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Chronic renal failure and sexual functioning: clinical status *versus* objectively assessed sexual response

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Abstract

Background. Sexual dysfunctions are common among patients with chronic renal failure. The prevalence was assessed in a population of 281 patients (20–60 years), and it was attempted to determine whether their mode of treatment (haemodialysis, peritoneal dialysis, or kidney transplantation), or biochemical and endocrine variables and neuropathy affect sexual functioning. Patients with rheumatoid arthritis served as a comparison group.

Methods. Assessment included clinical history, physical and laboratory examinations, questionnaires measuring erotosexual dysfunctions, and a psychophysiological test procedure. The latter is a laboratory method which measures, in a waking state, subjective and physiological sexual arousal.

Results. Men on haemodialysis or peritoneal dialysis suffered significantly more often from 'Hypoactive Sexual Desire Disorder', 'Sexual Aversion Disorder' and 'Inhibited Male Orgasm' than men with kidney transplantation or rheumatoid arthritis. Interestingly, the prevalence of 'Male Erectile Disorder' did not differ significantly between the four groups and ranged between 17 and 43%. Of the women, transplanted patients suffered significantly less from 'Hypoactive Sexual Desire Disorder' than the other three groups; the prevalence of other sexual dysfunctions did not differ between the groups. Although 'Male Erectile Disorder' and 'Female Sexual Arousal Disorder' had a relatively high prevalence there were no differences in the four groups of patients in genital responses during psychophysiological testing. Genital responses during psychophysiological assessment had no relationship to the duration of renal replacement treatment, biochemical/endocrine variables, or the presence/absence of neuropathy.

Conclusion. The prevalence of sexual dysfunction was high. Sexual dysfunction in men on haemodialysis or peritoneal dialysis was not so much due to erectile failure but largely to loss of sexual interest, subjectively ascribed to fatigue. The latter was also found in women on haemodialysis or peritoneal dialysis.

Key words: chronic renal failure; prevalence; biochemical variables; psychophysiology; sexual dysfunctions

Introduction

Sexual dysfunctions are common in patients with chronic renal failure (CRF). Prevalence estimates run from 9% before starting dialysis to 60–70% in dialysing male and female patients [1,2]. Several somatic factors have been implicated in the aetiology of sexual dysfunctions in patients with CRF (for a review see Handelsman [3]). However, most of these factors lack empirical support. Severe malnutrition, and vitamin and zinc deficiencies were problems in the early days of dialysis, but are relatively rare now. Uraemic toxins and 'middle molecules' have not been convincingly implicated. CRF is associated with disturbances of reproductive hormones and prolactin, but their pharmacotherapeutic correction has not been proved beneficial. Atherosclerosis is accelerated in patients with CRF, but the rapid onset of improvement of sexual function following renal transplantation renders it unlikely that this is an important factor. This also applies to uraemic neuropathy, the progression of which is being slowed by adequate dialysis. Several drugs used in the treatment of patients with CRF may interfere with sexual functioning, but their replacement with more modern drugs has not reduced sexual dysfunction.

None of the somatic mechanisms mentioned above has satisfactorily explained the high incidence of sexual dysfunctions in patients with CRF. Thus, psychological mechanisms have to be taken into consideration. In view of the psychosomatic nature of human sexuality, these psychological studies have gained in importance [1,4,5]. Depression in reaction to the handicap of CRF and a sense of loss (of one's job, financial security,

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freedom, and attractiveness as a sexual partner) could all be significant factors.

Modern insights into the sexual response cycle compel us to consider somatic and psychological factors integrally and simultaneously. Bancroft [6] has designed a scheme to symbolize the complexity of the sexual response system, the so-called psychosomatic circle of sex. This system contains emotional, cognitive, and genital components. In view of the circularity of the psychosomatic sexual schema, it can be broken into at any point; the circle relies on positive and negative feedback between different parts of the system. Failure in any of these areas may lead to sexual difficulties.

In the late seventies, Procci *et al.* [2] investigated whether the registration of spontaneous, sleep-related nocturnal penile tumescence (NPT) could provide objective psychophysiological criteria for evaluation of erectile dysfunction in uraemia. One of the main assumptions of the technique of NPT is that psychological factors interfering with sexual functioning are non-operative during sleep. Thus, NPT could differentiate between somatic and psychogenic factors in sexual dysfunction. However, this assumption has proved to be an oversimplification. Psychological factors such as depression may negatively affect the occurrence of sleep erections [7]. In addition, it is increasingly realized that NPT registration during sleep needs not to reflect real-life sexual situations. Several investigations on erections, in both the waking and sleeping state, have shown discrepancies in outcome [8].

The laboratory method of visual erotic stimulation in the waking state more closely reflects real-life sexual situations [7,8]. The psychophysiological system of sexual arousal is elicited by means of erotic video material. The essential difference with the NPT measurement is the conscious and communicative experience of sexual arousal by the test subject. The method is applicable in both men and women. In men the instrument has been called the Waking Erectile Assessment (WEA), and has proven to be a valuable diagnostic instrument [7]. The parallel female version used in the present study is modelled after the WEA and further based on the research of Laan *et al.* [9]. This female version of the test is denoted by the Visual Erotic Stimulation (VES).

