Supplementary file

Supplement to: Renal outcomes with renin-angiotensin system blockers after unilateral nephrectomy

Sehun Lee et al.

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Table S1. Characteristics of patients who developed end-stage kidney disease

Variables	RAS blockers (+) (N=1)	RAS blockers (-) (N=6)
Male	1 (100%)	4 (67%)
Age, years	58	61 (43;78)
BMI, kg/m^2	28	23.8 (22.0;31.9)
Cancer type		
Renal cell carcinoma	1 (100%)	2 (33%)
Urothelial cell carcinoma	0	2 (33%)
Liposarcoma	0	0
Other	0	2 (33%)
Cancer stage		
1	1 (100%)	3 (50%)
2	0	1 (17%)
3	0	1 (17%)
4	0	1 (17%)
DM	0	2 (33%)
PCI or CABG	0	0
CVA	0	0
Dyslipidemia	0	0
β-blocker	1 (100%)	4 (67%)
Calcium channel blocker	1 (100%)	4 (67%)
Diuretics	1 (100%)	0
Adjuvant Tx., systemic	0	0
Adjuvant Tx., localized	0	1 (17%)
Laboratory findings, preoperative		
eGFR, ml/min/1.73 m^2	34.1	24.6 (15.5;104.2)
eGFR < 60 ml/min/1.73 m^2	1 (100%)	5 (83%)
eGFR < 30 ml/min/1.73 m^2	0	4 (66%)
BUN, mg/dl	27.2	34.5 (15.1;54.5)
Hb, g/dl	14.8	11.15 (10.4;16.2)
Potassium, mmol/l	4.7	4.6 (4.2;4.9)
Urine albumin		
Negative	0	1 (17%)
Trace	0	0
1+	0	1 (17%)
2+	0	1 (17%)
3+	1 (100%)	3 (50%)
Laboratory findings, at discharge		
eGFR, ml/min/1.73 m^2	21.5	16.05 (11.5;51)

eGFR < 30 ml/min/1.73 m^2	1 (100%)	5 (83%)
Death after ESKD	0	2 (33%)

Continuous variables are expressed as median (range) and categorical variables are expressed as numbers (%).

BMI, body mass index; DM, diabetes mellitus; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft; CVA, cerebrovascular accident; Tx, treatment; eGFR, estimated glomerular filtration rate; BUN, blood urea nitrogen; Hb, hemoglobin; ESKD, end stage kidney disease

Table S2. Differences in laboratory findings according to RAS blocker use after nephrectomy

Variables	Time after surgery	RAS blocker (+) (N=308)	RAS blocker (-) (N=272)	*P*
eGFR, ml/min/1.73 m^2	Discharge	54.6 ± 13.8	51.3 ± 15.9	0.009
	1 month	53.0 ± 13.6	50.5 ± 16.1	0.041
Hemoglobin, g/dl	Discharge	12.2 ± 1.7	12.3 ± 1.6	0.522
	1 month	12.6 ± 1.5	12.6 ± 1.5	0.852
Potassium, mmol/l	Discharge	4.5 ± 0.4	4.4 ± 0.5	0.197
	1 month	4.5 ± 0.4	4.5 ± 0.5	0.857
BUN, mg/dl	Discharge	19.7 ± 7.6	20.9 ± 8.4	0.063
	1 month	21.3 ± 6.9	22.6 ± 9.0	0.052

