Kidney Function Reserve Capacity in early and later stage Autosomal Dominant Polycystic Kidney Disease

Supplemental Material

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Kidney function measurements and Kidney Function Reserve Capacity

After a loading dose of 20 mL NaCl 0.9% with 0.3 MBq ^{125}I-iothalamate and 0.4 MBq ^{131}I-hippuran, a continuous infusion consisting of 0.0075 MBq/ml ^{125}I iothalamate and 0.02 MBq/ml ^{131}I-hippuran was given at a rate of 9 mL/hr over 7.5 hours. During the final two hours of this investigation, kidney function reserve capacity was determined by adding a constant infusion of dopamine of 4.4 mg/h in subjects less than 100 kg and 6.0 mg/h in subjects of 100 kg or more. The coefficient of variation is 2.5% for measured GFR and 5% for effective kidney plasma flow using this method[13].

Infusion of a low dose of dopamine, by binding to specific dopaminergic vascular receptors in the kidney, causes vasodilatation of especially afferent arterioles. This results in an increase in single nephron blood flow. In addition, nephrons can be recruited which normally do not or only minimally contribute to the GFR. Both phenomena allow the kidney to utilize its full filtrating capacity, which in normal conditions results in an increase in GFR[22, 23]. When the kidney already utilizes its full filtrating capacity, the GFR will not increase in response to dopamine, which indicates hyperfiltration.

Supplemental material is neither peer-reviewed nor thoroughly edited by CJASN. The authors alone are responsible for the accuracy and presentation of the material.

Table S1: Clinical characteristics of ADPKD patients and matched healthy controls according to age group

	Age (years)											
	18-29		30-39		40-49		50-59		≥60		P for trend	
Variables	**ADPKD**	**Control**	**ADPKD**	**Control**	**ADPKD**	**Control**	**ADPKD**	**Control**	**ADPKD**	**Control**	**ADPKD**	**Control**
N	17	17	26	26	41	41	50	50	16	16	-	-
Female, n (%)	12 (71)*	4 (24)	15 (58)	14 (54)	26 (63)	27 (66)	25 (50)	25 (50)	10 (63)	10 (63)	0.33	0.12
Age (years)	24±3	25±3	36±3	35±3	45±3	45±3	55±3	54±3	63±4	63±3	<0.001	<0.001
Weight (kg)	79.4±22.5	75.9±11.9	85.7±17.5	81.1±14.4	85.8±19.6	80.1±10.9	82.4±16.1	83.0±13.5	77.7±12.9	81.3±10.7	0.62	0.18
Height (cm)	176±11	177±8	177±11	177±9	178±10	175±9	176±11	176±10	174±8	172±7	0.50	0.08
BMI (kg/m^2)	25.5±6.2	24.1±3.9	27.4±5.8	25.7±3.5	27.0±5.1	26.3±3.0	26.5±3.8	26.6±2.9	25.8±3.9	27.3±2.6	0.90	0.002
Systolic blood pressure (mmHg)	126±13*	118±9	128±8*	121±10	127±12*	122±11	129±14	126±12	127±15	126±12	0.80	0.008
Diastolic blood pressure (mmHg)	74±11	69±6	79±7*	72±9	79±9*	74±8	80±10	77±8	73±9	76±8	0.72	0.002
Antihypertensive use, n (%)	9 (53)**	0 (0.0)	15 (58)**	2 (8)	32 (78)**	0 (0.0)	44 (88)**	8 (16)	14 (88)**	2 (13)	<0.001	0.03
RAAS-inhibitor use, n (%)	9 (53)**	0 (0.0)	14 (54)**	0 (0.0)	30 (73)**	0 (0.0)	39 (78)**	2 (4)	12 (75.0)**	0 (0.0)	0.02	0.30
Protein intake (g/24hr)	76±20	85±17	93±25	88±23	90±21	93±39	85±25	94±29	75±16	82±16	0.54	0.99
Sodium intake (mmol/24hr)	139±66	183±74	181±58	204±67	158±58	186±92	155±62*	195±71	140±53*	193±72	0.59	0.84
eGFR (ml/min/1.73m^2)	110±22	113±11	85±20*	98±13	58±25**	91±10	50±21**	86±12	34.5±20.7**	83.1±13.1	<0.001	<0.001
CKD stage, n (%)											<0.001	-
- 1	13 (77)	-	8 (31)	-	5 (12)	-	1 (2)	-	0 (0.0)	-		
- 2	4 (24)	-	16 (62)	-	13 (32)	-	16 (32)	-	3 (19)	-		
- 3A	0 (0.0)	-	0 (0.0)	-	9 (22)	-	12 (24)	-	1 (6)	-		
- 3B	0 (0.0)	-	2 (8)	-	7 (17)	-	11 (22)	-	3 (19)	-		
- 4	0 (0.0)	-	0 (0.0)	-	6 (15)	-	9 (18)	-	8 (50)	-		

