

Results from Phase One of The Missy Project Community Screening Program

Research Update from Dr. Craig Kemper's Research Pilot Community Program for Education, Prevention and Screening in First Degree Relatives of Patients with Intracranial Aneurysms.

Subarachnoid hemorrhages (SAH) occur in about 21,000 adults in the U.S. each year, of which approximately 75-99% are the result of a ruptured intracranial aneurysm (IA). The mortality rate following rupture IA is around 30-50% within 30 days of hemorrhage, with significant morbidity, including physical, emotional, and cognitive deficits associated with survival. 1 2 3 4

About 10 to 15 million people in the U.S. already have or will be found to have an intracranial aneurysm. Research on how these aneurysms form, what modifiable and nonmodifiable risk factors are associated with development and rupture, and the best medical treatment options has occurred over the last several decades. 2 3 5 6. Studies demonstrate the mean onset of rupture frequently occurs in the fourth or fifth decade of life and has a higher incidence in women. Age is another nonmodifiable risk factor, proving that older patients (over the age of 50) are more at risk of harboring an aneurysm. The number of subarachnoid hemorrhages also increases with age, and reaches a peak around 50 years old. 7 "A recent meta-analysis by Vlak et al. that included 68 studies with 94,912 participants (1450 had IAs) from 21 countries identified female sex, older age, family history of IAs as risk factors for harboring aneurysms". 8 The number of aneurysms found in females compared to males is notably higher. In a study conducted with 335 patients, there was about a 3:1 ratio of females to males that harbored at least one aneurysm. 9 Another study shows that out of a patient population containing 511 participants, 417 (81.6%) patients were women. 10

Risk factors identified in SAH victims and ruptured IA patients include hypertension, tobacco use, and possibly alcohol consumption. Another risk factor identified in numerous studies is a positive family history of SAH. First degree relatives of patients with a ruptured aneurysm have a 4% likelihood of having IAs compared to the general population incidence rate of about 2.3%. In families with 2 or more members identified with rupture IAs, the risk to first degree relatives increases to 8-9%. This familial predisposition also is associated with an earlier age of rupture in the third to fourth decade of life. 5

Familial incidence proves that patients are more at risk of harboring at least one aneurysm. In the "largest multinational descriptive comparison of familial and

nonfamilial as [intracranial aneurysms]" patients with a family history of aneurysms proved to be more at risk for multiple intracranial aneurysms. 10 Familial aneurysms not only put patients more at risk for intracranial aneurysms, but they also lead to a worse outcome. Once the familial intracranial aneurysm(s) burst, 52% of the familial subarachnoid hemorrhages had a poor result, compared to the 37% of the nonfamilial subarachnoid hemorrhages. It has been reported that unruptured intracranial aneurysms affect about 1-2% of the general population.¹⁰ Relatives of patients with a familial subarachnoid hemorrhage have an 8% chance of harboring an aneurysm, at least 4 times as prevalent than the general population. 11

Given the higher risk and known morbidity and mortality associated with intracranial hemorrhage, studies have been performed to detect and treat unruptured IAs of first degree family members. 6 Screening studies have been controversial in their utility regarding unruptured IAs. However, certain risks have been shown to suggest a higher risk of aneurysm formation and rupture rate. Smoking and hypertension are the two strongest risk factors that increase the chance of harboring an unruptured intracranial aneurysm. 8 Smoking increases the development of new aneurysms as well as that of established aneurysm. Hypertension proves to weaken the wall repair of the blood vessels. Rupture is a potential risk because the hemodynamic fluid will be stronger than the vessel wall, causing the artery to burst. 7

Primary (mother, father, sister, or brother) and secondary (grandmother, grandfather, aunt, or uncle) family members of those who have had at least one brain aneurysm and have a past of smoking and/or hypertension should be screened for an aneurysm. 12

Both CT angiography and MRA have demonstrated a specificity of about 95% and a sensitivity of 75-90% for aneurysms 5mm and larger. Current thought is that aneurysms smaller than this have a lower incidence of rupture and thus risk. Stroke now represents the most common cause of major disability in the U.S. and aneurysmal SAH are 8-10% of strokes. The health care cost of this disability is staggering. A recent audit in the state of Texas estimated that one stroke victim will incur \$100,000 of medical care and costs per year of life. If SAH can be prevented by early detection and appropriate intervention, an economic argument for screening studies is valid. Use of limited resources and funding must be prudent and efficient for society as a whole. However, these arguments do not negate the potential benefit that prevention efforts, increased awareness and screening can afford those who have increased risk of IAs. As advances in technology continue, the methods and benefit of screening for this disease must be continually assessed.

We propose to conduct a community based program on aneurysm screening, prevention and awareness. The purpose of the program will be to increase the awareness of aneurysms and stroke; to educate families on risk factors; to provide community resources on smoking cessation hypertension and healthy lifestyle promotion; and to provide screening to first degree relatives of known IA patients. All program efforts will be provided free of charge to these family members.

For the pilot program, we approached family members of 20 patients who have been hospitalized at University Medical Center Brackenridge (formerly Brackenridge Hospital) 601 East 15th Street, Austin, Texas 78701, for subarachnoid hemorrhage identified as being caused by a ruptured aneurysm. Family members were provided educational literature, a review of studies demonstrating familial risk and were notified that screening was available for qualified candidates.

Screening was provided for first degree siblings who were at least 16 years old using Magnetic Resonance Angiography (MRA) at UMC Brackenridge, Austin, Texas. The goal of the screening was to identify people with a previously unknown aneurysm. Upon identification, participants were provided counseling about risks of rupture and treatment alternatives. The pilot program began 11/2004. At the completion of the original study, data was reviewed and it was proposed to launch into a larger community based screening program

The next phase of the study intends to look at the incidence of detectable IAs using MRA (1.5T) screening in three cohort groups. The first group is a cohort of 100 representing first order relatives of patients with known aneurysms. The exclusion criteria are to be maintained throughout all cohorts of the study. The second cohort is 100 people with second order relatives harboring known aneurysms. The third cohort is a general population screening of 100 patients with no family history of IA. The need for the large cohort is an effort to achieve statistical significance in the findings.

Exclusion criteria were:

- 1) Age less than 12 or greater than 80.
- 2) Known pregnancy
- 3) Hardware implant precluding MRI imaging.

Data/Results

Of the 20 initial patients studied, no adverse events were encountered.

Current total screenings number 132. Cohort tabulation has not been completed and preliminary data is under review.

IRB approval has been obtained and updated throughout this study.

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