Epidemiology of patients in England and Wales with autosomal dominant polycystic kidney disease and end-stage renal failure

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ABSTRACT

Background. Autosomal dominant polycystic kidney disease (ADPKD) is the leading genetic cause of end-stage renal failure (ESRF). The epidemiology of the incident ADPKD patient cohort requiring renal replacement therapy (RRT) in England and Wales has not been described.

Methods. We used a retrospective cohort design. Incident adult patients commencing RRT between 1 January 2000 and 31 December 2011 in England and Wales were identified from the UK Renal Registry. Patients were stratified into three groups based on primary renal diagnosis (PRD): (i) ADPKD, (ii) diabetes as PRD, (iii) individuals with another PRD (‘other’). Baseline demographics, comorbidity, care-related measures and outcomes including patient survival are described.

Results. A total of 52 608 individuals started RRT during the study period, 3598 (6.8%) had ADPKD, 12 137 (23.1%) diabetes as PRD and 36 873 had another PRD diagnosis. The median age of commencing RRT was 55 years in the ADPKD group compared with 62 and 66 years in those with diabetes or ‘other’ PRD, respectively. The median age of starting RRT did not change within the ADPKD group over the 10-year period. Median age at death was similar across all groups. The ADPKD group had a lower hazard for all-cause mortality compared with the ‘other’ PRD group (adjusted hazard ratio 0.45, 95% CI 0.38–0.53). In all PRD groups, crude mortality rates had improved between 2000–06 and 2007–11.

Conclusion. Although engaged in renal services earlier than some other patient groups, individuals with ADPKD start RRT at a younger age and this has remained unchanged over the last decade. Developing a nationwide cohort and an enhanced disease-specific dataset would facilitate a wide range of research and quality improvement initiatives to try to modify progression to ESRF and the course of RRT.

Keywords: ADPKD, end-stage kidney disease, epidemiology and outcomes, renal replacement therapy

BACKGROUND

Autosomal dominant polycystic kidney disease (ADPKD) is the most common genetic cause of end-stage renal failure (ESRF) [1]. In the UK, ADPKD affects ~70 000 people and accounts for 7% of all incident adult cases accepted for renal replacement therapy (RRT) [2]. ESRF typically develops in the 6th decade of life in 50% of patients but the disease course is highly variable even within families.

Currently, several large international observational studies, including OVERTURE [3] and EuroCYST [4], are capturing information about the natural history of the condition, to facilitate identification of risk factors that may influence and therefore predict progression. The Consortium for Radiologic Imaging Studies of Polycystic Kidney Disease (CRISP) study provided valuable prospective longitudinal data identifying renal volume as a measure of disease progression [5].

Age-related renal volume and underlying disease mutation are important predictors of progression in chronic kidney disease [6, 7]. In terms of therapeutics, Tolvaptan, a vasopressin receptor antagonist may slow disease progression in patients with ADPKD and preserved kidney function [8]. To date however no specific intervention has been widely accepted or licensed for use in routine clinical care.

Although several studies have defined the characteristics of ADPKD patients and risk factors for disease progression to ESRF [5, 9–12] relatively little focus has been recently placed on understanding the epidemiology of patients with the combination of ADPKD and who reach ESRF and start RRT. Over recent decades renal survival in some centres has been improving; the increasing use of RAAS blockers has been suggested as
demography, clinical characteristics, care-related measures and outcomes of the incident RRT ADPKD population.

METHODS

Study population and measurements
Data were obtained from the UK Renal Registry (UKRR) [15], which monitors standards of care of patients requiring RRT in England, Wales and Northern Ireland. In brief, each patient entry contains information collected from the initiation of RRT, including demographic factors, primary renal diagnosis (PRD) and biochemical and mortality data. Renal units return data electronically to the UKRR on a quarterly basis. Data are prospectively validated. The UKRR operates within a comprehensive governance framework and has exemption granted by the Secretary of State under section 251 of The National Health Service Act (2006) to hold patient identifiable data.

This study included anonymized data from the incident adult patient population commencing RRT between 1 January 2000 and 31 December 2011. Northern Ireland joined the UKRR in 2005; hence their data were not included.

