# Sexual Function and Testosterone Level in Men With Conservatively Treated Chronic Kidney Disease

American Journal of Men's Health 2017, Vol. 11(4) 1069–1076 © The Author(s) 2017 Reprints and permissions: sagepub.com/journalsPermissions.nav DOI: 10.1177/1557988317703207 journals.sagepub.com/home/ajmh SAGE

Kerstin S. Fugl-Meyer, PhD<sup>1,2</sup>, Marie Nilsson, PhD<sup>1,2</sup>, Britta Hylander, MD<sup>1,2</sup>, and Mikael Lehtihet, MD<sup>1,3</sup>

## Abstract

Sexual dysfunctions are common, but underrecognized, in patients with chronic kidney disease (CKD) and are inversely associated with the glomerular filtration rate (GFR). Sexual dysfunctions may affect quality of life in males with CKD. The aim of this study was to analyze the relationship among sex hormones, sexual function, and sexual satisfaction in a group of men between 18 and 50 years of age with CKD Stages 1 to 5 not treated with hemodialysis or peritoneal dialysis. Fasting blood samples for hemoglobin, testosterone, prolactin, and luteinizing hormone and questionnaire surveys (Sexual Complaints Screener for Men, International Index of Erectile Function, and Aging Male Symptom scale) were evaluated in 100consecutive men. Higher CKD stage (i.e., lower renal function) had a statistically significant (p < .01) correlation with lower total testosterone, free testosterone, and hemoglobin levels, and higher luteinizing hormone and prolactin levels. Sexual function/dysfunctions were not significantly associated with CKD stage, even after adjustment for age and serum testosterone. The results indicate that CKD stage is a factor affecting testosterone levels in combination with age in men between 18 and 50 years of age at different stages of CKD but not treated with hemodialysis or peritoneal dialysis. Sexual dysfunctions are common but not strongly correlated to testosterone levels, prolactin levels, and survey (Sexual Complaints Screener for Men, International Index of Erectile Functional Index of Erectile Function, and Aging Male Symptom scale) with hemodialysis or peritoneal dialysis. Sexual dysfunctions are common but not strongly correlated to testosterone levels, prolactin levels, and survey (Sexual Complaints Screener for Men, International Index of Erectile Function, and Aging Male Symptom scale) responses in patients with CKD.

#### Keywords

chronic kidney disease, hypogonadism, sexual function, prolactin, testosterone

Received September 13, 2016; revised February 11, 2017; accepted February 16, 2017

## Introduction

Worldwide, chronic kidney disease (CKD) is reported to occur in more than 10% of the general population, and the incidence is increasing (Hallan et al., 2006; Jha et al., 2013). CKD affects not only the kidneys but all other vital organs and systems as well (Liu et al., 2014; Panocchia et al., 2016). Sexual dysfunctions are common in patients with CKD and an underrecognized problem (Anantharaman & Schmidt, 2007; Finkelstein, Shirani, Wuerth, & Finkelstein, 2007). In addition to CKD stage, other factors-such as diabetes mellitus, cardiovascular problems, sex hormone disturbances, and psychosocial factors-may contribute to sexual dysfunctions (Anantharaman & Schmidt, 2007; Palmer, 2003). Previous prevalence studies on sexual dysfunctions in men with CKD reported a wide range, from 20% to 80% (Anantharaman & Schmidt, 2007; Finkelstein et al., 2007), and an inverse association with glomerular filtration rate (GFR; Mehrsai et al., 2006). Gonadal dysfunctions with elevation of serum gonadotropin concentrations (mainly luteinizing hormone, LH) are a frequent finding, affecting 26% to 66% of men at different stages of CKD (Holley, 2004; Hylander & Lehtihet, 2015; Iglesias, Carrero, & Diez, 2012; Lehtihet & Hylander, 2015). Sexual dysfunctions profoundly affect quality of life in patients with CKD, because of anxiety and low selfconfidence, self-esteem, and self-image (Finkelstein et al., 2007).

<sup>1</sup>Karolinska Institute, Stockholm, Sweden
<sup>2</sup>Karolinska University Hospital, Stockholm, Sweden
<sup>3</sup>Karolinska University Hospital, Huddinge, Sweden

**Corresponding Author:** Mikael Lehtihet, Karolinska Institute, Sjukhusgatan I, Stockholm SE141 86, Sweden. Email: mikael.lehtihet@ki.se

Creative Commons Non Commercial CC BY-NC: This article is distributed under the terms of the Creative Commons Attribution-NonCommercial 3.0 License (http://www.creativecommons.org/licenses/by-nc/3.0/) which permits non-commercial use, reproduction and distribution of the work without further permission provided the original work is attributed as specified on the SAGE and Open Access pages (https://us.sagepub.com/en-us/nam/open-access-at-sage).