eGFR, estimated glomerular filtration rate; BUN, blood urea nitrogen

Table S3. Comparison between survived and deceased patients

Variables	Survived patients (N=502)	Deceased patients (N=78)	*P*
Male	352 (70.1%)	54 (69.2%)	0.979
Age, years	65.0 (58.0;72.0)	71.0 (65.0;76.0)	< 0.001
BMI, kg/m2	25.6 (23.6;27.9)	24.4 (22.5;26.7)	0.01
SBP, mmHg	125.0 (115.0;139.0)	128.5 (118.0;140.0)	0.191
DBP, mmHg	73.0 (67.0;80.0)	71.0 (66.0;77.0)	0.118
DM	139 (27.7%)	25 (32.1%)	0.509
PCI or CABG	16 (3.2%)	4 (5.1%)	0.589
CVA	29 (5.8%)	3 (3.8%)	0.668
Dyslipidemia	32 (6.4%)	3 (3.8%)	0.537
β-blocker	105 (20.9%)	13 (16.7%)	0.474
Calcium channel blocker	334 (66.5%)	56 (71.8%)	0.429
Diuretics	137 (27.3%)	20 (25.6%)	0.866
Cancer types			0.004
Renal cell carcinoma	346 (68.9%)	41 (52.6%)	
Urothelial cell carcinoma	105 (20.9%)	23 (29.5%)	
Liposarcoma	14 (2.8%)	7 (9.0%)	
Other	14 (2.8%)	5 (6.4%)	
Non-cancer	23 (4.6%)	2 (2.6%)	
Cancer stages			< 0.001
stage 1	235 (46.8%)	11 (14.1%)	
stage 2	85 (16.9%)	9 (11.5%)	
stage 3	135 (26.9%)	36 (46.2%)	
stage 4	24 (4.8%)	20 (25.6%)	
Non-cancer	23 (4.6%)	2 (2.6%)	
Cancer stages			< 0.001
limited stage (1 and 2)	320 (63.7%)	20 (25.6%)	
advanced stage (3 and 4)	159 (31.7%)	56 (71.8%)	
Non-cancer	23 (4.6%)	2 (2.6%)	
Laboratory findings, preoperative			
BUN, mg/dl	16.0 (13.2;19.6)	17.2 (13.5;21.0)	0.26
Hb, g/dl	13.7 (12.6;14.7)	12.4 (10.4;13.8)	< 0.001
K, mmol/l	4.3 (4.1; 4.5)	4.4 (4.2; 4.7)	0.003
Urine albumin			0.33
Negative	352 (70.5%)	48 (61.5%)	
Trace	65 (13.0%)	10 (12.8%)	
+	39 (7.8%)	9 (11.5%)	

++	27 (5.4%)	8 (10.3%)	
+++	16 (3.2%)	3 (3.8%)	
eGFR[a], preoperative	80.8 (68.1;90.8)	73.4 (59.4;88.0)	0.008
eGFR, preoperative < 60	76 (15.1%)	20 (25.6%)	0.031
eGFR, preoperative < 30	4 (0.8%)	3 (3.8%)	0.082
eGFR, at discharge	54.0 (45.0;62.2)	48.6 (36.5;59.8)	0.01
eGFR, at discharge < 30	28 (5.6%)	10 (12.8%)	0.031
eGFR, at 1 mo	52.4 (42.9;61.0)	49.8 (36.0;59.2)	0.066
eGFR, at 6 mo	52.0 (42.7;61.0)	48.9 (34.5;62.2)	0.145
eGFR, at 12 mo	52.0 (42.7;61.7)	43.1 (33.0;54.5)	0.001
ESKD	5 (1.0%)	2 (2.6%)	0.001

Continuous variables are expressed as mean ± standard deviation or median (interquartile range), and categorical variables are expressed as numbers (%)

[a]eGFR was expressed as mL/min/1.73 m^2

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; DM, diabetes mellitus; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft; CVA, cerebrovascular accident; eGFR, estimated glomerular filtration rate; BUN, blood urea nitrogen; Hb, hemoglobin; ESKD, end stage kidney disease

Table S4. Comparison between survived and deceased patients, according to RAS blocker use

