

SPECIAL REPORT

ARISE I Consensus Review on the Management of Intracranial Aneurysms

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BACKGROUND: Intracranial aneurysms (IAs) remain a challenging neurological diagnosis associated with significant morbidity and mortality. There is a plethora of microsurgical and endovascular techniques for the treatment of both ruptured and unruptured aneurysms. There is no definitive consensus as to the best treatment option for this cerebrovascular pathology. The Aneurysm, Arteriovenous Malformation, and Chronic Subdural Hematoma Roundtable Discussion With Industry and Stroke Experts discussed best practices and the most promising approaches to improve the management of brain aneurysms.

METHODS: A group of experts from academia, industry, and federal regulators convened to discuss updated clinical trials, scientific research on preclinical system models, management options, screening and monitoring, and promising novel device technologies, aiming to improve the outcomes of patients with IA.

RESULTS: Aneurysm, Arteriovenous Malformation, and Chronic Subdural Hematoma Roundtable Discussion With Industry and Stroke Experts suggested the incorporation of artificial intelligence to capture sequential aneurysm growth, identify predictors of rupture, and predict the risk of rupture to guide treatment options. The consensus strongly recommended nationwide systemic data collection of unruptured IA radiographic images for the analysis and development of machine learning algorithms for rupture risk. The consensus supported centers of excellence for preclinical multicenter trials in areas such as genetics, cellular composition, and radiogenomics. Optical coherence tomography and magnetic resonance imaging contrast-enhanced 3T vessel wall imaging are promising technologies; however, more data are needed to define their role in IA management. Ruptured aneurysms are best managed at large volume centers, which should include comprehensive patient management with expertise in microsurgery, endovascular surgery, neurology, and neurocritical care.

CONCLUSIONS: Clinical and preclinical studies and scientific research on IA should engage high-volume centers and be conducted in multicenter collaborative efforts. The future of IA diagnosis and monitoring could be enhanced by the incorporation of artificial intelligence and national radiographic and biologic registries. A collaborative effort between academic centers, government regulators, and the device industry is paramount for the adequate management of IA and the advancement of the field.

Key Words: cerebral angiography ■ computed tomography angiography ■ intracranial aneurysm ■ stroke ■ subarachnoid hemorrhage

Intracranial aneurysms (IAs) are vascular abnormalities of the brain, which pose significant morbidity and mortality due to rupture or mass effect. Although unruptured IA (UIA) may have a low annual risk of rupture, the potentially devastating sequelae of subarachnoid

hemorrhage (SAH) underline the importance of appropriate diagnosis, management, and follow-up.¹ The estimates of UIA prevalence vary between 0.2% and 10% with higher incidence in females (relative risk [RR], 2.1 [95% CI, 1.1–3.9]), patients with autosomal polycystic

The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

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For Sources of Funding and Disclosures, see page 1435.

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Nonstandard Abbreviations and Acronyms	
ARISE	Aneurysm, Arteriovenous Malformation, and Chronic Subdural Hematoma Roundtable Discussion With Industry and Stroke Experts
aSAH	aneurysmal subarachnoid hemorrhage
CAM	Comprehensive Aneurysm Management
CTA	computed tomography angiography
FDA	Food and Drug Administration
GRS	genetic risk score
IA	intracranial aneurysm
ISAT	International Subarachnoid Aneurysm Trial
ISUIA	International Study of Unruptured Intracranial Aneurysms
MRA	magnetic resonance imaging angiography
OCT	optical coherence tomography
RR	relative risk
SAH	subarachnoid hemorrhage
STAT	Stent-Assisted Coiling in the Treatment of Unruptured Intracranial Aneurysms
UIA	unruptured intracranial aneurysm

kidney disease (RR, 4.4 [95% CI, 2.7–7.2]), familial predisposition (RR, 4.0 [95% CI, 2.7–6.0]), or atherosclerosis (RR, 2.3 [95% CI, 1.7–3.1]).² The Aneurysm, Arteriovenous Malformation, and Chronic Subdural Hematoma Roundtable Discussion With Industry and Stroke Experts (ARISE) comprised of academic, government, and industry cerebrovascular experts who convened to identify and address critical research issues pertaining to IA. This article presents consensus from the expert discussion and research presentations on the subject. This consensus does not cover a comprehensive management of IAs.

DIAGNOSIS OF IAS

The mainstay of the diagnosis of cerebral aneurysms is detection via a neuroimaging modality. Conventional diagnostic studies include noninvasive magnetic resonance imaging angiography (MRA), computed tomography angiography (CTA), and invasive catheter cerebral angiography. Initial noninvasive cross-sectional imaging includes noncontrast computed tomography, which will detect the presence of SAH, intraventricular hemorrhage, calcifications (such as in giant aneurysms), and local mass effect. Magnetic resonance imaging could provide additional diagnostic information, including associated cerebral edema surrounding the aneurysm (fluid-attenuated inversion recovery and T2 sequences), prior hemorrhage

(gradient-recalled echo, susceptibility-weighted imaging, or T2* sequence), and the detection of scant SAH.