- 5	0 (0.0)	-	0 (0.0)	-	1 (2)	-	1 (2)	-	1 (6)	-		
htTKV (ml/m)	445 (347-749)	-	723 (486-1009)	-	929 (523-1395)	-	1121 (511-1505)	-	998 (507-1362)	-	0.03	-
Mayo htTKV class, n (%)											0.006	-
- 1A	0 (0.0)	-	0 (0.0)	-	3 (7)	-	5 (10)	-	1 (6)	-		
- 1B	2 (12)	-	4 (15)	-	8 (20)	-	13 (26)	-	4 (25)	-		
- 1C	6 (35)	-	9 (35)	-	11 (27)	-	18 (36)	-	6 (38)	-		
- 1D	1 (6)	-	7 (27)	-	13 (32)	-	8 (16)	-	1 (6)	-		
- 1E	7 (41)	-	4 (15)	-	5 (12)	-	0 (0.0)	-	0 (0.0)	-		
- 2	1 (6)	-	1 (4)	-	0 (0.0)	-	1 (2)	-	4 (25)	-		
- Missing	0 (0.0)	-	1 (4)	-	1 (2)	-	5 (10)	-		-		
APKD mutation											0.009	-
PKD1 T, n (%)	8 (47)	-	16 (62)	-	13 (32)	-	16 (32)	-	8 (50)	-		
PKD1 n-T, n (%)	5 (29)	-	4 (15)	-	16 (39)	-	11 (22)	-	5 (31)	-		
PKD2, n (%)	2 (12)	-	1 (4)	-	6 (15)	-	13 (26)	-	1 (6)	-		
NMD, n (%)	1 (6)	-	2 (8)	-	2 (5)	-	0 (0.0)	-	0 (0.0)	-		
Missing, n (%)	1 (6)	-	3 (12)	-	4 (10)	-	10 (20)	-	2 (13)	-		

Variables are presented as mean ± SD, or as median (IQR) in case of non-normal distribution or otherwise stated. P values are obtained using one-way ANOVA in case of normal distribution, Kruskal-Wallis test in case of non-normal distribution and linear chi-squared test in case of categorical data.

Abbreviations are: N, number; ADPKD, autosomal dominant polycystic kidney disease; BMI, body mass index; eGFR, estimated glomerular filtration rate; CKD, chronic kidney disease; htTKV, height adjusted total kidney volume; *PKD*, polycystic kidney disease; T, truncating; n-T, non-truncating; NMD, no mutation detected.

[*] $p<0.05$ compared to HC same age group

[**] $p<0.001$ compared to HC same age group

Figure S1: Absolute kidney function reserve capacity in ADPKD patients and healthy controls according to age group (upper panel) and CKD stage (lower panel). Data are expressed as Tukey boxplots with median, IQR, and minimum and maximum within 1.5 IQR and outliers. *p<0.05 **p<0.001. *Abbreviations are*: ADPKD, autosomal dominant polycystic kidney disease; CKD, chronic kidney disease.