Variable	RAS blocker (+)			RAS blocker (-)		
	Survived patients (N=274)	Deceased patients (N=34)	*P*	Survived patients (N=228)	Deceased patients (N=44)	*P*
Male	195 (71.2%)	25 (73.5%)	0.931	157 (68.9%)	29 (65.9%)	0.835
Age, years	63.4 ± 10.5	67.0 ± 9.5	0.057	67.0 (59.0;74.0)	73.0 (69.0;78.0)	<0.001
BMI, kg/m2	25.8 (23.7;28.6)	24.4 (23.2;26.7)	0.053	25.5 (23.5;27.4)	24.4 (22.1;26.8)	0.111
SBP, mmHg	124.0 (114.0;138.0)	128.0 (117.0;144.0)	0.271	128.6 ± 16.7	130.0 ± 14.6	0.604
DBP, mmHg	72.8 ± 10.2	72.6 ± 8.9	0.910	73.0 (68.0;80.0)	70.0 (62.5;77.5)	0.067
DM	80 (29.2%)	12 (35.3%)	0.593	59 (25.9%)	13 (29.5%)	0.750
PCI or CABG	12 (4.4%)	1 (2.9%)	1.000	4 (1.8%)	3 (6.8%)	0.155
CVA	13 (4.7%)	1 (2.9%)	0.968	16 (7.0%)	2 (4.5%)	0.785
Dyslipidemia	17 (6.2%)	1 (2.9%)	0.706	15 (6.6%)	2 (4.5%)	0.865
β-blocker	46 (16.8%)	4 (11.8%)	0.615	59 (25.9%)	9 (20.5%)	0.568
Calcium channel blocker	155 (56.6%)	22 (64.7%)	0.471	179 (78.5%)	34 (77.3%)	1.000
Diuretics	95 (34.7%)	10 (29.4%)	0.676	42 (18.4%)	10 (22.7%)	0.649
Cancer types			0.010			0.212
Renal cell carcinoma	193 (70.4%)	19 (55.9%)		153 (67.1%)	22 (50.0%)	
Urothelial cell carcinoma	54 (19.7%)	8 (23.5%)		51 (22.4%)	15 (34.1%)	
Liposarcoma	8 (2.9%)	4 (11.8%)		6 (2.6%)	3 (6.8%)	
Other	6 (2.2%)	3 (8.8%)		8 (3.5%)	2 (4.5%)	
Non-cancer	13 (4.7%)	0 (0.0%)		10 (4.4%)	2 (4.5%)	
Cancer stages			<0.001			<0.001
stage 1	128 (46.7%)	2 (5.9%)		107 (46.9%)	9 (20.5%)	
stage 2	42 (15.3%)	4 (11.8%)		43 (18.9%)	5 (11.4%)	
stage 3	79 (28.8%)	18 (52.9%)		56 (24.6%)	18 (40.9%)	
stage 4	12 (4.4%)	10 (29.4%)		12 (5.3%)	10 (22.7%)	
Non-cancer	13 (4.7%)	0 (0.0%)		10 (4.4%)	2 (4.5%)	
Cancer stages			<0.001			<0.001
limited stage (1 and 2)	170 (62.0%)	6 (17.6%)		150 (65.8%)	14 (31.8%)	
advanced stage (3 and 4)	91 (33.2%)	28 (82.4%)		68 (29.8%)	28 (63.6%)	
Non-cancer	13 (4.7%)	0 (0.0%)		10 (4.4%)	2 (4.5%)	
Laboratory findings, preoperative						
BUN, mg/dl,	16.0 (13.1;19.6)	17.3 (13.4;20.6)	0.450	16.0 (13.2;19.6)	17.1 (13.6;21.4)	0.415
Hb, g/dl,	13.8 (12.5;14.8)	12.4 (10.4;13.6)	<0.001	13.6 ± 1.7	12.4 ± 2.3	0.002
K, mmol/l	4.3 (4.1; 4.6)	4.5 (4.2; 4.9)	0.047	4.3 (4.0; 4.5)	4.4 (4.2; 4.7)	0.020
Urine albumin			0.907			0.154

