석 사 학 위 논 문

Clinical Characteristics and Risk Factors for Kidney Failure in Patients with Autosomal Dominant Polycystic Kidney Disease

계 명 대 학 교 대 학 원

의   학   과

박   한   일

지 도 교 수   진 규 복

2 0 2 2 년 8 월

Clinical Characteristics and Risk Factors for Kidney Failure in Patients with Autosomal Dominant Polycystic Kidney Disease

지도교수 진 규 복

이 논문을 석사학위 논문으로 제출함

2 0 2 2 년 8 월

계 명 대 학 교 대 학 원

의학과 내과학 전공

박 한 일

박한일의 석사학위 논문을 인준함

주 심 박 우 영

부 심 진 규 복

부 심 백 진 혁

계 명 대 학 교 대 학 원

2 0 2 2년 8월

Acknowledgements

Table of Contents

List of Tables

List of Figures

1. Introduction

Autosomal dominant polycystic kidney disease (ADPKD) is an inherited and progressive condition with the formation of numerous fluid-filled kidney cysts resulted from mutations in the PKD1 and PKD2 genes (1). These cysts press the adjacent renal tissue, and lead to the ongoing loss of kidney function (2). By the age of 65 years, 45%-70% of patients with ADPKD proceed to end-stage renal disease (ESRD) (3). In Korea, ADPKD is the fourth principal cause of ESRD (4). It also involves other organs and manifests as cardiovascular diseases, cerebral aneurysms, or colon diverticula (5).

In the 1990s, a few studies regarding therapeutic interventions using taxol (6), methylprednisolone (7), and lovastatin (8) to delay the progression of ADPKD in animal models were published. Recently, phase 3 clinical trials concerning the effect of tolvaptan on ADPKD progression were conducted (9-11). These trials demonstrated a sustained disease-modifying effect of tolvaptan on the estimated glomerular filtration rate (GFR). Hence, an ADPKD outcome model was developed for implementing tolvaptan treatment (12,13).

The cause and pathogenesis of ADPKD have been well identified, but there is no standard therapy to slow its progression, despite the development of various therapeutic approaches. Hence, when treating ADPKD, it is helpful to understand the factors affecting disease progression. The present study discussed the clinical features of patients with ADPKD and the risk factors associated with its progression.

2. Materials and Methods

This study enrolled 350 adult patients with ADPKD who received medical care at Keimyung University Dongsan Medical Center between January 1989 and August 2018. ADPKD was defined as more than two cysts in an unilateral kidney or a single cyst in each kidney in patients aged < 30 years, more than two cysts in each kidney in patients aged 30-59 years, and more than four cysts in each kidney in patients older than 60 years (14). Subjects who had insufficient data regarding certain factors were excluded from the analysis. Finally, the medical records of 288 patients with ADPKD who received care at the center were analyzed retrospectively.

Demographic information that included age at diagnosis, sex, family history of ADPKD, hypertension, diabetes mellitus, cerebral aneurysm, cerebrovascular accident (CVA), and cardiovascular disease were collected. Furthermore, clinical outcomes, such as cyst complication, which included infection and hemorrhage, number of patients that progressed to ESRD, number of patients receiving renal replacement therapy (RRT), duration from diagnosis to RRT, mortality, and the cause of mortality were investigated. Kidney failure was defined as ESRD requiring RRT, and the primary outcome was the kidney survival rates. The criterion for the age at diagnosis was selected as 30 years because studies regarding the linkage between the PKD1 gene and ultrasonography results found a 100% penetrance of renal cysts after the age of 30 years (14,15). The baseline serum creatinine levels over the upper normal limit were considered >1.3 mg/dL according to the reference value of the center.

Numerical values are marked as mean ± standard deviation (SD), and

categorized variates are represented by numbers and percentages. Overall and kidney survival rates were calculated with Kaplan-Meier survival analysis. In addition, log rank test made a comparison between the survival curves. Clinical risk factors for kidney failure were investigated using the Cox proportional hazards model. Furthermore, multivariable analysis was performed as forward conditional method, using the variables that showed significant results in univariable analysis. Statistical analyses were conducted with the version 28 of the IBM SPSS Statistics for Windows. A P value of <.05 was regarded as statistical significance.

The institutional review board of Dongsan Medical Center approved the present study (DSMC 2022-03-008).