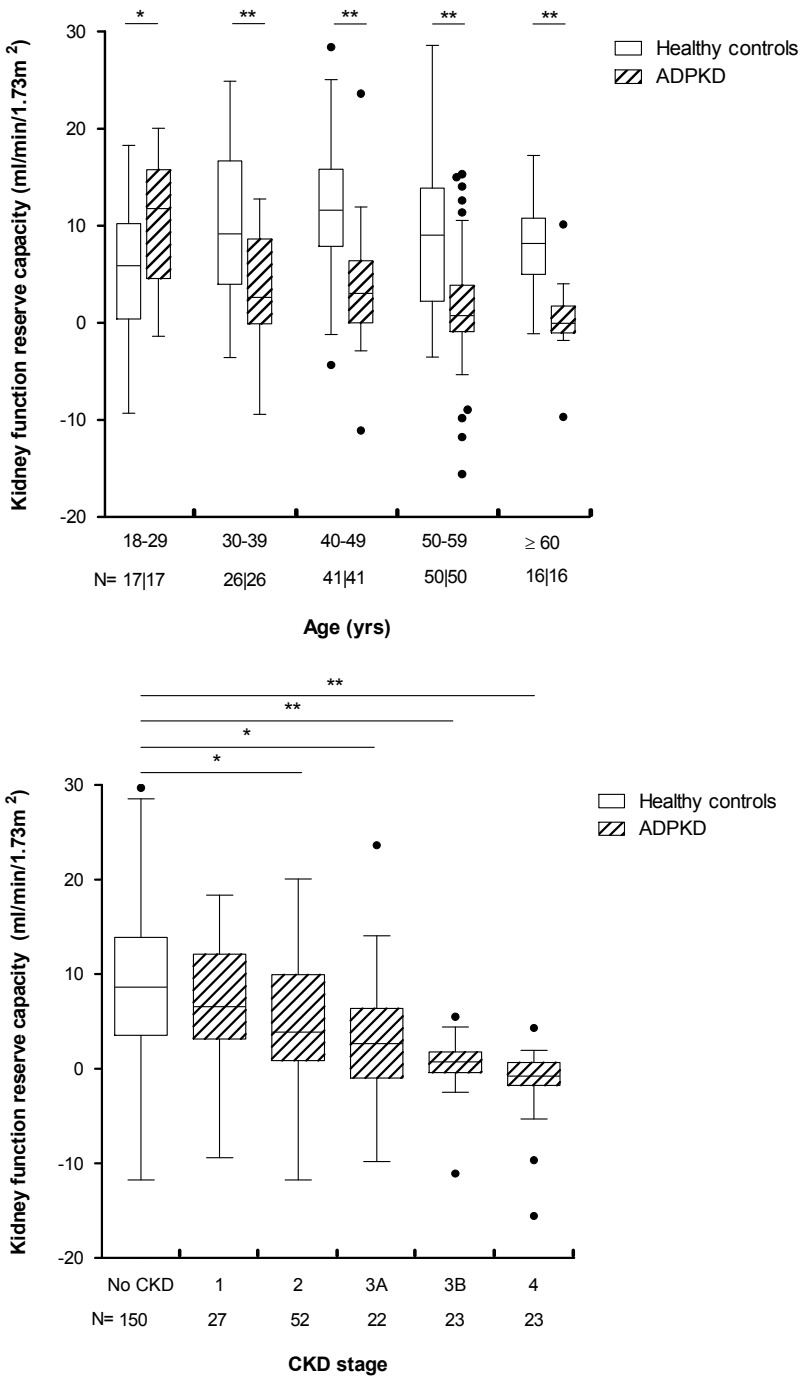
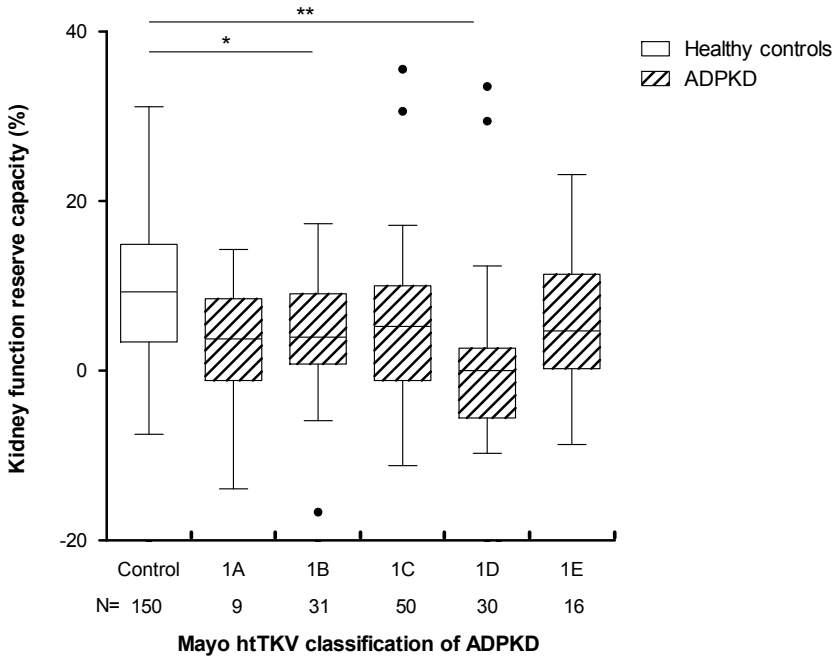


