom and had a confirmed diagnosis of ESRD (estimated GFR <15 mL/min/1.73m^2) were recruited. HD patients completed the Functional Assessment of Chronic Illness Therapy (FACIT) questionnaire and handgrip strength (HGS) was recorded. All patients were able to read and write English and were over 18 years of age. Data were collected between September 2017 and April 2018.

Study 2: Conservative management (CM) patients

This study collected data on QoL in a CM patient group (18) recruited to a randomised controlled trial of oral bicarbonate therapy vs placebo. This study included CM patients (n=263) who attended 24 study sites within the United Kingdom aged >60 years, with an eGFR ≤30 mL/min/1.73m^2, with serum bicarbonate levels <22 mmol/L and not on dialysis. This group

includes CKD stage 4 who do not have ESRD, and so are not (yet) at a point where one would have to make a choice about dialytic vs non-dialytic therapy. However, these patients are under conservative management insofar as they are not being dialysed and may never need to be dialysed. In addition to QoL measures, the six-minute walk test (6MWT) was completed by patients and handgrip strength (HGS) was recorded. Data were collected between 2014 and 2016.

Data collection

HD and CM patients in each study were asked to complete Likert subscales of the Kidney Disease Quality of Life (KDQoL-36 (HD) or the original 134-item KDQoL version (CM); 1) Symptoms of kidney disease, 2) Effects of kidney disease, 3) Burden of kidney disease, 4) SF12 physical component score (PCS), 5) SF-12 mental component score (MCS). These sub-scales can be compared across the two tools, the appropriateness of which is outlined in the literature (19). The raw scores are transformed linearly ranging from 0 to 100 using an Excel scoring template. A higher score indicates better QoL. KDQoL-36 has confirmed reliability and validity in measuring QoL in an ESRD population (19) (reliability across subscales [a =.81-.87] and construct validity [r =.4-.5]). It has also been validated and translated into various languages (20, 21, 22). HGS was measured in all patients. It is a reliable screening assessment for functional limitations and strongly correlates with other functional assessments such as 6MWT. (23) The 6MWT was recorded for CM patients whereas the HD patients completed the Functional Assessment of Chronic Illness Therapy (FACIT) questionnaire; a measure of fatigue. (24) Additional patient information was also collated (e.g. marital status, ethnicity and comorbidities (yes/no for hypertension, myocardial infarction, peripheral vascular disease, diabetes mellitus).

Data analysis

Patients were age matched. Descriptive statistics were generated for baseline demographics (sex, age) and QoL subscales. ANOVA was performed to compare KDQoL subscales between HD and CM (CKD stage 4 and CKD stage 5) populations. Bivariate correlations were conducted to assess any associations between KDQOL-36 subscales and functionality. Scale scores are computed with the KDQOL-36^{TM} scoring program. Participants with any missing data on the relevant measures were excluded from analysis (n=22). The significance level for all statistical

analyses was p<.05. All analyses were conducted using SPSS version 24 (IBM Corp. Released 2016, IBM SPSS, Statistics for Windows, Version 24.0, IBM Corp, Armonk, NY).

Results:

Data from 263 CM (CKD stage 4 n=188, mean age 73.6 years, 48 females; CKD stage 5 n=75, mean age 74.4 years, 26 females) and 74 patients on HD (mean age 73.8 years, 24 female) were analysed (table 1). Mean scores for KDQoL subscales are presented in Table 2. Higher scores indicate better QoL. Symptom or problem list subscale was significantly different between groups ($F(2,334)= 9.170$; $p<.001$). HD patients had significantly better scores compared to CM CKD stage 5 ($p<.001$). Scores for CM CKD stage 4 patients were also significantly better when compared to CM CKD stage 5 ($p<.001$) only. There were no significant differences between patient groups for the Effects of Kidney Disease subscale ($F(2,334)= 2.414$; $p=.091$). The burden of kidney disease subscale was significantly different between patient groups ($F(2,334)= 133.339$; $p<.001$). CM CKD stage 4 (M=87.88; SD=13.62) and CKD stage 5 (M=82.80; SD=15.39) scores were not dissimilar but were significantly better than HD patients ($p<.001$). There were no significant differences between patient groups for SF-12 Physical Component Subscale ($F(2,334)= .573$; $p=.565$) or SF-12 Mental Component Subscale between patient groups ($F(2,334)= .317$; $p=.302$).