Stage	Description	Estimated GFR (mL/min per 1.73 m <sup>2</sup> )
	Kidney damage with normal or increased GFR	≥90
2	Kidney damage with mildly decreased GFR	60-89
3	Moderately decreased GFR	30-59
4	Severely decreased GFR	15-29
5	, Kidney failure	<15 or dialysis

**Table 1.** Stages of Chronic Kidney Disease Defined According to the Presence or Absence of Kidney Damage and Level of Kidney Function, Irrespective of the Type of Kidney Disease.

Note. CKD = chronic kidney disease; GFR = glomerular filtration rate. GFR values were normalized to an average surface area of 1.73 m<sup>2</sup>. The National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF KDOQI).

# Aim

There are a limited number of studies of sexual dysfunctions and sexual well-being in younger men at different CKD stages and on conservative treatment. Therefore, the present study aimed to analyze the relationship among sex hormones, sexual function, and sexual satisfaction in younger men living with CKD at different stages but not on hemodialysis or peritoneal dialysis. The study hypothesis was that sexual satisfaction is affected in men with CKD and is related to stage of disease as well as hormonal status.

# Methods

## Participants

The authors performed a cross-sectional analysis from December 2012 to December 2013. The inclusion criteria were (a) age 18 to 50 years at inclusion and (b) being a patient at the Department of Nephrology, Karolinska University Hospital, Stockholm, Sweden. Participants were excluded if they were smokers or former smokers (>3 months), were diagnosed with diabetes mellitus, had a previous renal transplantation, were treated with erectile stimulation drugs or herbal compounds with erectile stimulating effect, or were treated with testosterone replacement therapy. This was done to avoid the wellknown confounding factors for sexual dysfunctions. The study was not designed to investigate the prevalence of sexual dysfunctions in men with CKD but to examine if there were associations among CKD, sexual function, and hormonal status. Patients with diabetes mellitus were excluded because of the well-known association between diabetes mellitus and sexual dysfunctions in men (Andersson, Ekstrom, & Lehtihet, 2015).

Of the 145 participants available, 100 (69%) met the inclusion criteria and volunteered to provide fasting blood samples and questionnaire responses at the clinical examination. Staging of CKD was done according to the extent of kidney damage and level of kidney function, irrespective of the type of kidney disease (Tsai, Grams, Inker, Coresh, & Selvin, 2014). Kidney function was

expressed as estimated GFR (ml/min per  $1.73 \text{ m}^2$ ), using standardized creatinine and cystatin C values and the CKD-EPI 2012 equation (Inker et al., 2012; Table 1).

The participants were then subdivided into three groups according to their stage of renal impairment (CKD stage): Group 1 (CKD Stage 1)—kidney damage with normal or slightly increased GFR ( $\geq$ 90 mL/min per 1.73 m<sup>2</sup>), n = 23; Group 2 (CKD Stages 2-3)—kidney damage with mild or moderate GFR impairment (30-89 mL/min per 1.73 m<sup>2</sup>), n = 46; and Group 3 (CKD Stages 4-5)—severely decreased GFR/kidney failure (15-29 mL/min per 1.73 m<sup>2</sup>), n = 31.

# Psychometric Evaluation With the Sexual Complaints Screener for Men, International Index of Erectile Function, and Aging Male Symptom Scale

Questionnaires were given to the participants during their scheduled visit to the clinic. The participants filled in the questionnaires at home and returned them by mail.

The main questionnaire was the Sexual Complaints Screener for Men (SCS-M), which is a rather new instrument, developed and constructed by an international expert group (Hatzichristou et al., 2010). The aim was to provide an evidence-based diagnostic tool for assessing sexual problems in medical practice. The instrument covers the past 6 months and includes six questions covering sexual function/dysfunctions, one about the size/shape of the penis, and one on sexual satisfaction. These items are followed by a question on whether a (possible) dysfunction was experienced as *distressing* (i.e., as a personal problem). In the present study, a dichotomization of the scale into No Complaint (occurring never/almost never or rarely), Complaint (occurring sometimes, often, or almost all the time/almost always), No Problem (experience not at all a problem or a very small problem), and Problem (experience somewhat a problem, a considerable problem, or a very great problem) was done.

Moreover, the questionnaire includes a question as to whether the responder is sexually active or not (not necessarily equal to sexual intercourse/penetration). Level of sexual satisfaction was dichotomized into Satisfying (very satisfying or satisfying) and Not Satisfying (rather satisfying, rather unsatisfying, unsatisfying, or very unsatisfying).

The International Index of Erectile Function (IIEF) is a widely used and validated instrument (Rosen et al., 1997). In this study, the brief screening version IIEF-5 was used. The total scores are categorized into No ED, Mild ED, Mild to Moderate ED, and Moderate and Severe ED.

