Yield of MRA screening of ADPKD young patients for intracranial aneurysms

Mahmoud Farid Bathalla[1], Hosam Eldeen Mostafa Ali[2], Khaled Esam Fawaz[3]

[1]Neurosurgery Department, Faculty of Medicine, Al-Azhar University, Cairo, Egypt
[2]Radiology Department, Faculty of Medicine, Benha University, Benha, Egypt
[3]Urology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt
faridneuro@yahoo.com

Abstract: Background and Purpose: Autosomal dominant polycystic kidney disease (ADPKD) correlates with an increased frequency of intracranial aneurysms (ICANs). The objective of the current study is to assess the utility of screening of ADPKD young adult patients less than 30-years-age group for intracranial aneurysms. **Methods:** 60 ADPKD Arabic young patients<30 year-age underwent screening for ICANs with non-contrast 3D Time-of-Flight MR angiography (MRA) of the intracranial arteries. **Results:** ICANs aneurysms prevalence in the study population was 5%. The depicted three aneurysms were followed up for 18months and showed no significant interval size or morphologic variation and required no neurosurgical intervention for present. No new aneurysms developed during the follow-up period. **Conclusions:** The prevalence of cerebral aneurysms in the study group was larger than that previously reported in the general population. The aneurysms were small and showed no significant interval size or morphologic variation on follow-up for 18 months. MRA is a non-invasive screening modality. Screening MRA should be considered especially in patients with positive family history of intracranial aneurysms or subarachnoid hemorrhage to avoid serious devastating squeal. Follow-up is advocated in case of depicted aneurysm regardless of its size.

[Mahmoud Farid Bathalla, Hosam Eldeen Mostafa Ali and Khaled Esam Fawaz. **Yield of MRA screening of ADPKD young patients for intracranial aneurysms.** *Life Sci J* 2016;13(7):83-90]. ISSN: 1097-8135 (Print) / ISSN: 2372-613X (Online). http://www.lifesciencesite.com. 11. doi:10.7537/marslsj130716.11.

Key words: intracranial aneurysm, ADPKD, MRI

1. Introduction

Autosomal dominant polycystic kidney disease (ADPKD) is one of the most common serious hereditary diseases, found in 1:400 to 1:1000 individuals, and by far the most common hereditary cause of end stage renal failure (ESRF). ADPKD is a systemic disorder associated with various extra-renal manifestations such as hypertension, hepatic cysts, and intracranial aneurysms (ICANs). Compared with the general population, patients with ADPKD have an increased frequency of ICANs with estimates of prevalence ranging from 4% to 41% and the morbidity of aneurysmal subarachnoid hemorrhage is higher in patients with ADPKD with half of those who survive having severe neurological deficits (1).

The association of intracranial aneurysms and autosomal dominant polycystic kidney disease (ADPKD) has been known for many years. Its prevalence has only been estimated reliably over the past decade owing to the development of noninvasive detection techniques, mainly magnetic resonance (MR) angiography. A prevalence of 8% of asymptomatic ICANs has been derived from three prospective series totaling 266 patients. A rate four to five times above that found in the general population. Although this association has been attributed in the past to the occurrence of hypertension in many affected patients, several lines of evidence strongly suggest a causal role of the mutated ADPKD gene (2).

The advent of non-invasive methods of imaging intracranial blood vessels such as MRA has facilitated screening for intracranial aneurysms in people who are at risk. In the current study, we screened 60 Arabic ADPKD patients younger than 30 years for ICANs in with non-contrast 3-D time-of-flight MR Angiography to determine the prevalence of ICANs in this subgroup and to assess the possible benefit from MRA screening.

2. Subjects and methods

Study Design

To evaluate the utility of MRA screening and the prevalence of cerebral aneurysms among young adult ADPKD patients younger than 30-years age group, non-contrast 3D time-of-flight MR cerebral angiography performed.

Patients

From January 2013 through December 2015, 60 consecutive Arabic ADPKD patients (36 men and 24 women; mean age 21 years; age range, 12–29 years) underwent non-contrast 3D time-of-flight MR cerebral angiography to depict possible intracranial aneurysms. The diagnosis with ADPKD was made on the basis of abdominal ultrasonography showed bilateral multiple renal cysts in addition to positive family history of

ADPKD. All patients underwent 3D time-of flight MR angiography at a 1.5 T MR system.

