Polycystic kidney disease among 4,436 intracranial aneurysm patients from a defined population

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ABSTRACT

Objective: To define the association of autosomal dominant polycystic kidney disease (ADPKD) with the characteristics of aneurysmal subarachnoid hemorrhage (aSAH) and unruptured intracranial aneurysm (IA) disease.

Methods: We fused data from the Kuopio Intracranial Aneurysm database (n = 4,436 IA patients) and Finnish nationwide registries into a population-based series of 53 IA patients with ADPKD to compare the aneurysm- and patient-specific characteristics of IA disease in ADPKD and in the general IA population, and to identify risks for de novo IA formation.

Results: In total, there were 33 patients with ADPKD with aSAH and 20 patients with ADPKD with unruptured IAs. The median size of ruptured IAs in ADPKD was significantly smaller than in the general population (6.00 vs 8.00 mm) and the proportion of small ruptured IAs was significantly higher (31% vs 18%). Median age at aSAH was 42.8 years, 10 years younger than in the general IA population. Multiple IAs were present in 45% of patients with ADPKD compared to 28% in the general IA population. Cumulative risk of de novo IA formation was 1.3% per patient-year (vs 0.2% in the general IA population). Hazard for de novo aneurysm formation was significantly elevated in patients with ADPKD (Cox regression hazard ratio 7.7, 95% confidence interval 2.8–20; $p < 0.0005$).

Conclusions: Subarachnoid hemorrhage occurs at younger age and from smaller IAs in patients with ADPKD and risk for de novo IAs is higher than in the general Eastern Finnish population. ADPKD should be considered as an indicator for long-term angiographic follow-up in patients with diagnosed IAs. ***Neurology*® 2017;89:1852–1859**

GLOSSARY

ADPKD = autosomal dominant polycystic kidney disease; **aSAH** = aneurysmal subarachnoid hemorrhage; **CI** = confidence interval; **CTA** = CT angiography; **DSA** = digital subtraction angiography; **HR** = hazard ratio; **IA** = intracranial aneurysm; **KUH** = Kuopio University Hospital; **MCA** = middle cerebral artery; **MRA** = MR angiography; **PKD** = polycystic kidney disease; **SAH** = subarachnoid hemorrhage; **sIA** = saccular intracranial aneurysm.

Autosomal dominant polycystic kidney disease (ADPKD) is a common hereditary disease with a prevalence of 1:400–1,000 live births. It is caused by mutations in either *PKD1* (~85%) or *PKD2* (~15%).[1] Together they are essential to vascular wall integrity and shear stress endurance.[2] The main feature of ADPKD is formation of cysts in the tubular epithelium of the nephron, resulting in loss of functional renal tissue, enlargement of the kidneys, and terminal uremia. Symptoms of ADPKD include hypertension, back pain, hematuria, and infections of the urinary tract and singular cysts. Extrarenal manifestations of the disease include intracranial aneurysms (IAs).[1]

IAs are usually pouch-like (i.e., saccular), sometimes spindle-shaped (fusiform), dilations at branching sites of major arteries in the circle of Willis. They are acquired lesions, most commonly diagnosed at around 50 years of age,[3] affecting approximately 3% of the adult population.[4] IA rupture leads to aneurysmal subarachnoid hemorrhage (aSAH), the most deadly subtype of stroke.[3]