The availability of the research tool of WEA and VES prompted us to study the prevalence and nature of sexual dysfunctions in patients with CRF. With regard to the inclusion of a comparison group with rheumatoid arthritis (RA), the study design was modelled after the work of Procci *et al.* [2]. However, in contrast to the former studies both men and women participated in the present study. There were two major research questions. First, is sexual dysfunctioning in CRF due to the underlying kidney disease and/or its treatment modality itself, or is it due more generally to having a chronic disabling physical condition, such as RA? Our second research question was to explore whether the mode of renal replacement therapy—haemodialysis (HD), peritoneal dialysis (PD), or transplantation (Tx)—influences the incidence and severity of sexual dysfunction.

Subjects and methods

Recruitment of patients

The research focus was on groups of *active* HD, PD, and Tx patients, aged 20–60 years, who were rehabilitated to a level at which they were able to manage their daily lives independently of medical institutions. Of the Tx patients, only those who received a kidney transplant between 1 and 7 years before the start of this study, and who had been dialysed before in one of our centres, were included. Patients who suffered from clinical depression or other major psychiatric diseases were excluded. Patients with classical, seropositive or seronegative, RA or with the diagnosis juvenile RA, were selected as controls. All were RA patients with Steinbröcker classification 2 or 3, i.e. hindrance of their disease in their daily lives to a degree comparable to the selected renal patients. Both renal and RA patients underwent at the same time the same study protocol.

One to three weeks after receiving a general introductory letter explaining the research project, patients were called by the principal investigator (AWFTT) and asked whether they were willing to participate. If the response was positive, patients and their spouses were invited to the clinic. Informed consent was obtained from all subjects and partners. The study protocol was approved by the hospital ethics committee. In case that patients refused to participate, they were asked whether they were willing to fill out a Sexual Attitude Questionnaire (SAQ) [10]. A high total score on this questionnaire indicates a 'liberal' sexual attitude; a low total score indicates a 'conservative' sexual attitude.

Clinical categorization

Assessment of clinical status of the participating patients consisted of a clinical interview, and a physical and biochemical examination. An inventory of sexual functioning adapted from Dekker *et al.* [11] was used and included items related to current erotic and current sexual functions, the severity of sexual problems, and sexual satisfaction. All patients were classified by a single researcher (AWFTT) according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-III-R) for their sexual functioning [12].

Existence of neuropathy was assessed by inquiring about the existence of restless leg symptoms, burning pain in the lower extremities, and loss of muscle power. Perception of deep sensibility was tested by examining the vibration threshold on the lower extremities, using a 128 Hz tuning key [13].

Psychophysiological assessment; stimuli, genital and subjective measures

At the end of the first part of the study patients were asked to make a second appointment for the psychophysiological assessment. HD patients were tested on a non-dialysing day [14]. Women were scheduled so that they would not have their menstrual period at the time of that assessment.

The video sequences consisted of six different excerpts in a fixed order, with explicit erotic scenes with sound, each lasting three min. All excerpts for women, and four of the six excerpts for men, were taken from films with female-

initiated, female-centred erotic activities. In the protocol for male patients, three film presentations were paired with vibrotactile stimulation of the penis [15]. Vibrotactile stimulation was administered by means of a ring-shaped vibrator (50 Hz), placed just below the coronal ridge of the penis.

To minimize negative cognitive interference, Janssen *et al.* [7,15] included arithmetic distraction tasks in the WEA, presented in the second and fifth film excerpt. These arithmetic tasks are employed to distract patients from their worries about not being able to get an erection. These tasks were also included in the VES. Subjects were instructed to perform the mental arithmetic while looking at the film, and to write down their answers on a form.

Analogous to the validation study of the WEA, two sequential order groups were created for the male patients: one group started with non-vibration/film conditions ('sequence one'), and one starting with vibration/film conditions ('sequence two'). Participants in WEA were randomly assigned to one of the two sequences. Vibration was not used in the VES procedure; therefore, there was only one sequence for the female patient group.

After the six film excerpts, male and female patients were asked to fantasize about a pleasurable sexual situation and to concentrate on pleasurable genital feelings. At the end, patients were asked whether they had been able to concentrate on the task of fantasizing. They were not asked about the contents of their fantasy.

Prior to each stimulus condition, a 3-min baseline measurement was taken. During baseline measurements patients listened to music of their own choice or watched a neutral video excerpt.

For male patients an electromechanical penile, Barlow strain gauge was used to assess penile circumference changes during all conditions [16]. Vaginal pulse amplitude (VPA) was measured using vaginal photoplethysmography [17].

Penile circumference change and VPA were sampled during baselines and subsequent stimulus presentation periods using a personal computer. Data were entered into computer programs that enabled off-line inspection and deletion of movement artefacts [7,9]. Penile data were scored as millimeters of circumference, based on pre-session calibration of the strain gauge. Mean VPA was expressed as millivolts change from preceding baseline. Differences between baseline measures and evoked measures provided indices of changes in genital responding.

