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Neurosurg Clin N Am 16 (2005) 309–312

NEUROSURGERY
CLINICS
OF NORTH AMERICA

Neuroepidemiology of Unruptured Intracranial Aneurysms: Implications for Decision Making Regarding Patient Management

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Unruptured intracranial aneurysms (UIAs) are relatively common, affecting up to 2–5% of the population at some point in life. These lesions are not congenital but rather develop with increasing age. Epidemiologic data from many vantage points suggest that most of these lesions do not rupture. Consequently, it is desirable to identify which unruptured aneurysms are at the greatest risk of subsequent rupture when considering which ones to repair. Optimal management of patients with UIAs also involves predicting which individuals have the greatest likelihood of success and lowest likelihood of complications from repairing their UIA and reconciling these data with natural history data involving these lesions.

It is important to recognize that ruptured intracranial aneurysms and UIAs constitute distinctly different clinical entities and need to be considered and managed accordingly. If it were possible to extrapolate the natural history of UIAs by studying series of patients with ruptured aneurysms, there would have been no need for natural history studies involving UIA patients. The findings of the International Study of Unruptured Intracranial Aneurysms (ISUIA) [1,2] and other natural history studies reinforce the fact that UIAs and ruptured aneurysms are different entities and that their natural histories are distinct from one another.

In the debate about the natural history of UIAs, some investigators have cited circumstances of patients with small unruptured aneurysms diagnosed after subarachnoid hemorrhage (SAH) and have argued on this basis that small unruptured aneurysms may have substantial rupture rates, even among patients with no history of SAH [3]. Others have also attempted to extrapolate the natural history of UIAs by considering incidence rates of SAH and inferred prevalences of UIAs in the population [4]. Considerable confusion has been added to the field by not recognizing the difference between the following two questions:

1. What is the probability of a ruptured aneurysm being a certain size?
2. What is the probability of future rupture of a given sized aneurysm discovered before rupture?

The second of these questions is relevant to the clinical management of patients with UIAs. This principle graphically applies not only to aneurysm size but to aneurysm location. The bottom line is that one does not learn about the natural history of UIAs by studying characteristics of patients or populations with ruptured aneurysms [5]. Available information suggests that most aneurysms that are going to rupture do so at the time of, or relatively soon after, they form and that the critical size for rupture is lower for those aneurysms that rupture early.

In contrast to the situation of patients with ruptured intracranial aneurysms, where one is attempting to repair virtually all aneurysms and an early focus involves which mode of treatment fits the particular situation at hand, patients with UIAs evoke much more emphasis on the

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doi:10.1016/j.nec.2004.08.018

Table 1
Five-year cumulative rupture rates according to size and location of unruptured aneurysm and according to patient group among patients in the unoperated cohort

	Aneurysm size/group				
Aneurysm location	<7 mm group 1[a]	<7 mm group 2[b]	7–12 mm	13–24 mm	>25 mm
Cavernous (n = 210)	0%	0%	0%	3 (0%)	6 (4%)
AC/MC/IC (n = 1037)	0%	1 (5%)	2 (6%)	14 (5%)	40%
Post-P comm (n = 445)	2 (5%)	3 (4%)	14 (5%)	18 (4%)	50%

Abbreviations: AC, anterior communicating or anterior cerebral artery; Cavernous, cavernous carotid artery; IC, internal carotid artery (not cavernous carotid artery); MC, middle cerebral artery; Post-P comm, vertebrobasilar, posterior cerebral arterial system, or posterior communicating artery.

[a] Patients in group 1 had no history of SAH.

[b] Patients in group 2 had a history of SAH from a separate aneurysm.

(*Reprinted from* International Study of Unruptured Intracranial Aneurysms Investigators. Unruptured intracranial aneurysms: natural history, clinical outcome, and risks of surgical and endovascular treatment. Lancet 2003;362;103–10.)

consideration of whether or not aneurysmal repair is warranted. This applies to UIAs of all sizes and locations, because many higher natural history risk patients are also at higher risk with regard to treatment morbidity and mortality.