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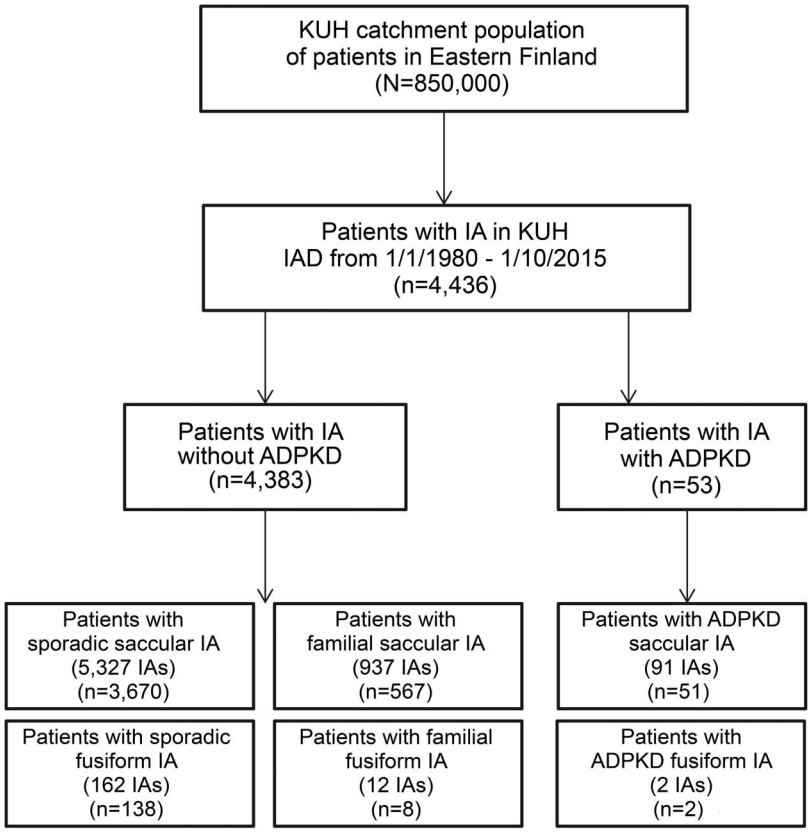
Estimates of prevalence of unruptured IAs in patients with ADPKD vary from 4%[5] to 33%.[6] Previous studies indicate that up to 6% of patients with ADPKD may have aSAH.[7] Our aim was to define the association of ADPKD with characteristics of aSAH and unruptured IA disease. We fused data from the Kuopio IA database and Finnish nationwide registries into a population-based cohort of patients with IA with ADPKD to compare the aneurysm- and patient-specific characteristics of IA disease in ADPKD and in the general IA population and to identify risks for de novo IA formation.

METHODS

The catchment population of Kuopio University Hospital. The Department of Neurosurgery at Kuopio University Hospital (KUH) is the exclusive center of both acute and elective neurosurgery for its catchment area in Eastern Finland. During the study period, the geographic area remained the same, the population decreased from 824,823 to 815,093, and the proportion of men rose from 49% to 49.5%. All the patients diagnosed with aSAH by CT or lumbar puncture in this area are imaged angiographically and treated in KUH if not moribund or very aged. Unruptured IAs detected by screening of IA family members or as occult findings are also referred to KUH to be evaluated for elective occlusion by the neurovascular team. All the IA diagnoses are confirmed by 4-vessel digital subtraction angiography (DSA), MR angiography (MRA), or CT angiography (CTA).[8–13]

Figure 1 Study population



ADPKD = autosomal dominant polycystic kidney disease; IA = intracranial aneurysm; IAD = intracranial aneurysm database; KUH = Kuopio University Hospital.

Kuopio IA patient and family database. The Department of Neurosurgery maintains a database of all cases of angiographically verified aSAH and patients with unruptured IAs admitted to KUH since 1977 (kuopioneurosurgery.fi/). The database, prospective since 1990, now includes over 4,900 patients with IA. The clinical data on their initial treatment and follow-up visits, alongside information on their concomitant diseases, prescribed medications, and aneurysm-related risk factors such as smoking and family history, are coded into an extensive list of variables. The database is maintained by a dedicated full-time nurse coordinator, who interviews all the new patients and enters follow-up data from follow-up visits and national statistics, including causes and circumstances on death. The criterion for saccular IA (sIA) family is at least 2 affected first-degree relatives, and sIA disease without family history is considered sporadic. The definition of hypertension was based on patient announcement, known hypertension diagnosis, or antihypertensive medication used at the time of IA diagnosis.

Follow-up for de novo IA formation. De novo IAs were defined as new IAs seen at a vascular location that was previously confirmed to be clean with CTA, MRA, or DSA. Follow-up times were calculated from the first angiography (CTA, MRA, or DSA) to the last angiography or the first angiography showing de novo IA formation. Decisions of selection to long-term angiographic follow-up were made in the neurovascular team on a case-to-case basis.

Data fusion from national registries. Using Finnish social security numbers, the use of prescribed medications was obtained from the national database by the Social Insurance Institution of Finland. The database of the National Institute of Health was consulted for ADPKD diagnoses and Statistics Finland provided the data on causes and times of death. These data were then fused with the Kuopio IA patient and family database.