During the third and sixth film excerpt, patients were asked to continuously self-monitor their estimated degree of genital response; i.e. the degree of erection in males, and the strongest degree of genital sensations in females. Patients were instructed to move a lever (connected to their armchair), which produced a signal calibrated to a 1–10 scale displayed under the TV monitor.

Measures of subjective arousal were collected prior to the first and after each following condition of the psychophysiological session. Subjects were asked to assess on a 7-point Likert scale: (a) their overall sexual arousal, (b) strongest feeling of sexual arousal, (c) degree of erection in men and strongest genital sensations in women, and (d) strongest extragenital sensations.

Data from the 'subjective' monitoring lever, and the discrete measures of subjective sexual arousal, were analysed separately. For a full description of the psychophysiological procedures the reader is referred to Janssen *et al.* [7,15], and Laan *et al.* [9].

Statistical analysis

The BMDP 4V program (1990 edition) was used for all multivariate and univariate ANOVAs. Repeated-measures ANOVAs were constructed with treatment groups as 'between-subjects' variables, and conditions as to genital responses and subjective measures as 'within-subjects' variables. For men there was another 'between-subjects' variable; two sequential order groups. In case there were group differences at the baseline measurement ANCOVAs were constructed with preceding baselines as covariates. The main focus in our paper is on differences between treatment groups, and results regarding condition effects and interactions between groups and conditions will not be discussed here.

The Greenhouse–Geisser epsilon procedure was applied to all repeated measures ANOVAs to correct for the violation of the spherity assumption in repeated-measures designs [18]. Following significant F ratios of main or interaction effects, *post hoc* contrast analyses (simple mean comparisons) were performed with the overall level of significance set at $\alpha = 0.05$ using the Bonferroni procedure [19].

Student's *t* tests and Chi-squared tests with Yates' continuity correction were used to compare questionnaire results, and physical, biochemical and endocrine examination of the four groups.

Results

General information

In total 166 men and 163 women were approached for participation. Fifty-three per cent of the men (88) and 27% of the women (44) decided to go through the complete assessment procedure. Ten per cent (16) of the men and 18% of the women (29) consented to an interview plus sexual history taking, a physical examination and a measurement of biochemical variables, but not to the psychophysiological assessment. Thirty-seven per cent of men (62) refused participation; however, 12% (20) of them were willing to fill out the Sexual Attitude Questionnaire (SAQ). In the female group 55% (90) refused participation, of whom 13% (21) filled out the SAQ. In women, Tx patients were significantly more willing to participate in VES (35%) than HD and PD patients (21 and 10% respectively, $P < 0.05$). In men, PD and Tx patients appeared to be most willing to participate in the research programme, but the difference in participation between groups was not significant.

Men who participated in WEA appeared to have a somewhat more 'liberal' sexual attitude ($n = 84$; total score 117) than the non-participants ($n = 32$; total score 106, $P < 0.005$). This pattern was not observed in female patients ($n = 44$, 115 vs $n = 21$, 111; $P > 0.2$). General characteristics regarding age, duration of disease or renal replacement therapy, and social status of male and female patients are summarized in Tables 1 and 2. More single men than men with a partner declined participation in the WEA ($P < 0.01$). In female patients this difference was not found.

Diagnosis of sexual dysfunction

In men, lack of desire for sexual activity and lack of sexual fantasies (i.e. 'Hypoactive Sexual Desire Disorder') were significantly more often present in dialysing men than in Tx and RA men (Table 3). For

Table 1. General information on men who filled out the sexual history questionnaire

Men	Haemodialyis	Peritoneal dialysis	Transplantation	Rheumatoid arthritis	*P*
n	23	21	33	22	
Ever HD	–	6	18	–	
Ever Tx	10	3	–	–	
Duration disease (years; mean ± SD)	13.2 ± 9.0	7.5 ± 8.3	12.1 ± 9.0	12.8 ± 7.7	0.12
Duration total RRTs	8.2 ± 6.0	2.5 ± 2.5¶	6.2 ± 4.9	–	<0.01
Duration current RRT	5.4 ± 6.0#	2.0 ± 1.9	3.3 ± 2.3	–	<0.01
Age	40.8 ± 10.6	40.0 ± 11.6	38.9 ± 10.3	47.3 ± 10.5†	0.02
Relational status					
Single	8 (36%)	7 (33%)	9 (27%)	3 (14%)	0.34
Divorced	5 (23%)‡	1 (5%)	1 (3%)	1 (5%)	0.04
No children	8 (36%)	6 (32%)	13 (41%)	5 (28%)	0.71
With partner	15 (74%)	14 (67%)	24 (73%)	19 (86%)	0.34
Assessment of relationship					0.77
Unhappy	0	0	1 (4%)	1 (5%)	
Indifferent	1 (7%)	0	1 (4%)	2 (11%)	
Happy	13 (93%)	14 (100%)	22 (92%)	16 (84%)	
Sexually active with partner	11 (79%)	13 (93%)	23 (89%)	18 (95%)	0.49

¶Significantly shorter than the other two groups of RRT.
#Significantly longer than the other two groups of RRT.
†Significantly older than patients with RRT.
‡Significantly more than the other groups of patients.