The study was performed in accordance with the recommendations of our institutional review board. The whole procedure was explained to all patients, and they gave their informed consent to be included.

MR Angiography

MRA was performed on a 1.5 T magnet, (SignaHDxt, GE Healthcare, Little Chalfont, Buckinghamshire, United Kingdom). TOF MRA was obtained using 3D gradient echo sequences (TE 7.15 ms, TR 24 ms, flip-angle 25°, multiple overlapping thin slab acquisition, in-plane pixel spacing 0.625 mm, slice spacing 0.8 mm, slab thickness 28.8 mm). No gadolinium contrast was administered.

The 3D TOF MRA slab was obliquely prescribed to include the intradural vertebral artery up to the ambient segment of the posterior cerebral artery and the cavernous internal carotid artery (ICA) up to the proximal portion of the insular segment (M2) of the middle cerebral artery (MCA) in 1 slab.

The acquired image data sets were transferred to the GE Advantage workstation (GE Healthcare) where the 3D images were reconstructed with a 1024 × 1024 matrix by maximum intensity projection (MIP) and volume rendering (VR) using the associated 3D software package.

Image Analysis

Diagnoses of aneurysms were performed after evaluating the maximum intensity projection (MIP) images and individual axial sections. The following five vessel segments were analyzed separately in each case: the axial and coronal rotations of whole intracranial arteries, the axial rotation of both internal carotid arteries (ICAs), the middle cerebral arteries (MCAs), anterior cerebral arteries (ACA), posterior communicating artery origins, and the basilar artery. Target MIP was tried when necessary. If an aneurysm was detected, the following items recorded: the size, shape, neck, and parent vessel. If an aneurysm was suspected after review of five sets of MIP images, the multiplanar reconstruction (MPR) image was also generated. The MPR technique involves reformatting (resectioning) the MR angiographic volumetric series into sets of sequential thin-section 2D images, with section orientation, section thickness, and intersection spacing prescribed by the operator. Sets of MPR images were obtained in the two orthogonal orientations perpendicular to the base set. Any abnormal saccular outpouching from intracranial arteries with defined neck clearly seen on MIP and MPR images was regarded as an aneurysm.

The results of MRA were defined as positive or negative. A positive MRA image was defined as a region of apparent dilatation that could not be explained by the normal course of an artery or an arterial branch.

Statistical Analyses

The target analysis of the present study is the estimation of the prevalence of ICANs in ADPKD patients younger than 30 years' age. The prevalence was estimated and a 95% CI constructed for the estimate. Other data were expressed as mean ±SD.

3. Results

The prevalence of ICANs of 60 ADPKD younger than 30 was 5%. Out of 60 patients of ADPKD younger than 30 years of age, three saccular aneurysms were depicted in three patients (two male and one female patient). The female patient gave a family history of cerebral aneurysms in contrary to the two male patients. The patients with normal blood pressure, no renal calculi, no cysts in other organs rather than the kidneys and normal kidney functions. The aneurysms were saccular, measured 2-3 mm and originated from the paraclinoid internal carotid and middle cerebral arteries. The aneurysms followed up for 18 months (MRA every 6 months) and showed no appreciable interval size or morphologic variation. No new aneurysms developed during the follow-up period. The three patients did not undergo any surgical intervention to the present.

Table 1: characteristics of the study group.

Characteristic	Value
Male/female%	60%, 40%
Mean age, range	21 years, age range, 12–29 years
Abnormal kidney functions	0
Hypertension	3
Renal or abdominal symptoms	7
Family history of aneurysms	3
Family history of ADPKD	57
Family history of SAH	1
Liver cysts	12
Splenic/pancreatic/epididymal cysts	0
Renal calculi	3

Table 2: characteristics of the aneurysm patient.

