

The correlation between hypertension and renal function, left ventricular hypertrophy and renal structure in autosomal dominant polycystic kidney disease

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The aim of this study was to evaluate the frequency of hypertension in autosomal dominant polycystic kidney disease (ADPKD) patients and its correlation with renal function, renal structure and its influence on left ventricular wall function.

Two hundred patients were included in the study. The patients were divided in two groups: the first group of 92 patients with normal renal function, and the second group of 108 patients with chronic renal failure. All patients had an abdominal ultrasound and a M-mode echocardiography.

Hypertension was observed in 140 ADPKD patients (70%): 56 of the first group (61%) and 84 of the second group (79%). The subjects who developed hypertension before the age of 35 had worse renal survival than those who remained normotensive after age 35 (50 years vs. 62 years; $p < 0.0001$; risk ratio = 4.3). Hypertensive patients had significantly higher serum creatinine concentration than those without hypertension ($p < 0.001$). Left ven-

tricular hypertrophy was found in 56 patients with hypertension (40%) and in 9 normotensive patients (16%) ($p < 0.005$). Patients with LVH had a worse renal survival than those without LVH ($p < 0.001$). We also, have studied the role of renal cystic enlargement in initiating hypertension in ADPKD and on renal function.

We conclude that hypertension is a common complication in our ADPKD patients, and an important factor of cardiac hypertrophy. LVH could be considered a more valid measure of blood pressure control than office blood pressure measurements. The blood pressure correlates with kidney size in ADPKD patients. Increased kidney volume was correlated with high blood pressure. These findings suggest that hypertension is a serious complication in ADPKD patients and may lead to both an increased incidence of cardiovascular complications and more rapid progression of renal functional impairment.

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Hypertension is a common complication of many renal diseases, and autosomal dominant polycystic kidney disease (ADPKD) is no exception. It has been reported to occur in 13% to 81% of ADPKD patients at the time of their initial presentation¹⁻³. Increased blood pressure in ADPKD often precedes renal failure⁴. It is thought to play a major role in the progression of renal failure in these patients⁵. Also hypertension plays an important role in deaths because of cardiovascular catastrophes and there is strong evidence that hypertension plays an important role in ADPKD patients mortality^{6,7}.

Left ventricular hypertrophy and atheromatosis are consequences of the early onset of hypertension

in adults⁸ and are causes of high mortality because of cardiovascular accidents in ADPKD patients. Left ventricular hypertrophy in adults undoubtedly is correlated to early onset and duration of hypertension^{9,10}.

Renal structure (kidney size and cystic renal volumes) has been shown to play an important role on the pathogenesis of hypertension in ADPKD and on the renal function¹¹.

We have evaluated the frequency of hypertension in 200 ADPKD patients during a period of 15 years, and have studied its influence on renal function and left ventricular wall. We also have studied the role of renal cystic enlargement in initiating hypertension in ADPKD.

Patients and Methods

Two hundred ADPKD patients were divided in two groups: the first group of 92 patients with normal renal function, and the second group of 108 patients with chronic renal failure (serum creatinine level > 1.5 mg/dl).

Subjects were considered to have ADPKD if there were five or more bilateral renal cysts, and a family history for ADPKD¹².

Hypertension was defined as diastolic pressure greater than 90 mm Hg, a systolic pressure greater than 150 mm Hg in the sitting position, or a known history of hypertension on therapy¹³.

All patients had an abdominal ultrasound and a M-mode echocardiography. An Aloka SSD-720 instrument coupled with 3.75- or 5-MHz transducers was used for echocardiography. The measurements were made according to the recommendations of the American Society of Echocardiography¹⁴. Renal volume was calculated using the following formula for a modified ellipse: $4/3 \pi (\text{length}/2) (\text{anterior-posterior diameter}/4 + \text{width}/4)^2$ ¹¹.

The data were transmitted to a personal computer and were transformed to a dBase-compatible data format. Risk ratio was calculated using the Cox proportion hazards regression model. Kaplan-Meier product-limit survival curves were constructed. The log rank test was used to compare survival curves.

Differences between groups were determined by nominal regression analysis. All variables are presented as mean \pm one standard error. Differences were considered significant at the $p < 0.05$ levels.

Results

Hypertension was observed in 140 ADPKD patients (70%): 56 patients of the first group, with normal renal function (61%) and 84 patients of the second group, with chronic renal failure (79%). The male-female ratio between the hypertensive patients was 1.7:1 (88 males and 52 females) (Table 1). The mean age of hypertensive patients was 46 ± 4.6 years (range 18-70 years) (Table 2). In 56 patients the hypertension developed before the age of 35, while in 84 patients it was developed after the age of 35 (Table 3). In the Table 4 are given the mean and standard deviation of systolic and diastolic blood pressure of the patients with hypertension before the age of 35, patients with hypertension after the age of 35 and normotensives.