Identification of patients with ADPKD. The Kuopio IA database was searched for patients with ADPKD, using data from the national database of hospital diagnoses of the National Institute of Health. The following diagnoses were identified to screen for ADPKD: Q61.2, polycystic kidney, adult type; Q61.3, polycystic kidney, nonspecified. Identified patient records were carefully reviewed for additional confirmation or exclusion of the diagnosis of ADPKD. A total of 53 patients with ADPKD and IA was identified (figure 1). Patients were defined as having ADPKD if they had a verified diagnosis of ADPKD at any time during the study period (January 1, 1980–October 1, 2015).

Study population of 4,436 patients with IA. The study population consists of the following patients (figure 1):

1. Those with Finnish citizenship and of Finnish ethnicity.
2. Those who were admitted alive to KUH with intracranial saccular or fusiform IAs or subarachnoid hemorrhage from a saccular or fusiform IA between January 1, 1980, and October 1, 2015.

Previous relevant literature. In order to summarize the previous studies on the relationship between ADPKD and IA disease, PubMed was searched for articles on studies on humans only published in English after January 1, 1990, with the terms (ADPKD or PKD or polycystic) and aneurysm* and (CNS or intracranial or brain or cerebral or subarachnoid*). On June 22, 2016, this search delivered 205 hits. We included studies (1)

examining the prevalence or characteristics of IAs or aSAH in the ADPKD population and (2) featuring a population of 3 or more patients with ADPKD with IAs or aSAH (3) verified by appropriate methods of diagnosis. Cohorts smaller than 3 patients with ADPKD with IA, case reports, and patient questionnaire surveys without imaging or autopsy data were excluded. From a single cohort, the largest or most recent study was included. These studies are presented in table 1.

Statistical analysis. IA characteristics (size, location, etiology, morphology) and patient characteristics (age at diagnosis of IA and ADPKD, sex, harboring multiple IAs, and de novo IA formation) were collected from the IA database and compared between patients with ADPKD and the general IA population. IBM SPSS Statistics, version 22.0 (IBM SPSS, Armonk, NY) was used for the analyses. Distributions were compared by Mann-Whitney *U* test and independent samples median test. For contingency, χ^2 and Fisher exact test were used as appropriate. Two-tailed *p* values ≤ 0.05 were considered statistically significant. Kaplan-Meier hazard curves were plotted to visualize the effect of ADPKD on de novo IA formation and log-rank test (Mantel-Cox) was used to examine the difference between the curves of the patients with ADPKD and the general IA population. Multivariable Cox regression analysis using the enter method was used to calculate hazard ratios (HRs) and 95% confidence intervals (CI) for de novo sIA formation with the following variables: age at first IA diagnosis, smoking, hypertension, family history of IAs, and ADPKD.

Standard protocol approvals, registrations, and patient consents. This study was approved by the ethical committee of KUH and informed consent was obtained from all patients. Data integration from the national registries was performed with approval from the Ministry of Social Affairs and Health of Finland.

RESULTS

Characteristics of the patients with ADPKD with IA. In our population-based IA database of 4,436 patients with IA, there were 53 (1.2%) patients with ADPKD (95% CI 0.9%–1.6%, 45% male). Their clinical characteristics are shown beside the characteristics of the general IA population without ADPKD in table 2. The median age at diagnosis of ADPKD was 48.5 years (SD 13.3). In 4 patients who died of subarachnoid hemorrhage (SAH), the polycystic kidneys were discovered postmortem. Hypertension was present in 74% of patients with ADPKD at the time of IA diagnosis. There were 12 (23%) patients with ADPKD who had known family history of IAs. Multiple IAs were present in 45% of the

Table 1 Previous cohorts of intracranial aneurysm (IA) and subarachnoid hemorrhage (SAH) in patients with autosomal dominant polycystic kidney disease (ADPKD)