Patients were stratified into three groups based on PRD [16]:

(1) ADPKD

(2) Diabetes as PRD

(3) Individuals with another PRD (‘other’ PRD)

We were concerned that patients with a PRD related to malignancy or primary amyloid may have a substantially poorer prognosis than other types of PRD groups. Individuals with a PRD of amyloidosis (n = 696), myeloma (n = 1477), renal cell carcinoma (n = 377), renal failure induced by chemotherapy (n = 20) or missing PRD (n = 1379) were excluded. Because ESRF resulting from diabetic nephropathy has been associated with a poorer outcome, individuals with diabetes as PRD were categorized separately.

Demographic and comorbidity data from the time of starting RRT were utilized. The estimated glomerular filtration rate (eGFR) within 2 weeks of starting dialysis was calculated using the Modified Diet in Renal Disease (MDRD) formula [17]. Data from the first 3 months after starting RRT were used for bone mineral measurements, haemoglobin, ferritin and erythropoietin prescription.

Full UKRR dataset definitions are available at www.renalreg.com.

Statistical analysis
All data analyses were conducted using SAS for Windows Version 9.3. Cross tabulations of baseline demographics, comorbidity and care-related measures were performed.

Frequencies and percentages were calculated for binary/categorical variables and means with standard deviations for continuous variables if normally distributed, or medians with interquartile ranges (IQR) if results were not normally distributed. For biochemical and haematological parameters comparison with current Renal Association standards were made when a standard was available (Supplementary data, Appendix 1) [18]. The proportion of patients and corresponding 95% confidence intervals within each PRD group meeting the standard were calculated stratified by PRD and dialysis modality.

Kaplan–Meier survival curves with censoring at death or renal transplantation were estimated to illustrate the probability of failure of peritoneal dialysis (PD) and a move in modality to haemodialysis (HD) for each PRD group.

Crude mortality rates by PRD group were calculated over the first 5 years of RRT. Cox proportional hazard models were used to estimate the adjusted hazard of all-cause mortality after commencing RRT. Patients categorized as ‘other’ PRD were utilized as the baseline group for comparison. Models were adjusted for age, sex and ethnicity and RRT modality. Patients with missing data on ethnicity were included in the analysis and categorized as ‘missing’. Due to observed non-proportional hazards between groups, patients with diabetes as PRD were excluded from the survival analyses. We hypothesized that patient outcomes may have changed over the time of the cohort and results are presented stratified by calendar period. Evidence of interaction between PRD and year of starting RRT (categorized into starting between 2000–06 and 2007–11) and the outcome was tested. Sensitivity analysis in a subgroup with complete data on diabetes as comorbidity was conducted.

RESULTS

Of 52,608 patients who commenced RRT during the study period with complete data on PRD, 100% had complete data on gender, age and first renal modality. Comorbidity data were less well completed, available in 55% of patients (Supplementary data, Appendix 2).

Demography and comorbidity at time of starting RRT
A total of 3598 individuals (7%) had ADPKD, 12,137 (23%) diabetes and 36,873 (70%) had another PRD diagnosis (Table 1). The proportion of males with a diagnosis of ADPKD was 52%; men were over-represented in the other PRD groups. Patients with ADPKD started RRT at a younger age than the other PRD groups (median age 55 years compared with 62 and 66 years in those patients with diabetes or ‘other’ PRD, respectively). After exclusion of patients preemptively transplanted, the median age of starting dialysis was 56 years in the ADPKD group, 63 years in those with diabetes as PRD and 67 years in those with ‘other’ PRD. The median age of starting RRT did not change within the ADPKD group over the 10-year period (Figure 1). There was a lower proportion of patients of black ethnicity in the ADPKD group (Table 1).

Comorbidity profile tended to be lower in the ADPKD group when commencing RRT, although these results must be
interpreted with caution due to a high frequency of missing data (Table 1 and Supplementary data, Appendix 2).

In 2000, the incident rate of individuals with ADPKD commencing RRT was 6.05 per million population (pmp). In 2011, the incident rate was 6.42 pmp.