The Aging Male Symptom scale (AMS) is a validated scale aiming to assess age-related decline in physical and mental capacity (Heinemann, 2005). The instrument includes 17 questions pertaining to three domains: psychological, somato-vegetative, and sexual. Based on normed values from a representative population (Heinemann, 2005), the following categories for total scores have been well defined with good sensitivity and specificity: No Impairment ( $\leq$ 5 points), Little Impairment (6-7 points), Moderate Impairment (8-10 points), and Severe Impairment ( $\geq$ 11 points).

## Assays

All blood samples were drawn in the morning (7.00-9.00 a.m.) after an overnight fast (12 h). Total testosterone level was measured with a chemiluminescent immunoassay for quantitative determination of total testosterone in human serum and plasma using the Access Immunoassay System (Beckman Coulter, Inc., Brea, CA). The intra-assay and inter-assay coefficients of variation for testosterone were less than 5.0%. Free serum testosterone was calculated by the method of Vermeulen (Vermeulen, Verdonck, & Kaufman, 1999).

LH was determined with an AutoDELFIA (PerkinElmer Life and Analytical Sciences, Turku, Finland) hLH twosite immunoradiometric assay. The intra-assay and interassay coefficients of variation for LH were 1.9% and 2.2%, respectively. Prolactin was measured with a paramagnetic particle chemiluminescent immunoassay (Access SHBG assay UniCel DxI 800, Beckman Coulter). The intra-assay and inter-assay coefficients of variation for prolactin were 3.5% and 5.0%, respectively.

Hemoglobin, creatinine, and cystatin C were measured by the routine chemistry accredited laboratory at the Karolinska University Hospital (Modular P, Roche Diagnostics, Mannheim, Germany).

Reference ranges for healthy men between 18 and 50 years of age are included in the following table.

Analysis	Reference range
Serum testosterone (nmol/L)	10-30
Serum LH (U/L)	1.2-9.6
Serum prolactin (µg/L)	2.6-13
Hemoglobin (g/L)	134-170
Creatinine (µmol/L)	<100
Cystatin C (mg/l)	<0.99

## Statistics

Data were analyzed using IBM SPSS Version 22 (SPSS Inc., Chicago, IL). For hormone analyses, hemoglobin, creatinine, and cystatin C data were expressed as means  $\pm$  standard deviation. The normality was tested with a probability plot and Kolmogorov-Smirnov one-sample test for normality to approximate normal distribution. Log-transformed values were used for prolactin in the analysis and then back-transformed for data presentation.

On continuous medical measures, one-way betweengroup analyses of variance were performed with Tukey's honest significant difference post hoc tests to detect differences in means between the three groups, and independent t test was performed to detect differences in means between two groups. To test the relationship between the (categorical) variables, cross-tabulations were performed with chi-square test and Fischer's exact test. Spearman rank order correlation was applied for correlation between the variables in SCS-M, IIEF and AMS. Trichotomization for CKD staging was done at CKD Stage 1 (low), CKD Stages 2 to 3 (moderate), and CKD Stages 4 or 5 (high). The decision to trichotomize was taken because Stage 1 constitutes normal GFR, Stages 2 to 3 require some medical treatment, and Stages 4 to 5 entail severely reduced kidney function, and also because five CKD stages would yield insufficient statistical power.

Significance level was set at p < .05 for all statistical analyses (two-tailed).

## Results

In Table 2, the characteristics of the participants' diagnosis and medications are given.

## Sexually Active

Five men had not been sexually active during the past 6 months. There were no statistically significant differences between those sexually active and those inactive concerning sexual complaints or their experiences of distress (Table 3). Nor were there any significant differences between the sexually active and the inactive men in terms of hormonal levels, CKD stage, or sexual satisfaction.

# SCS-M: Prevalence and Distress

No sexual complaints were reported by 36% of the men. One complaint was reported by 24%, two complaints were reported by 6%, and 34% had experienced three to seven complaints during the past 6 months (Table 3). However, the number of responders who experienced these complaints as distressful was less than the actual reported number of complaints. Thus, 65% reported one or more sexual complaints during the past 6 months, but 54% experienced these as distressful.

	CKD Stage I ( $n = 23$ )	CKD Stages 2 and 3 $(n = 46)$	CKD Stages 4 and 5 $(n = 31)$
Diagnosis			
Glomerular disease	11	27	18
Hypertensive nephrosclerosis	2	5	3
Tubulointerstial disease	2	5	2
Vascular disease	3	2	4
Polycystic kidney disease	5	7	4
Medications			
Statins	5	17	14
Angiotensin-converting enzyme inhibitors	11	23	17
Angiotensin receptor blockers	2	20	18
Diuretic	0	8	16
Beta-blockers	3	10	17
Calcium channel blockers	4	18	13

**Table 2.** Diagnosis and Medications of Participants in Chronic Kidney Disease (CKD) Stages 1 to 5 Subdivided Into Three Groups According to Their Stage of Renal Impairment (N = 100).

