Prevalence of Cardiovascular Events in Patients with Autosomal Dominant Polycystic Kidney Disease

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Key Words

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Abstract

Background: This study evaluates the prevalence of cardiovascular events in autosomal dominant polycystic kidney disease (ADPKD) patients. **Methods:** We distributed surveys to 1,439 subjects from our ADPKD research database. In total, 426 subjects completed and returned surveys; 7 of these were from children and were excluded from the study. **Results:** The patients who responded were female (63.2%), non-Hispanic (88.1%) and white (93.6%). The mean age of the total group was 53.2 ± 13.7 years; 82.8% had a family history of ADPKD and 32.5% had reached end-stage renal disease (ESRD). With respect to cardiovascular risk factors, 86.6% were hypertensive with a mean age at diagnosis of 36.9 ± 12.9 years and hypertension was significantly more prevalent in males. In addition, 19.6% of the subjects were obese, 20.8% were smokers, 8.7% had diabetes, 45.7% had high cholesterol and 17.8% were sedentary. The most prevalent self-reported cardiovascular events were arrhythmias (25.9%), evidence of peripheral vascular disease (16.5%), heart valve problems (14.4%), cardiac enlargement (9.5%), stroke or cerebral bleeding (7.5%), myocardial infarction (6%) and brain aneurysm (5.0%). The most commonly used antihypertensive medications were renin-angiotensin inhibitors used by 75% of

ADPKD patients. Older ADPKD patients and those at ESRD had a significantly higher incidence of cardiovascular events.

Conclusion: These findings support the high prevalence of cardiovascular risk factors and events in ADPKD patients which contribute to a greater mortality risk. Due to the prevalence of cardiovascular risk factors in the ADPKD population, early diagnosis and clinical intervention are recommended.

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Introduction

Approximately 6 million Americans have chronic cardiovascular and kidney disease combined, resulting in an increasing epidemic of heart and kidney failure [1]. This morbid association represents unique challenges to the clinician. Approximately 600,000 Americans are affected with autosomal dominant polycystic kidney disease (ADPKD), with over 2000 patients starting dialysis every year [2]. Patients with ADPKD have an increased incidence of early onset hypertension, left ventricular hypertrophy (LVH) and cardiovascular abnormalities [3, 4]. The reported relative mortality rate in patients with ADPKD ranges between 1.6-fold [95% confidence interval (CI) 1.3–2.0] and 3.2-fold higher (95% CI 2–4.8) in comparison to the general population [5].

Table 1. Demographic characteristics of 419 survey respondents with ADPKD

Variable	Patients	
	n	%
Sex		
Male	145	34.6
Female	265	63.2
Not reported	9	2.2
Ethnicity		
Hispanic or Latino	18	4.3
Not Hispanic or Latino	369	88.1
Unknown or not reported	32	7.6
Race		
American Indian/Alaska native	3	0.7
Asian	3	0.7
Black or African American	3	0.7
White	381	93.6
More than one race	12	3.0
Unknown or not reported	17	4.1
Family history of ADPKD	347	82.8
No	37	8.8
Unknown	35	8.4
ESRD	136	32.5
No	271	64.7
Unknown	12	2.9
Hemodialysis or peritoneal dialysis	83	19.8
No	329	78.5
Unknown	7	1.7
Transplantation	117	27.9
No	291	69.5
Unknown	11	2.6
Dialysis and transplantation	66	16
Preemptive transplantation (never on dialysis)	51	12.2
Mean age $\pm$ SD, years ¹	53.2 $\pm$ 13.7	

¹ Age at the time of survey available for 418 patients.

Cardiovascular complications are the most common cause of morbidity and mortality in patients with ADPKD [6]. Primary prevention is important to reduce early morbidity and mortality, thus the need for detection and treatment of cardiovascular risk factors in the ADPKD population. There is evidence that blockade of the renin-angiotensin-aldosterone system (RAAS) with better control of blood pressure has improved ADPKD patient and renal survival [7–9]. There also are results in hypertensive ADPKD patients which demonstrate that initial therapy with RAAS inhibition compared to diuretics necessitates significantly fewer antihypertensive medications for comparable control of blood pressure [10].

