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Original Investigation

Health-Related Quality of Life in Patients With Autosomal Dominant Polycystic Kidney Disease and CKD Stages 1-4: A Cross-sectional Study

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Background: In people with early autosomal dominant polycystic kidney disease (ADPKD), average total kidney volume (TKV) is 3 times normal and increases by an average of 5% per year despite a seemingly normal glomerular filtration rate (GFR). We hypothesized that increased TKV would be a source of morbidity and diminished quality of life that would be worse in patients with more advanced disease.

Study Design: Cross-sectional.

Setting & Participants: 1,043 patients with ADPKD, hypertension, and a baseline estimated GFR (eGFR) >20 mL/min/1.73 m^2.

Predictors: (1) eGFR, (2) height-adjusted TKV (htTKV) in patients with eGFR >60 mL/min/1.73 m^2.

Outcomes: 36-Item Short Form Health Survey (SF-36) and the Wisconsin Brief Pain Survey.

Measurements: Questionnaires were self-administered. GFR was estimated from serum creatinine using the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) equation. htTKV was measured by magnetic resonance imaging.

Results: Back pain was reported by 50% of patients, and 20% experienced it "often, usually, or always." In patients with early disease (eGFR >60 mL/min/1.73 m^2), there was no association between pain and htTKV, except in patients with large kidneys (htTKV $>1,000$ mL/m). Comparing across eGFR levels and including patients with eGFRs <60 mL/min/1.73 m^2, patients with eGFRs of 20-44 mL/min/1.73 m^2 were significantly more likely to report that pain impacted on their daily lives and had lower SF-36 scores than patients with eGFRs of 45-60 and $\geq$60 mL/min/1.73 m^2. Symptoms relating to abdominal fullness were reported by 20% of patients and were related significantly to lower eGFRs in women, but not men.

Limitations: TKV and liver volume were not measured in patients with eGFR <60 mL/min/1.73 m^2. The number of patients with eGFRs <30 mL/min/1.73 m^2 is small. Causal inferences are limited by cross-sectional design.

Conclusions: Pain is a common early symptom in the course of ADPKD, although it is not related to kidney size in early disease (eGFR >60 mL/min/1.73 m^2), except in individuals with large kidneys (htTKV $>1,000$ mL/m). Symptoms relating to abdominal fullness and pain are greater in patients with more advanced (eGFR, 20-45 mL/min/1.73 m^2) disease and may be due to organ enlargement, especially in women. More research about the role of TKV in quality of life and outcomes of patients with ADPKD is warranted.

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INDEX WORDS: Autosomal dominant polycystic kidney disease (ADPKD); quality of life (QoL); chronic kidney disease (CKD); patient-reported outcomes; extrarenal symptoms; renal disease; activities of daily life.

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Autosomal dominant polycystic kidney disease (ADPKD) is unique among forms of chronic kidney disease (CKD) for the growth of cysts and enlargement of the kidneys, which occur well before kidney function declines. Past studies show that >60% of adult patients and 35% of children with ADPKD report pain, often despite normal kidney function (ie, decades before they reach end-stage renal disease [ESRD]).[1,2] There are many causes of pain in ADPKD, including cyst expansion under the renal capsule, traction on the renal pedicle, compression of nearby structures by kidney or liver cysts, or mechanical back pain that arises from an exaggerated pelvic tilt and increased lumbar lordosis.[3] The average rate of kidney growth among individuals with early disease (estimated glomerular filtration rate [eGFR] > 60 mL/min/1.73 m^2) was estimated at 5.3% ± 4.0% per year in the Consortium for Radiologic Imaging for the Study of Polycystic Kidney Disease (CRISP) Study, and this has been consistent across studies.[4-6] The kidneys are estimated to double in size over 8 years.[7] Liver cysts are very common, found in 85% of individuals older than 30 years in the CRISP cohort at baseline,[8] and contribute further to abdominal distension and symptoms related to increased abdominal mass. The continuous enlargement of the kidneys and liver occurs well before reaching ESRD and can be the source of severe morbidity that is different from that associated with declining kidney function or its treatment.

