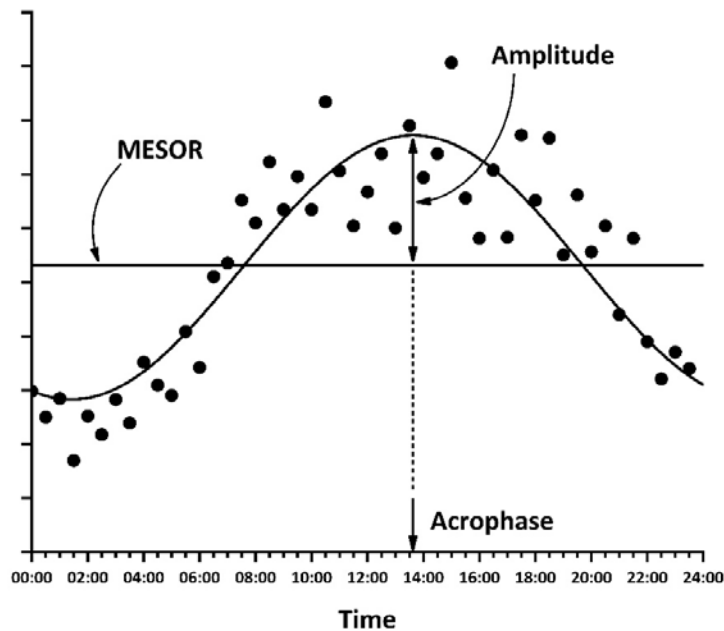


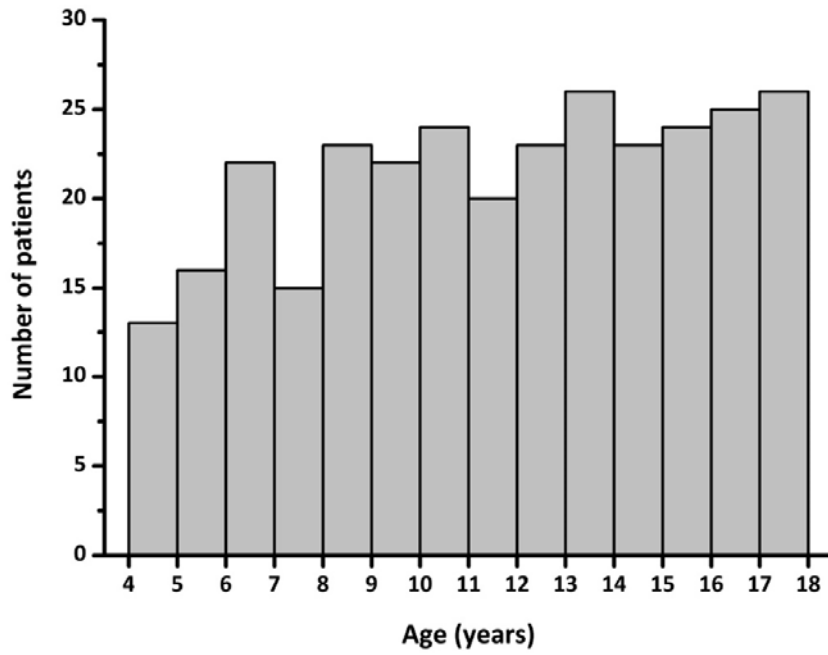
Supplementary Figure 1. Rhythm analysis parameters



