Asymptomatic unruptured intracranial aneurysms

Approach to screening and treatment

John T. Lysack MD FRCPC **Annalee Coakley** MD CCFP

ABSTRACT

OBJECTIVE To review the current knowledge of screening and treatment of asymptomatic unruptured intracranial aneurysms (AUIAs) using a case-based approach.

SOURCES OF INFORMATION PubMed was searched from January 1995 to January 2008 using the phrase *unruptured intracranial aneurysm.* Scientific statements of the Stroke Council of the American Heart Association pertaining to intracranial aneurysms were also reviewed.

MAIN MESSAGE Most small AUIAs (≤5 mm) do not rupture, and the risks of treatment are substantial. Most small AUIAs can therefore be managed conservatively. Endovascular coiling or surgical clipping of larger aneurysms (>5 mm) should be considered on a case-by-case basis.

CONCLUSION There is currently a lack of sound scientific evidence to support treatment of unruptured intracranial aneurysms. A prospective randomized controlled trial—Trial on Endovascular Aneurysm Management—is now under way to address this issue. It is expected to conclude in 2021.

RÉSUMÉ

OBJECTIF Revoir les données actuelles sur le dépistage et le traitement des anévrysmes intracrâniens non rompus asymptomatiques (AINA) en utilisant une méthode de cas par cas.

SOURCES DE L'INFORMATION On a consulté PubMed entre janvier 1995 et janvier 2008 à l'aide de l'expression *unruptured intracranial aneurysm*. On a aussi relevé les déclarations scientifiques du *Stroke Council* de l'*American Heart Association* à propos des anévrysmes intracrâniens.

PRINCIPAL MESSAGE La plupart des petits AINA (≤5 mm) ne se rompent pas tandis que les risques de traiter sont importants. La plupart des petits AINA peuvent donc être traités de façon conservatrice. Dans le cas des anévrysmes plus importants (>5 mm), l'insertion d'un coil endovasculaire ou le clampage chirurgical devraient être envisagés en fonction de chaque cas.

CONCLUSION À l'heure actuelle, il n'y a pas de preuve scientifique solide justifiant de traiter un anévrysme intracrânien non rompu. Cette question fait présentement l'objet d'un essai randomisé prospectif (Trial on Endovascular Aneurysm Management), qui doit se terminer en 2021.

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Brain imaging, for a variety of reasons, is being performed more frequently in Canada. As a result, an increasing number of asymptomatic unruptured intracranial aneurysms (AUIAs) are being discovered, either on purpose (ie, via screening) or as an incidental finding (ie, incidentaloma). As more aneurysms are discovered, family physicians can expect to be further involved in their management.

For screening to be considered effective, the screened population must have a better outcome than the unscreened population. Differences in outcome between screened and unscreened populations are primarily a reflection of the risks related to diagnosis and treatment versus the natural history of the condition. Similarly, differences in outcome between patients with treated and conservatively managed incidentalomas are a reflection of the risks related to treatment versus the natural history of the condition. In other words, the natural history of a lesion must be sufficiently poor to justify the risks of intervention.

Case 1

Ms A. is a 45-year-old woman who has recently moved to the city and presents to her new family physician for an initial visit. She is in good health, but during a routine review of her family history it is revealed that her father died of a ruptured intracranial aneurysm. She is unaware of any other family history of intracranial aneurysm. She is asymptomatic and in good health. Should Ms A. be screened for an intracranial aneurysm?

Case 2

Ms B. is a 45-year-old woman who was struck in the face by a softball during a recreational game. She reported to the local emergency department for management of a laceration. In case of underlying injury, a computed tomography scan of the head and facial bones was performed. There was no fracture or intracranial hemorrhage; however, focal prominence of the left middle cerebral artery (MCA) raised the possibility of an incidental unruptured intracranial aneurysm. A computed tomography angiogram was performed, which confirmed the presence of a 3-mm saccular aneurysm at the left MCA bifurcation. Does this aneurysm require treatment?

Case 3

Ms C. is a 45-year-old woman who comes to her family physician for follow-up of an incidentally discovered 3-mm left MCA bifurcation aneurysm. Although she remains asymptomatic, she has been researching her condition on the Internet and is now considering prophylactic treatment. She has heard that coiling is better than clipping. Is that true?

Sources of information

PubMed was searched using the phrase *unruptured intracranial aneurysm*. Results were limited to human studies published in the English language from January 1995 to January 2008. Relevant papers were selected for review. Additional articles were identified from the reference lists of relevant papers. Scientific statements of the Stroke Council of the American Heart Association that pertained to intracranial aneurysms were also reviewed.

