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Kaushik, K.; Eijkholt, M.M.; Graeff, N. de; Banerjee, G.; Werring, D.J.; Terwindt, G.M.; ... ; Wermer, M.J.H.

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PERSPECTIVE

Ethical considerations of disclosure of iatrogenic cerebral amyloid angiopathy

Kanishk Kaushik[1] | Marleen M. Eijkholt[2] | Nienke de Graeff[2] | Gargi Banerjee[3] | David J. Werring[4] | Gisela M. Terwindt[1] | Ellis S. van Etten[1] | Marieke J. H. Wermer[5]

[1]Department of Neurology, Leiden University Medical Centre (LUMC), Leiden, the Netherlands

[2]Department of Medical Ethics and Health Law, LUMC, Leiden, the Netherlands

[3]MRC Prion Unit, Institute of Prion Diseases at University College London (UCL), London, UK

[4]Stroke Research Centre, Department of Brain Repair and Rehabilitation, UCL Queen Square Institute of Neurology and the National Hospital for Neurology and Neurosurgery, London, UK

[5]Department of Neurology, University Medical Center Groningen (UMCG), Groningen, the Netherlands

Correspondence
Kanishk Kaushik, Department of Neurology, Leiden University Medical Centre (LUMC), LUMC, Albinusdreef 2, 2300RC Leiden, the Netherlands.
Email: k.kaushik@lumc.nl

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Abstract

Cerebral amyloid angiopathy (CAA) causes stroke and cognitive decline. The recently identified iatrogenic CAA subtype (iCAA) is thought to be transmitted through medical procedures involving cadaveric human material and potentially neurosurgical instruments or blood transfusions. This raises ethical questions concerning disclosure of iCAA. We consider ethical arguments concerning three disclosure-related questions. Should clinicians disclose their suspicion of iCAA to patients presenting with CAA and a history of relevant exposure? Should clinicians recommend the additional tests needed for iCAA diagnosis? Should clinicians proactively identify and notify asymptomatic at-risk individuals who are unaware of their risk? We conclude that disclosure of the iCAA-diagnosis and communication of diagnostic uncertainties are warranted, based on professional responsibility to facilitate autonomous decision-making, despite limited clinical benefits. While certain diagnoses are impossible, recommending additional diagnostics can provide diagnostic support and exclude other causes. Notification of known exposure-confirmed, asymptomatic, at-risk individuals seems warranted; however, proactive identification remains challenging.

KEYWORDS
amyloid beta, cerebral amyloid angiopathy, disclosure, ethics, iatrogenic, intracerebral hemorrhage, prion, small-vessel disease, stroke, transmission

Highlights

- iCAA may result from Aß transmission via medical treatments.
- We discuss three clinically relevant disclosure-related ethical questions that arise due to the uncertainty surrounding the discovery of iCAA.
- We focus on disclosing to patients with suspected iCAA the recommendation of additional diagnostics and proactive identification and notification of asymptomatic persons at risk.

- This analysis supports clinicians in their decision to disclose a presumed iCAA diagnosis and when informing patients about additional CAA diagnostics.
- Our findings serve as a reference tool for handling disclosure of future discoveries of presumed iatrogenesis (e.g., that of iatrogenic Alzheimer's disease).

1 | INTRODUCTION

Cerebral amyloid angiopathy (CAA) causes stroke and cognitive decline due to cerebrovascular amyloid beta (Aβ) accumulation.[1] We can distinguish hereditary and non-hereditary (sporadic) CAA, the latter being a more prevalent, age-related disease that is typically diagnosed at age >50 years.[2] Iatrogenic CAA (iCAA) may result from Aβ transmission via medical treatments involving cadaveric human material and potentially via neurosurgical instruments and blood transfusions.[3–5] After transmission, propagation of the exogenous Aβ in the recipient is thought to occur in a proteinopathic or "prion-like" manner.[6] The prevalence of iCAA might be 4% in patients with CAA aged >50 years and 45% in patients aged <55 years at presentation.[4] To date, >125 patients with presumed iCAA have been identified, most of whom were related to intracranial use of cadaveric dura mater. Currently, in the absence of disease-modifying treatments, clinical management aims to relieve neuro(psycho)logical symptoms and prevent intracerebral hemorrhage (ICH) recurrence through antihypertensive management.[2]