3. Results

The mean age at the time of diagnosis was 43.1 ± 14.1 years, and there were 146 males (50.7%). A family history of ADPKD was identified in 113 cases (39.2%). Overall, Hypertension was found in 197 patients (68.4%) and 11 patients (3.8%) had cerebral aneurysm. CVA was detected in 35 patients (12.1%), which included 11 cases of cerebral hemorrhage and 24 cases of cerebral infarction. Cardiovascular disease developed in 17 patients (5.9%). Table 1 displays the demographic data of patients with ADPKD.

During the follow-up period, 28 patients (9.7%) died. The most common cause of death was infection (42.9%), and the second most common cause was sudden cardiac death (25.0%). Cyst complications such as cyst infection and hemorrhage developed in 43 patients (14.9%). In total, 132 patients (45.8%) advanced to ESRD and 104 patients (36.1%) required RRT. The mean duration from diagnosis to RRT was 110.8 ± 93.9 months. Table 2 shows the clinical outcomes of the patients.

There were 104 cases of kidney failure, which indicated the cases of ESRD requiring RRT. In univariable Cox analysis, age at diagnosis after 30 years (odd's ratio [OR], 3.648; 95% confidence interval [CI], 1.771-7.517; $p < 0.001$), baseline serum creatinine levels (OR, 1.347; 95% CI, 1.281-1.418; $p < 0.001$), hypertension (OR, 1.596; 95% CI, 1.008-2.525; $p = 0.046$), cardiovascular disease (OR, 2.106; 95% CI, 1.095-4.049; $p = 0.026$), and cyst infection (OR, 2.671; 95% CI, 1.618-4.411; $p < 0.001$) significantly increase the risk for kidney failure. In multivariable Cox test, the independent risk factors for kidney failure were age at diagnosis after 30 years (OR, 2.737; 95%

CI, 1.320-5.675; *p* = 0.007), baseline serum creatinine levels (OR, 1.326; 95% CI, 1.259-1.396; *p* < 0.001), and cyst infection (OR, 2.065; 95% CI, 1.242-3.433; *p* = 0.005). Table 3 shows the clinical risk factors for kidney failure in patients with ADPKD.

Figure 1 presents the overall survival rates wherein the 1-year survival rate was 97.3%, 5-year survival rate was 89.9%, and 10-year survival rate was 87.8%. Figure 2 shows the kidney survival rates according to age at diagnosis. Patients diagnosed with ADPKD after 30 years old showed worse kidney survival rates than those diagnosed before 30 years old (*p* < 0.001). Figure 3 shows the kidney survival rates according to the baseline serum creatinine levels. Patients with baseline serum creatinine levels over the upper normal limit showed worse kidney survival rates compared with those having baseline serum creatinine levels below the upper normal limit (*p* < 0.001). Figure 4 shows the kidney survival rates according to cyst infection. Patients with cyst infection showed worse kidney survival rates compared with those who had no cyst infection (*p* < 0.001).

Table 1. Demographics of Patients with ADPKD

Variables	All patients (n = 288)
Age at diagnosis (years)	43.1 ± 14.1
Male gender (%)	146 (50.7)
Family history of ADPKD (%)	113 (39.2)
Hypertension (%)	197 (68.4)
Diabetes mellitus (%)	21 (7.3)
Cerebral aneurysm (%)	11 (3.8)
Cerebral vascular accident (%)	35 (12.1)
Cerebral hemorrhage	11 (31.4)
Cerebral infarction	24 (68.6)
Cardiovascular disease (%)	17 (5.9)

Values are expressed as mean ± SD, n (%).

ADPKD, autosomal dominant polycystic kidney disease

Table 2. Clinical Outcomes of The Patients with ADPKD

Variables	All patients (n = 288)
Cyst complication (%)	43 (14.9)
Cyst infection	28 (65.1)
Cyst hemorrhage	15 (34.9)
ESRD (%)	132 (45.8)
RRT (%)	104 (36.1)
Hemodialysis	74 (71.1)
Peritoneal dialysis	2 (1.9)
Kidney transplantation	28 (26.9)
Duration from diagnosis to RRT (months)	110.8 ± 93.9
Follow-up duration (months)	117.1 ± 102.1
Mortality (%)	28 (9.7)
Causes of mortality (%)	
Infection	12 (42.9)
Cyst infection	3 (10.7)
Urinary tract infection	2 (7.1)
Pneumonia	2 (7.1)
Catheter-related infection	2 (7.1)
Bacterial meningitis	1 (3.6)
Pseudomembranous colitis	1 (3.6)
Colitis	1 (3.6)
Cerebral hemorrhage	1 (3.6)
Sudden cardiac death	7 (25.0)
Pulmonary thromboembolism	2 (7.1)
Others	6 (21.4)

Values are expressed as mean ± SD, n (%).

