Review

Long-term neuropsychiatric complications of aneurysmal subarachnoid hemorrhage: a narrative review

Jose Danilo Bengzon Diestro ,[1,2] Manav Vyas,[1,2] Youngkyung Jung,[3] Teruko Kishibe,[2,4] Carl Leochico,[1,5,6,7] Adrian Espiritu,[1,5,8,9] Maria Kristina Dorotan,[10] Nico Dimal,[1] Abdelsimar Tan Omar,[11] April Sienes,[12] Gustavo Saposnik,[1,2] Thomas R Marotta,[13] Atif Zafar,[1] Vitor Mendes Pereira ,[3] Julian Spears[3]

For numbered affiliations see end of article.

Correspondence to
Dr Jose Danilo Bengzon Diestro, Department of Medicine, University of Toronto, Toronto, Canada; danni.diestro@gmail.com

Received 13 February 2024
Accepted 31 March 2024

Listen to Podcast
jnis.bmj.com

ABSTRACT

This review focuses on the often-neglected long-term neuropsychiatric consequences of aneurysmal subarachnoid hemorrhage (aSAH), beyond traditional randomized trial outcomes of mortality and retreatment. While current guidelines recommend screening for these sequalae, it may not be routinely practiced. This review will underscore the prevalence and management of common neuropsychiatric sequalae, including anxiety, depression, cognitive dysfunction, headaches, seizures, and sexual dysfunction, all of which can significantly impact the quality of life of survivors of aSAH. We emphasize the critical role neurointerventionalists can play by going beyond the customary practice of radiological monitoring for treated aneurysms by screening for and helping guide management of these common neuropsychiatric complications.

BACKGROUND

Randomized trials examining the consequences of aneurysmal subarachnoid hemorrhage (aSAH) primarily concentrate on conventional outcomes, such as mortality, aneurysm recurrence, and aneurysm retreatment.[1 2] While there is available data on functional outcomes assessed through the modified Rankin Scale (mRS), there is a paucity of studies dedicated to investigating long-term neuropsychiatric consequences, including anxiety, depression, epilepsy, chronic headaches, cognitive dysfunction, and sexual dysfunction. These outcomes can significantly impact patients' quality of life, even among those perceived to have favorable functional outcomes based on the mRS.[3 4]

Guidelines from the American Heart Association (AHA) recommend screening for these outcomes at discharge and during follow-up visits to facilitate timely intervention.[5] As healthcare providers who routinely monitor treated aneurysms throughout patients' lifetimes, neurointerventionalists are well-situated to observe the progression and impact of these complications on patients' quality of life. Our review aims to primarily elucidate the prevalence and management approaches for these long-term outcomes, offering practical screening tools suitable for the neurointerventional clinic setting. By doing so, we expect to enhance the long-term neuropsychiatric care of survivors of aSAH.

METHOD/SEARCH STRATEGY

An information specialist (TK) worked with the lead author (JDBD) to develop the search strategy. We conducted the search on Medline (Ovid), Embase (Ovid), the Cochrane Central Register of Controlled Trials (Ovid), and Scopus (Elsevier). Keywords and Medical Subject Heading (MeSH) terms related to our research question were used. The search terms used included the combinations and truncations of the following: subarachnoid hemorrhage, mood disorders, depression, anxiety, seizure, epilepsy, convulsion, sexual dysfunction, dyspareunia, erectile dysfunction, impotence, vaginismus, premature ejaculation, cognition, mental fatigue, brain fog, neuropsychiatric, headache, cephalgia, and migraine. The full search strategy according to each database is available from the authors upon reasonable request.

Each outcome was addressed using a tailored search strategy for prevalence, and a separate distinct search strategy for questionnaires was employed across all outcomes. The results were then integrated into Covidence, an online systematic review tool aimed at enhancing collaboration and streamlining literature review processes. Lead authors (YJ, CL, AE, MKD, ND) were assigned to specific topics and provided access to a curated list of potential publications within their respective subtopics. Collaborating with the primary author (JDBD), they assessed the relevance and significance of these publications for inclusion in the review. Relevant articles were additionally manually searched to identify further pertinent literature.

Ethics

The study did not require ethics approval as it does not involve any patient data.

Anxiety and depression

Symptoms of depression and anxiety are relatively common in patients with intracranial aneurysms. Multiple evidence synthesis studies indicate that approximately three out of ten individuals who survived aSAH may develop symptoms of

To cite: Diestro JDB, Vyas M, Jung Y, *et al*. *J NeuroIntervent Surg* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/jnis-2023-020979

