Original Article

Retrospective Analysis of Factors Affecting the Progression of Chronic Renal Failure in Adult Polycystic Kidney Disease

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ABSTRACT. Autosomal dominant polycystic kidney disease (ADPKD) is the commonest congenital cystic renal disease. Factors such as hypertension, urinary tract infection, hematuria, and proteinuria may affect the progression to chronic renal failure in ADPKD patients. Therapeutic interventions, such as the use of angiotensin converting enzyme inhibitors (ACEI) or diet modification, may impact the natural progression of the disease. We aim in this study to review a registry of ADPKD patients in order to compare the slow and fast progressors and identify possible predictors of progression and interventions that slow the progression of this disease. Sheffield Kidney Institute (SKI), one of the largest kidney institutes in Northern Europe, has registered a large number of ADPKD patients since 1981. SKI’s computer network contains a wide range of information on these patients. We selected 94 adult polycystic patients from the SKI for retrospective analysis of factors affecting progression to chronic renal failure. Patients who doubled their s. creatinine in ≤ 36 months were considered fast progressors (FP), while those who doubled their s. creatinine in > 36 months were regarded as slow progressors (SP). There were 70 patients in the FP group and 24 patients in the SP group. A third group of 137 patients consisted of non-progressors (NP) who had stable s. creatinine levels during the same period. We found that the incidence of hypertension, UTI, macroscopic and microscopic hematuria, and overt proteinuria in the FP group was higher than in the SP and NP groups. Modification of some factors, such as hypertension and UTI, may decrease the rate of the deterioration of renal function.

Key Words: Adult, Polycystic, Kidney, Disease, Hypertension, Hematuria, Proteinuria, Urinary, Infection.

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Introduction

Autosomal dominant polycystic kidney disease (ADPKD) is the commonest congenital cystic renal disease. However, its pathogenesis and progression to chronic renal failure are not
clearly understood. Factors such as hypertension, urinary tract infection, hematuria, and proteinuria may affect the progression to chronic renal failure in ADPKD patients. 1-9

Therapeutic interventions, such as the use of angiotensin converting enzyme inhibitors (ACEI) or diet modification, may impact the natural course of progression of the disease. 10-14

We aim in this study to review a registry of ADPKD patients in order to compare the slow and fast progressors and identify possible predictors of progression and interventions to slow down the progression of this disease.

Materials and Methods

Sheffield Kidney Institute (SKI), one of the largest kidney institutes in Northern Europe, has registered a large number of ADPKD patients since 1981. SKI is a computer network that contains a wide range of information on these patients. 94 adult polycystic patients were selected from the SKI for retrospective analysis of factors affecting progression to chronic renal failure. Patients who doubled their s. creatinine in < 36 months were considered fast progressors (FP), while those who doubled the s. creatinine in over 36 months were regarded as slow progressors (SP). A third group consisted of non progressors (NP) whose renal function remained stable during the study period. There were 70 patients in the FP group, 24 patients in the SP group, and 137 patients in NP group.

The effects of gender, documented active and recurrent urinary tract infection (UTI), gross and microscopic hematuria, >300mg/24hrs or 2+ proteinuria, hypertension (defined as systolic values of ≥160 mmHg and a diastolic values ≥ 90mmHg during the time of progression prior to any replacement therapy), and use of angiotensin converting enzyme inhibitors on progression in the study groups were analyzed.

The mean systolic and mean diastolic pressures were calculated for each patient from at least three readings before therapeutic intervention. The duration of hypertension prior to any replacement therapy was also calculated. In order to evaluate the severity of the hypertension, the number of drugs used to control hypertension was also compared among the study groups.

Statistical Analysis

We compared the groups by using non-parametric tests. The significance of the differences of the continuous variables (i.e. blood pressure) between the study groups was tested by the Wilcoxon Ranksum test. The significance of discontinuous variables (UTI, hematuria, and drugs) among the study groups were estimated by the Chi-squared test. The P value was set as significant if P< 0.05.

Results

Table 1 shows the characteristics and risk factors of progression in the different study groups. There was no significant difference in the gender composition among the study groups. A total of 29 patients in the progressors group had UTIs, mostly in the FP group; 11 patients had recurrent UTIs. The prevalence of UTI in the NP group was 18 patients (13.1%). There was a significant statistical difference in the prevalence of UTI between the FP and NP groups (p value <0.01). The prevalence of proteinuria was 5.7% and 4.1% in the fast and slow progressors, respectively. In the NP group, the incidence of proteinuria was 2.9%. None of these patients had proteinuria of more than 1 g/24h. Because of this very small number, statistical tests were not performed. The prevalence of microscopic hematuria was 25.7%, 29%, and 8.7% in the FP, SP, and NP groups, respectively. On
the other hand, the incidence of macroscopic hematuria in the FP group was 7.1%. This was higher than in the SP and NP groups, where the prevalence of macroscopic hematuria was 4.1% and 1.5%, respectively. However, a statistically significant difference was found between the FP and NP groups (p<0.05). The prevalence of microscopic hematuria was not significantly different between the FP and SP groups but was significant between both of these and the NP group (p <0.01). The prevalence of recurrent hematuria was higher in the FP group than in the other groups. In the FP and SP groups, 81 out of 94 (86%) patients were hypertensive. The prevalence of hypertension was significantly lower in the NP group, since only 55 out of 137 (40%) patients were hypertensive, (p <0.001). The mean arterial pressure, mean systolic pressure, and mean diastolic pressure in the FP group were found to be slightly higher than in the SP group, but this was statistically not significant. Furthermore, the difference in duration of hypertension between the FP and SP groups was not significant. The prevalence of drug resistant hypertension (requiring 3 or more antihyper-tensives for satisfactory control of BP) was found to be slightly higher in FP group than in the SP and the NP groups. However, there was no statistically significant difference in the use of multiple antihypertensives or ACEIs between the FP and SP groups. Because of lack of data, the blood pressure values of non progressors could not be obtained.

**Discussion**

With the limitations inherent in retrospective analysis, the factors affecting the progression of chronic kidney disease (CKD) in ADPKD were analyzed. We found that the prevalence of UTI, macroscopic and microscopic hematuria, and overt proteinuria in the FP group was higher than in the SP and NP groups. This suggests an association between these factors and the progression of CKD in ADPKD patients.
An association with the fast progression of CKD in ADPKD patients who had macro-hematuria, especially before the age of 30 years, has been shown by other studies. The same result was obtained for overt proteinuria.

The prevalence of hypertension was significantly higher in the FP and SP groups than in the NP group. This implies that hypertension may be an important factor for the progression of CKD in ADPKD patients. Other investigators also observed the deleterious effect of hypertension on the progression of CKD when they compared hypertensives with and without any interventions.

The utilization of ACEIs was not significantly different between the FP and SP groups. This is largely due to a small number of patients in our study. The observations described in the MDRD study suggested a low benefit of the ACEIs in the prevention of progression of CKD in ADPKD patients.

We found no gender effect on the progression of CKD in ADPKD patients after the GFR falls below 25 ml/min/1.73m². The MDRD study reported the same conclusion on the gender effect on CKD progression.

We conclude that the progression of CKD in ADPKD patients can be affected by several factors, such as hypertension, proteinuria, hematuria, and UTI. These factors may result in the rapid deterioration of renal function and progression towards end-stage renal failure. Modification of some factors, such as hypertension and UTI, may decrease the rate of the deterioration of renal function.

References