Figure S2: Kidney function reserve capacity (as percentage) according to Mayo height adjusted total kidney volume class 1A-1E (upper panel) and *PKD* mutation (lower panel). Data are expressed as Tukey boxplots with median, IQR, and minimum and maximum within 1.5 IQR and outliers. *p<0.05 **p<0.001. *Abbreviations are:* htTKV, height adjusted total kidney volume; ADPKD, autosomal dominant polycystic kidney disease; *PKD*, polycystic kidney disease; NMD, no mutation detected.



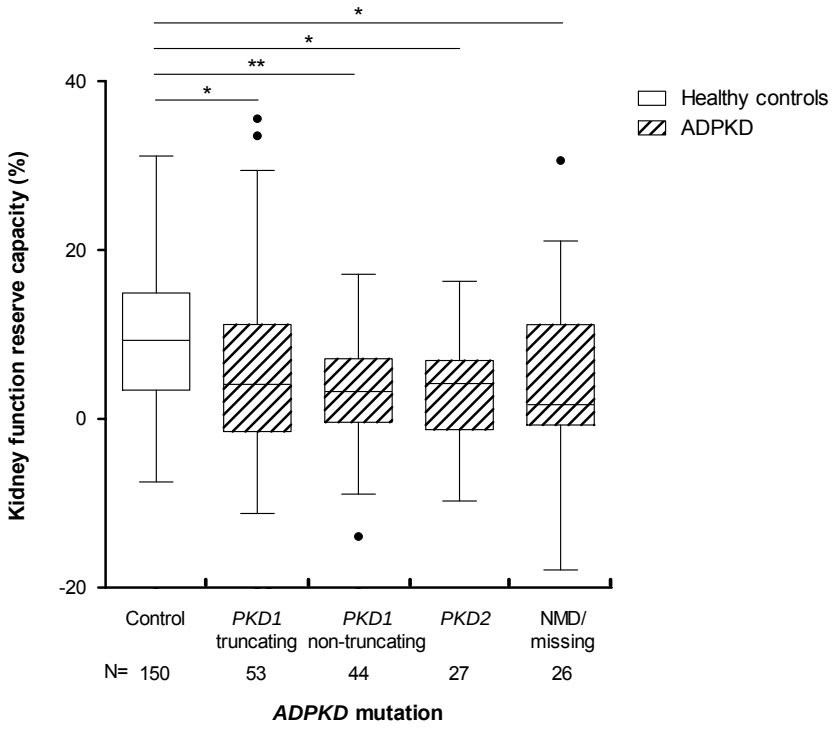
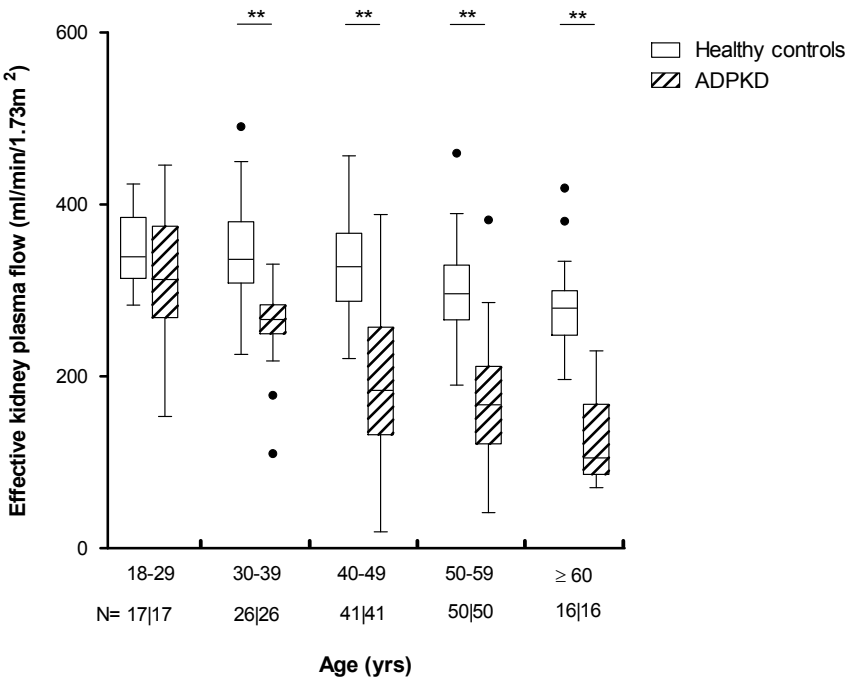