Table 2. General information on women who filled out the sexual history questionnaire

Women	Haemodialyis	Peritoneal dialysis	Transplantation	Rheumatoid arthritis	*P*
n	11	9	27	18	
Ever HD	–	6	18	–	
Ever Tx	2	4	–	–	
Duration disease (years; mean ± SD)	11.3 ± 7.7	10.0 ± 8.0	16.1 ± 9.5	16.0 ± 9.8	0.19
Duration total RRT	5.7 ± 5.4	3.6 ± 4.0¶	7.0 ± 4.0	–	<0.01
Duration current RRT	4.5 ± 4.8	2.4 ± 1.5¶	4.0 ± 2.7	–	<0.01
Age	41.7 ± 12.7	39.5 ± 9.7	43.2 ± 9.3	46.0 ± 9.8	0.33
Relational status					
Single	3 (27%)	2 (22%)	3 (11%)	6 (33%)	0.33
Divorced	1 (9%)	1 (13%)	0	2 (11%)	0.36
No children	6 (55%)#	1 (13%)	5 (19%)#	1 (17%)	0.01
With partner	8 (73%)	7 (78%)	24 (89%)	12 (67%)	0.33
Assessment of relationship					0.54
Unhappy	0	0	2 (8%)	0	
Indifferent	2 (25%)	1 (14%)	1 (4%)	2 (15%)	
Happy	6 (75%)	6 (86%)	21 (88%)	11 (85%)	
Sexually active with partner:	6 (75%)†	7 (100%)	24 (100%)	12 (100%)	<0.01

¶Significantly shorter than the other two groups of RRT.
#Significantly more than the other groups of patients.
†Significantly less than the other three groups.

the male patients the percentages were 57% in HD, 60% in PD, 12% in Tx, and 9% in RA. Failure to attain or maintain erection until completion of the sexual activity, or lack of a subjective sense of sexual excitement and pleasure during sexual activity is defined as 'Male Erectile Disorder'. Erectile disorder, present in 43% of HD men and in 25% of PD men, was not significantly less prevalent in Tx men (21%) or in RA men (17%).

The significant differences pertaining to 'Inhibited Male Orgasm' and 'Premature Ejaculation' are possibly influenced by the number of men without a sexual partner.

In female patients, prevalence of lack of desire for sexual activity and lack of sexual fantasies (Hypoactive Sexual Desire Disorder) were 100% in HD, 67% in PD, 31% in Tx, and 76% in RA patients (Table 4). In female RA patients (in contrast to male RA patients) prevalence of Hypoactive Sexual Desire Disorder did not differ significantly from prevalence in dialysing women. Hypoactive Sexual Desire Disorder of Tx women was significantly less prevalent in comparison

Table 3. Sexual dysfunction according to DSM-III-R in men

Men	Haemodialyis	Peritoneal dialysis	Transplantation	Rheumatoid arthritis	*P*
Participation in interview or also VES	22	21	37	24	–
No classifying sexual diagnosis	1	1	3	1	–
Hypoactive Sexual Desire Disorder	57% (12)¶	60% (12)¶	12% (4)	9% (2)	<0.01
Male Erectile Disorder	43% (9)	25% (5)	21% (7)	17% (4)	0.21
Sexual Aversion Disorder	24% (5)¶	15% (3)	0	4% (1)	0.01
Not relevant to respondent	3	3	5	1	–
Inhibited Male Orgasm	37% (7)¶	12% (2)	3% (1)	4% (1)	<0.01
Not relevant to respondent	2	3	–	–	–
Premature Ejaculation	11% (2)	12% (2)	15% (5)	22% (5)	0.77
Not relevant to respondent	3	3	1	–	–
Dyspareunia	0	0	0	0	0.51
Not relevant to respondent	4	4	6	–	–
Marked feelings of inadequacy concerning body habitus	24% (5)	15% (3)	12% (4)	0	0.09

¶Significantly more frequent than the other groups.

to the other three groups of women. Failure to attain or maintain the lubrication-swelling response of sexual excitement until completion of the sexual activity, or lack of a subjective sense of sexual excitement and pleasure during sexual activity is defined as Female Sexual Arousal Disorder. It was present in 71% of HD women. It was observed in 50% of cases on PD. Differences between the four groups of female patients were not significant. This so-called 'Female Sexual Arousal Disorder' was present in 26% of Tx, and in 40% of RA female patients. Prevalences of other sexual dysfunctions are presented in Table 4.