ADPKD, autosomal dominant polycystic kidney disease; ESRD, end-stage renal disease; RRT, renal replacement therapy

Table 3. Clinical Risk Factors for Kidney Failure in Patients with
ADPKD

Variables	Univariable			Multivariable		
	OR	95% CI	P value	OR	95% CI	P value
Age at diagnosis after 30 years	3.648	1.771-7.517	<0.001	2.737	1.320-5.675	0.007
Baseline serum creatinine levels	1.347	1.281-1.418	<0.001	1.326	1.259-1.396	<0.001
Male gender	0.878	0.593-1.301	0.517			
Hypertension	1.596	1.008-2.525	0.046	1.064	0.660-1.716	0.799
Diabetes mellitus	1.832	0.979-3.428	0.058			
Cerebral aneurysm	2.012	0.976-4.147	0.058			
Cardiovascular disease	2.106	1.095-4.049	0.026	0.852	0.410-1.767	0.666
Cyst infection	2.671	1.618-4.411	<0.001	2.065	1.242-3.433	0.005
Cyst hemorrhage	0.907	0.369-2.230	0.832			

OR, odds ratio; CI, confidence interval; ADPKD, autosomal dominant polycystic kidney disease
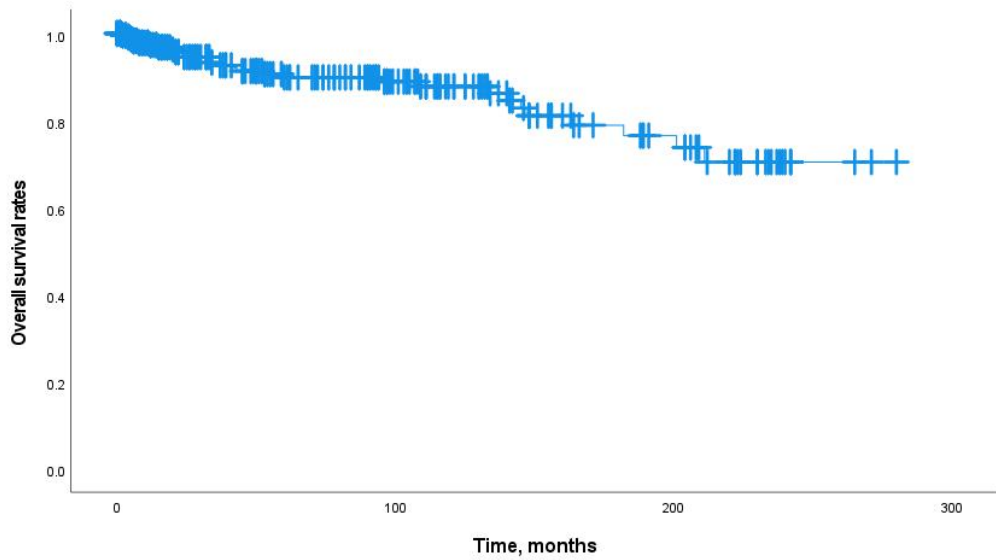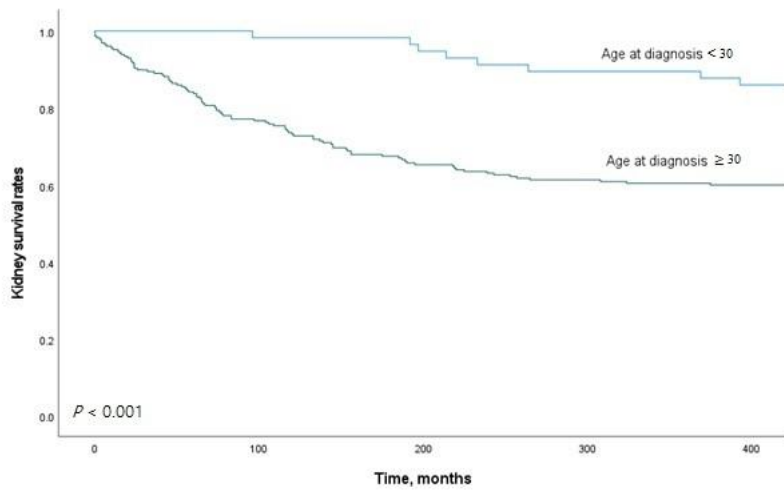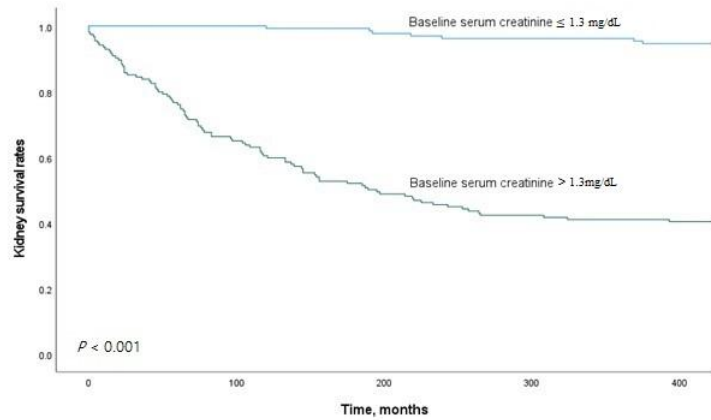
Figure 1. Overall survival rates in patients with ADPKD.
ADPKD, autosomal dominant polycystic kidney disease.

