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RADIOLOGICAL EDUCATION



Are we ready for amyloid-related imaging abnormalities (ARIA) monitoring? A European survey among neuroradiologists and neurologists by the ESNR/EAN Working Group

Tiago Gil Oliveira^{1,2,3} , Meike W. Vernooij^{4,5,6}, Giovanni B. Frisoni^{7,8}, Roland Wiest^{9,10*} and Frederik Barkhof^{11,12*}

Abstract

Objectives Amyloid-lowering immunotherapies can cause amyloid-related imaging abnormalities (ARIA), requiring brain MRI for detection and monitoring. The European Society of Neuroradiology (ESNR)/European Academy of Neurology (EAN) ARIA Working Group conducted a survey to assess European clinicians' readiness for this logistical challenge and need for further education on ARIA.

Materials and methods An online questionnaire with 32 items (multiple choice, single best choice, and free text) was distributed to ESNR and EAN members. Between June and July 2024, we collected 422 responses from 41 European countries, including 47% neurologists and 51% (neuro)radiologists; 15% were residents, and 58% worked in academic hospitals.

Results Of respondents, 69% were familiar with the concept of ARIA, and 60% reportedly understood its risk factors. Confidence in evaluating ARIA-E (edema/effusion) and ARIA-H (hemorrhage) subtypes was reported by 60% and 69%, respectively, with (neuro)radiologists more confident than neurologists. However, 34% of respondents felt poorly equipped to meet logistical demands, and 82% lacked a dedicated ARIA imaging protocol. Key barriers included limited organizational adaptability and radiology expertise. Notably, 72% saw potential in having support by artificial intelligence approaches, and 93% expressed the wish for further training on how to monitor ARIA.

Conclusions Despite the current unavailability of amyloid-lowering therapies, European neurologists and (neuro) radiologists report reasonable ARIA awareness. There is a clear need for additional practical preparation and training in ARIA assessment, which can inform future ESNR/EAN educational initiatives.

Key Points

Question Are neurologists and neuroradiologists ready for ARIA monitoring?

Findings Neurologists and neuroradiologists were moderately familiar with the concept of ARIA, its risk factors, and its identification on MRI, but felt poorly equipped to meet the logistical demands.

Tiago Gil Oliveira, Meike W. Vernooij and Frederik Barkhof represent the European Society of Neuroradiology (ESNR).

Giovanni B. Frisoni and Roland Wiest represent the European Academy of Neurology (EAN). This publication is endorsed by both ESNR and EAN.

Tiago Gil Oliveira and Meike W. Vernooij contributed equally to this work.

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Clinical relevance With the potential introduction of amyloid-lowering therapies in European countries, identifying key barriers, such as limited organizational adaptability and radiology expertise, highlights the need for further practical preparation by clinical departments and additional training in ARIA assessment.

Keywords Amyloid-related imaging abnormalities, Alzheimer, Anti-amyloid, MRI

Graphical Abstract

Are we ready for amyloid-related imaging abnormalities (ARIA) monitoring? A European survey among neuroradiologists and neurologists by the ESNR/EAN working group

The ARIA Working Group conducted a survey to assess European clinicians' readiness for the logistical challenge to handle ARIA cases and the need for further education on ARIA.

An online questionnaire with 32 items was distributed to European Society of Neuroradiology and European Academy of Neurology members.

European
neurologists &
radiologists

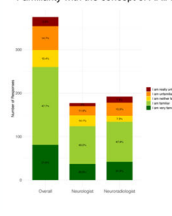
Survey



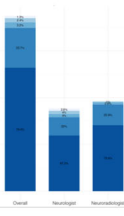
Multi
center



Familiarity with the concept of ARIA



Need for extra training?



Although European neurologists and neuroradiologists were moderately familiar with the concept of ARIA, its risk factors, and its identification on MRI, many felt poorly equipped to meet the logistical demands, and most lacked a dedicated ARIA imaging protocol.

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EUROPEAN SOCIETY OF RADIOLOGY

European Radiology

Introduction

Alzheimer's disease (AD) is the most common cause of dementia. At the pathophysiological level, AD is defined by the accumulation in different brain regions of amyloid plaques, mainly constituted by amyloid beta ($A\beta$), and neurofibrillary tangles, constituted by hyperphosphorylated forms of tau [1]. These protein aggregates are considered to drive neurodegeneration, leading to brain atrophy on computed tomography (CT) and magnetic resonance imaging (MRI) [2]. Fluid biomarkers allow detection of amyloid- and tau-linked pathologies by measuring pathological forms of $A\beta$ or phosphorylated tau (p-tau) in the cerebrospinal fluid and serum, while amyloid and tau deposition can be shown using positron emission tomography [3].

In order to halt the neurodegenerative process, various therapies have been designed to slow disease progression, and among these, anti-amyloid immunotherapies were the first class of disease-modifying therapies shown to slow down cognitive decline upon clearing amyloid

plaques from the brains of AD patients. This was shown for three different drugs, with lecanemab and donanemab currently in the process of being considered to be used in Europe [4, 5], with the extent of amyloid removal correlating with the delay in cognitive decline [6]. Concerns, however, have been raised due to the frequent occurrence of treatment-related MRI findings, so-called amyloid-related imaging abnormalities (ARIA). Ranging in clinical sequelae from (most often) completely asymptomatic to (infrequent) severe impairment or death, ARIA constitutes the major side-effect observed during clinical trials, occurring in up to 40% of individuals depending on the drug [7]. ARIA can manifest in two ways: ARIA-E with hyperintense vasogenic edema and sulcal effusions on T2-fluid-attenuated inversion recovery (T2-FLAIR); and ARIA-H, standing for hemorrhage, with hypointense microhemorrhages and superficial siderosis on susceptibility-sensitive images [7] (Fig. 1). Several rating scales for ARIA severity exist [8], both for its clinical and imaging presentation, with direct



Fig. 1 ARIA-E and ARIA-H are identified on brain MRI. ARIA-E is identified on T2-FLAIR (top panels) by the presence of edema (left) and/or sulcal effusion (right), and ARIA-H is identified on T2* (or alternatively on SWI) (lower panels) by the presence of microhemorrhages (left) or cortical siderosis (right). ARIA-specific changes highlighted within orange circles. Images available at www.ariaeducation.eu

consequences for dose-adaptation or even discontinuation of therapy.