Sex/age	Family history of ADPKD	Family history of aneurysms	Family history of SAH	Hypertension	Renal calculi	Other organs cysts	Abnormal kidney functions	Renal or abdominal symptoms	Symptoms related to the aneurysm
F/27	+	+	-	-	-	-	-	-	-
M/25	+	-	-	-	-	+	-	-	-
M/21	+	-	-	-	-	-	-	-	-

+=present, -= absent

Table 3: MRA characteristics of the depicted aneurysm.

Sex/age	Type	Number	Size	Location	Follow-up size variation			Visibility on		
						MIP	targeted MIP	SE	MPR	source MR angiogram
F/27	Saccular	1	3 mm	Left paraclinoid ICA	-	+	+	-	+	+
M/25	Saccular	1	3 mm	Middle cerebral	-	+	+	+	+	+
M/21	Saccular	1	2 mm	Middle cerebral	-	+	+	-	+	+

+=present, -= absent

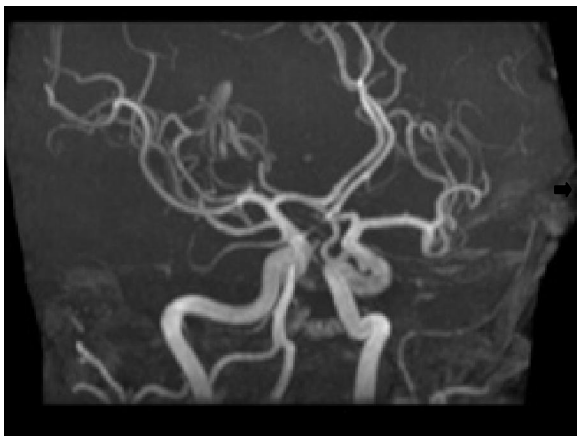

Fig.1: 3D TOF MRA MIP reconstruction elicited left paraclinoid internal carotid small saccular aneurysm (black arrow).

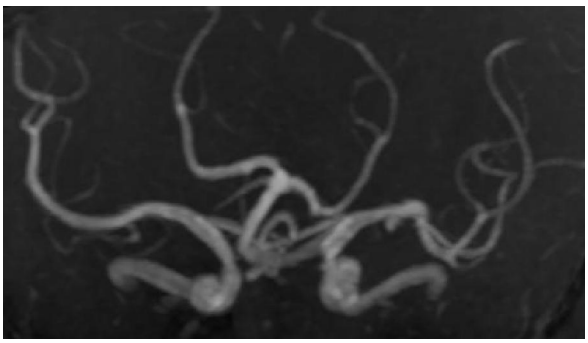

Fig.2: 3D TOF MRA MIP reconstruction elicited leftMCA small saccular aneurysm (black arrow)

4. Discussion

ADPKD is a common systemic disorder. It is the most common monogenic hereditary disease, affecting 1 of every 1000 people. However, although ADPKD leads to end-stage renal disease in a large proportion of patients, its symptoms are not limited to the kidney. Extrarenal manifestations include, among others, cysts in other organs (eg, liver and pancreas); arterial hypertension; and ICANs which are more likely to occur in patients with ADPKD than in the general population (3).

There is also a higher incidence of ICAN rupture in younger patients than is seen in the general population which correlates with a high risk for serious complications like subarachnoid hemorrhage or mortality (4).

The incidence of ICANs rupture in patients with ADPKD has been estimated to be □1/2000 person. This rate is five times higher than in the general population (5).

ADPCKD was found to be the single greatest risk factor for ICAN development, greater than atherosclerosis and family history of ICAN. In fact, 10% of patients with undiagnosed ADPCKD will have ICAN rupture as their presenting symptom, and 6% of all patients with ADPCKD will die due to subarachnoid hemorrhage. ICAN rupture is considered the most severe complication of ADPCKD (6).

The most serious possible complication of ADPKD is a ruptured cerebral aneurysm leading to subarachnoid hemorrhage or cerebral hemorrhage. If not treated before the aneurysm ruptures, this can lead to irreversible brain damage or even death.

Approximately 3 to 7 % of young adults with ADPKD may have brain aneurysms, and the frequency increases to 12 to 15 percent if someone else in the patient's family has had an intracranial aneurysm. Compared with the general population, the

risk of developing an aneurysm in ADPKD is approximately fivefold greater. People with a first-degree relative with a history of intracranial aneurysm or subarachnoid hemorrhage are at the highest risk of forming an aneurysm.