Waking Erectile Assessment results in men; physiology

Table 5 shows means (SD) of maximum penile circumference changes measured by the strain gauge for all four groups during the eight conditions. Baseline values remained constant during the five baseline measurements ($P>0.40$), and there were no differences between baselines for the four groups ($P>0.40$). A repeated measures ANOVA was performed to test the assumption that the three groups of men with CRF were different on their erectile responses, it revealed that there was not a main effect for mode of renal replacement therapy ($P>0.30$). However, a significant effect of sequence was found ($F=12.74$, $df=1$, 57, $P<0.001$): patients allotted to 'sequence one' (receiving film conditions before vibration to the penis was added) showed a greater mean penile response than patients of 'sequence two'. This effect was congruent in the three modes of renal replacement therapy. It was found that erectile responses were dependent on the sequence of presentation of the conditions, signifying a difference associated with the set-up of the experiment, not with the underlying medical condition. In addition, a main effect of condition was found ($F=8.81$, $df=7$, 399, $\varepsilon=0.70$, $P<0.0001$), signifying that

Table 4. Sexual dysfunction according to DSM-III-R in women

Women	Haemodialyis	Peritoneal dialysis	Transplantation	Rheumatoid arthritis	*P*
Participation in interview or also VES	11	10	27	25	–
No classifying sexual diagnosis	–	1	1	–	–
Hypoactive Sexual Desire Disorder	100% (11)	67% (6)	31% (8)¶	76% (19)	<0.01
Female Sexual Arousal Disorder	71% (5)	50% (4)	26% (6)	40% (8)	0.16
Not relevant to respondent	2	1	3	5	–
Inhibited Female Orgasm	50% (4)	50% (4)	23% (5)	30% (6)	0.37
Not relevant to respondent	3	1	4	5	–
Sexual Aversion Disorder	38% (3)	25% (2)	12% (3)	9% (2)	0.21
Not relevant to respondent	3	1	0	2	–
Dyspareunia	17% (1)	50% (4)#	4% (2)	8% (2)	0.05
Not relevant to respondent	5	4	5	–	
Vaginismus	0	0	5% (1)	5% (1)	0.87
Not relevant to respondent	5	1	3	6	–
Marked feelings of inadequacy concerning body habitus	9% (1)	22% (2)	24% (6)	20% (5)	0.89
Not relevant to respondent	0	0	1	0	–

¶Significantly less frequent than the other groups.
#Significantly more frequent than the other groups.

Table 5. Millimetres penile circumference changes for each erotic condition in men with renal replacement therapy and men with rheumatoid arthritis (mean and SD in parentheses)

	Haemodialysis		Peritoneal dialysis		Transplantation		Rheumatoid arthritis	
	Sequence 1 $n=10$	Sequence 2 $n=9$	Sequence 1 $n=6$	Sequence 2 $n=7$	Sequence 1 $n=16$	Sequence 2 $n=15$	Sequence 1 $n=10$	Sequence 2 $n=11$
Film	11.7 (15.1)	10.2 (5.9)	28.2 (19.3)	15.6 (13.6)	28.8 (15.7)	11.1 (10.2)	26.6 (19.6)	17.1 (19.4)
Film & distraction	20.7 (17.7)	13.9 (9.0)	28.7 (25.3)	16 (18.1)	30.3 (18.1)	11.1 (10.7)	22.7 (25.1)	18.0 (20.6)
Film & monitoring	23.4 (13.2)	10.1 (9.6)	39.5 (32.9)	14.4 (14.2)	36.1 (23.9)	10.6 (10.2)	31.7 (23.6)	21.9 (25.1)
Vibration	22.2 (19.3)	9.3 (10.5)	16.7 (9.2)	9.7 (13.4)	19.2 (23.4)	12.2 (14.9)	17.9 (20.4)	26.2 (18.6)
Vibration & film	28.1 (24.1)	16.7 (16)	42.2 (21.6)	18.6 (15.4)	38.5 (19.3)	16.7 (14.6)	22.1 (16.1)	37.4 (25.7)
Vibration & film & distraction	24.9 (25.1)	15.7 (10.1)	34 (29.3)	19.3 (13.7)	25.2 (22.4)	20.1 (16.8)	22.9 (15.3)	32.5 (31.5)
Vibration & film & monitoring	25.6 (23.2)	28 (28.3)	32 (29.2)	16.3 (13.7)	21.9 (13.3)	26.7 (17.8)	23.7 (15.6)	31.8 (28.4)
Fantasy	5.2 (4.7)	4.6 (6.0)	22.2 (17)	7.3 (8.1)	11.1 (7.7)	14.9 (13.8)	7.5 (7.4)	19.7 (18.9)

the eight conditions differed in the extent to which they evoked erectile responses.

In an additional repeated measures ANOVA, it became clear that penile circumference changes of renal patients were not different from the responses of the RA comparison group ($P>0.20$). Although calculations made clear that age showed a (weak) negative correlation with the results in WEA ($r\ (88)=-0.32$, $P<0.005$), and although these comparison patients were significantly older than the renal patients ($P<0.05$), no main effect of disease category was found. However, the latter analysis revealed a significant interaction between sequence of stimuli and 'underlying disease' ($F=4.97$, $df=1, 80$, $P<0.05$). The previously described sequence effect was unique for the renal patients, independent of mode of RRT. The so-called sequence effect did not occur in the comparison patients.