Mean scores between groups were not statistically dissimilar for Effects of Kidney Disease, SF-12 PCS or SF-12 MCS. However, CM CKD stage 4 patients tended to have better KDQoL scores compared to HD and CM CKD stage 5 patients (Burden of Kidney Disease; SF-12 PCS, SF-12 MCS). CM individuals with CKD stage 5 also tended to have worse KDQoL scores (Symptoms/Problem List, Effect of Kidney Disease, SF-12 MCS). Bivariate analysis (Table 3) was conducted comparing associations between quality of life subscales and HGS for patient groups. Significant associations were reported for Burden of Kidney Disease and HGS in CM CKD stage 5 (r = .233) and SF-12 PCS and HGS in HD patients (r=.319).

Table 1: Patient characteristics

	CM CKD 4 (N=188)	*CM CKD 5 (N=75)*	*HD (n=74)^*

sex Male (%)	*140 (74%)*	*49 (65%)*	*58 (78%)*
Mean AGE years (SD)	*73.6 (6.6)*	*74.4 (7.9)*	*73.8 (7.6)*
Ethnicity White (%)	*184 (98%)*	*70 (93%)*	*74 (100%)*
Living arrangements			
Living alone (%)	*55 (29%)*	*23 (33%)*	*22 (30%)*
Co-morbidities			
Hypertension	*164 (89%)*	*67 (89%)*	*60 (81%)*
Myocardial infarction	*32 (17%)*	*4 (5%)*	*11 (15%)*
Peripheral Vascular Disease	*16 (9%)*	*6 (8%)*	*24 (31%)*
Diabetes mellitus	*62 (33%)*	*22 (29%)*	*56 (75%)*
^ reference group for ANOVA			

1

2 *Table 2: KDQOL-36 subscales*

KDQOL-36 subscales	*CM CKD 4 (N=188)*	*CM CKD 5 (N=75)*	*HD (n=74)^*
Symptom or problem list	*77.8 (24.4)a**	*66.5 (25.2)**	*81.3 (13.7)*
Effects of kidney disease	*80.9 (12.5)*	*79.0 (13.4)*	*83.8 (15.2)*
Burden of kidney disease	*87.9 (13.6)**	*82.8 (15.4)**	*47.0 (29.2)*
SF-12 PCS	*38.8 (11.3)*	*37.7 (8.9)*	*37.5 (9.8)*
SF-12 MCS	*51.9 (10.6)*	*49.8 (9.6)*	*51.4 (9.3)*
*^ reference group for ANOVA; * p<.001, a* respective post-hoc t-test of CM CKD 4 vs. CM CKD 5*			

3 *Table 3: Bivariate correlations between quality of life subscales and measures of functionality*

4 *for CM (CKD stage 4 & 5) and HD*

KDQoL subscales		CM CKD 4 (N=188)	CM CKD 5 (N=75)	HD (N=74)
Symptoms/problem list	*HGS (higher score =*	.096	.174	.217
Effects of Kidney Disease		-.018	.153	.085
Burden of Kidney Disease		.117	***.233****	.064

SF-12 PCS	*higher function)*	-.135	-.011	***.319****
SF-12 MCS		.063	.140	-.029
Symptoms/problem list	*6MWT (higher score = greater distance covered)*	.108	.038	-
Effects of Kidney Disease		***.263****	.202	-
Burden of Kidney Disease		***.234****	.108	-
SF-12 PCS		***.385****	**.251***	-
SF-12 MCS		***.158****	.218	-
Symptoms/problem list	*FACIT (higher score = lower fatigue)*	-	-	***.628****
Effects of Kidney Disease		-	-	***.374****
Burden of Kidney Disease		-	-	***.357****
SF-12 PCS		-	-	***.540****
SF-12 MCS		-	-	***.557****

*(*p=<.05; **p=<.001) HGS: handgrip strength; 6MWT: six-minute walk test; FACIT: Functional Assessment of Chronic Illness Therapy*