Negative	192 (70.8%)	24 (70.6%)		160 (70.2%)	24 (54.5%)	
Trace	35 (12.9%)	3 (8.8%)		30 (13.2%)	7 (15.9%)	
+	21 (7.7%)	4 (11.8%)		18 (7.9%)	5 (11.4%)	
++	16 (5.9%)	2 (5.9%)		11 (4.8%)	6 (13.6%)	
+++	7 (2.6%)	1 (2.9%)		9 (3.9%)	2 (4.5%)	
eGFR[a], preoperative	81.5 (69.0;91.0)	74.2 (67.8;91.1)	0.403	78.5 (66.3;90.6)	67.8 (51.7;85.4)	0.010
eGFR, preoperative < 60	32 (11.7%)	6 (17.6%)	0.471	44 (19.3%)	14 (31.8%)	0.098
eGFR, preoperative < 30	2 (0.7%)	0 (0.0%)	1.000	2 (0.9%)	3 (6.8%)	0.038
eGFR, at discharge	54.8 (46.9;62.7)	49.7 (44.2;58.4)	0.105	52.3 ± 15.2	46.6 ± 18.9	0.068
eGFR, at discharge < 30	10 (3.6%)	1 (2.9%)	1.000	18 (7.9%)	9 (20.5%)	0.023
eGFR, at 1 mo.	53.8 (44.9;61.0)	50.0 (41.3;58.3)	0.137	50.9 ± 15.3	48.2 ± 19.7	0.397
eGFR, at 6 mo.	52.0 (43.7;61.3)	49.4 (41.3;62.5)	0.544	51.8 (40.3;61.0)	47.7 (30.2;61.9)	0.191
eGFR, at 12 mo.	52.9 ± 15.0	50.2 ± 17.4	0.425	51.8 ± 15.8	39.9 ± 18.8	<0.001
ESKD before death	1 (0.4%)	0 (0.0%)	1.000	4 (1.8%)	2 (4.5%)	0.553

Continuous variables are expressed as mean ± standard deviation or median (interquartile range), and categorical variables are expressed as numbers (%)

[a]eGFR was expressed as mL/min/1.73 m^2

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; DM, diabetes mellitus; PCI: percutaneous coronary intervention; CABG, coronary artery bypass graft; CVA, cerebrovascular accident; eGFR, estimated glomerular filtration rate; BUN, Blood urea nitrogen; Hb, hemoglobin, K, potassium; ESKD, end stage kidney disease.

Table S5. The risk of mortality and composite outcome of ESKD and mortality according to RAS blocker use with calcium channel blocker instead of β-blocker

	Mortality			ESKD or mortality		
	HR	**95% CI**	***P***	**HR**	**95% CI**	***P***
Univariable	0.644	0.412, 1.008	0.054	0.603	0.390, 0.932	0.023
Model 1	0.694	0.434, 1.110	0.128	0.653	0.412, 1.034	0.069
Model 2	0.625	0.389, 1.004	0.052	0.6	0.377, 0.953	0.030
Model 3	0.584	0.361, 0.944	0.028	0.557	0.348, 0.890	0.014

Model 1 was adjusted for age, sex, body mass index, medical history (diabetes mellitus, coronary artery bypass graft or percutaneous coronary intervention, cerebrovascular accident, and dyslipidemia), and the use of calcium channel blockers.

Model 2: Model 1 + was adjusted for initial laboratory tests including estimated glomerular filtration rate, blood urea nitrogen, hemoglobin, potassium, and urine albumin