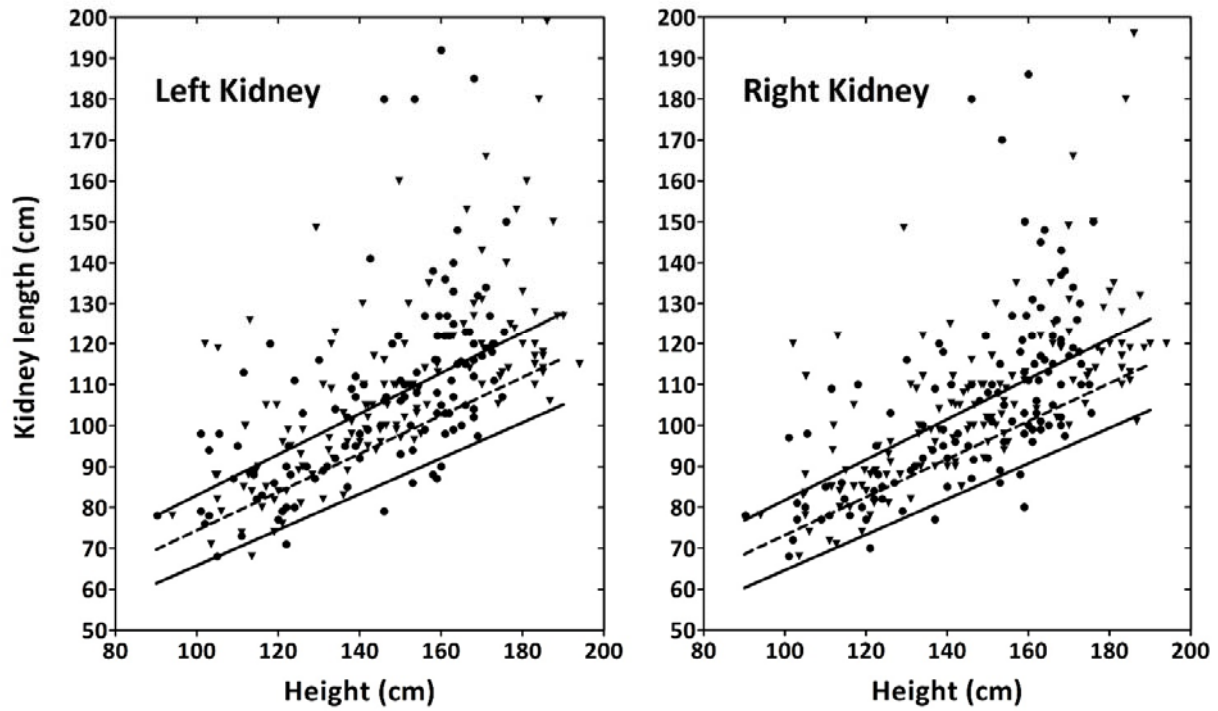
Several biological activities are characterized by rhythmic variations that are under the control of specialized suprachiasmatic nuclei and are influenced by external stimuli such as seasons, temperature, daylight, or feeding, resulting in ultradian (<24h), circadian (24h) and infradian (>24h) rhythmicity⁴⁰. Periodic activities, such as sleep/wake cycles, or therapies, such as treatment with BP medications, also generate biological rhythms.

The figure illustrates an example of cosine function fitting on data points obtained by ABPM on a full day/night cycle. Partial Fourier analysis is used to fit the function. For circadian (24h) rhythms, the analysis is applied to the recorded BP or HR values. Ultradian rhythms (12h, 8h, 6h) correspond to rhythms that are superimposed on the circadian rhythm. The Fourier analysis is performed on the residual values between the observed data points and the circadian function. ABPM files are considered to contain rhythms if cosine functions can be fitted with a p value <0.05 by least-squares method analysis. In addition, the software calculates the *MESOR* (Midline Estimating Statistic of Rhythm) value, which corresponds to the mean value of the fitted curve, the rhythm *amplitude*, which corresponds to the distance between the MESOR and the curve's peak value, and the *acrophase*, which is the hour past midnight that corresponds to the peak value.

