Value of Magnetic Resonance Angiography for the Detection of Intracranial Aneurysms in Autosomal Dominant Polycystic Kidney Disease\textsuperscript{1,2}

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ABSTRACT

The association of intracranial aneurysms with autosomal dominant polycystic kidney disease (ADPKD), the 30-day mortality rate exceeding 50\% for aneurysmal rupture, the effectiveness of surgical repair of unruptured aneurysms with a low surgical risk, and the development of noninvasive imaging techniques for their detection have led physicians to consider the value of screening patients with ADPKD for unruptured intracranial aneurysms. The sensitivity and specificity of high-resolution computed tomography and magnetic resonance imaging for the diagnosis of small intracranial aneurysms have been disappointing. To determine the value of magnetic resonance angiography (MRA), 85 patients with ADPKD without symptoms related to an intracranial aneurysm and 2 patients with ADPKD presenting with a subarachnoid hemorrhage or a suspected aneurysmal leak were studied. MRA was performed with the Multisequence Vascular Package (GE Medical Systems) with use of three-dimensional time-of-flight and three-dimensional phase-contrast techniques, and postprocessing maximum intensity projection images were generated to eliminate the problem of overlapping vessels. Asymptomatic intracranial aneurysms were detected in 6 (22\%) of 27 patients with and 3 (5\%) of 56 patients without a family history of intracranial aneurysm or subarachnoid hemorrhage ($P = 0.02$, information missing in 2 patients) and in the 2 patients who presented with a symptomatic aneurysm. A stepwise logistic regression analysis indicated that a family history of intracranial aneurysm or subarachnoid hemorrhage was independently associated with the presence of intracranial aneurysms. All of the aneurysms were $\leq 6.5$ mm in diameter. These observations, together with previous experience with high-resolution computed tomography and magnetic resonance imaging, suggest that MRA is superior to computed tomography and magnetic resonance imaging in the presymptomatic detection of intracranial aneurysms and confirm a familial clustering of intracranial aneurysms in ADPKD.

Key Words: Aneurysm, autosomal dominant polycystic kidney disease, magnetic resonance angiography, subarachnoid hemorrhage

The association of intracranial aneurysms with autosomal dominant polycystic kidney disease (ADPKD)\textsuperscript{1–4} combined with a 30-day mortality rate exceeding 50\% after aneurysmal rupture\textsuperscript{5} and the effectiveness of surgical repair of unruptured aneurysms with a low surgical risk (6–8) have led physicians to consider the value of screening patients with ADPKD for unruptured intracranial aneurysms. A decision analysis has not supported the routine use of cerebral arteriography\textsuperscript{9}. With the development of high-resolution computed tomography (CT) and magnetic resonance, noninvasive visualization of intracranial aneurysms has become possible\textsuperscript{10,11}. Although the sensitivity of high-resolution CT and magnetic resonance imaging to detect large intracranial aneurysms appears to be adequate, the specificity of these techniques to diagnose small intracranial aneurysms has been low\textsuperscript{10,11}. The purpose of this study was to determine the value of magnetic resonance angiography (MRA) in the presymptomatic diagnosis of intracranial aneurysms in patients with ADPKD.
MATERIAL AND METHODS

Patients

The patients with ADPKD seen by the authors during the period from 1989 to 1992 were given detailed information regarding the association of intracranial aneurysms and ADPKD and the possible indications for noninvasive presymptomatic evaluation for intracranial aneurysms in this disease. This information was based in part on the results of our previous studies (10,12). Eighty-five asymptomatic ADPKD patients from 80 families agreed to undergo MRA. Indications included a family history of intracranial aneurysms (N = 26), evaluation before major elective surgery or renal transplantation (N = 31), or request by the patient for the purpose of reassurance (N = 28). One patient evaluated before renal transplantation was later classified as having a positive family history when, as part of the study, her son was discovered to have an intracranial aneurysm. In addition, two symptomatic patients with histories of subarachnoid hemorrhage or suspected aneurysmal leak were studied during the same period. Information abstracted for the study included gender, age, presence of hypertension defined as a diastolic blood pressure ≥95 mm Hg or treatment with antihypertensive medications, serum creatinine level at the time of MRA, and family history of intracranial aneurysm or subarachnoid hemorrhage as diagnosed by a neurologist or a pathologist at our center or elsewhere. Eighty of the 87 patients had computed tomographies of the abdomen available for review. The severity of the polycystic liver disease was graded according to the extent of the cross-sectional area occupied by cysts as follows: mild, <10%; moderate, 10 to 40%, and severe, >40%.

