The Relation of Hypertension, Renal Function and Cardiovascular Events in Autosomal Dominant Polycystic Kidney Disease

A. Idrizi[1], M. Barbullushi[1], A. Strakosha[1], E. Zaimi[2], S. Kodra[1], N. Thereska[1] and E. A. Petrela[3]

[1]Department of Nephrology, [2]Department of Cardiology, [3]Department of Biostatistique, University Hospital Center "Mother Teresa", Tirana, Albania; ² Institute for developement of water resources, Jaroslav Cerni, Belgrade, Serbia

Abstract

Backround. 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 the left ventricular wall.

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

Results. Hypertension was observed in 140 ADPKD patients (70%): 56 of the first group (61%) and 84 of the second group (79%). Subjects who developed hypertension before age 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 ventricular hypertrophy was present 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 ($p < 0.001$). Also, we have studied the role of renal cystic enlargement in initiating hypertension in ADPKD and on renal function.

Conslusions. We conclude that hypertension is a common complication in our ADPKD patients, considering it as 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. Along with the increased kidney volume, the highest blood pressure is observed. These findings suggest that hypertension is a serious complication in ADPKD that may lead to both, an increased incidence of cardiovascular complications and more rapid progression of renal functional impairment.

Key words: Autosomal dominant polycystic kidney disease, Hypertension, Left ventricular hypertrophy, Renal volume.

Introduction

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 presentation (1-3). Increased blood pressure in ADPKD often precedes renal failure (4). It is thought to play a major role in the progression of renal failure in these patients (5). Also hypertension plays an important role in deaths because of cardiovascular events and there is a 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 adults (8) and are causes of high mortality because of the cardiovascular accidents in ADPKD patients. Left ventricular hypertrophy in adults undoubtedly relates to an early onset and duration of hypertension (9, 10).

Renal structure (kidney size and cystic renal volumes) has been shown to play an important role in the pathogenesis of hypertension in ADPKD and in the renal function (11).

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: first group of 92 patients with normal renal function, and 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 at least five or more bilateral renal cysts, and a family history for ADPKD (12).

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 therapy (13).

All patients performed an abdominal ultrasound and M-mode echocardiography. 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 Echocardiography (14). Renal volume was calculated using the following formula for a modified ellipse: $4/3\ \pi$ (length/2) (anterior-posterior diameter/4 + 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

Correspodence to: Alma Idrizi, Department of Nephrology, University Hospital Center "Mother Teresa", Tirana, Albania; E-mail: alma_idrizi@yahoo.com

mean ± 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 first group, with normal renal function (61%) and 84 patients of second group, with chronic renal failure (79%), and male-female ratio between the hypertensive patients 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 was 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.

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

	Renal function		Start of hypertension	
Gender	Normal function (56 pts)	Chronic renal failure (84 pts)	Before age 35 (56 pts)	After age 35 (84 pts)
Female	22	30	22	30
Male	34	54	34	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)	
Gender	Female	Male	Female	Male
No. of patients (140)	22	34	30	54

Table 4. The correlation between systolic and diastolic blood pressure

Patients	Blood Pressure	Mean values (mmHg)	Standard Deviation (mmHg)
	Systolic	155.0	16.6
	Diastolic	97.25	4.06
	Systolic	150.5	11.1
	Diastolic	97.7	7.1
	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	2.3 mg/dl	1.6 mg/dl	1.5-5.3
before age 35	3.6 mg/dl	1.9 mg/dl	3.1-5.6
after age 35	1.8 mg/dl	1.5 mg/dl	1.3-3.2
Normotensive	1.45 mg/dl	0.8 mg/dl	0.6-1.6

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 same 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).