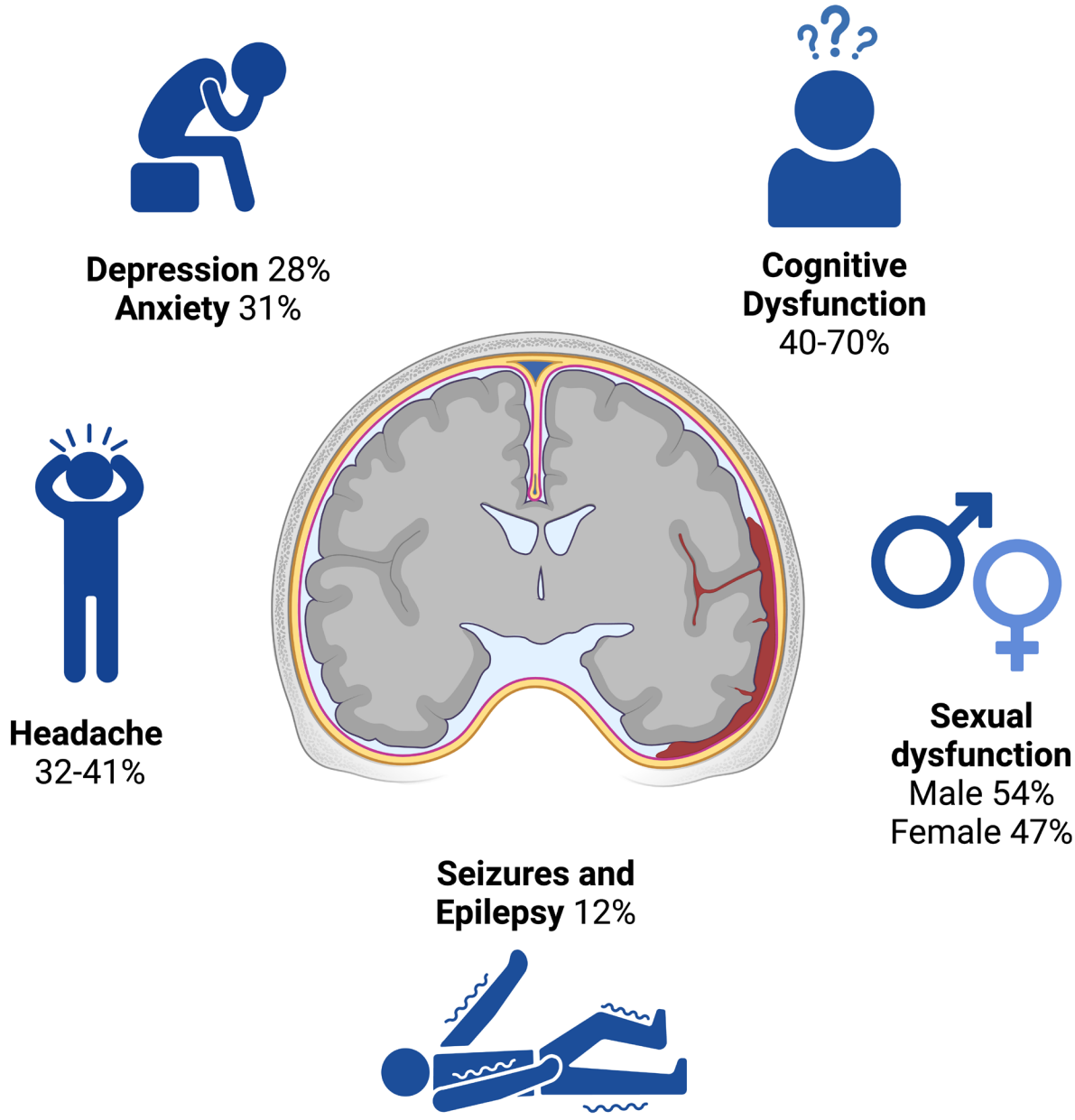

Figure 1 Summary of prevalence of long-term neuropsychiatric complications following aneurysmal subarachnoid hemorrhage (figure created with BioRender.com).

depression and anxiety (figure 1).[6 7] Depression and anxiety symptoms associated with aSAH may have a substantial effect on patients' lives. Systematic reviews revealed a negative association between depression/anxiety and health-related quality of life, and the presence of depression may also predict poorer quality of life in aSAH survivors.[6 7] Depression was also found to be a significant predictor of unemployment.[8] Depression after aSAH was found to be more common among females, those with premorbid depression or psychiatric illness, and those with substance use disorder. Further, having cognitive symptoms, fatigue, and higher physical disability also increases the risk of having depression after SAH.[9]

The 2023 American Heart Association (AHA)/American Stroke Association (ASA) guideline indicates that patients with aSAH with depression are recommended to undergo psychotherapy and drug therapy.[5] Potential treatments for these symptoms were derived from therapies used for people with mental health conditions and from data on stroke survivors. Selective serotonin reuptake inhibitors (SSRIs) have been considered first-line therapy for major depressive and anxiety disorders.[10] Among the SSRIs, fluoxetine has been recommended based on several randomized controlled trials (RCTs) in stroke patients.[5] Furthermore, a recent 2023 Cochrane Living Systematic Review involving 65 trials on patients with stroke (n=5831) indicated

significant reductions in reducing the prevalence of depression when they compared pharmacological therapies (SSRIs and other antidepressants) versus placebo (relative risk (RR) 0.70; 95% CI 0.55 to 0.88; 8 RCTs; n=1025), psychological (cognitive–behavioral therapy and others) versus usual care/attention control (RR 0.77; 95% CI 0.62 to 0.95; 6 trials; n=521), and the combination of non-invasive brain stimulation (transcranial magnetic stimulation) with pharmacological intervention versus pharmacological therapy only (RR 0.77; 95% CI 0.64 to 0.91; 3 RCTs; n=392).[11]