Supplementary Figure 2. Age distribution of patients included in the study

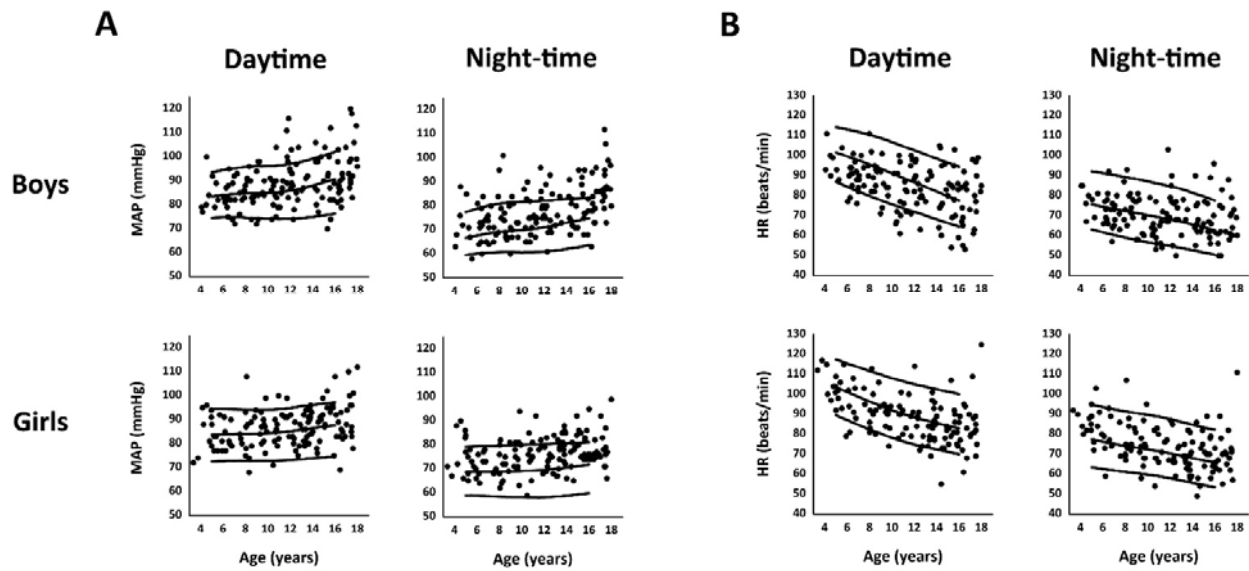


Supplementary Figure 3. Right and left kidney length.



Boys are indicated with filled inverted triangles; girls with filled circles. Reference data (mean, -2SD and +2SD) are derived from: Di Zazzo, G, Stringini, G, Matteucci, MC, Muraca, M, Malena, S, Emma, F: Serum creatinine levels are significantly influenced by renal size in the normal pediatric population. *Clin J Am Soc Nephrol*, 6: 107-113, 2011.

Supplementary Figure 4. Daytime and nighttime mean ABPM values



Panels A and B show mean values for mean arterial pressure (MAP) and heart rate (HR) in daytime and nighttime. Continuous lines show the reference ranges (5th, 50th, and 95th percentiles) for age as described in reference: Wuhl, E, Witte, K, Soergel, M, Mehls, O, Schaefer, F, German Working Group on Pediatric, H: Distribution of 24-h ambulatory blood pressure in children: normalized reference values and role of body dimensions. *J Hypertens*, 20: 1995-2007, 2002.

Supplementary Table 1. Analysis of center effect

	Adjusted OR	95% C.I.	p
Center 1	2,07	0,49 - 8,77	0,324
Center 3	0,73	0,20 - 2,62	0,630
Center 4	1,65	0,32 - 8,62	0,550
Center 7	0,33	0,04 - 2,78	0,306
Center 8	1,03	0,19 - 5,50	0,970
Center 9	0,90	0,18 - 4,47	0,894
Center 10	1,56	0,48 - 5,11	0,461
Center 11	0,26	0,06 - 1,11	0,069
Center 12	0,40	0,08 - 1,90	0,250
Center 13	1,85	0,70 - 4,90	0,218
Center 14	1,06	0,22 - 5,16	0,942
Center 15	0,56	0,16 - 1,99	0,374
Center 17	4,32	0,80 - 23,4	0,089
Center 19	0,31	0,04 - 2,40	0,259
Center 20	2,46	0,71 - 8,54	0,158
Center 21	8,77	2,41 - 32,0	0,001
Center 22	1,77	0,52 - 6,01	0,359

The table shows the results of a univariate logistic regression analysis, testing the effect of each center on the risk of having hypertension. Odds ratios (OR) were adjusted for age and gender. Data could not be calculated for 5 centers due to the limited number of patients.