Main message

When intracranial aneurysms rupture the results are devastating; half of patients die and up to half of those who survive are disabled.[1] Fortunately, although the prevalence of intracranial aneurysms in the general population is relatively high (2%),[2] the incidence of subarachnoid hemorrhage (SAH) in the general population is relatively low (6 to 9 cases per 100 000 person-years).[3,4] This implies that most intracranial aneurysms never rupture.

The best estimate of the rupture risk of intracranial aneurysms is arguably from a recent meta-analysis,[5] which yielded an annual rupture risk of 0.6% to 1.3%. Subgroup analyses showed that asymptomatic aneurysms were 4 to 5 times less likely to rupture than symptomatic aneurysms; small aneurysms (≤5 mm) were 2 to 3 times less likely to rupture than larger (>5 mm) aneurysms; and anterior circulation aneurysms were 2 to 3 times less likely to rupture than posterior circulation aneurysms (those involving the vertebrobasilar system or posterior cerebral arteries).[5] An earlier study suggested that the annual rupture risk for small aneurysms (<10 mm) might be as low as 0.05%, although this claim is controversial.[6]

Patients with a family history of aneurysmal SAH are at increased risk of harbouring an intracranial aneurysm compared with the general population. Epidemiologic studies have shown that patients with a single first-degree relative with aneurysmal SAH have a 3% to 6% risk of harbouring AUIAs (twice the baseline risk of the general population),[7,8] while patients with 2 or more first-degree relatives with aneurysmal SAH have an 8% to 10% risk of harbouring AUIAs (4 to 5 times the baseline risk of the general population).[8,9]

In deciding whether or not to intervene, the risk of intervention (ie, treatment-related mortality and morbidity) must be weighed against the risk of nonintervention (ie, risk of rupture). Treatment-related risks are substantial. In a recent, large retrospective study (2535 cases from 18 American states), 11.5% of patients had an adverse outcome following elective treatment of their unruptured intracranial aneurysm and 53 patients (2.1%) died.[10] A prospective study of the risks and benefits of screening for intracranial aneurysms in first-degree relatives of patients with sporadic SAH showed that although screening resulted in a small increase in life expectancy (4 weeks per person screened), this was

overshadowed by a substantial decrease in quality of life (19 years of decreased function per person screened).[7] The study also showed that in order to prevent 1 SAH, 149 first-degree relatives would need to be screened; to prevent 1 fatal SAH, 298 would need to be screened. From a societal perspective, the cost-effectiveness of various management strategies is also of interest. In a recent comprehensive cost-effectiveness analysis,[11] conservative management (no treatment) was the only cost-effective strategy for small (<7 mm) intracranial aneurysms (using an incremental cost-effectiveness ratio threshold of $100 000 per quality-adjusted life-year).

Given the relatively high risks of treatment and the comparatively modest anticipated benefits, the Stroke Council of the American Heart Association has concluded that screening for AUIAs in the general population is not indicated.[12] Despite increased risk of harboured AUIAs, screening patients with a single first-degree relative with aneurysmal SAH is also not generally recommended.[12] Screening patients with 2 or more first-degree relatives with aneurysmal SAH is controversial—although this population is at a substantially greater risk of harbouring AUIAs, the effectiveness of screening has not been studied and therefore remains unknown.[12] Treatment is not generally advocated in patients with small (<10 mm) asymptomatic intracranial aneurysms in patients without a personal history of SAH.[12]

The prospective, randomized International Subarachnoid Aneurysm Trial (ISAT)[13] showed that endovascular coiling of ruptured intracranial aneurysms was associated with improved outcomes when compared with surgical clipping (24% versus 31% morbidity or severe disability at 1 year). Although not as rigorously studied, coiling of unruptured intracranial aneurysms might improve short-term outcomes as well. In a recent nonrandomized retrospective study,[10] adverse outcomes at discharge following endovascular treatment of unruptured intracranial aneurysms were less frequent than those following surgical treatment (7% versus 13%), and in-hospital mortality rates were lower (0.9% versus 2.5%).

Because coiling is a relatively new technique, however, its long-term outcomes are not yet known. Questions remain about the durability of endovascular repair. For example, follow-up with the ISAT[13] study population has shown that retreatment occurs almost 7 times more frequently for coiled aneurysms than for clipped aneurysms.[14]

Case resolutions

Based on the evidence presented, the cases should be resolved as follows:

Case 1. Ms A. does not need to be screened for an intracranial aneurysm. Given the relatively high risks of treatment and the modest anticipated benefits, screening for AUIAs in patients with a single first-degree relative with a ruptured intracranial aneurysm is not generally recommended (level II evidence).

