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Sex Disparities and Adverse Clinical Outcomes in Patients with Chronic Kidney Disease: Results from KNOW-CKD

Ga Young Heo¹, Tae Ik Chang², Ea Wha Kang², Tae-Hyun Yoo¹, Shin-Wook Kang¹, Kook Hwan Oh³, Curie Ahn³, Jung Tak Park¹, Seung Hyeok Han¹

¹Department of Internal Medicine, Severance Hospital, Korea, Republic of

²Department of Internal Medicine, National Health Insurance Service Ilsan Hospital, Korea, Republic of

³Department of Internal Medicine, Seoul National University Hospital, Korea, Republic of

Objectives: There are substantial differences in public health issues between men and women. However, longitudinal studies of the relationship between sex disparities and adverse clinical outcomes in patients with chronic kidney disease (CKD) are scarce. Here, we studied whether major outcomes including cardiovascular outcomes, all-cause mortality, and CKD progression may differ between men and women among Korean CKD patients

Methods: The KoreaN cohort study for Outcome in patients with Chronic Kidney Disease (KNOW-CKD) enrolled a total of 2,238 patients with non-dialysis CKD. The primary outcome was a composite of non-fatal cardiovascular events or death from any cause. The secondary outcome was CKD progression, which was defined as a $\geq 50\%$ decline in eGFR from baseline or the onset of end-stage kidney disease.

Results:

There were 1,367 (61.1%) men and 871 (38.9%) women in this cohort. During 8517 person-years of follow-up, 208 primary outcome events occurred; 150 (11.0%) in men and 58 (6.7%) in women with the corresponding incidence rates of 29.4 and 17.0 per 1,000 person-years, respectively. In multivariable-adjusted Cox model, men were associated with a 64% higher risk of the composite outcome compared with women (HR, 1.64; 95% CI, 1.06-2.53). In secondary outcome analysis, adverse kidney outcome events occurred in 583 patients with the incidence rate of 76.8 per 1,000 person-years. Similar to the results of primary outcome analysis, men had a 1.41-fold (95% CI, 1.10-1.80) higher risk of CKD progression than women.

Conclusions: In Korean CKD patients, men are more likely to have adverse clinical outcomes than women.

Composite outcome of non-fatal CV events or all-cause mortality

. stir SEX

failure _d: CV_DEATH == 1
analysis time _t: CV_DEATH_YEAR

note: Exposed <-> SEX==female and Unexposed <-> SEX==male

	SEX		Total
	Exposed	Unexposed	
Failure Time	58 3418.662	150 5098.879	208 8517.541
Incidence rate	.0169657 .0294182		.0244202
	Point estimate		[95% Conf. Interval]
Inc. rate diff.	-.0124525		-.0188734 -.0060317
Inc. rate ratio	.5767072		.4183577 .7858084 (exact)
Prev. frac. ex.	.4232928		.2141916 .5816423 (exact)
Prev. frac. pop	.1698959		
	(midp) Pr(k<=58) =		0.0001 (exact)
	(midp) 2*Pr(k<=58) =		0.0002 (exact)

. stcox b1.SEX AGE BMI1_0 CCI_S1 EPI_CR_0 PR_CR C_TC_0 C_LDL_0 C_ALB_0 ln_CRP_0 PTH_ALL C_SMK_B0 C_EDU C_ES C_ACEI_0 C_ARB_0 C_DIU_0 C_PRD

failure _d: CV_DEATH == 1
analysis time _t: CV_DEATH_YEAR

Iteration 0: log likelihood = -1267.5781
Iteration 1: log likelihood = -1182.4633
Iteration 2: log likelihood = -1174.5184
Iteration 3: log likelihood = -1174.3944
Iteration 4: log likelihood = -1174.3942
Iteration 5: log likelihood = -1174.3942
Refining estimates:
Iteration 0: log likelihood = -1174.3942

Cox regression -- Breslow method for ties

No. of subjects = 1,861 Number of obs = 1,861
No. of failures = 179
Time at risk = 7439.189943
LR chi2(18) = 186.37
Log likelihood = -1174.3942 Prob > chi2 = 0.0000