Figure S3: Effective kidney plasma flow in ADPKD patients and healthy controls according to age group (upper panel) and CKD stage (lower panel). Data are expressed as Tukey boxplots with median, IQR, and minimum and maximum within 1.5 IQR and outliers. *p<0.05 **p<0.001. *Abbreviations are*: ADPKD, autosomal dominant polycystic kidney disease; CKD, chronic kidney disease.



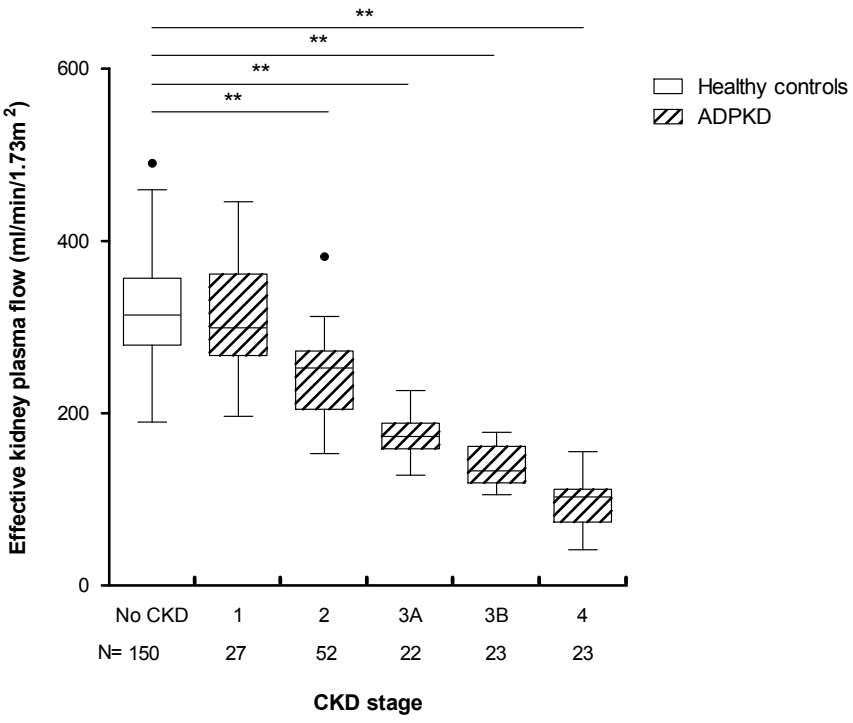
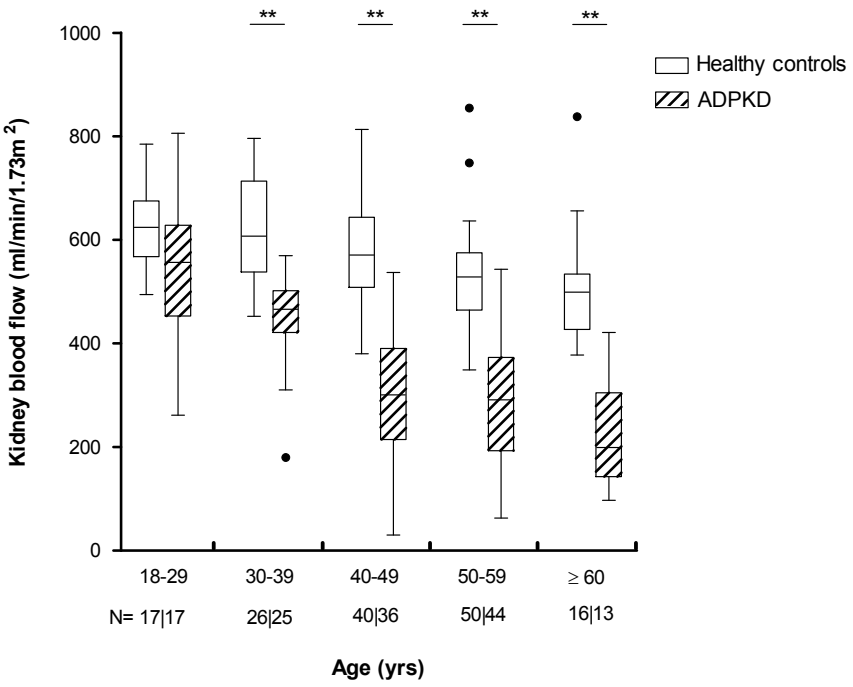