Similar to when acquired Creutzfeldt Jakob disease (CJD) was identified, ethical dilemmas arise regarding disclosure of diagnosis in clinical practice due to uncertainty about iCAA etiology, prognosis, and lack of treatments. CJD is the classic example of a human prion disease, of which the acquired variant has been related to treatments with cadaveric human materials but with a higher mortality rate than CAA. In both iCAA and CJD, the uncertainties differ from regular probabilistic medicine, in which (scientific) uncertainties remain, primarily because of the sensitive nature of presumed iatrogenesis. Lessons from recognizing and managing acquired CJD highlight that the identification of iCAA today can have important public health implications, and the fact that a historical medical procedure, initially performed with the intention of improving patient outcomes, now causes an existentially transforming disease characterized by ICH, cognitive decline, and disability warrants a reflection on the communication strategy of the medical community with respect to such conditions.

We discuss three important questions. First, should patients presenting with symptoms and MRI findings suggestive of CAA be informed about an iatrogenic cause if they had a relevant exposure? Second, if disclosure is warranted, should clinicians recommend the additional diagnostic tests needed to differentiate "probable" from "possible" iCAA? Third, should asymptomatic at-risk recipients of cadaveric human materials, who are unaware of their risk of iCAA, be proactively identified and notified? We scrutinize various arguments and offer recommendations for clinical practice. Our analysis addresses practical approaches for patients suspected to have, or at risk of having, iCAA.

2 | CONTEXT AND SCOPE

2.1 | Clinical context

Patients who present with ICH or cognitive decline can have underlying CAA. Clinical work-up is done in patients presenting with spontaneous ICH, transient focal neurological episodes, convexity subarachnoid hemorrhage, or cognitive decline and encompasses radiological imaging (CT/MRI) and exclusion of other causes (e.g., cerebral cavernous malformations).[2] Genetic causes are routinely explored in patients presenting with unexplained ICH or early-onset cognitive decline.[7] In brief, according to the Boston Criteria 2.0, a definite CAA diagnosis can be made with a full *post mortem* investigation demonstrating severe CAA vasculopathy in the absence of other diagnostic lesions; "probable CAA" is diagnosed when the presenting patient is aged ≥50 years and has either (i) at least two strictly lobar hemorrhagic CAA-related lesions or (ii) one lobar hemorrhagic lesion and one white matter feature in the absence of other causes of hemorrhagic lesions on MRI. In addition, "possible CAA" can be diagnosed in patients ≥50 years with only one strictly lobar hemorrhagic feature or one white matter feature. The "probable CAA" diagnosis can be made more certain when supporting histopathology (e.g., obtained from biopsy) is available.[2] In clinical practice, however, supporting histopathology is seldom available, so a distinction between probable and definite CAA can generally not be made in clinical practice. Similarly, exclusion of other causes can be difficult in clinical practice due to clinical mimics, the presence of comorbidities, or practical difficulties in performing diagnostic work-up.

Some patients presenting with CAA have a history of potential exposure to exogenous Aβ and might therefore have iCAA. The diagnostic criteria for iCAA distinguish probable from possible iCAA based on relative certainty and imaging features (which, in contrast to the Boston Criteria, allow for some, but not predominantly, deep hemorrhagic imaging features). Patients have probable iCAA if (i) positron emission tomography (PET), cerebrospinal fluid (CSF), or biopsy findings provide evidence of Aβ accumulation in the CNS and (ii) genetic causes are excluded. Possible iCAA is considered when supporting diagnostics are not available or performed, but the patient has a history of relevant exposure.[3]

The ethical dilemmas at hand arise because the newly recognized iCAA diagnosis comes with uncertainties regarding diagnosis, disease risks, and prognosis. In clinical practice, in non-hereditary cases, the alternative diagnosis to iCAA would be sporadic CAA, "young-onset CAA" (age < 50 years), or CAA mimics.