### Biochemical and haematological measurements at start of dialysis

**eGFR at start of dialysis.** In all three PRD groups, mean eGFR in patients starting PD or HD has increased over the last 11 years (Figure 2a and b). For example, in the ADPKD group mean eGFR at start of dialysis has increased from 6.6 mL/min/1.73 m² to 8.7 mL/min/1.73 m². People with ADPKD tended to start dialysis at a slightly lower mean eGFR than the comparison PRD groups, although this difference has diminished over time.

In 2011, individuals with ADPKD undergoing pre-emptive transplantation had a mean eGFR of 11.2 mL/min/1.73 m² compared with 14.0 mL/min/1.73 m² in the diabetes PRD group and 12.0 mL/min/1.73 m² in the ‘other’ PRD group.

**Serum phosphate, adjusted calcium and PTH levels at start of dialysis.** In the first 3 months of dialysis, 65.7% of the incident PD patients in 2011 had a phosphate level within 1.1–1.7 mmol/L compared with 57.4% in HD cohort. For each PD and HD cohort by calendar year, phosphate control by PRD group was similar (Figure 3a and 3b). A similar pattern was observed in adjusted calcium measures and PTH control (Supplementary data, Appendix 3a and 3b/Appendix 4a and 4b). A trend to improved PTH control was also observed. These trends were observed across all PRD groups.

**Haemoglobin, ferritin levels and erythropoietin prescription at start of dialysis.** In 2000, the median haemoglobin values for patients in the ADPKD group, ‘other’ group and diabetes group were 6.6 mmol/L, 6.1 mmol/L and 6.1 mmol/L, respectively; in 2011 the median values remained similar (6.7 mmol/L, 6.2 mmol/L and 6.1 mmol/L, respectively) (Supplementary data, Appendix 5a/5b). There was a trend to lower ferritin levels in ADPKD patients than other PRD groups in the population starting HD (Supplementary data, Appendix 6a/6b). The data on ferritin levels however must be interpreted with caution as there was a relatively high proportion of missing data, particularly in the patients categorized as ‘other’ PRD (21%). The proportion of patients prescribed erythropoietin (EPO) was similar across all PRD groups for those starting HD; more variation was seen in those starting PD, with the highest proportion of patients with diabetes as PRD being prescribed EPO (68%) compared with ADPKD or ‘other’ PRD groups (60%) (Supplementary data, Appendix 7a/7b).

### PRD and first RRT modality.

Over 80% of patients were reviewed >1 year prior to commencing RRT (versus 60% of

Table 1. Baseline characteristics of the incident cohort starting RRT between 1 January 2000 and 31 December 2011

