Intracranial Aneurysms: A Game of Millimeters

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Rationale and Objectives: In this review we will discuss the historic development of intracranial aneurysms as a pathologic entity and the potential for overdiagnosis.

Materials and Methods: We conducted a literature search to assess the prevalence, rupture rate, and treatment of intracranial aneurysms.

Results: Intracranial aneurysms represent a necessary example of overdiagnosis.

Conclusions: A change in the nomenclature of small aneurysms is a possible solution to mitigate patient anxiety from a diagnosis of intracranial aneurysm.

Key Words: Aneurysm; overdiagnosis; vascular imaging.©AUR, 2015

Since the 18th century, intracranial aneurysms were recognized by physicians as a silent scourge, which could kill indiscriminately. In 1927, when Moniz introduced cerebral angiography to the world, the diagnostic and therapeutic outlook of intracranial aneurysms changed forever (1). As with any technologic innovation, the moment a new medical diagnostic tool arrives, a rush to prove its utility and effectiveness ensues. Expectedly, cerebral angiography quickly became an integral component in the workup and identification of cerebral aneurysms (2). The study of intracranial aneurysms continued to grow, and clinicians required epidemiologic data to better understand the prevalence of this phenomenon and to develop appropriate treatment algorithms. A 42-year autopsy series published in 1958 by Housepian and Pool described the prevalence of aneurysms as 2% in adults (1). Approximately, 71% of identified aneurysms produced a fatal hemorrhage, which they subdivided into initial and subsequent bleeding episodes (1). Notably, 6.6% of ruptured aneurysms measured 1–2 mm and 38.7% of ruptured aneurysms measured 3–5 mm (1). More recently, the mean prevalence of intracranial aneurysms varies, being quoted as high as 5%–10% by Caranci et al. (3). The discrepancy in prevalence over time is likely multifactorial, with more inclusive characterization, larger data sampling, and an increase in imaging volume serving as contributing factors.

One factor which did not contribute to this increased prevalence is size criteria. The autopsy series by Housepian and Poole classified intracranial aneurysms according to the following criteria: 1–2 mm, 3–5 mm, 6–10 mm, 11–20 mm, 21–40 mm, >40 mm (1). The presence of aneurysms was based on alterations in the histologic morphology of the vessel wall as identified on microscopic section (1). Additionally, histologic changes were present at vascular bifurcations in keeping with the expected evolution of histologic changes associated with the development of aneurysms (1).

Currently, diagnosticians try their utmost to accurately identify the smallest of cerebral aneurysms on a variety of imaging modalities. Whether in the reading room or the angiography suite, they may question if a finding is real, but they do not question whether a 2-mm aneurysm is worth reporting.

This categorical approach harkens back to their training in pathophysiology, where they learned about the catastrophic consequence of aneurysm rupture. In their eyes, it is unacceptable to dismiss a 2-mm aneurysm with the aim of sparing the patient the psychological trauma of overdiagnosis, as this would constitute a preventable serious harm. As diagnosticians improve their ability to perceive and document a 2-mm aneurysm, perhaps they should ask themselves, now what?

EPIDEMIOLOGY OF CEREBRAL ANEURYSM RUPTURE

Though catastrophic, there is an approximately 0.006% chance of developing an aneurysmal subarachnoid hemorrhage each year, which translates to approximately 15,000 annual cases in the United States (4). For patients with a
known aneurysm, the likelihood of rupture varies based in part on whether or not the patient suffered a subarachnoid hemorrhage from a separate aneurysm, anatomic location of the aneurysm, and the size of the aneurysm in question. Data published from the International Study of Unruptured Intracranial Aneurysms (ISUIA) in 2003 demonstrated that the lowest risk of aneurysmal ruptures occurs in patients anterior circulation aneurysms <7 mm in diameter the anterior circulation, without prior history of rupture (5). The overall risk for patients who have an aneurysm <7 mm in diameter without a prior history of rupture is approximately 0.1% per year (5). For aneurysms >10 mm in diameter, the rate of rupture increases to approximately 1% per year (4).

A review on the natural history of aneurysms performed by Brown and Broderick demonstrated that among retrospective studies, for unruptured aneurysms <10 mm in diameter, the risk of rupture is 0%–1.1% per year (6). For aneurysms 10 mm in diameter, the risk of rupture has been published as 0.7%–6.7% per year, noting the absence of an upper size limit in these studies (6). In Brown and Broderick's analysis of prospective studies on unruptured aneurysms, they noted that the 5-year cumulative rupture rate for aneurysms <7 mm in diameter was zero if they were in the anterior circulation or in the cavernous carotid artery (6). Posterior circulation aneurysms, <7 mm in diameter, had a rupture rate of 2.5% (6). The rupture rates increased to 3.0% when the aneurysm grew to 13–24 mm in the cavernous carotid (6). Rupture rates were 2.6% and 14.5% in anterior circulation aneurysms that were 7–12 and 13–24 mm in diameter, respectively (6). Rupture rates were 14.5% and 18.4% in posterior circulation aneurysms that were 7–12 and 13–24 mm in diameter, respectively (6).