2.2 | Scope

Our analysis addresses practical approaches for patients suspected of having or at risk of iCAA. The full range of medical procedures causing iCAA is unknown. However, inferences have been drawn from the only other iatrogenic disease caused by protein transmission in humans, iatrogenic CJD.[8] Potential exposure to exogenous Aβ encompasses, but is not limited to, the use of cadaveric dura mater, cadaveric human growth hormone (hGH), and relevant neurosurgical procedures. For clarity, we consider exposure to cadaveric materials in our paper, expecting generalizability to other exposure mechanisms or outcomes as they arise.[5,9] We omit ethical neurogenetic considerations, as they were discussed elsewhere.[10] We simplify by not considering legal aspects (e.g., concerning product manufacturer liability) of our research questions, acknowledging that such concerns may be relevant but raise a whole different level of complexity.

3 | SHOULD CLINICIANS DISCLOSE THEIR SUSPICION OF IATROGENIC CAA TO PATIENTS PRESENTING WITH SYMPTOMS, SUGGESTIVE MRI FINDINGS, AND HISTORY OF RELEVANT EXPOSURE?

While standards of informed consent require informing patients about their diagnosis and prognosis, questions arise when elements of the diagnosis are uncertain, to some degree, as in the case of iCAA. We can imagine a spectrum of reasons why or why not to disclose this suspicion to a patient. This all might depend on the level of certainty of diagnosis, as we discuss below. This analysis leads us to conclude that disclosure is warranted in nearly all cases.

3.1 | Arguments for disclosure

3.1.1 | Respect for patient autonomy

The main argument to disclose is based on respect for autonomy, allowing individuals to be independent, self-governing agents motivated by their authentic selves and not by externally imposed conditions.[11]

Providing patients with incomplete or filtered information is not compatible with this principle. Withholding information limits patients in acquiring the understanding of their (health) state required for autonomous decision-making.[12] Full understanding might incentivize patients to actively take control of their health, for example, by participating in secondary (stroke) prevention strategies.[13,14] Additionally, disclosure might increase patient understanding of the causes of their complaints, yield a better sense of control over their health, and aid in working toward acceptance.[13,15,16] Moreover, this understanding can influence non-medical life choices (e.g., concerning education, financial, or legal issues), and it can matter for patients' personal identity, including their creation of a coherent life story to understand themselves (personal narrative).[12,17] Furthermore, disclosure in the context of respect for autonomy is endorsed by vascular neurologists, who, in the context of diagnosing sporadic CAA with new biomarkers, viewed non-disclosure due to a lack of treatment options as paternalistic.[13]

One might argue that disclosure of presumed iatrogenesis is not required for patients to actively take control of their health, for example, because secondary (stroke) prevention strategies and clinical management are similar for iCAA and any alternative CAA diagnosis. However, it is yet to be determined if this is correct, as is discussed in the next section. Moreover, even if the prognosis and therapeutic options would later turn out to be the same, a patient could make different non-medical choices (e.g., concerning legal recourse) when presumed iatrogenesis is disclosed.

3.1.2 | Clinical benefit: Disclosure might prevent harm

Although no disease-modifying treatments for CAA are available, some of its symptoms (e.g., seizures, neuropsychiatric symptoms) can be managed. Importantly, antihypertensive management, and ideally avoidance of anticoagulative therapy, can reduce ICH incidence or recurrence.[18,19] In the current literature, the ICH-recurrence rate in iCAA appears to be higher than in sporadic CAA, although this might reflect reporting bias.[4] Although it is not yet known if early intervention in iCAA is beneficial, the absolute benefit will be greater in iatrogenic than in sporadic CAA if the baseline recurrence risk in iCAA is greater.[18] Having iCAA might therefore increase the urgency of and absolute benefit from secondary prevention.