The occurrence of ARIA-E and ARIA-H in lecanemab and donanemab-treated patients varied from 5.4–34.4%

and 11.9–30.5%, respectively, depending on the dose and type of drug administered, and on *APOE4* carriership, which increases the likelihood of developing ARIA [5, 9, 10]. Microhemorrhages at baseline before treatment

increase the risk of developing ARIA-E [9, 10], and data from other trials show extensive white matter hyperintensities and the severity of amyloid pathology as additional risk factors that should be taken into account [11]. Further reports showed evidence connecting ARIA with cerebral amyloid angiopathy pathology and the risk of developing intracerebral hemorrhage [12]. Therefore, the choice of which patients to be submitted to anti-amyloid therapies can impact the risk of developing ARIA, while recognizing that in population-based studies, microhemorrhages are present in 17.8% of participants aged 60–69, 38.3% in those aged ≥ 80 years [13].

The clinical community faces several challenges related to the market introduction of anti-amyloid therapies and the associated risk of developing ARIA. These include the selection of eligible patients, regular monitoring for ARIA with clinical and MRI assessments, and adequate communication protocols and organization to manage ARIA cases in a timely manner [14]. During treatment, at least four MRIs are expected to be performed within the first year, and in both symptomatic patients and cases with identified ARIA, even a higher number of scans will be required [15]. Overall, monitoring of ARIA is expected to impose a substantial additional burden on clinical workflows, since it implies that for each patient, a baseline MRI exam is performed to assess for potential contraindications and to identify pre-existing abnormalities. In the USA, where these therapies have already been introduced in clinical practice, a survey was recently conducted by the American Society of Neuroradiology (ASNR), among neuroradiologists only. They reported variable degrees of confidence in their ability to identify ARIA, and only 39.4% had specific ARIA dedicated MRI protocols [8]. As these therapies are currently being considered to be implemented in Europe (with approval of lecanemab and donanemab by the European Medicines Agency) [16, 17], we conducted a survey to assess European clinicians' readiness and the need for further education on ARIA. This survey included questions regarding the knowledge about ARIA and its risk factors, logistic preparation and the need for further training, which can inform future educational initiatives.

Materials and methods

The survey was conducted by the authors as members of an ad-hoc ARIA working group of the European Society of Neuroradiology (ESNR) and the European Academy of Neurology (EAN). An online questionnaire was designed using Google Forms open access toolbox (Google.com) and sent through SurveyMonkey to collect answers from participants. Questions were assembled by the members of the ESNR/EAN ARIA Working Group with further feedback from the ESNR and EAN scientific panel and

board members. The questionnaire contained 33 items, divided into multiple choice, single best choice and free text questions (see supplement for entire list of questions). There were 10 questions addressing characteristics of respondents, 6 questions on prior knowledge and confidence in ARIA rating and management, 7 questions addressing how well institutions are prepared to deal with ARIA, 8 questions on reporting, interpretation and AI approaches in ARIA, and 2 questions regarding additional information. Survey invitations were emailed to all ESNR and EAN members, and recipients were encouraged to forward them to any colleagues who were (likely to be) involved in ARIA monitoring and one final question for additional comments. Requests for responses were also sent through national neuroradiological societies across Europe. The survey was open for about 1 month from June 7 to July 10, 2024. Descriptive analyses were performed for the answers to each question. We analyzed results for the entire sample of European respondents and, where appropriate, stratified between (neuro)radiologists (aggregating both radiologists and neuroradiologists) and neurologists, and/or between academic versus non-academic institutes. All analyses and figures were created using RStudio Version 1.4.1103.

Results

Demographics

A total of 476 entries were received, of which 422 were from European institutions. Responses originated from 41 countries, with a map of respondents shown in Fig. 2. Countries with the most respondents were Italy ($n = 75$), Portugal ($n = 42$), France ($n = 30$), the Netherlands ($n = 25$), Switzerland ($n = 25$) and Germany ($n = 22$). Among the respondents, 51% were (neuro)radiologists, and 47% neurologists (Fig. 3A). Of all respondents, 15% were residents (Fig. 3B), 58% worked in academic hospitals (Fig. 3C), 61% had a dedicated memory clinic with a neurologist being the primary care provider, and about 80% used MRI as the primary imaging modality to assess patients with suspected dementia, with 3-T MRI as the top option. The experience of the respondents was quite diverse, ranging from 31% with 0–5 years, to 11% of participants with over 25 years of experience in dementia care (Fig. 3D).

Prior knowledge and confidence in ARIA rating and management

The concept of ARIA is recent and has been proposed in the context of clinical trials with the administration of antibodies directed to A β species. Most hands-on experience in identifying ARIA thus comes from European clinicians involved with these trials, whereas others will have primarily theoretical knowledge. Despite ARIA

