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Suppl. Table S1.

Prediction of TKV stereology (TKVs) by
TKV ellipsoid (TKVe)

	R-Square	Coeff Var	Root MSE	PRESS Statistic
TKVe coronal	0.9997	1.6201	0.1668	17.112
TKVe sagittal	0.9998	1.5441	0.1590	15.544
TKVe average	0.9998	1.4180	0.1460	13.109

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Comparison of TKV stereology (TKVs) measurements with MR or CT images

We identified 43 patients who had abdominal CT and MR images obtained within 15 days. Axial non-contrast CT and MR images, of 5-10 mm, were used to calculate TKVs, using Analyze software. TKV measurements from CT and MRI were strongly correlated ($R^2=0.9998$, Supplementary Figure S3A). A plot of the % difference between the measurements against their mean is more informative to assess between measurements differences (Supplementary Figure S3B). The mean % difference in TKV was 0.29 ± 1.68 . Difference in TKV (MRI-CT) was within 3.1% below to 3.6% above true TKV (MRI, CT mean). This is less than the annual mean increase of 5.3% reported in ADPKD. The probability that an MRI-CT switch could account for a change of this magnitude is extremely small (0.0008). This data suggested that MRI and CT images could be used interchangeably if necessary to measure TKV.

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3 **Classification of Class 1 ADPKD by HtTKV0 and age at HtTKV0.**
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5 Class 1 patients were stratified into five subclasses based on estimated kidney growth rates, <1.5 (subclass
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7 1A), 1.5-3 (1B), 3-4.5 (1C), 4.5-6 (1D) or >6% (1E) (Supplemental Table S2).
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Suppl. Table S2. Annual of the American Society of NEPHROLOGY

Years	Class 1 A*	Class 1 B*	Class 1 C*	Class 1 D*	Class 1 E†
15	188	234	290	359	359
16	190	241	303	381	381
17	193	248	317	404	404
18	196	255	331	428	428
19	199	263	346	454	454
20	202	271	362	481	481
21	205	279	378	510	510
22	208	287	395	541	541
23	211	296	413	573	573
24	214	305	431	607	607
25	218	314	451	644	644
26	221	323	471	682	682
27	224	333	492	723	723
28	228	343	514	767	767
29	231	353	538	813	813
30	234	364	562	862	862
31	238	375	587	913	913
32	242	386	613	968	968
33	245	398	641	1026	1026
34	249	410	670	1088	1088
35	253	422	700	1153	1153
36	256	435	732	1222	1222
37	260	448	765	1295	1295
38	264	461	799	1373	1373
39	268	475	835	1456	1456
40	272	489	872	1543	1543
41	276	504	912	1635	1635
42	280	519	953	1734	1734
43	285	535	996	1838	1838
44	289	551	1040	1948	1948
45	293	567	1087	2065	2065
46	298	584	1136	2189	2189
47	302	602	1187	2320	2320
48	307	620	1241	2459	2459
49	311	638	1297	2607	2607
50	316	658	1355	2763	2763
51	321	677	1416	2929	2929
52	325	698	1480	3105	3105
53	330	719	1546	3291	3291
54	335	740	1616	3488	3488
55	340	762	1688	3698	3698
56	345	785	1764	3919	3919
57	350	809	1844	4155	4155
58	356	833	1927	4404	4404
59	361	858	2014	4668	4668
60	366	884	2104	4948	4948
61	372	910	2199	5245	5245
62	378	938	2298	5560	5560
63	383	966	2401	5893	5893
64	389	995	2509	6247	6247
65	395	1024	2622	6622	6622
66	401	1055	2740	7019	7019
67	407	1087	2863	7440	7440
68	413	1119	2992	7887	7887
69	419	1153	3127	8360	8360
70	425	1188	3268	8861	8861
71	432	1223	3415	9393	9393
72	438	1260	3568	9957	9957
73	445	1298	3729	10554	10554
74	451	1337	3897	11187	11187
75	458	1377	4072	11859	11859
76	465	1418	4255	12570	12570
77	472	1461	4447	13324	13324
78	479	1505	4647	14124	14124
79	486	1550	4856	14971	14971
80	494	1596	5075	15869	15869

*Upper limits shown for classes A, B, C and D.

†Minimal values shown for Class 1E

Suppl. Table S3. Expected predicted error (EPE) in validation set

	EPE		
	All patients	Patients <60mL/min/1.73m ²	Patients ≥60mL/min/1.73m ²
	(eGFR)	(eGFR)	(eGFR)
Class 1 patients by TKV ellipsoid (TKVe) Internal Validation	181 (13.5)	102 (10.1)	261 (16.2)
Class 1 patients by TKV ellipsoid (TKVe) External Validation	293 (17.1)	221 (14.9)	313 (17.7)

Supplementary Table S4: Comparison between modeling eGFR with and without PKD classes using validation data.

eGFR at baseline	Sensitivity for last eGFR ≤45: % TP (no. TPs)		Specificity for last eGFR ≤45: % TN (no. TN)		AUC last eGFR ≤45 vs. predicted	
	With PKD Classes	Without PKD Classes	With PKD Classes	Without PKD Classes	With PKD Classes	Without PKD Classes
All (n=333, 106)	81.1 (86)	71.7 (76)	90.7 (206)	89.4 (203)	0.945	0.929
<60 (n=65, 61)	96.7 (59)	95.1 (58)	25.0 (1)	0.0 (0)	0.934	0.900
≥60 (n=268, 45)	60.0 (27)	40.0 (18)	91.9 (205)	91.0 (203)	0.901	0.864
≥70 (n=243, 36)	55.6 (20)	30.6 (11)	93.7 (194)	92.7 (192)	0.907	0.873
≥80 (n=202, 23)	47.8 (11)	17.4 (4)	95.5 (171)	96.6 (173)	0.912	0.883

Note: TN=true negative, TP=True positive.

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Supplementary Table S5: Comparison of concordance statistics between modeling time to ESRD using baseline eGFR plus PKD class versus baseline eGFR alone.

Concordance		
eGFR at baseline (ESRD events)	Baseline eGFR and PKD Class (ordinal)	Baseline eGFR
All (143)	95.7	95.1
≥30 (74)	92.5	90.6
≥60(21)	97.4	73.6
≥70(13)	87.9	73.3
≥80(10)	89.9	77.5

Suppl. Table S6. Cox-regression model of time to ESRD for Class 1, typical ADPKD patients, controlling by eGFR at HtTKV0

		ESRD Hazard Ratio	95% CI		p value
Mayo	eGFR at HtTKV0	0.909	0.896	0.921	<0.0001
	Type 1 class	1.835	1.488	2.262	<0.0001
CRISP	eGFR at HtTKV0	0.90	0.83	0.97	0.0086
	Type 1 class	4.67	1.03	21.20	0.0458

Web application to facilitate the estimation of TKVe and Class 1 subclassification

A web application that allows a fast estimation of TKV based on the ellipsoid equation from simple MRI or CT measurements (Supplemental Figure S2) can be found at <http://www.mayo.edu/research/centers-programs/translational-polycystic-kidney-disease-pkd-center/overview>. Once TKV has been estimated (or if TKV has been already obtained by stereology technique) patient's classification can be obtained with additional input of patient's height and age at the time of TKV.

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