<table>
<thead>
<tr>
<th></th>
<th>ADPKD</th>
<th>Diabetes</th>
<th>Other PRD</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>3598</td>
<td>12 137</td>
<td>36 873</td>
</tr>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age in years, median (IQR)</td>
<td>55 (47–63)</td>
<td>62 (50–71)</td>
<td>66 (49–75)</td>
</tr>
<tr>
<td>Age in years for men, median (IQR)</td>
<td>54 (46–63)</td>
<td>62 (51–71)</td>
<td>67 (51–76)</td>
</tr>
<tr>
<td>Age in years for women, median (IQR)</td>
<td>56 (48–65)</td>
<td>63 (50–71)</td>
<td>65 (49–75)</td>
</tr>
<tr>
<td>Male gender, N (%)</td>
<td>1875</td>
<td>9068</td>
<td>27 092</td>
</tr>
<tr>
<td>Smoker, N (%)</td>
<td>262</td>
<td>903</td>
<td>1660</td>
</tr>
<tr>
<td><strong>1st RRT modality, N (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HD</td>
<td>1938</td>
<td>9068</td>
<td>27 092</td>
</tr>
<tr>
<td>PD</td>
<td>1237</td>
<td>2691</td>
<td>8121</td>
</tr>
<tr>
<td>Transplant</td>
<td>423</td>
<td>378</td>
<td>1660</td>
</tr>
<tr>
<td><strong>Ethnicity, N (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>3069</td>
<td>7715</td>
<td>27 293</td>
</tr>
<tr>
<td>Black</td>
<td>112</td>
<td>989</td>
<td>1939</td>
</tr>
<tr>
<td>Asian</td>
<td>130</td>
<td>1895</td>
<td>2743</td>
</tr>
<tr>
<td>Other</td>
<td>46</td>
<td>297</td>
<td>629</td>
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<tr>
<td>Missing</td>
<td>241</td>
<td>1241</td>
<td>4269</td>
</tr>
<tr>
<td><strong>Comorbidity, N (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>117</td>
<td>NA</td>
<td>2218</td>
</tr>
<tr>
<td>Previous MI</td>
<td>114</td>
<td>1187</td>
<td>2329</td>
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<tr>
<td>Previous CABG</td>
<td>97</td>
<td>758</td>
<td>1385</td>
</tr>
<tr>
<td>CVSD</td>
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<td>985</td>
<td>1923</td>
</tr>
<tr>
<td>PVD</td>
<td>58</td>
<td>1531</td>
<td>1925</td>
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<tr>
<td>Malignancy</td>
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<td>372</td>
<td>2197</td>
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<tr>
<td>COPD</td>
<td>68</td>
<td>375</td>
<td>1509</td>
</tr>
<tr>
<td>Liver disease</td>
<td>61</td>
<td>171</td>
<td>534</td>
</tr>
<tr>
<td>All-cause death, N (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Died</td>
<td>749</td>
<td>5823</td>
<td>15 813</td>
</tr>
</tbody>
</table>

Column percentages are shown throughout.

ADPKD, autosomal dominant polycystic kidney disease; RRT, renal replacement therapy; HD, haemodialysis; PD, peritoneal dialysis; MI, myocardial infarction; CABG, coronary artery bypass graft; CVSD, cerebrovascular disease; PVD, peripheral vascular disease; COPD, chronic obstructive airways disease; NA, not applicable data field for the diabetes PRD group.

a% shown is out of those patients with co morbidity data completed.
individuals with diabetes as PRD and 68% individuals with another PRD, data not shown). A total of 11.8% patients with ADPKD started RRT with a pre-emptive transplant, compared with 3.1% in those with diabetes as PRD and 4.5% with ‘other’ PRD (Table 1). Within each PRD group, the relative proportions of each RRT modality as first RRT modality have remained static between 2000–06 and 2007–11 (data not shown).

PD as first RRT modality was also more prevalent in the ADPKD group than the other PRD groups (Table 1). There was no evidence that individuals with ADPKD were more likely to switch modality to HD than the other two PRD groups (Figure 4).

PRD and all-cause mortality. Patients were followed up for a median of 2.7 years (IQR 1.0–5.0 years). A total of 22,386 patients (42.6%) died. The median (IQR) age at death was 70 years (IQR 62–78) for individuals with ADPKD and 69 years (IQR 59–76) and 76 years (IQR 68–82) in those with diabetes as PRD or another PRD, respectively.

Table 2 lists the crude mortality rates by PRD group and by calendar period of starting RRT. Crude mortality rates were lowest in the ADPKD group, in both time frames. For all three PRD groups, crude mortality rates were lower in the 2007–11 cohort compared with the 2000–06 cohort (Table 2). The adjusted hazard ratio for all-cause mortality in patients in the ADPKD group compared with those in the ‘other’ PRD group was 0.53 (95% CI 0.48–0.59) in the 2000–06 cohort, and 0.45 (0.38–0.53) in the 2007–11 cohort (Table 3). In the ADPKD group, the adjusted hazard ratio for all-cause mortality was lower at 0.77 (95% CI 0.63–0.94) comparing those who started RRT in 2007–11 to the 2000–06 incident cohort (Table 4). No change in the effect estimates was observed in the subgroup analysis with complete data on diabetes status as comorbidity (data not shown).

In a subgroup of patients with cause of death data available (n = 11,085), cardiac disease was the most frequently identified specific cause of death in all PRD groups; infection as the leading cause of death was relatively more common in the ADPKD group than in the other two groups (Table 5).

