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Research article

Chronic kidney disease report differently on change in sexual function dependent on treatment: a cohort study

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Abstract: Patients with Chronic Kidney Disease (CKD) report sexual dysfunction to a large extent. The objective of this study was to investigate if CKD-stage and mode of treatment correlate to selfreported experience in sexual function before and after onset of symptomatic CKD in patients without active treatment, after transplantation or on dialysis. Participants (N = 234) answered a questionnaire on frequency of sexual desire, initiative, intercourse, erection (men) /vaginal lubrication (women), and orgasm, currently and compared with before onset of symptomatic CKD. Clinical data were taken from medical charts. Within-group differences in sexual function were compared for patients without active treatment (PreT), patients with a renal transplant (Tx) and patients on dialysis treatment (D). In a subgroup analysis, five patient groups were created based on mode of treatment and CKD stage. Between-group differences in sexual function were analyzed as differences in mean composite scores and 95% CI and were estimated using ordinary least square regression with robust standard errors. In the first analysis of the study, all CKD patients reported a decrease in the frequency of sexual desire, initiative, intercourse, erection (men)/vaginal lubrication (women), and orgasm (Bonferroni p < 0.001) compared to before disease onset, irrespective of treatment mode. In the subgroup analysis, when adjusting for sex and age, dialysis patients reported a statistically significant decrease in their average score of sexual function (-2.65; 95% CI: -4.19 to -1.11; p = 0.001) compared to patients without active treatment CKD 2-3 (the reference group). The self-reported experience of CKD-patients of a deteriorating sexual function over time correlates to treatment modality and CKD stage. It is important for health-care personnel to be aware of the patients' experience of a deterioration in sexual function over time regardless of treatment modalities.

Keywords: chronic kidney disease; sexual dysfunction; erectile dysfunction; predialysis; transplantation; uremia

Abbreviations: CKD: Chronic kidney disease; CKD 1–5: Chronic kidney disease stage 1–5; PreT: Pretreatment; PreT 2–3: Pretreatment patients in CKD stages 2–3; PreT 4–5: Pretreatment patients in CKD stages 4–5; D: Dialysis; Tx: Transplanted patients; Tx 2–3: Patients with a renal transplant in CKD stages 2–3; Tx 4–5: Patients with a renal transplant in CKD stages 4–5; BMI: Body Mass Index; GFR: Glomerular Filtration Rate; IIEF: International Index of Erectile function questionnaire; FSFI: Female Sexual Function Index questionnaire; ED: Erectile Dysfunction; RSS: Relationship and Sexuality Scale; ACE: Angiotensin converting enzyme; ARB: Angiotensin II receptor blockers; PTH: Parathyroid Hormone; OLS regression: Ordinary least square regression; IQR: Interquartile range; SLE: Systemic lupus erythematosus; EPO: Erytropoietin

1. Introduction

Chronic Kidney Disease (CKD) is a worldwide disease with increasing incidence. In Sweden, 10% of the population is living with CKD and approximately 10 000 patients are on active dialysis treatment or have a renal transplant. Patients with CKD report high rates of depression and decreased quality of life [1–3].

It is known that CKD patients have reduced sexual function, especially dialysis (D) patients [4–11]. Increasing age, underlying comorbidities and different treatment modalities have been suggested to contribute to such deterioration [5,6].

The stage of CKD at which sexual dysfunction becomes overt has been less investigated, and few studies have focused on patients without active treatment (Pretreatment, PreT) [1,12–15].

In our previously published study, using a self-comparator design, we found that patients reported a decrease in sexual desire, initiative, erection/vaginal lubrication and frequency of intercourse but that PreT patients (CKD 4–5) reported less sexual dysfunction than D and transplanted patients (Tx) [4].

We hypothesized that 1: treatment modality correlates to a self-reported experience of decreasing sexual function over time. 2: CKD stage correlates to a self-reported experience of decreasing sexual function i.e. CKD 2–3 patients would report less change in sexual function compared to patients with CKD 4–5.