The availability of non-invasive screening methods for asymptomatic aneurysms and the major advances in microsurgical and endovascular techniques raise the question of whether systematic screening of those patients is warranted.

Subarachnoid hemorrhage (SAH) from ruptured intracranial saccular aneurysms of the circle of Willis is a devastating event with a mortality rate of over 25% and an additional high risk of permanent disability (7).

The advent of non-invasive methods of imaging intracranial blood vessels has facilitated screening for intracranial aneurysms in people who are at risk. A strong risk factor is polycystic kidney disease. People who have this risk factor are potential candidates for screening. Even if screening does not find abnormality, there is a high risk of new aneurysms 5 years later. Repeated screening might be done, although the optimum interval between screening assessments and the duration of repeated screening is unclear. Patients who have survived a subarachnoid hemorrhage are at increased risk of another from a newly developed aneurysm, but whether screening is beneficial in such patients is not clear (8).

Conventional 4-vessel angiography or DSA used to evaluate ICANs which yields high spatial resolution. The quality of DSA is operator-dependent, varying with the degree of vessel super-selection, injection rates and volumes, and number of projections, including any supplementary 3D DSA with post-processed reconstructions. Regions of competitive flow such as at the vertebral-basilar junction and anterior communicating artery may be difficult to opacify due to a lack of contrast in the blood pool. Differences in geographic distortion and 2D planar imaging views can make subtle changes in aneurysm size difficult to assess on serial studies, unless 3D imaging is performed. The risk of death and permanent neurological injury of this procedure is approximately 0.5% and it might be higher in patients with ADPKD (9).

Chapman *et al.*, reported a 25% rate of transient complications, *i.e.* in eight of 32 patients: vasospasm with headache and nausea in two, severe headache in two, scotoma in two, scotoma and numbness of the hand in one, and asymptomatic dissection of one vertebral artery in one patient. All patients recovered completely after 48 h. None of the patients had significant elevation of the creatinine level after administration of contrast medium (10).

MDCT and MR imaging largely replaced 4-vessel conventional angiography and DSA for IA screening. Multidetector CTA and 3T time-of-flight MRA can generate spatial resolutions up to 0.5-mm^2 per pixel. CTA relies on attenuation differences between iodinated contrast and surrounding tissues that can be suboptimal at the skull base in the presence of heavy mural calcification or metallic hardware. Venous contamination could be encountered with inadequately bolus-timed CTA can also limit assessment of the intracranial circulation.

Time of flight (TOF) MRA is a modality that has been investigated within the past two decades in the diagnosis of intracranial aneurysms and can be performed without gadolinium enhancement. TOF imaging exploits the differential effects of rapid, slice-selective, radiofrequency (RF) pulses on stationary *versus* flowing protons. The repetitive RF pulses suppress the signal from saturated stationary protons within the slice but enhance the signal from fully magnetized protons flowing into the slice, leading to high flow-related contrast. Rapidly flowing arterial blood is not saturated because it sees a limited number of magnetic pulses compared to the surrounding tissue and is thus highlighted against a saturated background (11).

The primary benefit of unenhanced MR angiography is its limited invasiveness, because it does not involve exposure to radiation or contrast materials. This allows repeated examinations, which makes it suitable for screening and follow-up studies. Another benefit is the lower susceptibility to calcification relative to that of CT, because calcification produces no signal at MR imaging. Similarly, MR angiography can easily depict vessels close to bones, vessels that are difficult to visualize with CT angiography, even with image postprocessing. One of the limitations of unenhanced MR angiography are the long acquisition times relative to those of contrast material–enhanced MR angiography or CT angiography (12).