At the same time, one could argue that, regardless of a potential risk difference, all patients with CAA should receive adequate antihypertensive management to reduce the risk of developing an(other) ICH. This would not require disclosure of presumed iatrogenesis. Therefore, though there is a potential gain from the increased urgency for secondary prevention, the expected clinical benefit of disclosure of presumed iatrogenesis is limited until further treatment becomes available.

3.1.3 | Scientific/societal benefit

We recognize that there might be a scientific benefit to disclosure because it might increase the willingness of patients to partake in scientific studies (further discussed under research question 2). However, it is not evident that we should weigh this societal benefit under the current research question, as disclosure of iatrogenesis motivated (predominantly) by scientific merits can also undermine the right of self-determination of an individual.

3.2 | Arguments against disclosure

3.2.1 | Diagnostic uncertainty

In newly identified diseases, limited data can cause diagnostic uncertainty. The current first version of the iCAA diagnostic criteria has not

yet been extensively applied, leaving their diagnostic testing accuracy (including sensitivity and specificity) to be determined. This poses the risk of misdiagnosing individuals through over- or underdiagnosis.

We acknowledge the potential for unnecessary psychological harm from misdiagnosis for a specific patient, but it is questionable whether this risk justifies non-disclosure (as discussed in the next section). In our view, the argument concerning diagnostic uncertainty is insufficiently convincing to forego disclosure of presumed iatrogenesis by default for all patients. Based on the combined experimental and clinical literature, the current evidence for the transmissibility of Aβ is beyond reasonable doubt, and currently no alternative explanation encompassing all reported patients exists.[3,4,6,20] In addition, obtaining further certainty through research can be time-consuming.[8,21]

Moreover, the basis for the iCAA diagnosis relies on historical records (patient notes) that may have been destroyed or lost or are ambiguous in content (e.g., mentioning "artificial dura"). This increases the diagnostic uncertainty for a specific patient.

Therefore, despite the best clinical and scientific efforts, the absence of crucial information might cause diagnostic and prognostic uncertainty to persist. Meanwhile, the current iCAA diagnostic criteria provide a useful framework for medical decision making. As we wait for science to advance, clinicians should communicate the diagnostic and prognostic uncertainties to suspected patients with iCAA out of respect for autonomy, rather than opt for non-disclosure.

3.2.2 | Psychological harm

Disclosure might lead to psychological harm because the true iCAA-related risks (e.g., concerning prognosis or the proportion of exposed patients that will develop symptoms) are still being discovered, prompting the argument that these risks therefore should not be fully communicated. According to this reasoning, physicians should withhold information about iatrogenesis from their patients because it could psychologically harm them.

However, non-disclosure of iCAA might not limit psychological harm. In addition to the previously mentioned arguments concerning diagnostic uncertainty, the additional psychological harm caused by disclosure of possible iatrogenesis rather than an alternative CAA diagnosis is unclear. We note that patients are often unaware that cadaveric materials were used during neurosurgery, which in itself can be perceived as a disturbing idea. Nevertheless, other examples show that the psychological harm is unlikely to be substantial. For example, in variant CJD, the majority of recipients of potentially contaminated blood, a mode of transmission that was later deemed to be very rare, preferred to be notified.[22–24] Moreover, these individuals experienced little sustained emotional distress afterward.[25] Similarly, patients at risk of iatrogenic CJD preferred to be notified.[26]

Moreover, to justify non-disclosure to prevent psychological harm, clinicians should have a clear and concrete understanding of the harm that is prevented for a specific patient.[12] Therefore, opting for non-disclosure by default for all patients does not appear to be justified. On the contrary, by providing transparency through disclosure, patient trust and, thus, the doctor-patient relationship might be cultivated. The societal preference for this transparency and honesty, even in the case of uncertainties or sensitive subject matter, can also be appreciated in various healthcare legislation.[27]

Additionally, we argue that, especially in younger patients, non-disclosure has the potential of doing more psychological harm than disclosure would, as withholding disclosure does not prevent them from searching the internet for information about (young-onset) CAA or finding media coverage regarding this topic. At the time of writing, on PubMed and Google, most search results for *"(young-onset OR young onset) AND CAA"* and some for CAA only (search date: January 2, 2024) relate to iatrogenic CAA. Thus, it is likely that patients could (un)intentionally find out about the possible iatrogenesis, but without the supportive contextual communication a physician could provide. This, in turn, could cause psychological harm.