Subjects who developed hypertension before the age of 35 had poorer renal survival than those who developed hypertension after the age of 35 (50 years vs. 62 years; $p < 0.0001$; risk ratio = 4.3) (Figure 1). At the mean time, hypertensive patients had significantly higher serum creatinine levels compared with normotensive patients (2.3 mg/dl vs. 1.45 mg/dl; $p < 0.001$) (Table 5).

Table 1. The correlation of hypertension, renal function and gender

Renal function	Normal function (56 pts)		Chronic renal failure (84 pts)	
	Female	Male	Female	Male
No. of patients (140)	22	34	30	54

Table 2. Patients' demographic data

Patients	No. of patients	Mean age	Range	Standard Deviation
Total	200	48.5 ± 12.1 ys	18 - 70	5.1
Hypertensive	140	46 ± 4.6 ys	18 - 70	4.6
Normotensive	60	38 ± 2.6 ys	20 - 62	2.6

Table 3. The correlation of hypertension start and gender

Start of hypertension	Before age 35 (56 pts)		After age 35 (84 pts)	
	Female	Male	Female	Male
No. of patients (140)	22	34	30	54

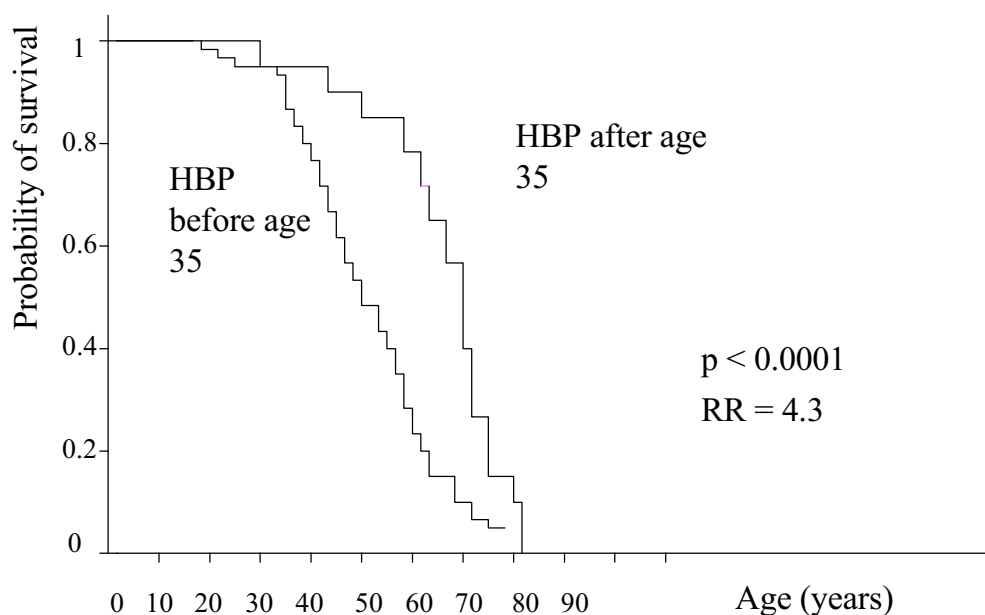


Fig. 1. Renal survival in pts diagnosed for HBP before age 35 vs. pts diagnosed for HBP after age 35

Left ventricular hypertrophy was present in 65 ADPKD patients (32.5%) (mean age 35.3 ± 2.1 years): 56 of the hypertensive patients had left ventricular hypertrophy (40%), and 9 of the normotensive patients had left ventricular hypertrophy (15%). Patients with LVH (with and without arterial hypertension) had a poorer renal sur-

vival than those without LVH (with and without arterial hypertension) ($p < 0.001$; risk ratio = 2.8) (Figure 2).

The kidney size (longitudinal diameter) was significantly greater in the hypertensive patients compared with those normotensive (16.36 ± 1.9 cm vs. 12.9 ± 1.06 cm, $p < 0.039$) (Table 6). Systolic and