Gadolinium should be used with caution in patients with an estimated glomerular filtration rate (eGFR) of less than 30 mL/min/1.73 m^2, including dialysis patients, to avoid nephrogenic systemic fibrosis. If iodinated contrast materials are used in patients with an eGFR of less than 60 mL/min/1.73 m^2 (except in dialysis patients), there is a high risk of contrast material–induced nephropathy. Even patients already undergoing dialysis may suffer damage to the already limited number of functioning nephrons that help sustain them between dialysis sessions. Therefore, unenhanced MR angiography is suitable for these patients as well as patients who may develop allergic reactions to contrast materials. It is also appropriate for young or essentially healthy people

who undergo a medical check-up, thus avoiding unnecessary radiation exposure or drug use, and for patients with severe calcification, for whom CT is not suitable (13).

Prior studies have demonstrated that TOF MRA may be as accurate as contrast-enhanced MRA and CTA in detecting intracranial aneurysms. Indeed, ongoing technical refinements have improved the quality of cerebral TOF MRA, including the use of 1) multiple overlapping thin slab acquisitions and variable flip-angle excitation to reduce progressive saturation of flowing spins in the acquisition volume; 2) fat saturation and magnetization transfer pulses to further suppress the signal from stationary tissues; and 3) higher magnetic field strengths (e.g. 3T) and parallel imaging to increase signal-to-noise ratio, increase spatial resolution, and decrease imaging time. However, previous studies have focused on the use of TOF MRA as a screening modality, with further characterization done through contrast modalities prior to surgical intervention (14).

Several studies have compared MRA and CTA with DSA with respect to diagnostic accuracy for IAs. 3D TOF MRA demonstrated a screening sensitivity of 67% for aneurysms of <3 mm, 79% for those of 3–5 mm, and 95% for those of >5 mm (15).

Many patients have multiple aneurysms (□30%). Per-patient screening sensitivity is a more reliable for assessment of the effectiveness of a technique. Multidetector CTA had a slightly lower per-patient screening sensitivity of 95% and a slightly higher screening specificity of 96% (16).

Noncontrast 3D TOF MRA has become the primary noninvasive screening technique for aneurysms in patients of ADPKD, with the advantage of avoiding the use of potentially nephrotoxic or allergenic contrast media and avoiding the placement of an IV line. Adding a gadolinium-enhanced MRA to the protocol may add the risk of the rare but serious nephrogenic systemic sclerosis. Nephrogenic systemic sclerosis is noted to occur in 1%–7% of patients with a GFR <30 mL/min due to the use of certain gadolinium-based compounds, though it is exceedingly rare in patients with normal eGFR.

Screening patients with autosomal dominant polycystic kidney disease (ADPKD) for asymptomatic intracranial aneurysms has been proposed as a method of reducing the morbidity and mortality associated with aneurysm rupture. However, recent studies have shown lower spontaneous rupture rates of small aneurysms and higher risks of significant complications with interventions than previously reported. Risk-benefit analysis has not demonstrated any benefit of screening ADPKD patients without a history of subarachnoid hemorrhage (SAH) for intracranial aneurysms, and has suggested that screening might cause harm (17).

The risks of screening asymptomatic ADPKD patients followed by treatment should be weighed against the risks of complications of aneurysm such as SAH. The strategy of choice is the one that provides a gain in life expectancy, or, even better, the best quality-adjusted survival, *i.e.,* the gain in years of good functional health.

Butler et al., compared an MRI screening strategy with a nonscreening strategy. The screening strategy specified MRI screening and then neurosurgical management of detected aneurysms. The nonscreening strategy specified cerebrovascular care only in the event of subarachnoid hemorrhage. The decision tree incorporated estimates derived from the clinical literature for the prevalence of asymptomatic aneurysms in patients with ADPKD (15%), the annual incidence of aneurysmal rupture (1.6%), the morbidity and mortality rates associated with subarachnoid hemorrhage (70 and 56%, respectively), the risk of transfemoral arteriography (0.2%), the sensitivity and specificity of MRI, the morbidity and mortality rates associated with surgical treatment of an unruptured aneurysm (4.1 and 1.0%, respectively), and the life expectancy of patients with ADPKD. The model predicted that the screening strategy would provide 1.0 additional year of life without neurological disability to a 20-year-old patient with ADPKD. A sensitivity analysis showed that the model was most sensitive to estimates of the prevalence of aneurysms in ADPKD, the annual incidence of rupture, and the morbidity and mortality rates associated with rupture. A financial analysis showed that a screening strategy is likely to cost less than a nonscreening strategy. The model predicts that an MRI screening strategy would increase the life expectancy of young patients with ADPKD and reduce the financial impact on society of ADPKD (18).