Figure 1. MIP image through the entire data set with overlapping vessels partially obscuring vascular detail (a). 3D image with the right carotid subvolume outlined (b). Right carotid subvolume isolated from other vascular structures (c). Nine of 19 projection images of the right carotid subvolume allow enhanced perception of the carotid siphon aneurysm (arrow in panel d).
Methods

Patients were examined with a 1.5-T superconducing imaging system (Signa; GE Medical Systems, Milwauke, WI). Standard magnetic resonance head imaging was performed with sagittal T1-weighted and transaxial T2-weighted sequences. In addition, high-resolution 3-mm transaxial T1-weighted imaging through the circle of Willis was performed. Vascular magnetic resonance imaging was performed with the Multisequence Vascular Package (GE Medical Systems, Milwaukee, WI) with the use of three-dimensional (3D) time-of-flight (TF) (13,14) and 3D phase-contrast (PC) (15,16) techniques. A coronal 2D PC scout image with 30 cm/s maximum velocity encoding was obtained to localize the volume for 3D TF and 3D PC imaging. Then, 3D PC angiography was performed in all patients (TR, 26 to 36; TE, 7.4 to 8.2, one excitation, 128 views, 15- to 20-degree flip angle, 18-cm field of view, 30 cm/s maximum velocity encoding) with the use of 60 axial sections between 0.7 and 1.0 mm thick. Additionally, 3D TF imaging was performed in 51 patients (TR, 40; TE, 4.3 to 6.0; one excitation, 192 to 256 views, 20-degree flip angle, 18-cm field of view) with the use of 60 axial sections between 0.7 and 1.0 mm thick. With both the 3D TF and 3D PC sequences, postprocessing maximum intensity projection (MIP) images were generated to eliminate the problem of overlapping vessels (Fig. 1) (17). This resulted in 19 MIP images perpendicular to the axial imaging plane at 10-degree increments. These subvolumes were selected from the MIP image along the axial imaging plane of both the 3D TF and the 3D PC series. Care was taken to include the anterior communicating artery in both carotid volumes. Viewing the individual subvolumes in a cine loop on an independent monitor enhanced the perception of the 3D relationship of the vessels and facilitated the identification of small aneurysms (Fig. 2).

Statistical Analysis

Two sample t tests, χ² and Mantel-Haenszel χ² analyses were used for comparisons between the groups of patients with and without intracranial aneurysms. In addition, a stepwise logistic regression analysis with backward elimination of variables that did not achieve a P = 0.05 level of significance was used to assess the predictive value of age, gender, family history of intracranial aneurysm or subarachnoid hemorrhage, history of hypertension, serum creatinine level, and severity of the polycystic liver disease on the presence of intracranial aneurysms detected by MRA (18). These analyses were done both including and excluding the two patients with ADPKD and symptomatic intracranial aneurysms. Only two-tailed P values are reported.

RESULTS

Intracranial aneurysms, one in each of 11 patients, were detected in 9 asymptomatic patients with ADPKD (Figs. 1 through 3) and in the 2 patients with ADPKD who presented with symptoms related to an aneurysmal rupture or suspected aneurysmal leak (Fig. 4). Multiple aneurysms were not detected in any of these patients. The latter two patients underwent conventional angiography and surgical clipping of the aneurysms without complications. The gender and age of the patients with intracranial aneurysms and the location and size of the aneurysms are summarized in Table 1. All of the aneurysms were ≤6.5 mm in maximal diameter.