**Table 3.** Number of Self-Reported Sexual Complaints and Experiences of Sexual Distress During the Past 6 Months (SCS-M) in79 Men With Chronic Kidney Disease.

	Sexual complaints, n (%)	Sexual distress, n (%)
None	28 (36%)	36 (46%)
I. One complaint/personal problem	19 (24%)	17 (22%)
2. Two complaints/personal problems	5 (6%)	2 (2%)
3. Three to seven complaints/personal problems	27 (34%)	24 (30%)

Note. SCS-M = Sexual Complaints Screener for Men.

The prevalence rates of sexual complaints, distress, and CKD stage are reported in Table 4. The most common complaint in all three groups was lack of, or low, sexual interest or desire, occurring in between 42% and 52% of the men, followed by difficulties with erectile and ejaculatory function.

In CKD Stage 1, distress was mostly expressed for difficulty in getting/maintaining an erection and difficulty in ejaculating/reaching orgasm (37%). In Stages 2 to 3, this was true for erectile function (29%), whereas participants in Stages 4 to 5 found the need for more stimulation to achieve erection to be stressful (40%). Pain during, and shortly after, sexual activity occurred more rarely, but concern about the size or shape of the penis was the case for almost 25% of the men in Stages 1 and Stages 2 to 3 and even more (32%) of those in Stages 4 to 5—leading to distress for almost all of them.

## SCS-M, IIEF-5, and AMS

There was no significant correlation between the SCS-M variables and CKD staging (Table 5) or IIEF-5, total AMS and AMS sexual subscale, or the separate variables and CKD staging (Table 6).

# CKD Stages, Age, Hemoglobin Levels, and Sex Hormones

CKD stage was significantly associated with increasing age (r = -.35, p < .001)—see Table 7. Furthermore, there was a significant decrease in hemoglobin and total testosterone levels with increasing CKD stage (p < .01), whereas LH and prolactin levels were increased significantly with CKD stage (p < .01).

No significant correlation was seen between hormonal levels and the different SCS-M variables, the total IIEF-5 score, or the separate variables, and the same was also noticed for total AMS as well as it's separate variables. There were no significant associations between CKD stage and AMS scale after adjustment for age and testosterone level.

## Discussion

It has been reported previously that there is a negative correlation between endogenous testosterone levels and CKD Stages 1 to 5 (Iglesias et al., 2012; Yilmaz et al., 2011). The mechanism for this is likely to involve, at least to some extent, some alteration or derangement of the male reproductive hormone profile (Holley, 2004). This supports the

SCS-M variable	CKD Stage I (GFR $\geq$ 90), $n = 23$ — Complaint/distress	CKD Stages 2-3 (GFR = 30-89), n = 46—Complaint/distress	CKD Stages 4-5 (GFR = 15-29), n = 31—Complaint/distress	p Value
Lack of/low sexual interest/desire	8 (42%)/6 (32%)	12 (48%)/9 (26%)	13 (52%)/8 (32%)	.39/.84
Need more stimulation to achieve erection	6 (32%)/5 (26%)	10 (29%)/8 (23%)	10 (40%)/10 (40%)	.64/.34
Difficulty getting/maintaining erection	5 (30%)/7 (37%)	8 (23%)/10 (29%)	5 (24%)/8 (33%)	.87/.81
Ejaculation before/shortly after penetration	3 (19%)/5 (26%)	8 (24%)/8 (24%)	4 (19%)/5 (20%)	.89/.88
Difficulty ejaculating/reaching orgasm	5 (31%)/7 (37%)	4 (11%)/6 (17%)	7 (32%)/6 (24%)	.12/.27
Pain during/shortly after sex	2 (14%)/3 (18%)	I (3%)/2 (7%)	I (6%)/I (5%)	.40/.32
Concerned about size/shape of penis	4 (24%)/4 (24%)	7 (24%)/6 (21%)	7 (32%)/6 (28%)	0.79/0.86
Sexual satisfaction				
Satisfied ( $n = 50$ )	16 (94%)	20 (69%)	14 (67%)	.10
Not satisfied $(n = 17)$	I (6%)	9 (31%)	7 (31%)	

**Table 4.** Prevalence of Reported Sexual Complaints, Experiences of Sexual Distress, and Sexual Satisfaction During the Past 6Months (SCS-M) in Relation to CKD Stages in 100 Men.

Note. CKD = chronic kidney disease; GFR = glomerular filtration rate; SCS-M = Sexual Complaints Screener for Men.

Table 5. Median of AMS Total, AMS Sexual, and IIEF in Relation to SCS-M.