This study analyzed the cardiovascular events and risk factors in a large number of ADPKD patients according to gender, age, hypertension, cholesterol, smoking and end-stage renal disease (ESRD). This observational study was undertaken in an era in which the majority of patients were receiving RAAS inhibition.

Methods

Data Source and Study Population

We developed a 6-page survey that was distributed to 1,439 study subjects listed as having ADPKD in our database. The survey asked basic demographic questions and specific questions related to the occurrence of cardiovascular disease in ADPKD patients, including the occurrence of stroke, peripheral arterial disease, abdominal aortic aneurysm, angina pectoris, myocardial infarction, atrial or ventricular arrhythmias, LVH and cardiac valvular abnormalities. The survey also collected information regarding the presence and treatment of cardiovascular risk factors, including hyperlipidemia, smoking, diabetes mellitus, hypertension and medication use (see appendix).

The survey was sent in a single mailing (January 2011) with instructions and an envelope provided in which to return it. A total of 426 (30%) subjects with ADPKD returned the survey completed; of these, 7 were from patients under the age of 18 years and these were excluded from the analysis.

Statistical Analysis

SAS version 9.3 PROC FREQ and PROC MEANS were used to obtain descriptive statistics for the surveys. The difference between the distribution of age categories for men and women was tested using a contingency table χ^2 test. $p < 0.05$ was considered significant.

Proportions for demographics were calculated as a percentage of all respondents. Proportions for other tables were calculated as a percentage of those who responded to that question.

Because multiple outcomes were tested, p values were adjusted using the Bonferroni method. Adjusted p values less than 0.0036 (0.05/14) or unadjusted p values < 0.05 were considered significant. This adjustment corrects for the probability of getting a significant p value purely by chance.

Results

Descriptive Analysis of the Patients Who Responded

ADPKD patients who responded were female (63.2%), nonHispanic (88.1%) and white (93.6%) (table 1). The mean age of the total group was 53.2 $\pm$ 13.7 years; 82.8% had a family history of ADPKD and 32.5% had reached ESRD. Analysis of cardiovascular risk factors (table 2) demonstrated that 86.6% had hypertension with a mean age of diagnosis of 36.9 $\pm$ 12.9 years with a significantly higher prevalence in males. In addition, 19.6% were obese, 20.8% were smokers, 8.7% had diabetes, 45.7% had high

cholesterol and 17.8% were sedentary. The most prevalent self-reported cardiovascular events (table 3) were arrhythmias (25.9%) with a mean age of diagnosis of 43.3 ± 16.4 years, evidence of peripheral vascular disease (16.5%; mean age of diagnosis 45 ± 13 years), heart valve problems (14.4%; mean age of diagnosis 41.2 ± 16.5 years), cardiac enlargement (9.5%; mean age of diagnosis 42.6 ± 13.9 years), stroke or cerebral bleeding (7.5%; mean age of diagnosis 50.8 ± 13.4 years), myocardial infarction (6%; mean age of diagnosis 53.4 ± 9.6 years) and brain aneurysm (5.0%; mean age of diagnosis 43.4 ± 13.7 years). Angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) were used in 75% of hypertensive ADPKD patients (table 4). Statins and antiplatelet medications (aspirin) were used in 11 and 22.5%, respectively.

Subgroup Analysis

Demographic parameters or cardiovascular risk factors were not significantly different between males and females (table 5). The occurrence of reported heart attacks was significantly higher in males (11.4%) than females (3.1%) (adjusted p value of 0.0136) (table 4).

ADPKD respondents over the age of 45 years were significantly more likely to report hypertension and high cholesterol than those 45 years or younger (table 6). Cardiovascular events were higher in older ADPKD respondents but did not reach significance (table 6).