Diagnostic cerebral angiography remains the gold standard in the diagnosis and management of IA. It provides a high spatial resolution of the angioarchitecture of the aneurysm, with a 3-dimensional reconstruction detailing a secondary excrescence (daughter sac), parent vessel anatomy, or dome irregularity. Furthermore, digital subtraction angiography offers a temporal resolution, therefore providing information on delayed aneurysm filling and wash-out, for example, with associated in-flow stenosis or a partially thrombosed aneurysm. Recent 4-dimensional rotational reconstruction (time-resolved 3-dimensional reconstruction) provides an additional temporospatial definition of neck and dome morphology with excellent resolution.³ Catheter cerebral angiography is a requirement for endovascular aneurysm treatment, as it allows the interventionalist to review and obtain optimal biplane angles in preparation for minimally invasive management. Although significant advancements have been made, cerebral angiography is still invasive and associated with some patient morbidity and mortality reported between 0.06% and 2.63%. However, this rate is potentially decreasing with advanced ultrasound-guided micropuncture techniques and radial access.⁴ In addition, especially in some patients with SAH, an initial digital subtraction angiography could be associated with a false negative result on initial angiography, requiring follow-up angiography for definitive diagnosis in 7% to 8% of patients.^{5,6}

MRA time of flight is a commonly used noninvasive imaging modality as the initial diagnostic method for IA. Its advantages include a lack of ionizing radiation or the need for intravenous contrast.⁷ However, disadvantages include limited availability, delayed acquisition time, low spatial resolution, lack of temporal resolution, metal screening requirement, and blood flow time of flight artifacts. An additional limitation is metallic (streak) artifact, which may impair visualization in areas of prior aneurysm clipping or intracranial stenting.

CTA is commonly used for the detection of IA, as it has higher sensitivity than MRA in the detection of IA, ranging from 96% to 98%.⁸ However, small and blister aneurysms may be missed, and a false positive result could be made, such as in the setting of an arterial infundibulum. Unlike MRA, its acquisition time is faster; however, it requires ionized radiation exposure, which could have cumulative side effects if repeated over time, and iodinated contrast, which could impair renal function or induce allergic reactions and anaphylaxis.⁹ Metallic implants pose a challenge for computed tomography imaging because of beam hardening artifact and blooming artifact. Bone artifact may also decrease its diagnostic accuracy in the vicinity of the skull base.

ARISE Consensus

Diagnostic catheter cerebral angiography remains the gold standard for the diagnosis of IA. The risk of diagnostic angiography should be weighed against its benefit for each individual patient. Noninvasive imaging, such as MRA and CTA, is a useful tool, however with limitations in sensitivity, as well as spatial and temporal resolution.

NEW DIAGNOSTIC MODALITIES FOR IA

Enhanced vessel wall imaging is a promising diagnostic technique, which may guide clinical decisions in aneurysm treatment and even follow-up. Contrast-enhanced high-resolution MRA may signal aneurysm instability and imminent rupture.¹⁰ In a meta-analysis of 12 studies and 1761 IAs, aneurysm wall enhancement was a predictor of rupture (prevalence ratio, 11.47 [95% CI, 4.05–32.46]) or interval growth (prevalence ratio, 4.62 [95% CI, 2.85–7.49]).¹⁰ Assessment of the performance of aneurysm wall enhancement showed high sensitivities, mixed specificities, low positive predictive values, and high negative predictive values. However, this diagnostic tool has a high sensitivity, but inconsistent specificity. Therefore, the absence of aneurysm wall enhancement is more important in establishing aneurysm stability, and its presence is still of uncertain diagnostic and clinical value, as it only provides a single snapshot of the aneurysm at that moment in time.⁶ In addition, its resolution for small cerebrovascular lesions is limited.

Intravascular vessel wall imaging is a promising new diagnostic technique that is gaining significant ground in its clinical applications for IA. Intravascular ultrasound and optical coherence tomography (OCT) may provide direct visualization of endovascular anatomy and aneurysmal intraluminal morphology.¹¹ OCT has a nearly 10× higher spatial resolution than intravascular ultrasound and a greater interobserver reliability.^{12,13} Thus far, OCT has multiple applications in cardiovascular and peripheral vascular interventional procedures, but the experience is limited in the cerebroendovascular domain. With the advent of improved OCT technology, including navigability and smaller diameter profiles (0.017-inch microcatheter delivery), there are increasing applications for cerebrovascular pathologies.⁶ Although the data are sparse, there is increasing evidence of OCT use in endovascular IA. It may provide critical information on stent vessel wall apposition, patency of perforators, presence of intraluminal thrombus, dissection and neointimal flaps, and aneurysm neck patency. Currently, there is no major neuroendovascular clinical trial data available, and commercial use is limited by a lack of Food and Drug Administration (FDA) approval.