The aim of this observational study was to compare self-reported experience of changes in sexual function over time before and after onset of symptomatic CKD in patient groups on different treatments and at different stages of renal dysfunction. We found that CKD-patients' self-reported experience of a deteriorating sexual function over time correlated to treatment modality and CKD stage.

2. Materials and methods

PreT, D and Tx patients with CKD 2–5 attending six nephrology units in Sweden were included in the study.

Exclusion criteria were: <18 years, factors affecting comprehension of the questionnaire (insufficient language understanding, psychiatric disease and cognitive disorder) and <3 months on current CKD treatment.

The attending nephrologist collected medical history and laboratory values from medical charts (underlying renal disease, concomitant diseases, blood pressure, body mass index (BMI), B-hemoglobin, S-albumin and glomerular filtration rate, GFR). The duration of the underlying renal disease was estimated by the nephrologist. CKD stages were defined according to the National Kidney Foundation (CKD 2: GFR 60–89 ml/min/1.73m², CKD 3: 30–59, CKD 4: 15–29, CKD 5: <15 or dialysis) [16].

We studied the difference in patients' self-reported experience of sexual function over time during the last 6 months compared to 6 months preceding the onset of symptoms from CKD (for questions see Supplement 1). The patients were instructed to compare their sexual function at the present time to a point in time preceding the onset of symptoms of CKD. In the first part of the study the self-reported experience of sexual function was analysed in predialysis patients, dialysis patients and transplanted patients. In a subgroup analysis, five patient groups were created based on mode of treatment and CKD stage. Patients without active treatment presently in CKD stages 2–3 (PreT 2–3) were used as reference group and compared with patients without active treatment presently in CKD stages 4–5 (PreT 4–5), patients with a renal transplant in CKD stages 2–3 (Tx 2–3), patients with a renal transplant in CKD stages 3–5 (Tx 4–5), as well as patients on dialysis treatment (D).

In this observational study we used the same questionnaire as in our previously published study [4], enabling a before-and-after comparison of the patients' self-reported experience of change in sexual function between the time before onset of symptoms of CKD and the time of the study (Supplement 1).

The questionnaire covered five aspects of sexual function (1) how often the participants had sexual desire/thoughts, (2) took sexual initiative, (3) had erection (men)/vaginal lubrication (women), and (4) how often they had intercourse, and (5) the ability to achieve an orgasm. The ability to achieve an erection (men)/vaginal lubrication (women) in combination with sexual performance was used to evaluate male/female physiological function. Frequency of sexual desire/thoughts, sexual initiative, intercourse, orgasm was of equal relevance to both sexes.

The item on orgasm had four possible answers "never/rarely", "sometimes", "half of the times", and "(almost) always". Responses were scored along an arbitrary scale, typical for Likert-type scales, where the response "once every week" were considered the highest possible score and "never" the lowest possible score. The distance between responses carried equal weight e.g. a decrease of one step from "once every week" to "once a week" rendered one minus point or from "once a week" to "never" rendered two minus points etc. The first four items each had four possible responses: "once every week", "once a week", "once a month", or "never". The item on orgasm was scored analogously as the first four items but in reverse direction.

The question of premature ejaculation was not studied in this report.

This resulted in a composite score (interval scale variable) describing the change in sexual function. The total range went from minus 15 to plus 10 where 0 represented no change, minus 15 to minus 1 represented a deterioration in sexual function, and 1–10 represented an improvement.

2.1. Statistical analysis

Categorical variables were expressed as frequencies (%) and proportions. Continuous variables were summarized as mean (±SD) or median values (IQR). Group differences were calculated using Chi-square tests for categorical variables. Missing observations (<5%) were omitted. P-values obtained from multiple testing were adjusted by Bonferroni correction or Benjamini-Hochberg correction [17]. Student's t-test (for mean values) or Mann-Whitney U-tests (for median values) were calculated for continuous variables. A double-sided p-value of <0.05 was considered statistically significant.