The seemingly benign course of small anterior circulation aneurysm came under scrutiny more recently, because of studies providing more detailed anatomic risk stratification. A retrospective review of the impact of aneurysm location on rupture risk by Gross et al. demonstrated that pericallosal and frontopolar aneurysms have an increased likelihood of rupture in comparison to more proximal anterior circulation aneurysms (7). The true anatomic predilection for rupture requires further research to fully quantitate, to account for small sample size.

Initial treatment evaluation for ruptured intracranial aneurysms demonstrated a 1-year morbidity and mortality risk of 12.6% with neurosurgical clipping and 9.8% with endovascular coiling (5). These risks vary based on patient age and aneurysm location (5). These values are difficult to extrapolate to unruptured aneurysms but are likely lower (6,8). The possibility of increased procedural risk in case of rupture can be used to justify early treatment of unruptured aneurysms.

Guidelines published by the Stroke Council state that because of the aforementioned risks associated with neurosurgical clipping or endovascular coiling, intervention for small asymptomatic aneurysms is not generally recommended (4,5). For aneurysms >10 mm, treatment should be strongly considered (4). In early 2014, PHASES, a new aneurysm risk calculator, was proposed to assess rupture versus treatment risk (9). The implications of this system and its impact on treatment recommendations have not yet been fully explored.

EVALUATION OF METHODOLOGY

Some of the discordance in the literature regarding the incidence of and natural history of aneurysms may reflect methodologic differences. Housepian and Poole's evaluation represents the only autopsy series. Therefore, its estimate of aneurysm incidence is generalizable to the entire population, but their work cannot be used to estimate the annual rate of rupture. The ISUIA, which used a prospective analysis of patients diagnosed with unruptured aneurysm, probably provides the best estimate of the natural history of aneurysm and mortality risk. However, this study excluded aneurysms <2 mm in diameter. The study by Gross et al., while provocative, may be confounded by factors related to its retrospective design (eg, survivorship bias and/or detection bias).

Moreover, aneurysms in early studies generally fell into the following classification categories: fusiform, saccular, luetic, and saccular with arteriosclerosis (1). More recent studies excluded fusiform aneurysms, thus at least partially limiting diagnostic correlation (5). Studies also differ in the extent to which they evaluate the distal vasculature (5,7). The evolution of these studies highlights how our current level of knowledge and technology frames our assessment of truth. Each study that further characterized vascular anatomy changed our perception of the occurrence of aneurysm rupture. This serves as a warning that although our data may at times appear complete, more representative studies along with more detailed anatomic evaluations always have the potential to disrupt our current diagnostic and treatment paradigm.

Given the minimal risk of rupture for incidental small aneurysms, patients should be told that despite the serious diagnosis, according to our current literature, no intervention is typically recommended. The large proportion of patients diagnosed with ultimately quiescent aneurysms compared to the few who will rupture, particularly in light of the lack of treatment options, suggests overdiagnosis. This premise of overdiagnosis, particularly with aneurysms <2 mm, is further corroborated by their absence from the ISUIA's analysis of the natural history and treatment of unruptured intracranial aneurysms.

THE COMPONENTS OF UNCERTAINTY IN A HEALTH CARE INTERACTION

A radiologist's practice revolves around uncertainty. Descriptions are often qualified: “diagnostic of,” “compatible with,” or “cannot exclude a particular disease entity” based on the level of uncertainty. Whether through conscious or subconscious effort, word choice communicates the level of
uncertainty to whoever reads their reports. To better understand how this impacts patient care, we must further breakdown the term uncertainty as it relates to health care interactions.

Uncertainty contains three components: probability, ambiguity, and complexity (10). Probability is the likelihood that an event will occur. Returning to the example of a 2-mm cerebral aneurysm, there is an approximately 1 in 1000 chance that the aneurysm will rupture each year (5). This value represents a good estimate; however, it is subject to experimental error. Different studies arrive at slightly different numbers, and experts disagree on a precise risk. Although confidence intervals can ground some of these findings, inherent variability leads to ambiguity, which muddles interpretation. Reconciling probabilities, conflicting expert opinions, and individual patient risk factors decrease comprehensibility of a particular statistic and thus generate complexity.

To illustrate how this relates to a health care interaction, imagine a primary care physician was consulted by a 46-year-old woman to assess her risk of developing breast cancer. With no additional risk factors, a typical 46-year-old woman to assess her risk of developing breast cancer (46). With no additional risk factors, a typical 46-year-old woman has a 1% chance of developing breast cancer within 5 years (11). However, women with dense breasts have shown to have a slightly increased risk of breast cancer. This adds ambiguity to the assessment. Moreover, suppose the patient was Hispanic. These statistics may not be generalizable to the Hispanic population. The physician might communicate to the patient that the risk of developing breast cancer within 5 years for a 46-year-old Caucasian woman without dense breasts is 1%. However, because this patient is of a different race and has dense breasts, her actual risk is difficult to calculate. It may be higher or lower, but 1% might still be a reasonable estimate. Similar conversations ensue when physicians discuss statistics regarding aneurysms, particularly small ones, with patients.