Publication year	Type of study	ADPKD/IA/SAH	Prevalence of IA/SAH, %	Mean age, y	Means of diagnosis, IA/SAH	Risk factors for IA
1990[14]	Retrospective	98/NA/3	NA/3.1 (2.2[a])	NA	NA/CT, DSA	NA
1992[15]	Prospective	75/6/NA	8.0/NA	51.4	DSA/NA	NA
1992[16]	Retrospective	41/41/33	NA/NA (1.7[a])	46.4	DSA, surgery, AUT/CT, surgery, AUT	NA
1992[5]	Prospective	92/4/0	4/NA	36	CT, DSA/NA	NA
1992[17]	Retrospective	142/NA/3	NA/2.1	55	NA/CT, DSA	NA
1994[18]	Retrospective	77/77/71	NA/NA	40	CT or DSA	FH, previous SAH[b]
1993[19]	Prospective	85/9/0	11/NA	45.3	MRA/NA	FH of IA or SAH; PLD
1994[20]	Prospective	93/10/0	10.8/NA	48.0	MRI, MRA, DSA/NA	FH of IA
1995[7]	Retrospective	129/10/7	NA/6	55[c]	75/129 AUT	NA
1998[6]	Retrospective	63/6/3	33/4.8	58.9	MRA or DSA (18)	NA
2000[21]	Retrospective	15/3/1	20/6.7	58.3	MRA	NA
2002[22]	Prospective	43/6/0	14/NA	45.7	MRA, DSA/NA	FH of IA or ICH
2003[23]	Retrospective	5/NA/1,147	NA/NA (0.4[a])	45	CTA, MRA, DSA, CT	NA
2006[24]	Prospective	92/3/2	7.1/2.2	35.6[d]	MRA, DSA (42)/NA	NA
2010[25]	Retrospective	647/NA/6	NA/0.9	NA	NA/CT, DSA	NA
2011[26]	Prospective	355/44/0	12.4/NA	46.5	MRA, DSA/NA	FH of IA/SAH, age, HT
2013[27]	Prospective	83/12/0	16.9[e]/NA	46	MRA, CTA/NA	NA
2014[28]	Retrospective	6 749/NA/48	NA/0.71	65.3[f]	NA	NA

Abbreviations: AUT = autopsy; CTA = CT angiography; DSA = digital subtraction angiography; FH = family history; HT = hypertension (duration, y); ICH = intracranial hemorrhage; MRA = MR angiography; NA = not available/not applicable; PLD = severe polycystic liver disease; SAH = subarachnoid hemorrhage.
[a] Prevalence of ADPKD in SAH, %.
[b] Risk factors for SAH.
[c] The cohort consisted of cadavers; mean age in the cohort at death.
[d] Mean age given among the screened, not available among the rest.
[e] Also including 2 patients with history of aneurysmal SAH.
[f] Mean age at start of dialysis, duration of which not specified.

Table 2 Comparison of characteristics among patients with autosomal dominant polycystic kidney disease (ADPKD) with aneurysmal subarachnoid hemorrhage (aSAH), patients with ADPKD with unruptured intracranial aneurysms (IAs), and patients with aSAH and patients with IA in the general population

	ADPKD (n = 53)		No ADPKD (n = 4,383)	
	SAH (n = 33)	Unruptured IA (n = 20)	SAH (n = 2,962)	Unruptured IA (n = 1,421)
Women, n (%)	17 (52)	12 (60)	1,627 (55)	785 (55)
Age at first diagnosis, y, median (SD)	42.8 (12.6)	50.0 (9.6)	52.8 (13.3)	57.8 (12.6)
Age group at first diagnosis, y				
<20	0 (0)	0 (0)	22 (0.7)	9 (0.6)
20-40	12 (36)	2 (10)	479 (16)	114 (8)
40-50	13 (39)	8 (40)	763 (26)	256 (18)
50-60	4 (12)	8 (40)	807 (27)	414 (29)
>60	4 (12)	2 (10)	891 (30)	628 (44)
Risk factors				
Family history	7 (21)	5 (25)	314 (11)	261 (18)
Hypertension	23 (70)	16 (80)	901 (30)	588 (41)
Smoking, current or former	8 (24)	6 (30)	835 (28)	576 (41)
Multiple aneurysms	15 (46)	9 (45)	821 (28)	399 (28)

Values are n (%) unless otherwise specified.

patients with ADPKD, compared to 28% in the general population ($p = 0.005$). The most common IA location was the middle cerebral artery (MCA): 44% in ADPKD and 40% in the general IA population. Median IA size was 4.0 mm in patients with ADPKD (n = 93) vs 6.0 mm in the general IA population (n = 6,080; $p < 0.0005$). Irregular IA morphology was present in 48% of patients with ADPKD and 55% of the general IA population; the difference was not significant. Ruptured IAs were more common in patients without ADPKD in the posterior communicating/anterior choroidal artery location (16% vs 3%; $p = 0.028$). Other statistically significant differences in IA location distribution between the patients with ADPKD and the general IA population were not found.