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

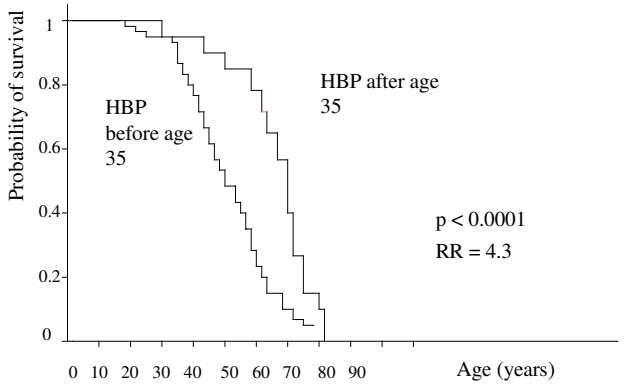
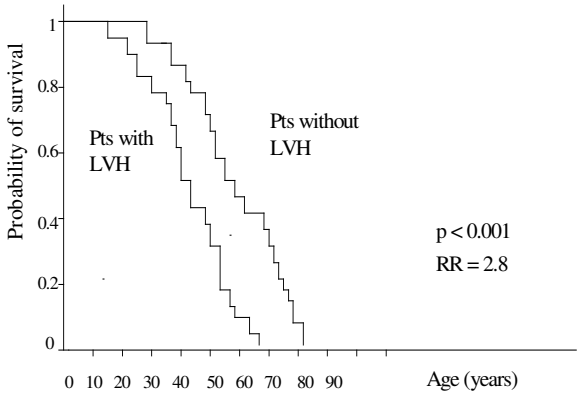


Table 6. The correlation of hypertension with kidney size and renal volume

	Hypertensive pts	Normotensive pts	p
Kidney size	16.36 ± 1.9 cm	12.9 ± 1.06 cm	<0.039
Mean renal volume	590 ± 43 cm^3	365 ± 45 cm^3	0.005

Left ventricular hypertrophy was present in 65 ADPKD patients (32.5%) (mean age 35.3 ± 2.1 years): 56/140 in the hypertensive (40%), and 9/60 in the normotensive group of patients (15%). Patients with LVH (with and without arterial hypertension) had a poorer renal survival when compared with those without LVH (with and without arterial hypertension) ($p < 0.001$; risk ratio = 2.8) (Figure 2).

Figure 2: Renal survival in pts with LVH vs. pts without LVH



The kidney size (longitudinal diameter) was significantly greater in the hypertensive patients compared with the normotensive ones (16.36 ± 1.9 cm vs. 12.9 ± 1.06 cm, $p < 0.039$) (Table 6). Systolic and diastolic blood pressure correlated with the kidney size ($r = 0.55$; $r = 0.63$). Also, mean renal volume was significantly greater in the

hypertensive patients compared to the normotensive patients (590 ± 43 cm^3 vs. 365 ± 45 cm^3, $p < 0.005$) (Table 7).

Discussion

Hypertension is one of the most important and variable complications of ADPKD. In our ADPKD patients it occurs in about 70%, which goes in line with the findings of the literature (1-3).

Furthermore, as reported in 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 ensuing of the renal dysfunction (15, 16) suggests that hypertension contributes to worsening of the renal function (12). Indeed, our study showed that our hypertensive ADPKD patients have a faster progression of renal disease than the normotensive patients.

The early onset of hypertension may also confer an important cardiovascular risk (17), especially if we consider that hypertension is an important factor of left ventricular hypertrophy. It has been shown to occur in 50% of hypertensive ADPKD patients, 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. In addition, LVH was found even in 20% to 40% of the normotensive ADPKD patients (18). The more frequent presence of left ventricular hypertrophy in ADPKD patients than that found in the general population supports the observation for the elevated blood pressure load to the heart. Since LVH is considered to be a more valid index of blood pressure control than the office blood pressure measurements, undetected and poorly controlled hypertension is a serious complication in ADPKD that may lead to an increased incidence of cardiovascular complications and more rapid progression of renal functional impairment.

Recently, a relationship between structural deformation and hypertension in the ADPKD patients has been suggested (11). In the present study, hypertension was associated with greater renal structural abnormalities. Especially, 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.

Conclusion

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

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