Genital responses in WEA in relation to erectile dysfunction

All participants in WEA were classified on the basis of their erectile function according the criteria of the DSM-III-R. They were classified as with No Erectile Disorder or having Erectile Disorder. No statistically significant differences in erectile responses between the 18 renal patients with erectile disorder and the 45 renal patients without erectile disorder were calculated ($P>0.10$) in a separate ANOVA.

Subjective sexual arousal in the WEA

During two conditions, patients continuously self-monitored their estimated degree of erection. Analysis of these data made clear that dialysing (HD and PD) men were equally capable of monitoring their estimated genital response as Tx patients or RA patients. In contrast, a difference became apparent in assessment of subjective sexual arousal as measured by the discrete items. 'Overall' and 'strongest sexual arousal' during the erotic conditions were investigated in an ANCOVA with preceding 'overall sexual arousal', assessed during baseline measurements, as covariates. A main trend for the factor mode of renal replacement therapy was found for both 'overall sexual arousal' ($F=2,40$, $df=2,54$, $P=0.09$) and 'strongest sexual arousal' ($F=2.39$, $df=2,54$, $P=0.10$). 'Overall sexual arousal' was rated lower by PD patients than Tx patients; *post hoc* test: $F=3.91$, $df=1,57$, $P=0.05$. For 'strongest sexual arousal' the *post hoc* revealed no differences between the treatment groups.

Visual Erotic Stimulation results in women; physiology

Table 6 shows means (SD) of maximum VPA changes measured by the vaginal photoplethysmograph for three groups during the seven conditions. In total seven dialysing women participated in the VES. Two of them were treated with PD, five with HD. Because of the small number of dialysing women, in comparison to the 20 Tx women and the 16 RA women, the seven women treated with HD and PD were regarded as one group in the analyses.

In contrast to the men, women participating in the psychophysiological test showed increasing baseline values during progression of the VES procedure ($F=13.20$, $df=4,160$, $\varepsilon=0.75$, $P<0.0001$). This effect was independent of the groups. To account for these baseline differences, VPA changes during erotic conditions

Table 6. Millivolts Vaginal Pulse Amplitude (VPA) changes for each erotic condition in women with renal replacement therapy and women with rheumatoid arthritis (mean and SD in parentheses)

	Dialysis $n=7$	Transplantation $n=20$	Rheumatoid arthritis $n=16$
Film 1	1.2 (2.2)	1.4 (1.3)	1.2 (1.2)
Film & distraction 1	1.3 (1.6)	1.0 (1.5)	1.1 (1.3)
Film & monitoring 1	2.3 (2.0)	2.2 (1.8)	2.4 (1.8)
Film 2	1.7 (1.9)	2.0 (1.9)	1.2 (1.8)
Film & distraction 2	0.7 (1.3)	0.5 (0.9)	0.6 (1.3)
Film & monitoring 2	2.5 (2.4)	1.6 (1.7)	1.9 (2.5)
Fantasy	0.7 (0.8)	0.8 (1.4)	1.3 (1.9)

were investigated in an ANCOVA, with preceding mean baselines as covariates. This ANCOVA revealed that there was no main effect of group ($P > 0.95$), indicating that dialysing women showed the same physiological response to the erotic stimuli as women with a renal graft or women with RA. However, the main effect of condition was significant ($F = 14.49$, $df = 6, 239$, $P < 0.0001$), signifying that the seven erotic conditions differed in the extent to which they evoked increases in the vaginal blood flow. Because the main focus of this paper is on group effects, these results will not be further discussed. No significant interaction effects were found.

Genital responses in VES in relation to sexual dysfunctions; physiology

Women with classifications 'not relevant to respondent' (see Table 4) were excluded from ANCOVAs testing the relation between sexual dysfunctions and sexual responses evoked in the VES. Because no significant main effect of group was found in the analysis reported above, all participating women to the VES were regarded as one group. In a next ANCOVA the assumption that sexual dysfunctions had effect on the vaginal haemodynamics was tested. No single diagnostic variable of sexual dysfunction in the DSM-III-R revealed an effect on vaginal blood flow.

Subjective sexual arousal in the VES

During two of the test conditions the women were asked to continuously monitor their genital arousal by moving a lever. A test design was used to answer the question whether dialysing women rated their perceived genital arousal differently from renal transplant or comparison subjects. Maximum and mean subjective responses were used as dependent variables. No group effects were found with regard to mean subjective ratings ($P > 0.60$) and maximal subjective ratings ($P > 0.95$). This indicates that dialysing women did not rate their genital responses differently from the other two groups of women.

No effects were found on genital responses when women with sexual dysfunctions were compared with women without sexual dysfunctions as described in the previous section. However, when data of monitoring genital arousal in relation to sexual dysfunctions were analysed, differences became manifest. Women with 'Female Sexual Arousal Disorder' and women with 'Inhibited Female Orgasm' reported less feelings of sexual arousal in their genitals than women without these dysfunctions. On the one hand, women with 'Female Sexual Arousal Disorder' showed a statistical trend that their self-monitored level of *mean* genital arousal was lower than in women without sexual arousal disorder ($F = 3.82$, $df = 1, 18$, $P = 0.06$). But, the women with 'Female Sexual Arousal Disorder' monitored significantly lower levels of *maximal* genital arousal than the women without this disorder ($F = 4.17$, $df = 1, 18$, $P < 0.05$). In the group of women with 'Inhibited Female Orgasm', *mean* as well as *maximal* genital arousal was significantly lower than in the group of women without 'Inhibited Female Orgasm'; test results were $F = 4.56$, $df = 1, 37$, $P < 0.05$, and $F = 4.28$, $df = 1, 37$, $P < 0.05$ respectively.

