The risk factors for end-stage renal disease in autosomal dominant polycystic kidney disease

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Introduction

The progression to renal failure in autosomal dominant polycystic kidney disease
(ADPKD) patients is influenced by factors that are considered as risk factors (1-3). Age at the moment of diagnosis, gene linkage and hypertension are some of these risk factors. 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). Patients with these factors may be those for whom therapeutic intervention would be of great benefit. We have studied those subpopulations with ADPKD with highest risk for end-stage renal disease (ESRD).

Patients and methods

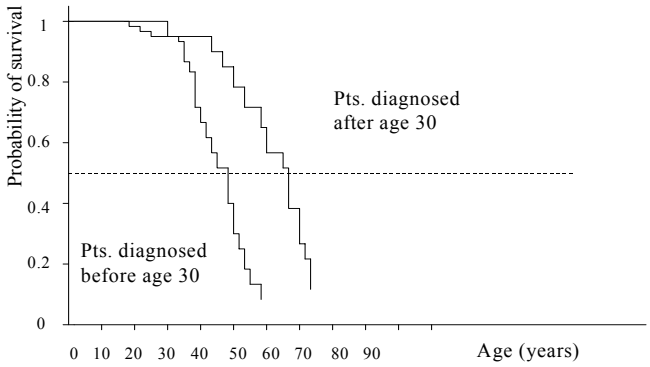
200 ADPKD patients (mean age 48.5±12.2 years) were studied retrospectively during 15 years. The selection of mean age of diagnosis before 30, hypertension before age 35 were chosen because these are the mean ages or approximate mean ages of these manifestation in this population (6). Gene linkage analysis was made in 36 patients from 13 families using a panel of markers for the locus of the putative PKD gene on the short arm of chromosome 16 (7). Absence of linkage to chromosome 16 markers defined a family as PKD2 (8).

All variables are presented as mean ± one standard error. Differences were considered significant at the $p < 0.05$ levels. Kaplan-Meier product-limit survival curves were constructed, and log rank test was used to compare the survival curves. Survival times were calculated as time to dialysis, transplantation or death (9). Risk ratio was calculated using the Cox proportion hazards model.

Results

55 pts entered in ESRD and 34 pts died. 60 patients were diagnosed before age 30 (mean age 34.7 ± 4.3 years), while 140 patients were diagnosed after age 30 (mean age 47.7 ± 5.2 years). Subjects who were diagnosed before age 30 had worse renal survival than those diagnosed after age 30 (48 years vs. 60 years; $p<0.0001$; risk ratio=3.6) (Fig. 1).

Figure 1. Renal survival in pts diagnosed before age 30 vs. pts diagnosed after age 30



30 patients were classified as PKD1 carriers (mean age 44.7 ± 4.8 years) and for 6 patients there wasn't a linkage with markers of chromosome 16, so they were classified as PKD2 carriers. PKD2 subjects had longer renal survival than PKD1 patients (median survival 58 vs. 41 yr; $p<0.001$; risk ratio=2.3).

Hypertension was observed in 140 ADPKD patients (70%). The mean age of hypertensive patients was 46±4.6 years (range 18-70 years). In 56 patients the hypertension was developed before the age of 35, while in 84 patients it was developed after the age of 35. 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) (Fig. 2). 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; $p < 0.001$) 55 patients entered in ESRD and 34 patients died.

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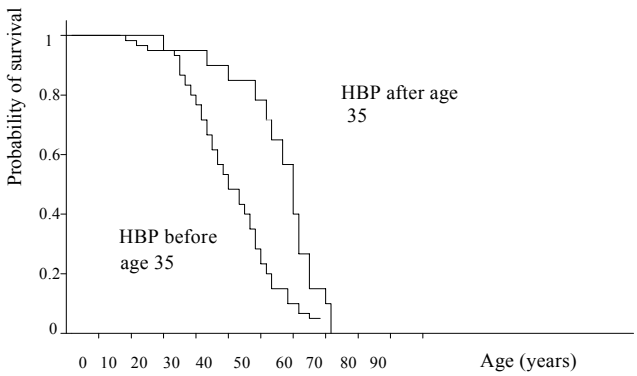
Figure 2. Renal survival in pts diagnosed for HBP before age 35 vs. pts diagnosed for HBP after age 35



Treated patients with urinary desinfectants had a significant lower frequency of urinary infections than those untreated ($p<0.001$). Moreover, treated patients demonstrated a slope of creatinine of 0.0007 vs. 0.0148 of untreated patients ($p<0.001$).

Conclusions

We conclude that the onset age of autosomal dominant polycyctic kidney disease influences its course; those subjects diagnosed later in life have more benign course disease than those diagnosed earlier. It is very important to diagnose and to treat hypertension and urinary infections early in the course of this disease.

References

1. Zeier M, Geberth S, Ritz E, et al. Adult dominant polycystic kidney disease-clinical problems. Nephron 1988; 49:177-183
2. Milutinovic J, Fialkow PJ, Aogodoa LY, et al. Autosomal dominant polycystic kidney disease: symptoms and clinical findings Q J Med 1984; 53:511-522
3. Gonzalo A, Rivera M, Quereda C, et al. Clinical features and prognosis of adult polycystic kidney disease. Am J Nephrol 1990; 10:470-474
4. Fick GM, Duley IT, Johnson AM, et al. The spectrum of autosomal dominant polycystic kidney disease in children. J Am Soc Nephrol 1994; 4:1654-1660
5. Zeier M, Fehrenbach P, Geberth S, et al. Renal histology of patients with autosomal dominant polycystic kidney disease with incipient or advanced renal failure. Kidney Int 1992; 42:1259-1265
6. Gabow PA, Ikle DW, Holmes JH. Polycystic kidney disease:
7. Prospective analysis of nonazotemic patients and family members. Ann Intern Med 1984; 101: 238-247
8. Reeders ST, Breuning MH, Davies KE, Nichols RD et al. A highly polymorphic DNA marker linked to adult polycystic kidney disease on chromosome 16. Nature 1985; 317: 542-544
9. Kimberling WJ, Kumar S, Gabow PA, Kenyon JB, Connolly CJ, Somlo ST. Autosomal dominant polycystic kidney disease: Localisation of the second gene to chromosome 4q 13-123. Genomics 1993; 18: 467-472
10. Gabow PA, Johnson AM, Kaehny WD et al.: Factors affecting the progression of renal disease in autosomal dominant polycystic kidney disease. Kidney Int 1992; 41: 1311-1319