The clinical data on the patients with ADPKD with and without intracranial aneurysms are shown in Table 2. A family history of intracranial aneurysms...
or subarachnoid hemorrhage and the presence of severe polycystic liver disease were associated with the presence of intracranial aneurysms detected by MRA. A stepwise logistic regression analysis with backward elimination of nonsignificant variables indicated that both the family history of intracranial aneurysm or subarachnoid hemorrhage and the presence of severe polycystic liver disease were independently associated with the presence of intracranial aneurysms (Table 3). Both patients with symptomatic intracranial aneurysms had severe polycystic liver disease, but neither one had a family history of intracranial aneurysm or subarachnoid hemorrhage. Excluding these two patients from the analysis, the univariate association between family history and presence of aneurysms continues to be significant ($P = 0.011$), whereas the association with severe polycystic liver disease is not ($P = 0.123$). Thus, the
presence of severe polycystic liver disease was not a significant predictor for the presence of an intracranial aneurysm in asymptomatic patients. Asymptomatic intracranial aneurysms were detected by MRA in 6 (22%) of 27 patients with and in 3 (5%) of 56 patients without a family history of intracranial aneurysm or subarachnoid hemorrhage \((P = 0.021)\).

Other vascular abnormalities noted in these patients included an ectatic middle cerebral artery in one patient, fetal origin of a posterior cerebral artery in two patients, hypoplastic cerebral arteries in two patients, and absence of a lateral sinus in one patient. Additional findings included an arachnoid cyst in five patients, cavum septum pellucidum in two, pineal cyst in one, and empty sella in one.

### DISCUSSION

Intracranial aneurysms were detected by MRA in 9 (11%) of 85 patients with ADPKD who had no symptoms related to the presence of aneurysms. Because of numerous referral and selection biases, this frequency should be viewed as only an approximation of the frequency of intracranial aneurysms in this disease. Similar biases have influenced previous autopsy and angiography studies and have resulted in highly variable frequencies ranging from 0 to 50% at autopsy (1–4, 12, 19) and from 8 to 60% in studies using conventional arteriography (11, 20–24). The most recent and comprehensive studies of this association suggest that the overall prevalence of intracranial aneurysms in ADPKD does not exceed 10% (11, 12), which is in agreement with the findings of this study.

With the development of high-resolution CT and magnetic resonance imaging, the noninvasive visualization of intracranial aneurysms became possible (10, 11). Although these imaging techniques have sensitivity adequate enough to detect large intracranial aneurysms, their specificity for the detection of small aneurysms has been disappointing. In our previous study of 96 patients with ADPKD, small areas (2 to 4 mm) of contrast enhancement or signal void,

### TABLE 1. Location and size of 11 intracranial aneurysms detected by MRA in nine asymptomatic and two symptomatic ADPKD patients

<table>
<thead>
<tr>
<th>Location</th>
<th>Size ((\text{mm}))</th>
<th>Figure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>58P</td>
<td>Rt carotid siphon</td>
<td>3 4 2.5</td>
</tr>
<tr>
<td>72F</td>
<td>Lt periphihalmic</td>
<td>2.5 2.5 2.5</td>
</tr>
<tr>
<td>45F</td>
<td>Basilar tip</td>
<td>1 1.5</td>
</tr>
<tr>
<td>47F</td>
<td>Rt MCA bifurcation</td>
<td>4.5 4.5 5</td>
</tr>
<tr>
<td>45F</td>
<td>Rt superior cerebellar</td>
<td>1 1.5 1</td>
</tr>
<tr>
<td>49F</td>
<td>Rt carotid siphon</td>
<td>4.5 5 6</td>
</tr>
<tr>
<td>52M</td>
<td>Lt carotid siphon</td>
<td>6 6.5 6 1</td>
</tr>
<tr>
<td>37F</td>
<td>Lt carotid siphon</td>
<td>2 2 3</td>
</tr>
<tr>
<td>27M</td>
<td>Rt MCA bifurcation</td>
<td>1 1 1.5</td>
</tr>
<tr>
<td>Symptomatic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>49F</td>
<td>Rt MCA bifurcation</td>
<td>4 4 5 4</td>
</tr>
<tr>
<td>43M</td>
<td>Lt anterior cerebral</td>
<td>3 3</td>
</tr>
</tbody>
</table>

*AP, anteroposterior; SI, superior-inferior; RL, right-left.