In the subgroup analysis, the outcome of a self-reported change in sexual function over time was modelled as an interval scale variable (-15 to +10) and between-group differences were estimated using ordinary least squares regression with robust standard errors. Between-group differences were expressed as unadjusted means and means adjusted for age divided at the median (≤ 58 or >58 years) and gender. A double-sided p-value of 0.05 was considered statistically significant. Analyses were performed in STATA 16.1 (Stata Corp, College Station, Texas, USA).

Ethics approval: This study was approved by the Regional Ethical Review Board of Stockholm (2009/4:1). Consent to participate: All patients gave their written informed consent.

3. Results

Two hundred and thirty-four patients attending six nephrology units answered the questionnaire: Karolinska Hospital Solna (123 patients), Danderyd Hospital (23), Nyköping (17), Linköping (32), Eskilstuna (30) and Karlstad (9) patients.

Differences in baseline characteristics between the treatment groups (PreT, Tx and D) are shown in Table 1. Differences in baseline characteristics between the five groups in the subgroup analysis (PreT 2–3, PreT 4–5, Tx 2–3, Tx 4–5 and D) are shown in Supplement 2.

	PreT (CKD 2–5)	D (CKD 5)	Tx (CKD 2–5)	p-value
N (%)	93 (39.7)	73 (31.2)	68 (29.1)	
Male	68 (73)	57 (78)	47 (69)	0.48
Female	25 (27)	16 (22)	21 (31)	
Age, median (IQR)	60.0 (46.0, 70.0)	59.0 (50.0, 67.0)	56.5 (46.0, 64.5)	0.21

Table 1. Baseline characteristics in the patient groups (PreT, D, Tx).

	PreT (CKD 2–5)	D (CKD 5)	Tx (CKD 2–5)	p-value
Renal disease				
Glomerulonephritis	20 (22)	19 (26)	24 (35)	0.18
Diabetic nephropathy	24 (26)	15 (21)	5 (7)	0.008
Nephrosclerosis/hypertension	21 (23)	16 (22)	5 (7)	0.026
Polycystic kidney disease	9 (10)	10 (14)	18 (26)	0.016
SLE and other systemic diseases	4 (4)	3 (4)	8 (12)	0.10
Comorbidity				
Hypertension	66 (76)	43 (59)	55 (82)	0.006
Diabetes type 1 and 2	28 (30)	19 (26)	14 (21)	0.27
Current/former smoker	25 (27)	25 (34)	14 (21)	0.19
Prostate cancer	7 (8)	6 (8)	2 (3)	0.001
Cardiovascular disease	23 (25)	30 (41)	8 (12)	< 0.001
Medication				
ACE/ARB	74 (80)	32 (44)	42 (62)	< 0.001
Beta blockers	44 (47)	47 (64)	42 (62)	0.010
Diuretics	57 (61)	38 (52)	27 (40)	0.010
Calcium inhibitors	46 (49)	22 (30)	33 (49)	< 0.001
Cortisol	15 (16)	15 (21)	62 (91)	< 0.001
EPO	26 (28)	54 (74)	7 (10)	< 0.001
Immunosuppressors	8 (9)	8 (11)	67 (99)	< 0.001
Anticoagulants	32 (34)	30 (41)	18 (26)	0.18
Lab. values, median (95% CI)				
Hemoglobin, g/L	124.0 (116.0–135.0)	119.5 (107.5–126.0)	133.0 (123.0–143.0)	< 0.001
Albumin, g/L	36.0 (34.0–38.0)	35.0 (33.5–39.0)	36.0 (35.0–38.0)	0.44
PTH, pmol/L	54.0 (27.5–111.0)	90.5 (51.0–123.0)	77.0 (35.0–118.0)	0.15
BMI kg/m ²	27.1 (24.0–30.1)	24.4 (22.6–26.7)	25.9 (24.0–28.1)	0.003
Systolic Blood Pressure, mm	130.0 (125.0–144.0)	140.0 (123.0–157.0)	130.0 (121.0–140.0)	0.098
Hg				
Diastolic Blood Pressure, mm Hg	80.0 (75.0–86.0)	75.0 (70.0–85.0)	80.0 (75.0–85.0)	0.031
GFR, mean (median; min-max), ml/min/1.73m ²	27.7 (21; 5–80)		46.2 (46; 12–84)	< 0.001

