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Prevalence and correlates of erectile dysfunction in men on chronic haemodialysis: a multinational cross-sectional study

Collaborative Depression and Sexual dysfunction (CDS) in Hemodialysis Working Group*

Correspondence and offprint requests to: Giovanni F.M. Strippoli; E-mail: strippoli@negrisud.it
*The committee details are given in the Appendix.

Abstract

Background. Factors associated with erectile dysfunction in men on haemodialysis are incompletely identified due to suboptimal existing studies. We determined the prevalence and correlates of erectile dysfunction and identified combinations of clinical characteristics associated with a higher risk of erectile dysfunction using recursive partitioning and amalgamation (REPCAM) analysis.

Methods. We conducted a multinational cross-sectional study in men on haemodialysis within a collaborative network. Erectile dysfunction and depressive symptoms were evaluated using the erectile function domain of the International Index of Erectile Function questionnaire and the Center for Epidemiological Studies-Depression Scale, respectively.

Results. Nine hundred and forty-six (59%) of 1611 eligible men provided complete data for erectile dysfunction. Eighty-three per cent reported erectile dysfunction and 47% reported severe erectile dysfunction. Four per cent of those with erectile dysfunction were receiving pharmacological treatment. Depressive symptoms were the strongest correlate of erectile dysfunction [adjusted odds ratio 2.41 (95% confidence interval (CI) 1.57–3.71)]. Erectile dysfunction was also associated with age (1.06, 1.05–1.08), being unemployed (1.80, 1.17–2.79) or receiving a pension (2.05, 1.14–3.69) and interdialytic weight gain (1.9–2.87 kg, 1.92 [CI 1.19–3.09]; >2.87 kg, 1.57 [CI 1.00–2.45]). Married men had a lower risk of erectile dysfunction (0.49, 0.31–0.76). The prevalence of erectile dysfunction was highest (94%) in unmarried and unemployed or retired men who have depressive symptoms.

Conclusions. Most men on haemodialysis experience erectile dysfunction and are untreated. Given the prevalence of this condition and the relative lack of efficacy data for pharmacological agents, we suggest that large trials of pharmacological and non-pharmacological interventions for erectile dysfunction and depression are needed.

Keywords: depression; erectile dysfunction; haemodialysis; sexual function

Introduction

Erectile dysfunction, defined as the inability to achieve or maintain an erection sufficient for satisfactory sexual performance [1], is common in men with chronic kidney disease. Existing studies have shown erectile dysfunction is present in ~50% of men with chronic kidney disease not requiring dialysis and in 80% of men receiving dialysis

treatment [2–4]. It is less prevalent in earlier stages of chronic kidney disease [5] and may be improved by kidney transplantation [5, 6]. Erectile dysfunction may profoundly affect the quality of life in men with chronic kidney disease [7–9] and be associated with anxiety, loss of self-esteem, depression and marital discord [8–11]. Previous studies have linked erectile dysfunction to adverse cardiovascular outcomes and death [12–15]. Increasing age, hypertension, diabetes mellitus, anaemia and dyslipidaemia may be associated with erectile dysfunction; however, existing studies in chronic kidney disease report conflicting results [2,3] and have not adequately accounted for the coexistence of depression and other major confounders [16, 17].

Our Collaborative Working Group on Depression and Sexual dysfunction (CDS) in haemodialysis recently explored the prevalence and predictors of erectile dysfunction reported in existing cohort studies of people with chronic kidney disease (50 studies, 8343 individuals) [18]. We observed a pooled prevalence of 70% for any category of erectile dysfunction in men [95% confidence interval (CI) 62–77%] but available studies were few and individually limited by small sample sizes, were single-centre analyses and had weaknesses in study design and conduct. Their pooled analysis was unreliable given the limitations inherent to the individual cohort studies and the potential for unknown confounding, necessitating a large study of correlates of erectile dysfunction in men receiving haemodialysis. The aims of the present study were to estimate the prevalence of erectile dysfunction and identify correlates for any erectile dysfunction and severe erectile dysfunction in men receiving haemodialysis. We also sought to develop an algorithm to identify men receiving dialysis who are at higher risk of erectile dysfunction.

Materials and methods

Population and data collection

We recruited men from 27 randomly selected public and private clinics located in seven countries within a collaborative dialysis network coordinated by Diaverum Renal Services. This dialysis network provides outpatient in-centre haemodialysis therapy for a population of ~16 500 people in 14 countries. Dialysis clinics were located in Argentina, Hungary, Italy, Poland, Portugal, Spain and Uruguay. Consecutive men aged ≥18 years who were receiving chronic haemodialysis between January and June 2008 were eligible. We approached all men in the participating dialysis clinics at the time of a haemodialysis treatment. Patients who were participating in any other clinical study were not considered eligible. There were no other exclusion criteria. Ethics approval was obtained from local ethics committees in each of the countries where the study was conducted and men were enrolled after providing written informed consent.

Erectile function was assessed by the five-item erectile function domain of the International Index of Erectile Function (IIEF) questionnaire (also known as the Sexual Health Inventory for Men) [19], which classifies erectile dysfunction into one of five categories: absent (score, 26–30), mild (22–25), mild to moderate (17–21), moderate (11–16) and severe (1–10) (Supplementary material) [20]. From these scores, we categorized erectile dysfunction as severe, mild to moderate (including the categories of mild, mild to moderate and moderate) or no erectile dysfunction. The Sexual Health Inventory for Men has high internal consistency (0.90), test–retest repeatability ($r = 0.84$) and construct (concurrent, convergent and discriminant) validity [19]. Depressive symptoms were evaluated using the Center for Epidemiological Studies-Depression (CES-D) Scale, a short self-report scale that can be used to screen for depression in people with end-stage kidney disease [21]. This depression measure is composed of 20 items measuring symptoms of depression during the previous 4 weeks. A score of ≥18 in individuals requiring dialysis is compatible with depression [22]. We used questionnaires and ratings instruments that were translated and validated in native languages by the MAPI Institute (http://www.mapi-institute.com). International harmonization techniques were used to maximize cultural equivalence of the questions in the translated languages. Questionnaires were completed by men anonymously and collated with de-identified socio-demographic and clinical data provided by the treating physician on a standardized case report form.

