Supplemental Table S1. Multivariable logistic regression model coefficients

Baseline covariates	**Outcome of CKD stage 3**[a]			**Outcome of CKD stage 4**[a]			**Outcome of CKD stage 5**[a] **or ESRD**		
	β	**S.D.**	**P value**	**β**	**S.D.**	**P value**	**β**	**S.D.**	**P value**
htTKV[b]	0.32	0.08	<0.001	0.35	0.07	<0.001	0.30	0.07	<0.001
Age	0.06	0.02	0.015	0.05	0.03	0.086	0.04	0.03	0.193
BMI	0.03	0.04	0.452	0.05	0.04	0.164	0.04	0.04	0.401
Sex[c]	0.35	0.39	0.367	-0.14	0.43	0.754	-0.35	0.46	0.450
Race[d]	0.23	0.59	0.692	0.88	1.01	0.382	0.19	0.96	0.846
GFR[e]	-0.03	0.01	0.003	-0.03	0.01	0.015	-0.03	0.01	0.029
Intercept	-1.74	1.83	0.253	-4.29	2.31	0.064	-3.10	2.41	0.275

[a] Defined by iothalamate GFR

[b] Per 100 mL/m

[c] Reference group is male

[d] Reference group is non-white

[e] Baseline corrected iothalamate GFR (mL/min/1.73 m^2)

Supplemental Table S2. Logistic regression analysis with different adjustments to the original cohort

Renal insufficiency endpoint by measured (iothalamate) GFR	**Full cohort[a]**			**Class I patients only[b]**		
	N	**OR**	**95% CI**	**N**	**OR**	**95% CI**
30–59 (CKD Stage 3)	184	1.38	(1.19-1.60)	180	1.58	(1.31-1.92)
15-29 (CKD Stage 4)	189	1.35	(1.19, 1.54)	185	1.42	(1.23-1.64)
<15 (CKD Stage 5) or ESRD	186	1.30	(1.15, 1.48)	182	1.34	(1.17-1.54)
GFR decreased ≥ 30%	192	1.42	(1.20, 1.67)	188	1.54	(1.27-1.88)
GFR decreased ≥ 57%	188	1.36	(1.20 1.54)	184	1.47	(1.27-1.71)

GFR values in mL/min/1.73 m^2

P values are <0.001 for all the analyses

OR, odds ratio of reaching CKD stage per 100 mL/m increment in baseline htTKV in multivariable model adjusted for age, sex, race, BMI and baseline GFR

[a] 12 patients with CKD stage 3 at baseline were considered part of the cohort for the analysis of CKD Stage 4, CKD Stage 5, GFR decreased ≥ 30% and GFR decreased ≥ 57%, and were included if they were informative of the outcome

[b] Excluded 4 patients with atypical (Class 2) imaging findings on kidney MRI

Supplemental Table S3. Logistic regression analysis with adjustments to the original cohort to exclude participants in interventional trials

Renal insufficiency endpoint by measured (iothalamate) GFR	**Full cohort[a]**			**Excluding HALT subjects[b]**			**Excluding TEMPO subjects[c]**		
	N	**OR**	**95% CI**	**N**	**OR**	**95% CI**	**N**	**OR**	**95% CI**
30–59 (CKD Stage 3)	184	1.38	(1.19-1.60)	125	1.32	(1.12-1.55)	162	1.40	(1.19-1.66)
15-29 (CKD Stage 4)	189	1.35	(1.19, 1.54)	130	1.30	(1.12-1.51)	166	1.37	(1.19-1.58)
<15 (CKD Stage 5) or ESRD	186	1.30	(1.15, 1.48)	128	1.28	(1.11-1.49)	164	1.28	(1.13-1.46)
GFR decreased ≥ 30%	192	1.42	(1.20, 1.67)	133	1.32	(1.11-1.60)	168	1.42	(1.18-1.70)
GFR decreased ≥ 57%	188	1.36	(1.20 1.54)	129	1.33	(1.15-1.54)	166	1.36	(1.18-1.55)

GFR values in mL/min/1.73 m^2

P values are ≤0.001 for all the analyses except P = 0.003 for GFR decreased ≥ 30% in the cohort excluding HALT subjects.

