PROGNOSTIC IMPACT OF THE SIMPLIFIED INTERNATIONAL INDEX OF ERECTILE FUNCTION IN PATIENTS WITH CHRONIC KIDNEY DISEASE STAGES 3-5

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Background

✓Erectile dysfunction (ED) is mainly due to atherosclerosis, with penile circulation being affected usually earlier, as a consequence of the smaller diameter of the penile arteries, when compared with other vessels. Thus, in the community, individuals who develop ED are at increased risk for cardiovascular disease (CVD) and all-cause mortality.

✓ The simplified international index of erectile function (IIEF-5) is an easily-accessible tool to assess and grade erectile function.

✓Chronic kidney disease (CKD), *per se*, associates with higher CVD risk, and although CKD patients have a high prevalence of erectile dysfunction, there are few studies evaluating the prognostic impact of ED, evaluated by means of IIEF-5 in this patient population.

Objective

We sought to evaluate the associations of IIEF-5, with a range of traditional and uremic related risk factors, and test its prognostic value in a carefully phenotyped cohort of non-dialysis dependent patients with CKD stages 3 to 5.

Methods

We cross-sectionally included 181 male patients (61, [53-68] years). Patients were followed for 35 (23 - 42) months, with no loss of follow-up, and all-cause mortality was recorded.

Results

✓ General characteristics of the studied population as well as patient's characteristics according to quartiles of IIEF-5 distribution (middle quartiles combined) are summarized in **Table 1**. With decreasing IIEF-5 quartiles (middle quartiles combined) patients were older, had higher prevalence of diabetes mellitus (DM), ischemic heart disease (IHD) and peripheral vascular disease (PVD), as well as higher serum brain natriuretic peptide levels; while diastolic blood pressure, and free testosterone levels were progressively reduced.

✓ During follow-up, 49 patients died, and the mortality risk decreased across the quartiles (36% vs. 32% vs. 14% log-rank X2 = 9.42; P = 0.009), **Figure 1**.

✓A 1 point higher IIEF-5 was associated with a reduced hazard ratio (HR) for mortality in crude Cox analysis (HR 0.95, 95% confidence interval (CI) 0.92-0.99). This association remained significant even after adjustment for confounders (age, glomerular filtration rate, DM and serum albumin (**Table 2)**. In search of potential mechanisms explaining the impact of IIEF-5 on the patient's mortality, we performed two different models, including IHD or PVD as covariates. While the inclusion of IHD did not change the association between IIEF-5 and mortality, the association lost its significance when PVD was included in the model, as shown in **Table 2**.

Results

Table 1. Demographics and clinical characteristics of the 181 non-dialysis dependent CKD stages 3 - 5 male patients included in the study, overall, and according to the quartiles (middle quartiles combineds) of the simplified international index of erectile function (IIEF-5).

	All-Patients (n=181)	IIEF – 5 Quartiles *Lower (≤5)* (n=39)	*Middles (6 – 19)* (n=85)	*Higher (≥ 20)* (n=57)	*P for trend*
IIEF-5	15 (6 – 21)	23 (22 – 25)	12 (8 – 17)	5 (5 – 5)	-----
Age (years)	61 (53 – 68)	64 (58 – 72)	62(55 – 68)	54 (47 – 64)	***<0.001***
Diabetes Mellitus (n, %)	87 (48%)	27 (69%)	47 (55%)	13 (23%)	***<0.001***
Ischemic heart disease (n, %)	74 (41%)	19 (49%)	40 (47%)	15 (26%)	***0.020***
Peripheral vascular disease (n, %)	81 (45%)	23 (59%)	45 (53%)	13 (23%)	***<0.001***
Smoking (n, %)	114 (63%)	24 (62%)	56 (66%)	34 (60%)	0.776
Glomerular Filtration Rate (ml/min)	26 (15 – 38)	30 (16 – 43)	22 (14 – 35)	28 (17 – 40)	0.643
Systolic BP (mmHg)	149 (134 – 170)	150 (131 – 165)	149 (136 – 172)	147 (132 – 168)	0.745
Diastolic BP (mmHg)	81 (71 – 91)	78 (69 – 88)	81 (71 – 89)	84 (73 – 97)	0.035
ACE inhibitors / ARB (n, %)	114 (63%)	25 (64%)	48 (57%)	41 (72%)	0.321
Calcium channel blockers (n, %)	121 (67%)	24 (62%)	62 (73%)	35 (61%)	0.822
β-blockers (n, %)	129 (71%)	24 (62%)	64 (75%)	41(72%)	0.344
Diuretics (n, %)	159 (88%)	33 (85%)	76 (89%)	50 (88%)	0.709
Total of antihypertensive drugs (n, %)	4 (3 – 5)	4 (3 – 5)	4 (3 – 5)	4 (3 – 5)	0.857
Body mass index (Kg/m^2)	29.1 ± 5.2	29.7 ± 4.7	29.0 ± 5.2	28.9 ± 5.4	0.414
Waist circumference (cm)	100 (90 – 108)	101 (91 – 108)	99 (90 – 107)	99 (90 – 107)	0.311
Hemoglobin (g/dL)	12.7 ± 2.8	12.6 ± 2.2	12.5 ± 2.1	12.9 ± 2.2	0.467
Total Cholesterol (mg/dL)	163 (139 – 206)	149 (130 – 199)	167 (145 – 214)	163 (139 – 211)	0.462
HDL Cholesterol (mg/dL)	38 (33 – 46)	39 (33 – 46)	40 (32 – 46)	37 (32 – 45)	0.484
Triglycerides (mg/dL)	150 (112 – 210)	152 (101 – 198)	142 (110 – 202)	153 (120 – 225)	0.520
Ionized Calcium (mmol/L)	1.14 (1.08 – 1.21)	1.15 (1.08 – 1.21)	1.14 (1.07 – 1.21)	1.13 (1.08 – 1.21)	0.459
Phosphorus (mg/dL)	4.1 (3.5 – 4.7)	4.1 (3.4 – 4.6)	4.2 (3.7 – 4.6)	4.0 (3.4 – 5.0)	0.704
Parathyroid hormone (pg/mL)	132 (90 – 260)	117 (73 – 209)	132 (95 – 275)	148 (92 – 367)	***0.038***
Albumin (mg/dL)	3.9 (3.6 – 4.2)	3.8 (3.3 – 4.2)	3.8 (3.6 – 4.2)	4.0 (3.7 – 4.3)	0.079
C-Reactive Protein (mg/L)	3.7 (1.4 – 8.9)	6.0 (1.4 – 9.0)	3.8 (1.4 – 8.4)	2.7 (1.4 – 9.6)	0.173
Free testosterone (ng/dL)	6.9 (5.0 – 8.1)	5.7 (4.2 – 5.1)	6.7 (5.1 – 8.2)	7.2 (5.5 – 8.6)	***0.004***
BNP (pg/mL)	76 (33 – 168)	45 (20 – 146)	76 (37 – 249)	124 (50 – 206)	***0.001***