Statistical analyses

Baseline variables were calculated as mean and SD or median and interquartile range for continuous variables and as frequencies and percentages for categorical variables. We compared the characteristics of men who provided responses to the erectile dysfunction questionnaire to those of non-respondents using the chi-square (χ^2) test and standard univariate statistics. Clinical characteristics of men in each category of erectile dysfunction (none, mild to moderate and severe) were compared for trend using the Mantel–Haenszel χ^2 test and analysis of variance for trend on ranks for categorical and continuous variables, respectively. Pearson χ^2 test and Mann–Whitney *U*-tests were also reported for any erectile dysfunction (all categories) versus no erectile dysfunction. We used a multivariable logistic regression analysis to identify correlates of erectile dysfunction. We included in the model: age, marital and occupational status, smoking, housing, highest educational level, alcohol abuse, co-morbidities [cardiovascular or cerebrovascular event, diabetes mellitus and endocrine (as defined by a physician) or neurological abnormality (spinal cord lesion, multiple sclerosis, Parkinson's disease or Alzheimer's disease)], cause of end-stage kidney failure (hypertension, diabetes mellitus or other), previous kidney transplant, being on the waiting list for a kidney transplant, medications (including: anxiolytics, antipsychotics and beta blockers), dry weight, interdialytic weight gain, time on dialysis, dialysis adequacy (*Kt*/*V*), laboratory variables (haemoglobin, parathyroid hormone, calcium, phosphorus and albumin) and CES-D score (≥18 versus <18). Results were expressed as adjusted odds ratios (AOR) and their 95% confidence interval (CI). For all multivariable logistic analyses, continuous variables were categorized according to tertiles or specific clinically relevant threshold values.

We then used the recursive partitioning and amalgamation (RECPAM) method to identify combinations of clinical characteristics that were associated with lower and higher risks of any category of erectile dysfunction [23]. This tree-growing method based on logistic regression chose at each step a covariate and its best binary split to maximize the difference in the risk of erectile dysfunction between two groups. The algorithm stopped when user-defined conditions (stopping rules) were met. Age served as the global predictor in our modelling (i.e. the effect of age was considered equally important in all subgroups identified by the algorithm). All statistical analyses were carried out in SAS® (release 9.1; SAS Institute, Cary, NC) including the RECPAM analysis which was conducted using a SAS macro routine [24].

Results

Between January and June 2008, 1700 men receiving long-term haemodialysis treatment from the selected participating haemodialysis clinics were included, representing ~10% of the source dialysis population. As shown in Figure 1, 89 men (5%) were excluded from the present study; 40 (2%) were excluded because they were taking part in other studies and 49 (3%) declined to participate. The remaining 1611 men (95%) were asked to complete two questionnaires; the five-item erectile function domain of the IIEF for erectile dysfunction (Sexual Health Inventory for Men) and the CES-D for depressive symptoms. Of these 1611 men, 1100 (68%) completed and returned the surveys to study personnel. Overall, 946 (59%) provided complete data for the erectile dysfunction domain of the sexual dysfunction questionnaire. Compared with respondents, the non-respondents who did not return the questionnaires were older, weighed less, and were more likely to be

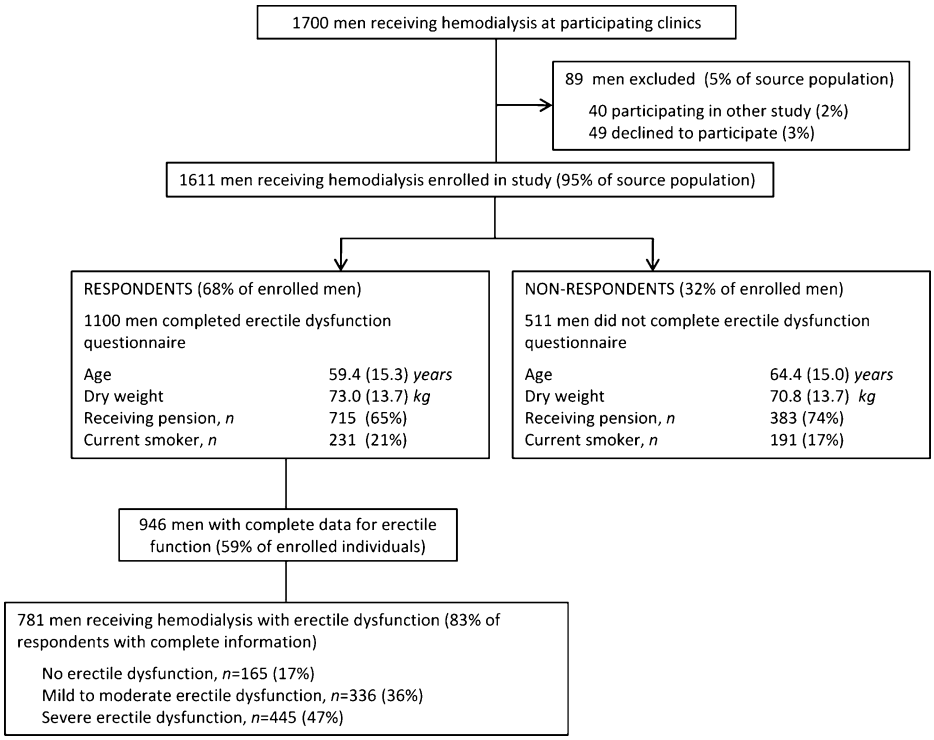

Fig. 1. Patient flow.

receiving a pension and to be non-smokers ($P < 0.05$ for all) (Figure 1). Of the respondents, 781 men (83%) reported experiencing any category of erectile dysfunction. Forty-seven per cent (445 men) reported severe erectile problems and 36% (336 men) reported mild to moderate erectile dysfunction. The clinical characteristics of the included men are shown in Table 1. Approximately 55% (522/946 men) reported being sexually active, including nearly all men [157/165 (98%)] without erectile dysfunction. Men without erectile dysfunction most often reported 3–4 sexual episodes/week [35/165 men (21.9%)], whereas those with mild to moderate erectile dysfunction most frequently reported 1–2 sexual episodes/week [135/336 (40.2%)] and men with severe erectile dysfunction most often reported no sexual episodes/week [376/445 (84.5%)].