DISCUSSION

In this retrospective study utilizing data collated by the UKRR for an incident RRT population between 2000 and 2012, we have described the demographics, clinical characteristics and outcomes for patients with ADPKD in England and Wales.

Patients with ADPKD commence RRT at a median age of 55 years, which is earlier than the UK median age of 65 years for all-cause ESRF [2]. Our data are consistent with historical reports in patients with ADPKD across several countries [6, 12, 19–21]. Determining the underlying genetic mutation is not currently part of standard diagnostic practice in the UK so the relative contribution of PKD1 and PKD2 mutations in our cohort is unknown. However, 55 years approximates to the median age of ESRF associated with truncating PKD1 mutations [6]. Over the 12-year period of our study, the median age of onset of RRT in patients with ADPKD has not substantially changed suggesting that standard care does not modify progression to ESRF. The static age at onset of RRT in the UK ADPKD population we observed is in contrast to a Danish cohort study in which the mean age of commencing RRT increased by 4.8 years, from 56 to 60 years between 2002 and 2007 [14]. Speculative explanations for this variation include differences in the frequency of PKD2 mutations or different...
biochemical/clinical influences on when to start RRT; it is possible that more elderly patients were accepted for RRT in the Danish cohort over time influencing the cohort mean age. The numbers of patients were smaller than in our cohort however, and alternatively the observed change may have been a chance finding.

In terms of the ethnic distribution of our cohort, the proportion of patients of black ethnicity in the ADPKD group is comparable to the national prevalence of black ethnicity groups in the UK (∼4%) [22]. The relative over-representation of people of Asian ethnicity in the diabetes PRD group likely reflects the high prevalence of type 2 diabetes in the Asian population [23].

It is an interesting observation that in individuals with ADPKD the mean eGFR at the time of starting dialysis tended to be slightly lower than in the other PRD groups. This could reflect the earlier engagement with renal services and managed symptomology of progressive CKD, or the lower comorbidity burden within this group resulting in enhanced tolerance of the complications of CKD. It is important to note that for

**FIGURE 2**: (a) Mean eGFR at time of commencing haemodialysis as first RRT modality, stratified by PRD. (b) Mean eGFR at time of commencing peritoneal dialysis as first RRT modality, stratified by PRD.
temporal comparison of haematological or biochemical parameters we used the current RA guidance in this analysis [18]. Standards changed between 2000 and 2012, which needs to be acknowledged when interpreting any trends observed. We were surprised by the similarity in haemoglobin parameters and the prevalence of EPO prescriptions in all three PRD groups. It has been previously postulated that the mechanism of relatively preserved EPO production in ADPKD patients may be offset by the inhibitory effect of uraemia [24] but the evidence is conflicting [25] and anecdotally we expected to see less EPO prescribed in the ADPKD population. Unfortunately we did not have information on dosage of EPO which may well have exposed differences between the PRD groups.

Early engagement with renal services, lower comorbid profile and younger age at ESRF help to account for the higher prevalence of renal transplantation as first modality of RRT in patients with ADPKD. We also highlight the interesting result that PD was more prevalent in patients with ADPKD as first modality than in the other two groups and patients with ADPKD were not more likely to switch to HD than the comparative PRD groups. Our data support the feasibility of PD in patients with ADPKD findings which are supported by

FIGURE 3: (a) Percentage of haemodialysis patients with serum phosphate within 1.1–1.7 mmol/L. (b) Percentage of peritoneal dialysis patients with serum phosphate within 1.1–1.7 mmol/L.
previous studies and refuting previous potential concerns of PD treatment failure [26–28].

Although there was a tendency to a lower comorbid profile at the start of RRT, ultimately the reported cause of death was similar in all three patient groups. Cardiovascular complications contributed to the single most substantial proportion, reflecting the accelerated cardiovascular risk generically associated with ESRF. Infection as a cause of death was more prevalent in the ADPKD population which likely reflects the higher transplant rate in this group. The median age at death was also similar in the ADPKD group, again reflecting the high risk nature of ESRF.

