Incidence of Symptomatic Hemorrhage in Patients With Lobar Microbleeds

Ellis S. van Etten, MD; Eitan Auriel, MD, MSc; Kellen E. Haley, BA; Alison M. Ayres, BA; Anastasia Vashkevich, BA; Kristin M. Schwab, BA; Jonathan Rosand, MD, MSc; Anand Viswanathan, MD, PhD; Steven M. Greenberg, MD, PhD; M. Edip Gurol, MD, MSc

Background and Purpose—Lobar microbleeds suggestive of cerebral amyloid angiopathy (CAA) are often identified on MRI in the absence of lobar intracerebral hemorrhage (ICH). We compared the baseline characteristics and risk of subsequent ICH among such patients to those presenting with CAA-related lobar ICH.

Methods—Clinical data (demographics, risk factors), apolipoprotein E genotype, neuroimaging markers of CAA severity (microbleed counts, leukoaraiosis volume), and clinical outcomes (incidence rates of ICH and death during a mean follow-up of 5.3±3.8 years) were compared between 63 patients enrolled because of incidentally found microbleeds and 316 with CAA-related ICH, in our prospectively enrolled cohort. Predictors of incident ICH were explored in the microbleed-only patients using multivariable Cox regression models.

Results—Microbleed-only patients shared similar demographic, apolipoprotein E, and vascular risk profiles with lobar ICH patients, but had more lobar microbleeds (median, 10 versus 2; P<0.001) and higher leukoaraiosis volumes (median, 31 versus 23 mL; P=0.02). Microbleed-only patients had a nontrivial incidence rate of ICH, not different from patients presenting with ICH (5 versus 8.9 per 100 person-years; adjusted hazard ratio, 0.58; 95% confidence interval, 0.31–1.06; P=0.08). Microbleed-only patients had a higher mortality rate (hazard ratio, 1.67; 95% confidence interval, 1.1–2.6) compared with ICH survivors. Warfarin use and increasing age were independent predictors of future ICH among microbleed-only patients after correction for other covariates.

Conclusions—Patients presenting with isolated lobar microbleeds on MRI have a genetic, neuroimaging, and hemorrhagic risk profile suggestive of severe CAA pathology. They have a substantial risk of incident ICH, potentially affecting decisions regarding anticoagulation in clinical situations. (Stroke. 2014;45:00-00.)

Key Words: cerebral amyloid angiopathy, cerebral hemorrhage, cerebral microbleeds, magnetic resonance imaging.
Hospital with neurological symptoms and enrolled in a longitudinal cohort study of the natural history of CAA. Patients were enrolled with definite or probable CAA according to the previously validated Boston criteria by which individuals aged ≥55 years with multiple hemorrhagic lesions restricted to lobar, cortical, or cortico-subcortical regions (cerebellar hemorrhage allowed) and no other definite cause (trauma, ischemic stroke, tumor, vascular malformation, vasculitis, coagulopathy, anticoagulation with international normalized ratio ≥3.0) are diagnosed as probable CAA. For the current analysis, we grouped the patients into 2 categories: those presenting with (1) ≥2 lobar microbleeds in the absence of lobar ICH (microbleed-only patients) or (2) those presenting with a lobar ICH with ≥1 lobar microbleed (ICH patients). Patients with a diagnosis of inflammatory CAA or autosomal dominant hereditary CAA were not included into this analysis. A full history was obtained, a neurological examination was performed, and head computed tomography, brain MRI, and computed tomography angiography or magnetic resonance angiography of the brain were performed to exclude an underlying vascular abnormality or other structural causes of hemorrhage. Microbleed-only patients underwent neurological and cognitive testing including mini mental state examination as part of the research protocol on which they scored ≥27. For the survival analysis, day zero for the ICH group was taken as the date of ICH. For the microbleed-only subjects who entered the prospective study without a prior ICH, day zero for survival analyses was taken as the date of study enrollment.