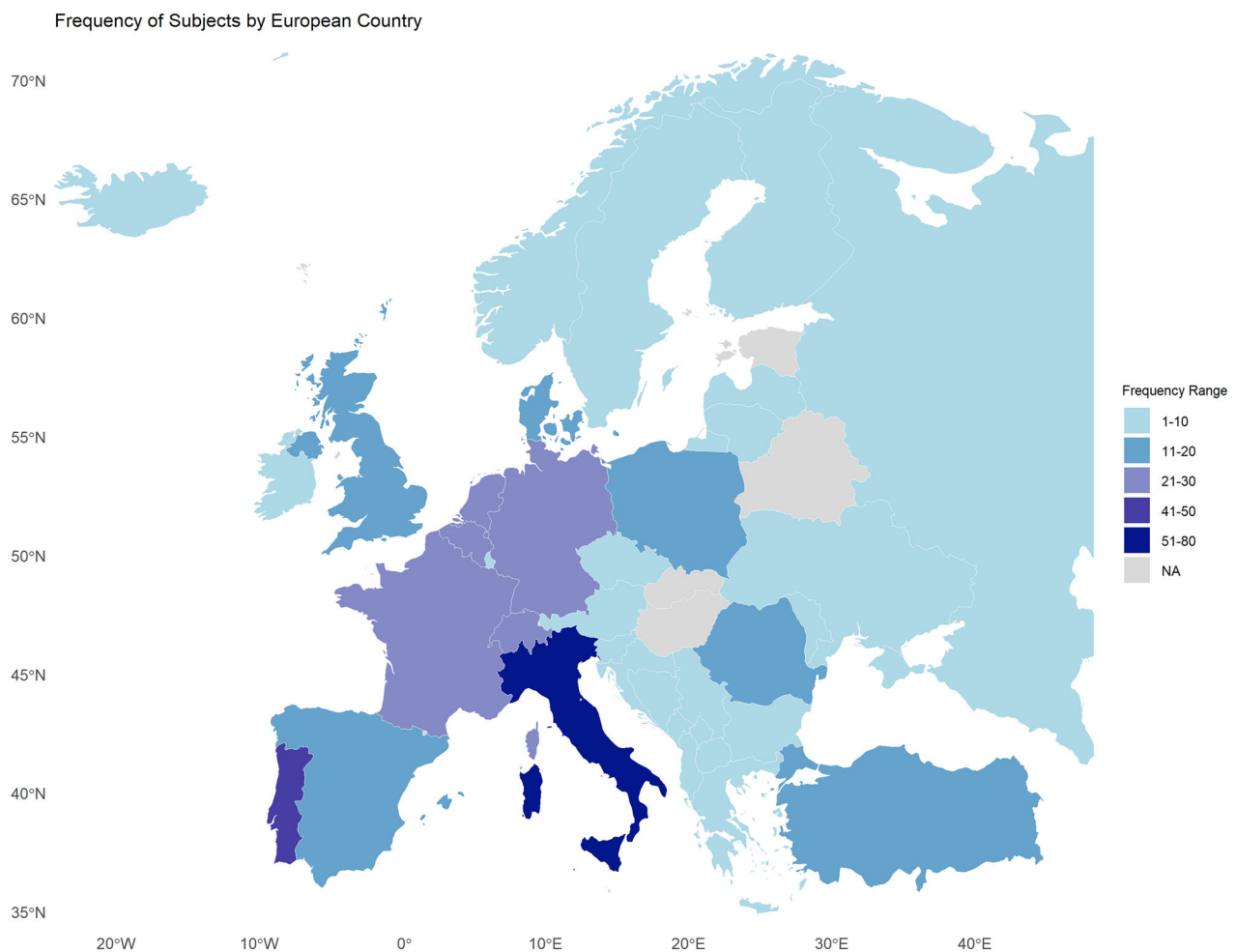


Fig. 2 Number of responses per country. Countries with no responses (NA) are shown in shaded gray. 422 responses were considered from European institutions in 41 different countries

being a relatively new concept, the majority of respondents indicated they were familiar to very familiar with the concept (69%), percentages not differing between neurology and (neuro)radiology respondents (Fig. 4A). However, 40% were not familiar with the risk factors to develop ARIA, with no major differences in the responses by either neurologists and (neuro)radiologists (Fig. 4B).

The overall confidence in identifying ARIA was slightly higher for ARIA-H, with 69% mentioning being confident to very confident in assessing it, while for ARIA-E, it was about 60%. Not unexpectedly, (neuro)radiologists reported having higher confidence in identifying both ARIA-E (70% vs 50%) and ARIA-H (83% vs 56%). Once ARIA is present, the rating of ARIA on MRI ranges from mild to moderate and severe, depending on the number of locations or size of edema areas for ARIA-E, and the number of new microhemorrhages or focal areas of superficial siderosis for ARIA-H [10]. Overall, only 9% of

respondents were very confident in rating ARIA, with a higher percentage of (neuro)radiologists (12%) than neurologists (5%) (Fig. 4E). Finally, the vast majority of respondents would find it useful to get extra training on ARIA (93%) (Fig. 4F). Even though there are no major differences between academic and non-academic centers, professionals in academic institutions appear to be slightly more familiar with ARIA and with its risks (Supplementary Fig. 1A–E).

How well are institutions prepared to deal with ARIA?

While the majority of (neuro)radiologists mentioned that clinical management was not applicable to them, among the neurologists, only 39% mentioned at least some level of confidence in managing a patient with ARIA (Fig. 5A), which was slightly higher in academic centers (Supplementary Fig. 1F). Overall, 34% of respondents consider their institutions to be badly equipped to meet the