The relative mortality rate was lower in the ADPKD group compared with those in other PRD groups, a finding supported by previous analyses [13, 14, 16, 29]. In all three PRD groups the crude mortality rates were lower in those starting RRT between 2007–11 and 2002–06, showing an overall improvement in survival between the two time frames in all of the PRD groups. Patients with ADPKD had a lower adjusted relative hazard for mortality when compared with the ‘other’ PRD group; however, there was no evidence of effect modification by year of starting RRT, when the two cohort time frames were compared, suggesting that the hazard for mortality has reduced by a similar degree in both the PRD groups. Although again speculative, these changes likely reflect improvements across the spectrum of medical care of all RRT patients.

In this study we have described a wide range of factors in a large nationally representative cohort of incident RRT patients with ADPKD and other PRDs. There are however limitations to our study. This is an observational study using an available registry that was not primarily designed or powered with the aim of examining heterogeneity in terms of PRD. The primary aim of this analysis was descriptive and the findings are hypothesis generating. Biochemical and haematological parameters included are reported from across many hospital laboratory systems with potential for measurement error—this has previously been discussed in detail in the UKRR annual report [30]. The results of the survival analysis are unadjusted for potentially important confounders, such as cardiovascular disease, blood pressure and medications. While the UKRR has complete coverage of all renal units, data completeness on some important variables including comorbidity does vary. Comorbidity data have historically been reported to the UKRR with only moderate completeness (∼50% of returns). Previous work from the UKRR showed that patients with missing comorbidity data have a higher mortality than those with reported data, suggesting a selection bias [31]. Reassuringly, our results in this analysis relating to improved patient survival in the ADPKD group are supported by other studies [29].

The choice of PRD groups in our analyses needs consideration. The group categorized as ‘other’ PRD in this analysis is a highly heterogeneous group, consisting of individuals with many different types of PRD likely to have varying mortality risks. We chose these PRD groupings based on previous studies, and on a pragmatic basis, but recognize this limitation. However, our study supports that reporting aggregate level results for patients with various PRDs may not be appropriate. Exploring further the heterogeneity of patient outcomes amongst patients with varying PRDs, categorizing at a more granular level, across different cohorts with more detailed information on possible confounders, would be valuable. A standardized approach across cohorts for categorization by PRD would be useful. Finally, the current UKRR dataset does not collect information on variables with specific relevance to patients with ADPKD including radiological parameters such as MRI renal volume or genetic information. Currently,
medication data are also limited, as is detailed information regarding cause of death. We did not have data on individuals with stage 5 CKD who do not commence RRT. Therefore our cohort does not represent the entire ESRF population.

This report of the national RRT cohort in England and Wales provides the most comprehensive description of the epidemiology of the ADPKD population at the time of starting RRT available to date. We have highlighted that despite early engagement with renal services, the median age of starting RRT in patients with ADPKD has not changed over the last decade. With the growing number of clinical trials in ADPKD, developing a nationwide cohort and an enhanced disease-specific dataset including linkage to other established data sources including radiology, primary and secondary care data would be a valuable contribution to studying the efficacy of new therapies outside the trial setting. This would facilitate a wide range of research and quality improvement initiatives to try to influence progression to ESRF and the course of RRT. A national ADPKD study group has been established to implement this agenda.

SUPPLEMENTARY DATA

Supplementary data are available online at http://ndt.oxfordjournals.org.

CONFLICT OF INTEREST STATEMENT

All authors have contributed to this paper and agree with the submission. The authors of this paper also declare that the results presented in this paper have not been published previously in whole or part, except in abstract format. C.S., D.P., R. J.S. have no conflicts of interest to declare. R.S. has previously been on an Otsuka-sponsored clinical advisory board. This was an ad hoc appointment and he holds no stock.