**ETHICAL ISSUES SURROUNDING TESTING AND UNCERTAINTY**

The push to improve patient autonomy has spurred interest in disclosing the risks of uncertainty. The most prominent example within radiology is the suggestion to include the discovery of incidental findings in the informed consent process (12). Although incidental findings typically refer to poorly understood hyperintense foci of signal within the abdominal organs, a 2-mm aneurysm could easily fall under this umbrella when an emergency physician orders an enhanced head computed tomography (CT), CT angiography, or magnetic resonance imaging for another reason.

Currently, the best analogy for this scenario derives from work on neurodegenerative disease and genetic testing. An allele of the apolipoprotein (APOE) gene, APOE e4, represents an autosomal dominant mutation that increases the risk of Alzheimer’s disease (13). Genetic testing can provide a categorical answer regarding the presence of the gene, however, the risk associated with it and the onset of Alzheimer’s is variable. There are many similarities between the possibility of developing a heritable malady and the finding of a small aneurysm. In both cases, there is the potential for increased psychological stress and the alteration of life-planning decisions and family dynamics due to uncertainty. For Alzheimer disease, the initiation of oral therapy represents a potential benign treatment option for patients. In contrast, the morbidity and mortality of treatment of tiny aneurysms may outweigh the benefits.

The association between uncertainty and stress has been extensively studied, with an increased illness rate associated with uncertainty (14). A study discussing the psychological impact of a genetic predisposition to fatal cardiac arrhythmias by Hidayatallah et al. demonstrated a bereavement trajectory for asymptomatic patients told they possessed this predisposition (15). These patients paralleled the emotional arc of a family coping with the unexplained death of a child, which begins with disbelief, followed by anxiety and concluding with acceptance (15). Like a fatal arrhythmia, a cerebral aneurysm can rupture at any time and kill without warning. Therefore, it is reasonable to assume that the aforementioned cardiac study can serve as a baseline estimate of how patients with small cerebral aneurysms may feel.

**NOMENCLATURE**

Returning to the discovery of a 2-mm aneurysm, an unfortunate dilemma persists. On the one hand, the 2 mm exists and has the potential for harm and therefore must be reported; on the other hand, no recommended treatment options exist, and therefore, they serve only as a nidus for patient anxiety. Superficially, this illustrates an example where “overdiagnosis” remains far from an ideal solution.

However, one option exists for the beleaguered diagnostician: alter the nomenclature to mitigate anxiety-provoking connotations. For example, the Fleischner Society defines a pulmonary mass as >3 cm; anything less and nodule is the appropriate term (16). Within vascular imaging, vessels can be defined as either ectatic or aneurysmal, depending on their physical tolerability limits (17).

In cases of tiny aneurysms, a change in nomenclature may be in order to prevent patients from hearing the word aneurysm and subsequently fearing a sudden end to their existence. Tiny aneurysms, defined as <7 mm and without suspicious features or vulnerable anatomic location, could be reclassified as VOIR: vascular outpouching of indeterminate relevance. This constitutes an anatomic description and an acknowledgment of the uncertainty associated with their prognosis. As a helpful mnemonic, VOIR is the French verb “to see.” This is an appropriate term for these findings, as diagnosticians see them without currently offering anything more helpful than a description to the patient.

Similar approaches have been used in other areas of medicine. In the field of oncology, there are myriad permutations
of irregular cellular growth patterns categorized as “cancer.” Although there is a marked difference between an invasive ductal carcinoma in situ, patients often hear the word cancer and let the remainder of the conversation fall on deaf ears. To combat this, authors have proposed nomenclature changes to precancerous conditions and indolent neoplasms in an attempt to mitigate patient anxiety. For example, Esserman et al. (18) coined the term “indolent lesion of epithelial origin” as a possible alternative for such lesions. Numerous examples of these lesions already exist within pathology and radiology, such as a follicular lesion of undetermined significance in the thyroid and indeterminate liver lesions in patients with underlying malignancy (19–21). As in these cases, acknowledging uncertainty will likely serve patients better than definitively stating the presence of a serious condition which may or may not be relevant to the patient.

CONCLUSIONS

Overall, the precise definition of an incidental small aneurysm remains controversial, but when found, there is a negligible chance of rupture and lack of recommended treatment options. Therefore, discovering a small aneurysm in a presumably otherwise healthy person suggests that diagnosticians are overwhelmingly labeling healthy people with a diseased state to identify the few who may rupture, without any potential benefit. Hence, small aneurysms fall into the category of overdiagnosis. If the reporting of small aneurysms remains a necessity, altering the nomenclature of these small aneurysms, such as renaming them VOIR, may be the best alternative to mitigate patient anxiety.

REFERENCES