Table 3 provides positive correlations between KDQoL-36 subscales and HGS. Although significant, weak correlations between Burden of Kidney Disease and HGS (r=.233, p=.044) in CM CKD 5, suggests better scores on Burden of Kidney Disease are associated with higher HGS. A significant but weak correlation between SF-12 PCS and HGS in HD patients (r=.319, p=.006) suggests increases in SF-12 PCS are associated with higher HGS. The 6MWT was administrated only to CM patients. With exception of Symptoms/Problems List subscale, higher scores of Effects (p<.001), Burden (p=.001), SF-12 PCS (p<.001) and SF-12 MCS (p=.031) were associated with longer walking distances in the 6MWT for CM CKD stage 4 patients. Correlations were of a similar magnitude for CKD stage 5 but did not reach significance in all cases due to the smaller sample size with exception of SF-12 PCS (r=.251; p=.031). Positive moderate correlations were reported for all KDQoL subscales (Symptoms (p<.001), Effect (p=.001), Burden (p=.002), PCS (p<.001), MCS (p<.001)) and FACIT (p<.001) in HD patients. This suggests better KDQoL is associated with better scores of fatigue.

*Insert [Fig 1: QoL **Symptom/Problem list** subscale for CM and HD patients by age and sex]*

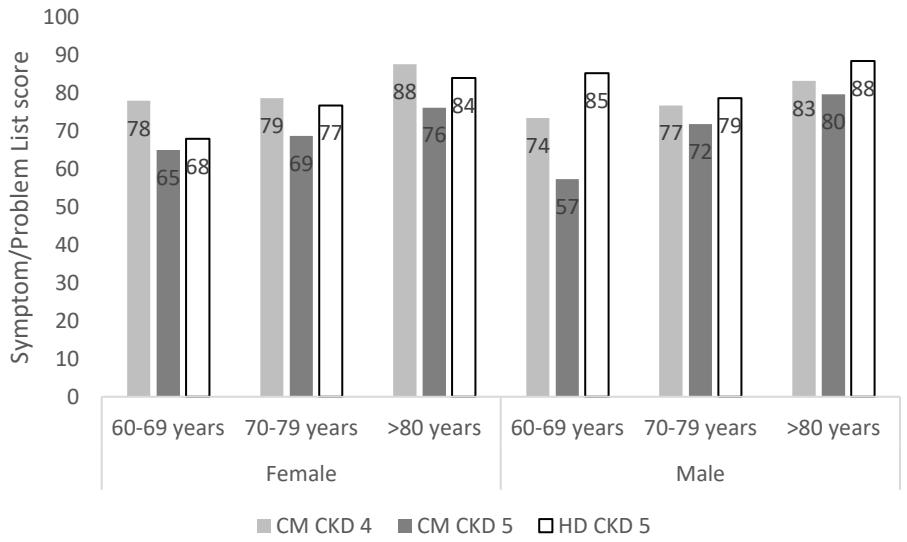

Figure 1 demonstrates the lower age group (60-69 years) tended to experience greater symptoms or problems in both males and females. In addition, as age increased, QoL symptom and problem list scores improve.

*Insert [Fig 2: QoL **Effects of Kidney Disease** subscale for CM and HD patients by age and sex]*

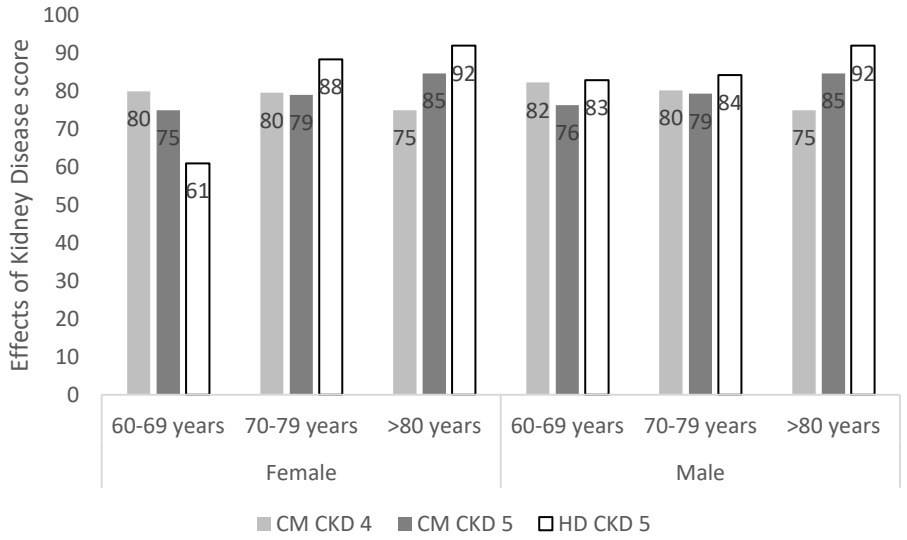

Figure 2 demonstrates higher scores were more common in HD groups for both males and females.