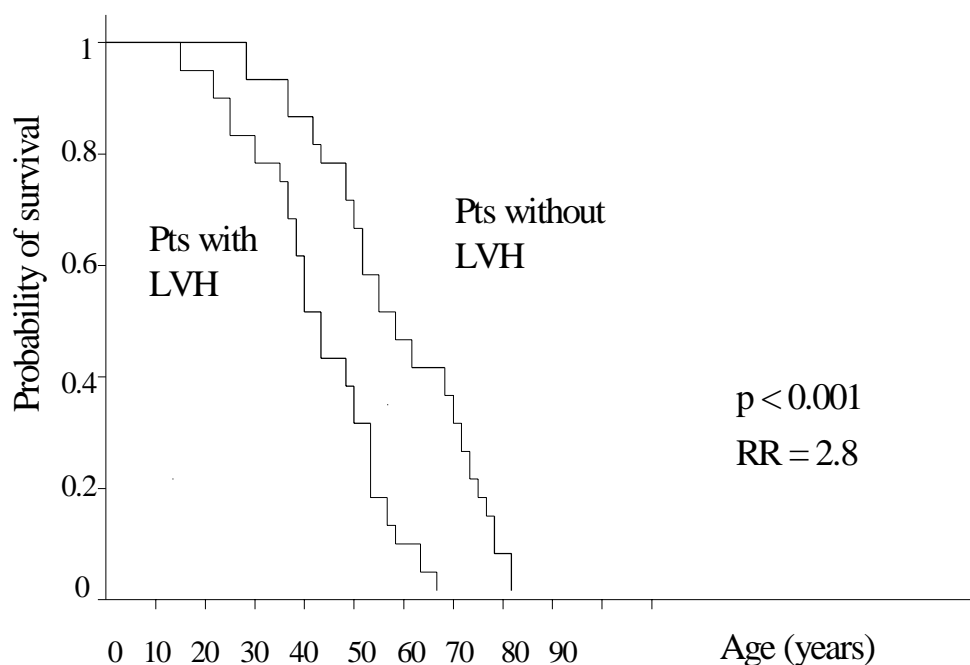


Fig. 2. Renal survival in pts with LVH vs. pts without LVH

Table 4. The correlation between systolic and diastolic blood pressure

Patients	Blood Pressure	Mean values (mmHg)	Standard Deviation (mmHg)
Hypertensive before age 35	Systolic	155.0	16.6
	Diastolic	97.25	4.06
Hypertensive after age 35	Systolic	150.5	11.1
	Diastolic	97.7	7.1
Normotensive	Systolic	141.2	13.7
	Diastolic	88.4	6.7

Table 5. Serum creatinine levels of hypertensives and normotensives patients

Patients	Mean values	Standard Deviation	Range
Hypertensive before age 35	2.3 mg/dl	1.6 mg/dl	1.5-5.3
	3.6 mg/dl	1.9 mg/dl	3.1-5.6
Hypertensive after age 35	1.8 mg/dl	1.5 mg/dl	1.3-3.2
	1.45 mg/dl	0.8 mg/dl	0.6-1.6

Table 6. The correlation of hypertension with kidney size

	Hypertensive pts	Normotensive pts	p
Kidney size	16.36±1.9 cm	12.9±1.06 cm	<0.039

Table 7. The correlation of hypertension with renal volume

	Hypertensive pts	Normotensive pts	p
Mean renal volume	590 ± 43 cm ³	365 ± 45 cm ³	0.005

diastolic blood pressure was correlated with kidney size ($r = 0.55$; $r = 0.63$). Also, the mean renal volume was significantly greater in the hypertensive patients versus the normotensive patients (590 ± 43 cm³ vs. 365 ± 45 cm³, $p < 0.005$) (Table 7).

Discussion

Hypertension is one of the most important and variable complications of ADPKD. In our ADPKD patients it was found in 70% of them in accord to the findings of the literature¹⁻³.

Also, according to the literature hypertension is more frequent in men than in women (66% and 41%, respectively)¹¹. The occurrence of hypertension in as many as 75% of ADPKD patients before renal dysfunction^{15,16} suggests that hypertension contributes to worsening renal function¹². In fact, in our

study our hypertensive ADPKD patients have a faster progression of renal disease than normotensive patients.

The early onset of hypertension may also confer an important cardiovascular risk¹⁷, especially if we consider that hypertension is an important factor of left ventricular hypertrophy, which has been shown to occur in 50% of hypertensive ADPKD patients, a proportion which is greater than that found in the general population. The mean age of our patients with LVH was about 36 years, which is considerably lower than that found in populations with essential hypertension. It was found even in 20% to 40% of normotensive ADPKD patients¹⁸. The more frequent presence of left ventricular hypertrophy in ADPKD patients than that found in the general population supports the notion that the blood pressure load to

the heart is elevated. LVH is considered to be a more valid index of blood pressure control than office blood pressure measurements. Undetected and poorly controlled hypertension is a serious complication in ADPKD that may lead to increased incidence of cardiovascular complications and more rapid progression of renal functional impairment.

It has been suggested that a relationship exists between structural deformation and hypertension in the ADPKD patients¹¹. In the present study, hypertension was associated with greater renal structural abnormalities. Specifically, the hypertensive ADPKD patients have greater renal volumes and cystic involvement than well-matched normotensive ADPKD patients. This supports the hypothesis that cyst decompression has been associated with a decrease in blood pressure and an improvement of renal function.

In conclusion, an early diagnosis and correct treatment of hypertension may be associated with improved cardiovascular and renal outcomes as well as increased patients survival in ADPKD.

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