	PreT (CKD 2–5)	D (CKD 5)	Tx (CKD 2–5)	p-value
CKD 2 No (%)	4 (4)		19 (28)	
CKD 3 No (%)	25 (27)		33 (49)	
CKD 4 No (%)	44 (47)		10 (11)	
CKD 5 No (%)	16 (28)		6 (9)	

Note: Values are frequencies (%) for binary and categorical variables, and median (95%Cis/IQR/min-max) for continuous variables. Chi-square tests (categorical/binary) and one-way Anova (or Kruskal-Wallis test for non-normal data) were applied to asses statistically significant group differences. A two-sided p-value < 0.05 was considered statistically significant. No (%): Number of patients (percent of total). Cardiovascular disease includes history of angina pectoris, acute myocardial infarction, intermittent claudication and/or stroke, hypertension not included. Diabetes includes type 1 and 2, on oral and/or insulin treatment. IQR: Interquartile range; SLE: Systemic lupus erythematosus; ACE: Angiotensin converting enzyme inhibitor; ARB: Angiotensin II receptor blocker; EPO: Erytropoietin; PTH: Parathyroid Hormone; BMI: Body mass index; GFR: Glomerular Filtration Rate.

Concerning relationships: 80.3% (mean) (D 80.8%, PreD 84.9%, Tx 73.5%) of all the patients stated that they were in stable relationships before their renal disease, compared to 73.5% (mean) (78.1%, 79.6%, 60.3) at their present condition.

Self-reported experience of change in sexual function before and after the onset of symptomatic CKD: All three patient groups in the initial analysis reported a deterioration in their experience of sexual function (5 out of 5 questions) at present time compared with 6 months before onset of symptomatic CKD (Bonferroni adjusted p-values < 0.001) (Table 2).

Table 2. Answers to the questionnaire by the groups PreT, D and Tx.

	PreT (CKD 2-	PreT (CKD 2-5) 93		D (CKD 5) 73		Tx (CKD 2-5) 68	
	Before onset of CKD†	Time of study†	Before onset of CKD ⁺	Time of study†	Before onset of CKD [†]	Time of study†	
Number of p	atients (N) and pe	rcent (%)					
1. How often	have you had sex	ual thoughts (desire) of any kind	l, e.g. wish for	sexual intercourse	?	
>1/week	53 (57)	36 (39)	43 (59)	20 (27)	40 (59)	27 (40)	
<1/week	31 (33)	35 (38)	19 (26)	21 (29)	22 (32)	20 (29)	
<1/month	2 (2)	8 (9)	5 (7)	13 (18)	3 (4)	14 (21)	
Never	4 (4)	10 (11)	4 (5)	18 (25)	3 (4)	7 (10)	
2. How often	did you take the	initiative for s	exual activities?				
>1/week	28 (30)	14 (15)	27 (37)	7 (10)	26 (38)	11 (16)	
<1/week	49 (53)	34 (37)	28 (38)	13 (18)	29 (43)	21 (31)	
<1/month	7 (8)	14 (15)	8 (11)	19 (26)	6 (9)	14 (21)	
Never	6 (6)	28 (30)	8 (11)	33 (45)	6 (9)	22 (32)	