3.2.3 | Respect for autonomy – right not to know

Finally, disclosure might be unjustified due to the right not to know (RNTK): the right that individual have to control the information provided to them by specific individuals and to express the will not to receive certain information in a specific institutional context.[28] To express their RNTK, patient need to be provided with a minimal degree of information to make an informed and autonomous decision regarding their willingness to become further informed about their disease.[28] In the current context, the RNTK might mean that a patient, after understanding the required minimal degree of information, might autonomously decide to wish to remain ignorant about iatrogenesis as the presumed cause. While providing the minimal degree of information that patients have *some* risk of iCAA is challenging, physicians would impair autonomous decision-making if they a priori assumed the RNTK for all patients in general and should therefore refrain from doing so.[28] Naturally, if an informed patient expresses a will not to know, this should be respected.

3.3 | Why disclosure is warranted

We conclude that disclosure is warranted for the most certain patient group (cadaveric exposure confirmed, no differential diagnosis) and in more uncertain cases (e.g., older age, non-typical neurosurgery, surgical notes unavailable) if diagnostic uncertainties are communicated. By disclosing, clinicians fulfill their professional responsibility of transparently informing patients, respecting their autonomy, and empowering autonomous decision-making, specifically with regard to non-medical choices. This outweighs the limited potential for causing psychological harm and the risk of misinforming patients, as it is based on the best available current knowledge. At the same time, because antihypertensive management and avoidance of anticoagulative therapy should be regular care for all CAA patients, regardless of whether iCAA is suspected, the specific clinical benefit of disclosure might be limited.

4 | SHOULD CLINICIANS RECOMMEND THE ADDITIONAL DIAGNOSTIC TESTS NEEDED TO CLASSIFY THE DIAGNOSIS AS PROBABLE OR POSSIBLE IATROGENIC CAA?

Having established that physicians should ideally disclose the diagnosis of iCAA, a further question, then, is if they should actively counsel for further diagnostic work-up to classify the diagnosis as probable or possible iCAA. This question arises because the interpretation of the relevant diagnostic tests can prove difficult and because there is wide local variation in views about the necessity of performing these tests, often influenced by their limited local availability. To answer this question, we considered the diagnostic value and proportionality of the diagnostic tests, which could be questioned, and their potential for societal/scientific benefit.

4.1 | Determining the appropriate test

According to the diagnostic criteria, the diagnostic tests encompass genetic testing (beyond the scope of this manuscript, as explained under Scope) and either brain biopsy, lumbar puncture, or amyloid-PET to demonstrate the presence of Aβ in the CNS.

The proportionality of these additional diagnostic tests might be questioned. Although brain or leptomeningeal biopsy can demonstrate the presence of histopathological CAA, it is invasive and comes with intra- and periprocedural complication risks (including hemorrhage). Additionally, biopsy could hypothetically cause further transmission of iCAA via surgical instruments. These risks render biopsy a less preferred modality for iCAA diagnosis.

This leaves two less invasive procedures: the lumbar puncture and amyloid-PET. Currently, the diagnostic value of these modalities is uncertain due to the absence of validation studies defining appropriate cut-offs to discern CAA from Alzheimer's disease.1 However, while this is a limitation in elderly patients, young patients generally do not have Alzheimer's disease (co-)pathology, and the Boston criteria were not validated for them. Therefore, decreased levels of CSF Aβ40 and Aβ42 or abnormal amyloid-PET could aid clinicians by supporting the CAA diagnosis.1,2 Moreover, in all patients, CSF/PET findings can aid in excluding alternative, potentially treatable diagnoses (e.g., cerebral vasculitis). Thus, recommending these diagnostic modalities seems appropriate.