	AMS Total		AMS Sexual		IIEF-5 Total	
SCS-M variable	Complaint	No complaint	Complaint	No complaint	Complaint	No complaint
Lack of/low sexual interest	32.0	31.0	10.0	9.0	7.0	8.0
Need more stimulation to achieve erection	32.0	30.0	10.0	9.0	6.5	8.0
Difficulty getting/maintaining erection	29.0	32.0	9.0	9.5	6.0	9.0
Ejaculation before/shortly after penetration	31.0	31.5	10.5	9.0	11.0	7.5
Difficulty ejaculating/reaching orgasm	32.0	30.0	10.0	9.0	7.0	8.0
Pain during/shortly after sex	34.5	30.5	8.5	9.0	7.0	7.0
Concerned about size/shape of penis	30.0	32.0	8.0	10.5	6.5	8.0
Sexual satisfaction	32.0	31.0	11.0	9.0	9.0	7.0

Note. AMS = Aging Male Symptom scale; IIEF = International Index of Erectile Function; SCS-M = Sexual Complaints Screener for Men.

	CKD Stage I (GFR $\ge$ 90)	CKD Stages 2-3 (GFR = 30-89)	CKD Stages 4-5 (GFR = 15-29)
IIEF-5	8.94	9.19	10.95
AMS Total	28.94	30.54	41.05
AMS Sexual	8.69	9.58	13.19

Table 6. Median of IIEF-5, AMS Total, and AMS Sexual in CKD Stages.

Note. AMS = Aging Male Symptom scale; CKD = chronic kidney disease; GFR = glomerular filtration rate; IIEF = International Index of Erectile Function.

current findings of a significant decrease in testosterone levels at the advanced CKD stages. At the advanced CKD stages, a significant increase in the LH level and a pattern of hypergonadotropic hypogonadism were seen. This suggests that uremic metabolites secondary to advanced CKD stage affect the testes more than the hypothalamic or pituitary function. Alternatively, the degradation of uremic metabolites in the hypothalamic or pituitary region is faster and more pronounced than in the testes. An alternative, more trivial, explanation might be that LH and prolactin are polypeptide protein hormones (whereas testosterone is not), whose renal clearance may be impaired as GFR decreases and, hence, the observed elevated levels of LH and prolactin are merely artifactual.

A novel finding is that although the testosterone levels decreased significantly as CKD progressed, this was not associated with the sexual dysfunctions measured with SCS-M, IIEF-5, and AMS in this study population.

	CKD Stages 1-2 (GFR $\geq$ 90), $n = 23$	CKD Stage 3 (GFR = 30-89), <i>n</i> = 46	CKD Stages 4-5 (GFR = 15-29), <i>n</i> = 31	þ Value
Age (year)	34.0 (9.1)	41.0 (6.3)	40.0 (7.5)	<.001
Hemoglobin level (g/L)	150.0 (7.2)	138.6 (13.2)	115.7 (13.5)	<.001
Testosterone level (nmol/L)	14.9 (3.9)	13.6 (4.0)	9.7 (4.2)	<.01
Free testosterone	0.33 ± 0.10	0.26 ± 0.05	0.19 ± 0.07	<.01
Prolactin <sup>ª</sup> level (U/L)	7.8 (2.0)	8.9 (2.9)	17.0 (11.3)	<.01

6.8 (4.2)

**Table 7.** Age and Levels of Hemoglobin, Serum Testosterone, Luteinizing Hormone, and Prolactin<sup>a</sup> in 100 men With CKD, Given as Mean Scores and Standard Deviations.

*Note*. CKD = chronic kidney disease; GFR = glomerular filtration rate.

<sup>a</sup>The conversion factor for prolactin concentration from mass to units is 21.2 ([µg/L] × 21.2 = mIU/L).

5.3 (1.7)

Previous descriptive as well as analytic epidemiological studies have reported that male sexual dysfunctions are quite common, though with great variation worldwide (Lewis et al., 2010). The reasons for this variation may pertain to differences in the definitions of the dysfunctions, the methods used for the evaluation, and the populations studied. It is, however, clear that ill health is a risk factor for sexual dysfunctions and sexual dissatisfaction (Lewis et al., 2010). In the present study, as many as 64% of the study participants had experienced one or more sexual dysfunctions during the past 6 months (according to the SCS-M questionnaire). The concurrence of more than one sexual dysfunction supports earlier findings (A. R. Fugl-Meyer, Melin, & Fugl-Meyer, 2002; K. Fugl-Meyer & Fugl-Meyer, 2002).

The prevalence of erectile dysfunction among men in the general population until the age of 50 to 55 years is estimated not to exceed 10% (Lewis et al., 2010). The corresponding figure for the somewhat younger patients in the current cohort at different CKD stages was higher and varied between 23% and 30%. Sexual interest/desire and other sexual dysfunctions showed the same pattern that is, a much higher prevalence of dysfunctions as well as distress compared with the general population.