	PreT (CKD 2-5) 93		D (CKD 5) 73	D (CKD 5) 73		Tx (CKD 2–5) 68	
	Before onset	Time of	Before onset	Time of	Before onset	Time of	
	of CKD†	study†	of CKD†	study†	of CKD†	study†	
3. How often	did you have sex	ual intercourse?					
>1/week	28 (30)	14 (15)	27 (37)	5 (7)	28 (41)	7 (10)	
<1/week	45 (48)	32 (34)	25 (34)	8 (11)	27 (40)	19 (28)	
<1/month	9 (10)	7 (8)	8 (11)	12 (16)	5 (7)	15 (22)	
Never	10 (11)	39 (42)	11 (15)	46 (63)	6 (9)	27 (40)	
4. How often	have you had ere	ction/vaginal lub	orication?				
>1/week	47 (51)	29 (31)	40 (55)	15 (21)	40 (59)	17 (25)	
<1/week	29 (31)	26 (28)	18 (25)	10 (14)	20 (29)	25 (37)	
<1/month	7 (8)	13 (14)	6 (8)	21 (29)	2 (3)	12 (18)	
Never	5 (5)	20 (22)	7 (10)	24 (33)	4 (6)	13 (19)	
5. How often	have you experie	nced difficulties	in achieving an	orgasm			
Never/rarely	49 (53)	31 (33)	30 (41)	11 (15)	32 (47)	21 (31)	
Sometimes	23 (25)	17 (18)	15 (21)	21 (29)	18 (26)	11 (16)	
>half of the	6 (6)	13 (14)	9 (12)	4 (5)	7 (10)	8 (12)	
times							
(Almost)	13 (14)	30 (32)	18 (25)	37 (51)	10 (15)	28 (41)	
always							

Note: Values are number of patients (N) and percent (%). PreT: Patients with CKD 2–5 attending the nephrology outpatient clinic; D: Patients on regular dialysis treatment; Tx: Patients with a functioning renal transplant, CKD 2–5. † All groups had statistically significant difference (Bonferroni adjusted p < 0.001) based on Wilcoxon signed rank test, for all questions of sexual function before and after symptomatic CDK onset.

Subgroup analysis. Comparing five groups with different treatment and different degree of CKD. Results from regression model: In the unadjusted model PreT 4–5, Tx 4–5 and D groups reported statistically significant deterioration in sexual function when being compared to PreT 2–3 (reference group) (Table 3).

Table 3. Subgroup analysis. Comparing five groups with different treatment and different degree of CKD.

	Unadjusted estimates (95% Intervals) ^a	Confidence	Adjusted estimates (95% Confidence Intervals) ^b		
PreT CKD 2–3	Reference	p-value	Reference	p-value	
N = 29					
PreT CKD 4–5	-1.58 (-3.12 to -0.044)	0.04	-1.08 (-2.54 to 0.38)	0.15	
N = 60					
Tx CKD 2–3	-1.58 (-3.32 to 0.16)	0.08	-1.53 (-3.19 to 0.12)	0.07	
N = 52					

	Unadjusted estimates (95% Intervals) ^a	Confidence	Adjusted estimates (95% Confidence Intervals) ^b		
Tx CKD 4–5	-2.22 (-4.24 to -0.20)	0.03	-1.95 (-3.91 to 0.02)	0.052	
N = 16					
D	-2.87 (-4.47 to -1.27)	0.001	-2.65 (-4.19 to -1.11)	0.001	
N = 73					

Note: Estimates and 95% confidence intervals are calculated from OLS regression with robust standard errors.

Answers to the questions by the groups PreD 2–3, PreD 4–5, Tx 2–3, Tx 4–5 and D are shown in Supplement 3.

In the adjusted model, adjusting for age and sex, dialysis patients reported a statistically significant deterioration in average sexual function compared with the reference group (-2.65; 95% CI: -4.19 to -1.11, p = 0.001). Similar deterioration in reported sexual function was also found for Tx 2-3 (1.53; 95% CI: -3.19 to 0.12, p = 0.07) and Tx 4-5 (1.95; 95% CI: -3.91 to 0.02; p = 0.05), however differences were not statistically significant (Table 3).

4. Discussion

All patient groups reported a decrease in their sexual function at the time of the study compared to before onset of CKD symptoms.

In the subgroup analysis, when comparing between-group differences, dialysis patients reported a decrease in their sexual function compared to PreT 2–3 (reference group) adjusting for age and sex. Similar associations were found for PreT 4–5, Tx 2–3 and Tx 4–5 albeit not statistically significant.

Few studies have reported on sexual function in PreT patients, and it is unknown at which CKD stage the sexual dysfunction is recognized by the patients [1,12–15].

Our results concerning dialysis patients are in accordance with the literature, where dialysis patients consistently report decreased sexual function regarding both desire and performance [5,9–10].