Model 3: Model 2 + adjusted for cancer type, stages and adjuvant treatment

Table S6. Characteristics of patients after propensity score matching

Variables	RAS blocker (+) (N=186)	RAS blocker (-) (N=186)	*P*
Male	135 (72.6%)	136 (73.1%)	1.000
Age, years	66.0 [58.0;72.0]	66.5 [59.0;73.0]	0.695
BMI, kg/m2	25.9 [23.6;28.4]	25.4 [23.4;27.5]	0.102
SBP, mmHg	127.7 ± 16.0	128.4 ± 16.5	0.688
DBP, mmHg	73.3 ± 10.3	73.8 ± 11.7	0.679
DM	53 (28.5%)	50 (26.9%)	0.817
PCI or CABG	8 (4.3%)	6 (3.2%)	0.785
Dyslipidemia	13 (7.0%)	11 (5.9%)	0.833
CVA	11 (5.9%)	10 (5.4%)	1.000
β-blockers	39 (21.0%)	48 (25.8%)	0.327
Calcium channel blockers	144 (77.4%)	136 (73.1%)	0.400
Diuretics	62 (33.3%)	41 (22.0%)	0.020
Antihypertensive medication count			< 0.001
1	18 (9.7%)	150 (80.6%)	
2	100 (53.8%)	33 (17.7%)	
3	59 (31.7%)	3 (1.6%)	
4	9 (4.8%)	0 (0.0%)	
Cancer	179 (96.2%)	180 (96.8%)	1.000
Cancer types			0.910
Renal cell carcinoma	130 (69.9%)	123 (66.1%)	
Urothelial cell carcinoma	34 (18.3%)	40 (21.5%)	
Liposarcoma	8 (4.3%)	7 (3.8%)	
Other	7 (3.8%)	9 (4.8%)	
Non-cancer	7 (3.8%)	7 (3.8%)	
Cancer stages			0.928
Stage 1	73 (39.2%)	77 (41.4%)	
Stage 2	32 (17.2%)	34 (18.3%)	
Stage 3	59 (31.7%)	51 (27.4%)	
Stage 4	15 (8.1%)	17 (9.1%)	
Non-cancer	7 (3.8%)	7 (3.8%)	
Cancer stage			0.811
Limited stage (1 and 2)	105 (56.5%)	111 (59.7%)	
Advanced stage (3 and 4)	74 (39.8%)	68 (36.6%)	
Non-cancer	7 (3.8%)	7 (3.8%)	
Adjuvant Tx., systemic	30 (16.1%)	26 (14.0%)	0.664

Adjuvant Tx., localized	11 (5.9%)	11 (5.9%)	1.000
Smoking History			0.265
None	106 (57.0%)	101 (54.3%)	
Ex	41 (22.0%)	55 (29.6%)	
Current	17 (9.1%)	16 (8.6%)	
No data	22 (11.8%)	14 (7.5%)	
Drinking History			0.623
None	102 (54.8%)	103 (55.4%)	
Ex	28 (15.1%)	28 (15.1%)	
Current	33 (17.7%)	39 (21.0%)	
No data	23 (12.4%)	16 (8.6%)	
Laboratory findings, preoperative			
eGFR, ml/min/1.73 m2	79.2 [67.8;90.2]	79.7 [67.0;91.5]	0.957
BUN, mg/dl	16.3 [13.2;20.1]	15.9 [13.2;19.3]	0.427
Hemoglobin, g/dl	13.8 [12.4;14.8]	13.7 [12.3;14.7]	0.952
Uric acid, mg/dl	5.8 ± 1.6	5.4 ± 1.6	0.024
Potassium, mmol/l	4.3 [4.1; 4.6]	4.3 [4.0; 4.6]	0.809
Urine albumin			0.788
Negative	127 (68.3%)	130 (69.9%)	
Trace	28 (15.1%)	24 (12.9%)	
+	13 (7.0%)	16 (8.6%)	
++	13 (7.0%)	9 (4.8%)	
+++	5 (2.7%)	7 (3.8%)	
Hospital stays, d	8 [8; 9]	8 [8;10]	0.155
Follow-up period, mo	35 [35;35]	35 [33;35]	0.024

Continuous variables are expressed as mean ± standard deviation or median (interquartile range), and categorical variables are expressed as numbers (%).

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; DM, diabetes mellitus; PCI: percutaneous coronary intervention; CABG, coronary artery bypass graft; CVA, cerebrovascular accident; Tx, treatment; eGFR, estimated glomerular filtration rate; BUN, blood urea nitrogen.

Table S7. Renal outcomes and hyperkalemia findings according to RAS blockers use after propensity score matching

Variables	Time from surgery	RAS blocker (+) N=186	RAS blocker (-) N=186	*P*
Renal adaptation, %	Discharge	69.0 ± 10.0	67.5 ± 11.6	0.210
	1 month	67.4 ± 10.1	66.8 ± 11.9	0.606
Acute kidney injury	1 month	8 (4.3%)	10 (5.4%)	0.629
ESKD (1000 PY)	3 years	0	8.3	0.038
Hyperkalemia	Discharge	5/186 (2.7%)	6/186 (3.2%)	1.000
	1 month	5/186 (2.7%)	6/186 (3.2%)	1.000
	6 months	4/148 (2.7%)	4/143 (2.8%)	1.000
	12 months	3/132 (2.3%)	2/121 (1.7%)	1.000

Continuous variables are expressed as mean ± standard deviation, and categorical variables are expressed as numbers (%).