Formal study of the impact of ADPKD on quality of life has been limited. Although some studies have described symptoms,[9-11] the impact on daily living and the changes that occur with disease progression have not been systematically characterized. The largest study to date consisted of 101 patients with preserved GFR (eGFR > 70 mL/min/1.73 m^2) who completed the 36-Item Short Form Health Survey (SF-36) and at the same time had total kidney volume (TKV) measured by magnetic resonance imaging.[12] Results showed that SF-36 scores were well preserved and much better than those of other patients with CKD, but did not correlate with TKV. However, this study was limited by its small sample size, use of a generic health-related quality of life (HRQoL) instrument only, and lack of selection for patients at high risk for progression to ESRD (eg, presence of hypertension).

The HALT PKD trials consist of 2 randomized clinical trials that are examining combination angiotensin-converting enzyme (ACE)-inhibitor/angiotensin receptor blocker use compared with ACE-inhibitor use alone in hypertensive patients with eGFRs > 60 mL/min/1.73 m^2 (study A) and eGFRs of 25-60 mL/min/1.73 m^2 (study B).[13] Participants completed the SF-36[14] and a modified[9] version of the Wisconsin Brief Pain Survey[15] at baseline, prior to intervention. This provides a unique opportunity to describe the symptoms and their interference with daily living at early through to more advanced stages of ADPKD. We hypothesized that symptoms, including pain and mass effects, would be worse in individuals with larger kidneys. Kidney volume was measured by magnetic resonance imaging at the time of questionnaire administration in study A patients only. Although TKV was not measured in study B patients, we hypothesized that there would be a relationship of pain and symptoms with disease severity (as defined by eGFR) in study B patients given the known strong inverse correlation of GFR with TKV.[7,16,17]

METHODS

Study Population

The design and implementation of the HALT-PKD trials and the baseline characteristics of this population have been reported in detail elsewhere.[13] Briefly, the HALT-PKD trials are 2 prospective, randomized, double-blind, placebo-controlled, multicenter, interventional trials testing whether multilevel blockade of the renin-angiotensin-aldosterone system using ACE-inhibitor plus angiotensin receptor blocker (lisinopril plus telmisartan) combination therapy will delay the progression of kidney disease compared with ACE-inhibitor (lisinopril plus placebo) monotherapy in studies A and B, and whether low blood pressure control (95-100/60-75 mm Hg) will delay progression compared with standard control (120-130/70-80 mm Hg) in study A. In study A, patients are aged 15-49 years with eGFRs > 60 mL/min/1.73 m^2, whereas in study B, patients are aged 18-64 years with eGFRs of 25-60 mL/min/1.73 m^2. All patients undergo a formal screening visit to verify eligibility, diagnosis of ADPKD, and assignment to study A or study B based on eGFR. All HALT-PKD participants have hypertension, defined as current use of antihypertensive medications for blood pressure control or systolic blood pressure >130 mm Hg and/or diastolic blood pressure >80 mm Hg on 3 separate readings within the past year.

HRQoL Measurement

Patients completed the SF-36[18] and a modified version[9] of the Wisconsin Brief Pain Survey[15] while attending the baseline visit. The pain questionnaire consisted of questions that asked about the location, frequency, and intensity of pain; treatments that had been used and their effectiveness in relieving pain; and the degree to which pain interfered with activities of daily life. Patients completed the questionnaires without assistance from study staff.

Statistical Analyses

Patients were categorized into 3 groups based on their baseline eGFRs. eGFR was estimated from the CKD-EPI (CKD Epidemiology Collaboration) creatinine equation standardized for body surface area of 1.73 m^2. The cutoff values for eGFR subgroups were 20-44, 45-60, and >60 mL/min/1.73 m^2. The lowest strata includes eGFR < 25 mL/min/1.73 m^2 (the cutoff eGFR for study eligibility) because this study is based on eGFR at the baseline visit, which declined from the screening visit eGFR in some subjects. Individual items on the pain questionnaire were primarily dichotomous (yes/no) and were analyzed as such. For questions that had Likert-type answers (never, rarely, sometimes, often, usually, and always), the first 2 responses were consolidated, as well as the last 3, resulting in 3 distinct groups. Pain questionnaire items were compared across eGFR groups within sexes using Fisher exact test or Kruskal-Wallis test. SF-36 component scores were summarized by sample means and compared across the 3 eGFR groups within sexes using the Kruskal-Wallis test. The