While improving outcomes in aSAH requires effective therapies for these psychiatric conditions, a prerequisite to this is the accurate identification of SAH survivors with anxiety and depressive disorders. A recent systematic review identified the nine most common depression and screening instruments used in patients with aSAH.[12] These instruments include the Beck Depression Inventory-II (BDI-II), Hospital Anxiety and Depression Scale (HADS), Center for Epidemiologic Studies Depression Scale (CESDS), Zung Self-Rating Depression Scale, Geriatric Depression Scale, Montgomery–Asberg Depression Rating Scale (MADRS), Patient Health Questionnaire-9 (PHQ-9), EQ-5D Anxiety/Depression, and Stroke Specific Quality of Life. HADS has been validated for post-stroke patients and found to have a sensitivity of 86.8% and a specificity of 69.9% with a total cut-off score of 11.[13] However, none of these tools have been validated for individuals with aSAH.[12] Conducting further studies is essential to verify the validity of these screening techniques for aSAH.

Cognitive dysfunction

Cognitive impairment is a major sequela of aSAH seen in 40–70% of survivors and has been associated with more reduced quality of life measures (figure 1).[14] It falls under the term post-stroke cognitive impairment, which refers to cognitive decline occurring 3 to 6 months after a stroke.[15] Known risk factors for subsequent cognitive dysfunction following aSAH include acute hydrocephalus requiring cerebrospinal fluid diversion, seizures, fever, prolonged intensive care unit stay, and development of delayed cerebral ischemia, although even those with good functional outcomes and postoperative scores may still harbor cognitive deficits within the first 3 months to years later.[14 16]

The type of cognitive dysfunction depends on factors including location of the hemorrhage, artery affected, time to treatment, and comorbid factors,[14 15] but domains more commonly involved include attention, executive function, and memory.[14 16] Impairment in emotion recognition and social cognition can also be seen[16] and may contribute to neuropsychiatric disturbances. Language deficits following aSAH remain understudied,[14] although high performance on animal naming and abstraction, which are language-driven subtests, on cognitive testing like the Montreal Cognitive Assessment (MoCA) is more closely associated with returning to work following aSAH.[17]

All aSAH patients may undergo neurocognitive assessment for screening and longitudinal follow-up regardless of functional outcome.[15] A proposed framework that captures the natural history of cognitive impairment and post-acute recovery involves a *screening test* done between onset up to 8–90 days later followed by *in-depth testing* done as early as 8–90 days up to 1 year and beyond if prior screening is positive.[15] A recommended screening test is a 5-minute protocol including the Orientation, Memory, and Phonemic fluency MoCA subtests for assessment in the acute setting in addition to screening for delirium, which may impact longer-term cognitive outcomes.[15] Following the acute phase, in-depth testing can be done using a validated global cognition screening test such as the full MoCA or the Mini-Mental State Examination (MMSE). The MoCA is an ideal and more sensitive screening tool than the MMSE as it affords a more granular assessment of executive, language, and visuospatial skills in addition to memory.[17] Establishing cognitive function using these tools at 3 months post-aSAH is a useful measure and predictor of health-related quality of life (HRQoL) at 1-year follow-up.[14]

Once cognitive impairment is recognized, a holistic approach to rehabilitation may be instituted. It is found to be most beneficial around 6 months following aSAH.[14] There remains, however, uncertainty as to the efficacy of cognitive rehabilitation interventions due to lack of robust data.[15] Currently, there is no pharmacotherapy approved for post-stroke cognitive impairment.[15]

Headaches

While headaches are a prominent clinical feature of aSAH, their persistence after initial management and stabilization remains unclear. Reported rates of persistent headaches after aSAH vary between 32% and 41% in the literature, with some reporting severe headache years after the inciting event (figure 1).[18 19] The natural history of post-aSAH headaches is also poorly defined, with no strict cut-off point after which SAH-related headaches should naturally subside. According to the International Classification of Headache Disorders (3rd edition), headaches persisting 3 months after resolution of aSAH are classified as "persistent headache attributed to past non-traumatic subarachnoid hemorrhage".[20]

Unlike the classic thunderclap headache associated with the onset of aSAH, post-aSAH headaches tend to be more insidious in onset, often described as a sensation of pressure.[18 21] There are no clear prognostic factors for developing chronic aSAH; clinical presentation, radiographic distribution, aneurysm type nor location, hydrocephalus, and management of the aSAH have not been associated with long-term headaches.[18 19]

In addition to knowing the type and character of the headaches, it is important to use questionnaires to understand their impact on a patient's daily life. One center utilized the Headache Disability Index and a series of pain questionnaires (eg, the Short-Form McGill Pain Questionnaire (SF-MPQ), the German Pain Questionnaire, and the Depression, Anxiety Stress Scale (DASS)), along with the Health-Related Quality of Life (HRQOL) questionnaire and 12-item Short Form Health Survey.[18] They found that higher headache scores correlated with reduced quality of life.

