When the neurosurgeon, neurologist, interventional neuroradiologist, or neuroradiologist sees a patient with an unruptured intracranial aneurysm, the patient wants to know two things: 1) What risk does this aneurysm pose to my life and to my quality of life? 2) If it is treated what are the risks of treatment and are those risks higher or lower than the risk of the disease? The patient wants to know what the physician would do if he or she had this aneurysm.

The Risk of Rupture of an Unruptured Aneurysm

To answer the first question about the risk of aneurysm rupture is challenging for any neurosurgeon. If we look at rates quoted from the literature in Tables 2 and 3 in the paper written by Morita, et al., the risks of rupture range from 0.3 to 6.9% per year. Actually in its first report the International Study of Unruptured Intracranial Aneurysms (ISUIA) demonstrated a low rupture rate of 0.05% per year in a retrospective study. This is a 10-fold difference in values according to the paper by Morita, et al., and more than a 100-fold difference if you compare the 6.9% rate with data provided in the first ISUIA study. For the patient the decision process is different if the risk is 0.3% per year or 6.9% per year. Therefore, the treating physician needs better data or a better way to screen the data that are reported.

The Ideal Study

If one were to think of the ideal study necessary to identify the risk of hemorrhage from unruptured intracranial aneurysms, one would want a study in which an unbiased sample of patients was selected from the universe of all patients with unruptured aneurysms to determine the risk of rupture. If one wanted to know what the risks are in patients who display symptoms from their aneurysms, those symptoms would have to be defined and the patient sample would be taken from the universe of symptomatic patients with unruptured aneurysms. For patients in whose aneurysms were found incidentally, one would sample the universe of those patients with incidentally found aneurysms. Unfortunately, no studies have been performed in these ways. Therefore, any data that are reported are biased by the referral source or a selection of some kind.

Prominent Studies in the Literature

To me, the best study in the literature is the one conducted by Juvela and colleagues. Before 1979 in Finland no patients with unruptured aneurysms were surgically treated; they were observed. These patients came primarily from a population of patients who harbored multiple aneurysms of which one had bled. The other aneurysms were then followed. It is assumed in the study of Juvela and colleagues that multiple aneurysms in the same patient have a rupture rate equal to that of a single unruptured aneurysm in a patient. This selection bias has been criticized. The patients who came to the investigators’ institution represented a large sample of the Finnish population and were not selected because aneurysm surgery was not performed at any other institution in Finland. In that study the risk of rupture was 1.4% per year.

The ISUIA was divided into two studies, one retrospective and the other prospective, both of which represent severely biased samples of the universe of patients with unruptured aneurysms. In the later study (2003) the groups were further subselected in a biased manner to undergo surgery, endovascular treatment, or no treatment. The rupture rate was calculated from data in the no-treatment group after subselection. Data on the rupture rate in both studies are virtually useless to me as a clinician for those reasons. The key question for neurosurgeons regarding the ISUIA studies is: “Is the patient discussed in these studies the patient I am seeing in consultation?” To me the answer is “no” or “I don’t know.” You can read a more detailed explanation of my criticisms of these studies in other papers.

The report from Europe by Rinkel, et al., provides an analysis of the literature and includes one Japanese study. This study is well done. Its discussion section provides a fair evaluation of the results, which indicate a 1.9% rupture rate per year. It must be remembered, however, that this report is also a compilation of selected series.

The study by Morita, et al., reported in this issue, was
performed in the same manner as the Rinkel study; they are both detailed reviews of published studies. The study by Morita, et al., however, only included Japanese reports. This study documents a rupture rate of 2.7%, reportedly higher than the rate in the Rinkel report and in others, perhaps, because of racial differences in the rupture rates. This leads us to another question: does all of this information help us decide what to recommend to the patient?

How to Use This Information

Symptomatic Unruptured Aneurysms. There are two circumstances in which the clinician will see a patient with an unruptured intracranial aneurysm. First, the patient will present with symptoms that ultimately can be related to the aneurysm. The patient will complain of persisting or progressively more frequent headaches, double vision (third nerve palsy), or visual loss—symptoms difficult to exclude as not being related to an aneurysm.\textsuperscript{3} In these circumstances most likely the clinician will want to treat the aneurysm. According to the paper by Morita, et al., the risk of rupture in symptomatic patients is 7.3\%, but there were only 42 patients in that category. In the paper by Rinkel, et al., the risk of rupture in this category is also increased. Among 463 patients the risk of rupture was 6.5\%.\textsuperscript{4} Using common sense, a category excluded by the statistical method, if one operates on an unruptured aneurysm and sees the blood swirling in the thinned dome of the aneurysm, it does not take much persuasion to know that this aneurysm is dangerous and will rupture sometime. From the Rinkel and Morita reports one has to conclude that there is a significant risk of choosing no treatment for this symptomatic unruptured aneurysm. The risk of rupture in the symptomatic group of patients ranges from 6.5 to 7.3\%. Thus, the only choice is whether the risk of treatment is worse than the risk of the disease or of no treatment. I will discuss this subject later in this editorial.