The enhancing effect of androgens on sexual desire/ interest and sexual function has been unequivocally established at the population level. However, the correlation between testosterone and sexual desire at the individual level is still open to question (Travison, Morley, Araujo, O'Donnell, & McKinlay, 2006). Furthermore, certain studies have reported a lack of association or only a modest association between testosterone and erectile dysfunction as assessed by IIEF-5 (Ahn, Park, & Lee, 2002; Kang, Ham, Oh, Kim, & Moon du, 2011; Rhoden, Teloken, Mafessoni, & Souto, 2002). In a previous study with older men, only a moderate improvement of sexual function was seen in those men who were put on testosterone therapy (Snyder et al., 2016). These findings were confirmed in the present study, even though the CKD stage and age affected testosterone levels in this group of relatively young men with various degrees of kidney disease.

8.0 (5.1)

<.01

Severe hyperprolactinemia, but not milder forms, has been reported to adversely impact affect sexual desire and erectile function (Corona et al., 2013). However, the relationship between hyperprolactinemia and erectile function is under debate. Controlled studies evaluating the effect of dopamine agonists on erectile function in men with hyperprolactinemia are inconclusive (Bhasin, Enzlin, Coviello, & Basson, 2007). In the present study, the men in CKD Stages 4 to 5 (GFR 15-29 mL/min per  $1.73 \text{ m}^2$ ) were reported to have hyperprolactinemia. However, no significant associations between hyperprolactinemia and sexual interest/desire or erectile function (as evaluated by SCS-M, two questions, and IIEF-5) were discernible.

Ejaculatory dysfunctions occurred more frequently in the current study's participants than in the general population, particularly in terms of retarded/delayed ejaculation. Difficulty in ejaculating/reaching orgasm was reported in 11% to 32% (Groups 2-3 and Groups 4-5, respectively) of the patients with kidney disease. Furthermore, and somewhat surprisingly, 23% of the patients with CKD expressed concern about the size or shape of their penis, which was distressing for almost all of them.

Fifty-six percent of the Swedish population (aged 18-74 years) have been reported to be sexually satisfied/very satisfied (A. R. Fugl-Meyer et al., 2002; K. Fugl-Meyer & Fugl-Meyer, 2002), which is much lower than what was expressed by the current study's participants with CKD. Altogether, these results point to the complexity of sexuality, because satisfaction is not only a reflection of sexual function and/or physical function. Multifactorial explanations seem necessary in understanding sexual life, perhaps especially when living with a chronic disease. Psychological and emotional problems, stress, anxiety, and depression (Pastuszak, Badhiwala, Lipshultz, & Khera, 2013) but also social problems, such as economic issues (Idung, Abasiubong, Udoh, & Akinbami, 2012), have been reported

Luteinizing hormone (U/L)

to affect sexual function and sexual satisfaction. The latter probably affects quality of life to a higher extent when dealing with the consequences of living with a severe chronic disease. This may also be an explanation for the nonsignificant association between decreased testosterone levels and sexual dysfunctions. Moreover, for those who have a partner, sexual dysfunctions and the distress caused by them should also be regarded from the partner's perspective as sexual dysfunctions concur to a significant degree (A. R. Fugl-Meyer et al., 2002; Skeppner & Fugl-Meyer, 2015; Wagner, Fugl-Meyer, & Fugl-Meyer, 2000). Thus, questionnaires may not be the only tool when investigating sexuality in populations with chronic diseases.

Admittedly, the current study has several limitations. First, this was a cross-sectional observational study performed with a small cohort of patients with different diagnoses and at different CKD stages under different treatment regimens, including antihypertensive treatment and statins. Moreover, a qualitative approach could be considered to deepen the understanding of sexuality when living with CKD. In future studies, evaluation of the partner should be included. This study lacked a healthy control group; however, the participants in CKD Stage 1 were almost healthy and with normal or slightly increased GFR ( $\geq$ 90 mL/min per 1.73m<sup>2</sup>), therefore a trichotomization for CKD staging with CKD Stage 1 as a reference group was performed.

In conclusion, sexual function/dysfunctions and distress measured by SCS-M and IIEF-5 did not show a significant association to CKD stage or to the AMS scale. Total testosterone and free testosterone levels decreased significantly with advanced CKD stage but without significant associations to sexual function in this subgroup of men between 18 and 50 years of age without diabetes and with CKD Stages 1 to 5 not treated with hemodialysis or peritoneal dialysis.

#### Acknowledgments

We thank Pia Brushammar, research nurse at the Department of Nephrology, Karolinska University Hospital, Solna, Stockholm, Sweden, for excellent logistic work. We are also grateful for constructive comments on the article by Professor Emeritus Stephan Rössner and are indebted to the study participants for willingly participating in the study.

#### **Authors' Note**

All participants gave their written and oral informed consent. The study was approved by the local committee on ethics at Karolinska Institute. All records were made anonymous and deidentified prior to analysis.