Supplementary Table 2. Logistic regression – effect of birth weight and renal function

24h hypertension

Variable	Units	Adj. OR	95% C.I.	P
Birth weight	1000 gr	0.70	0.22 - 2.20	0.54
eGFR	100 ml/min/1.73 m ²	0.80	0.25 - 2.58	0.71

Daytime hypertension

Variable	Units	Adj. OR	95% C.I.	P
Birth weight	1000 gr	0.37	0.11 - 1.26	0.11
eGFR	100 ml/min/1.73 m ²	1.59	0.36 - 6.90	0.54

Nighttime hypertension

Variable	Units	Adj. OR	95% C.I.	P
Birth weight	1000 gr	1.05	0.40 - 2.77	0.92
eGFR	100 ml/min/1.73 m ²	0.86	0.29 - 2.56	0.79

Isolated nocturnal hypertension

Variable	Units	Adj. OR	95% C.I.	P
Birth weight	1000 gr	2.35	0.74 - 7.51	0.15
eGFR	100 ml/min/1.73 m ²	0.78	0.25 - 2.46	0.67

Non-dipping

Variable	Units	Adj. OR	95% C.I.	P
Birth weight	1000 gr	2.03	0.95 - 4.31	0.07
eGFR	100 ml/min/1.73 m ²	0.64	0.25 - 1.62	0.35

The table shows the results of a univariable logistic regression to analyze the impact of birth weight and eGFR on different ABPM outcomes. Odds ratios are adjusted (Adj. OR) for age, gender, use of BP medications and center effect, and are indicated with their corresponding 95% confidence intervals (95% C.I.).

Abbreviations: eGFR = estimated glomerular filtration rate

Supplementary Table 3. Cardiovascular rhythm analysis.

A. Comparison of MAP rhythm amplitudes and acrophases with reference control subjects.

	Controls		ADPKD		Trend	p
	Median	IQR	Median	IQR		
MAP amplitude						
24h	10.1	4.4	7.7	4.2	↓	<0.001
12h	5.9	2.4	5.0	3.5	↓	<0.001
8h	5.5	2.6	3.7	1.8	↓	<0.001
6h	5.2	2.2	3.6	1.6	↓	<0.001
MAP acrophase						
24h	13.9	1.9	14.6	2.4	↑	<0.001
12h	8	1.9	8.9	2.1	↑	<0.001
8h	2.1	1.8	2.7	2.4	↑	0.002
6h	2	1.5	2.4	2.3	↑	0.045

B. Comparison of HR rhythm amplitudes and acrophases with reference control subjects.

	Controls		ADPKD		Trend	p
	Median	IQR	Median	IQR		
HR amplitude						
24h	13.4	6.9	10.4	5.7	↓	<0.001
12h	7.7	4.0	5.9	3.7	↓	<0.001
8h	6.8	3.5	5.3	2.2	↓	<0.001
6h	6.4	2.7	4.2	2.2	↓	<0.001
HR acrophase						
24h	13.5	2.0	14.1	2.4	↑	<0.001
12h	8.4	2.0	8.7	2.1	↑	<0.04
8h	1.8	2.8	2.4	2.6	↑	<0.11
6h	2.0	1.4	2.6	2.1	↑	<0.04

C. χ^2 test for association of MAP and HR ultradian rhythms.

	MAP 12h	MAP 8h	MAP 6h	HR 12h	HR 8h	HR 6h
Age¹	0.07	0.58	0.61	0.27	0.58	0.36
Hypertension and or BP medications	0.53	0.77	0.99	0.77	0.65	0.22
Non-dipping	0.13	0.41	0.92	0.04*	0.40	0.14

Reference values for control subjects in panels A and B are from: Hadtstein, C, Wuhl, E, Soergel, M, Witte, K, Schaefer, F, German Study Group for Pediatric, H: Normative values for circadian and ultradian cardiovascular rhythms in childhood. *Hypertension*, 43: 547-554, 2004.