The latest and most robust data regarding natural history and treatment morbidity and mortality among patients with UIAs emanating from the ISUIA allow a more individualized and detailed assessment of the risks of natural history versus the risk of surgical or endovascular repair based on much more than aneurysm size. It continues to be a general principle, however, that for group 1 patients (no history of SAH from another aneurysm) with aneurysms less than 7 mm in diameter, it is unlikely that one will improve on the natural history of these lesions, particularly in older patients and those with aneurysms in the anterior circulation. It must be kept in mind, however, that available natural history studies, including the ISUIA, include few asymptomatic patients with small UIAs, particularly those with acute or changing symptoms or observed aneurysmal growth; thus, these rare circumstances may constitute exceptions to the previously stated principle. Current data do not allow one to establish that a positive family history of intracranial aneurysm or SAH increases the risk of future rupture of an unruptured aneurysm.

For group 1 patients with aneurysms 7 mm or greater in diameter and group 2 patients, rupture rates are more substantial than for group 1 patients with aneurysms less than 7 mm in diameter and generally vary according to aneurysmal size and location. It is now possible to be more sophisticated in making comparisons between natural history and treatment morbidity and mortality on the basis of more than aneurysmal size, and it is important that one considers size-, site-, and group-specific natural history rates for comparison with size, site, and age treatment morbidity and mortality rates (Table 1, Figs. 1–3). The age of the patient has emerged as a crucial decision-making element, largely because age has a major impact on operative morbidity and mortality but relatively little impact on natural history. The age range in which impact is greatest begins at approximately 50 years and older for open surgery and at approximately 70 years and older for endovascular procedures.

Overall, the rupture risk is lowest for asymptomatic group 1 patients with UIAs less than 7 mm in diameter in the anterior circulation. Surgical morbidity and mortality are most favorable for asymptomatic patients less than 50 years of age with UIAs less than 24 mm in diameter in the anterior circulation and no history of cerebrovascular ischemic events. Endovascular morbidity and mortality seem to be less age dependent, and this could favor endovascular procedures, particularly in those patients between 50 and 70 years of age. Another issue of major importance, however, involves the question of immediate versus long-term risk with regard to treatment effectiveness and durability. This issue emphasizes the importance of long-term follow-up in patients after surgical and endovascular procedures so as to assess not only the immediate and short-term complications but the long-term effectiveness.

In circumstances in which repair of UIAs is considered, it is important to recognize that available data suggest substantially lower

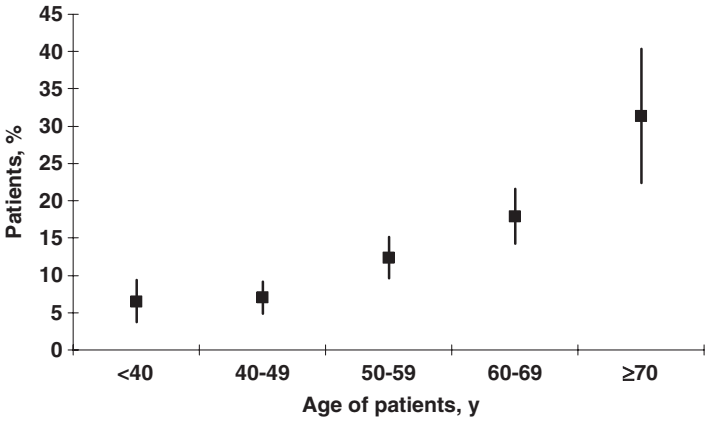

Fig. 1. Poor outcome at 1 year in the surgical cohort by age. Poor outcome is death, a Rankin score between 3 and 5, or impaired cognitive status. Bars show 95% confidence intervals. (*Reprinted from* International Study of Unruptured Intracranial Aneurysms Investigators. Unruptured intracranial aneurysms: natural history, clinical outcome, and risks of surgical and endovascular treatment. Lancet 2003;362;103–10.)

complication rates are associated with institutions and individuals treating large numbers of patients with cerebral aneurysms on an ongoing basis [3,6–8]. It is therefore of great importance to seek out individuals and institutions with substantial ongoing experience with treatment procedures.