#### **Declaration of Conflicting Interests**

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

#### Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

#### References

- Ahn, H. S., Park, C. M., & Lee, S. W. (2002). The clinical relevance of sex hormone levels and sexual activity in the ageing male. *BJU International*, 89, 526-530.
- Anantharaman, P., & Schmidt, R. J. (2007). Sexual function in chronic kidney disease. *Advances in Chronic Kidney Disease*, 14, 119-125. doi:10.1053/j.ackd.2007.01.002
- Andersson, D. P., Ekstrom, U., & Lehtihet, M. (2015). Rigiscan evaluation of men with diabetes mellitus and erectile dysfunction and correlation with diabetes duration, age, BMI, lipids and HbA1c. *PLoS One*, *10*, e0133121. doi:10.1371/ journal.pone.0133121
- Bhasin, S., Enzlin, P., Coviello, A., & Basson, R. (2007). Sexual dysfunction in men and women with endocrine disorders. *Lancet*, 369, 597-611. doi:10.1016/S0140-6736(07)60280-3
- Corona, G., Rastrelli, G., Ricca, V., Jannini, E. A., Vignozzi, L., Monami, M., . . . Maggi, M. (2013). Risk factors associated with primary and secondary reduced libido in male patients with sexual dysfunction. *Journal of Sexual Medicine*, 10, 1074-1089. doi:10.1111/jsm.12043
- Finkelstein, F. O., Shirani, S., Wuerth, D., & Finkelstein, S. H. (2007). Therapy insight: Sexual dysfunction in patients with chronic kidney disease. *Nature Clinical Practice: Nephrology*, 3, 200-207. doi:10.1038/ncpneph0438
- Fugl-Meyer, A. R., Melin, R., & Fugl-Meyer, K. S. (2002). Life satisfaction in 18- to 64-year-old Swedes: In relation to gender, age, partner and immigrant status. *Journal of Rehabilitation Medicine*, 34, 239-246.
- Fugl-Meyer, K., & Fugl-Meyer, A. R. (2002). Sexual disabilities are not singularities. *International Journal of Impotence Research*, 14, 487-493. doi:10.1038/sj.ijir.3900914
- Hallan, S. I., Coresh, J., Astor, B. C., Asberg, A., Powe, N. R., Romundstad, S., . . . Holmen, J. (2006). International comparison of the relationship of chronic kidney disease prevalence and ESRD risk. *Journal of the American Society of Nephrology*, *17*, 2275-2284. doi:10.1681/ ASN.2005121273
- Hatzichristou, D., Rosen, R. C., Derogatis, L. R., Low, W. Y., Meuleman, E. J., Sadovsky, R., & Symonds, T. (2010). Recommendations for the clinical evaluation of men and women with sexual dysfunction. *Journal of Sexual Medicine*, 7(1, Pt. 2), 337-348. doi:10.1111/j.1743-6109.2009.01619.x
- Heinemann, L. A. (2005). Aging Males' Symptoms Scale: A standardized instrument for the practice. *Journal of Endocrinological Investigation*, 28(11, Suppl.), 34-38.
- Holley, J. L. (2004). The hypothalamic-pituitary axis in men and women with chronic kidney disease. *Advances in Chronic Kidney Disease*, 11, 337-341.
- Hylander, B., & Lehtihet, M. (2015). Testosterone and gonadotropins but not SHBG vary with CKD stages in young and middle aged men. *Basic and Clinical Andrology*, 25, 9. doi:10.1186/s12610-015-0027-y
- Idung, A. U., Abasiubong, F., Udoh, S. B., & Akinbami, O. S. (2012). Quality of life in patients with erectile dysfunction

in the Niger Delta region, Nigeria. Journal of Mental Health, 21, 236-243. doi:10.3109/09638237.2012.664300