On univariate analysis (Table 1), all grades of erectile dysfunction were significantly associated with increasing age. The proportion of men with any erectile dysfunction was 69, 77, 90 and 95% for those <50 years, between 50 and 59 years, between 60 and 69 and ≥70 years, respectively. Symptoms of depression, frequency of sexual activity, limited education, receiving a pension or being unemployed, alcohol abuse, diabetic nephropathy or hypertensive nephrosclerosis as a cause for end-stage kidney disease, a history of diabetes mellitus or cardiovascular disease, lower diastolic blood pressure, shorter dialysis treatment duration or lower urea clearance (Kt/V_{urea}), a lower serum albumin, and prescription of nitrates or diuretics were associated with any erectile dysfunction. Conversely, those with a previous kidney transplant who had returned to dialysis or men awaiting a kidney transplant had a lower risk of erectile dysfunction. The presence of any erectile dysfunction was unrelated to haemoglobin and serum cholesterol levels. Severe erectile dysfunction was additionally associated with previous smoking ($P = 0.009$) and living alone ($P < 0.05$). Of men with severe erectile dysfunction, 10/445 (2.2%) reported receiving phosphodiesterase inhibitor treatment.

Figures 2 and 3 summarize the clinical and sociodemographic characteristics that correlated either with any category of erectile dysfunction or with severe erectile dysfunction in multivariate regression analysis. Age was an important correlate of erectile dysfunction; for each 1-year increase in age, men had a 6% increase in risk of any category of erectile dysfunction (95% CI 5–8%) and a 10% increase in the risk of severe erectile dysfunction (95% CI 8–12%). A higher score on the self-administered depression questionnaire (CES-D score ≥ 18) was the strongest correlate of any erectile dysfunction. In addition, being unemployed or receiving a pension also correlated with any erectile dysfunction as well as interdialytic weight gain, while married men were half as likely to report any erectile dysfunction. Symptoms of depression were also a strong independent correlate of severe erectile dysfunction in addition to presence of diabetic nephropathy or hypertensive nephrosclerosis and endocrine abnormalities. Compared to unmarried men, married men had one-third the risk of severe erectile dysfunction. Men who were on the waiting list for a kidney transplant had a lower risk of severe symptoms.

Figure 4 shows groups of men with differing risks of erectile dysfunction based on combinations of key clinical characteristics that were identified by the REPCAM analysis. The depression score (assessed by the CES-D questionnaire) dichotomized at a score of 18 (presence of

Table 1. Demographic and clinical characteristics of men receiving haemodialysis according to severity of erectile dysfunction ($n = 946$)[a]