*Insert [Fig 3: QoL **Burden of Kidney Disease** subscale for CM and HD patients by age and sex]*

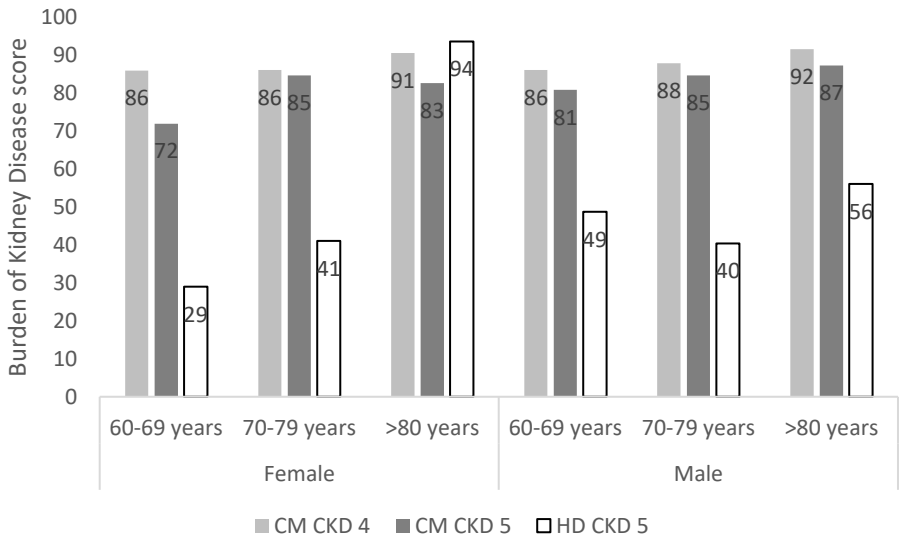

Figure 3 demonstrates males experiences less Burden of Kidney Disease compared to females. HD patients experienced greatest Burden of Kidney Disease across age groups with exception of females >80 years, indicated by lowest QoL scores.

*Insert [Fig 4: QoL **SF-12 Physical Component** Subscale for CM and HD patients by age and sex]*

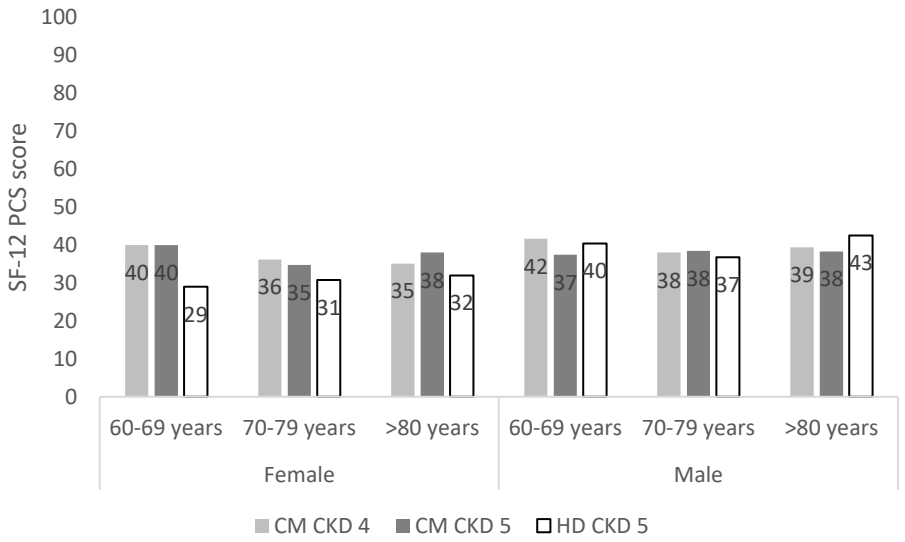

Figure 4 demonstrates males patients had better scores of SF-12 PCS compared to females. Males tended to have similar scores across age groups.