At the same time, we note that not PET, CSF, or biopsy could prove iatrogenesis and that, unlike genetic testing, normal CSF/PET findings did not exclude a CAA diagnosis. Therefore, the implications of results should be clearly communicated, as normal findings might lead to a false sense of security.

Moreover, we note that these diagnostics are costly and not widely available, which can cause healthcare discrepancies in countries where medical care is not freely accessible. In such cases, or if a patient prefers not to undergo them, regular clinical and radiological follow-up to evaluate progression of CAA over time might be a pragmatic alternative approach. Of note, this approach does not exclude or confirm iatrogenesis and does not differentiate probable from possible iCAA, though it does aid in supporting the CAA diagnosis.

4.2 | Scientific/societal benefit

There might be a societal benefit of differentiating probable from possible iCAA in patients, as the increased relative diagnostic certainty might improve the scientific accuracy of findings in studies on iCAA, thereby hopefully advancing the CAA field as a whole. Patient interests would seem indirectly served by the increase in knowledge in the field. In our clinical experience, several patients proactively expressed their willingness to partake in scientific studies or donate their brains after death due to the rarity of the disease without being asked by their physician after they had their diagnoses disclosed. Thus, one might argue that clinicians have a responsibility, within the boundaries of the legal and medical-ethical frameworks, to facilitate patient engagement in scientific research.

4.3 | Counsel through shared decision-making

Overall, recommending a (brain or leptomeningeal) biopsy for iCAA diagnosis seems unjustified due to the invasive nature of the procedure, with risks of complications and a theoretical and, as of yet, unquantified risk of Aβ transmission to other patients via contaminated surgical instruments. However, patients can be empowered in deciding what medical information they (do not) want to know through informed discussions about clinical follow-up options, such as MRI or CSF/PET diagnostics – modalities that are not able to provide absolute diagnostic certainty. In our view, there is a place for CSF/PET diagnostics, as they provide diagnostic support for the CAA part of the diagnosis and help exclude other diagnoses. Clinicians should note that CSF/PET diagnostics can help exclude other causes but do not confirm iatrogenesis. Therefore, the results could lead to a false sense of security if they are not clearly communicated. Finally, there is an important scientific benefit in these diagnostics, and as furthering science also aids in re-evaluating the weighing of ethical arguments raised in this manuscript, it seems appropriate that clinicians also make patients aware of iatrogenic CAA research endeavors that exist.

5 | SHOULD CLINICIANS PROACTIVELY IDENTIFY AND NOTIFY ASYMPTOMATIC "AT-RISK" RECIPIENTS OF CADAVERIC HUMAN MATERIALS WHO ARE CURRENTLY UNAWARE OF THEIR RISK?

The context of being asymptomatic and at risk of iCAA differs from, for example, hereditary CAA. Unlike in hereditary disease, there is no test available to exclude or unequivocally confirm iCAA, and key information, such as confirmation of exposure status, is often lacking. This prevents the adoption of widely used strategies for counseling of

asymptomatic at-risk individuals. Therefore, we discuss whether we should proactively identify and notify these persons in case of iCAA.

5.1 | On notification

Arguments to notify asymptomatic at-risk individuals are similar to those raised concerning disclosure of presumed iatrogenesis, including the professional responsibility of transparently informing recipients and the facilitation of autonomous decision-making of those at risk. In addition to those arguments, notification might improve clinical outcome by increasing health literacy, for example, concerning the importance of primary prevention and recognition of cognitive decline or stroke-related symptoms.[29] Timely diagnosis of CAA at pre-symptomatic or early symptomatic stages might have consequences for antithrombotic management, as is the case in other CAA-subtypes (although no iCAA-specific literature is currently available). Additionally, in case they do develop neurological symptoms, persons who were notified can help inform clinicians about their medical history.