Figure 2. Kidney survival rates according to age (years) at
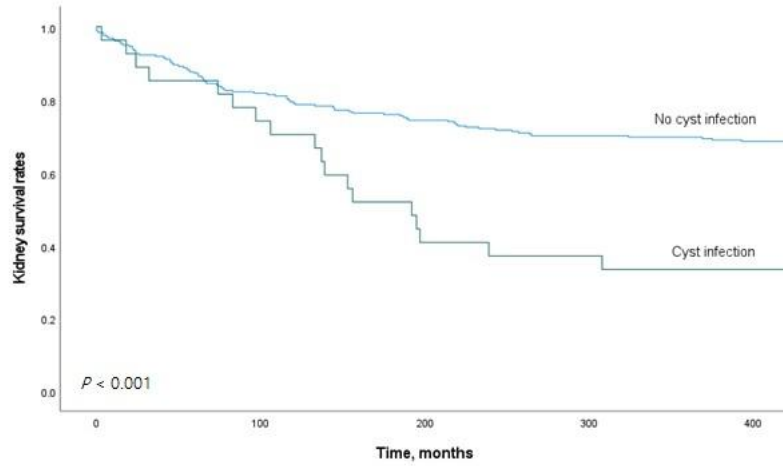diagnosis.

Figure 3. Kidney survival rates according to baseline serum
creatinine levels (mg/dL).

Figure 4. Kidney survival rates according to cyst infection.

4. Discussion

ADPKD is the most common inherited kidney disease with a single gene mutation (16). The major problem of this condition is the inevitably decreasing renal function of the patients, which ultimately results in ESRD requiring RRT. However, standard treatments have not yet been established. Hence, it is important to predict the kidney outcomes and outline the clinical risk factors for such patients. Age at diagnosis after 30 years, baseline serum creatinine levels, and cyst infection are the independent risk factors for kidney failure, as found in this study.

The demographics of the current study group were similar to that of another Korean cohort study that enrolled 364 patients with ADPKD from 9 hospitals (17). In the present study, the mean age at the time of diagnosis was 43.1 ± 14.1 years, whereas in the other Korean cohort study, it was 37.9 ± 10.6 years. In both the studies, the male-to-female ratio was almost equal. A large proportion of patients had hypertension: 68.4% in this study versus 87.6% in the other Korean cohort study.

Several studies have been conducted for predicting kidney survival in patients with ADPKD. Gall et al. proposed a predicting renal outcome in ADPKD scoring system ranging from 0 to 9 points: being male as 1 point, hypertension before 35 years old as 2 points, first urologic event (gross hematuria, flank pain, and cyst infection) before 35 years old as 2 points, PKD2 mutation as 0 point, non-truncating PKD1 mutation as 2 points, and truncating PKD1 mutation as 4 points. There are 3 risk groups for the progression of ESRD: 0-3 points as low risk, 4-6 points as intermediate risk, and 7-

9 points as high risk, with corresponding median ages for the onset of ESRD as 70.6, 56.9, and 49 years, respectively (18). Another study presented the total kidney volume (TKV) as a powerful and independent predictor for developing advance of chronic kidney disease (CKD) (19). Moreover, Johnson et al. suggested age at diagnosis before 30 years, male gender, PKD1 gene mutation, hypertension before 35 years old, gross hematuria before 30 years old as risk factors for ESRD in patients with ADPKD (20).