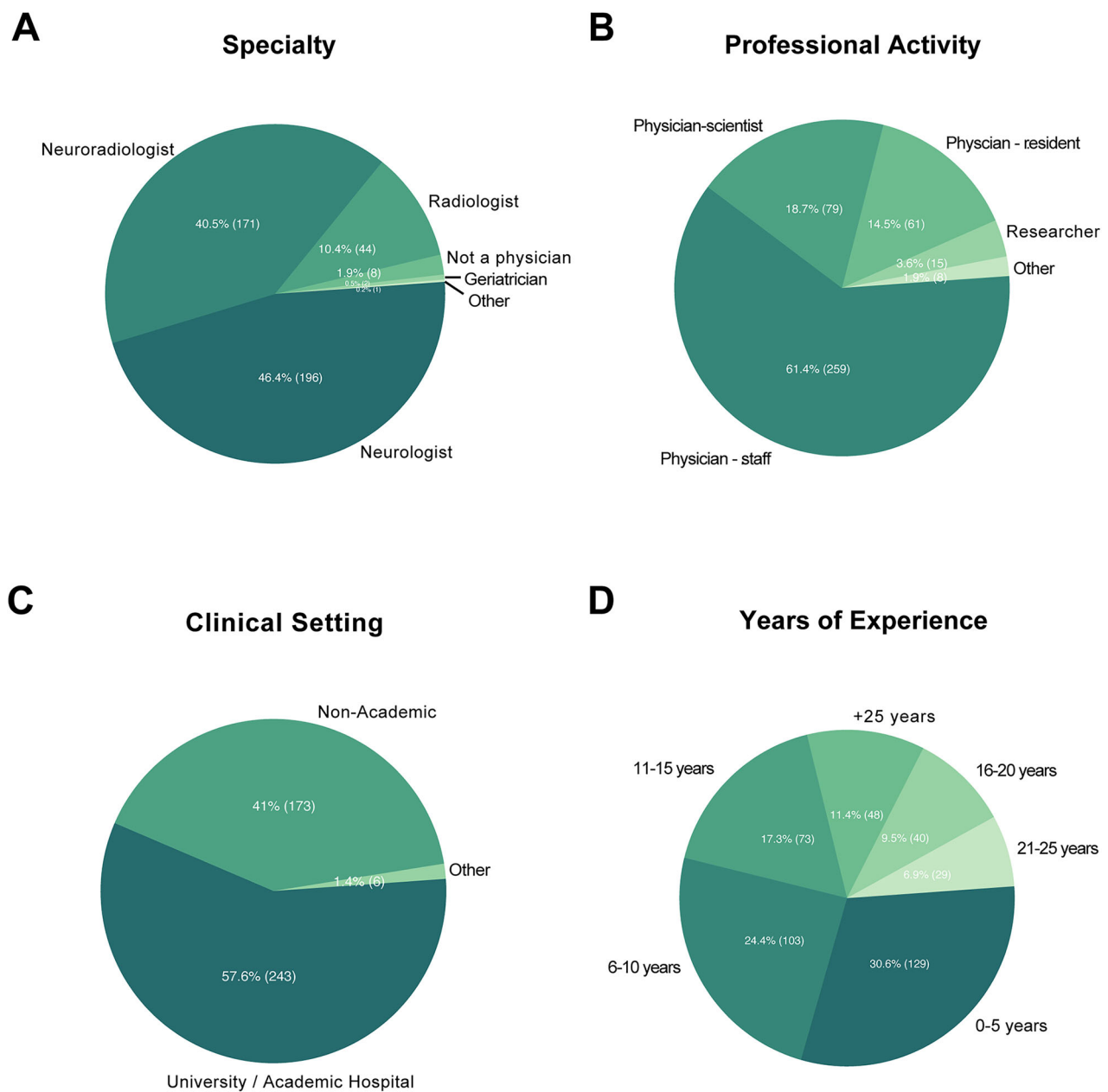


Fig. 3 Characteristics of respondents. **A–D** Total number of respondents was 422, with percentages shown and number of responses between brackets. In **A**, neuroradiologists and radiologists are separately represented, while in subsequent analyses, they were pooled together as neuroradiologists

demands of the expected increase in ARIA monitoring and management of cases (Fig. 5B).

Regarding the ability of clinical centers to perform emergency ARIA assessments, 65% reported being able to do so, with notable differences between academic centers (73%) and non-academic centers (53%) (Supplementary Fig. 2A). Similarly, 66% reported that their centers have a mechanism in place to communicate urgent ARIA findings detected on MRI, with a higher percentage in

academic centers than in non-academic centers (73% vs 56%) (Supplementary Fig. 2B).

Among the most relevant barriers to the implementation of ARIA monitoring, the major ones mentioned were lack of organizational adaptability, such as scheduling slots, scanner capacity and radiology expertise (Fig. 5C). Importantly, 82% mentioned they had no ARIA protocol implemented, with no major differences between academic and non-academic centers (Supplementary

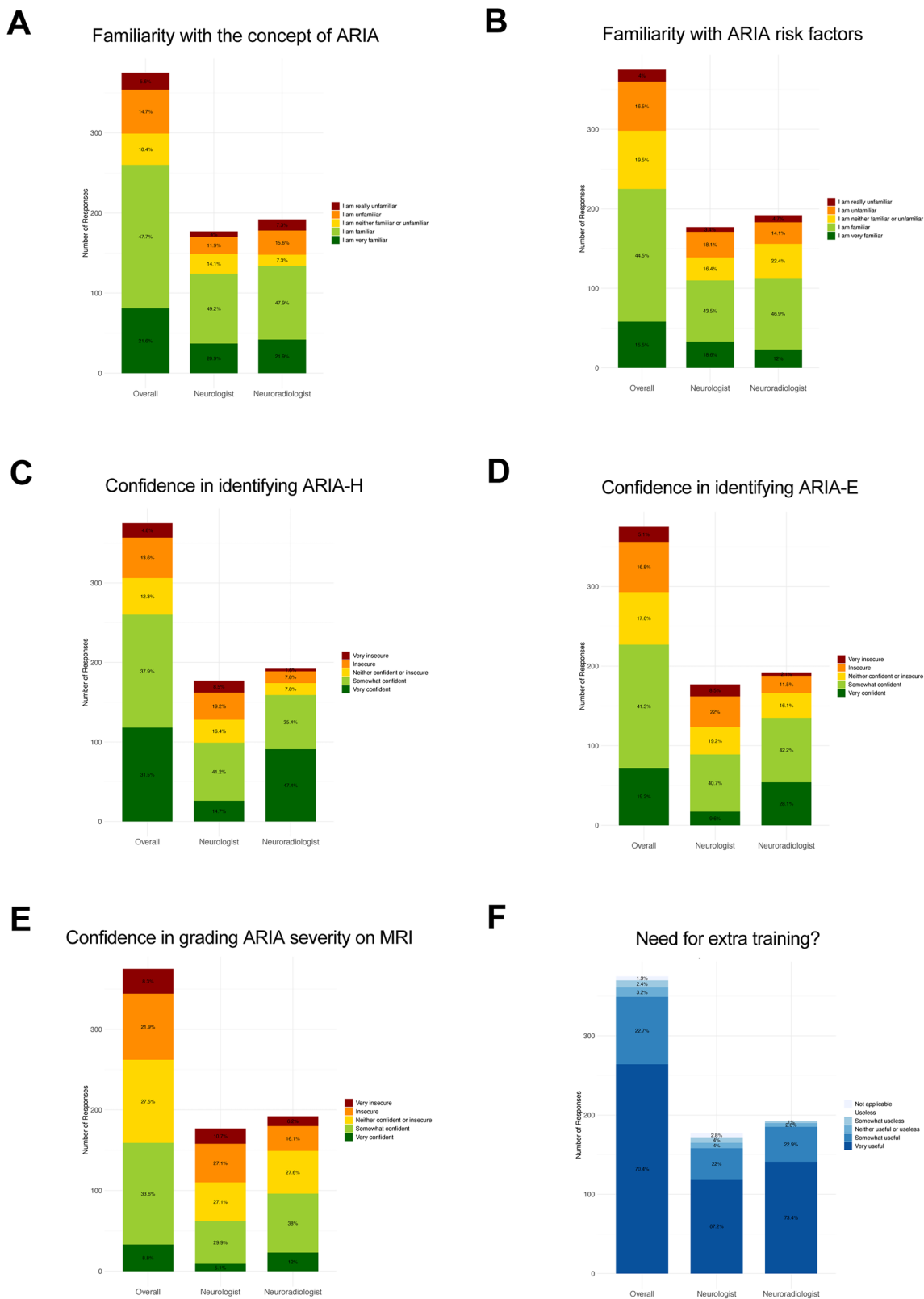


Fig. 4 Prior knowledge and confidence in ARIA rating and management. **A–F** Total number of responses considered was 375, with 177 from neurologists and 192 from neuroradiologists. Neuroradiologist designation includes the responses from both neuroradiologists and radiologists