ARISE Consensus

Promising new technology, such as vessel wall and intravascular imaging, may be useful in the assessment

and management of IA. However, large clinical trials are required before their widespread clinical.

SCREENING AND MONITORING

Preventive screening for IA might provide early life-saving measures and prevent potential future SAH. However, the overall low incidence of IA makes general population screening studies unlikely due to the large number of patients, which would be required to reach statistical significance. Therefore, attention has been given to established high-risk patient groups.

Familial IA syndrome is defined as the presence of ≥2 first-degree relatives affected by the aneurysmal rupture and carries up to a 20% lifelong risk of SAH.¹⁴ Furthermore, screening in this patient population may have a positive yield of 4% to 11%.¹⁵ Furthermore, additional risk factors, such as smoking, may increase the likelihood of positive screening. Follow-up screening for patients with familial intracranial aneurysm is recommended every 5 years. People with a single first-degree relative of SAH should be considered for screening, as they carry a 3% to 4% lifetime risk of aneurysm rupture.¹⁶ There is no solid evidence to recommend screening in patients with relatives harboring UIA, and if this incidence is sporadic, then the recommendation is to not screen, unless there are other associated high-risk clinical features, including severe headaches, uncontrolled hypertension, and smoking.

Adult dominant polycystic kidney disease is an autosomal dominant genetic disorder with a higher incidence of cerebral aneurysms and SAH. In a large systematic review and meta-analysis of 1490 patients with autosomal dominant polycystic kidney disease, the approximate incidence of IA was noted to be ≈10%.¹⁷ Thus, an initial screening for these patients is recommended and cost-effective, followed by surveillance monitoring every 5 years.¹⁸

Additional conditions associated with IA include rare disorders, such as vascular Ehlers-Danlos syndrome, Marfan syndrome, and Loeys-Dietz syndrome, in addition to other more frequent connective tissue disorders, such as fibromuscular dysplasia. Due to the low incidence of these pathologies, strong clinical evidence for screening is lacking. Therefore, decision-making should be individualized considering every patient's clinical profile. International consortia have suggested initial screening for patients with fibromuscular dysplasia, type IV Ehlers-Danlos syndrome, and Loeys-Dietz syndrome.¹⁴

According to the 2015 guidelines for the management of patients with a UIA published by the American Heart Association/American Stroke Association MRA or CTA is recommended for the noninvasive management of UIA at regular intervals; however, the optimal interval and duration of follow-up remains uncertain (class I; level of evidence B).¹⁹ A first follow-up at 6- to 12-month intervals from initial diagnosis followed by yearly or every

other year surveillance may be reasonable (class IIb; level of evidence C).

Early results on machine learning algorithms allowed the development of convolutional neural networks to detect and analyze IAs on CTA with a 93.8% sensitivity (95% CI, 0.87–0.98), 94.2% specificity (95% CI, 0.90–0.97), and a positive predictive value of 88.2% (95% CI, 0.80–0.94).²⁰ A large multicenter Chinese study utilizing machine learning–based prediction of small aneurysm rupture status based on CTA hemodynamics found that concentrated in-flow streams, a small (<50%) flow-impingement zone, and the oscillatory shear index coefficient of variation were the best predictors of aneurysm rupture.²¹ Specifically, aneurysm stability and changes over time could be assessed, providing an early indication of an evolving rupture risk factor.

ARISE Consensus

There is a lack of strong evidence and therefore consensus on optimal screening protocol for patients with IA. Patients in high-risk categories, such as adult dominant polycystic kidney disease, family history of IA, and specific connective tissue disorders, should be strongly considered for initial screening and follow-up. Similarly, there is a lack of strong evidence for the appropriate frequency or modality of follow-up monitoring of IA. Collection of large multicenter data may be helpful in the implementation of artificial intelligence and machine learning algorithms to screen, monitor IA at a prerule stage, and predict the risk of rupture to guide treatment options. In all, the ARISE group supports to follow screening recommendations for high-risk patients, such as familial intracranial aneurysm syndrome, adult dominant polycystic kidney disease, and selective connective tissue disorders. It is also essential to note that artificial intelligence may be incorporated to help physicians with screening and detection but should not replace physician training in diagnosing and recognizing IAs in imaging studies.