According to a risk-benefit screening analysis conducted by Butler et al, a single initial screening MRA in all 20-year-old patients with ADPCKD would increase the mean life expectancy without neurologic disability by 1 year.(18)

In a post-mortem study on 89 ADPKD patients, Schievink et al, reported a 22.5% prevalence of intracranial aneurysms (19). Huston *et al,* reported a prevalence of 10% in 85 ADPKD patients screened by MR angiography (20). **Ruggieri *et al*.** found a similar prevalence of 11.7% in 93 patients and a higher frequency in 27 patients with a definite or suspected family history for aneurysms. In those clinical studies, only one patient with an aneurysms was younger than 30 years, i.e. 24 years (21). He had a 3-mm aneurysm of the petrous segment of the internal carotid artery, which is associated with a very low risk of bleeding.

All of the detected aneurysms were smaller than 7 mm in diameter. These findings were confirmed by **Ronkainen *et al,*** (22).

No much available studies in the imaging literature dedicated for identifying the prevalence of cerebral aneurysms in the young ADPKD population (younger than 30 years) and the yield of screening for intracranial aneurysms in such age group.

The current study revealed three aneurysms in three ADPKD patients (5%) younger than 30 years. The saccular aneurysm ranged 2-3 mm size and emerged from the middle cerebral artery (M1 segments) and paraclinoid internal carotid artery. The depicted silent saccular aneurysms patients are not hypertensive and had normal kidney functions.

In a study conducted by Xu et al, the prevalence of ICANs in ADPKD group younger than 29 year-old was 2.3%. The study of Xu et al included 42 patients younger than 29 years and depicted one aneurysm among them.

Several studies have compared MRA and CTA with DSA with respect to diagnostic accuracy for ICANs. According to a recent study, 3T TOF MRA demonstrated a screening sensitivity of 67% for aneurysms of 3 mm, 79% for those of 3–5 mm, and 95% for those of 5 mm. Because many patients have multiple aneurysms (30%), 37a per-patient screening sensitivity is a more accurate metric for assessing the effectiveness of a technique. In this study, the per-patient screening sensitivity and specificity were 96% and 92%, respectively. Multidetector CTA had a slightly lower per-patient screening sensitivity of 95% and a slightly higher screening specificity of 96%. Another recent study focused on CTA revealed a similar screening sensitivity of 95% for aneurysms of7 mm. Due to the relatively invasive nature of DSA and the small but definite risk of stroke as well as the cost, dedicated staff and time commitment, and patient discomfort involved in the procedure, DSA has become less attractive as a screening technique for ICANs. One study estimates the complication risk at 1.3%, with a 0.5% risk of permanent neurologic complications (23).

Non-contrast TOF MRA has become the primary noninvasive screening technique, with the advantage of avoiding the use of potentially nephrotoxic or allergenic contrast media and avoiding the placement of an IV line. Adding a gadolinium-enhanced MRA to the protocol may add the risk of the rare but serious nephrogenic systemic sclerosis. Nephrogenic systemic sclerosis is noted to occur in 1%–7% of patients with a GFR 30 mL/min due to the use of certain gadolinium-based compounds, though it is exceedingly rare in patients with normal GFR.

Time-of-Flight MR angiography carries no risk compared to conventional four-vessel angiography and avoids the hazards of ionizing radiation and iodinated contrast agents associated with CTA. Its value in the detection of aneurysms is now well established. Angiographically confirmed aneurysms of 6 mm or more in diameter have been detected with 100% sensitivity by two or more blinded readers with time-of-flight-MRA. The sensitivity decreased to 87.5, 68.2, 60 and 55.6% for aneurysms with a diameter of 5,4,3 and 2 mm respectively. There were no false positive results in these studies (24).