Subjective sexual arousal was measured at the beginning of the VES and after each test condition. The main objective of measurement of subjective sexual arousal was to know whether there were differences between the three groups. At baseline measurements there were differences between the three groups; therefore it was necessary to use an analysis of variance with baseline values as covariates (ANCOVA). Although baseline measurement showed differences in subjective sexual arousal between the three treatment groups, during the VES these group differences were no longer apparent ($0.12 < P < 0.85$).

Genital responses in VES in relation to sexual dysfunctions; physiology

Women with classifications 'not relevant to respondent' (see Table 4) were excluded from ANCOVAs testing the relation between sexual dysfunctions and sexual responses evoked in the VES. Because no significant main effect of group was found in the analysis reported above, all participating women to the VES were regarded as one group. In a next ANCOVA the assumption that sexual dysfunctions had effect on the vaginal haemodynamics was tested. No single diagnostic variable of sexual dysfunction in the DSM-III-R revealed an effect on vaginal blood flow.

Biochemical, endocrinological, neuropathic variables, and the results in WEA or VES

Correlations were computed between both haemoglobin, biochemical and endocrinological variables, and genital responses to the eight WEA conditions, in order to explore possible biochemical parallels of sexual dysfunction. Dialysing patients with haemoglobin levels smaller than or equal to 5.5 mmol/l were treated with erythropoietin. Haemoglobin levels, in men and women, differed between the four groups. In men haemoglobin was 7.6 ± 0.8 mmol/l, 6.7 ± 1.2 mmol/l, 8.8 ± 1.5 mmol/l, and 8.8 ± 0.6 mmol/l in HD, PD, Tx, and RA respectively ($P < 0.01$). In women level of haemoglobin was 7.2 ± 0.7 mmol/l, 7.4 ± 0.9 mmol/l, 8.5 ± 1.0 mmol/l, and 7.8 ± 1.0 mmol/l in HD, PD, Tx, and RA respectively ($P < 0.05$). Biochemical variables were creatinine clearance, serum albumin, total serum protein, potassium, haemoglobin, calcium, and phosphate. The endocrinological variables were prolactin, total serum testosterone, parathormone, oestradiol, luteinizing hormone, thyroid hormone, and thyroid stimulating hormone. Correlations were calculated for male patients as one group, and for the four treatment groups separately. Although there were differences in biochemical and endocrinological variables between groups, no significant correlations with results in WEA

were found. Because no consistent pattern of correlation of biochemical and endocrinological variables with results in WEA was found, these tests have not been repeated for the results of women in VES. The effects of presence or absence of menstual cycles, and its relationship with hormone status and genital responses are not reported here.

In addition, no effect of neuropathy was found in our measures of circumference changes or vaginal blood flow responses to the conditions in WEA or VES. To further evaluate the influence of polyneuropathic complaints and signs on genital responses, absence or presence of 'restless leg' symptoms, 'burning pain' in the distal extremities, and the result of the deep sensibility test with the tuning key were tested in separate ANOVAs. There was no main effect of neuropathic signs or symptoms on genital responses to the conditions in WEA or VES.

Discussion

Sex research is generally characterized by a bias due to volunteer participation [20]. Therefore, introduction of the Sexual Attitude Questionnaire (SAQ) [10] was thought to be helpful in describing some aspects of volunteer bias in our study. Patients who declined participation were asked to complete the questionnaire to assess their sexual attitudes, and their scores were compared with the scores of the participants. The answers in the SAQ demonstrated that there was a higher degree of conservatism in sexual attitudes in men who refused to participate in the WEA. In the male group of non-participants there were also more single men. In contrast, there were no differences in sexual attitudes between women who went through the whole protocol and women who declined. Notwithstanding, readiness of dialysing women to participate in the VES was low. There were no age differences between male and female patients who refused, and those who participated. Men who declined felt more insecure in discussing their sexual lives with the investigator than men who consented. The former refused to give any information about their sex lives. In women this was different; women gave personal reports of their sex lives in an interview. However, for most of them participation in the VES proved too intimate.

There were no significant differences between the four (HD, PD, Tx, and RA) groups of patients in both sexes, with respect to the prevalence of sexual arousal-related problems ('Male Erectile Disorder' and 'Female Sexual Arousal Disorder'). A difference became apparent with the subject describing whether there was a 'Hypoactive Sexual Desire Disorder' in men as well as in women. Unexpectedly, the duration of dialysis had no relationship to the severity of sexual dysfunction.