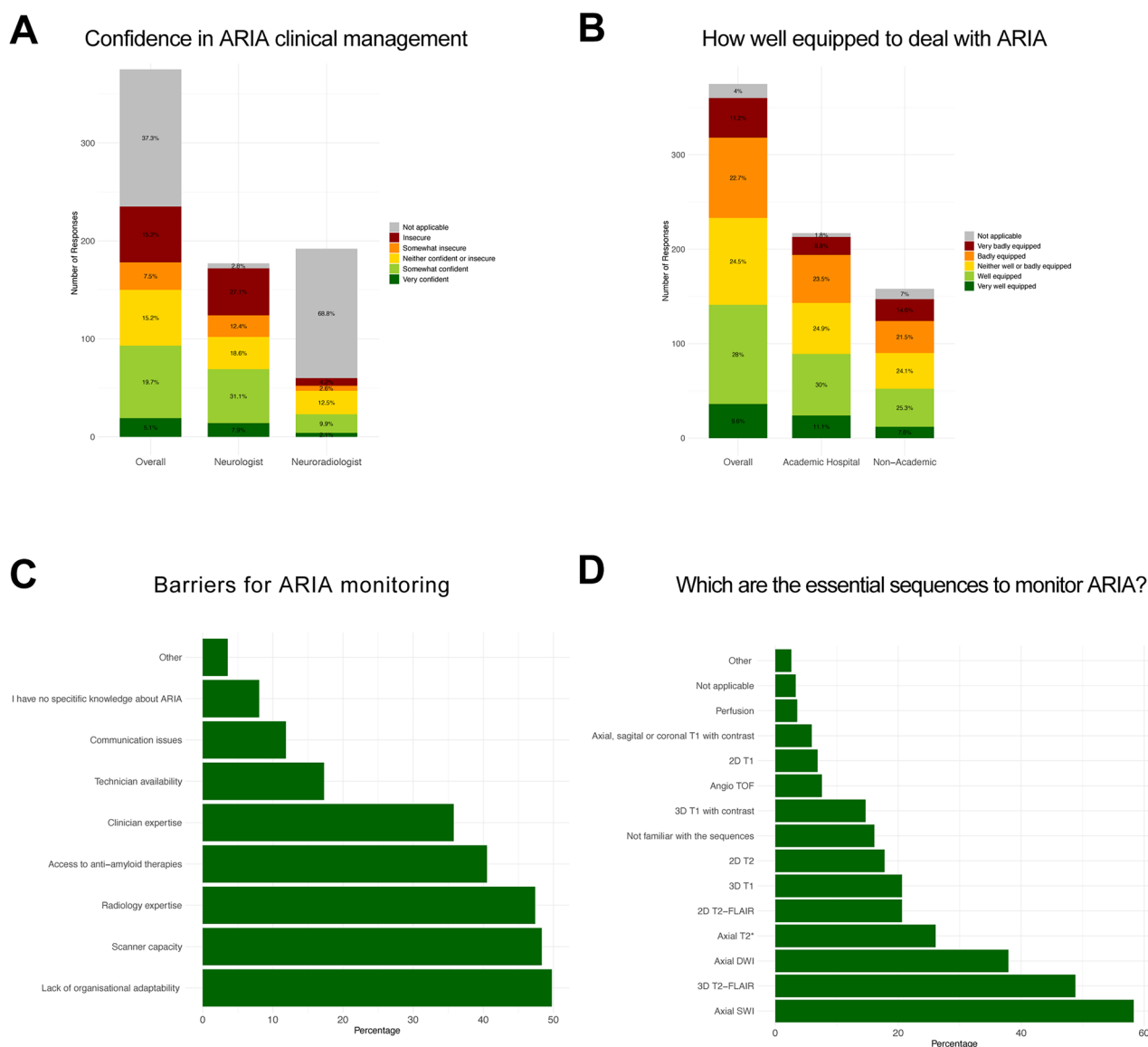


Fig. 5 How well are institutions prepared to deal with ARIA. **A** Total number of responses considered was 235, with 172 from neurologists and 60 from neuroradiologists. **B** Total number of responses considered was 360, with 213 from academic institutions and 147 from non-academic institutions. **C, D** Percentages of responses were calculated considering all 422 respondents. Multiple responses were considered per respondent. Neuroradiologist designation includes the responses from both neuroradiologists and radiologists

Fig. 2C), most likely since only a few European centers participated in anti-A β clinical trials. Indeed, when asked about the sequences needed for monitoring, the top responses were axial SWI and 3D T2-FLAIR (Fig. 5D), which differ from the ones optimized for clinical trials and generally advised for monitoring [8], which are axial T2*/gradient echo (GRE) and 2D T2-FLAIR.

Reporting, interpretation and AI approaches in ARIA

The expected increase in scans being performed will lead to a higher demand for reporting and require

communication protocols for MRI findings. Overall, respondents mentioned that provision of a report template would be preferred (65%) (Supplementary Fig. 3A), and that their preferred option for reporting cases in the context of ARIA would be local reading complemented with central reading for challenging cases (66%), with a higher percentage for neurologists (75%) compared with (neuro)radiologists (59%) (Supplementary Fig. 3B). Respondents also mentioned that follow-up discussion should be performed in a multidisciplinary meeting, either for all cases (40%) or a selected number of cases (54%),