REFERENCES

3. Observational Study in Patients with Autosomal Dominant Polycystic Kidney Disease (OVERTURE) http://clinicaltrials.gov/ct2/show/NCT01430494

Table 3. Adjusted hazard ratios for patient mortality (all-cause) comparing patients on RRT with a PRD of ADPKD with patients categorized as ‘other’ PRD

<table>
<thead>
<tr>
<th>Year</th>
<th>PRD Group</th>
<th>Crude HR (95% CI)</th>
<th>P-value</th>
<th>Adjusted HR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000–06</td>
<td>Other</td>
<td>1.00</td>
<td>&lt;0.001</td>
<td>1.00</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2007–11</td>
<td>ADPKD</td>
<td>0.53 (0.48–0.59)</td>
<td>&lt;0.001</td>
<td>0.53 (0.48–0.59)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2007–11</td>
<td>Other</td>
<td>1.00</td>
<td>&lt;0.001</td>
<td>1.00</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2007–11</td>
<td>ADPKD</td>
<td>0.45 (0.38–0.53)</td>
<td>&lt;0.001</td>
<td>0.45 (0.38–0.53)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

PRD, primary renal diagnosis; ADPKD, autosomal dominant polycystic kidney disease; HR, hazard ratio.

Where percentages do not total 100% this is due to rounding.

Table 4. Adjusted hazard ratios for patient mortality (all-cause) comparing patients with ADPKD who started RRT in 2007–11 compared with patient starting RRT in 2000–06

<table>
<thead>
<tr>
<th>Year</th>
<th>Crude HR (95% CI)</th>
<th>P-value</th>
<th>Adjusted HR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000–06</td>
<td>1.00</td>
<td>&lt;0.001</td>
<td>1.00</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2007–11</td>
<td>0.66 (0.54–0.81)</td>
<td>&lt;0.001</td>
<td>0.77 (0.63–0.94)</td>
<td>0.012</td>
</tr>
</tbody>
</table>

PRD, primary renal diagnosis; ADPKD, autosomal dominant polycystic kidney disease; HR, hazard ratio.

Table 5. Cause of death

<table>
<thead>
<tr>
<th>Cause of death</th>
<th>PRD Group</th>
<th>ADPKD</th>
<th>Diabetes</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=390</td>
<td>n=2949</td>
<td>n=7746</td>
<td></td>
</tr>
<tr>
<td>Cardiac disease, N (%)</td>
<td>86 (22.1)</td>
<td>901 (30.6)</td>
<td>1701 (22.0)</td>
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</tr>
<tr>
<td>Cerebrovascular disease, N (%)</td>
<td>27 (6.9)</td>
<td>166 (5.6)</td>
<td>338 (4.4)</td>
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<tr>
<td>Infection, N (%)</td>
<td>83 (21.2)</td>
<td>534 (18.1)</td>
<td>1389 (17.9)</td>
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</tr>
<tr>
<td>Malignancy, N (%)</td>
<td>34 (8.7)</td>
<td>112 (3.8)</td>
<td>618 (8.0)</td>
<td></td>
</tr>
<tr>
<td>Treatment withdrawal, N (%)</td>
<td>44 (11.3)</td>
<td>439 (14.9)</td>
<td>1258 (16.2)</td>
<td></td>
</tr>
<tr>
<td>Other, N (%)</td>
<td>103 (26.4)</td>
<td>652 (22.1)</td>
<td>2114 (27.3)</td>
<td></td>
</tr>
<tr>
<td>Uncertain, N (%)</td>
<td>13 (3.3)</td>
<td>145 (4.9)</td>
<td>328 (4.2)</td>
<td></td>
</tr>
</tbody>
</table>

PRD, primary renal diagnosis; ADPKD, autosomal dominant polycystic kidney disease.

As a proportion of patients who died with data available on cause of death.

Number of patients who died with cause of death data available.
Tacrolimus therapy in adult-onset steroid-resistant nephrotic syndrome due to a focal segmental glomerulosclerosis single-center experience

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ABSTRACT

Introduction. Management of adults with steroid-resistant (SR) nephrotic syndrome due to focal segmental glomerulosclerosis (FSGS) is a challenging task. Is tacrolimus (TAC) effective in this situation without serious adverse effects? This prospective study was done to answer this question. Materials and methods. In patients with SR nephrotic syndrome due to FSGS, oral TAC (0.1 mg/kg/day) was started targeting a trough level of 5–10 ng/mL along with oral prednisolone (0.15 mg/kg/day) for 48 weeks. In patients with complete


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