Patients with ADPKD with aSAH (n = 33). The median age at aSAH diagnosis in patients with ADPKD (n = 33, 48% male) was 42.8 years, significantly younger than in the general population (52.8 years; $p = 0.002$). Percentage of patients with aSAH with ADPKD <35 years was 3.2%, but in patients ≥55 years it was only 0.4%. In 18 (55%) patients with aSAH, ADPKD had not been diagnosed before the aSAH occurred. The age at first diagnosis of ADPKD was known for 17 patients with aSAH, with a median of 42 years. Multiple IAs were present in 46% of patients with ADPKD with aSAH compared to 28% in the general aSAH population ($p = 0.024$). The 15 patients with aSAH had a total of 25 additional unruptured IAs at initial diagnosis. Median size of ruptured IAs was significantly smaller (6.00 mm) in patients with ADPKD than in other patients with aSAH (8.00 mm; $p = 0.031$). Size and other characteristics of IAs in ADPKD and in the general IA population are described in detail in table 3. The most common locations for ruptured IAs were the anterior communicating artery (44%) and MCA (39%). Ruptured IA shape was confirmed to be irregular in 89% of patients with ADPKD vs 88% of other patients with aSAH. One of the ruptured IAs in patients with ADPKD was fusiform.

Patients with ADPKD with unruptured IAs (n = 20). The most common location for unruptured IAs was the MCA (48% in ADPKD, 47% in controls) (table 3). Median size of unruptured IA was 4.00 mm in both groups. Unruptured IA shape was irregular in 24% vs 23%. Only one unruptured fusiform IA was found in patients with ADPKD.

Incidence of de novo sIAs. Patients were followed up for a total of 20,645 patient-years with a median follow-up of 6.3 years. Eight de novo IAs were diagnosed in 5 patients with ADPKD a median of 10 years after the initial diagnosis. All of them were women ($p = 0.044$) and had originally presented with an aSAH at their first diagnosis. Two patients had second aSAH from a de novo aneurysm. The cumulative risk of de novo IA formation was 1.3% per patient-year for patients with ADPKD and aSAH and 0.2% in the general aSAH population of Eastern Finland. In the Kaplan-Meier analysis, the cumulative hazard for de novo IA formation in

Table 3 Comparison of characteristics between aneurysms of patients with autosomal dominant polycystic kidney disease (ADPKD) and the general intracranial aneurysm population

	ADPKD		No ADPKD	
	Ruptured (n = 36)	Unruptured (n = 59)	Ruptured (n = 3,122)	Unruptured (n = 3,337)
Size, mm				
<4	5 (14)	23 (39)	240 (8)	1,197 (36)
4–6	11 (31)	22 (37)	576 (18)	835 (25)
6–8	7 (19)	8 (14)	621 (20)	434 (13)
8–10	5 (14)	1 (2)	470 (15)	240 (7)
>10	7 (19)	4 (7)	999 (32)	468 (14)
Size, mm, median (SD)	6.00 (3.03)	4.00 (2.47)	8.00 (6.06)	4.00 (6.84)
Location, n (%)				
ICA bifurcation	1 (3)	4 (7)	112 (4)	126 (4)
PCom/anterior choroidal artery	1 (3)	6 (10)	509 (16)	395 (12)
Ophth ICA	0	3 (5)	48 (2)	160 (5)
Extradural ICA	1 (3)	0	6 (0.2)	167 (5)
ACom	16 (44)	9 (15)	932 (30)	400 (12)
Pericallosal artery	2 (6)	6 (10)	161 (5)	159 (5)
MCA	14 (39)	28 (48)	1,031 (33)	1,581 (47)
Basilar apex/SCA	1 (3)	3 (5)	177 (6)	235 (7)
Vertebral artery/PICA	0	0	101 (3)	56 (2)
Other	0	0	45 (1)	58 (2)
Shape				
Irregular	32 (89)	14 (24)	2,753 (88)	772 (23)
Smooth	2 (6)	43 (73)	250 (8)	2,476 (74)

Abbreviations: ACom = anterior communicating artery; ICA = internal carotid artery; MCA = middle cerebral artery; Ophth ICA = ophthalmic segment of ICA; PCom = posterior communicating artery; PICA = posterior inferior cerebellar artery; SCA = superior cerebellar artery.
Values are n (%) unless otherwise specified. Data on aneurysm shape were available on 34 ruptured ADPKD, 57 unruptured ADPKD, 3,003 ruptured non-ADPKD, and 3,248 unruptured non-ADPKD aneurysms. Data on size were available on 35 ruptured ADPKD, 58 unruptured ADPKD, 2,906 ruptured non-ADPKD, and 3,174 unruptured non-ADPKD aneurysms.