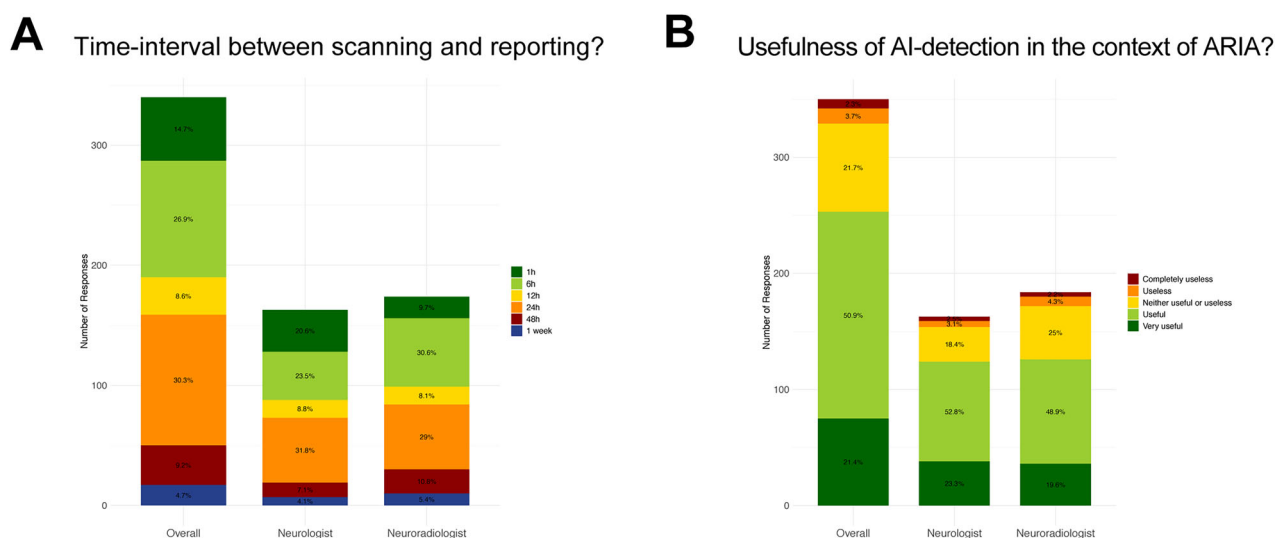


Fig. 6 Reporting, interpretation and AI approaches in ARIA. **A** Total number of responses considered was 340, with 163 from neurologists and 174 from neuroradiologists. **B** Total number of responses considered was 350, with 163 from neurologists and 184 from neuroradiologists. Neuroradiologist designation includes the responses from both neuroradiologists and radiologists

with no major differences between neurologists and (neuro)radiologists (Supplementary Fig. 3C). With the expected increased demands, the time estimated for an ARIA reading and report was either 10–15 min (29%) or 15–30 min (24%), with a higher percentage of neurologists (28% vs 6%) mentioning not knowing the estimated time, and specifically 67% (neuro)radiologists responding to estimate an ARIA report to take less than 15 min (Supplementary Fig. 3D). Regarding the optimal time interval for the report to be available after the scan is performed, overall the majority of respondents considered it desirable to be either within 24 h (30%) or even 6 h (27%). The percentage of neurologists expecting communication within 1 h was higher than (neuro)radiologists (21% vs 10%) (Fig. 6A).

AI approaches are being used increasingly by (neuro) radiologists, and in particular applications with algorithms offering lesion detection support. Overall, 25% of respondents mentioned that they currently use any AI approaches in dementia imaging, while those who do so mainly use it for volumetric assessments. In contrast, 72% of the respondents answered that AI approaches would be useful to very useful in the detection of ARIA, with a slightly higher percentage in neurologists compared to (neuro)radiologists (76% vs 69%) (Fig. 6B), and the majority would value quantitative features to support the grading of ARIA to be included in such a report. Finally, the majority of respondents (74%) were interested in contributing to a central database on ARIA (Supplementary Fig. 3E).

Discussion

With the introduction of anti-amyloid antibody therapies in clinical practice in Europe, drug labels will prescribe strict patient inclusion rules and standardized imaging monitoring for the detection of ARIA. As a consequence of the high prevalence of these side effects, a high number of brain MRI scans will need to be performed to exclude ARIA, which is expected to put significant pressure on both neurology and (neuro)radiology departments and emergency rooms, bringing with them the need for further management and imaging. We present the results of a European survey among neurologists and neuroradiologists, enquiring about overall knowledge on ARIA, rating and management, institutional readiness, and current views from the community regarding how interpretation, communication and AI approaches are employed to deal with ARIA findings. Though overall our results demonstrate reasonable awareness, there is a clear need for further action toward preparedness and additional training in ARIA assessment; therefore, we provide practical recommendations and highlight potential areas of research (Table 1 and 2).

Even though most hands-on experience in identifying ARIA by European clinicians comes from their involvement in trials, the majority of respondents—neurologists and neuroradiologists alike—perceived they were familiar to very familiar with the concept of ARIA and its risk factors. Though we did not actually test factual knowledge, it is likely that the surge in recent scientific and non-scientific publications on ARIA, as well as attention in several international

Table 1 Recommendations to professionals for ARIA monitoring

- Baseline and monitoring MRI scans should be performed under similar conditions (at minimum same protocol, same field strength, and preferably the same scanner).
- If the above cannot be accomplished, scan reading and reporting should mention and, if possible, account for differences in field strength (1.5 T vs 3 T) and/or differences in protocol.
- Current severity grading criteria are based on 2D T2*/GRE and axial 2D T2-FLAIR, since these sequences were used during clinical trials. More sensitive sequences, such as SWI and 3D T2-FLAIR, can be used, but consider doing them in parallel until new grading criteria are validated [8].
- Risk factors for ARIA, such as baseline microhemorrhages, extensive white matter hyperintensities, *APOE4* carriership, and dosage of anti-amyloid treatment, should be considered in the neuroradiological reporting, keeping in mind that (severe) ARIA can also occur without risk factors.
- Use of a standard template for reporting the severity of ARIA cases will facilitate communication of results between radiologists and treating physicians.
- A pre-established communication system should be in place and adapted to each institution to communicate urgent findings, and a periodic multidisciplinary clinical board should occur to discuss selected cases.
- Symptomatic ARIA cases should be scanned and reported urgently to exclude and/or differentiate from stroke.
- Routine monitoring ARIA scans should be read and reported in a timely fashion (preferably within 72 h), and any severe cases should be communicated urgently.
- More hands-on training is needed, and web-based interactive training could address this gap in part. The EAN and ESNR can have a relevant role in providing qualified training. A first example is the ARIA educational website www.ariaeducation.eu.