Whether or not the patients with UIAs undergo aneurysmal repair, it is important to emphasize that patients avoid smoking (including passive smoke). In situations in which UIAs are left alone and monitored, it also seems advisable to suggest that patients avoid heavy alcohol consumption and that they avoid stimulant medications and drugs as well as excessive straining and Valsalva maneuvers resulting in major increases in blood pressure. It is not generally necessary to alter daily physical activities. Although there are many other medical reasons to treat chronic hypertension, data from the ISUIA and other studies indicate that chronic hypertension may have little or no effect on aneurysmal

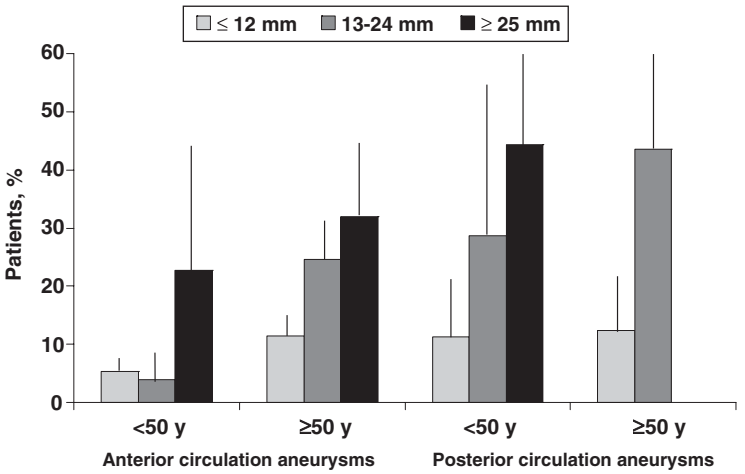

Fig. 2. Poor surgical outcome at 1 year by age, site, and size of aneurysm. Poor outcome is death, a Rankin score between 3 and 5, or impaired cognitive status. Bars show 95% confidence intervals. (*Reprinted from* International Study of Unruptured Intracranial Aneurysms Investigators. Unruptured intracranial aneurysms: natural history, clinical outcome, and risks of surgical and endovascular treatment. Lancet 2003;362;103–10.)

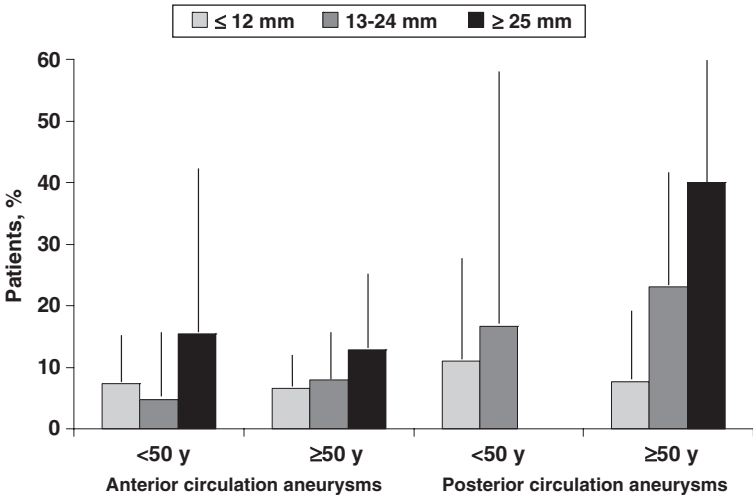

Fig. 3. Poor endovascular outcome at 1 year by age, site, and size of aneurysm. Poor outcome is death, a Rankin score between 3 and 5, or impaired cognitive status. Bars show 95% confidence intervals. (*Reprinted from* International Study of Unruptured Intracranial Aneurysms Investigators. Unruptured intracranial aneurysms: natural history, clinical outcome, and risks of surgical and endovascular treatment. Lancet 2003;362;103–10.)

development or future rupture of UIAs. For situations in which UIAs are not repaired, patients are often monitored annually with magnetic resonance angiography (MRA) or CT angiography for 2 to 3 years and then every 2 to 5 years thereafter if they are stable clinically and radiographically.

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