Data Collection
Subject enrollment, baseline data collection, and MRI acquisition and analysis were performed as described previously. Baseline characteristics were compared between ICH patients and microbleed-only patients among all patients enrolled. Individuals who consented to longitudinal follow-up and ICH patients who survived the first 90 days after their index event were studied for incident lobar ICH or death as described. Forty-six patients who died within the first 3 months after their index ICH were not included into the longitudinal analyses. Thirty-three patients who did not consent for the longitudinal study were older (P=0.003), but other baseline characteristics (sex, vascular risk factors, apolipoprotein E [APOE], number of microbleeds, and leukoaraiosis volume) did not differ from the longitudinal cohort (n=300; all P>0.2). Information on antithrombotic medication use, incident lobar ICH, and occurrence and cause of death was obtained by follow-up phone calls at 3 months after enrollment and every 6 months thereafter. Chart review was performed when needed to adjudicate the nature of an event reported as a new lobar ICH. We accrued the date of death by consulting the Social Security Death Index as described previously. All patients were followed from their date of enrollment until the occurrence of ICH, death, or the end of follow-up in June 2012. This study was performed with the approval of and in accordance with the guidelines of the institutional review board of Massachusetts General Hospital and with informed consent of all subjects or authorized family members. Radiological and genetic analyses were performed by separate study personnel and the results recorded without the knowledge of the subjects’ clinical information.

Clinical and Laboratory Data
Data on demographics (age, sex) and vascular risk factors (hypertension, diabetes mellitus, and hypercholesterolemia) were obtained by interviewing the patients (or their families or surrogates) at enrollment. APOE genotype was determined in a large subset of patients who provided research blood samples.

MRI Acquisition and Analysis
Images were obtained using a 1.5-T magnetic resonance scanner (GE Sigma). Whole-brain axial gradient-echo images (repetition time/echo time, 750/50 ms; 5 mm slice thickness; 1 mm interslice gap) and fluid-attenuated inversion recovery images (repetition time/echo time, 10000/140 ms; inversion time, 2200 ms; number of excitations, 1; 5 mm slice thickness; 1 mm interslice gap) were performed. Lobar microbleeds were classified as punctate, hypointense foci (<5 mm in diameter) selectively involving the cortex and underlying white matter on gradient-echo images, distinct from vascular flow voids and leptomeningeal hemosiderosis. White matter hyperintensity (WMH or leukoaraiosis) volume was quantified as previously validated using a computer-assisted algorithm that involves MRcron, a freely available tool. All MRI analyses were performed and recorded by investigators blinded to clinical and genetic data.

Statistical Analysis
Univariate analyses were used to compare clinical characteristics, frequencies of the APOE ε2 and ε4 alleles, and radiological markers between the 2 groups. Subsequently, multivariate analyses were performed to look for independent associations between these predictors and diagnostic categories. For multivariate models, APOE genotype was analyzed as a categorical variable according to the presence or absence of the ε2 and ε4 alleles. As blood samples for genotyping were not available in 28% of subjects, multivariate models were built with and without APOE; addition of this variable did not change the associations observed among other variables. In the follow-up cohort, the mean follow-up time was calculated and the incidence rates of ICH and death were determined using the incidence per 100 person-years of follow-up. We used multivariable Cox regression analyses to calculate the crude and adjusted hazard ratios for occurrence of ICH and death. For the adjusted Cox regression model, patient group (with ICH as the control group), age, sex, hypertension, WMH volume, and lobar microbleed counts were entered in the model. In the microbleed-only patients, a multivariable Cox regression model was built to test the association between anticoagulant use and incident ICH after adjustment for demographics, hypertension, WMH, and microbleeds. All analyses were performed with SPSS 22.0 (released 20/12, IBM SPSS Statistics for Windows, version 22.0, IBM Corp, Armonk, NY). All tests of significance were 2 tailed.

Results
We analyzed a total of 379 patients who were enrolled between January 1993 and January 2012, of whom 63 patients presented with lobar microbleeds only and 316 with lobar ICH. Of the 63 microbleed-only patients, 26 patients underwent their index MRI for evaluation of symptoms suggestive of an ischemic event, 27 because of mild cognitive symptoms, 4 because of a gait disorder, and 6 because of transient sensory spells. None of the microbleed-only patients was found to have ischemic stroke, dementia, mass lesion, or other neurodegenerative conditions after complete evaluation.