	Overall[b] ($n = 946$)	No erectile dysfunction ($n = 165$)	Mild to moderate erectile dysfunction ($n = 336$)	Severe erectile dysfunction ($n = 445$)	P -value (any versus no erectile dysfunction)	P -value (trend across increasing severity)
Age (years), mean (SD)	58.6 (14.9)	49.6 (12.9)	54.1 (13.9)	65.3 (13.1)	<0.001	<0.001
Highest school education, *n* (%)					0.006	0.11
≤5 years	306 (34.3)	40 (25.6)	110 (35.1)	156 (36.8)		
Middle school	375 (41.9)	69 (44.4)	134 (42.8)	172 (40.6)		
High school	146 (16.4)	38 (24.4)	48 (15.3)	60 (14.2)		
University degree	66 (7.4)	9 (5.8)	21 (6.7)	36 (8.5)		
Depression score (CES-D scale), mean (SD)	17.5 (9.8)	13.3 (8.5)	17.2 (9.4)	19.3 (10.1)	<0.001	<0.001
Married, *n* (%)	651 (68.8)	119 (72.1)	230 (69.3)	302 (68.6)	0.31	0.40
Waiting list for kidney transplant, *n* (%)	174 (18.4)	49 (29.7)	81 (24.0)	44 (9.9)	<0.001	<0.001
Occupational status, *n* (%)					<0.001	<0.001
Employed	223 (24.1)	72 (44.4)	87 (26.7)	64 (14.6)		
Unemployed	118 (12.7)	23 (14.2)	59 (17.8)	36 (8.4)		
Receiving pension	586 (63.2)	67 (41.4)	181 (55.5)	338 (77.0)		
Living alone, *n* (%)	100 (10.6)	11 (6.8)	33 (9.9)	56 (12.6)	0.08	0.03
Alcohol abuse, *n* (%)	31 (3.3)	3 (1.8)	16 (4.8)	12 (2.7)	0.25	0.97
Sexually active, *n* (%)	522 (55.1)	157 (98.1)	297 (89.2)	68 (15.3)	<0.001	<0.001
Frequency of sexual activity, episodes/week					<0.001	<0.001
None	415 (44.3)	3 (1.9)	36 (10.8)	376 (84.7)		
1–2 episodes	213 (22.7)	27 (16.9)	135 (40.5)	51 (11.5)		
3–4 episodes	141 (15.0)	35 (21.9)	97 (29.1)	9 (2.0)		
5–6 episodes	66 (7.0)	32 (20.0)	30 (9.0)	4 (0.9)		
7–10 episodes	55 (5.9)	30 (18.8)	24 (7.2)	1 (0.2)		
>11 episodes	47 (5.0)	33 (20.3)	11 (3.3)	3 (0.7)		
Co-morbid conditions, *n* (%)						
Diabetes mellitus	238 (25.1)	30 (18.8)	66 (19.9)	142 (32.6)	0.03	<0.001
Hypertension	638 (73.8)	105 (72.4)	235 (76.2)	298 (72.4)	0.69	0.68
Prior cardiovascular event	237 (25.1)	12 (7.3)	63 (18.7)	151 (34.0)	<0.001	<0.001
Kidney transplant	71 (7.5)	19 (11.5)	36 (10.7)	16 (3.6)	0.03	<0.001
Endocrine dysfunction	28 (3.0)	7 (4.2)	12 (3.6)	9 (2.0)	0.28	0.11
Neurological function	12 (1.3)	1 (0.6)	4 (1.2)	7 (1.6)	0.40	0.34
Primary renal disease, *n* (%)					<0.001	<0.001
Diabetic nephropathy	202 (21.7)	26 (16.1)	61 (18.4)	115 (26.2)		
Hypertensive nephrosclerosis	223 (23.9)	25 (15.4)	70 (21.1)	128 (29.2)		
Other	508 (53.7)	111 (67.3)	201 (59.8)	196 (44.0)		
Smoking history, *n* (%)					0.13	0.08
Current smoker	495 (52.3)	82 (49.7)	186 (55.3)	227 (51.0)		
Former smoker	199 (21.0)	43 (26.0)	81 (24.1)	75 (16.9)		
Never smoked	228 (24.1)	33 (20.0)	64 (19.0)	131 (29.4)		
Dialysis characteristics, mean (SD) or median (interquartile range)						
Interdialytic weight gain, kg	2.4 (1.1)	2.4 (1.2)	2.5 (1.1)	2.3 (1.1)	0.55	0.20
Dialysis vintage, months	33.8 (15.3–68.6)	31.3 (16.1–67.8)	36.5 (16.5–77.8)	33.9 (14.5–65.2)	0.74	0.52
Duration of dialysis, minutes per /session	240.8 (19.6)	243.7 (18.4)	242.6 (18.9)	238.3 (20.3)	0.03	<0.001
KT/V	1.48 (0.23)	1.51 (0.25)	1.47 (0.23)	1.47 (0.24)	0.03	0.07
Clinical parameters, mean (SD) or median (interquartile range)						
Body mass index, kg/m^2	25.3 (4.1)	25.1 (3.9)	25.4 (4.2)	25.3 (4.1)	0.34	0.45
Systolic blood pressure, mmHg	132.7 (18.0)	133.7 (17.4)	133.7 (17.2)	131.6 (18.9)	0.62	0.25
Diastolic blood pressure, mmHg	75.4 (9.3)	77.4 (9.6)	76.6 (8.9)	73.8 (9.2)	0.003	<0.001
Haemoglobin, g/lL	111 (14)	110 (15)	114 (14)	110 (13)	0.42	0.17
Ferritin, µg/lL	408 (227–633)	457 (259–696)	450 (248–675)	420 (242–616)	0.27	0.16
Albumin, g/lL	39 (5)	40 (4)	39 (4)	38 (5)	0.04	0.002
LDL cholesterol, mmol/L	2.38 (0.86)	2.30 (0.76)	2.53 (0.94)	2.28 (0.80)	0.63	0.35
Phosphorus, mg/dldL	4.7 (1.4)	4.8 (1.4)	4.7 (1.5)	4.6 (1.3)	0.18	0.10
Calcium, mg/dldL	8.9 (0.8)	8.9 (0.8)	8.9 (0.8)	8.8 (0.8)	0.89	0.83
Parathyroid hormone, pg/mlmL	286 (170–468)	295 (173–634)	295 (198–481)	262 (158–419)	0.12	0.002
Medication, *n* (%)						
Phosphodiesterase inhibitors	33 (3.5)	8 (4.8)	15 (4.5)	10 (2.2)	0.29	0.07
Beta blocker	364 (38.5)	57 (34.6)	131 (38.9)	176 (39.6)	0.25	0.30
ACE inhibitor	401 (42.4)	65 (39.4)	152 (45.1)	184 (41.1)	0.39	0.9
Angiotensin receptor blocker	127 (13.4)	24 (14.5)	40 (11.9)	63 (14.2)	0.64	0.84
Diuretic	175 (18.5)	21 (12.7)	47 (14.0)	107 (24.0)	0.009	0.001
Erythropoietin	799 (85.7)	133 (14.3)	288 (30.9)	378 (40.6)	0.10	0.14
Nitrate	152 (16.0)	17 (10.3)	47 (14.0)	88 (19.8)	0.03	0.002
Lipid -lowering therapy	256 (27.0)	44 (26.7)	80 (23.7)	132 (29.7)	0.90	0.22
Anti-depressant	38 (4.0)	5 (3.0)	10 (3.0)	23 (5.2)	0.48	0.13

Continued

Table 1. *Continued*

	Overall[b] ($n = 946$)	No erectile dysfunction ($n = 165$)	Mild to moderate erectile dysfunction ($n = 336$)	Severe erectile dysfunction ($n = 445$)	P -value (any versus no erectile dysfunction)	P -value (trend across increasing severity)
Antipsychotic	15 (1.6)	3 (1.8)	5 (1.5)	7 (1.6)	0.79	0.88
Anxiolytic	115 (12.2)	18 (10.9)	34 (10.1)	63 (14.2)	0.59	0.14

[a]ACE, angiotensin-converting enzyme; LDL, low-density lipoprotein.
[b]Numbers may not sum to group totals or percentages may not total 100% where data for the variable are missing.