_t	Haz. Ratio	Std. Err.	z	P> z	[95% Conf. Interval]	
SEX						
male	1.639572	.3626749	2.24	0.025	1.062781	2.529397
AGE	1.060458	.0094232	6.61	0.000	1.042148	1.079088
BMI1_0	.9398287	.0246133	-2.37	0.018	.8928047	.9893294
CCI_S1	1.343963	.0829884	4.79	0.000	1.190766	1.516869
EPI_CR_0	1.00919	.004273	2.16	0.031	1.00085	1.0176
PR_CR	1.008082	.0410446	0.20	0.843	.9307618	1.091825
C_TC_0	.9984641	.0039234	-0.39	0.696	.9908039	1.006183
C_LDL_0	.9998723	.005036	-0.03	0.980	.9900504	1.009792
C_ALB_0	.4938067	.1091186	-3.19	0.001	.3202309	.7614664
ln_CRP_0	1.135357	.0604346	2.38	0.017	1.022877	1.260206
PTH_ALL	1.001673	.0008713	1.92	0.055	.9999665	1.003382
C_SMK_B0	.9027562	.0946455	-0.98	0.329	.7350721	1.108692
C_EDU	.9398169	.0701637	-0.83	0.406	.8118864	1.087906
C_ES	1.157821	.1431227	1.19	0.236	.9087011	1.475236
C_ACEI_0	.9896389	.2401176	-0.04	0.966	.6151038	1.592227
C_ARB_0	.9955204	.1914364	-0.02	0.981	.6829138	1.451224
C_DIU_0	.7909477	.1291199	-1.44	0.151	.5743697	1.089191
C_PRD	1.100841	.0401463	2.63	0.008	1.024902	1.182407

Composite outcome of a $\geq 50\%$ decline in GFR or ESKD

. stir SEX

failure_d: RE_EVENT == 1
analysis time_t: RE_YEAR

note: Exposed <-> SEX==female and Unexposed <-> SEX==male

	SEX		Total
	Exposed	Unexposed	
Failure Time	235 3041.341	348 4635.51	583 7676.85
Incidence rate	.0772686	.0750727	.0759426
	Point estimate		[95% Conf. Interval]
Inc. rate diff.	.0021959		-.0104457 .0148375
Inc. rate ratio	1.02925		.8685271 1.217981 (exact)
Attr. frac. ex.	.028419		-.1513745 .1789692 (exact)
Attr. frac. pop	.0114554		
	(midp) Pr(k>=235) =		0.3655 (exact)
	(midp) 2*Pr(k>=235) =		0.7311 (exact)

. stcox b1.SEX AGE BMI1_0 CCI_S1 EPI_CR_0 PR_CR C_TC_0 C_LDL_0 C_ALB_0 ln_CRP_0 PTH_ALL C_SMK_B0 C_EDU C_ES C_ACEI_0 C_ARB_0 C_DIU_0 C_PRD

failure_d: RE_EVENT == 1
analysis time_t: RE_YEAR

Iteration 0: log likelihood = -3588.5312
Iteration 1: log likelihood = -3396.2541
Iteration 2: log likelihood = -3092.8924
Iteration 3: log likelihood = -3054.6089
Iteration 4: log likelihood = -3052.7451
Iteration 5: log likelihood = -3052.7389
Iteration 6: log likelihood = -3052.7389
Refining estimates:
Iteration 0: log likelihood = -3052.7389

Cox regression -- Breslow method for ties

No. of subjects = 1,861 Number of obs = 1,861
No. of failures = 513
Time at risk = 6693.914784
LR chi2(18) = 1071.58
Log likelihood = -3052.7389 Prob > chi2 = 0.0000

_t	Haz. Ratio	Std. Err.	z	P> z	[95% Conf. Interval]	
SEX						
male	1.405243	.1759121	2.72	0.007	1.099501	1.796003
AGE	.9674839	.0044077	-7.26	0.000	.9588834	.9761614
BMI1_0	.9922347	.0141595	-0.55	0.585	.964867	1.020379
CCI_S1	1.165374	.0550216	3.24	0.001	1.062373	1.278361
EPI_CR_0	.943923	.0034109	-15.97	0.000	.9372614	.9506319
PR_CR	1.244605	.0281793	9.66	0.000	1.190582	1.301079
C_TC_0	1.000861	.0021774	0.40	0.692	.9966028	1.005138
C_LDL_0	.9973272	.0027194	-0.98	0.326	.9920114	1.002671
C_ALB_0	.5828968	.0745164	-4.22	0.000	.4537073	.7488719
ln_CRP_0	.9130337	.0318112	-2.61	0.009	.852766	.9775606
PTH_ALL	1.001918	.0004391	4.37	0.000	1.001058	1.002779
C_SMK_B0	.9798031	.0638232	-0.31	0.754	.8623678	1.11323
C_EDU	.9356082	.0464198	-1.34	0.180	.8489108	1.03116
C_ES	1.185622	.0863199	2.34	0.019	1.027955	1.367472
C_ACEI_0	1.038587	.1536643	0.26	0.798	.7771474	1.387978
C_ARB_0	.817221	.1020363	-1.62	0.106	.6398239	1.043803
C_DIU_0	.8654175	.085709	-1.46	0.144	.7127292	1.050816
C_PRD	1.013616	.0273235	0.50	0.616	.9614534	1.06861