Figure S4: Kidney blood flow in ADPKD patients and healthy controls according to age group (upper panel) and CKD stage (lower panel). Data are expressed as Tukey boxplots with median, IQR, and minimum and maximum within 1.5 IQR and outliers. $^{*}p<0.05$ $^{**}p<0.001$. *Abbreviations are*: ADPKD, autosomal dominant polycystic kidney disease; CKD, chronic kidney disease.



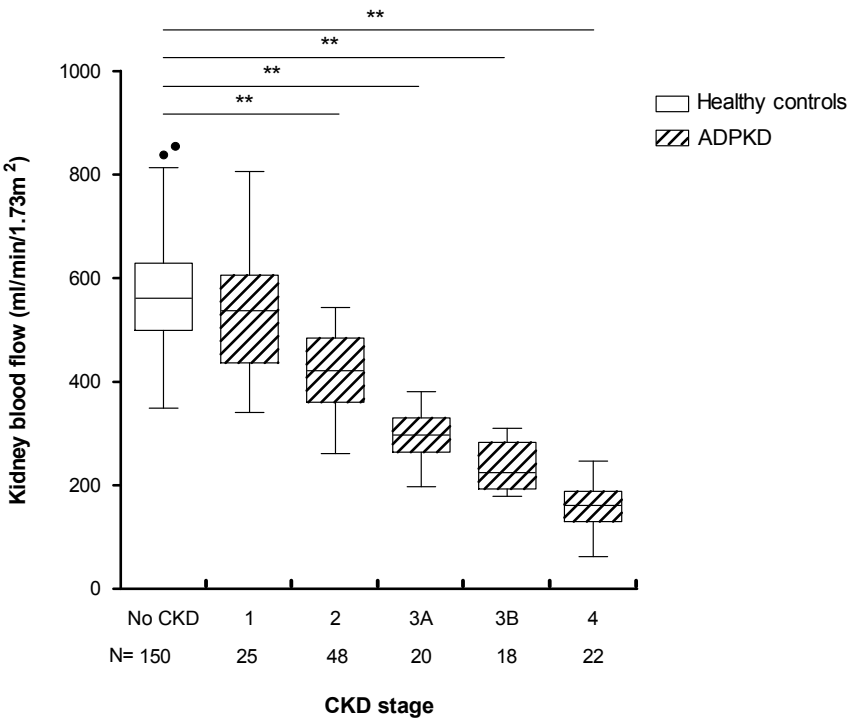
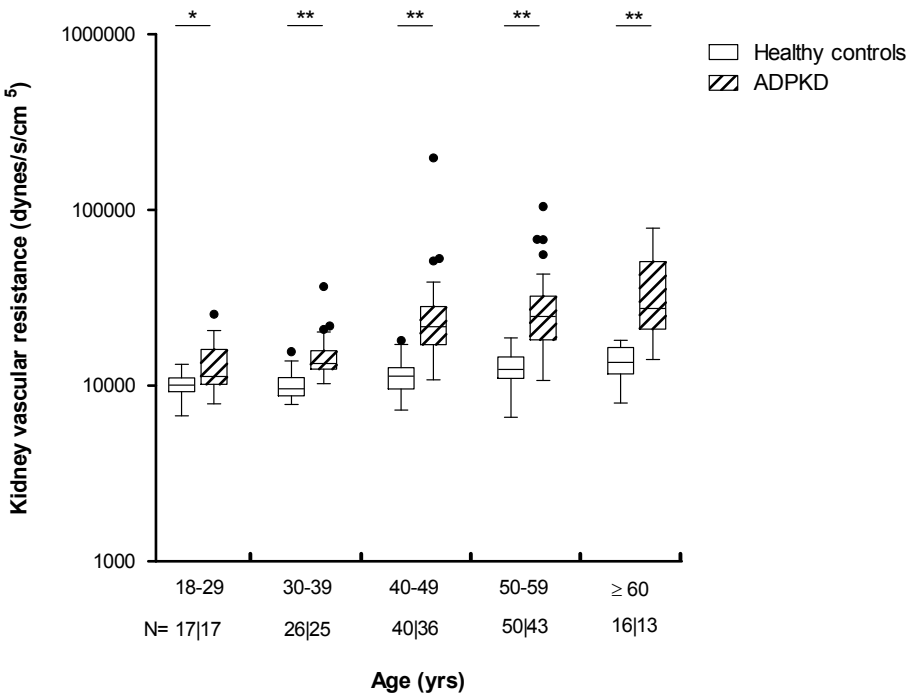