ADPKD respondents with ESRD were significantly more likely to report diabetes, hypertension and high cholesterol levels (table 7). They also reported a significantly higher incidence of stroke or cerebral bleeding, heart attack and cardiac enlargement (table 7).

Discussion

The most common extra-renal complications that contribute to morbidity and mortality in ADPKD patients are of a cardiovascular nature [4]. Hypertension is the most frequent cardiovascular complication and contributes to both an increased incidence of cardiovascular mortality and a faster progression to ESRD [6, 11, 12]. Hypertension develops early in the course of ADPKD [13] and occurs in 50–70% of ADPKD patients with normal kidney function [14, 15]. We previously reported a median age at diagnosis for hypertension in ADPKD of 32 years in males and 34 years in females [16]. The current results support the presence of early hypertension in ADPKD. Hypertension is a widespread feature of this disease

Table 2. Incidence of cardiovascular risk factors in 419 survey respondents with ADPKD

Variable	Patients	
	n	%
Obesity (BMI ≥ 30)	77/392	19.6
Ever smoked	156/412	37.9
Current Smoker	32/154	20.8
Diabetes	36/412	8.7
Hypertension	356/411	86.6
High cholesterol	188/411	45.7
Sedentary	73/411	17.8

Table 3. Prevalence of cardiovascular events of 419 survey respondents with ADPKD

Variable	Patients		Mean age at diagnosis $\pm$ SD
	n	%	
Stroke or cerebral bleeding	31/412	7.5	50.8 ± 13.4
Brain aneurysm	20/397	5.0	43.4 ± 13.7
Circulation problems in legs	66/400	16.5	45 ± 13
Abdominal aortic aneurysm	3/397	0.8	35.7 ± 26.8
Angina	13/399	3.3	48.9 ± 15.9
Heart attack	24/399	6	53.4 ± 9.6
Irregular heart beat (arrhythmia)	103/398	25.9	43.3 ± 16.4
Enlarged heart	38/400	9.5	42.6 ± 13.9
Heart valve problem	57/397	14.4	41.2 ± 16.5
Heart surgery	23/393	5.9	50.7 ± 11.9
Angioplasty	4/23	17.4	
Stents	8/23	34.8	
Angioplasty + stents	3/23	13	
Coronary bypass	4/23	17.4	
Cardiac valve surgery	4/23	17.4	

and has been reported in up to 80% of ADPKD patients with ESRD on dialysis [17]. Thus, the main and most effective therapy in ADPKD remains control of hypertension primarily by including RAAS inhibition [7, 8]. For the definitive answer of whether treatment with either ACEIs and/or ARBs results in a decreased rate of renal disease progression in ADPKD, we await the results of the HALT-PKD (Halt Progression of PKD) study [18]. However, the control of hypertension in ADPKD patients is important as it is a specific risk factor for intracerebral hemorrhage and aneurysm ruptures [19].

Our study demonstrates a high prevalence of cardiovascular risk factors including hypertension, obesity, diabetes and hypercholesterolemia in an ADPKD popula-

Table 4. Use of antihypertensive drugs among 419 survey respondents with ADPKD

Drug	ADPKD patients					
	hypertensive		nonhypertensive		all	
	n	%	n	%	n	%
Diuretics	78/333	23.4	1/53	1.9	79/387	20.4
Sympathetic blocking agents	92/329	28	2/54	3.7	94/385	24.4
Vasodilators	14/331	4.2	1/53	1.9	15/387	3.9
Calcium channel blockers	87/330	26.4	0/54	0	87/386	22.5
ACEIs	155/331	46.8	6/54	11.1	161/387	41.6
ARBs	92/331	27.8	2/51	3.9	94/384	24.5

Table 5. Analysis of cardiovascular risk factors and events by gender among 419 survey respondents with ADPKD