Demographics (age, sex), vascular risk factors, and APOE genotype did not differ significantly between microbleed-only and ICH groups (Table 1). The lobar microbleed count was significantly higher in microbleed-only patients (median, 10; interquartile range, 4–30) compared with the ICH patients (median, 2; interquartile range, 1–9; P<0.001). This difference remained significant after adjusting for demographics and vascular risk factors (P<0.001). Within the lobar microbleed-only group, no significant correlation was found between microbleed counts and other factors such as demographics, vascular risk factors, or APOE. Microbleed-only patients had a larger median WMH volume compared with the patients with ICH (31 versus 23 mL; P=0.02; Table 1). Higher WMH volume remained independently associated with the microbleed-only category (P=0.04) after correction for age, sex, and vascular risk factors.
Three hundred patients (240 ICH who survived the first 90 days after their index ICH and 60 microbleed-only) were followed longitudinally for 5.3±3.8 years after their index event. Twelve microbleed-only patients (20% of the microbleed-only group, 5 per 100 person-years) developed a lobar ICH during follow-up versus 86 patients (36%) presenting with ICH (8.9 per 100 person-years). Details of the incident event rates, hazard ratios, and confidence intervals are presented in Table 2. Cox regression analysis showed a mildly lower risk of incident ICH for the microbleed-only versus the lobar ICH patients, but this difference did not reach statistical significance (Figure 1A; hazard ratio, 0.58; 95% confidence interval, 0.31–1.06; P=0.08). The ICH rate observed in either group of CAA patients was orders of magnitude greater than that of the general elderly population (estimated at 0.015–0.05 incident ICHs per 100 people per year).16,17 Figure 2 shows the baseline and follow-up imaging of an microbleed-only patient who later developed a symptomatic ICH.

We analyzed the predictors of incident ICH in the microbleed-only group. Warfarin use (P=0.02) and older age (P=0.04) were independently associated with time to incident ICH in a multivariable Cox regression model that also adjusted for age, sex, hypertension, microbleed count, and white matter hyperintensity volume.

### Table 1. Clinical and Radiological Characteristics of the 2 Patient Groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. of Patients Presenting With</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lobar Microbleed-Only (n=63)</td>
<td>Lobar ICH (n=216)</td>
</tr>
<tr>
<td>Definite/probable CAA All</td>
<td>All</td>
<td>All</td>
</tr>
<tr>
<td>Clinical variables</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male sex (%)</td>
<td>40 (63)</td>
<td>162 (51)</td>
</tr>
<tr>
<td>Age, y</td>
<td>73.6±8.3</td>
<td>73.6±9</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>34 (54)</td>
<td>194 (61)</td>
</tr>
<tr>
<td>Hypercholesterolemia (%)</td>
<td>26 (41)</td>
<td>136 (43)</td>
</tr>
<tr>
<td>Diabetes mellitus (%)</td>
<td>9 (14)</td>
<td>55 (17)</td>
</tr>
<tr>
<td>Genotype APOE ε2 frequency</td>
<td>15.6%</td>
<td>12%</td>
</tr>
<tr>
<td>Genotype APOE ε4 frequency</td>
<td>25%</td>
<td>23%</td>
</tr>
<tr>
<td>Radiological markers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lobar microbleed count</td>
<td>10 (4–30)</td>
<td>2 (1–9)</td>
</tr>
<tr>
<td>WMH volume, mL</td>
<td>31 (18–46)</td>
<td>23 (12–40)</td>
</tr>
</tbody>
</table>

Values are displayed as mean±SD, median (25th–75th quartile), or n (%). APOE genotypes were available in 48 subjects with microbleed-only and 224 with ICH. APOE indicates apolipoprotein E; CAA, cerebral amyloid angiopathy; ICH, intracerebral hemorrhage; and WMH, white matter hyperintensity.

### Table 2. Incidence Rates and Hazard Ratios for the Occurrence of ICH and Death in Both Groups During Follow-Up

<table>
<thead>
<tr>
<th>Event Rate</th>
<th>No. of Patients Presenting With</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Event: occurrence of lobar ICH</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Observed person-years</td>
<td>241</td>
<td>968</td>
</tr>
<tr>
<td>No. of occurrence (%)</td>
<td>12 (20)</td>
<td>86 (36)</td>
</tr>
<tr>
<td>Incidence of ICH per 100 person-years (95% CI)</td>
<td>5 (2.6–8.7)</td>
<td>8.9 (7.1–11)</td>
</tr>
<tr>
<td>Crude hazard ratio (95% CI)</td>
<td>0.57 (0.3–1.04)</td>
<td>Ref</td>
</tr>
<tr>
<td>Adjusted hazard ratio* (95% CI)</td>
<td>0.58 (0.31–1.06)</td>
<td>Ref</td>
</tr>
<tr>
<td>Event: occurrence of death</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Observed person-years</td>
<td>261</td>
<td>1316</td>
</tr>
<tr>
<td>No. of occurrence (%)</td>
<td>31 (52)</td>
<td>105 (44)</td>
</tr>
<tr>
<td>Incidence of death per 100 person-years (95% CI)</td>
<td>11.9 (8.16)</td>
<td>8 (6.5–9.7)</td>
</tr>
<tr>
<td>Crude hazard ratio (95% CI)</td>
<td>1.8 (1.2–2.8)</td>
<td>Ref</td>
</tr>
<tr>
<td>Adjusted hazard ratio* (95% CI)</td>
<td>1.67 (1.1–2.6)</td>
<td>Ref</td>
</tr>
</tbody>
</table>

CI indicates confidence interval; ICH, intracerebral hemorrhage; and ref, reference for hazard ratios.

