Autosomal Dominant Polycystic Kidney Disease and Intracranial Aneurysms: Is There an Increased Risk of Treatment?

M.N. Rozenfeld, S.A. Ansari, P. Mohan, A. Shaibani, E.J. Russell, and M.C. Hurley

ABSTRACT

BACKGROUND AND PURPOSE: Autosomal dominant polycystic kidney disease is associated with an increased risk of intracranial aneurysms. Our purpose was to assess whether there is an increased risk during aneurysm coiling and clipping.

MATERIALS AND METHODS: Data were obtained from the National Inpatient Sample (2000–2011). All subjects had an unruptured aneurysm clipped or coiled and were divided into polycystic kidney ($n = 189$) and control ($n = 3555$) groups. Primary end points included in-hospital mortality, length of stay, and total hospital charges. Secondary end points included the International Classification of Diseases, Ninth Revision codes for iatrogenic hemorrhage or infarction; intracranial hemorrhage; embolic infarction; and carotid and vertebral artery dissections.

RESULTS: There was a significantly greater incidence of iatrogenic hemorrhage or infarction, embolic infarction, and carotid artery dissection in the patients with polycystic kidney disease compared with the control group after endovascular coiling. There was also a significantly greater incidence of iatrogenic hemorrhage or infarction in the polycystic kidney group after surgical clipping. However, the hospital stay was not longer in the polycystic kidney group, and the total hospital charges were not higher. Additional analysis within the polycystic kidney group revealed a significantly shorter length of stay but similar in-hospital costs when subjects underwent coiling versus clipping.

CONCLUSIONS: Patients with polycystic kidney disease face an increased risk during intracranial aneurysm treatment, whether by coiling or clipping. This risk, however, does not translate into longer hospital stays or increased hospital costs. Despite the additional catheterization-related risks of dissection and embolization, coiling results in shorter hospital stays and similar mortality compared with clipping.

ABBREVIATIONS: ADPCKD = autosomal dominant polycystic kidney disease; ICD9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification; NIS = National Inpatient Sample

Autosomal dominant polycystic kidney disease (ADPCKD) is a genetic disorder affecting 1 in 1000 individuals worldwide and is associated with an increased risk of intracranial aneurysms, ranging from 4% to 23%[1-6] compared with the general population risk of 2%–3%.[7-10] Patients with ADPCKD are also at increased risk for aneurysm rupture earlier in life (mean age, 35–45 years),[1,11-13] compared with the general population (mean age, 50–54 years).[14,15]

There is evidence that the associated vascular defects in

ADPCKD may be due to mutations in the *PKD1* and *PKD2* genes, located on the short arm of chromosomes 16 and 4.[16,17] Abnormalities of these genes in mouse models correspond with increased rates of arterial dissection, arterial rupture, and intracranial vascular abnormalities.[18] To our knowledge, only 1 study to date has investigated whether these issues engender an increased risk when treating intracranial aneurysms (whether by endovascular coiling or surgical clipping).[2] The purpose of this investigation was to assess whether ADPCKD confers an increased peri- and immediate postprocedural risk of aneurysm coiling and clipping.

MATERIALS AND METHODS

Data for this study were obtained from the National Inpatient Sample (NIS; http://www.entnet.org/content/nationwide-inpatient-sample-nis) provided by the Healthcare Cost and Utilization Project, sponsored by the Agency for Healthcare Research and Quality under the US Department of Health and Human

Services. The NIS is a stratified sample of 20% of all US nonfederal hospitals. Data derived for this study spanned the years 2000–2011.

All patients in this study received a diagnosis of "cerebral aneurysm–nonruptured" (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD9-CM] code 437.3) and a procedural code of either "clipping of aneurysm" (ICD9-CM code 39.51) or any 1 of 3 possible codes for aneurysm coiling: "endovascular total embolization or occlusion of head and neck vessels" (ICD9-CM code 39.72), "endovascular embolization or occlusion of vessels of head and neck by using bare coils" (ICD9-CM code 39.75), or "endovascular embolization or occlusion of vessels of head and neck by using bioactive coils" (ICD9-CM code 39.76). The codes 39.75 and 39.76 were not created until 2009. The ADPCKD group also had a diagnosis of "polycystic kidney disease, autosomal dominant" (ICD9-CM code 753.13), while the control group did not. Patients with a diagnosis of "subarachnoid hemorrhage" (ICD-CM code 430) were excluded from this study as in prior similar investigations due to the concern of potential coding errors and patients with ruptured intracranial aneurysms being included in our study. Primary end points investigated in this study included in-hospital mortality, length of stay, and total hospital charges. Secondary end points included the diagnoses "iatrogenic cerebrovascular hemorrhage or infarction" (ICD9-CM code 997.02), "intracerebral hemorrhage" (ICD9-CM code 431), "unspecified intracranial hemorrhage" (ICD9-CM code 432.9), "cerebral embolism with cerebral infarction" (ICD9-CM code 434.11), "dissection of carotid artery" (ICD9-CM code 443.21), and "dissection of vertebral artery" (ICD9-CM code 443.24).