Variable	Male		Female		p value ^a	Adjusted p value
	n	%	n	%		
Obesity (BMI ≥30)	33/140	23.6	44/248	17.7	0.1668	1
Current smoker	9/60	15.0	22/91	24.2	0.1719	1
Diabetes	12/144	8.3	23/264	8.7	0.8961	1
Hypertension	127/143	88.8	225/264	85.2	0.3127	1
High cholesterol	68/143	47.6	119/264	45.1	0.6322	1
Stroke or cerebral bleeding	10/144	6.9	20/144	7.6	0.8154 ^a	1
Brain aneurysm	5/138	3.6	14/255	5.5	0.4101 ^a	1
Abdominal aortic aneurysm	2/138	1.5	1/255	0.4	0.2808 ^b	1
Angina	8/140	5.7	5/255	2.0	0.0726 ^b	1
Heart attack	16/140	11.4	8/255	3.1	0.0010 ^a	0.0136
Irregular heart beat (arrhythmia)	32/139	23.0	71/255	27.8	0.2980 ^a	1
Enlarged heart	21/140	15.0	17/256	6.6	0.0069 ^a	0.0971
Heart valve problem	17/138	12.3	40/255	15.7	0.3655 ^a	1

^a χ^2 test. ^b Fisher's exact test.

tion. In a previous study, 22% of ADPKD patients (age 35.9 ± 11.1 years) with normal kidney function also fulfilled the International Diabetes Federation criteria of metabolic syndrome [20].

LVH is a significant risk factor for cardiovascular morbidity and mortality and a common finding in hypertensive and even normotensive ADPKD patients [21–24]. However, a recent study in ADPKD patients with preserved renal function reported a prevalence of LVH of 3.9% [25]. Increased LV mass index does occur in children and young adults with ADPKD [13, 26–28]. The early onset of hypertension in ADPKD may be associated with LVH in nearly 50% of ADPKD patients by their 40s [22]. Increased LV mass index has been found to be associated with poor renal and overall outcomes in ADPKD patients

[12], and a significant correlation between hypertension and increased LV mass index has been demonstrated in both children and adult patients [13, 26–28]. RAAS inhibition in hypertensive ADPKD patients has led to the long-term reversal of LVH [29, 30]. This finding was significantly greater in association with a rigorous control of blood pressure (<120/80 mm Hg) in ADPKD patients [30].

Structural cardiac abnormalities are found more often in ADPKD patients than in non-ADPKD family members or in normal controls [31]. A prospective echocardiographic study in ADPKD subjects found mitral valve prolapse in 26% and mitral regurgitation in 31% [27]. Tricuspid regurgitation and aortic regurgitation were also found, in 15% and 8%, respectively [29]. In our study, overall heart valve problems were found in 14.4% of patients.

Table 6. Analysis of cardiovascular risk factors and events by age among 419 survey respondents with ADPKD

Variable	Patients ≤45 years		Patients >45 years		p value ^a	Adjusted p value
	n	%	n	%		
Obesity (BMI ≥30)	17/86	19.8	60/305	19.7	0.9843	1
Current smoker	11/28	39.3	21/125	16.8	0.0082	0.1146
Diabetes	3/91	3.3	33/320	10.3	0.0367	0.5140
Hypertension	59/91	64.8	296/319	92.8	<0.0001	<0.0001
High cholesterol	14/91	15.4	174/319	54.6	<0.0001	<0.0001
Stroke or cerebral bleeding	1/92	1.1	30/319	9.4	0.0078 ^a	0.1089
Brain aneurysm	2/90	2.2	18/306	5.9	0.1634 ^a	1
Abdominal aortic aneurysm	0/92	0	3/304	1.0	n/a	1
Angina	1/92	1.1	12/306	3.9	0.3141 ^b	1
Heart attack	1/92	1.1	23/306	7.5	0.0231 ^a	0.3236
Irregular heart beat (arrhythmia)	14/91	15.4	89/306	29.1	0.0089 ^a	0.1239
Enlarged heart	2/91	2.2	36/308	11.7	0.0067 ^a	0.0943
Heart valve problem	8/91	8.8	49/305	16.1	0.0828 ^a	1

^a χ^2 test. ^b Fisher's exact test.