A controversial issue concerning age exists, with different studies presenting contrary results. Johnson et al. reported that patients diagnosed with ADPKD before 30 years old are diagnosed with ESRD earlier than those diagnosed with ADPKD after 30 years old (risk ratio, 3.2; 95% CI, 2.3-4.5; p < 0.0001) (20). Since seven tenths of young patients with ADPKD are symptomatic, the symptoms are often likely to provoke the diagnosis. Therefore, these patients diagnosed with ADPKD earlier can experience a more severe course of disease. On the contrary, Ozkok et al. suggested age as a significant and independent factor for predicting the advanced stages of CKD (hazard ratio, 1.05; 95% CI, 1.01-1.09; p = 0.01) (21). Similar to the latter study, the risk for kidney failure was greater in the patients who were diagnosed later in the present study. Owing to good medical accessibility in Korea, the progression of ADPKD to ESRD may be slow because of close monitoring and management following early diagnosis. However, further researches are needed to clarify the influence of age on kidney prognosis.

Recently, a number of studies have reported that baseline TKV is the most important predictor of the disease progression (22-24). Numerous researches have suggested an inverse relationship between TKV and GFR (25,26). Estimated GFR is inversely proportional to serum

creatinine levels in accordance with the Modification of Diet in Renal Disease study equation. Therefore, a direct proportional relationship between TKV and serum creatinine levels exists. In the current study, multivariable analysis revealed that baseline serum creatinine levels are a significant and independent risk factor for kidney failure. There are no data regarding the TKV of the study group, but the relationship between baseline serum creatinine levels, TKV, and kidney prognosis may be established.

During the lifetime, 30%-50% of patients with ADPKD experience urinary tract infections (UTIs), with cyst infection and acute pyelonephritis being the most common causes of upper UTIs in such patients (27). Several studies have reported that multiple UTIs are related to a more faster decrease in kidney function. In a retrospective study, the fast progressor group defined by the doubling of serum creatinine levels within 36 months showed a greater prevalence of UTIs than the slow progressor group (28). Another study presented that chronic asymptomatic pyuria and overt UTIs were related to a rapid decline in kidney function. The researchers proposed that UTIs might be a direct cause of cystogenesis (29). When renal tubular epithelial cells were subjected to ischemic damage or nephrotoxic injury, abnormal cell proliferation and cyst formation appeared (30,31). Furthermore, other studies have reported the influence of tumor necrosis factor-alpha (TNF-α) on cyst formation and lipopolysaccharide on peritubular capillary dysfunction (32,33). Hence, inflammation provoked by UTIs may result in cell proliferation, cyst formation, fibrosis, and renal function deterioration. Similar to the results of former studies, cyst infection appeared to be an independent risk factor for kidney failure in this study.

The present study has few limitations. TKV has been suggested as a significant predictor of ADPKD in several studies (19,34,35). However, in the absence of magnetic resonance imaging stereology and automated methods for TKV determination, data regarding TKV cannot be collected. In addition, PKD1 and PKD2 gene mutations have frequently been presented as a risk factor in various studies (20,36,37). Since genetic testing is rarely performed, this could not be further analyzed. Moreover, data regarding the treatment of patients have not been investigated.

In conclusion, age at diagnosis after 30 years, baseline serum creatinine levels, and cyst infection were found to be the significant and independent risk factors for kidney failure. Early diagnosis and close observation for the onset of cyst infection may be helpful in delaying the advance to ESRD in patients with ADPKD.

5. Summary

ADPKD is a progressive renal disease resulting in ESRD that requires RRT in numerous patients. Since its standard treatment is not yet established, it is important to understand the risk factors for kidney failure in patients with ADPKD. The medical records of 288 patients with ADPKD at Keimyung University Dongsan Medical Center were retrospectively analyzed using the Cox proportional hazards model and Kaplan-Meier survival analysis. Age at diagnosis after 30 years, baseline serum creatinine levels, and cyst infection were the significant and independent risk factors for kidney failure in the current study. To delay the progression to kidney failure, early diagnosis and close observation for the onset of cyst infection are vital.

References

1. Chapman AB, Devuyst O, Eckardt KU, Gansevoort RT, Harris T, Horie S, et al.: Autosomal-dominant polycystic kidney disease (ADPKD): executive summary from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. Kidney International 2015 Jul; 88(1): 17-27.

2. Churchill DN, Bear JC, Morgan J, Payne RH, McManamon PJ, Gault MH: Prognosis of adult onset polycystic kidney disease re-evaluated. Kidney International 1984 Aug; 26(2): 190-3.

3. Lentine KL, Xiao H, Machnicki G, Gheorghian A, Schnitzler MA: Renal function and healthcare costs in patients with polycystic kidney disease. Clinical Journal of the American Society of Nephrology 2010 Aug 1; 5(8): 1471-9.