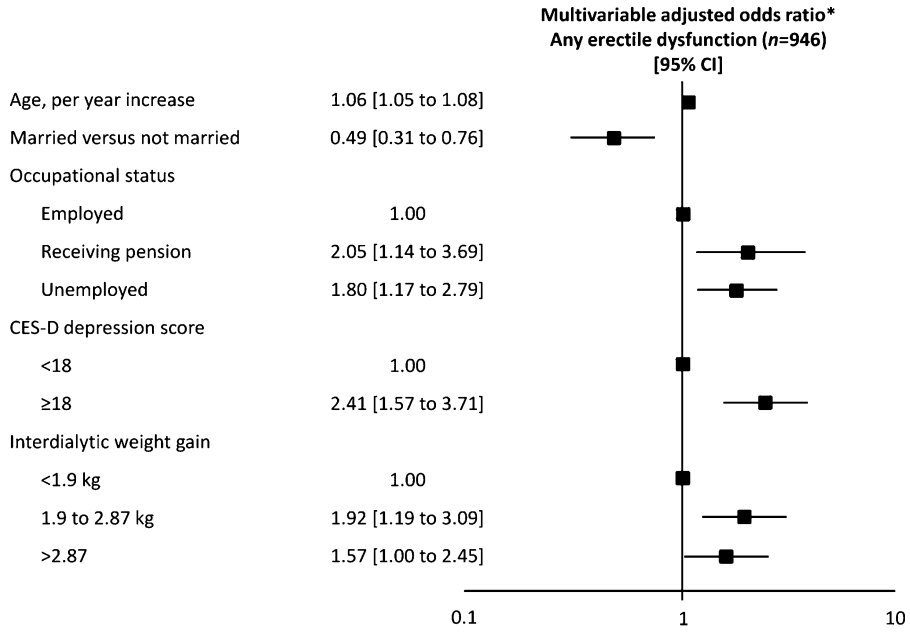

Fig. 2. Socio-demographic and clinical predictors of any erectile dysfunction displayed as multivariate adjusted odds ratios. *The multivariate model included: age, marital and occupational status, smoking, housing, highest educational level, alcohol abuse, co-morbidities [cardiovascular or cerebrovascular event or diabetes mellitus and endocrine (as defined by a physician) or neurological abnormality (spinal cord lesion, multiple sclerosis, Parkinson's disease or Alzheimer's disease)], cause of end-stage kidney failure (hypertension, diabetes mellitus or other), previous kidney transplant, being on the waiting list for a kidney transplant, medication (including: anxiolytics, antipsychotics and beta blockers), dry weight, interdial 10/10/2011 weight gain, time on dialysis, dialysis adequacy (Kt/V), laboratory variables (haemoglobin, parathyroid hormone, calcium, phosphorus and albumin) and CES-D score.

depression if $\geq$18) was the most discriminating variable for differentiating higher and lower erectile dysfunction risk. Married men with a lower depressive symptoms score were less likely to experience erectile dysfunction (292/381 men (77%); reference category). In contrast, unmarried and unemployed men with CES-D score compatible with depression had the highest risk of erectile dysfunction [111/118 (94%) men; AOR, 9.49; 95% CI 4.01–22.45]. Unmarried men with CES-D score compatible with depression and serum albumin levels outside the range of 3.8–4.1 g/dL were also identified as having a higher risk of erectile dysfunction [152/160 men (95%); AOR, 5.12; 95% CI 2.38–11.02].

Discussion

This large multinational cross-sectional study has shown that erectile dysfunction, assessed by a validated measure, is experienced by most men receiving haemodialysis. It is almost always present in some men such as those who are depressed, unmarried and unemployed or retired. In nearly half of men on dialysis, symptoms of erectile dysfunction are severe. The prevalence of erectile dysfunction in men receiving haemodialysis is markedly higher than that of the general population, in which 10–40% of men report one or more features of sexual dysfunction [25–27]. Men with erectile dysfunction were considerably more likely to be sexually inactive. Although erectile dysfunction in men on haemodialysis is common and often severe, very few men (3%) with erectile dysfunction and only 2% of men with severe erectile dysfunction report receiving specific pharmacological treatment. The reasons behind such a low intervention rate are unclear and require additional research, although are likely to include low awareness from treating clinicians, patient embarrassment and the importance of the symptoms relative to the patients' overall health concerns. It is also plausible that the low

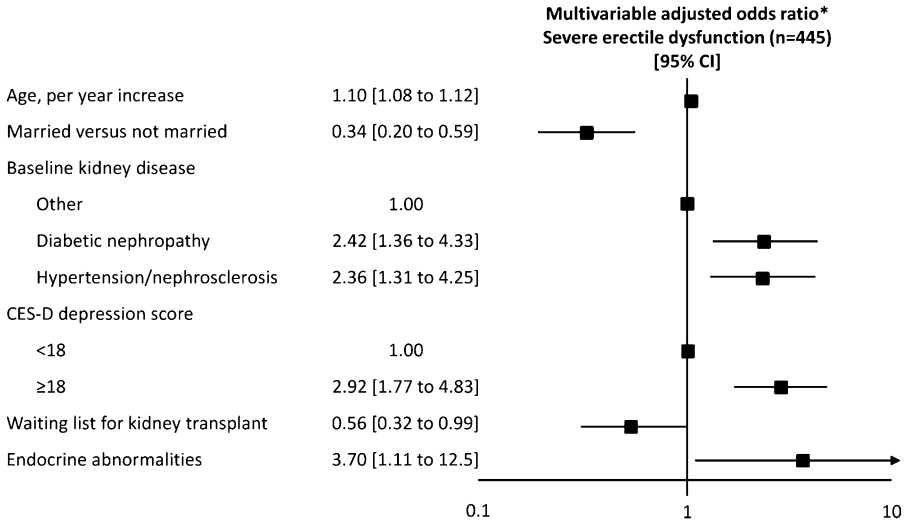

Fig. 3. Socio-demographic and clinical predictors of severe erectile dysfunction displayed as multivariate adjusted odds ratios. *The multivariate model included: age, marital and occupational status, smoking, housing, highest educational level, alcohol abuse, co-morbidities [cardiovascular or cerebrovascular event or diabetes mellitus and endocrine (as defined by a physician) or neurological abnormality (spinal cord lesion, multiple sclerosis, Parkinson's disease or Alzheimer's disease)], cause of end-stage kidney failure (hypertension, diabetes mellitus or other), previous kidney transplant, being on the waiting list for a kidney transplant, medication (including: anxiolytics, antipsychotics and beta blockers), dry weight, interdialytic weight gain, time on dialysis, dialysis adequacy (*Kt*/*V*), laboratory variables (haemoglobin, parathyroid hormone, calcium, phosphorus and albumin) and CES-D score.