The 3D TOF technique is the preferred MRA imaging method, since it provides high-quality images, without contrast administration. It has better resolution and signal-to-noise ratio (SNR) and requires less time than PC MRA. 3D TOF is prone to artifacts produced by turbulent blood flow. Turbulent flow is most commonly observed at the carotid siphon and in large-size aneurysms. Performing 3D TOF reduces such artifact with the application of short TE. Nevertheless, 3D TOF sequence acquires a large slab with resulting signal loss, which may reduce signal intensity within the aneurysm, and thus may underestimate the size of the aneurysm. Moreover, turbulent flow artifact at the base of the skull, in combination with susceptibility artifacts, may exacerbate this phenomenon, thus decreasing the sensitivity of this method in depicting aneurysms at the skull base. The introduction of MIP reconstruction, flow compensation, application of short TE, and smaller slice thickness may eliminate these artifacts.

The risk of aneurysm rupture depends mainly on its size, on a history of previous bleeding from another aneurysm, and on its location (the posterior circulation is at higher risk). Owing to low prevalence and because most aneurysms detected in ADPKD patients are less than 10 mm in diameter the yearly risk of bleeding is low. However, the cumulated risk remains significant. It obviously depends on the expected survival, which may be about 60 years in ADPKD patients (25).

SAH from aneurysms is responsible for death in a relatively small proportion of patients with ADPKD. However, the mean age at rupture in patients with ADPKD is between 35 and 40 years, that is 10–20 years earlier than in patients with sporadic SAH. This suggests that ADPKD per se is a risk factor for aneurysm rupture (26).

Screening for ICANs in the ADPKD population younger than 30 years may positively influence patient outcome and is cost-effective. ICANs detected by screening are usually small, with a very low expected rupture rate. Unfortunately, except for a positive family history of subarachnoid hemorrhage, no risk factors for ICANs in patients with ADPKD have been defined meaning that it is not able to identify all patients with a risk for subarachnoid hemorrhage from

ICAN rupture. some authors support systematic screening for ICANs in patients with ADPKD (27-28).

Conclusion

Owing to considerably high prevalence of ICANs in the present study group of ADPKD patients younger than 30-years relative to the estimated prevalence in the general population, the MRA screening for ICANs in such age-group should be considered owing to the significant annual risk of rupture, and the potential catastrophic sequelae of SAH. Screening is specially indicated in patients with family history of aneurysms and subarachnoid hemorrhage or hypertensive patients. There is higher incidence of ICANs rupture in young ADPKD patients than that in the general population with consequent serious complications.

Screening young patients with ADPCKD via MRA will improve life expectancy in a cost-effective and, at times, cost-saving manner. We recommend screening all young patients with ADPCKD by non-contrast 3D TOF MRA at the time of initial diagnosis of ADPKD with follow-up scans at intervals of those with diagnosed aneurysm. The follow-up interval depends on patient-specific risk factors, including the family history of intracranial aneurysms or SAH, prior SAH, neurologic symptoms, hypertension, smoking, alcohol abuse, high-risk professions (such as pilots), or those undergoing major elective surgery.