*Adjusted for age, sex, hypertension, microbleed count, and white matter hyperintensity volume.

![Figure 1. Survival curves of the 2 groups for occurrence of intracerebral hemorrhage (ICH; A) and death (B). MB indicates microbleed.](http://stroke.ahajournals.org/DownloadedFrom)
CAA patients presenting with ICH. The risk of subsequent ICH, and an overall higher mortality than isolated lobar microbleeds were in the same age range and had similar vascular risk factors. APOE genotypes were also similar between the groups. Two microbleed-only and microbleed-only CAA, but this finding is in line with previous studies.

In this study, we have identified similar genetic and radiological characteristics at presentation between individuals with nonspecific symptoms who had lobar microbleeds on MRI (white arrows, A). Four months later, the patient presented to the emergency department with acutely altered mental status. Her head computed tomography showed a right-sided posterior lobar ICH with ventricular extension (black arrow, B).

Discussion

In this study, we have identified similar genetic and radiological characteristics at presentation between individuals with nonspecific symptoms who had lobar microbleeds on T2* MRI and patients with CAA diagnosed after a lobar ICH. Compared with the lobar ICH CAA patients, the patients with isolated lobar microbleeds were in the same age range and had similar vascular risk factors. APOE genotypes were also similar, with relatively high frequencies for the ε2 and ε4 alleles as previously observed in nontraumatic lobar ICH. There also seemed to be notable differences between the 2 groups. The microbleed-only group demonstrated higher microbleed counts, a finding that might in part reflect a higher likelihood that patients with large numbers of microbleeds would be identified and referred to our longitudinal research study. Patients with lobar microbleed-only in this study demonstrated increased WMH volume, a previously identified consequence of severe CAA pathology, as well as a substantial risk of subsequent ICH, and an overall higher mortality than CAA patients presenting with ICH.

The Boston criteria for diagnosis of CAA during life originally assumed the presence of ≥1 lobar hemorrhage, the presence of lobar microbleeds strengthening the diagnosis. The ongoing question in the field has been the diagnostic and prognostic importance of finding multiple lobar microbleeds on MRI of an older adult without any symptomatic ICH and without other causes for microbleeds. The results of our baseline comparisons that show similar demographic, genetic, and vascular risk profiles between the groups support the view that the lobar microbleed-only pattern can reliably be considered as probable CAA. The finding of a more severe marker of CAA-related cerebral damage (high WMH volume) also suggests vascular amyloid-related small vessel dysfunction as the principal pathological mechanism in these cases.

The current data bear on the important question of which patients should receive anticoagulant therapy. Individuals with isolated lobar microbleeds are being increasingly detected by more frequent use of sensitive MRI techniques, with prevalences in the range of 11% to 24% of the community-dwelling elderly. As the risk of ICH in these patients is largely unknown, however, there has been insufficient evidence to conclude that the presence of lobar microbleeds alone should preclude anticoagulant therapy. A neuropathologic study also suggested that CAA patients with multiple microbleeds might have different vessel pathology (with thicker amyloid-positive vessel walls) compared with CAA patients with few lobar microbleeds, suggesting that the ICH risk might be different across these groups. For these reasons, it has not been possible to extrapolate ICH risk estimates in a population with isolated lobar microbleeds based on prior studies of patients with past ICH. The current study suggests that microbleed-only CAA patients, though at mildly lower risk for future ICH than those with past ICH, are nonetheless at substantial risk.

Despite our relatively small sample size, we have also found that aspirin use was introduced into the model, and aspirin was not associated with increased ICH risk (P>0.2).

Thirty-one microbleed-only patients (11.9 per 100 person-years) died during follow-up versus 105 patients in the ICH group (8 per 100 person-years). After adjusting for age, sex, hypertension, WMH volume, and microbleed counts, the case-fatality rate was higher in microbleed-only patients (Table 2 and Figure 1B; adjusted hazard ratio, 1.67; 95% confidence interval, 1.1–2.6; P=0.02). Introduction of APOE status into multivariate models did not change any of the associations presented under the Results section. Two microbleed-only and 9 lobar ICH patients underwent autopsy. Presence of moderate-to-severe CAA was pathologically confirmed in all of these patients.