Table 2 Key areas where research is needed

- Validation of ARIA grading criteria for 1.5 T vs 3 T, T2*/GRE vs SWI, and 2D T2-FLAIR vs 3D T2-FLAIR. Since using 3 T, SWI and 3D T2-FLAIR increases the sensitivity to detect ARIA, re-adjusted criteria need to be defined for equivalent ARIA severity grading.
- Address potential differences in ARIA detection between vendors. This is an underexplored question that can have an impact on ARIA sensitivity detection and, consequently, severity grading.
- Clinical evaluation of the use of AI-based software that could aid in ARIA detection. Different tools are entering the market with this purpose, and research is needed to assess if they improve clinically relevant outcomes and/or impact workflow positively.
- Implementation and validation of accelerated acquisition protocols. Reducing the time of scan acquisition can be useful to deal with the expected increase in the number of scans to be performed in the context of ARIA monitoring; however, additional studies will be needed to see whether these faster protocols translate to higher throughput in clinical practice.
- Assessment of brain regional volumetric impact of anti-amyloid therapies is currently not recommended. It has been widely observed across anti-amyloid therapy studies that upon amyloid removal, the brain volume tends to decrease [4]. The significance of this observation and its potential effects and long-term consequences requires further study.
- Further identification of ARIA predictors. Even though risk factors for ARIA have been identified, such as *APOE4* carriership, microhemorrhages, extensive white matter hyperintensities and severity of amyloid pathology [9, 10], more research is needed to clarify if these differentially occur in all anti-amyloid drugs, and whether other factors could play a role.
- Relationship between radiologic and clinical severity. Evidence suggests that even though symptomatic ARIA-E events tend to be radiologically more severe and associated with ARIA-H, ARIA-E did not have a long-term impact on cognitive and functional performance [11]. More research is needed to clarify the characteristics of symptomatic ARIA and the long-term effects of ARIA.

conferences and courses, has brought about a basic level of knowledge among these professionals. It is of note, however, that due to a response bias, survey respondents may reflect a sample with a higher than average interest in these topics, and that average knowledge among European clinicians is likely to be lower.

In our survey, there was an overall high familiarity with both the concept of ARIA and risk factors to develop ARIA, and (neuro)radiologists showed higher confidence in identifying and rating ARIA than neurologists. Interestingly, (neuro)radiologists showed higher confidence in

identifying ARIA-H than ARIA-E, which underscores the lower degree of familiarity in visually finding ARIA-E on T2-FLAIR images than ARIA-H on SWI or T2*/GRE images, which may occur in other diseases as well. Importantly, the confidence in grading ARIA severity was lower than in identifying its presence, which underlines the need for further training, as radiological severity grading directly impacts clinical management, and radiologists should have a basic understanding of how their report affects further treatment decisions. This is reinforced by showing that most respondents would find extra

training useful. With respect to ARIA risk, *APOE* genotype is considered one of the most important risk factors, and *APOE4* carriers have an increased risk of developing ARIA [9, 10]. Consequently, the European Medicines Agency recently determined that patients with two *APOE4* copies have a contraindication to start either lecanemab or donanemab [16, 17]. Therefore, since patients with one *APOE4* copy still have an increased risk of developing ARIA, albeit less than with two copies, and can still be under anti-amyloid treatment, *APOE* genotyping information should be taken into account during MRI assessments, as it will determine the a priori chance of ARIA. Since the European Medicines Agency decision was made after the closure of our survey, we did not specifically ask about preparedness or hurdles with respect to genotyping. While in the U.S., the Food and Drug Administration has issued appropriate use recommendations for both lecanemab [15] and donanemab [18], in Europe, these still need to be implemented, and each European country will follow its own rules for reimbursement and/or availability of these drugs.

In order to meet the expected demands in brain MRI scans for ARIA assessment, health providers need to be properly equipped, and based on our results, only a minority mention being well-equipped to deal with this surge. According to our survey, most centers have either MRI 1.5 T or MRI 3 T available; however, the choice between which one to use is not trivial. It has been reported that MRI 3 T is more sensitive than MRI 1.5 T in detecting ARIA-like findings, such as microhemorrhages [19]. Even though recommendations for clinical trial scans were to be performed using either MRI 1.5 T or MRI 3 T, this was an acknowledged source of variability [10, 20]. Given that the diagnosis of ARIA is based on the comparison with a baseline brain MRI, acquired before initiation of anti-amyloid therapy [8], it is highly desirable that follow-up ARIA-monitoring brain scans are performed at equivalent MRI field strength as baseline, if not on the same scanner. This may introduce further logistical challenges that need further efforts. An additional challenge is the potential difference introduced by MRI equipment from different vendors, which is not yet resolved.

Our results further highlight that the most relevant barriers to the implementation of optimized ARIA procedures are the lack of organizational adaptability, such as the availability of MRI slots, which is directly connected with scanner capacity, and may be alleviated by accelerated scan protocols. Other barriers, such as radiological and clinical expertise to deal with ARIA, highlight the need for additional training. Additionally, the regional diversity in access to anti-amyloid therapies is pointed out as an important uncertainty, and even though it is unclear

which centers will be predominantly dedicated to implement these therapies in Europe, it is important to note that any patient undergoing anti-amyloid therapy is at risk to develop ARIA, underscoring the importance that all clinicians should be aware of how to handle an ARIA case.

