ESRD From Autosomal Dominant Polycystic Kidney Disease in the United States, 2001-2010

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Background: Autosomal dominant polycystic kidney disease (ADPKD) is amenable to early detection and specialty care. Thus, while important to patients with the condition, end-stage renal disease (ESRD) from ADPKD also may be an indicator of the overall state of nephrology care.

Study Design: Retrospective cohort study of temporal trends in ESRD from ADPKD and pre–renal replacement therapy (RRT) nephrologist care, 2001-2010 (n = 23,772).

Setting & Participants: US patients who initiated maintenance RRT from 2001 through 2010 (n = 1,069,343) from US Renal Data System data.

Predictor: ESRD from ADPKD versus from other causes for baseline characteristics and clinical outcomes; interval 2001-2005 versus 2006-2010 for comparisons of cohort of patients with ESRD from ADPKD.

Outcomes: Death, wait-listing for kidney transplant, kidney transplantation.

Measurements: US census data were used as population denominators. Poisson distribution was used to compute incidence rates (IRs). Incidence ratios were standardized to rates in 2001-2002 for age, sex, and race/ethnicity. Patients with and without ADPKD were matched to compare clinical outcomes. Poisson regression was used to calculate IRs and adjusted HRs for clinical events after inception of RRT.

Results: General population incidence ratios in 2009-2010 were unchanged from 2001-2002 (incidence ratio, 1.02). Of patients with ADPKD, 48.1% received more than 12 months of nephrology care before RRT; preemptive transplantation was the initial RRT in 14.3% and fistula was the initial hemodialysis access in 35.8%. During 4.9 years of follow-up, patients with ADPKD were more likely to be listed for transplantation (IR, 11.7 [95% CI, 11.5-12.0] vs 8.4 [95% CI, 8.2-8.7] per 100 person-years) and to undergo transplantation (IR, 9.8 [95% CI, 9.5-10.0] vs 4.8 [95% CI, 4.7-5.0] per 100 person-years) and less likely to die (IR, 5.6 [95% CI, 5.4-5.7] vs 15.5 [95% CI, 15.3-15.8] per 100 person-years) than matched controls without ADPKD.

Limitations: Retrospective nonexperimental registry-based study of associations; cause-and-effect relationships cannot be determined.

Conclusions: Although outcomes on dialysis therapy are better for patients with ADPKD than for those without ADPKD, access to predialysis nephrology care and nondeclining ESRD rates may be a cause for concern.

Am J Kidney Dis. 64(4):592-599. © 2014 by the National Kidney Foundation, Inc.

INDEX WORDS: Dialysis; end-stage renal disease (ESRD); autosomal dominant polycystic kidney disease (ADPKD); renal replacement therapy (RRT); renal transplant; incidence; clinical outcome; registry data.

Autosomal dominant polycystic kidney disease (ADPKD) is the most common hereditary form of kidney disease and has been described in all racial and ethnic groups. In the United States, for example, ADPKD is thought to be responsible for 1 in every 20 cases of end-stage renal disease (ESRD).[1] Enumerating the clinical epidemiology of ESRD from ADPKD could be useful for several reasons. Although much

research is ongoing in genetics and diagnostic and therapeutic domains, up-to-date disease-specific information for risk factors and outcomes of ESRD from ADPKD would help long-term decision making for at-risk individuals. In addition, nationally representative epidemiologic data could help with trial design and cost-benefit analysis of innovative interventions designed specifically to slow disease progression.[2-4] From a broader perspective, ADPKD differs from most other causes of ESRD because it can be detected early in life. Hence, it has the potential to illuminate issues such as non–disease-specific interventions to prevent ESRD and patterns of nephrology care in late-stage chronic kidney disease.

Because information of this nature is surprisingly sparse, we set out to describe the clinical epidemiology of ESRD from ADPKD in the United States from 2001 through 2010. The principal objectives of this study were to elucidate trends in incidence ratios, standardized to rates in 2001-2002, of ESRD due to

ADPKD in the United States from 2001 through 2010. Regarding clinical outcomes after beginning renal replacement therapy (RRT), we set out to compare rates of wait-listing for a kidney transplant, transplantation, and death in matched patients with and without ADPKD. An additional objective was to calculate hazard ratios for these outcomes specific to patients with ADPKD.

METHODS

Patients

In this retrospective study, US Renal Data System (USRDS) standard analysis files were used to evaluate US patients who initiated maintenance RRT from 2001 through 2010 (n = 1,069,343). Baseline characteristics at initiation of RRT were obtained from the Centers for Medicare & Medicaid Services (CMS) Medical Evidence Report (form CMS-2728) and corresponding data fields residing in the USRDS Medevid95 and Medevid05 files. By federal requirement, the Medical Evidence Report must be submitted for all new maintenance RRT patients in the United States. The form underwent structural changes in 1995 and 2005. Unlike previous versions, the 2005 version collects information regarding duration of nephrologist care before RRT initiation and hemodialysis vascular access at initiation. In both the 1995 and 2005 versions, 1 of 82 causes is entered as the primary cause of ESRD; options are identical between forms.