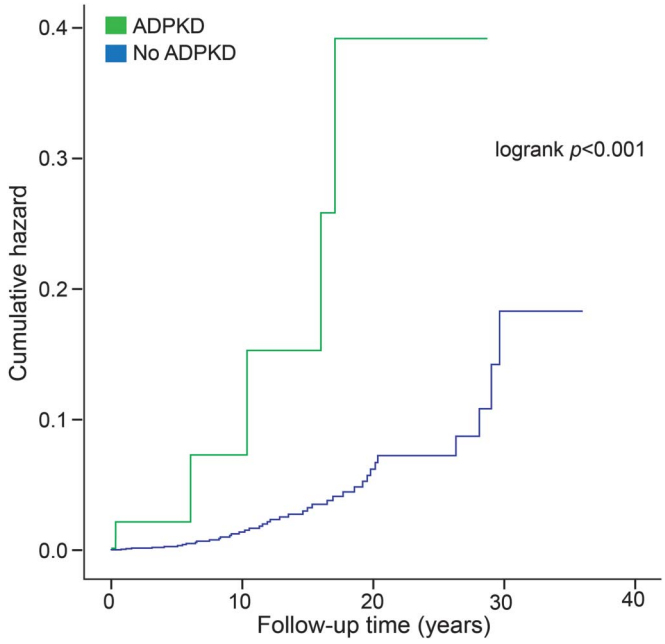
patients with ADPKD was significantly higher (log-rank $p < 0.001$) than in the general IA population (figure 2). In multivariable Cox regression model with age, smoking, hypertension, and family history of IAs and ADPKD as variables, ADPKD was an independent risk factor for de novo IA formation (HR 7.7, CI 95% 2.8–20; $p < 0.0005$). Other independent risk factors were age at first presentation of IA disease (HR 0.92 per year, 95% CI 0.92–0.97; $p < 0.0005$), smoking (HR 4.3, 95% CI 2.3–8.2; $p < 0.0005$), and female sex (HR 2.0, 1.1–3.6; $p = 0.029$).

DISCUSSION We studied differences in clinical characteristics of IA disease in a large population-based series of 53 patients with ADPKD with IA disease and 4,383 patients with IA without ADPKD. The median age at aSAH for the patients with ADPKD was 43 years, significantly lower than in the general IA population (53 years). In patients with ADPKD, ruptured IAs were significantly smaller than in the general population. De novo IA formation was significantly more common in patients with ADPKD than in the general IA population.

In previous cohorts, the mean age at aSAH in ADPKD has ranged from 37 to 47 years.[7,16,18,23] Our finding of the young onset age of aSAH in ADPKD is well in line with the previous data.

According to the Dutch meta-analysis of 53 cohorts and 369 patients with ADPKD with IA, 9%–36% of ruptured IAs (n = 40) were less than 5 mm.[23] In our study population, the median size of ruptured IAs in patients with ADPKD was only 6 mm. Furthermore, of the 36 ruptured IAs, 31% were 4 mm or smaller. Our results suggest that patients with

Figure 2 Kaplan-Meier curves of de novo aneurysm formation in patients with autosomal dominant polycystic kidney disease (ADPKD) and patients with intracranial aneurysm without ADPKD



ADPKD may be at risk of aSAH from smaller IAs than the general population. Increased rate of aneurysm formation in patients with ADPKD may be a contributing factor to this finding.

In previous studies, prevalence of multiple IAs in patients with ADPKD and IA has varied from 0%[19] to 75%.[5] In the Dutch meta-analysis, 16% of patients with ADPKD and IA had multiple IAs.[23] This is significantly fewer than in our population, where multiple IAs were present in 45% of the patients with ADPKD. All the patients in our study population underwent MRA or DSA, and even very small IAs were discovered if present.