### TABLE 2. Clinical data on the patients with ADPKD with and without ICA at the time of MRA

<table>
<thead>
<tr>
<th></th>
<th>With ICA ((N = 11))</th>
<th>Without ICA ((N = 76))</th>
<th>(P) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>48 ± 11 (29–72)</td>
<td>45 ± 12 (17–67)</td>
<td>NS</td>
</tr>
<tr>
<td>Sex (M:F)</td>
<td>3:8</td>
<td>31:45</td>
<td>NS</td>
</tr>
<tr>
<td>Family history of ICA (^a)</td>
<td>6/11 (55%)</td>
<td>21/74 (28%)</td>
<td>0.08</td>
</tr>
<tr>
<td>Hypertension</td>
<td>10/11 (91%)</td>
<td>66/76 (87%)</td>
<td>NS</td>
</tr>
<tr>
<td>Serum Creatinine (mg/dL)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤1.2</td>
<td>2 (18%)</td>
<td>28 (34%)</td>
<td></td>
</tr>
<tr>
<td>1.3–3.0</td>
<td>5 (46%)</td>
<td>27 (32%)</td>
<td></td>
</tr>
<tr>
<td>3.1–10</td>
<td>3 (27%)</td>
<td>13 (18%)</td>
<td></td>
</tr>
<tr>
<td>ESRF</td>
<td>1 (9%)</td>
<td>8 (10%)</td>
<td>NS</td>
</tr>
<tr>
<td>Polycystic liver disease(^c)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>1 (10%)</td>
<td>14 (20%)</td>
<td></td>
</tr>
<tr>
<td>Mild (&lt;10% SA)</td>
<td>2 (20%)</td>
<td>26 (38%)</td>
<td></td>
</tr>
<tr>
<td>Moderate (10–40% SA)</td>
<td>2 (20%)</td>
<td>16 (23%)</td>
<td></td>
</tr>
<tr>
<td>Severe (&gt;40% SA)</td>
<td>5 (50%)</td>
<td>13 (19%)</td>
<td>0.05</td>
</tr>
</tbody>
</table>

\(^a\) ICA, intracranial aneurysm; ESRF, end-stage renal failure; SA, cross-sectional area on CT; NS, not significant.

\(^b\) Information not available in two patients without ICA.

\(^c\) Information not available in seven patients without and one patient with ICA.
Several investigators have suggested that patients with ADPKD and a family history of intracranial aneurysm or subarachnoid hemorrhage are more likely to have an intracranial aneurysm (25–27). The results of our study are consistent with these observations. Intracranial aneurysms were detected in 5% of our patients without and in 22% of our patients with a family history of intracranial aneurysm or subarachnoid hemorrhage. Our study also suggests a possible association between the severity of the polycystic liver disease and the presence of an intracranial aneurysm. This association, however, only reaches statistical significance when two patients with symptomatic intracranial aneurysms detected by MRA are included in the analysis. This observation, along with the report by Chauveau et al. of intracranial aneurysms in two patients with severe polycystic kidney disease and renal failure at an early age (28), may suggest an increased risk for the presence of aneurysms in patients with a severe expression of polycystic kidney or liver disease. Age, gender, history of hypertension, and renal function were not found to be significant predictors for the presence of an aneurysm.

The value of presymptomatic detection of intracranial aneurysms by MRA in patients with polycystic kidney disease is dependent upon the natural history of unruptured intracranial aneurysms and the risk/benefit ratio of interventional therapy. In the general population, aneurysmal size is an important variable for predicting the future rupture of unruptured intracranial aneurysms in the absence of prior subarachnoid hemorrhage from a different source (29,30). For unruptured aneurysms less than 10 mm in diameter in patients with no prior subarachnoid hemorrhage, the risk of subsequent rupture appears to be low. Whether this is also true in patients with ADPKD is uncertain, because it has been suggested that familial intracranial aneurysms in general rupture at a smaller size and when the patient is younger in comparison with sporadic intracranial aneurysms (31). In addition, several studies have suggested that intracranial aneurysms in ADPKD rupture with the patients at a younger age than do intracranial aneurysms in the general population (12,32,33).

ACKNOWLEDGMENTS

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