Figure S5: Kidney vascular resistance in ADPKD patients and healthy controls according to age group (upper panel) and CKD stage (lower panel). Data are expressed as Tukey boxplots with median, IQR, and minimum and maximum within 1.5 IQR and outliers. *p<0.05 **p<0.001. *Abbreviations are*: ADPKD, autosomal dominant polycystic kidney disease; CKD, chronic kidney disease.



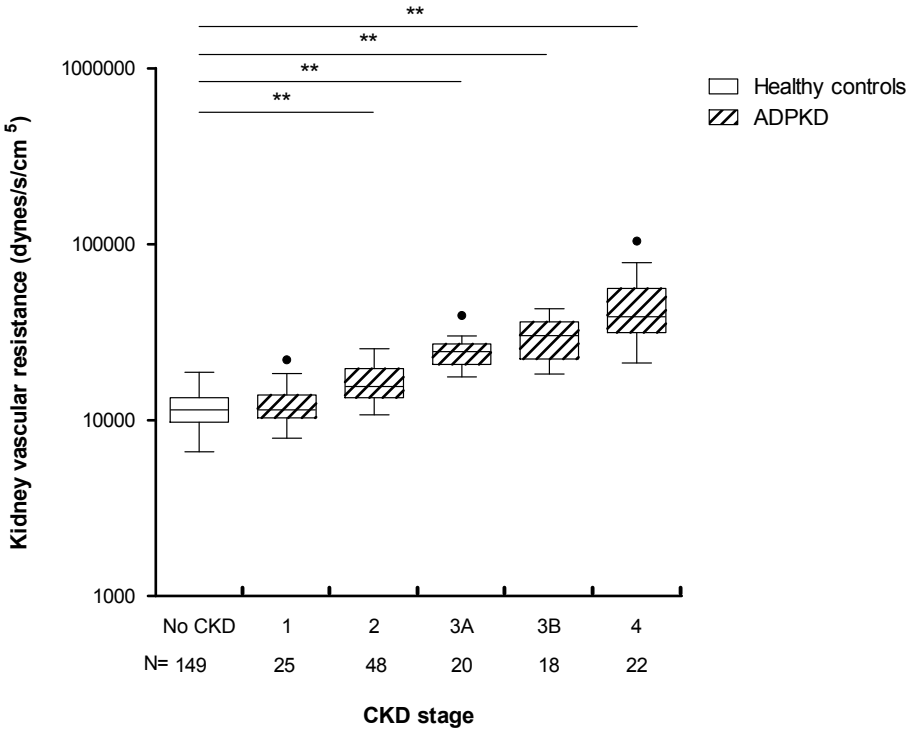


Figure S6: Filtration fraction according to Mayo height adjusted total kidney volume class 1A-1E (upper panel) and *PKD* mutation (lower panel). Data are expressed as Tukey boxplots with median, IQR, and minimum and maximum within 1.5 IQR and outliers. $^{*}p<0.05$ $^{**}p<0.001$. *Abbreviations are:* htTKV, height adjusted total kidney volume; ADPKD, autosomal dominant polycystic kidney disease; *PKD*, polycystic kidney disease; NMD, no mutation detected.