The management of post aSAH headaches is not well-defined, with no specific targeted therapies. In their narrative review of this topic, Sorrentino *et al* note the overall paucity of evidence in this area, with no evidence specifically focused on the outpatient management of post-aSAH headaches.[21] Pharmaceutical management of headaches after aSAH heavily relies on a combination of acetaminophen, opioids, and steroids, with the vast majority of patients requiring more than one type of analgesic.[22] Select studies also demonstrate a role for gabapentin, pregabalin, and intravenous lidocaine for the inpatient management of persistent headaches; however, the long-term effects are not well-known.[21] Of note, most patients (95%) receive inpatient opioids and over 70% are discharged home with a prescription for opioids; however, there is little evidence that opioids improve headaches after the immediate SAH event.[22]

Seizures and epilepsy

Seizures and epilepsy are well-described complications of aSAH. Seizures are distinct from the diagnosis of epilepsy, which

is characterized by an enduring predisposition for epileptic seizures.[23] Seizures that occur within 24 hours to 14 days following ictus are considered acute symptomatic seizures which will likely not require long-term treatment, whereas those that occur >14 days are consistent with the diagnosis of epilepsy, requiring early diagnosis and long-term management.

An analysis of the ISAT study showed a higher risk of seizures for open surgery (9.6%) compared with endovascular therapy (5.2%) at 5 years.[24] A population-based study showed a 5-year cumulative incidence of 12% (figure 1).[25] Differences in reported incidence are likely related to inconsistencies between definitions of epilepsy, length of follow-up, confounding factors such as anti-seizure medications (ASM) prescribing practices, among others. Risk factors for developing epilepsy following aSAH include acute symptomatic seizures or seizures at onset, non-convulsive status epilepticus, middle cerebral artery aneurysms, higher Hunt and Hess and Fisher grades, and the presence of a large intracerebral hemorrhage.[24 25]

There is currently no gold standard or evidence-based guideline regarding the choice of ASM from epilepsy following aSAH. An earlier retrospective study of aSAH patients identified phenytoin exposure as a predictor of poor functional and cognitive outcomes.[26] However, a subsequent observational study comparing levetiracetam to phenytoin showed no significant difference in functional outcome, seizures, or delayed cerebral ischemia.[27] Considerations of ASM choice includes efficacy, safety, and tolerability as well as comorbid conditions. For patients who do not achieve seizure-freedom following the use of more than two well-tolerated ASMs, epilepsy surgery may be considered, assuming a focal area is identified using advanced functional imaging and neuropsychiatric testing, an evaluation similar to that done in other patients with focal epilepsy.

No standardized test or screening tool is available to help aid in the diagnosis of epilepsy in the clinic setting following an aSAH. Most epilepsy screening questionnaires are designed for community screening in epidemiological studies. Since seizures can present with different semiologies and can often be subtle, a high index of suspicion should be maintained in patients with a history of aSAH. Electroencephalography (EEG) is utilized in patients who present with paroxysmal events concerning for seizures such as sudden jerking movements, discreet episodes of cognitive changes, loss of consciousness, or awareness to assess for epileptiform patterns.

The diagnosis of epilepsy significantly impacts quality of life, particularly driving restrictions, employment prospects, and psychosocial stigma. Appropriate diagnosis and treatment are indispensable in high-risk groups of patients such as those with a history of aSAH.

Sexual dysfunction

Sexual dysfunction after aSAH is frequently overlooked in the clinical setting despite its significant impact on psychosocial functioning and quality of life. Nonetheless, a cross-sectional study of 33 patients with good clinical grade aSAH and favorable neurological outcome found a high prevalence of erectile dysfunction in men (54%) and sexual dysfunction (47%) and hypoactive sexual desire (100%) in women (figure 1).[28]

Limited epidemiological data associate sexual dysfunction with various factors. Hypothalamic–pituitary dysfunction occurs in 11–50% of cases and may cause growth hormone, corticotropin, and gonadal hormone deficiencies predominantly.[29] Regions key to sexual experience (anterior/mesial temporal lobes; basal forebrain) may also be affected, being intimately related to the most frequent sites of ruptured intracranial aneurysms (anterior/posterior communicating arteries; middle cerebral artery bifurcation).[28] Symptoms may include decreased libido, arousal difficulties, orgasmic dysfunction, reduced lubrication, pain/discomfort, body image concerns, and psychological disturbances such as lower self-esteem, emotional lability, and fear of stroke recurrence.[28]

As sexual health is an integral aspect of overall well-being, physicians should actively probe for symptoms of sexual dysfunction in their patients.[5] Utilizing validated self-report tools specific to sexual dysfunction can then be done when appropriate. The 15-item International Index of Erectile Function and 19-item Female Sexual Function Index are multidimensional questionnaires widely used among men and women, respectively.[28] The Changes in Sexual Functioning Questionnaire measures the impact of illness and medications and can be used in both sexes.[30] Before adopting any screening tool, clinicians should consider the specific needs and characteristics of patients.