IA TREATMENT

Unruptured IAs

Natural History

The decision to treat UIAs is complex and requires careful evaluation of radiographic and clinical findings in each patient. The ISUIA (International Study of Unruptured Intracranial Aneurysms) was provided with guidelines for the management of UIA, including aneurysm size, location, and history of SAH.^{18,22} The rupture rate for anterior circulation aneurysms <7 mm was 0% per year in patients with no prior SAH and 0.3% per year in patients with previous SAH; 7- to 12-mm aneurysms, 0.5% per year; 13- to 24-mm aneurysms, 3% per year; and giant aneurysms, 8% per year. The rupture rate for posterior circulation aneurysms

is higher at all sizes: <7 mm was 0.5% per year in subjects with no prior SAH, 0.7% in those with prior SAH; 7 to 12 mm, 3% per year; 13 to 24 mm, 3.7% per year; and giant aneurysms, 10% per year.^{1,23} Subsequently, the natural course of unruptured aneurysms was investigated in a large Japanese cohort in the UCAS study (Unruptured Cerebral Aneurysm Study).²⁴ Of the 6997 aneurysms studied, 91% were incidental and asymptomatic, mainly in the carotid circulation (36% middle cerebral and 34% internal carotid arteries). Like ISUIA, the risk of rupture increased with aneurysm size. Specifically, the rupture risk with reference to a 3- to 4-mm aneurysm was 5 to 6 mm, 1.13 (95% CI, 0.58–2.22); 7 to 9 mm, 3.35 (95% CI, 1.87–6.00); 10 to 24 mm, 9.09 (95% CI, 5.25–15.74); and ≥25 mm, 76.26 (95% CI, 32.76–177.54). Also, both studies showed that posterior circulation aneurysms have a higher risk of rupture (hazard ratio, 1.90 [95% CI, 1.12–3.21]). UCAS also added anterior communicating artery aneurysms in the high rupture risk group with a hazard ratio of 2.02 (95% CI, 1.13–3.58).

Scoring Systems

Several UIA scoring systems have been proposed as a means of facilitating the clinical decision for treatment. In 2013, the PHASES score pooled data from 6 prospective cohort studies to analyze predictors of IA aneurysm rupture.²⁵ In 29 166 patient-years of follow-up, the mean annual risk of rupture was 1.4%, and the cumulative 5-year rupture risk was 3.4%. Predictors of SAH included age, hypertension, history of SAH, aneurysm size, aneurysm location, and geographic region (Finnish and Japanese highest risks). A criticism of the PHASES score includes the overselection of high-risk patient populations (Japanese), therefore increasing their calculated rupture risk. An international multidisciplinary investigation (Neurosurgery, Neuroradiology, Neurology Clinical Epidemiology) of 69 specialists reached a consensus in the development of a grading score to aid in the UIA treatment decision process, Unruptured Intracranial Aneurysms Treatment Score.²⁶ The score incorporates 29 key factors, including age, risk factors (smoking, hypertension, prior SAH, and adult dominant polycystic kidney disease), life expectancy, aneurysm location, morphology, and treatment risk. Although it was not a predictive model, it attempted to create international guidelines and consensus from the variability noted in aneurysm treatment clinical decisions.

ARISE Consensus

Understanding the natural history and rupture risk for UIA is complex and involves a thorough consideration of patient-specific factors (age, sex, family history, comorbidities, smoking, and symptoms) and aneurysm factors (size, location, and morphology). Therefore, combined with poor data on the true natural history of UIA, current practices may include treatment decisions for lower

risk aneurysms in terms of size and location. The group strongly recommends consideration of a new UIA scoring system, with respect to detection of medical risk factors and radiographic characteristics/changes. The group is looking forward to the results of the CAM trial (Comprehensive Aneurysm Management) proposed by Darsaut et al²⁷ in 2020, which aims to identify the optimal management of patients with UIA through randomization to conservative versus curative treatment. With 403 patients included up till July 2021, the trial was able to randomize patients with UIA into subgroups of conservative versus endovascular management, conservative versus surgical management, and surgical versus endovascular management.²⁸ As the trial is underway, the group recommends individualized decision-making for the treatment of UIA, with consideration of current aneurysm data and incorporation of physician discretion based on clinical and radiographic criteria.