References

1. Schievink WI, Torres VE, Piepgras DG, et al. Saccular intracranial aneurysms in autosomal dominant polycystic kidney disease. J Am Soc Nephrol 1992; 3:88–95.
2. Rinkel GJE, Djibuti M, Algra A, van Gijn J: Prevalence and risk of rupture of intracranial aneurysms: a systematic review. Stroke 1998; 29:251–56.
3. Vlak MH, Algra A, Brandenburg R, et al. Prevalence of unruptured intracranial aneurysms, with emphasis on sex, age, comorbidity, country, and the time period: a systematic review and meta-analysis. Lancet Neurol 2011; 10:626–36.
4. Gieteling EW, Rinkel GJ. Characteristics of intracranial aneurysms and subarachnoid hemorrhage in patients with polycystic kidney disease. J Neurol 2003; 250:418–23.
5. Schievink WI: Intracranial aneurysms. N Engl J Med 336: 28–40, 1997.
6. Bonneville, F., Sourour, N., and Biondi, A. Intracranial aneurysms: an overview. Neuroimaging Clin. N. Am., 2006 16, 371–382, vii.
7. Schievink WI, Wijdicks EFM, Parisi JE, Piepgras DG, Whisnant JP. Sudden death from aneurysmal subarachnoid hemorrhage. Neurology 1995; 45: 871–874.
8. Rinkel GJ. Intracranial aneurysm screening: indications and advice for practice. Lancet Neurol 2005; 4:122–28).
9. Gouliamos A, Gotsis E, Blahos L. et al. Magnetic resonance angiography compared to intra-arterial digital subtraction angiography in patients with subarachnoid hemorrhage. Neuroradiology1992; 35: 46–49).
10. Chapman AB et al. Intracranial aneurysm in adult polycystic kidney disease. N Engl J Med 1992; 327: 916–920.
11. Hiratsuka Y, Miki H, Kiriyama I, Kikuchi K, Takahashi S, Matsubara I, et al. Diagnosis of unruptured intracranial aneurysms: 3T MR angiography versus 64-channel multi-detector row CT angiography. Magn Reson Med Sci. 2008; 7:169–178).
12. Kramer H, Quick H, Tombach B, Schoenberg S, Barkhausen J, Whole-body MRA. Eur Radiol 2008; 18(9):1925-1936.
13. Levey A, Coresh J, Balk E, et al. National Kidney Foundation practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Ann Intern Med 2003;139(2):137–147.
14. Papke K, Brassel F. Modern cross-sectional imaging in the diagnosis and follow-up of intracranial aneurysms. Eur Radiol. 2006; 16:2051–2066.
15. Adams W. M., Laitt R. D., and Jackson A., "The role of MR angiography in the pretreatment assessment of intracranial aneurysms: a comparative study," American Journal of Neuroradiology, 2000 vol. 21, no. 9, pp. 1618–1628.
16. Van Gelder JM. Computed tomographic angiography for detecting cerebral aneurysms: implications of aneurysm size distribution for the sensitivity, specificity, and likelihood ratios. Neurosurgery 2003; 53:597–605, discussion 605–06.
17. Hughes PD, Becker GJ. Screening for intracranial aneurysms in autosomal dominant polycystic kidney disease.
18. Butler WE, Barker FG 2nd., Crowell RM. Patients with polycystic kidney disease would benefit from routine magnetic resonance angiographic screening for intracerebral aneurysms: a decision analysis. Neurosurgery 1996; 38:506–15.
19. Schievink WI et al. Saccular intracranial aneurysms in autosomal dominant polycystic kidney disease. J Am Soc Nephrol1992; 3: 88–95

20. Huston J III, Torres VE, Sullivan PP, Offord KP, Wiebers DO. Value of magnetic resonance angiography for the detection of intracranial aneurysms in autosomal dominant polycystic kidney disease. J Am Soc Nephrol1993; 3: 1871–1877.
21. Ruggieri PM *et al.* Occult intracranial aneurysms in polycystic kidney disease: screening with MR angiography. Radiology1994; 191: 33–39.
22. Ronkainen A. *et al.* Familial intracranialaneurysms. Lancet 1997; 349: 1478–1479.
23. Willinsky RA, Taylor SM, Ter Brugge K, et al. Neurologic complications of cerebral angiography: prospective analysis of 2,899 procedures and review of the literature. Radiology 2003;227:522–28).
24. Huston J III, Nichols DA, Luetmer PH et al. Blinded prospective evaluation of sensitivity of MR angiography to known intracranial aneurysms: importance of aneurysm size. Am J Neuroradiol 1994; 15: 1607–1614).
25. Fick GM, Johnson AN, Hammond WS, Gabow PA. Causes of death in autosomal dominant polycystic kidney disease. J Am Soc Nephrol 1995; 5: 2048–2056.
26. Lozano AM, Leblanc R. Cerebral aneurysms and polycystic kidney disease: a critical review. Can J Neurol Sci 1992; 19: 222–227.
27. Mariani L, Bianchetti MG, Schroth G, et al. Cerebral aneurysms in patients with autosomal dominant polycystic kidney disease—to screen, to clip, to coil? Nephrol Dial Transplant 1999; 14:2319–22.
28. Xu HW, Yu SQ, Mei CL, *et al.* Screening for intracranial aneurysm in 355 patients with autosomal-dominant polycystic kidney disease. Stroke 2011; 42:204–06.

7/25/2016