Our review demonstrated a lack of literature focused on therapeutic options for aSAH with sexual dysfunction. Generally, the treatment of post-stroke sexual dysfunction is often multifaceted, combining medical, psychological, and rehabilitative approaches. A thorough review of medications likely contributing to sexual dysfunction is recommended, with dose adjustments being done as needed. Comorbid conditions such as depression, anxiety, and other health issues affecting sexual functioning should also be addressed. Lastly, various non-pharmacological modalities can also be offered by trained professionals. These include psychotherapy (eg, sex therapy, individual/couples counseling, support groups), physiotherapy (eg, pelvic floor exercises, mobility/balance/endurance training), occupational therapy (eg, adaptive devices, task modifications), and proper patient/partner education and communication skills training.[31]

How to put this in practice?

Rinkel *et al* emphasize the crucial role of multidisciplinary clinics within their institution, where a comprehensive evaluation for aSAH patients involves collaboration among a neuropsychology assistant, stroke nurse, and physiatrist.[3] Acknowledging the substantial financial commitment associated with such clinics, particularly in smaller centers, we propose an alternative approach that can be implemented in smaller clinic settings. We suggest that self-administered questionnaires be used to screen for neuropsychiatric outcomes. This may be followed by management of conditions aligned with the neurointerventionalist's expertise and a streamlined referral system.

Apart from the targeted questionnaires discussed earlier, a 40-item self-administered questionnaire for the Screening of Symptoms in aSAH (SOS-SAH) is also available to be used in the clinic setting (see table 1).[32] The questionnaire has allotted questions for caregivers as well to either supplement patient inputs or serve as proxy answers for patients who are unable to communicate or have poor insight into their condition. The 14 domains of patient-reported outcomes designed with inputs from patients and healthcare professionals included all the outcomes we reviewed except for seizures. As the questionnaire is also self-administered it may be accomplished in the waiting room prior to the consult. Although the questionnaire has shown utility in organizing consultations for aSAH, its precise psychometric characteristics, particularly its predictive capacity regarding long-term neuropsychiatric outcomes, have yet to be investigated.[33]

Lastly, support groups specifically designed for individuals and their families affected by brain aneurysms offer a valuable resource to potentially enhance psychosocial well-being,

Table 1 Questionnaire for the screening of symptoms in aneurysmal subarachnoid hemorrhage (SOS-SAH)[35]

Item number	Items					
1	I have been able to bring to mind words that I wanted to use while talking to someone.	Not at all	A little bit	Somewhat	Quite a bit	Very much
2	I have been able to focus my attention.	Not at all	A little bit	Somewhat	Quite a bit	Very much
3	I have been able to remember to do things, like take medicine or buy something I needed.	Not at all	A little bit	Somewhat	Quite a bit	Very much
4	I have been able to think clearly.	Not at all	A little bit	Somewhat	Quite a bit	Very much
5	I have been able to remember the name of a familiar object.	Not at all	A little bit	Somewhat	Quite a bit	Very much
6	I have been able to concentrate.	Not at all	A little bit	Somewhat	Quite a bit	Very much
7	I have been able to pay attention and keep track of what I am doing without extra effort.	Not at all	A little bit	Somewhat	Quite a bit	Very much
8	I have been able to learn new things easily, like telephone numbers or instructions.	Not at all	A little bit	Somewhat	Quite a bit	Very much
9	In a busy environment I find myself quickly bothered by excessive stimuli.	Not at all	A little bit	Somewhat	Quite a bit	Very much
10	I feel tense or 'wound up'.	Most of the time	A lot of the time	Frome time to time, occasionally	Not at all	
11	I still enjoy the things I used to enjoy.	Definitely as much	Not quite so much	Only a little	Hardly at all	
12	I get a sort of frightened feeling as if something awful is about to happen.	Very definitely and quite badly	Yes, but not too badly	A little, but it doesn't worry me	Not at all	
13	I can laugh and see the funny side of things.	As much as I always could	Not quite so much now	Definitely not so much now	Not at all	
14	Worrying thoughts go through my mind.	A great deal of the time	A lot of the time	From time to time but not too often	Only occasionally	
15	I feel cheerful.	Not at all	Not often	Sometimes	Most of the time	
16	I can sit at ease and feel relaxed.	Defintely	Usually	Not often	Not at all	
17	I feel as if I am slowed down.	Nearly all the time	Very often	Sometimes	Not at all	
18	I get a sort of frightened feeling like 'butterflies' in the stomach.	Not at all	Occasionally	Quite often	Very often	
19	I have lost interest in my appearance.	Defintely	I don't take so much care as I should	I may not take quite as much care	I take just as much care as ever	
20	I feel restless as I have to be on the move.	Very much indeed	Quite a lot	Not very much	Not at all	
21	I look forward with enjoyment to things.	As much as I ever did	Rather less than I used to	Definitely less than I used to	Hardly at all	
22	I get sudden feelings of panic.	Very often indeed	Quite often	Not very often	Not at all	
23	I can enjoy a good book or radio or TV programme.	Often	Sometimes	Not often	Very seldom	
24	I feel fatigued.	Not at all	A little bit	Somewhat	Quite a bit	Very much