4. Jin DC, Han JS: Renal replacement therapy in Korea, 2012. Kidney Research and Clinical Practice Elsevier 2014; 33: 9-18.

5. Gabow PA: Autosomal Dominant Polycystic Kidney Disease. New England Journal of Medicine 1993 Jul 29; 329(5): 332-42.

6. Woo DD, Miao SY, Pelayo JC, Woolf AS: Taxol inhibits progression of congenital polycystic kidney disease. Nature 1994; 368: 750-3.

7. Gattone VH, Cowley BD, Barash BD, Nagao S, Takahashi H, Yamaguchi T, et al.: Methylprednisolone Retards the Progression of

Inherited Polycystic Kidney Disease in Rodents. American Journal of Kidney Diseases 1995; 25(2): 302-13.

8. Gile RD, Cowley BD, Gattone VH, O'donnell MP, Swan SK, Grantham JJ: Effect of Lovastatin on the Development of Polycystic Kidney Disease in the Han:SPRD Rat. American Journal of Kidney Diseases 1995; 26(3): 501-7.

9. Torres VE, Meijer E, Bae KT, Chapman AB, Devuyst O, Gansevoort RT, et al.: Rationale and design of the TEMPO (tolvaptan efficacy and safety in management of autosomal dominant polycystic kidney disease and its outcomes) 3-4 study. American Journal of Kidney Diseases 2011 May; 57(5): 692-9.

10. Torres VE, Chapman AB, Devuyst O, Gansevoort RT, Perrone RD, Koch G, et al.: Tolvaptan in Later-Stage Autosomal Dominant Polycystic Kidney Disease. New England Journal of Medicine 2017 Nov 16; 377(20): 1930-42.

11. Torres VE, Chapman AB, Devuyst O, Gansevoort RT, Perrone RD, Dandurand A, et al.: Multicenter, open-label, extension trial to evaluate the long-term efficacy and safety of early versus delayed treatment with tolvaptan in autosomal dominant polycystic kidney disease: The TEMPO 4:4 Trial. Nephrology Dialysis Transplantation 2018 Mar 1; 33(3): 477-89.

12. McEwan P, Bennett WH, Ong ACM, Ørskov B, Sandford R, Scolari F, et al.: A model to predict disease progression in patients with autosomal dominant polycystic kidney disease (ADPKD): The ADPKD

Outcomes Model. BMC Nephrology 2018 Feb 13; 19(1): 1-12.

13. Bennett H, McEwan P, Hamilton K, O'Reilly K: Modelling the long-term benefits of tolvaptan therapy on renal function decline in autosomal dominant polycystic kidney disease: An exploratory analysis using the ADPKD outcomes model. BMC Nephrology 2019 Apr 23; 20(1): 1-9.

14. Ravine D, Sheffield L, Danks DM, Gibson RN, Walker RG, Kincaid-Smith P: Evaluation of ultrasonographic diagnostic criteria for autosomal dominant polycystic kidney disease 1. The Lancet 1994 Apr 2; 343(8901): 824-7.

15. Elles RG, Hodgkinson KA, Mallick NP, O'Donoghue DJ, Read AP, Rimmer S, et al.: Diagnosis of adult polycystic kidney disease by genetic markers and ultrasonographic imaging in a voluntary family register. Journal of Medical Genetics 1994; 31(2): 115-20.

16. Garcia IC, Torres VE, Offord KP, Holley KE, Beard CM, Kurland LT: Epidemiology of Adult Polycystic Kidney Disease, Olmsted County, Minnesota: 1935-1980. American Journal of Kidney Diseases 1983 May 1; 2(6): 630-9.

17. Kim H, Koh J, Park SK, Oh KH, Kim YH, Kim Y, et al.: Baseline characteristics of the autosomal-dominant polycystic kidney disease sub-cohort of the KoreaN cohort study for outcomes in patients with chronic kidney disease. Nephrology 2019 Apr 1; 24(4): 422-9.

18. Gall EC, Audrézet MP, Rousseau A, Hourmant M, Renaudineau E, Charasse C, et al.: The PROPKD score: A new algorithm to predict renal survival in autosomal dominant polycystic kidney disease. Journal of the American Society of Nephrology 2016 Mar 1; 27(3): 942-51.

19. Yu ASL, Shen C, Landsittel DP, Harris PC, Torres VE, Mrug M, et al.: Baseline total kidney volume and the rate of kidney growth are associated with chronic kidney disease progression in Autosomal Dominant Polycystic Kidney Disease. Kidney International 2018 Mar 1; 93(3): 691-9.