- Iglesias, P., Carrero, J. J., & Diez, J. J. (2012). Gonadal dysfunction in men with chronic kidney disease: Clinical features, prognostic implications and therapeutic options. *Journal of Nephrology*, 25, 31-42. doi:10.5301/JN.2011.8481
- Inker, L. A., Schmid, C. H., Tighiouart, H., Eckfeldt, J. H., Feldman, H. I., Greene, T., . . . Levey, A. S. (2012). Estimating glomerular filtration rate from serum creatinine and cystatin C. *New England Journal of Medicine*, 367, 20-29. doi:10.1056/NEJMoa1114248
- Jha, V., Garcia-Garcia, G., Iseki, K., Li, Z., Naicker, S., Plattner, B., . . . Yang, C. W. (2013). Chronic kidney disease: Global dimension and perspectives. *Lancet*, 382, 260-272. doi:10.1016/S0140-6736(13)60687-X
- Kang, J., II, Ham, B. K., Oh, M. M., Kim, J. J., & Moon du, G. (2011). Correlation between serum total testosterone and the AMS and IIEF questionnaires in patients with erectile dysfunction with testosterone deficiency syndrome. *Korean Journal of Urology*, 52, 416-420. doi:10.4111/ kju.2011.52.6.416
- Lehtihet, M., & Hylander, B. (2015). Semen quality in men with chronic kidney disease and its correlation with chronic kidney disease stages. *Andrologia*, 47, 1103-1108. doi:10.1111/and.12388
- Lewis, R. W., Fugl-Meyer, K. S., Corona, G., Hayes, R. D., Laumann, E. O., Moreira, E. D., Jr., . . . Segraves, T. (2010). Definitions/epidemiology/risk factors for sexual dysfunction. *Journal of Sexual Medicine*, 7(4, Pt. 2), 1598-1607. doi:10.1111/j.1743-6109.2010.01778.x
- Liu, M., Li, X. C., Lu, L., Cao, Y., Sun, R. R., Chen, S., & Zhang, P. Y. (2014). Cardiovascular disease and its relationship with chronic kidney disease. *European Review for Medical and Pharmacological Sciences*, 18, 2918-2926.
- Mehrsai, A., Mousavi, S., Nikoobakht, M., Khanlarpoor, T., Shekarpour, L., & Pourmand, G. (2006). Improvement of erectile dysfunction after kidney transplantation: The role of the associated factors. *Urology Journal*, 3, 240-244.
- Palmer, B. F. (2003). Sexual dysfunction in men and women with chronic kidney disease and end-stage kidney disease. Advances in Renal Replacement Therapy, 10, 48-60. doi:10.1053/jarr.2003.50003
- Panocchia, N., Tazza, L., Di Stasio, E., Liberatori, M., Vulpio, C., Giungi, S., . . . Bossola, M. (2016). Mortality in hospitalized chronic kidney disease patients starting unplanned urgent hemodialysis. *Nephrology (Carlton)*, 21, 62-67. doi:10.1111/nep.12561

- Pastuszak, A. W., Badhiwala, N., Lipshultz, L. I., & Khera, M. (2013). Depression is correlated with the psychological and physical aspects of sexual dysfunction in men. *International Journal of Impotence Research*, 25, 194-199. doi:10.1038/ijir.2013.4
- Rhoden, E. L., Teloken, C., Mafessoni, R., & Souto, C. A. (2002). Is there any relation between serum levels of total testosterone and the severity of erectile dysfunction? *International Journal of Impotence Research*, 14, 167-171. doi:10.1038/sj.ijir.3900852
- Rosen, R. C., Riley, A., Wagner, G., Osterloh, I. H., Kirkpatrick, J., & Mishra, A. (1997). The International Index of Erectile Function (IIEF): A multidimensional scale for assessment of erectile dysfunction. *Urology*, 49, 822-830.
- Skeppner, E., & Fugl-Meyer, K. (2015). Dyadic aspects of sexual well-being in men with laser-treated penile carcinoma. *Sexual Medicine*, *3*, 67-75. doi:10.1002/sm2.59
- Snyder, P. J., Bhasin, S., Cunningham, G. R., Matsumoto, A. M., Stephens-Shields, A. J., Cauley, J. A., . . . Ellenberg, S. S. (2016). Effects of testosterone treatment in older men. *New England Journal of Medicine*, 374, 611-624. doi:10.1056/NEJMoa1506119
- Travison, T. G., Morley, J. E., Araujo, A. B., O'Donnell, A. B., & McKinlay, J. B. (2006). The relationship between libido and testosterone levels in aging men. *Journal of Clinical Endocrinology and Metabolism*, 91, 2509-2513. doi:10.1210/jc.2005-2508
- Tsai, C. W., Grams, M. E., Inker, L. A., Coresh, J., & Selvin, E. (2014). Cystatin C- and creatinine-based estimated glomerular filtration rate, vascular disease, and mortality in persons with diabetes in the U.S. *Diabetes Care*, 37, 1002-1008. doi:10.2337/dc13-1910
- Vermeulen, A., Verdonck, L., & Kaufman, J. M. (1999). A critical evaluation of simple methods for the estimation of free testosterone in serum. *Journal of Clinical Endocrinology and Metabolism*, 84, 3666-3672. doi: 10.1210/jcem.84.10.6079
- Wagner, G., Fugl-Meyer, K. S., & Fugl-Meyer, A. R. (2000). Impact of erectile dysfunction on quality of life: Patient and partner perspectives. *International Journal of Impotence Research*, 12(Suppl. 4), S144-S146.
- Yilmaz, M. I., Sonmez, A., Qureshi, A. R., Saglam, M., Stenvinkel, P., Yaman, H., . . . Carrero, J. J. (2011). Endogenous testosterone, endothelial dysfunction, and cardiovascular events in men with nondialysis chronic kidney disease. *Clinical Journal of the American Society of Nephrology*, *6*, 1617-1625. doi:10.2215/CJN.10681210