SURGICAL TREATMENT MODALITIES

Microsurgery

Microsurgical clipping ligation is a durable UIA therapy that remains an effective treatment option. In ISUIA, the overall rate of surgery-related morbidity and mortality was 17.5% in group 1 and 13.6% in group 2 at 30 days and 15.7% and 13.1%, respectively, at 1 year; age was the independently predicted surgical outcome.²² Most studies reporting the morbidity and mortality of surgical clipping are single-center retrospective reviews. Most recently, Darsaut et al²⁹ performed a pragmatic randomized trial comparing UIA clipping ligation to endovascular treatment in 7 centers over 10 years. Morbidity and mortality (modified Rankin Scale score ≥ 2) at 1 year occurred in 3/143 and 3/148 (2% [95% CI, 1%–6%]) patients allocated to surgery and endovascular treatments, respectively. Neurological deficits (RR, 1.74 [95% CI, 1.04–2.92]; $P=0.04$) and hospitalizations beyond 5 days (RR, 0.18 [95% CI, 0.11–0.31]; $P<0.001$) were more frequent after surgery. However, there are several large systematic reviews and meta-analyses that investigate the overall surgical risk in UIA. In 2011, a review of 9845 patients from 60 studies reported an overall mortality rate of 1.7%, a morbidity rate of 5%, and an unfavorable outcome estimate of 6.7% up to 1 year after surgery.³⁰ In 2019, Algra et al's systemic review and meta-analysis of 114 studies reported a complication risk of 4.9% and a case-fatality risk of 0.3%.³¹

However, microsurgical techniques have evolved over the years, with improvement in microsurgical instruments, intraoperative diagnostic tools (catheter angiography, indocyanine-green, Doppler, ultrasound, and flow cytometry), and avoidance of fixed brain retractors causing cerebral contusions. A decisive factor in good surgical outcomes has been associated with high-volume centers

for the treatment of UIA. In a review of 3498 patients in 463 hospitals, the overall reported mortality was 2.1%.³² High-volume centers (>20 case volume per year) had a discharge destination other than home 15.6%, as opposed to low-volume centers (<4 case volume per year) 23.8%. Mortality was equally lower at high-volume hospitals (1.6% versus 2.2%), as well as neurological complications ($P=0.04$). Therefore, high-volume centers were associated with significantly lower morbidity and moderately lower mortality in the treatment of UIA.

ARISE Consensus

Microsurgery comprises a mainstay treatment for UIA. Multicenter prospective studies that are focused on microsurgical clipping of UIA could provide insight into contemporary safety and efficacy rates. Careful patient selection based on aneurysm location and patient characteristics is critical for safety and efficacy. Surgical clipping in high-volume centers (>20) offering a multidisciplinary team contributes to optimal patient outcomes.

ENDOVASCULAR

Guglielmi detachable coils were initially approved by the FDA in 1995.³³ Since then, advancements in endovascular technology have increased treatment options and improved outcomes of patients with IA. Initial coil architecture improvement, with complex and 3-dimensional shapes, was followed by adjunctive devices to facilitate coiling, such as balloons and stents. Large systematic reviews and meta-analyses, such as by Phan et al,³⁴ showed that stent-assisted coiling reached immediate aneurysm occlusion in 57.7% of 2698 patients, as opposed to coiling alone 48.7% in 28 388 patients. The occlusion was progressive, and future aneurysm thrombosis occurred in an additional 29.9% of patients. Furthermore, recurrence was significantly lower in stent-assisted coiling (12.7%) compared with coiling-only (27.9%; odds ratio, 0.43 [95% CI, 0.28–0.66]).^{35–37} However, according to the STAT trial (Stent-Assisted Coiling in the Treatment of Unruptured Intracranial Aneurysms), stent-assisted coiling was not superior to coiling alone in terms of functional and angiographic outcomes when used in the treatment of large, wide-neck, or recurrent unruptured aneurysms.³⁸ Balloon-assisted coiling has similar results with complete occlusion rates at the end of the treatment comparable to stent-assisted coiling in a large systematic review and meta-analysis by Wang et al.^{39–42} Stented patients had higher progressive aneurysm occlusion at 6-month follow-up (odds ratio, 1.82 [95% CI, 1.21–2.74]) compared with balloon patients.

An equally defining innovation for the endovascular IA treatment was flow diversion.⁴³ The Conformite Europeenne approval of the SILK flow diverter