ESKD, end-stage kidney disease; PY, person-year; RAS, renin-angiotensin system

Table S8. The risk of mortality and composite outcome of ESKD and mortality according to RAS blocker use after propensity score matching

	Mortality			ESKD or mortality		
	HR	**95% CI**	***P***	**HR**	**95% CI**	***P***
Univariable	0.620	0.361, 1.063	0.082	0.609	0.360, 1.031	0.065
Model 1	0.620	0.360, 1.068	0.085	0.615	0.362, 1.046	0.073
Model 2	0.564	0.323, 0.984	0.044	0.560	0.326, 0.962	0.036
Model 3	0.495	0.278, 0.879	0.016	0.504	0.289, 0.881	0.016

Model 1 was adjusted for age, sex, body mass index, and medical history (diabetes mellitus, coronary artery bypass graft or percutaneous coronary intervention, cerebrovascular accident, and dyslipidemia) + beta-blocker use.

Model 2: Model 1 + was adjusted for initial laboratory tests including estimated glomerular filtration rate, blood urea nitrogen, hemoglobin, potassium, and urine albumin.

Model 3: Model 2 + adjusted for cancer type, stages, and adjuvant treatment

Cl, confidence interval; ESKD, end-stage kidney disease; HR, hazard ratio; RAS, renin-angiotensin system

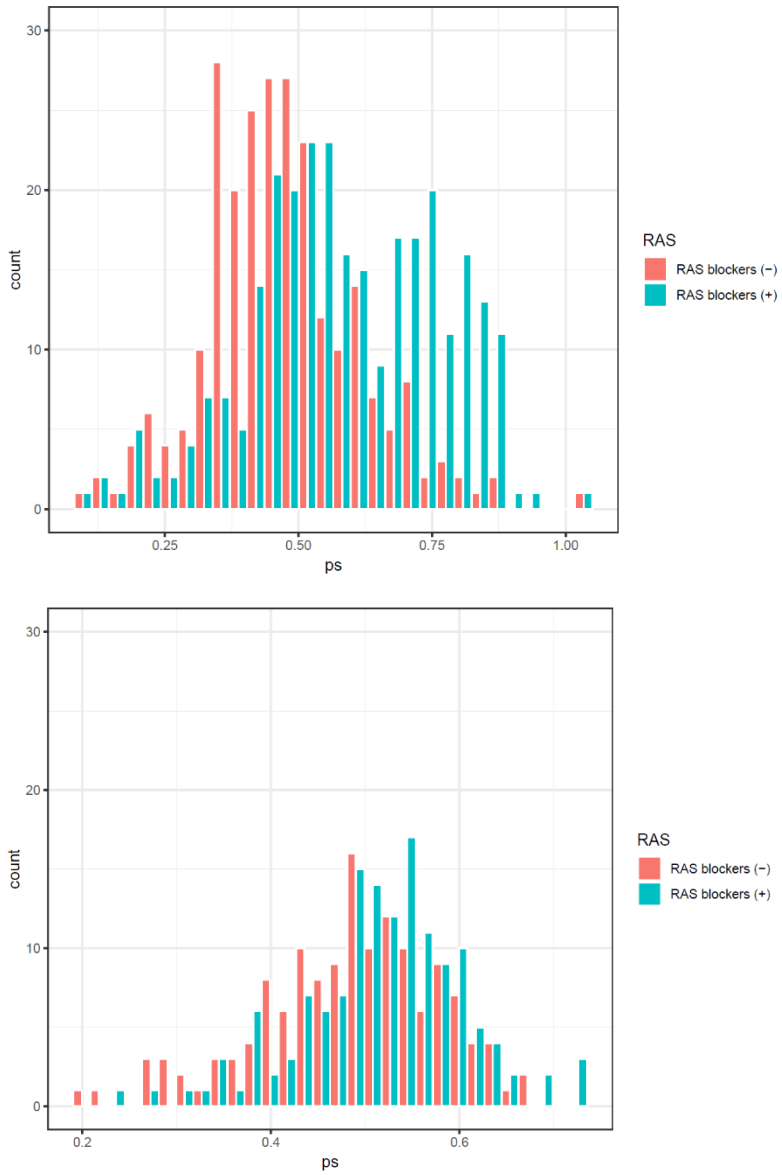
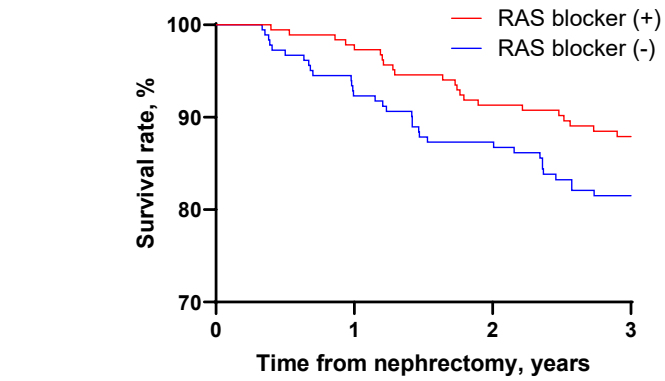