The NIS data were imported into SPSS (IBM, Armonk, New York), and searches were performed by using scripts containing the above codes. Statistical analyses of the data were performed by using χ^2 for categoric variables and t test for continuous variables.

RESULTS

During 2000–2011, 189 patients with ADPCKD and unruptured intracranial aneurysms presented for either surgical clipping ($n = 136$) or endovascular coiling ($n = 53$). A control group of 3555 patients without ADPCKD was also analyzed, presenting for either surgical clipping ($n = 1707$) or endovascular coiling ($n = 1848$).

The average age at endovascular coiling in the ADPCKD group was significantly lower than that of the control group (53 versus 58 years) ($P = .02$). The average age at surgical clipping was also significantly lower than that of the control group (50 versus 55 years) ($P = .00$).

There was a mildly increased in-hospital mortality rate in the control group after both coiling and clipping without reaching statistical significance. The mean length of stay was also slightly longer in control subjects compared with patients with ADPCKD after coiling and clipping—only reaching statistical significance in the clipping group. The mean total hospital charges in the control group were significantly greater than those in the ADPCKD group after coiling and clipping (Table 1).

There was a significantly greater incidence of "iatrogenic cerebrovascular hemorrhage or infarction," "cerebral embolism with cerebral infarction," and "dissection of carotid artery" in the patients with ADPCKD compared with the control group after endovascular coiling. There was also a significantly greater incidence of "iatrogenic cerebrovascular hemorrhage or infarction" in the ADPCKD group compared with the control group after surgical clipping (Table 2). However, the mean length of hospital stay was not longer in the ADPCKD group, and the total hospital charges were not higher.

Additional analysis within the ADPCKD group revealed a significantly shorter length of stay when the subjects underwent endovascular coiling versus surgical clipping (2.57 versus 5.72 days) ($P < .01$). There was no significant difference in age or total in-hospital charges when comparing clipping and coiling in this population.

DISCUSSION

Our study used the NIS data base to draw from the largest possible sample of patients, and despite the failure of ICD disease codes to fully distinguish primary conditions from adverse events, it suggests that patients with ADPCKD have a significantly increased risk of iatrogenic hemorrhage and infarction, em-

Table 1: Primary end points

	ADPCKD	Controls	P Value
In-hospital mortality			
Coiling	0.0%	0.3%	NS
Clipping	0.0%	0.5%	NS
Mean length of stay (days)			
Coiling	2.57	2.99	NS
Clipping	5.72	6.91	<.01
Mean total hospital charges			
Coiling	$61,874	$85,568	<.01
Clipping	$67,133	$89,787	<.01

Note:—NS indicates not significant.

Table 2: Secondary end points

	ADPCKD	Controls	P Value
Iatrogenic cerebrovascular hemorrhage or infarction			
Coiling	5 (9.4%)	55 (3.0%)	<.01
Clipping	16 (11.8%)	109 (6.4%)	<.02
Intracerebral hemorrhage			
Coiling	0 (0%)	11 (0.6%)	NS
Clipping	0 (0%)	39 (2.3%)	NS
Unspecified intracranial hemorrhage			
Coiling	0 (0%)	0 (0%)	NS
Clipping	0 (0%)	0 (0%)	NS
Cerebral embolism with cerebral infarction			
Coiling	5 (9.4%)	14 (0.8%)	.00
Clipping	0 (0%)	5 (0.3%)	NS
Dissection of carotid artery			
Coiling	5 (9.4%)	0 (0%)	.00
Clipping	0 (0.0%)	0 (0%)	NS
Dissection of vertebral artery			
Coiling	0 (0%)	0 (0%)	NS
Clipping	0 (0%)	0 (0%)	NS

Note:—NS indicates not significant.

bolic infarction, and carotid artery dissection when undergoing endovascular coiling and a significantly increased risk of iatrogenic hemorrhage or infarction when undergoing surgical clipping. The lack of increased risk of embolic infarction and dissection in the surgical clipping group is presumably due to these adverse outcomes being secondary to catheter manipulation; surgical clipping bypasses the abnormal vessels in these patients.