Table 7. Analysis of cardiovascular risk factors and events by gender among 419 ADPKD survey respondents with and without ESRD

Variable	Patients with ESRD		Without ESRD		p value ^a	Adjusted p value
	n	%	n	%		
Obesity (BMI ≥30)	21/129	16.3	56/257	21.8	0.2012	1
Current smoker	8/57	14.0	24/94	25.5	0.0938	1
Diabetes	22/135	16.3	13/270	4.8	0.0001	0.0015
Hypertension	132/135	97.8	218/269	81.0	<0.0001	<0.0001
High cholesterol	86/134	64.2	97/270	35.9	<0.0001	<0.0001
Stroke or cerebral bleeding	20/135	14.8	10/271	6.7	<0.0001 ^a	0.0008
Brain aneurysm	12/131	9.2	8/259	3.1	0.0102 ^a	0.1434
Abdominal aortic aneurysm	2/131	1.5	1/259	0.4	0.2621 ^b	1
Angina	8/132	6.1	5/260	1.9	0.0387 ^b	0.5417
Heart attack	16/133	12.0	8/259	3.1	0.0005 ^a	0.0066
Irregular heart beat (arrhythmia)	44/133	33.1	57/258	22.1	0.0187 ^a	0.2614
Enlarged heart	21/132	15.9	16/261	6.1	0.0017 ^a	0.0240
Heart valve problem	23/130	17.7	32/260	12.3	0.1498 ^a	1

^a χ^2 test. ^b Fisher's exact test.

The occurrence rate of coronary events, such as angina, myocardial infarction, and the need for coronary revascularization in ADPKD patients with normal renal function has not been previously reported in the literature. Our survey reported that 3.3% of respondents had angina, 6% had suffered a heart attack and 5.9% had undergone angioplasty, angioplasty and stent or cardiac valve surgery. The mean age for heart surgery was 50.7 ± 11.9 years. ADPKD patients with ESRD had less coronary events than matched ESRD patients of other causes

[32, 33]. This has been attributed to less severe anemia in ADPKD patients [32, 33], which is probably due to increased endogenous erythropoietin production [34].

Arterial aneurysms, particularly intracranial aneurysms, are more prevalent in ADPKD patients than in the general population (4.0–11.7 vs. 1.0%) [35, 36]. Moreover, it has been suggested that ADPKD is a risk factor for coronary artery aneurysms [37]. Abdominal aortic aneurysm also appears to be more prevalent in ADPKD patients [38–40], although in our cohort, the incidence was

actually very low (0.8%). However, a tendency towards larger aortic diameters in ADPKD patients compared to a control population has previously been reported [39].

The other major vascular abnormality in ADPKD is intracranial aneurysms (ICA). The prevalence ranges from 5% in patients with no family history of ICA to 21% in those with a positive family history of ICA rupture [32, 35, 41]. The prevalence may be even higher in ADPKD patients on dialysis, as observed in our study. An occurrence rate of both asymptomatic and ruptured ICA of 33.3% has been reported in ADPKD patients with ESRD [42]. Another study [43] found no difference in incidence of cerebrovascular accidents between ADPKD patients on dialysis and a non-PKD dialysis patient population. Only 25–50% of cerebrovascular accidents in ADPKD patients have been reported to result from ICA rupture [6, 44]. In our cohort, brain aneurysm and stroke prevalence or intracerebral bleeding were 5 and 7.5%, respectively. ICA rupture accounts for a 35–55% risk of combined morbidity and mortality [19, 45], so identification and screening of patients at risk for developing symptomatic ICA are recommended. Systematic screening of ICA with 3-dimensional magnetic resonance angiography (MRA) is recommended for ADPKD patients, particularly for adults (≥ 30 years), with a positive family history of hemorrhagic stroke or ICA, those undergoing major surgery with potential hemodynamic instability and those with high-risk occupations [46, 47]. It has been recommended that MRA be conducted every 5 years if initially negative and every 2–3 years if positive [46]. However, recent data support a requirement for less screening for ICAs in ADPKD patients and therefore widespread screening is not indicated [48].