In light of the substantial risk for future ICH observed among the microbleed-only subjects, it is reasonable to consider this condition as a potential precursor or early form of CAA-related ICH. In other respects, however, the microbleed-only patients in the current study demonstrate markers of CAA equal to or greater than those in the ICH group. Among these markers were increased microbleed counts (possibly a reflection of referral preferences as noted above), higher WMH burden, and earlier mortality. We were unable to determine the potential causes of increased mortality in patients with microbleed-only CAA, but this finding is in line with...
recent studies that show higher mortality in older adults with microbleeds.33,34 Although clearly requiring further analysis, the current data suggest that microbleed-only CAA may represent an alternative pathway by which this pathology can cause progressive neurological damage, even in the absence of major hemorrhagic stroke. Pathological confirmation of the CAA diagnosis in all 11 patients who underwent autopsy also supports the view that Boston criteria can accurately establish this diagnosis during life.

Our study has limitations. It is indeed likely that many of the microbleed-only patients were referred to our clinic because of finding relatively high number of lobar microbleeds, an issue that might be related to higher WMH load and mortality in this particular cohort. We do note, however, that the number of lobar microbleeds was not related to the risk of incident ICH in these subjects, suggesting that this possible referral bias did not account for the relatively high incidence of future hemorrhage in microbleed-only patients. The question of CAA diagnosis is typically raised when a brain MRI obtained for neurological complaints in an older adult shows lobar microbleeds. In that sense, our study population is similar to patients seen in clinical practice. None of our microbleed-only patients had dementia, stroke, or other neurodegenerative conditions at enrollment, limiting the contribution of potential confounders to the outcomes observed. A second limitation was our sample size, which limited our ability to assess the risk of antithrombotic use in better multivariate models. A larger study would be necessary to address the risk of ICH with or without antithrombotic use, in patients with isolated lobar microbleeds who are at high risk of ischemic events because of the presence of atrial fibrillation, deep venous thrombosis, or pulmonary embolism. Data from randomized clinical trials are unlikely to be forthcoming, however, as such trials to rule out harmful medication effects in high-risk subjects are difficult to justify and perform.

Conclusions
The vascular risk factors as well as genetic and radiological characteristics of patients with isolated lobar microbleeds are similar to patients with CAA diagnosed after a lobar ICH, therefore suggestive of substantial CAA pathology. In this sense, lobar microbleeds on MRI, a common finding in otherwise healthy elderly individuals with or without nonspecific symptoms, seem to be a promising diagnostic marker of advanced CAA. We also find that patients presenting with isolated lobar microbleeds are at considerable risk of future lobar ICH, a risk made worse by the use of warfarin. Given the high prevalence of isolated lobar microbleeds in the elderly, our findings support the importance of developing early detection markers for CAA in asymptomatic individuals, studying its impact in this population, and determining the feasibility of treating CAA before it becomes symptomatic.

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Disclosures
Dr Rosand serves as a consultant for Boehringer Ingelheim. Drs Rosand, Greenberg, and Gurol receive research support from National Institutes of Health. The other authors report no conflicts.

References


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背景和目的：脑叶微出血常提示脑淀粉样血管病（CAA）,常在不伴有脑叶脑出血（ICH）时被MRI发现。脑微出血能够在磁共振T2*加权像上被检出,已被证实为致死致残率较高的颅内出血的危险因素,但其与ICH之间的因果关系仍不明确。CAA是β淀粉样蛋白沉积在脑内小、中径血管管壁内继发的出血及缺血性脑损伤,波士顿诊断标准最初是在脑叶ICH的患者中得以验证,然而随着T2*加权像成像技术的不断发展,CAA的脑叶IICH患者具有相似的血管危险因素和遗传/影像学特征,而且多个研究发现CAA患者发生ICH的风险很高。因此本文对CAA和ICH患者进行比较研究,以探索CAA患者发生ICH的风险。

方法：本研究前瞻性纳入了63例检查发现的脑微出血患者和316例CAA相关的ICH患者,并比较分析了两组患者的临床资料(人口统计数据,危险因素),载脂蛋白E(APOE)基因型,CAA严重程度的神经影像学标志物(微出血的数量,白质疏松的体积)和临床结局(平均随访5.3±3.8年期间ICH和死亡的发生率)。通过多因素Cox回归模型探索单纯脑微出血患者发生脑出血的预测因子。