Defining ADPKD

Cases of ESRD due to ADPKD were those with primary cause of ESRD listed as "Polycystic kidneys, autosomal dominant" on the Medical Evidence Report (form CMS-2728).

Covariates

The covariates used for analysis were obtained from the USRDS Medevid95 and Medevid05 files and included sex; ethnicity, defined as Hispanic or Latino or not Hispanic or Latino; race, defined as white, black or African American, and other, defined as nonwhite, non–African American; and several comorbid conditions, including atherosclerotic heart disease and any history of diabetes. Information for prior ESRD therapy, including nephrology care and access type at initiation, was obtained from the Medevid05 file only because previous versions did not include this information. Continuous variables, including albumin, creatinine, and hemoglobin levels, were converted to categorical variables for analysis. Body mass index expressed as kilograms per meter squared was calculated based on reported height and weight in the Medevid95 and Medevid05 files. Two eras used for comparison were defined as 2001-2005 and 2006-2010.

Outcome Assessment

Dates of death and first kidney transplantation were obtained from the USRDS Patients file, and first wait-listing for a transplant, from the USRDS Waitlist_ki and Waitlist_kp files.[5] Using death as an outcome of interest, the interval was defined as [Death date] − [Date of dialysis initiation]. Specific outcomes of interest included dates of death, wait-listing for a kidney transplant, and kidney transplantation.

Analysis

US Census data were used as population denominators for the years examined, with age in 5-year increments and race/ethnicity classified as non-Hispanic white, non-Hispanic black, Hispanic, and other.[6] Poisson distribution was used to compute incidence rates of ESRD due to ADPKD. For standardized incidence ratios (SIRs; with observed rates as numerator and expected rates as denominator), expected incidence rates were calculated by applying incidence rates from 2001-2002 to each individual permutation of age, sex, race, and ethnicity to the corresponding subgroup of the US population in subsequent 2-year periods. Chi-square analysis was used for unadjusted comparisons of patients with and without ESRD due to ADPKD, and logistic regression with adjustment for age, sex, race, and ethnicity was used for adjusted comparisons. Percentages of missing values were calculated and reported. To compare clinical outcome rates of patients with and without ADPKD, patients were matched according to age (in 1-year intervals), sex, race, and ethnicity. Poisson regression was used to calculate incidence rates and adjusted hazard ratios for clinical events after inception of RRT, with follow-up ending on June 30, 2011. Person-time was calculated with start time as first service date and end of follow-up time as the date of first occurrence of the outcome of interest, death, or survival to June 30, 2011. Similar calculations for follow-up time were performed for wait-listing for a kidney transplant and transplantation. For data analysis, SAS, version 9.1.3 (SAS Institute Inc), was used.

RESULTS

In 2001-2002, a total of 4,282 patients began RRT because of chronic kidney failure due to ADPKD, a rate of 7.5 cases per million per year (Table 1); rates were higher for groups characterized by age 40-64 and 65 or more years and non-Hispanic white and African American race/ethnicity (incidence rates per million of 17.3, 15.3, 8.2, and 7.8, respectively). Mean age at initiation in 2001-2002 was 55.7 ± 13.2 (SD) years and was largely unchanged over time. For the overall population, SIRs exceeded 1 for all biennia after 2003-2004, with significant increases in 2005-2006 (1.07) and 2007-2008 (1.06). For patients aged 40-64 years, the ratios increased and remained significantly higher in 2003-2004 (1.11), 2005-2006 (1.16), 2007-2008 (1.16), and 2009-2010 (1.11). The SIR appeared to decrease for patients of Hispanic ethnicity in the most recent biennium (0.84) and to increase significantly for patients of other race/ethnicity in 2007-2008 (1.64) and 2009-2010 (1.48).

Table 2 shows comparisons of patients with ESRD with and without ADPKD and of patients with ESRD due to ADPKD in 2 eras. Patients with ESRD from ADPKD were more likely than patients without ADPKD to be aged 40-64 years (68.1% vs 41.2%), female (46.1% vs 44.4%), white (72.9% vs 52.9%), and non-Hispanic (90.7% vs 86.5%). After adjustment for age, sex, race, and ethnicity, associations of ESRD from ADPKD at baseline included younger age, female sex, white race, non-Hispanic ethnicity, absence of ischemic heart disease, absence of diabetes, peritoneal dialysis, preemptive transplantation for RRT, fistulas for hemodialysis, longer duration of nephrologist care, lower estimated glomerular filtration rate (eGFR), lower body mass index, and higher serum albumin and hemoglobin levels. Ranked by magnitude, odds ratios adjusted for age, sex, race, and ethnicity (aORs) for ADPKD were ≥2.0 for