Panel C shows the p values for each χ^2 test assessing the association between ultradian rhythms and age,

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the presence of hypertension and/or the use of blood pressure medications, or the absence of nocturnal dipping.

(¹) The population was divided in three age classes (<10 years, 10-13 years and >13 years), corresponding approximately to the terciles boundaries of the cohort.

(*) $p < 0.05$.

Abbreviations: MAP: mean arterial pressure; HR = heart rate; IQR: inter-quartile range.

Supplementary Table 4. Sensitivity analysis – ABPM results

	All patients (N=292)	All patients except patients from center 21 (N=275)	
	Prevalence	Prevalence	p
Day - Hypertension	14,9%	10,9%	0,163
Night - Hypertension	29,9%	26,1%	0,323
24h - Hypertension	20,7%	17,0%	0,279
Non Dippers	51,9%	51,5%	0,927
Isolated Nocturnal Hypertension	18,2%	18,7%	0,903
Day - Hypertension and/or BP medications	31,3%	27,1%	0,294
Night - Hypertension and/or BP medications	41,6%	37,7%	0,363
24h - Hypertension and/or BP medications	34,8%	30,9%	0,338
Day - BP <p75 without BP medications	51,6%	54,7%	0,486
Night - BP <p75 without BP medications	34,7%	37,0%	0,582
24h - BP <p75 without BP medications	46,4%	49,0%	0,539

The table shows in columns 2 the prevalence of ABPM diagnoses as reported in table 1.

In the following columns, the same numbers have been calculated after removing seventeen patients from center 21, in which the prevalence of hypertension was significantly higher compared to the rest of the cohort. The impact of removing patients from center 21 was evaluated by the p value of χ^2 tests and was found to be statistically non-significant.

Supplementary Table 5. Sensitivity analysis – Rhythm analysis

	All patients (N=137)	Only patient not taking BP medications (N=111)	
	Prevalence	Prevalence	<i>P</i>
MAP – prepubertal - 24h rhythm	90,3%	90,6%	0.999
MAP – prepubertal - 12h rhythm	69,4%	71,7%	0.623
MAP – prepubertal - 8h rhythm	58,1%	56,6%	0.877
MAP – prepubertal - 6h rhythm	51,6%	52,8%	0.901
MAP – pubertal - 24h rhythm	88,0%	86,2%	0.759
MAP – pubertal - 12h rhythm	78,7%	77,6%	0.884
MAP – pubertal - 8h rhythm	53,3%	50,0%	0.703
MAP – pubertal - 6h rhythm	46,7%	46,6%	0.999
HR – prepubertal - 24h rhythm	95,2%	94,3%	0.844
HR – prepubertal - 12h rhythm	75,8%	77,4%	0.846
HR – prepubertal - 8h rhythm	58,1%	60,4%	0.802
HR – prepubertal - 6h rhythm	51,6%	52,8%	0.901
HR – pubertal - 24h rhythm	92,0%	89,7%	0.634
HR – pubertal - 12h rhythm	82,7%	81,0%	0.809
HR – pubertal - 8h rhythm	49,3%	44,8%	0.606
HR – pubertal - 6h rhythm	49,3%	55,2%	0.504

The table shows the prevalence of circadian and ultradian rhythms in the entire cohort and after removing patients treated with blood pressure medications. The *P* value refer to the significance of χ^2 tests comparing the prevalence in the entire cohort with the prevalence after removing patients under blood pressure treatment.