Patients with non-PKD chronic kidney disease demonstrate significantly increased cardiovascular events and risk factors [49]. However, ADPKD is unique, due to the early occurrence of hypertension, heart valve problems and ICA. As expected, older ADPKD patients and those with ESRD are at a higher risk for cardiovascular events; male gender, however, may be losing its importance as a risk factor. The early and effective treatment of hypertension in ADPKD is critical for the prevention of cardiovascular events in ADPKD.

Conclusion

There are intrinsic limitations to the survey-based nature of this study and the reported frequencies may be underestimated. Nevertheless, these findings confirm the

high prevalence of cardiovascular risk factors and events in ADPKD patients which are associated with an increased risk for mortality. Moreover, older ADPKD subjects and those with ESRD had an increased risk for cardiovascular events, and this increased morbidity and mortality. Due to the prevalence and early onset of cardiovascular risk factors in the ADPKD population, early diagnosis and intervention by aggressively treating blood pressure in ADPKD patients is considered important for the prevention of LVH, cardiovascular complications and mortality.

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Appendix

Survey on Polycystic Kidney Disease

Please mark answers with an X or fill in the information in the box as indicated.

By returning this form, I indicate my consent to participate in this survey.

Information will be kept strictly confidential.

Feel free to attach a sheet of paper if needed to clarify an answer.

Date: _____

1. Name: _____

(Last)(First)(Middle)(Maiden)

2. Date of birth: ☐☐☐☐☐☐

MonthDayYear

3. Gender: ☐ male ☐ female

4. Ethnic categories (select one):

☐ Hispanic or Latino ☐ Unknown

☐ Not Hispanic or Latino ☐ decline to report

☐ Decline to report

5. Racial categories (select one):

☐ American Indian/Alaska Native ☐ White

☐ Asian ☐ More Than One Race

☐ Native Hawaiian or other Pacific Islander ☐ Unknown

☐ Black or African American ☐ Decline to report

6. Do you have other family members with PKD?
☐ Yes ☐ No ☐ Unknown

7. Have you had either hemodialysis or peritoneal dialysis treatment?
☐ Yes ☐ No
 If yes, what was your age at the time you had your first dialysis treatment? ☐ ☐

8. Have you received a kidney transplant? ☐ Yes ☐ No
 If yes, what was your age at the time of your first transplant? ☐ ☐

9. Weight (pounds) ☐ ☐ ☐ Height (feet) ☐ ☐ ☐

10. Have you ever smoked Cigarettes or Cigars: ☐ Yes ☐ No
 If yes: How many packs/day: ☐ ☐
 Number of years you have smoked: ☐ ☐
 Do you still smoke? ☐ Yes ☐ No

11. Have you ever been told by a doctor that you have diabetes?
☐ Yes ☐ No If yes, what was your age at diagnosis? ☐ ☐
 If yes, Type: ☐ 1 ☐ 2 ☐ Gestational
☐ Unknown (only during pregnancy)
 If yes, initial treatment: ☐ Diet ☐ Medication ☐ Insulin injection
 If yes for medication(s), which diabetes medication(s) do you take?
 Current diabetes treatment (if different from above):
☐ Diet ☐ Medication ☐ Insulin injection
 What was your age when you began your current treatment? ☐ ☐
 If yes for medication(s), which diabetes medication(s) do you currently take?

12. Have you ever been told by a doctor that you have high blood pressure
☐ Yes ☐ No If yes, what was your age at diagnosis? ☐ ☐
 Have you been on medication for high blood pressure ?
☐ Yes ☐ No
 If yes, which high blood pressure medication(s) do you take?

13. Have you ever been told by a doctor that you have high cholesterol?
☐ Yes ☐ No If yes, what was your age at diagnosis? ☐ ☐
 Current treatment: ☐ Diet ☐ Medication
 If yes for medication, which high cholesterol medication(s) do you take?