(Balt, Montmorency, France) in 2007 and the FDA approval of the Pipeline embolization device (eV3 Neurovascular, Irvine, CA) in 2011 was a significant development in minimally invasive treatment of giant and large complex IA, especially in the paraclinoid internal carotid artery region. Since then, a plethora of flow diversion devices have been developed, and several prospective multicenter trials reported on their safety and efficacy. In a 2023 systematic review and meta-analysis of UIA treated with flow diversion stents, the cumulative aneurysm occlusion was progressive over the years, at 77%, 87.4%, 84.5%, 89.4%, and 96% for 1-, 1- to 2-, 2-, 3-, and 5-year follow-ups, respectively.⁴⁴ These devices require dual-antiplatelet medical therapy during the endothelialization process, which averages 6 months after placement. There is wide variation in clinical practice with respect to the type of dual-antiplatelet agent (aspirin, 81 versus 325 mg; clopidogrel, 75 mg; ticagrelor, 60 versus 90 mg bid; and prasugrel, 5 mg), loading strategy, testing (platelet function test), and posttreatment dose modification. A systematic review and meta-analysis in 2017 showed that despite the clinical practice variability, there was no statistically demonstrable difference in thrombotic events between centers that conducted at least 1 platelet function test and centers that did not test their patients with a platelet function test.⁴⁵ In a systematic review of 2526 patients in 49 studies, the use of ticagrelor or prasugrel was associated with a lower risk of mortality compared with clopidogrel (RR, 4.57 [95% CI, 1.23–16.99]; $P=0.02$) with comparable hemorrhagic complications (RR, 0.92 [95% CI, 0.27–3.16]; $P=0.89$).⁴⁵ Recently, surface modification of flow diversion stents became available to facilitate the endothelialization process and improve aneurysm wall reconstruction.⁴⁶ This surface enhancement with antithrombogenic material is engineered to facilitate device deployment and decrease ischemic complications.⁴⁷ In a systematic review and meta-analysis of 911 patients and 1050 aneurysms treated with surface-modified flow diversion, 6- and 12-month aneurysm occlusions were reported at 80.5% and 85.6%, respectively. Pooled estimates for mortality, morbidity, total ischemia, and serious ischemia rates were 0.7%, 6.0%, 6.7%, and 1.8%, respectively.

A more recent technological advancement that has contributed to the treatment of wide-neck bifurcation aneurysms is the endosaccular device (WEB; Microvention FDA approval 2017). The WEB-IT trial (Woven EndoBridge Intracapsular Therapy) reported 12-month device safety and efficacy in 148 patients with 53.8% complete aneurysm occlusion, 84.6% adequate occlusion, and 0.7% adverse events.⁴⁸ The long-term outcomes were recently updated in 2 large European combined trial populations (WEBCAST [Woven EndoBridge Clinical Assessment of Intracapsular Aneurysm Therapy] and WEBCAST-2) in 100 patients, with 1% procedure-related mortality, complete aneurysm occlusion in 51.6%, neck remnant in

26.3%, and aneurysm remnant in 22.1%.⁴⁹ The retreatment rate at 5 years was 11.6% (11/95 aneurysms). These data supported the stability of aneurysm occlusion with 77.9% 5-year-adequate aneurysm occlusion and a retreatment rate of 11.6%. New generation flow diversion and endosaccular devices are constantly being investigated (Contour by Cerus, Trezza by Styker, Nautilus by Endostream Medical, and Lattice by Galaxy, Inc), and this promising field of endovascular aneurysm treatment is ever-evolving with improving radiographic and patient outcomes. One of the most recent advancements is a bioabsorbable flow diverter. The goal of bioabsorbable flow diverters is that these devices occlude the aneurysm, heal the parent artery, and are harmlessly resorbed by the body.⁵⁰ Potential advantages of bioabsorbable flow diverters are reducing the risk of chronic device-induced thrombogenesis, minimizing the chronic inflammation that leads to in-stent stenosis via neointimal hyperplasia, reducing the risk of late side-branch occlusion, restoring physiological contraction and relaxation of micro arteries, and diminishing imaging artifacts.⁵⁰

ARISE Consensus

The endovascular treatment of UIA is an established modality with constantly improving technologies and, therefore, a better safety and efficacy profile. The group recommends new device development to involve physician leaders along with industry and an emphasis on outcome safety. Large postmarket device registries facilitate continued evaluation of device safety and efficacy. The group failed to reach a consensus on the type, duration, and testing of dual-antiplatelet medical therapy in conjunction with flow diversion. Practitioners should use institutional protocols for the best individualized outcomes. The group was in full support and recommended patient education in terms of compliance with the recommended antiplatelet regimen to prevent ischemic events. Bioabsorbable stents are a promising new technology and, however, require long-term safety data, as their absorption introduces them to systemic circulation. To improve future endovascular device investigation due to the lack of randomized control trials comparing devices or assessing the feasibility, safety profile, and efficacy of these new technologies, the group suggested the consideration of multilateral regulation and collaboration with international regulatory agencies, for example, between the FDA, European Medicines Agency, Medical and Healthcare Products Regulatory Agency, and other organizations, in large international clinical trials.

Overall ARISE Consensus

The treatment modality for UIA should be individualized based on a thorough review of the patient's physiological age, comorbidities, aneurysm location, and

angioarchitecture. Careful patient selection for surgical clipping or endovascular treatment should occur in a multidisciplinary high-volume environment with expertise in both treatment options to ensure optimal patient outcomes.