Furthermore, due to the sensitive nature of iatrogenesis, there is extra value in transparency from the medical profession through precautionary disclosure to maintain societal trust. Failure to disclose or communicate might be perceived as more erroneous than the potential negative publicity of notification.[30]

Conversely, the knowledge of potentially developing a non-preventable, non-modifiable disease that can result in significant disability carries a potential for psychological harm.[15,31] This would be unjustified if notification were inaccurate and the person never developed iCAA (argued under *diagnostic uncertainty*). Therefore, notification might best be targeted only to known exposure-confirmed individuals (Appendix 1).

5.2 | Identification and notification: a limited obligation

In summary, notification may be justified for known exposure-confirmed at-risk asymptomatic individuals, based on the arguments concerning patient autonomy, transparency, and (although limited) potential for clinical benefit through increased health literacy. As with disclosure, uncertainties should be well communicated. As in predictive genetic testing, individuals should receive post-notification (psychological) care as required.[10,14]

At the same time, proactive identification of the potentially exposed (e.g., through review of historical surgical lists for operations using cadaveric dura) has the potential to be inaccurate and unfeasible, resulting in substantial psychosocial impact in the absence of sufficient clinical benefit. This weighing might change if the infectiousness of cadaveric material for developing CAA is greater than currently expected or if other causative agents, such as blood transfusions, are established.

6 | LIMITATIONS

Our ethical appraisal has limitations. First, we acknowledge that diagnostic uncertainty increases in older patients as the incidence and prevalence of sporadic CAA increase with age.[32] However, as no pathophysiological basis exists for an age limit to iatrogenesis, we did not restrict our argumentation to young patients. Second, we did not assess legal aspects. We believe that the assessment of the urgency and the resolution of potential legal issues are best entrusted to legal experts or left until more research on iCAA has been done. In general, we presume that legal aspects might favor disclosure to patients by improving autonomy but, given potential financial and other benefits for a patient, might result in clinicians becoming more conservative in making the iCAA diagnosis. Third, as we focused on the doctor–patient relationship, societal implications, such as questions concerning disclosure to public health bodies, were not considered and might be investigated in the future. Finally, in our analysis, we drew parallels between iCAA and iatrogenic CJD, as the presumed (prion) mechanisms and exposures (medical procedures involving cadaveric dura mater) are similar. However, their disease course and prognosis are different. This might cause the weighting of the arguments related to patient values to change. Similarly, as certainty about the transmissibility of Aβ as the cause of iCAA increases, other considerations might be at stake. Future studies might investigate these patient preferences in CAA to evaluate if such differences exist, which in turn could help in future similar disclosure-related dilemmas.

7 | CONCLUSIONS

In conclusion, physicians should fulfill their professional responsibility to inform patients of presumed iatrogenesis and communicate the related uncertainties. Disclosure likely outweighs psychological harm. While a definite iCAA diagnosis is unattainable, CSF/PET tests can aid diagnosis and rule out other causes. Notification of known exposure-confirmed asymptomatic at-risk individuals seems reasonable as it facilitates patient autonomy, potentially provides clinical benefits, and maintains trust in the medical profession. However, proactive identification at a population level of potentially exposed individuals is challenging and risks unaffected individuals being incorrectly informed. Our arguments should be viewed as part of an evolving discussion, aiming to optimize care for all CAA patients and aid the medical community in case of future iatrogenic diseases.

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There are no conflicts of interest for any of the authors (K. Kaushik, M.M. Eijkholt, N. de Graeff, G. Banerjee, D.J. Werring, G.M. Terwindt, E.S. van Etten, M.J.H. Wermer). Author disclosures are available in the Supporting Information.

CONSENT STATEMENT

Consent for this study was not necessary, as no human subjects other than the authors were included in this study.

ORCID

Kanishk Kaushik https://orcid.org/0000-0003-1429-6853

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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