14. Do you exercise? ☐ Yes ☐ No If yes, how many hours/week? ☐ ☐
 What type of exercise? ☐ Walking ☐ Running ☐ Biking
☐ Other

15. Have you ever been told by a doctor that you had a stroke or bleeding in your head?
☐ Yes ☐ No If yes, what was your age at diagnosis? ☐ ☐
 What was the problem (Mark all that apply)?
☐ Symptoms of stroke lasting less than 24 hours
☐ Stroke ☐ Bleeding ☐ Ruptured aneurysm

16. Have you ever been told by a doctor that you have a brain aneurysm?
☐ Yes ☐ No If yes, what was your age at diagnosis? ☐ ☐
 If yes, have you ever had surgery for your aneurysm? ☐ Yes ☐ No

17. Has anyone in your family been told by a doctor that they have a brain aneurysm or had a ruptured aneurysm in their head?
☐ Yes ☐ No ☐ Unknown
 If yes, what was their age at diagnosis? ☐ ☐
 How are they related to you? _____
 If yes, what was their age at diagnosis? ☐ ☐
 How are they related to you? _____
 If yes, what was their age at diagnosis? ☐ ☐
 How are they related to you? _____

18. Have you ever had circulation problems in your legs?
☐ Yes ☐ No
 If yes, what was your age when this first occurred? ☐ ☐

19. Have you ever been told by a doctor that you had an abdominal aortic aneurysm?
☐ Yes ☐ No If yes, what was your age at diagnosis? ☐ ☐

20. Have you ever been told by a doctor that you have Angina?
☐ Yes ☐ No If yes, what was your age at diagnosis? ☐ ☐

21. Have you ever been told by a doctor that you had a heart attack?
☐ Yes ☐ No If yes, what was your age at diagnosis? ☐ ☐

22. Have you ever been told by a doctor that you have an irregular heart beat?
☐ Yes ☐ No If yes, what was your age at diagnosis? ☐ ☐

23. Have you ever been told by a doctor that you have an enlarged heart?
☐ Yes ☐ No If yes, what was your age at diagnosis? ☐ ☐

24. Have you ever been told by a doctor that you have a heart valve problem?
☐ Yes ☐ No If yes, what was your age at diagnosis? ☐ ☐

25. Have you ever had heart surgery? ☐ Yes ☐ No
 If yes: ☐ Angioplasty ☐ Stents ☐ Angioplasty + Stent
☐ Coronary bypass
 If yes, what was your age at surgery? ☐ ☐

26. If working, how many days have you missed work in the last year due to symptoms related to your PKD?

27. Have you ever been told by a doctor that you have osteoporosis?
☐ Yes ☐ No If yes, what was your age at diagnosis? ☐ ☐

28. Have you ever been told by a doctor that you have low vitamin D?
☐ Yes ☐ No If yes, what was your age at diagnosis? ☐ ☐

29. Have you ever been told by a doctor that you had kidney stones, or other problems from kidney stones?
☐ Yes ☐ No If yes, what was your age at diagnosis? ☐ ☐
☐ In one kidney ☐ In both kidneys
 How were the kidney stones treated?
☐ Surgery ☐ Medication ☐ Other
 If yes for medication, which medication(s) did you take for your kidney stones?

30. What were your symptoms of kidney stones (mark all that apply):
☐ Back pain ☐ Flank/side pain ☐ Abdominal/stomach pain
☐ Bloody urine ☐ A doctor found blood in my urine
☐ Kidney infection ☐ Abnormal laboratory or radiology results

31. Do you know what kind of stone you had?
☐ Uric acid stone ☐ Calcium-containing stone ☐ Unknown

32. Any other medical conditions not mentioned above?

33. Are you currently taking prescription or over the counter medication(s) or vitamins?
☐ Yes ☐ No, not currently taking medication ☐ Decline to report
 Please list all current medicine(s) and the first date on which you started taking this medicine:
 Name of medication: _____
 Date began taking medication: _____
 Name of medication: _____
 Date began taking medication: _____

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