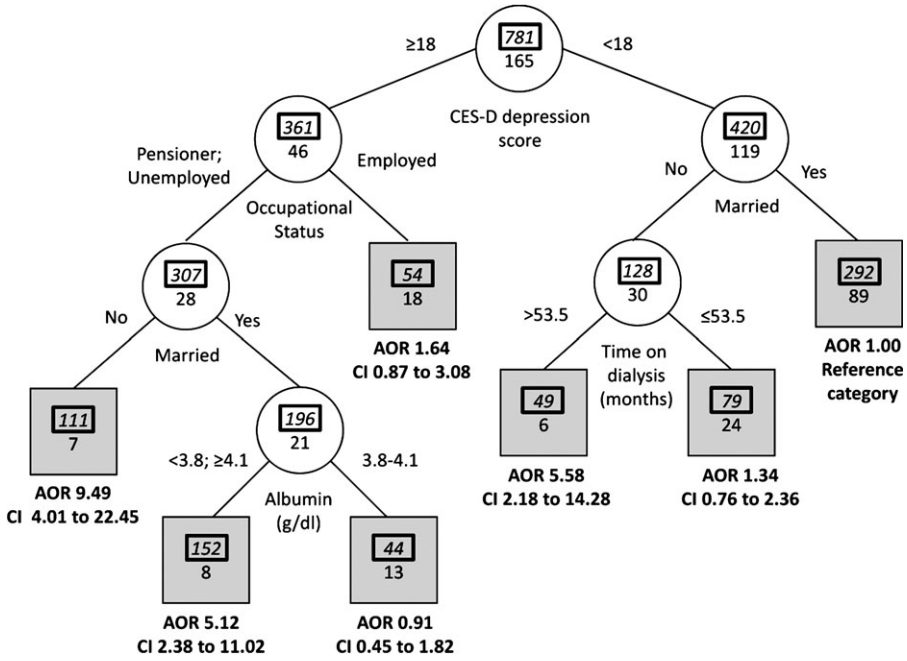

Fig. 4. Recursive partitioning and amalgamation (RECPAM) analysis identifying combinations of individual characteristics associated with different risks for any kind of erectile dysfunction. A tree growing algorithm modelled age-adjusted odds ratios for predicting risk of erectile dysfunction. The splitting variables are shown between branches, while the characteristic assigning men to different groups is above the corresponding branch. Married men without depression had the lowest prevalence of erectile dysfunction and were designated as the reference category. Circles indicate subgroups of patients. Shaded squares indicate men with different combinations of clinical and socio-demographic characteristics and the associated combined risk of erectile dysfunction. Numbers inside circles and squares represent number of patients with (upper number; dark border) and without erectile dysfunction (lower number), respectively.

intervention rate is the result of suboptimal evidence relating to the benefits and harms of existing specific interventions for erectile dysfunction in chronic kidney disease [28] or that patients self-administered but did not report using these treatments, as a result of the difficulties in discussing the topic with their physicians and/or the lack of routine screening for sexual dysfunction in the dialysis facilities.

We found that having symptoms of depression was the strongest independent correlate of erectile dysfunction of any severity in these men, suggesting that treating

concurrent depression might present a potential strategy for managing erectile dysfunction in this setting. Depression in people with end-stage kidney disease can be secondary to losing a primary role in occupation or family, decreased physical function, diminution of cognitive skills or a decline in sexual function [29]. While the association of erectile dysfunction with depression does not establish that treating this factor will improve symptoms of erectile dysfunction, identifying depression as a strong independent correlate of erectile dysfunction represents an important prelude to designing trials that evaluate the relative benefits and harms of treating sexual dysfunction in men with chronic kidney disease. The strength of the association and evidence of a dose–response effect also advocate for a potential causal relationship between depression and erectile dysfunction in these patients. Accordingly, trials of treating erectile dysfunction that include depression as an outcome and vice versa are warranted in men receiving haemodialysis.

Of interest, prescription of anti-depressants did not differ significantly between those with and without erectile dysfunction. This may be because anti-depressants not infrequently cause sexual dysfunction (which is one of the predominant reasons for drug discontinuation), even though amelioration of depression could have a beneficial effect on erectile dysfunction. Selective serotonin reuptake inhibitors (SSRIs), frequently prescribed anti-depressants, have negative effects on arousal and orgasm compared with other anti-depressants [30]. In addition, these agents, as well as psychological support as interventions for depression, have been poorly studied in chronic kidney disease [31].

Older age, receiving a pension or unemployment and larger interdialytic weight gains were all important indicators of erectile dysfunction, whereas married men were considerably less likely to report symptoms, indicating that these characteristics might assist the clinician to identify men at particularly high risk for erectile dysfunction. Married men had one-third the risk of severe erectile dysfunction of unmarried men, suggesting that either being married is protective or that erectile dysfunction may lead to marital difficulties, as has been reported previously [32]. Endocrine abnormalities, not further defined, were associated with a large increase in the prevalence of severe erectile dysfunction and diabetic nephropathy as the underlying cause of end-stage kidney disease nearly tripled the risk for more severe erectile dysfunction. These findings are consistent with the possibility that generalized microvascular disease secondary to diabetes or hormonal dysregulation contributes to the pathophysiology of erectile dysfunction. Of potential importance for possible screening strategies is the finding that the combination of depressive symptoms, unemployment and not being married identified men who were exceedingly likely to experience any erectile dysfunction. Married men with fewer depressive symptoms were the least likely to report erectile problems, although nearly 80% of these men still reported erectile dysfunction. These data overall suggest that all men receiving dialysis should be screened for erectile dysfunction, regardless of their individual characteristics.