20. Johnson AM, Gabowt PA: Identification of Patients with Autosomal Dominant Polycystic Kidney Disease at Highest Risk for End-Stage Renal Disease. Journal of the American Society of Nephrology 1997; 8(10): 1560-7.

21. Ozkok A, Akpinar TS, Tufan F, Kanitez NA, Uysal M, Guzel M, et al.: Clinical characteristics and predictors of progression of chronic kidney disease in autosomal dominant polycystic kidney disease: A single center experience. Clinical and Experimental Nephrology 2013 Jun; 17(3): 345-51.

22. Grantham JJ, Chapman AB, Torres VE: Volume progression in autosomal dominant polycystic kidney disease: the major factor determining clinical outcomes. Clinical journal of the american society of Nephrology 2006; 1(1): 148-57.

23. Chapman AB, Bost JE, Torres VE, Guay-Woodford L, Bae KT,

Landsittel D, et al.: Kidney volume and functional outcomes in autosomal dominant polycystic kidney disease. Clinical Journal of the American Society of Nephrology 2012 Mar 1; 7(3): 479-86.

24. Xue C, Zhou C, Mei C: Total kidney volume: the most valuable predictor of autosomal dominant polycystic kidney disease progression. Kidney International 2018 Mar 1; 93(3): 540-2.

25. Thomsen HS, Madsen JK, Hess Thaysen J, Damgaard-Petersen K: Urologic Radiology Volume of Polycystic Kidneys During Reduction of Renal Function. Urologic radiology 1981; 3(2): 85-9.

26. Fick-Brosnahan GM, Belz MM, McFann KK, Johnson AM, Schrier RW: Relationship between renal volume growth and renal function in autosomal dominant polycystic kidney disease: A longitudinal study. American Journal of Kidney Diseases 2002 Jun 1; 39(6): 1127-34.

27. Chebib FT, Torres VE: Autosomal Dominant Polycystic Kidney Disease: Core Curriculum 2016. American Journal of Kidney Diseases 2016 May 1; 67(5): 792-810.

28. Ahmed ER, Tashkandi MA, Nahrir S, Maulana A: Retrospective Analysis of Factors Affecting the Progression of Chronic Renal Failure in Adult Polycystic Kidney Disease. Saudi Journal of Kidney Diseases and Transplantation 2006; 17(4): 511.

29. Hwang JH, Park HC, Jeong JC, Baek SH, Han MY, Bang K, et al.: Chronic asymptomatic pyuria precedes overt urinary tract

infection and deterioration of renal function in autosomal dominant polycystic kidney disease. BMC Nephrology 2013; 14(1): 1-9.

30. Amin MA: Molecular genetics and pathogenesis of autosomal dominant polycystic kidney disease. Annual review of medicine 2001; 52(1): 93-123.

31. Weimbs T: Third-hit signaling in renal cyst formation. Journal of the American Society of Nephrology 2011; 22(5): 793-5.

32. Wu L, Tiwari MM, Messer KJ, Holthoff JH, Gokden N, Brock RW, et al.: Peritubular capillary dysfunction and renal tubular epithelial cell stress following lipopolysaccharide administration in mice. American Journal of Physiology-Renal Physiology 2007; 292(1): 261-8.

33. Pirson Y: Does TNF-α enhance cystogenesis in ADPKD?. Nephrology Dialysis Transplantation 2008; 23(12): 3773-5.

34. Alam A, Dahl NK, Lipschutz JH, Rossetti S, Smith P, Sapir D, et al.: Total Kidney Volume in Autosomal Dominant Polycystic Kidney Disease: A Biomarker of Disease Progression and Therapeutic Efficacy. American Journal of Kidney Diseases 2015 Oct 1; 66(4): 564-76.

35. Soroka S, Alam A, Bevilacqua M, Girard LP, Komenda P, Loertscher R, et al.: Assessing risk of disease progression and pharmacological management of autosomal dominant polycystic

kidney disease: A canadian expert consensus. Canadian Journal of
Kidney Health and Disease 2017; 4: 1-12.

36. Rossetti S, Harris PC: Genotype-phenotype correlations in
    autosomal dominant and autosomal recessive polycystic kidney
    disease. Journal of the American Society of Nephrology 2007;
    18(5): 1374-80.

37. Schrier RW, Brosnahan G, Cadnapaphornchai MA, Chonchol M, Friend
    K, Gitomer B, et al.: Predictors of autosomal dominant polycystic
    kidney disease progression. Journal of the American Society of
    Nephrology 2014; 25(11): 2399-418.