结果：两组患者的人口统计学资料、危险因素(高血压、糖尿病、高胆固醇血症)、血管危险因素等并无统计学差异。相比脑叶ICH患者,单纯微出血患者脑叶微出血灶更多(中值,10:2;P<0.001),脑白质疏松体积更大(中值,31:23ml,P=0.02)且远期病死率较高(HR,1.67;95%CI,1.1-2.6),孤立性脑微出血患者脑出血率较高,但与ICH患者并无显著统计学差异(5:8.9/100人·年;校正后HR,0.58;95%CI,0.31-1.06;校正数据P=0.08)。在校正相关变量后,华法林的应用和高龄是单纯脑微出血患者发生脑出血的独立危险因素。

结论：孤立性脑微出血患者的基因、神经影像及脑出血危险因素等方面提示有重度CAA的病理机制参与,这类患者发生ICH的风险很大,在抗凝治疗时会潜在影响临床决策。

(Stroke. 2014;45:2280-2285. 郑州大学第一附属医院神经内科 宋波 译；许予明 校)
脑出血发生率之间的关系。所有分析均用 SPSS 20.0 软件完成。所有事件(16,17)16高于一般的老年人(估计每年每 100 人发生 0.015–0.05 例脑出血 P=0.08)。任何一组脑淀粉样血管病患者的脑出血发生率呈数量级水

平,这种差异未达到统计学差异(图 1A;HR 0.58;95%CI 0.31–1.06; P=0.08)。将 APOE 引入多因素模型未对结果造成影响。2 例单纯微出血的患者(占该组的 20%,5 例 /100 人 - 年)在随访中进展为

既往非外伤性脑叶 ICH 患者的研究中已经发现

出血及 9 例脑叶出血患者进行了尸检。均经病理证实存在中到重度的

变所致,这也可能是由偏倚引起,即微出血病灶多的患者更容易发现并转诊纳

者也存在明显不同之处。单纯脑微出血患者的微出血灶数量更多,但

前也无统计学差异。如果单纯脑微出血患者不能接受抗凝治疗

单 纯 微 出 血 组(表 2 和 图 1B; 校 正 HR1.67;95% CI 为 1.1-2.6; P=0.02)。2 例单纯微出血的患者(占该组的 20%,5 例 /100 人 - 年)在随访中进展为

者有相对较高的整体 ICH 发生率这一结果。对于因神经系统相关症

卒中治疗和试验数据下撤治的立场,鼓励影像学检查时发现脑叶微出血

没有症状性 ICH 及其它引起脑微出血因素的

出血患者可以诊断为可能的 CAA。同时,该研究还发现了单纯脑叶

相 等 于 中 轻 度 的 新 发 脑 出 血 病 变, 包 括 脑 出 血

的影像学标志物,这些标志物包括微出血病灶数目多(可能存在上述偏倚)、

患者相比有更大的白质高信号平均体积(31:23ml;P=0.02; 表 1)。载脂蛋白 E 等其他因素之间没有相关性。仅有微出血的患者与脑出血

异常。在进行完整的评估后,单纯微出血的患者中无一例发现有缺血

前非外伤性脑叶 ICH 患者的研究中已经发现

也验证了 Boston 标准诊断 CAA 的准确性。根据

这提示我们 ICH 发生的风险可能更高。但是,我们目前不能排除

患者有更高的整体 ICH 发生率。这也进一步支持了脑叶 ICH 发生的危

这为我们理解 CAA 相关 ICH 的早期表现形式。另一方面,研

既往有 ICH 的

更多 ICH 危险因素来分析其影响程度。31

血栓相关性疾病的预测意义。33,34

这支持了 ICH 风险与血管淀粉样变的相关性,提示动脉性脑血管病患者

患者 Pareto 了单账户的 CAA。但是,我们对这些患者罹患 ICH 的风险所知甚少,目

这提示我们 ICH 的风险可能更高。然而,我们目前不能确定

这为我们理解 CAA 相关 ICH 的早期表现形式。另一方面,研

阶段新发脑出血的风险降低;与此同时,这些患者也发现有更高的 ICH 风险,且

同时该组患者存在较高的 ICH 风险,整体死亡率亦较以脑

患者,提示动脉性脑血管病(CAA)患者有更高的 ICH 风险。31

本研究发现,虽然单纯微出血的 CAA 患者相对于没有 ICH 患者发生

高危患者影响的临床试验短时间内还难以开展和实施。然而,探讨抗栓药物对