EDITOR'S KEY POINTS

- Brain imaging is being performed more frequently in Canada and, as a result, an increasing number of asymptomatic unruptured intracranial aneurysms (AUIAs) are being discovered. How should such AUIAs be managed?
- While ruptured intracranial aneurysms are devastating—half of patients die and up to half of those who survive are disabled—most intracranial aneurysms never rupture. Management decisions are currently made based on estimations of natural history versus expected treatment outcomes. Treatment-related risks are substantial, and there is currently insufficient evidence to support surgical or endovascular treatment of AUIAs in most cases.
- Should the natural history of a lesion be estimated to be sufficiently poor to justify the risks of intervention, some evidence suggests that endovascular coiling of unruptured intracranial aneurysms might improve outcomes compared with surgical clipping. Because coiling is a relatively new technique, however, its long-term outcomes are not yet known and questions remain about the durability of endovascular repair.

POINTS DE REPÈRE DU RÉDACTEUR

- Comme l'imagerie cérébrale est utilisée de plus en plus souvent au Canada, un nombre croissant d'anévrysmes intra-crâniens non rompus asymptomatiques (AINA) sont découverts. Comment doit-on traiter ces AINA?
- Alors que la rupture d'un anévrysme intracrânien est désastreuse—la moitié des patients meurent et plus de la moitié des survivants sont handicapés—la plupart de ces lésions ne se rompent jamais. À l'heure actuelle, la décision de traiter tient compte de l'évolution naturelle prévue de l'anévrysme par rapport aux résultats escomptés du traitement. Les traitements comportent des risques importants et il n'y a actuellement pas de preuves suffisantes pour justifier un traitement chirurgical ou endovasculaire dans la majorité des cas d'AINA.
- Pour les anévrysmes dont l'évolution naturelle est suffisamment inquiétante pour justifier le risque d'une intervention, certaines données suggèrent que l'insertion d'un coil dans un anévrysme intracrânien non rompu pourrait avoir une meilleure issue qu'un clampage chirurgical. Toutefois, comme l'insertion du coil est une technique relativement nouvelle, ses résultats à long terme ne sont pas encore connus, et on ignore toujours la durabilité de cette intervention.

Case 2. Ms B.'s aneurysm does not need to be treated. The risks of treatment might be greater than the risk of rupture for her small (≤5 mm) AUIA (level II evidence). Endovascular coiling or surgical clipping of larger aneurysms should be considered on a case-by-case basis. Consultation with an interventional neuroradiologist or neurosurgeon should be considered for patients with AUIAs larger than 5 mm (level III evidence).

Case 3. Ms C. might be correct that coiling is better than clipping. There is some evidence that short-term outcomes are better with coiling than with clipping (level II evidence), but whether or not long-term outcomes are similar has yet to be determined.

Conclusion

The optimal management of patients with AUIAs is controversial. There is currently a lack of good scientific evidence to support surgical or endovascular treatment of unruptured intracranial aneurysms.[15] Screening is therefore difficult to justify at the present time. In the absence of a randomized controlled trial of intervention versus observation, management decisions are currently made based on estimations of natural history versus expected treatment outcomes (**level III evidence**). A prospective randomized controlled trial (Trial on Endovascular Aneurysm Management, known as the TEAM study)[16] is now under way to address this issue. It is expected to conclude in 2021.

Levels of evidence

Level I: At least one properly conducted randomized controlled trial, systematic review, or meta-analysis
Level II: Other comparison trials, non-randomized, cohort, case-control, or epidemiologic studies, and preferably more than one study
Level III: Expert opinion or consensus statements

Dr Lysack is an Assistant Professor of Radiology and Clinical Neurosciences at the University of Calgary in Alberta and is a neuroradiologist based at the Foothills Medical Centre in Calgary. **Dr Coakley** is a family physician in Calgary, Alta.

Contributors
Drs Lysack and **Coakley** contributed to the concept of the article, the literature search, the review of selected articles, and preparing the manuscript for submission.

Competing interests
None declared

Correspondence
Dr John T. Lysack, Diagnostic Imaging, Foothills Medical Centre, 1403-29 St NW, Calgary AB T2N 2T9; e-mail **john.lysack@gmail.com**

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