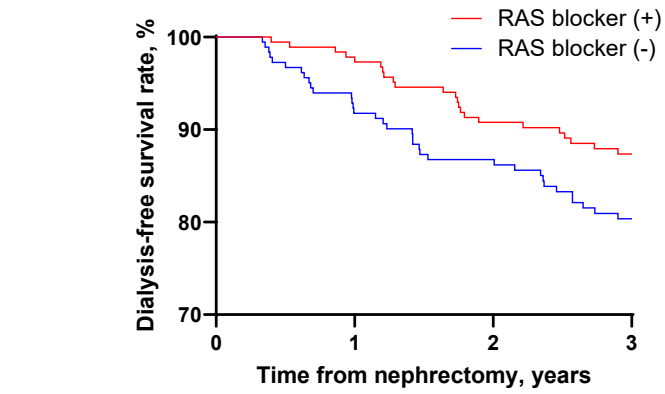
Figure S1. Distribution of propensity scores before and after matching. (A) Distribution of propensity scores before matching. (B) Distribution of propensity scores after matching

(A)



Numbers at risk				
RAS blocker (+)	186	179	165	153
RAS blocker (-)	186	167	155	138

(B)



Numbers at risk				
RAS blocker (+)	186	179	164	152
RAS blocker (-)	186	166	154	136

Figure S2. Kaplan-Meier curves according to RAS blocker use after propensity score matching. After propensity score matching, (A) overall survival (*P*-value = 0.079) and (B) dialysis-free survival (*P*-value = 0.062) tended to be better in the RAS blockers group compared with the control group, but this was not statistically significant.

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1,3
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3,4
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	7,9
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-10
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7,8
Bias	9	Describe any efforts to address potential sources of bias	7,11
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9,10
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	10-12
		(*b*) Describe any methods used to examine subgroups and interactions	10
		(*c*) Explain how missing data were addressed	11
		(*d*) If applicable, explain how loss to follow-up was addressed	11
		(*e*) Describe any sensitivity analyses	11-12
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	7
		(c) Consider use of a flow diagram	Fig1.
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	12
		(b) Indicate number of participants with missing data for each variable of interest	12 Table1
		(c) Summarise follow-up time (eg, average and total amount)	12
Outcome data	15*	Report numbers of outcome events or summary measures over time	12-18

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10-16, Table2, Table3, Figure2, Figure3
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	16-18 Table4, Figure4, Figure5, Figure6
Discussion			
Key results	18	Summarise key results with reference to study objectives	18-19
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	22
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	19-21
Generalisability	21	Discuss the generalisability (external validity) of the study results	20,21
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	24

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.