RUPTURED IAS

Aneurysmal SAH (aSAH) remains a significant threat to public health with a nationwide incidence of 6.1 per 100 000 and in-patient mortality rates of in-patient mortality rates 13.7% in 2006 to 13.1% in 2018 (in the United States).⁵¹ Globally, in-hospital aneurysmal aSAH mortality rates are ≈20%.⁵² The American Heart Association/American Stroke Association 2023 SAH management guidelines recommend a prompt evaluation to prevent rerupture with associated poor outcomes and utilization of patient clinical scales, such as the World Federation of Neurosurgical Society grade and the Hunt and Hess grade. Furthermore, the document strongly emphasizes the importance of a multidisciplinary approach for the management of aSAH by recommending a timely transfer from hospitals with low case volume (eg, <10 aSAH cases per year) to higher volume centers (eg, >35 aSAH cases per year) for treatment by experienced cerebrovascular surgeons, neuroendovascular interventionalists, and multidisciplinary neurointensive care services. The coordinated medical management of these critical patients should involve experienced physicians in Neurological Intensive Care Units, with blood pressure monitoring/control with avoidance of blood pressure fluctuation, severe variability, and emergent reversal of anticoagulant usage. The surgical or endovascular treatment of the ruptured aneurysm should be performed as early as feasible following presentation to improve the outcome, preferably within 24 hours of ictus. In 2002, the ISAT (International Subarachnoid Aneurysm Trial) compared outcomes of 2143 patients with ruptured aneurysms randomized into endovascular coiling and clipping treatment and demonstrated that when both modalities are therapeutic, endovascular coiling provides significantly higher rates of survival free of disability at 1 year of follow-up.⁵³ Thus, although the goal of treatment is complete aneurysm occlusion, it needs to be balanced against the risks of the procedure. Careful patient selection for endovascular or microsurgical management and individualized recommendations should be made based on the assessment of patient age and clinical severity, aneurysm geometry and location, and the presence of intraparenchymal hemorrhage.

ARISE Consensus

The group agrees that high-volume centers are recommended for the treatment of ruptured IA; however, defining centers of excellence for aSAH is challenging based on reimbursement trends and a lack of systematic certification for hemorrhagic stroke (unlike ischemic stroke).

The group strongly encourages federal and private funding to support the development of a distinct hemorrhagic network platform, like its ischemic counterpart, National Institutes of Health StrokeNet. The group recommends continued collaboration for the development of organized advocacy groups for patients with IA. Some examples of advocacy groups are, but are not limited to, the Brain Aneurysm Foundation and the Bee Foundation whose work in funding aneurysm research and increasing public awareness about symptomology, risk factors, and the importance of screening has bridged the gap between aneurysm detection and catastrophic consequences. It reached a consensus in identifying the need to redefine patient outcomes to include neurocognitive, neuropsychological (eg, depression), and return-to-work criteria.

FUTURE RESEARCH

One of the fastest evolving branches of medicine is radiogenomics, which refers to the linking of imaging phenotypes to a genetic profile. Though the field is rapidly advancing in areas such as neuro-oncology, the literature on IA is scant.⁵⁴ A recent review on the genetics of IA reported 19 different loci commonly observed in patients including 2q33.1, 4q31.22, 5q31.1, 6q16.1, 7p21.1, 8q11.23, 9p21.3, 10q23.33, 10q24.33, 11p15.5, 12p12.2, 12q21.33, 12q22, 13q13.1, 15q25.1, 16q23.1, 18q11.2, 20p11.23, and 22q12.2.⁵⁵ Recent advancements in biogenetics have allowed the correlation of these loci to specific genes utilizing expressive quantitative trait loci data, and analysis led to the identification of 11 potential causative genes: SLC22A5, SLC22A4, P4HA2, SOX17, NT5C2, MARCKSL1P1, FGD6, NR2C1, PSMA4, BCAR1, and RP11-252K23.2. The continued evolution of biogenetic analysis of IA and translational applications to risk prediction via genetic risk scores, the discovery of causal risk factors utilizing genetic data, and the development of therapeutic targets by linking to drug bioactivity data could prevent the incidence of aSAH and improve outcomes in patients with IA.

ARISE Consensus

The overall low incidence of IA demands the support of centers of excellence in brain aneurysms for preclinical multicenter trials in areas such as genetics and cellular composition. Radiogenomics and somatic mutation research require large patient population samples and extensive data collection and processing. Utilization of existing National Institutes of Health–funding venues, such as the Clinical and Translational Science Awards program to obtain samples from nationwide centers coupled with the development of artificial intelligence algorithms, may facilitate such a daunting task. An exciting new research area that requires funding support and development includes endovascular biopsy (via stent

retrievers or microcatheter blood samples), which may shed light on the molecular and endothelial mechanisms of aneurysm development, growth, and rupture.

ARTICLE INFORMATION

Received October 24, 2023; final revision received March 15, 2024; accepted March 19, 2024.