Men on dialysis spontaneously reported significantly lower levels of sexual desire than the Tx men. Interestingly, during the clinical interview Tx men not infrequently mentioned a very quick return of their spontaneous erections and libido once they had received a donor kidney. Nevertheless, prevalence of 'Erectile Disorder' in Tx men was not significantly lower than in dialysis patients.

In women, prevalences of 'Hypoactive Sexual Desire Disorder', 'Female Sexual Arousal Disorder', 'Inhibited Orgasm', and 'Sexual Aversion Disorder' were at least the same but most often higher as compared to the male patients (see Tables 3 and 4). More or less the same pattern of sexual dysfunctions was found as in the men. Again as in men, more sexual desire was reported by renal-grafted women, compared to women on dialysis. As opposed to what was found for men with RA, women with RA reported more sexual problems than the Tx women. In contrast to the Tx men, Tx women did not mention a strikingly quick return of their libido once they had received a donor kidney.

Although at present, dialysis sessions have a shorter duration and the technique has been improved, prevalence of sexual dysfunctions in renal patients in our study is comparable to prevalence rates reported in earlier studies of the seventies and eighties [1,2,4,5]. Unfortunately we have insufficient data to determine whether there is a relationship between quality of dialysis of the individual patient and their sexual (dys)functioning.

While differences between the four groups were found in the self-reported data and clinical judgment of the severity of their sexual dysfunctions, in particular of libido, there was surprisingly never a difference between the four groups in the outcome of the more objective WEA and VES laboratory assessments of erectile function and vaginal pulse amplitude. Similarly, in the comparison between self-reported presence of sexual arousal disorders and physiological responses in the laboratory, no differences were found. We did, however, find differences between groups the subjective experience of sexual arousal. PD men in the WEA reported significantly lower levels of 'overall sexual arousal' than the Tx men. In the female patients, the clinical diagnosis of 'Female Sexual Arousal Disorder' paralleled the ratings of perceived sexual arousal during VES; women with this disorder, independent of group, reported lower levels of sexual arousal than women without affected libido.

Male renal patients showed a difference in genital responding in the WEA depending on the sequence of stimulus presentation used in the test. Those male renal patients who started with vibration-and-film conditions showed a significant smaller genital response in the film-only conditions (which were presented after they had received the vibration-and-film conditions). This effect was not observed in male renal patients who had been alloted to the reverse sequence of testing in WEA. In the comparison patients with arthritis this so-called sequence effect was not found. The effect of stimulus order in male renal patients was unexpected, since it had not been found in the validation study of the

WEA procedure [7]. Our explanation can only be speculative. The observation may show that in patients with CRF the psychophyiological substrate of sexual arousal becomes quickly exhausted, and, genital arousal cannot be maintained at a high level for a prolonged period if a strong stimulus is provided already at the beginning of the test.

It has been speculated that uraemic polyneuropathy is an important determinant of erectile dysfunction in renal patients [2]. Vibration sensitivity with the tuning key appears to have satisfactory qualities for a meaningful clinical impression of the degree of uraemic polyneuropathy [13]. In this study the results of vibration sensitivity and the results in the psychophysiological assessment of sexual arousal were unrelated. A meta-analysis of the effects of antihypertensive medication on genital function in non-uraemic patients has been published [21]. Effects of these drugs in uraemic patients are anecdotal, however, with either no effect or a negative effect. The potential negative effect of antihypertensive medication on erectile capacity or vaginal haemodynamic changes could not be tested in this study because of imbalance between the number of patients with and without antihypertensive agents.

Our findings indicate that CRF *per se* does not explain sexual dysfunction in renal patients. It appeared that in renal patients before transplantation sexual functioning is not so much impaired by genital problems. Therefore we come to a different conclusion from that of Procci and colleagues [2]. Procci *et al.* tested spontaneous penile tumescence during sleep (NPT), a situation characterized as non-sexual. Nocturnal erections are strongly dependent on testosterone, while erections associated with erotosexuality are much less dependent [22,23]. From the self-reported data of patients as well as from the differences in emotional sexual arousal during the VES and WEA, the lack of sexual desire or libido was a prominent characteristic of our patient population. We were not able to relate any of the biochemical or endocrine variables to sexual (dys)functioning.

A variable frequently mentioned in the clinical interview, but in retrospect regrettably not quantified in our study, was fatigue. It was also a prominent feature in women with RA, with possibly the same effect on their sexual functioning as in dialysing women, while there are in the women with RA no metabolic disturbances comparable to those in women with CRF. Male, but not female, Tx patients recalled their rapid recovery from physical tiredness and listlessness very shortly after the transplantation. We speculate that mental symptoms of fatigue and listlessness, associated with the affliction, seem to be major factors in the poor sexual functioning in dialysing patients. An objectively reasonable degree of erectile potency or vaginal engorgement, as measured in the laboratory, combined with a subjectively moderate degree of sexual arousal are apparently not enough to perform sexually. From our interviews we got the strong impression that the successfulness of coping with the sexual self-image, and with the situation of being a renal patient, is even more important than uraemia, but this has not been objectively assessed.

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