OR, odds ratio of reaching CKD stage per 100 mL/m increment in baseline htTKV in multivariable model adjusted for age, sex, race, BMI and baseline GFR

[a] 12 patients with CKD stage 3 at baseline were considered part of the cohort for the analysis of CKD Stage 4, CKD Stage 5, GFR decreased ≥ 30% and GFR decreased ≥ 57%, and were included if they were informative of the outcome

[b] Exclude subjects in HALT trial

[c] Exclude subjects in TEMPO trial

Supplemental Table S4. P values for likelihood ratio tests comparing models that include ADPKD genotype and/or htTKV

Model comparison	Outcome				
	CKD Stage 3	CKD Stage 4	CKD Stage 5 or ESRD	GFR decreased ≥ 30%	GFR decreased ≥ 57%
Model 2 vs. Model 1	0.012	0.004	0.008	<0.001	0.005
Model 3 vs. Model 1	<0.001	<0.001	<0.001	<0.001	<0.001
Model 4 vs. Model 1	<0.001	<0.001	<0.001	<0.001	<0.001
Model 4 vs. Model 2	<0.001	<0.001	<0.001	<0.001	<0.001
Model 4 vs. Model 3	0.396	0.308	0.275	0.133	0.482

Model 1 (Base model): Sex, race, BMI, baseline age and GFR

Model 2: Base model + genotype

Model 3: Base model + htTKV

Model 4: Base model + genotype + htTKV

Supplemental Table S5. Net reclassification indices for models that include ADPKD genotype and/or htTKV

Model comparison	Outcome				
	CKD Stage 3	CKD Stage 4	CKD Stage 5 or ESRD	GFR decreased ≥ 30%	GFR decreased ≥ 57%
Model 2 vs. Model 1	0.004	0.083	0.079	0.183	0.109
Model 3 vs. Model 1	0.202 (0.018, 0.425)	0.249 (0.077, 0.493)	0.218 (0.015, 0.500)	0.308 (0.099, 0.607)	0.303 (0.113, 0.545)
Model 4 vs. Model 1	0.205 (0.056, 0.462)	0.245 (0.089, 0.522)	0.250 (0.050, 0.537)	0.381 (0.148, 0.655)	0.307 (0.128, 0.582)
Model 4 vs. Model 2	0.189 (0.002, 0.401)	0.150 (0.008, 0.444)	0.200 (-0.037, 0.349)	0.238 (0.014, 0.482)	0.268 (0.078, 0.488)
Model 4 vs. Model 3	0.094 (-0.066, 0.183)	0.055 (-0.070, 0.228)	0.050 (-0.062, 0.201)	-0.030 (-0.102, 0.230)	0.070 (-0.074, 0.168)

Numbers in each cell represent the net reclassification index for the indicated model comparison (by row) and outcome (by column), with 95% confidence intervals in parentheses.

Model 1 (Base model): Sex, race, BMI, baseline age and GFR
Model 2: Base model + genotype
Model 3: Base model + htTKV
Model 4: Base model + genotype + htTKV

Supplemental Table S6. Net reclassification indices for models that include ADPKD genotype and/or Irazabal class

Model comparison	Outcome				
	CKD Stage 3	CKD Stage 4	CKD Stage 5 or ESRD	GFR decreased ≥ 30%	GFR decreased ≥ 57%
Model 2 vs. Model 1	0.004	0.083	0.079	0.183	0.109
Model 3 vs. Model 1	0.166 (0.044, 0.474)	0.334 (0.125, 0.618)	0.275 (0.084, 0.628)	0.302 (0.108, 0.594)	0.339 (0.079, 0.546)
Model 4 vs. Model 1	0.234 (0.093, 0.503)	0.285 (0.141, 0.629)	0.329 (0.095, 0.674)	0.318 (0.158, 0.675)	0.290 (0.114, 0.608)
Model 4 vs. Model 2	0.234 (0.043, 0.425)	0.182 (0.068, 0.542)	0.236 (0.000, 0.495)	0.226 (0.016, 0.461)	0.244 (0.036, 0.473)
Model 4 vs. Model 3	0.032 (-0.072, 0.191)	0.055 (-0.082, 0.224)	0.071 (-0.093, 0.200)	0.142 (-0.067, 0.280)	0.031 (-0.069, 0.295)

Numbers in each cell represent the net reclassification index for the indicated model comparison (by row) and outcome (by column), with 95% confidence intervals in parentheses.

Model 1 (Base model): Sex, race, BMI, baseline age and GFR
Model 2: Base model + genotype
Model 3: Base model + Irazabal class
Model 4: Base model + genotype + Irazabal class