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Sources of Funding

None.

Disclosures

Dr Tjoumakaris reports compensation from Medtronic for consultant services, MicroVention, Inc, for consultant services, and MicroVention, Inc, for consultant services. Dr Hanel reports compensation from Cerenovus for consultant services; stock holdings in eLum and BlinkTBI; compensation from Medtronic for consultant services; stock holdings in Endostream; compensation from Stryker for consultant services; stock holdings in Scientia, Cerebrotech, and Rist; compensation from MicroVention, Inc, for consultant services; compensation from Balt USA, LLC, for consultant services; stock holdings in Corindus, Inc, InNeuroCo, NTL, and Three Rivers Medical, Inc; and compensation from phenox, Inc, Q'Apel, and Rapid Medical Ltd for consultant services. Dr Mocco reports compensation from CVAid for consultant services; stock options in Tulavi; compensation from Penumbra, Inc, for other services; stock holdings in Q'Apel, Spinaker, Endostream, Sim&Cure, and Cerebrotech; compensation from Perflow for consultant services; stock options in Songbird, NRT, and Borvo; grants from PCORI; stock options in E8; employment by Mount Sinai Health System; stock holdings in Imperative Care, Inc; compensation from CVAid and RIST for consultant services; stock holdings in Viseon, Inc, Radical, Vastrax, and Neuroolutions; compensation from Synchron for consultant services; stock options in Spinaker; compensation from MicroVention, Inc, for other services; stock holdings in Blinktbi, Echovate, NTL Managers, and Vizai; and compensation from Stryker for other services. Dr Ali-Aziz Sultan reports compensation from MicroVention, Inc, for other services. Dr Froehler reports compensation from OCULUS, Inc, Cerenovus, and Siemens for consultant services; grants from Genentech, Inc; grants from Siemens; and compensation from Balt USA, LLC, for consultant services. Dr Lieber reports stock holdings in Prometheus Therapeutics, Inc. Dr Coon reports compensation from Medtronic, Inc, Imperative Care, Inc, MicroVention, Inc, Rapid Medical Ltd, Stryker Corporation, and Johnson and Johnson for consultant services. Dr Tateshima reports compensation from Rapid Medical Ltd, Medtronic, phenox, Inc, Cerenovus, MicroVention, Inc, and Stryker for consultant services. Dr Altschul reports securities holdings in Von Vascular, Inc, and compensation from Johnson and Johnson International, Stryker Corporation, Medtronic USA, Inc, and MicroVention, Inc, for consultant services. Dr Narayanan reports compensation from MicroVention, Inc, Johnson & Johnson Health Care Systems, Inc, and Imperative Care, Inc, for consultant services. Dr Taussky reports compensation from Medtronic for consultant services; compensation from phenox, Inc, for data and safety monitoring services; and compensation from Johnson & Johnson Health Care Systems, Inc, for consultant services. Dr Hoh reports stock options in Progressive Neuro; compensation from AstraZeneca for other services; stock op-

tions in Galaxy Therapeutics; grants from the National Institutes of Health; compensation from Janssen Pharmaceuticals for other services; employment by the College of Medicine, University of Florida; grants from the Brain Aneurysm Foundation; and stock options in Proprio Vision. Dr Gounis reports compensation from Wallaby Medical, Imperative Care, Inc, and Mivi Neurosciences for consultant services; stock holdings in Galaxy Therapeutics; compensation from Medtronic Neurovascular for consultant services; stock holdings in InNeuroCo, LLC; compensation from Q'Apel Medical, phenox, Inc, Cerenovus, Route 92 Medical, Inc, Alembic, LLC, and Stryker Corporation for consultant services; and stock holdings in Imperative Care, Inc, and Synchron. Dr Liebeskind reports compensation from Stryker, Medtronic, Rapid Medical Ltd, Cerenovus, and Genentech for consultant services. Dr Volovic reports employment by Erasmus Medisch Centrum and compensation from JAMA for consultant services. Dr Toth reports compensation from Medtronic USA, Inc, for other services and compensation from EBSCO and Penumbra, Inc, for consultant services. Dr Arthur reports compensation from Balt USA, LLC, Penumbra, Inc, MicroVention, Inc, Johnson and Johnson International, Siemens Medical Solutions USA, Inc, Stryker Corporation, Perfuzo, Scientia, and Medtronic USA, Inc, for consultant services. Dr Wakhloo reports compensation from Stryker Corporation for consultant services, an ownership stake in Deinde Medical, compensation from Acotec for consultant services, an ownership stake in Prometheus Therapeutics, grants from Philips, an ownership stake in Neurofine, and compensation from Cerenovus Johnson & Johnson for consultant services. The other authors report no conflicts.

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