Estimates of the frequency of erectile dysfunction in men receiving haemodialysis have been variable. Previous studies have reported prevalence rates ranging between 20 and 80% [2,7,8,33–48]. Our results are consistent with those of our recent systematic review, which found that erectile dysfunction was experienced by 70% (95% CI 62–77%; 20 studies, 4332 individuals) of men with chronic kidney disease [18]. Of note, previous cohort studies of erectile dysfunction in men requiring dialysis were small; the largest existing study of erectile dysfunction included 302 men requiring haemodialysis [2], while nearly half of all studies have included <100 men. Enrolling few participants limits the power of such studies to identify the key correlates of erectile dysfunction by adequately adjusting for potentially confounding variables. Indeed, many previous studies of erectile dysfunction have not used multivariable adjustment to determine independent correlates of erectile dysfunction or adjusted for depression. Due to these methodological limitations, it was not possible to rely on the pooled estimate from the meta-analysis, which may well be confounded by unknown factors inherent to the individual studies. It also has been difficult to reliably identify factors associated with erectile dysfunction in men requiring haemodialysis that might be promptly addressed, although the presence of diabetes mellitus or depression has been the most frequently reported.

Most previous studies of sexual dysfunction in individuals with chronic kidney disease are from single centres and have combined populations of both men and women treated with haemodialysis or peritoneal dialysis and kidney transplant recipients. Nearly half of existing studies have used an unvalidated instrument to assess sexual dysfunction and, accordingly, may have unpredictably over- or underestimated the true prevalence of erectile dysfunction. Studies using abbreviated assessment tools generally report a higher prevalence of erectile dysfunction [18]. Furthermore, previous studies have included mostly younger men with chronic kidney disease (typically 30–50 years) and might have underestimated the risk of erectile dysfunction in men receiving dialysis overall. In our study, we deliberately did not have an inclusion criterion for age, and all patients in the participating centres were invited to contribute information.

Another interesting finding of our study was that specific treatments for erectile dysfunction, principally phosphodiesterase inhibitors, were prescribed to a small minority of the men who reported erectile dysfunction. The underutilization of erectile dysfunction treatment, such as phosphodiesterase inhibitors, in men with chronic kidney disease is surprising, given that only 17% of such men were prescribed nitrates, a recognized contraindication to phosphodiesterase inhibitors. Phosphodiesterase inhibitors are potentially effective in men with chronic kidney disease. Our recent systematic review of randomized trials in chronic kidney disease showed that phosphodiesterase inhibitors improve erectile function scores, although the review also identified a need for additional larger trials to evaluate the complete benefit-harm trade-off for these agents [28]. The low prescription rate of phosphodiesterase inhibitors in men receiving haemodialysis is, however, consistent with the underutilization of standard care that is generally observed in patients with chronic kidney disease [49–51]. It remains possible that the use of interventions for

erectile dysfunction in the current study was under-reported due to procurement of such medications without prescription by men in our population. Given the near universal experience of erectile dysfunction in men requiring haemodialysis, systematic investigation of erectile dysfunction should be considered by clinicians involved in their care, which in turn may also avoid inappropriate self-administration of potentially harmful drugs. The burden of erectile dysfunction in this population suggests that there is an unmet need for appropriate identification of the problem and trialing of appropriate interventions.

Finally, and important in our view, we were not able to confirm previous observations that anaemia, hypertension or dyslipidaemia were associated with the risk of erectile dysfunction. Anaemia correction to achieve higher haemoglobin levels with use of erythropoiesis-stimulating agents in particular has previously been recommended to prevent or treat erectile dysfunction in chronic kidney disease [52]. We could not confirm this.

Our study has a number of strengths. The eligibility criteria were deliberately broad, including no upper age limitation, to capture information from an unselected population receiving haemodialysis. The study is the largest to date and included men from several haemodialysis centres and countries, facilitating our ability to identify the key correlates of erectile dysfunction by adjusting for important confounding variables that have not previously been accounted for, particularly depressive symptoms. Of importance, we collected data for both erectile dysfunction and depression using validated instruments. These strengths, in comparison with most previous existing studies, should be balanced against potential limitations. The overall response rate of 59% raises the potential for responder bias. The response rate is, however, consistent with or better than any other previous studies of erectile dysfunction in patients with chronic kidney disease [18] and is likely to reflect the reticence of men to discuss sexual issues even with the assurance of anonymity. Non-respondents were older, had a lower body weight and were more likely to receive a pension, such that the prevalence and correlates of erectile dysfunction in non-responders is probably different to those who responded to the questionnaires. It is possible that older patients who may have lower sexual activity were less inclined to respond to surveys of erectile dysfunction. Erectile dysfunction was also self-reported by respondents, without verification by objective measures of erectile function. Importantly, we did not interview men to collect information about partner factors or the effects of erectile dysfunction on well-being. Partner sexual dysfunction and the length and quality of a relationship may impact on sexual functioning and require further exploration in our cohort [53]. The study also did not collect information on the presence of substance abuse, autonomic neuropathy, peripheral vascular disease, anxiety scores, prostatic pathology or lower urinary tract symptoms or residual kidney function such that the relative influence of these clinical characteristics on erectile dysfunction cannot be determined. The Sexual Health Inventory for Men may not adequately measure erectile dysfunction in men who have sex with men, such that data for erectile dysfunction in this population on haemodialysis are not captured by our study design. The study was limited to the haemodialysis setting only and confirmation of the findings in other populations with chronic kidney disease including men receiving peritoneal dialysis is warranted. Finally, the cross-sectional design does not allow us to draw definitive conclusions about the causal link between erectile dysfunction and the factors we identified or whether the symptoms experienced by the men were sustained over time.

In conclusion, erectile dysfunction as measured by the Sexual Health Inventory for Men is present in almost all men requiring haemodialysis and is frequently severe. In spite of the high prevalence of erectile dysfunction and its previously demonstrated links with impaired quality of life, only a small proportion of affected men receive specific treatment. We propose that all men receiving haemodialysis should be routinely asked about erectile dysfunction using existing and easily accessible validated instruments. Additional information about the relevance of erectile dysfunction to the well-being of men on haemodialysis should be characterized by future qualitative research. Large-scale randomized trials of interventions for erectile dysfunction depression are warranted. Erectile dysfunction is a prevalent condition in men receiving haemodialysis with an unmet need for valid strategies for both prevention and treatment.

Supplementary data

Supplementary data are available online at http://ndt.oxfordjournals.org.

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Conflict of interest statement. None declared.