Asymptomatic Unruptured Aneurysms. The second category of patients with unruptured aneurysms only pertains to those patients who were found incidentally to harbor aneurysms. These patients present with symptoms or another reason indicating the need for an imaging study unrelated to the aneurysm. The papers by Juvela and colleagues\textsuperscript{7,8,11,12} fall into this category. In the paper by Morita, et al., there are 876 cases in this category and the risk of rupture is 1.8\%. In the paper by Rinkel, et al., the risk of rupture is reported to be 0.8\%.\textsuperscript{11} Now the problem with the asymptomatic group is what to recommend. Dickey and Kailasnath\textsuperscript{10} reported that the risk of rupture increases exponentially—to the third power—with the diameter of the aneurysm: the larger the aneurysm, the higher the risk of rupture. The Rinkel, Morita, and ISUIA studies all support that general conclusion. In contrast to what Wieber and colleagues\textsuperscript{13} wrote in 1998 and 2003, that an aneurysm must reach 7 to 10 mm in diameter before it ruptures, these other papers do not dictate any size limitation to aneurysm rupture.\textsuperscript{4,14} Juvela, et al.,\textsuperscript{11} arrived at the same conclusion in the Finnish study reported in 1993. These researchers also reported that cigarette smoking, size of the unruptured aneurysm, patient age, and female sex carry higher risks of rupture.\textsuperscript{11,12} If we assume that the rupture rate for asymptomatic intracranial aneurysms is 1 to 2\% per year, the cumulative rupture rate over a 10-year period is 10 to 20\%.\textsuperscript{12} These factors—aneurysm size, cigarette smoking, age, and female sex—should thus be included when presenting data to the patient. What would you want done if the aneurysm was yours is the key question.

Incidence of Mortality and Morbidity Associated With Surgical Treatment and With No Treatment

Now, what is the risk of treatment of these aneurysms? Let’s assume a zero mortality rate, which has been reported and used as a justification for surgery. But death is not the only risk: there is also the risk of morbidity. Here is where the ISUIA provides us with excellent data.\textsuperscript{13} In the ISUIA patients were followed up for incidences of mortality and morbidity including cognitive deficits, which were evaluated using neuropsychological studies. Most neurosurgeons perform a cursory examination postoperatively and do not evaluate any cognitive deficits the patient may have. In the ISUIA the combined morbidity and mortality rate was approximately 11 to 15\% at 1 year. This is very significant. Cognitive morbidity constituted one third of the combined morbidity–mortality rate and both mortality and morbidity were associated with the surgery.

Incidence of Mortality and Morbidity From Endovascular Treatment

What is the combined mortality–morbidity rate in patients undergoing endovascular treatment? In a superselected group treated endovascularly the ISUIA found a 9.8\% mortality–morbidity rate with 3.2\% of patients experiencing cognitive disorders after interventional treatment.\textsuperscript{7} In a study of 247 unruptured intracranial aneurysms treated with coil embolism Gonzalez, et al., reported 5.5\% morbidity and mortality.\textsuperscript{6} Investigators in the International Subarachnoid Aneurysm Trial (ISAT) reported a morbidity–mortality rate that was lower than the rate associated with surgery and the difference had statistical significance.\textsuperscript{9} There is much criticism of this study by neurosurgeons; yet, the conclusions of the study are valid based on the questions asked.\textsuperscript{1} An additional report of the ISAT group should be published in 2005 and will reveal cognitive defects in the surgery and endovascular groups, which were randomly selected. My guess is that the cognitive deficits after coil placement will be much lower than those after surgery.

The Future

In the future we will observe detected unruptured intracranial aneurysms by using magnetic resonance angiography. When the aneurysm enlarges it can be treated.\textsuperscript{17} Juvela, et al.,\textsuperscript{11} made this observation based on repeated conventional angiography studies obtained during the follow-up period of their study in 1993.

My Answer Concerning What to Do

So, what does the clinician tell the patient with a symptomatic or asymptomatic unruptured intracranial aneurysm about the risks of treatment? Will surgery provide treatment that can be viewed favorably even in light of the 10 to 15\% rate of mortality and morbidity to which you will subject the patient if you operate? That is the choice the patient must make given the data. To me the data can be used to argue for treatment. What would I want done if it were my unruptured aneurysm? For me, get me to the most experienced inter-