Previous studies have reported 1.6%[29]–4.4%[21] risk per patient-year for de novo IA formation in patients with ADPKD with previously diagnosed sIA disease. In this study, during cumulative follow-up of 382 patient-years, risk of de novo IA formation after aSAH was 1.3% per patient-year. A total of 8 de novo IAs were diagnosed in 5 patients. The risk is significantly higher than that observed in the Eastern Finnish IA population in general (0.2% per patient-year). In Cox regression, ADPKD was an independent risk factor for de novo IA formation in addition to smoking, indicating that smoking does not explain the elevated risk in patients with ADPKD. However, it should be noted that risk of de novo aneurysm formation is likely not constant over time, but our small study population does not allow reliable calculation of de novo formation rates for specific age groups.

Of the 148 patients with fusiform IA in the Kuopio IA database, 2 (1.4%) also have ADPKD, slightly higher than the percentage of ADPKD carriers among patients with sIA (1.2%). Few fusiform IAs in patients with ADPKD have been reported in the literature,[16,30] probably due to their rarity. It seems probable that patients with ADPKD are prone to fusiform IAs as well, either by the weakened vessel wall due to the polycystin defect or by hypertension (and subsequent arteriosclerosis) provoked by the disease.

It is unlikely that there were patients with IA with autosomal recessive polycystic kidney disease (PKD) among our IA population. Recessive PKD is rare at 1 in 20 000 live births, and is usually characterized by more aggressive kidney disease and hepatic fibrosis manifesting in utero or in infancy.[31] None of our patients with PKD developed end stage renal disease or severe portal hypertension at a young age.

In this study population, ADPKD was often diagnosed after the IA disease (55% of the aSAH group), even though the disease is congenital. It is likely some of the patients now perceived as having regular IA will be diagnosed with ADPKD in the future. Furthermore, in some patients, ADPKD remains undiagnosed, as in 4 of our patients the polycystic kidneys were discovered postmortem. On the other hand, Ronkainen et al.[32] prospectively screened 438 members of IA families in the KUH IA database with abdominal ultrasound and discovered no undiagnosed cases of PKD among them. It is possible that some patients with ADPKD are missed and considered not to have ADPKD, but the bias is not likely to be significant. It should be noted that aSAH may be the first symptom of ADPKD. Renal ultrasound examination should be considered when treating young patients with SAH, especially if they are hypertensive.

Our results are based on a population of patients with IA collected prospectively from a well-defined population. However, it remains possible that the Finnish ethnicity of the patients may have biased our results, even though a recent study indicated that aSAH incidence in Finland is comparable to other Western populations.[33] The number of patients with ADPKD with de novo aneurysms was small, which should be taken into account when interpreting the results.

The Scandinavian governmental health care system provides this study with significant benefits. Finland is divided into mutually exclusive catchment areas of 5 university hospitals, enabling a large and minimally biased study population. We report data from a large population-based study of patients with ADPKD and IA with a sizable control population. Patients with ruptured as well as unruptured IAs are

included. However, it remains possible that Finnish ethnicity may reduce the generalizability of the results and the findings should be confirmed in other populations. The effect of ADPKD on the long-term outcome after aSAH requires further research, and we are planning to address that in a separate article.

SAH occurs at younger age and from smaller IAs and risk for de novo IAs is higher in patients with ADPKD than in the general Eastern Finnish population. Abdominal ultrasound should be considered when treating young patients with aSAH, especially if they are hypertensive, to rule out undiagnosed ADPKD. Our results suggest that ADPKD should be considered as an indicator for long-term angiographic follow-up in patients with diagnosed IAs.

AUTHOR CONTRIBUTIONS

H.J. Nurmonen: study concept and design, acquisition of data, analysis and interpretation of data. Dr. Huttunen: critical revision of the manuscript for intellectual content. Dr. Huttunen: critical revision of the manuscript for intellectual content. Dr. Kurki: critical revision of the manuscript for intellectual content. K. Helin: acquisition of data, critical revision of the manuscript for intellectual content. Dr. Koivisto: critical revision of the manuscript for intellectual content. Dr. von und zu Fraunberg: acquisition of data, critical revision of the manuscript for intellectual content. Dr. Jääskeläinen: acquisition of data, study concept and design, critical revision of the manuscript for intellectual content, study supervision. Dr. Lindgren: acquisition of data, study concept and design, analysis and interpretation of data, critical revision of the manuscript for intellectual content, study supervision.

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DISCLOSURE

The authors report no disclosures relevant to the manuscript. Go to Neurology.org for full disclosures.

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