Clinical Characteristics and Risk Factors for Kidney Failure in Patients with Autosomal Dominant Polycystic Kidney Disease

Park, Han Il

Department of Internal Medicine

Graduate School

Keimyung University

(Supervised by Professor Jin, Kyu Bok)

(Abstract)

Autosomal dominant polycystic kidney disease (ADPKD) is a hereditary and progressive renal disease. By the age of 65 years, 45%-70% of patients with ADPKD reach end-stage renal disease (ESRD). Although there are various treatments for this condition, no standard therapy exists to delay the progression of ADPKD. Hence, understanding the factors that affect disease progression may be helpful for the treatment of ADPKD.

The medical records of 288 patients with ADPKD at Keimyung University Dongsan Medical Center between January 1989 and August 2018 were analyzed retrospectively. Furthermore, we inspected the risk factors involved in the progression of ADPKD and the kidney

survival rates of patients using the Cox proportional hazards model and Kaplan-Meier survival analysis.

The mean age at the time of diagnosis was 43.1 ± 14.1 years, and there were 146 males (50.7%). In total, 197 patients (68.4%) had hypertension and 11 patients (3.8%) had cerebral aneurysm. Cerebrovascular accident occurred in 35 patients (12.1%), including 11 cases of cerebral hemorrhage and 24 cases of cerebral infarction. Twenty-eight patients (9.7%) died during the follow-up period (117.1 ± 102.1 months). Infection (42.9%) was the most common cause of mortality, followed by sudden cardiac death (25.0%). Overall, 132 patients (45.8%) progressed to ESRD and 104 patients (36.1%) required renal replacement therapy (RRT). The mean duration from diagnosis to RRT was 110.8 ± 93.9 months. Age at diagnosis after 30 years (odd's ratio [OR], 2.737; 95% confidence interval [CI], 1.320-5.675; p = 0.007), baseline serum creatinine levels (OR, 1.326; 95% CI, 1.259-1.396; p < 0.001), and cyst infection (OR, 2.065; 95% CI, 1.242-3.433; p = 0.005) were the independent risk factors for kidney

failure in multivariable analysis.

To delay the advance of ADPKD to ESRD, early diagnosis and close

observation for the onset of cyst infection are crucial.

상염색체 우성 다낭콩팥병 환자의
임상적 특징과 신부전의 위험 인자

박 한 일

계명대학교 대학원

의학과 내과학 전공

(지도교수 진 규 복)

(초록)

상염색체 우성 다낭콩팥병은 유전성, 진행성 신장 질환이다. 65세가 되면 환자의 45~70%가 말기 신장 질환에 도달한다. 치료법은 다양하나 질병의 진행을 늦추는 표준 치료는 아직 없다. 질병의 진행에 영향을 미치는 요인에 대해 이해하는 것이 질환의 치료에 도움이 될 수 있다.

1989년 1월부터 2018년 8월까지 계명대학교 동산의료원에서 진료받은 환자 288명의 의무 기록을 후향적으로 분석하였다. 콕스 비례 위험 모델과 카플란-마이어 생존 분석을 사용하여 질환의 진행에 관련된 위험 인자와 신장 생존율을 조사하였다.

진단 시 평균 연령은 43.1 ± 14.1세였으며 146명(50.7%)의 환자가 남성이었다. 고혈압은 197명(68.4%), 뇌동맥류는 11명(3.8%)에서 관찰되었다. 뇌혈관 사고는 뇌출혈 11건, 뇌경색 24건 등 환자 35명(12.1%)에서 발견되었다. 관찰 기간(117.1 ± 102.1개월) 동안 28명(9.7%)의 환자가 사망하였

다. 감염(42.9%)이 사망 원인 중 가장 많았고, 두 번째로 흔한 원인은 돌연사(25.0%)였다. 말기 신장 질환으로 진행한 환자는 132명(45.8%)이었으며, 104명(36.1%)이 신대체요법을 받았다. 진단에서 신대체요법까지의 평균 기간은 110.8 ± 93.9개월이었다. 진단 당시 30세 이상의 연령, 증가된 기저 혈청 크레아티닌 수치와 낭종 감염은 다변수 분석에서 신부전에 대한 독립적인 위험 인자로 나타났다.

상염색체 우성 다낭콩팥병 환자가 말기 신장 질환으로 진행하는 것을 늦추기 위해, 조기 진단과 낭종 감염의 발생에 대한 면밀한 관찰이 필요하다.