EDITORIAL

Managing Unruptured Intracranial Aneurysms

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Unruptured intracranial saccular aneurysms are discovered in the following different ways: 1) incidentally on brain imaging done for other reasons; 2) when asymptomatic individuals with a family history of aneurysms are screened with vascular imaging; 3) in patients who have suffered an aneurysmal subarachnoid hemorrhage (SAH) and who possess one or more additional and unrutpured aneurysms; 4) when they grow to compress and/or irritate adjacent neural structures such as cranial nerves or the brain itself causing corresponding symptoms and signs; and 5) when they either thrombose or embolize causing brain ischemia or infarction. Increased use of high definition brain imaging has resulted in more frequent discovery of asymptomatic aneurysms, which after silent cerebral infarcts were the second commonest incidental MRI finding in one recent general population survey[1]. As Dr. Raymond eloquently emphasizes in his commentary found in this issue of the Journal, this creates a common and serious dilemma for patients and their treating physicians: what should we do about newly discovered, asymptomatic intracranial aneurysms?

Firstly, let it be known that Jean Raymond is one of the world's leading neurovascular and endovascular scientists, researchers and therapists. His main points are that no matter what we think or read, in fact the natural history of unruptured aneurysms is poorly understood and cannot be predicted in any given patient, that there is no evidence to support treating asymptomatic aneurysms despite the fact that we frequently do so, and that the only ethical solution to this dilemma is to conduct randomized trials comparing observation to aneurysm repair. For logistical reasons Raymond believes two types of trials are needed, one with endovascular coiling in the treatment arm and the other with microsurgical clipping.

But are we as lost at sea on this subject as Dr. Raymond suggests? No one would argue that there is zero risk of an asymptomatic aneurysm rupturing, but we do debate about exactly how small that risk is. Raymond reminds us of imperfect data indicating a risk of bleeding from around 1 to 3 percent per year for "average" saccular aneurysms, the risk leaning towards either the lower or higher end of this small range according to the absence or presence of certain risk factors, including (to name just a few) bigger or more irregularly shaped aneurysms, aneurysms located on the basilar or posterior communicating arteries, and aneurysms found in a person with a strong family history of aneurysms. However the evidence supporting many risk factors is weak, and we do not have an exact size threshold beneath which an aneurysm is known to be completely safe. We can agree that the annual risk of spontaneous bleeding from a non-giant and asymptomatic aneurysm is very small, and our first job in the clinic is to reassure a stressed patient of that nothing is going to happen later that day, that week, month or even that year, and that they can resume normal physical activities and exertions (that some well-meaning doctor told them to cease "until they saw you!"). Our second job (making this discussion a delicate one) is to inform our patient that while the event rate of rupture is very low, we also know for certain that the consequence of any single rupture is enormous, in fact fatal in over one-half of patients. The discussion then necessarily turns to our patient's general health and age, and what his or hers' lifetime, cumulate risk of hemorrhage might be. Here Raymond argues that the many factors impacting rupture risk make this an extremely nuanced if not impossible estimate. However many would argue that it is useful to employ the equation of cumulative probability, or an actuarial table derived from that equation in order to provide some rough idea of relative lifetime risk, providing our patient manages what we all hope for, and that is living to an average old age. So for example an otherwise healthy, non-smoking 45 year-old found to be harboring a 8 mm aneurysm, may, depending on the presence or absence of risk factors, have between a 1% to 3% annual risk of rupture as already mentioned, meaning that if he or she lives to 80 there is between a 30% and 65% lifetime risk of rupture and catastrophe. Properly presented, this information is helpful to patients weighing their options.

It is true that at present there no proof that prophylactic repair of aneurysms is beneficial, and at the same time there is ample documentation of the harm that can result from aneurysm repair. In the International Study of Unruptured Intracranial Aneurysms (ISUIA) the one-year mortality and morbidity rates in patients who underwent microsurgical aneurysm repair were 2.3% and 9.7 % respectively, although in 5.7% (over one-half of those in that group) morbidity consisted of impaired cognitive status only, determined by way of a telephone interview[2]. Death and disability increased with increased patient age and aneurysm size, and with symptomatic aneurysms. In comparison, the cohort treated with endovascular coiling in that same study had one-year overall mortality and morbidity rates of 3.1% and 6.4%, with 3.5% having impaired cognition only. Aneurysm location and size correlated with poor endovascular outcome, but not age. Aggregate and data-base analyses also point to coiling as safer than clipping—and certainly associated with shorter hospitalizations and recovery times[3,4], although no direct or randomized comparisons of the two treatments has been made to date. Endovascular treatment has the important drawback, however, of a substantially lower complete aneurysm occlusion rate. In the recently reported ATENA study only 59% of 739 aneurysms were completely occluded, a neck remnant remained in 21.7%, a larger remnant in 15% and in the remaining 4.3% treatment failed for a variety of reasons[5]. Compared to microsurgery, far fewer patients can be considered "cured"

following coiling (which is associated with a greater than 90% complete occlusion rate), all will require follow-up, and some retreatment[6]. This is a significant consideration for unruptured aneurysms where life-time protection, rather than short-term prevention of rerupture, is the goal.

Randomized trials attempting to sort out these issues and establish if there is any efficacy of intervention are much needed, but I suspect will be difficult to conduct. Patients will be faced with random allocation to either a group where nothing is done, or a group that undergoes a delicate and risky brain aneurysm procedure. The two managements are so extremely opposite that I think many patients offered participation in such a trial will be left baffled, vexed, and unlikely participants.

Dr. Raymond's argument in support of randomized trials is irreproachable, his accomplishment in launching the TEAM study admirable and that study's goal of determining the effectiveness of endovascular coiling in altering the natural history of unruptured aneurysms is certainly required if we are to make "Level 1" evidence-based recommendations regarding that intervention in this setting. However not all patients or physicians will have the equipoise necessary to participate in this trial, or another comparing observation to microsurgical clipping of unruptured aneurysms. Despite the gaps in our knowledge it seems best that patients over 70 and/or unhealthy patients with asymptomatic aneurysms be managed conservatively outside of any trial, and that for patients less than 60 found to have sizable aneurysms (6 mm or greater), it is reasonable and ethical to discuss treatment, either coiling if it looks suitable for complete occlusion with that modality, or clipping if it is readily accessible without excessive brain retraction or risk to perforating vessels. Patients require an accurate and full account of what we presently know about the natural history of these lesions (which I have discussed above), and the real risks of treatment if it is being offered—stroke and disability, which vary according to aneurysm size, location and the experience of the surgeon or interventional radiologist. Patients who have survived and recovered from a prior aneurysm rupture and repair and who harbor another aneurysm not yet treated, as well as those patients who have had a relative or friend harmed or killed by the same condition come to us insisting on treatment, and it is a hard job to convince them otherwise when we think that approach unwise and dangerous. Jean Raymond's commentary is an argument and plea for true clinical equipoise when faced not just with patients between the ages 60 and 70, but all patients with treatable aneurysms. Read his commentary and see where you stand.

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