*Insert [Fig 5: QoL **SF-12 Mental Component** Subscale for CM and HD patients by age and sex]*

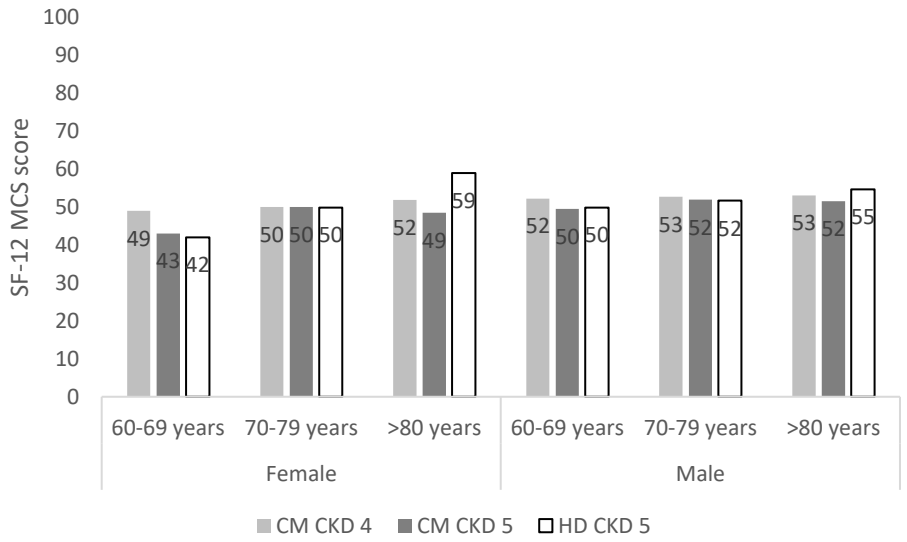

Figure 5 demonstrates males patients had better scores of SF-12 MCS compared to females. Males tended to have similar scores across age groups. Females in the lower age group (60-69 years) had the poorest quality of life for mental health.

Discussion

Few studies have examined QoL outcomes between patients opting for CM and HD treatment. This study directly compares QoL between age-matched CM and HD populations using the KDQoL-36 taking account of the CKD stage. In the current study, CM patients with CKD stage 5 tended to have poorer mean scores across more of the KDQoL subscales. This was significantly lower for the Symptom/Problems List subscale when compared to CM CKD stage 4 and HD patients. Conversely, it has been suggested that KDQoL-36 is an insensitive measure for HD patients (25) which includes a symptom and burden list that may be less prevalent since its publication. This may help to explain findings in the current study. Ceiling effects have been reported within other studies. (25) Severity of symptoms continues to be under recognised in ESRD (26) and further work is required to identify key symptoms and the impact on patient's quality of life.

Effects of Kidney Disease scores were not dissimilar between groups. CM CKD stage 5 patients had the poorest scores whereas HD patients had better scores. The Effects of Kidney Disease questions relate to a wide range of issues such as fluid restriction and dietary limitation, financial hardship, impact of sexual dysfunction, work status and being dependent on medical

personnel. (27) Answers to these issues are likely to be influenced by other patient factors such as current functionality and support needs. It is essential to explore these aspects.

Similar to Seow et al. (13) the Burden of Kidney Disease subscale was significantly poorer in HD patients compared to those receiving CM (CKD 4 and 5) in the current study. The nature of dialysis treatment is more likely to burden daily life as it includes invasive interventions, medicalisation and a significant time commitment required for dialysis therapies. (14) Also, post-dialysis treatment is associated with a wide range of adverse effects. (28)

The physical (PCS) and mental component (MCS) in HD and CM patients reported similar scores across groups. PCS and MCS scores were better for those managed conservatively with less severe renal disease i.e. CKD 4. As CKD progresses, patients typically have more comorbidities and have a higher mortality. ESRD patients experience a continual functional decline over time as well as an increasing risk of hospitalisation and premature death. (29-31) Monitoring physical function longitudinally (e.g. PCS scores) can be important assessment measures. However, Hall and colleagues (29) suggest that SF-12 PCS changes may not be meaningful for older dialysis patients. Objective physical performance measures (e.g. 6MWT) are more sensitive to subtle changes in physical function and therefore, may be more useful in tracking functional decline.