Another important issue is the appropriate protocol to implement for ARIA monitoring. This is particularly pertinent as the majority of respondents did not yet have any protocols in place, their responses suggested heterogeneity in their views, and not an optimal understanding of current recommendations. During clinical trials, the protocol to identify ARIA-E relied on axial 2D T2-FLAIR and for ARIA-H on 2D T2*/GRE, which led to cut-offs for ARIA severity based on these basic acquisitions as they were widely available and optimized more homogeneously in clinical departments [20]. However, in current clinical practice, often other sequences are available, such as 3D T2-FLAIR and (3D) SWI, that provide higher sensitivity to detect ARIA-E and ARIA-H, respectively. Since the criteria for ARIA severity during clinical trials were established using axial T2-FLAIR and T2*, the usage of 3D T2-FLAIR and SWI for ARIA monitoring, if performed, should be done as add-on sequences, with the goal for future validation of ARIA severity grading with these more sensitive acquisitions. Whether T2*/GRE or SWI acquisitions are performed as either 2D or 3D should be taken into account, since it has been shown that 3D T2*/GRE is more sensitive than 2D T2*/GRE in detecting microhemorrhages [13]. Importantly, diffusion-weighted imaging should also be included in the basic ARIA monitoring protocol to differentiate from ischemic changes, in particular in the evaluation of symptomatic cases, since ARIA can present with symptoms that mimic a clinical presentation of stroke. Furthermore, stroke management in patients with suspected ARIA will require modifications in the “code stroke” and cardiology emergency protocols, securing direct access to MRI. In emergent situations, interdisciplinary and personalized decision-making between stroke and dementia teams is required, since patients on amyloid-lowering therapies will remain eligible for mechanical thrombectomy, but usually are contraindicated for thrombolytic therapy.

The identification of an ARIA case can therefore impact clinical decisions of whether to continue or interrupt treatment, and only a minority of respondents were confident in clinically managing an ARIA case. Additionally, (neuro)radiologists also mentioned that further clinical management was not as applicable to them. This highlights the specific roles that clinicians, such as neurologists, can play compared with (neuro)radiologists, the need for close communication and collaboration between them, and the need for extra training on how to manage these cases.

For the communication to flow effectively between physicians who diagnose ARIA on MRI and those who manage clinical decisions (e.g., interrupting dosing due to severe ARIA), a pre-established communication system should be in place, adapted to each institution, which would be particularly relevant for ARIA cases that require immediate intervention. A pre-established reporting template can also be helpful in clearer communication, and indeed, the majority of respondents concurred with that possibility. Such communication protocols should also contain agreements on the maximum time interval between scan and radiology report, on which opinions differed in our survey between (neuro)radiologists and neurologists.

With the expected increase in cases to be scanned, time is of the essence, both concerning the duration of acquisition, and the time spent on assessing the scan to provide the report for clinical decision. Even though the majority of respondents do not currently use AI-based approaches, there are already tools designed to help clinicians for ARIA identification [21], which could be implemented in clinical practice depending on local experience and preference. This is an active area of research, with various innovations coming up in the near future, which, complemented with advances in ultra-fast MRI protocols that reduce the time of acquisition by > 50% [22], can optimize the physical resources and lead to a focus on training physicians in handling patients undergoing ARIA monitoring.

In Europe, amyloid-lowering monoclonal antibodies are being introduced in stages. The EMA approved lecanemab in 2024 and donanemab in July 2025 for early AD with confirmed amyloid pathology [4, 5]. Formal European guidance on patient selection, MRI monitoring, and ARIA management is still in development, with national authorities and professional societies expected to adapt these frameworks to local settings. Evidence from pivotal trials such as CLARITY AD (lecanemab) and TRAILBLAZER-ALZ (donanemab) has informed these approvals, and ongoing follow-up studies may further refine ARIA risk estimates and monitoring recommendations. Our survey was conducted during this transitional phase, before unified protocols were established. Real-world implementation will also depend on economic and infrastructural feasibility. Pricing and reimbursement will be decided nationally, guided by health technology assessments and cost-effectiveness evaluations. Such heterogeneity will shape access, imaging capacity, and multidisciplinary coordination. The reported lack of readiness in our survey thus reflects not only training and logistical gaps, but also the ongoing uncertainty surrounding regulatory and financial implementation.

An important strength of our survey is the pan-European approach in which we leveraged the membership base of both the ESNR and EAN to reach neurologists and (neuro)radiologists of various levels of expertise (from trainees to experts) across Europe. An inherent limitation of surveys is the response bias caused by limited response rates, which may not be evenly distributed across regions and expertise levels. Although we do not know the exact number of persons who received the survey, as we allowed forwarding of the invitation, we do know that it was distributed at least to several thousands of EAN and ESNR members, yielding a modest amount of 476 responses, of which 422 were from European institutes. Though this amounts to a low response rate, it is not different from previous ESNR surveys using a similar approach, which yielded either a similar or lower amount of responses [23, 24]. Even though responses were biased by countries where dissemination was more efficient, it still covered the vast majority of European countries, with a good balance between neurologists and (neuro)radiologists, and years of clinical experience. We cannot exclude that participation is skewed toward respondents more engaged in EAN and ESNR activities, and potentially more likely to be aware of current baseline knowledge on ARIA. It is still unclear whether anti-amyloid antibody therapies will be widely available to be administered regardless of the differentiation level of the clinic center, but the pool of candidate patients potentially benefiting from these therapies will likely be followed from primary care centers to academic hospitals. In accordance with the majority of respondents who would find it useful to get additional training on ARIA, we propose that multiple initiatives should be promoted to improve the knowledge on how to handle ARIA cases. Among the initiatives undertaken by this working group is the development of an educational website on ARIA, specifically designed for the European clinical community to provide a platform for training and testing the knowledge regarding ARIA pathophysiology, identification and management (www.ariaeducation.eu).

Conclusions

With this survey, we provide an overview of the current state regarding the knowledge, preparation and expectations on the expected increase in ARIA cases in the near future by the European clinical community. Based on this survey, our working group has identified key questions, with recommendations of how to handle ARIA cases in Europe and unresolved challenges that should be tackled with research and educational approaches (Table 1).

Abbreviations

AD	Alzheimer's disease
AI	Artificial intelligence
ARIA	Amyloid-related imaging abnormalities
ARIA-E	ARIA-edema/effusion
ARIA-H	ARIA-hemorrhage/hemosiderin
A β	Amyloid beta
EAN	European Academy of Neurology
ESNR	European Society of Neuroradiology
GRE	Gradient echo
MRI	Magnetic resonance imaging
p-tau	Phosphorylated tau
SWI	Susceptibility-weighted imaging
T2-FLAIR	T2-fluid-attenuated inversion recovery

Supplementary information

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Compliance with ethical standards

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Statistics and biometry

No complex statistical methods were necessary for this paper.

Informed consent

Written informed consent was not required for this study because the results presented were based on a voluntary online survey.

Ethical approval

The questionnaire was reviewed and approved by the ESNR and EAN scientific panels.

Study subjects or cohorts overlap

Not applicable.

Methodology

- Observational study based on an online survey

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