Patients with ADPCKD undergo aneurysm treatment earlier in life than controls, but it is unclear whether this is because they develop these aneurysms earlier in life or simply because they are detected earlier due to screening.

Most interesting, patients with ADPCKD had a significantly shorter length of hospital stay after clipping compared to patients without ADPCKD and significantly lower in-hospital costs after coiling and clipping. This finding is theorized to be secondary to their lower average age at the time of treatment, which may correlate with fewer comorbidities.

To the authors' knowledge, only 1 similar study to date has been performed.[2] In that study, which was published in 1992 at a time of presumably higher complication rates, 32 patients with ADPCKD underwent diagnostic cerebral angiography and 25% had transient complications versus 10% in the control group. Two patients with ADPCKD had asymptomatic transient severe occlusive carotid vasospasm, and 1 additional patient had an asymptomatic vertebral artery dissection. The authors of the study concluded that additional caution should be taken in this patient population. Other case reports have also suggested an increased risk of spontaneous dissection of the aorta and internal carotid, vertebral, basilar, and coronary arteries in ADPCKD.[2,19,20] As with any case report, however, conclusions must be interpreted with caution. Our study builds on this body of knowledge by offering a much larger sample size and additional data analysis and a comparison between endovascular coiling and microsurgical clipping risks.

In our NIS dataset, the in-hospital coiling-related mortality rate in the control group (0.3%) is similar but lower than reported rates in other studies: 2.0%,[21] 1.8%,[22] and 0.6%.[23] Our in-hospital clipping-related mortality rate in the control group (0.5%) is also similar but lower than those reported rates in other studies: 1.8%[21] and 1.2%.[23] These small differences may be accounted for by a combination of more recent data in our study (2000–2011) and differences in study design ("in-hospital mortality" ICD9 code in our study versus various methods of determining procedure-related mortality in other studies), suggesting accuracy in defining end points with our methodology. Any potential artifactual risk reduction compared with other studies would be spread equally across both the ADPCKD and control groups.

While it has been established that there is an increased risk of intracranial aneurysm formation in patients with ADPCKD, screening and treatment algorithms are controversial. Treatment risks have been extensively studied in the general population,[21-23] but data are sparse regarding the risk in patients with ADPCKD. This study assists in expanding our awareness for this susceptible patient group. Patients with ADPCKD face a significantly increased risk during intracranial aneurysm treatment, whether by clipping or coiling. While this population is exposed to additional risks of embolic infarction and carotid dissection when undergoing endovascular coil embolization, this treatment method was still associated with shorter hospital stays and equivalent in-hospital mortality compared with microsurgical clipping. The final decision of whether to treat, when to treat, and how to treat must be made on an individual patient and aneurysm basis by a multidisciplinary team; the additional overall treatment risks and the additional endovascular catheter-related risks must be considered.

There are limitations in using an administrative data base such as the NIS, given the possibility of coding errors or omissions. Additionally, comorbid patient conditions, patient medications, aneurysm-specific size and anatomy, and/or the complexity of surgical/endovascular treatments cannot be controlled. Unfortunately, there is no way to distinguish a code representing an in-hospital event versus a preadmission event; an issue that may be corrected in ICD-10. ICD-9 codes have, however, been found to have a 66% positive predictive value in correlating with in-hospital adverse events in the surgical population.[24] The lack of data on short-term but out-of-hospital mortality is another limitation. It is the authors' opinion that these limitations are at least partially offset by the use of a large dataset, and that any coding errors would be distributed evenly across the patient and control groups.

CONCLUSIONS

Compared with controls, patients with ADPCKD face an increased risk during intracranial aneurysm treatment, whether by endovascular coil embolization or microsurgical clipping. This risk, however, does not translate into longer hospital stays or increased hospital costs. Despite the additional catheterization-related risks of dissection and embolization, coiling results in shorter lengths of stay and no increased risk of mortality compared with clipping.

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