Editorial

Unruptured aneurysms

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The treatment of patients with unruptured intracranial aneurysms (UIAs) is controversial and one of the most important issues confronting neurosurgeons today. In this issue of the Journal of Neurosurgery, Dr. Chang reports on an intriguing mathematical simulation of the natural history of unruptured cerebral aneurysms, which is similar in methodology to the imaginative earlier work of Chang and Kirico in which they quantified the operative benefit for UIAs.

Patients harboring a UIA are afflicted by a potentially devastating disease, and preventing the rupture of such lesions with surgical or endovascular treatment is believed to be the most effective strategy for lowering associated mortality rates. Note, however, that all current therapies carry some risk; therefore, recommendations for treatment require careful consideration of the natural history of the UIA given that complications usually occur at or around the time that treatment is administered. The International Study of Unruptured Intracranial Aneurysms (ISUIA) generated much controversy when its data revealed a hemorrhage rate of 0.05%/year for aneurysms less than 10 mm in size and approximately 1% for those greater than 10 mm in size.

In the present publication, Chang describes a mathematical formula for the natural history of UIAs, which was developed to validate the ISUIA data. The mathematical simulation allowed for the determination of aneurysm formation, growth, and rupture probability, from which could be calculated: 1) the prevalence and size distribution of UIAs in the general population; 2) the annual incidence of subarachnoid hemorrhage (SAH) in that population; 3) the age and size of distribution of ruptured aneurysms; and 4) the lifetime lesion rupture probability and life expectancy in a patient of a certain age with a certain-sized aneurysm.

We draw the reader’s attention to the following concerns. First, in determining the origination rate of aneurysms, Dr. Chang used a 4% prevalence rate (see Clinical Material and Methods in his paper) in the model (and computed a 4.2% incidence for 5-mm aneurysms), stating that 4% is “...a figure commonly reported in the literature.” Yet, a review of these same citations revealed that more reasonable prevalence rate is approximately 2%. For example, Weir comprehensively reviewed prevalence rates and provided a range of figures, with very few being greater than or equal to 4%. Rinkel, et al., concluded that the prevalence of UIAs in the general population is 2%. The study by Ujiie and colleagues was based on cerebral angiography and demonstrated that 2.7% of 1612 patients had an unsuspected UIA. Data from a variety of additional studies also suggested that a prevalence rate well below 4%. For example, Fox reviewed data from 20 autopsies from a total of 164,764 and reported an aneurysm prevalence rate of 0.8%. In another autopsy series conducted by McCormick and Nofzinger, 153 patients were identified as harboring saccular intracranial aneurysms from among 7650 patients, for a prevalence of 2%. Rosenorn and Eskesen estimated a 0.6% prevalence of UIAs (range 0.1–2.9%) based on data from autopsy studies, and a prevalence of 0.4% (range 0.18–0.61%) based on data from radiological studies. A report by Winn and associates on 4568 cerebral arteriograms revealed 24 cases of asymptomatic aneurysms, yielding a prevalence rate of 0.65%. We conclude that the prevalence rate of 4% used by Chang is, at a minimum, two times too high. In summary, it is worthwhile to recall Weir’s observation in regard to a 5% prevalence rate: “This figure is frequently quoted, but, in my opinion, it is a considerable exaggeration.”

Our second concern relates to the constant c, which was developed by Dr. Chang to determine the growth rate of a cerebral aneurysm. This constant was based on an assumption that an aneurysm grows at a rate proportional to the cubic root function of the aneurysm’s age. As noted by the author, this cubic root assumption is based on data reported by Phan, et al., and Juvela, et al. The analysis by Phan and colleagues consisted of magnetic resonance imaging studies revealing that only large aneurysms grew and that any aneurysm smaller than 9 mm did not grow. The limitations of this analysis were well described in an accompanying editorial by Weir. The angiographic study data collected by Juvela and coworkers showed that the growth rate of aneurysms was quite varied. Furthermore, an additional angiographically based study by Allcock and Canham, which was not cited by Chang, revealed totally random growth of aneurysms. Thus, the validity of the assumption by Chang that aneurysms grow as a cubic root function of their age is at best unproven and probably incorrect.

Third, Dr. Chang assumed as correct the hypothesis by Dickey and Kailasnath that the rupture rate of aneurysms...
increases in proportion to the third order of its diameter. Furthermore, the actual coefficient used in the equation for calculating the lesion rupture rate was determined based on the prospective portion of the ISUIA (whose results have been questioned by many), and therefore it is not surprising that Dr. Chang’s results were similar to those of the ISUIA. Note the possible circular reasoning involved in Dr. Chang’s attempt to validate the ISUIA data.

A fourth concern is related to Chang’s claim that the calculated SAH incidence of 19.6/100,000 persons is compatible with that reported in the literature, although no reference was cited. Most incidence figures for aneurysmal SAH are lower, perhaps by half. For example, the following values are frequently quoted and commonly accepted: 10/100,000 persons. There are, however, higher incidences from authors in Japan,7 Finland,15,21 and Massachusetts.20

Last, Chang computed a mean age at rupture of 61.4 years and stated that this age “. . . corresponded well with the figures reported in the literature.” In fact, authors of most studies have found that the mean age at rupture is younger by a decade. In fact, according to cited references, we discovered the following: the study by Kassell and Torner,10 which was based on a very large international study, revealed a mean age at rupture of 51 years; in 1971 McCormick11 documented the most common decade of rupture as that between 50 and 59 years; and Weir25 indicated that the mean age at rupture is 48.5 years.

In conclusion, Chang reports on a very sophisticated mathematical modeling analysis, which is based on data from the ISUIA. He asserts that the model has produced reasonable statistical values: 4.2% prevalence rate of UIAs in the general population and 19.6/100,000 persons for the yearly incidence of SAH in a population with a mean age of 61.4 years. He concludes that his model validates the ISUIA. As noted previously, however, there are in fact significant variances from the accepted figures and statistics in the literature—that is, 50% higher prevalence rate, 50% higher incidence rate, and 20% older population—which suggests considerable caution in accepting Dr. Chang’s conclusions.

References

RESPONSE: I appreciate Drs. Winn and Britz for their detailed criticisms on my article, and I appreciate the Editor of