Continued

Table 1 Continued

Item number	Items					
25	I have trouble starting things because I am tired.	Not at all	A little bit	Somewhat	Quite a bit	Very much
26	How run-down did you feel on average?	Not at all	A little bit	Somewhat	Quite a bit	Very much
27	How fatigued were you on average?	Not at all	A little bit	Somewhat	Quite a bit	Very much
28	I have trouble doing all of my regular leisure activities with others	Never	Rarely	Sometimes	Usually	Always
29	I have trouble doing all of the family activities that I want to do	Never	Rarely	Sometimes	Usually	Always
30	I have trouble doing all of my usual work (include work at home)	Never	Rarely	Sometimes	Usually	Always
31	I have trouble doing all of the activities with friends that I want to do	Never	Rarely	Sometimes	Usually	Always
32	I am a different person than I was before the (subarachnoid) hemorrhage.	Not at all	A little bit	Somewhat	Quite a bit	Very much
33	How difficult do you find it to hold a conversation?	Not at all	A little bit	Somewhat	Quite a bit	Very much
34	How difficult do you find it to follow a conversation?	Not at all	A little bit	Somewhat	Quite a bit	Very much
35	How much difficulty do you have with your sight?	Not at all	A little bit	Somewhat	Quite a bit	Very much
36	How much difficulty do you have with your sense of taste?	Not at all	A little bit	Somewhat	Quite a bit	Very much
37	How much difficulty do you have with your sense of smell?	Not at all	A little bit	Somewhat	Quite a bit	Very much
38	How much difficulty do you have with your hearing?	Not at all	A little bit	Somewhat	Quite a bit	Very much
39	How bothered are you by headaches?	Not at all	A little bit	Somewhat	Quite a bit	Very much
40	Has the (subarachnoid) hemorrhage affected your sex life?	Not at all	A little bit	Somewhat	Quite a bit	Very much
41	My family member is a different person than he/she was before the (subarachnoid) hemorrhage.	Not at all	A little bit	Somewhat	Quite a bit	Very much
42	My family member has been able to bring to mind words that he/she wanted to use while talking to someone.	Not at all	A little bit	Somewhat	Quite a bit	Very much
43	My family member has been able to focus his/her attention.	Not at all	A little bit	Somewhat	Quite a bit	Very much
44	My family member has been able to remember to do things, like take medicine or buy something he/she needed.	Not at all	A little bit	Somewhat	Quite a bit	Very much
45	My family member has been able to think clearly.	Not at all	A little bit	Somewhat	Quite a bit	Very much

Continued

Table 1 Continued

Item number	Items					
46	My family member has been able to remember the name of a familiar object.	Not at all	A little bit	Somewhat	Quite a bit	Very much
47	My family member has been able to concentrate.	Not at all	A little bit	Somewhat	Quite a bit	Very much
48	My family member has been able to pay attention and keep track of what he/she is doing without extra effort.	Not at all	A little bit	Somewhat	Quite a bit	Very much
49	My family member has been able to learn new things easily, like telephone numbers or instructions.	Not at all	A little bit	Somewhat	Quite a bit	Very much

The questionnaire was previously published in *BMC Neurology*. The authors obtained permission from Prof. Jeroen D Boogarts to publish the questionnaire as part of their narrative review.

particularly in the context of challenges associated with aSAH. This is particularly pertinent for patients who despite the absence of overt neurological deficits, grapple with neuropsychiatric comorbidities impacting their capacity to lead fulfilling and productive lives. The Brain Aneurysm Foundation serves as a conduit for access to over 75 aneurysm support groups dispersed across North America as detailed on their website (https://www.bafound.org/support/).

Future directions

Utilizing insurance claims databases for population-based research presents a viable avenue to assess the disease burden. However, the identification of neuropsychiatric outcomes such as chronic headaches and cognitive dysfunction within these extensive datasets is often challenging due to their lack of detailed information. Thus, it is essential to establish large prospective cohorts to determine the incidence of the long-term neuropsychiatric complications of aSAH. Therapeutic trials addressing these outcomes can benefit from utilizing patients already in these cohorts as there may be significant challenges in recruiting patients for randomized trials. For instance, a trial targeting depression in aSAH patients faced significant recruitment difficulties, enrolling only 5 of 64 eligible patients.[34] Additionally, advanced neuroimaging studies focused on elucidating the pathomechanisms of neuropsychiatric outcomes in this population are crucial for identifying therapeutic targets.

Currently, ClinicalTrials.gov lists 50 ongoing studies related to aSAH, but only two actively recruiting trials directly examine long-term outcomes. One trial evaluates the efficacy of huperazine in alleviating cognitive dysfunction post-aSAH (bit.ly/3IQCS2V), while another focuses on a neuroimaging prospective cohort study assessing hippocampal volume and memory functions following aSAH (bit.ly/3IQCS2V). While there are trials for aSAH headache, they are limited to the period immediately following rupture. The paucity of active trials underscores the need for more research in this area.

CONCLUSIONS

In summary, this review underscores the significance of comprehending and addressing enduring neuropsychiatric concerns such as anxiety, depression, cognitive impairments, headaches, seizures, and sexual dysfunction following aSAH. Neurointerventionalists, who often oversee the long-term care of treated aneurysm patients, could play a pivotal role in early identification of these issues and, if their training permits, in managing certain aspects before referring patients to other subspecialties. The review also highlights the need for more research to prove the validity of screening tools and improve evidence-based treatments for these neuropsychiatric complications.