CM CKD stage 5 patients reported lower MCS suggesting poorer mental health outcomes. Although scores <50 indicate poorer health related quality of life (HRQoL; 32), overall scores of MCS were not dissimilar to 'national norms' reported by Peipert and colleagues. (19) However, these scores refer to dialyzed patients. Further work is required to provide normative values for non-dialysis patients. In addition, it has been suggested that the PCS and MCS may not appropriate measures for CM CKD patients, as these do not include domains which become increasingly important at the end of life (such as existential concerns, comfort and peace of mind). (32) Global assessments such as the Integrated Palliative Care Outcome Scale (33), used alongside HRQoL measures, have been recommended. (32)

There is an undisputed strong relationship between physical functional assessments such as HGS and ability to perform daily living. (30) Assessment of functionality in this study has also helped to reinforce this finding. Better QoL was associated with stronger HGS in CM CKD stage

5 and HD, longer walking distance in CM CKD stage 4 and more energy in HD patients. The ability to engage in activities of daily living should be used in combination with other assessments to understand the likely impact on QoL. KDQoL subscale scores also were similar across sex and different ages however females in the lower age group (60-69 years) tended to have poorer QoL scores. This is in keeping with QoL trends. For example, during the "third age" of life (65-85 years), QoL is reported to improve. In addition, women tend to have poor health related QoL. (34) With a growing older patient population, further research is needed to understand how QoL changes with increasing age and co-morbidity.

Strengths and limitations

This is a cross-sectional data and therefore cannot infer causality. CM tends to be offered more frequently to older patients than dialysis in part due to greater perceived frailty and comorbidities (35) however this study did not control for this. This study was also not adjusted for sex and co-morbidities. Also, CKD 4 patients have been included who do not have end-stage renal failure however, there is merit in including people with CKD 4 in our comparisons, in part because it demonstrates the relationship of severity of renal impairment with QoL. Other limitations include a lack of ethnic diversity which may influence findings as ethnic minorities tend to report lower QoL than white patient populations in self-rated health surveys. (36) Also, it is important to acknowledge the likely variability in the conservative management service provision between institutions which requires further exploration. Caution should be applied in the comparison of samples from two different studies conducted at different times, involving different demographic sites, however this work contributes to a small but growing evidence base investigating utility of QoL in older patients with ESRD.

Implications of clinical practice

Testing the utility of QoL clinical tools for prognostication is important; however, there is a need to update current KDQoL assessments (particularly symptom-related) taking account of evolving ESRD treatment (25). In addition, a prospective multicentre, ethnically diverse study overtime is required to provide a stronger evidence base for patient and clinician decision making.

Conclusion

QoL for CM patients was better for those patients with less advanced kidney disease (CKD stage 4 vs. CKD stage 5). CM CKD 4 patients tended to have better QoL scores on more subscales than HD or CM CKD 5. HD patients experienced a significantly greater burden of disease state and treatment compared to the other groups. However, admission rates, complications and other comorbidities require further exploration within these groups. (37) All groups demonstrated low mental health scores highlighting a greater need for supportive care across ESRD. Despite the challenges of studying QoL in this frail ESRD population, it is important to determine what matters to individuals with ESRD. (35-37) Currently, this study highlights the urgent need to provide enhanced support and services for patients conservatively managed.

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Competing interests

No conflict of interest has been declared by the author(s).

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Authors' contributions

JR is the principal investigator of the HD study and MDW is the principal investigator of the CMK study. All authors have assisted in the design of the study and have revised and given approval for the final version of the protocol. CMK completed data analysis. CMK, JR and MDW

completed the initial draft of this manuscript. All authors read and approved the final manuscript.

Ethical approval

Governance approval for the HD study was obtained from the Office of Research Ethics Committees Northern Ireland (ORECNI; HD study 1- REC reference: 16/NI/0233) and was funded by the Northern Ireland Public Health Agency / Northern Ireland Kidney Research Fund. The BicARB trial, from which the CM data were obtained, was approved by the East of Scotland NHS research ethics committee (approval 12/ES/0023), the Medicines and Healthcare Regulatory Authority (EudraCT number 2011-005271-16; Clinical Trial Authorisation number 41692/0001/001-0001), and was funded by the National Institute for Health Research Health Technology Assessment programme (reference 10/71/01).

Data availability statement

Data are available upon reasonable request.

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