In this study Tx patients do not differ from the D patient group. This is interesting considering that Tx patients in our study have fewer diseases usually associated with vascular disease like diabetic nephropathy, nephrosclerosis and cardiovascular disease. Tx patients had more polycystic kidney disease which is generally associated with less vascular disease and less inflammatory disease. Tx patients in our study also had a better renal function (GFR) than D patients. However, findings from previous literature are not conclusive [11].

In a metanalysis [5] the mode of renal replacement therapy significantly influenced the prevalence of erectil dysfunction (ED): hemodialysis and peritoneal dialysis patients had a higher prevalence of ED than transplanted patients. Also age, diabetes and hypertension were associated with sexual dysfunction [5], although results are conflicting.

In our study there was no significant difference between the sexes concerning sexual dysfunction. It has previously been suggested that women are more affected than men, but we could not find support for this in our study. In a metanalysis [5] including 50 studies, the overall prevalence of ED in men was 70%. In women the prevalence of sexual dysfunction was 30% to 80%. In our previous study

^a Estimates are mean differences compared to pre-dialysis patients with CKD stage 2–3 (Reference).

^b Estimates are mean differences compared to pre-dialysis patients with CKD stage 2–3 (Reference) adjusted for sex and age (below/above median age = 58 years).

using this methodology including both sexes [4] no gender difference was found. Other studies show conflicting results [1,2,18,19]

This study has several limitations. We cannot rule out the possibility of recall bias. However, any systematic differences in factors relating to how patient groups recall their sexual function before onset of symptomatic CKD seems unlikely to have influenced the results observed in this study.

A factor that may influence the results could be relationship status. However, the patients in this study were equally likely to be in a relationship regardless of their group status, so this factor did not seem to influence the results.

Another factor that could influence the risk of recall bias is the duration of CKD. Defining the time of onset of symptomatic CKD is a possible limitation of this study. The exact time when symptoms of CKD occur is methodologically challenging to ascertain because they are often insidious in onset and become more manifest at an advanced stage of CKD many years later. Thus, it is possible that time influenced recollection of sexual function differently for CKD patients which partly could explain the observed within-group and between-group differences. However, we did not find a correlation between the total duration of the underlying renal disease and reported sexual dysfunction in this study, which argues against such an explanation. The disease duration will be an important aspect for future large and multivariable prospective cohort studies.

A small sample size is a well-known problem in this type of study and most published studies have included less than 200 patients [5], which makes our study of 234 patients one of the largest in comparison. We chose the self-comparator design used in our previous study to highlight the intrapersonal change in sexual function. The patients were asked to compare their sexual function at two time points—before onset of symptomatic CKD and during the six months preceding the study, thus making both within-group and between-group comparison possible. Many studies use IIEF for men [20] and FSFI for women [21]. Both are well documented and standardized. IIEF and FSFI illustrate the current situation for the patients. Other methods have been used as well, such as the Arizona Sexual Experience Scale [2] and the Relationship and Sexuality Scale (RSS) [7]. However, differences in methodology makes comparisons between studies difficult.

This is a descriptive and observational study. Many factors have been suggested as important for sexual function in CKD, for instance testosterone [22]. This will be an interesting subject for future studies.

The patients in this study can be considered representative concerning age and gender of patients with CKD in Sweden found in the Swedish Renal Register (SRR, www.medscinet.net/snr).

5. Conclusions

We conclude that D patients reported a more severe sexual dysfunction than PreD and that there was a surprisingly less pronounced difference between the D patients and the Tx patients, despite Tx patients having less concomitant disease and improved renal function.

There was also an indication of a difference between Tx 2–3 and Tx 4–5 compared to PreT 2–3, although not statistically verified. Verifying such differences will require a larger number of patients which we can only suggest for future studies.

It is obviously important for nephrologists and other healthcare professionals to recognize and address the question of sexual dysfunction in CKD patients irrespective of treatment mode and CKD-stage.

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Use of AI tools declaration

The authors declare they have not used Artificial Intelligence (AI) tools in the creation of this article.

Conflict of interest

All authors declare no conflict of interest in this paper.

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