Author affiliations
[1]Division of Neurology, Department of Medicine, University of Toronto, Toronto, Ontario, Canada
[2]Li Ka Shing Knowledge Institute, St Michael's Hospital- Unity Health Toronto, Toronto, Ontario, Canada
[3]Division of Neurosurgery, Department of Surgery, University of Toronto, Toronto, Ontario, Canada
[4]Health Sciences Library, St Michael's Hospital- Unity Health Toronto, Toronto, Ontario, Canada
[5]Department of Psychiatry, University of Toronto, Toronto, Ontario, Canada
[6]Department of Rehabilitation Medicine, University of the Philippines Manila, Manila, Philippines
[7]Department of Physical Medicine and Rehabilitation, St. Luke's Medical Center, Quezon City, Philippines
[8]Ontario Shores Centre for Mental Health Sciences, Whitby, North Yorkshire, Canada
[9]Department of Clinical Epidemiology, College of Medicine, University of the Philippines Manila, Manila, Philippines
[10]Division of Epilepsy, Department of Neurology, Yale School of Medicine, New Haven, Connecticut, USA
[11]Division of Neurosurgery, Department of Surgery, McMaster University, Hamilton, Ontario, Canada
[12]Trauma and Neurosurgery Program, St Michael's Hospital, Toronto, Ontario, Canada
[13]Division of Diagnostic and Therapeutic Neuroradiology, Department of Medical Imaging, University of Toronto, Toronto, Ontario, Canada

X Jose Danilo Bengzon Diestro @dannidiestro and Vitor Mendes Pereira @VitorMendesPer1

Contributors All the authors meet all the following criteria: (1) substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; (2) drafting the work or revising it critically for important intellectual content; (3) final approval of the version to be published; and (4) agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests Dr Diestro is an Assistant Editor of the Journal of NeuroInterventional Surgery.

Patient consent for publication Not applicable.

Ethics approval Not applicable.

Provenance and peer review Commissioned; externally peer reviewed.

ORCID iDs
Jose Danilo Bengzon Diestro http://orcid.org/0000-0001-8450-2021
Vitor Mendes Pereira http://orcid.org/0000-0002-6804-3985