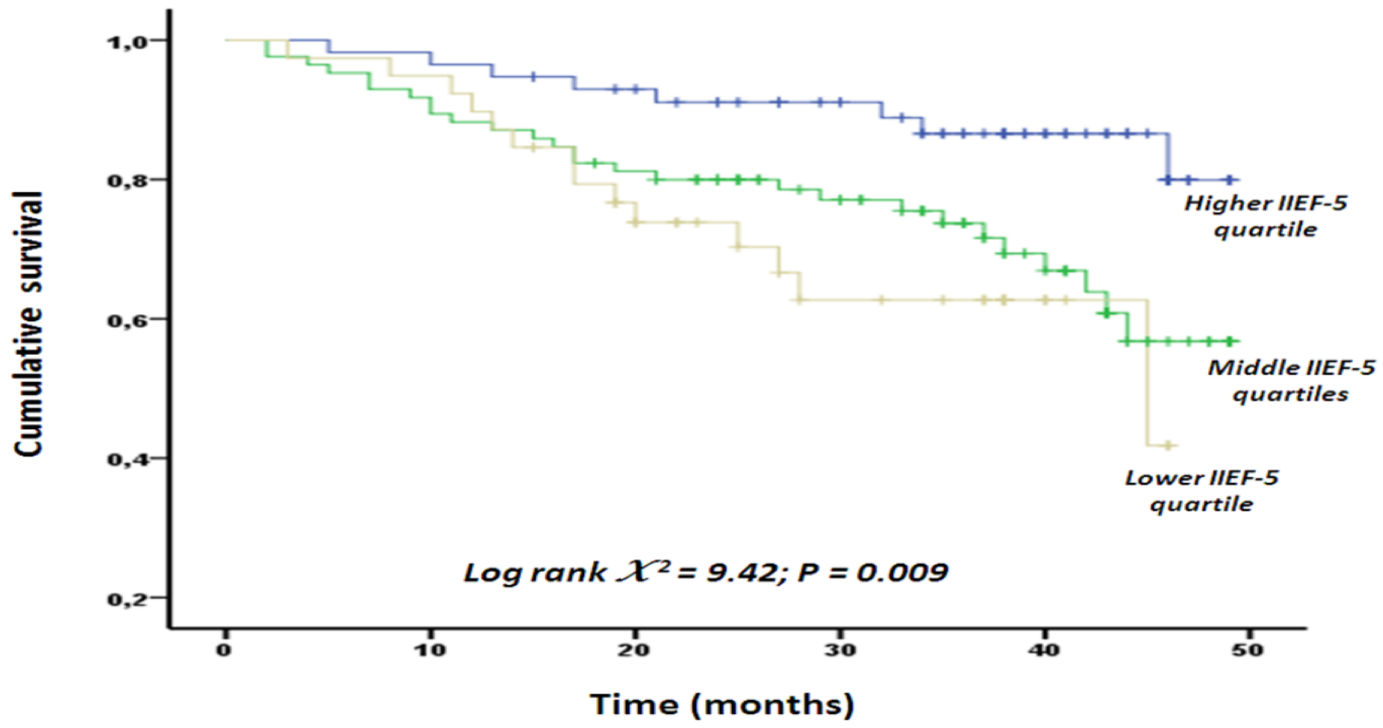

Figure 1. Kaplan-Meier curves for overall mortality, according to the IIEF-5 quartiles (middle quartiles combined) in 181 male CKD stage 3-5 patients

Table 2. Hazard ratios for all cause mortality according to the simplified international index of erectile function (IIEF-5) in 181 male patients with CKD stages 3 – 5.

Model		*All-cause mortality (n=49)* *Hazard ratio (95% CI)*
1	IIEF-5 (per unit of increase)	***0.95 (0.92 – 0.99)***
2	1 + Age and diabetes	***0.94 (0.90 – 0.99)***
3	2 + Glomerular filtration rate	***0.95 (0.90 – 0.99)***
4	3 + Albumin	***0.95 (0.91 – 0.99)***
	Model 4 + ischemic heart disease	***0.95 (0.91 – 0.99)***
	Model 4 + peripheral vascular disease	0.96 (0.91 – 1.01)

Conclusion

IIFE-5 associates with CVD risk factors and predicts overall mortality among non-dialyzed patients with CKD stages 3-5, probably reflecting peripheral vascular disease. These results support the routine evaluation of erectile dysfunction in CKD patients. Future studies are warranted to establish IIEF-5 as a risk stratification tool in this patient population.

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