Appendix

Writing, steering, executive committee

Mariacristina Vecchio, MSc, Suetonia Palmer, MB ChB, PhD, Giorgia De Berardis, MSc, Jonathan Craig, MB ChB, DCH, MM, PhD, David Johnson, MB ChB (Hons),

PhD, Fabio Pellegrini, MSc, Antonio Nicolucci, MD, Michela Sciancalepore, MSc, Valeria Saglimbene, MSc, Letizia Gargano, MSc, Carmen Bonifati, MD, Marinella Ruospo, MSc, Sankar D Navaneethan MD, MPH, Vincenzo Montinaro, MD, Paul Stroumza, MD, Marianna Zsom, MD, Mariatta Torok, MD, Eduardo Celia, MD, Ruben Gelfman, MD, Anna Bednarek-Skublewska, MD, Jan Dulawa, MD, Giusi Graziano, MSc, Giuseppe Lucisano, MSc, Giorgio Gentile, MD, Juan Nin Ferrari, MD, Antonio Santoro, MD, Annalisa Zucchelli, MD, Giorgio Triolo, MD, Stefano Maffei, MD, Jörgen Hegbrant, MD, PhD, Charlotta Wollheim, MSc, Salvatore De Cosmo, MD, Valeria M Manfreda, MD, Giovanni FM Strippoli, MD, PhD, MPH, MM.

Author affiliations: Department of Medicine, University of Otago, Christchurch, New Zealand (Dr Palmer); Department of Clinical Pharmacology and Epidemiology, Mario Negri Sud Consortium, S. Maria Imbaro, Italy (Ms Vecchio, De Berardis, Sciancalepore, Saglimbene, Mr Pellegrini and Lucisano, Drs Nicolucci, Graziano, Strippoli); School of Public Health, University of Sydney, Australia (Drs Craig and Strippoli); Department of Nephrology, University of Queensland at Princess Alexandra Hospital, Brisbane, Australia (Dr Johnson); Unit of Biostatistics, IRCCS Casa Sollievo della Sofferenza, San Giovanni Rotondo (Fg), Italy (Mr Pellegrini); Diaverum Medical-Scientific Office, Sweden (Ms Gargano and Ruospo, Drs Bonifati, Stroumza, Zsom, Torok, Celia, Gelfman, Bednarek-Skublewska, Dulawa, Gentile, Ferrari, Hegbrant, Wollheim, Strippoli); Department of Nephrology and Hypertension, Clevelan Clinic, Cleveland, OH, United States (Dr Navaneethan); Department of Emergency and Organ Transplantation, University of Bari (Ba), Italy (Dr Montinaro); Department of Nephrology, Medical University School of Lublin, Poland (Dr Bednarek-Skublewska); Department of Internal Medicine and Metabolic Diseases, Medical University of Silesia, Poland (Dr Dulawa); Department of Internal Medicine, University of Perugia, Italy (Dr Gentile); Department of Nephrology, Dialysis, Hypertension, Policlinico S. Orsola-Malpighi, Bologna (Bo), Italy (Dr Santoro); Department of Nephrology, Dialysis, Hypertension, Policlinico S. Orsola-Malpighi, Bologna (Bo), Italy (Dr Zucchelli); SCDO Nefrology and Dialysis, Azienda Ospedaliera CTO/CRF/M. Adelaide, Torino (To), Italy (Dr Triolo, Maffei); Unit of Endocrinology, Scientific Institute Casa Sollievo della Sofferenza, San Giovanni Rotondo, Italy (Dr De Cosmo); Ospedale "A Perrino, Brindisi, Italy (Dr Manfreda).

Participating centres, facilitators and organizing committee

DIAVERUM Argentina; D. Rubio, W. Labonia, M Prado, A. Vinockur, R. Paparone, C. Mato Mira, A. Peñalba, M. Gravielle, E. Mojico, M. Vargas, S. Tirado, M. Paz, G. Rodriguez, L. López, R. Beistegui, C. Bonelli, M. Arias, G. Coira, D. Florio, L. León, O. Hermida, S. Kapnik, K. García, J. De Francesco, H. Altman, F. Cravzoff, S. Mandri; **DIAVERUM Hungary;** K. Albert, M. Kassai, E. Kiss, D. Kosa, A. Orosz, J. Redl, G. Rozsahegyi, E. Varga, Zs. Vezekenyi, E. Zajko, A. Bereczki, L. Czikos, A. Kuti, A. Mike, K. Steiner, A. Takacs, K. Tolnai, A. Toth, I. Ven, R. Mogyorosi, E. Ligeti; **DIAVERUM Italy;** N. Dambrosio, F. Dagostino, M.L. Sambati, G. Giannoccaro, V. Greco, R. Di Toro Mammarella, A. Flammini, E. Boccia, D. Di Franco, P. Steri, A. M. Murgo, M. Fici, S. La Rosa, G. Montalto, M. Falco, F. Grisafi, S. Pagano, S. Amarù, D. Rallo, A. Conticello, G. Martucci, N. Sanfilippo, L. Leonardo, V. M. Liguigli, G. Matera, C. Saturno, V. Origlia, G. Paparella, A. D'Angelo, N. Falsitta, G. De Leo, S. Maldera, C. Riccardi, F. Pedone, L.Moscardelli, M. Mantuano, A. Lupo, P.G. Pellegrino, R. Antinoro, S. Cantarella, G. Randazzo, G. Marino, M. Meconizzi, A. Maniscalco, C. Donatelli, F. Torsello; **DIAVERUM Poland;** M. Drobisz, T. Gregorczyk, G. Wyrwicz, W. Dżugan, J. Ostrowski, W. Załuska, E. Bocheńska-Nowacka, A. Jaroszyński, J. Drabik, M. Birecka, J. Śliwarska- Strońska, T. Gauda, St. Dzimira, P. Rutkowski; **DIAVERUM Portugal;** J. Lopes, J.A. Lopes, M. Leal, M. Raimundol; **DIAVERUM Mataró, Spain;** J. Gabás; **DIAVERUM Uruguay;** M. Pimato, P. Berti, L. Goro.

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