REFERENCES

1 Molyneux A. International Subarachnoid Aaneurysm Trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised trial. *Lancet* 2002;360:1267–74.
2 Spetzler RF, McDougall CG, Zabramski JM, *et al*. Ten-year analysis of saccular aneurysms in the Barrow Ruptured Aneurysm Trial. *J Neurosurg* 2020;132:771–6.
3 Rinkel GJE, Algra A. Long-term outcomes of patients with aneurysmal subarachnoid haemorrhage. *Lancet Neurol* 2011;10:349–56.
4 Visser-Meily JMA, Rhebergen ML, Rinkel GJE, *et al*. Long-term health-related quality of life after aneurysmal subarachnoid hemorrhage. *Stroke* 2009;40:1526–9.
5 Hoh BL, Ko NU, Amin-Hanjani S, *et al*. Guideline for the management of patients with aneurysmal subarachnoid hemorrhage: a guideline from the American Heart Association/American Stroke Association. *Stroke* 2023;54:e314–70.
6 Tang WK, Wang L, Kwok Chu Wong G, *et al*. Depression after subarachnoid hemorrhage: a systematic review. *J Stroke* 2020;22:11–28.
7 Tang WK, Wang L, Tsoi KK, *et al*. Anxiety after subarachnoid hemorrhage: a systematic review and meta-analysis. *J Affect Disord Rep* 2021;3.
8 Boerboom W, Heijenbrok-Kal MH, van Kooten F, *et al*. Unmet needs, community integration and employment status four years after subarachnoid haemorrhage. *J Rehabil Med* 2016;48:529–34.
9 Yang NR, Seo EK, Cho Y, *et al*. Health-related quality of life of patients with aneurysmal subarachnoid hemorrhage who were classified as having "good outcomes". *J Clin Neurosci* 2024;119:143–8.
10 Lam RW, Kennedy SH, Parikh SV, *et al*. Canadian Network for Mood and Anxiety Treatments (CANMAT) 2016 clinical guidelines for the management of adults with major depressive disorder: Section 3. *Can J Psychiatry* 2016;61:506–9.
11 Allida SM, Hsieh C-F, Cox KL, *et al*. Pharmacological, non-invasive brain stimulation and psychological interventions, and their combination, for treating depression after stroke. *Cochrane Database Syst Rev* 2023;7.
12 Leung KYQ, Cartoon J, Hammond NE. Depression screening in patients with aneurysmal subarachnoid haemorrhage and their caregivers: a systematic review. *Aust Crit Care* 2023;36:1138–49.
13 Aben I, Verhey F, Lousberg R, *et al*. Validity of the Beck Depression Inventory, Hospital Anxiety and Depression Scale, SCL-90, and Hamilton Depression Rating Scale as screening instruments for depression in stroke patients. *Psychosomatics* 2002;43:386–93.
14 Nussbaum ES, Mikoff N, Paranjape GS. Cognitive deficits among patients surviving aneurysmal subarachnoid hemorrhage. A contemporary systematic review. *Br J Neurosurg* 2021;35:384–401.
15 Rost NS, Brodtmann A, Pase MP, *et al*. Post-stroke cognitive impairment and dementia. *Circ Res* 2022;130:1252–71.
16 Buunk AM, Groen RJM, Veenstra WS, *et al*. Cognitive deficits after aneurysmal and angiographically negative subarachnoid hemorrhage: memory, attention, executive functioning, and emotion recognition. *Neuropsychology* 2016;30:961–9.
17 Schweizer TA, Al-Khindi T, Macdonald RL. Mini-Mental State Examination versus Montreal Cognitive Assessment: rapid assessment tools for cognitive and functional outcome after aneurysmal subarachnoid hemorrhage. *J Neurol Sci* 2012;316:137–40.
18 Huckhagel T, Klinger R, Schmidt NO, *et al*. The burden of headache following aneurysmal subarachnoid hemorrhage: a prospective single-center cross-sectional analysis. *Acta Neurochir (Wien)* 2020;162:893–903.
19 Gerner ST, Reichl J, Custal C, *et al*. Long-term complications and influence on outcome in patients surviving spontaneous subarachnoid hemorrhage. *Cerebrovasc Dis* 2020;49:307–15.
20 Olesen J. Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition. *Cephalalgia* 2018;38:1–211.
21 Sorrentino ZA, Laurent D, Hernandez J, *et al*. Headache persisting after aneurysmal subarachnoid hemorrhage: a narrative review of pathophysiology and therapeutic strategies. *Headache* 2022;62:1120–32.
22 Glisic EK, Gardiner L, Josti L, *et al*. Inadequacy of headache management after subarachnoid hemorrhage. *Am J Crit Care* 2016;25:136–43.
23 Fisher RS, Acevedo C, Arzimanoglou A, *et al*. ILAE official report: a practical clinical definition of epilepsy. *Epilepsia* 2014;55:475–82.
24 Hart Y, Sneade M, Birks J, *et al*. Epilepsy after subarachnoid hemorrhage: the frequency of seizures after clip occlusion or coil embolization of a ruptured cerebral aneurysm. *J Neurosurg* 2011;115:1159–68.
25 Huttunen J, Kurki MI, von und zu Fraunberg M, *et al*. Epilepsy after aneurysmal subarachnoid hemorrhage. *Neurology* 2015;84:2229–37.
26 Naidech AM, Kreiter KT, Janjua N, *et al*. Phenytoin exposure is associated with functional and cognitive disability after subarachnoid hemorrhage. *Stroke* 2005;36:583–7.
27 Karamchandani RR, Fletcher JJ, Pandey AS, *et al*. Incidence of delayed seizures, delayed cerebral ischemia and poor outcome with the use of levetiracetam versus phenytoin after aneurysmal subarachnoid hemorrhage. *J Clin Neurosci* 2014;21:1507–13.
28 Epprecht L, Messerli M, Samuel R, *et al*. Sexual dysfunction after good-grade aneurysmal subarachnoid hemorrhage. *World Neurosurg* 2018;111:e449–53.
29 Dimopoulou I, Kouyialis AT, Tzanella M, *et al*. High incidence of neuroendocrine dysfunction in long-term survivors of aneurysmal subarachnoid hemorrhage. *Stroke* 2004;35:2884–9.
30 Clayton AH, McGarvey EL, Clavet GJ. The Changes in Sexual Functioning Questionnaire (CSFQ): development, reliability, and validity. *Psychopharmacol Bull* 1997;33:731–45.
31 Auger LP, Grondin M, Aubertin M, *et al*. Interventions used by allied health professionals in sexual rehabilitation after stroke: a systematic review. *Top Stroke Rehabil* 2021;28:557–72.
32 Nobels-Janssen E, Abma IL, Verhagen WIM, *et al*. "Development of a patient-reported outcome measure for patients who have recovered from a subarachnoid hemorrhage: the "questionnaire for the screening of symptoms in aneurysmal subarachnoid hemorrhage" (SOS-SAH)". *BMC Neurol* 2021;21.
33 Nobels-Janssen E, Abma IL, de Ridder IR, *et al*. The SOS-SAH questionnaire in clinical practice: a multi-method evaluation study. *BMC Neurol* 2023;23.
34 Keen J, Lim D, Prijoles K, *et al*. E-194 A randomized double-blind placebo-controlled trial of prophylactic antidepressant medication for the prevention of depression post aneurysmal subarachnoid hemorrhage. SNIS 19th Annual Meeting Abstracts; July 2022
32 Nobels-Janssen E, Abma IL, Verhagen WIM, *et al*. Development of a patient-reported outcome measure for patients who have recovered from a subarachnoid hemorrhage: the "questionnaire for the screening of symptoms in aneurysmal subarachnoid hemorrhage" (SOS-SAH)". *BMC Neurol* 2021;21:162.