Use of Antithrombotic Therapy and Long-Term Clinical Outcome Among Patients Surviving Intracerebral Hemorrhage

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Background and Purpose—The effectiveness and safety of antithrombotic therapy (AT) among patients with a history of intracerebral hemorrhage remain uncertain. We therefore determined the prevalence of indication for AT among patients hospitalized with first-time intracerebral hemorrhage and examined the impact of subsequent AT use on the long-term clinical outcome.

Methods—We performed a population-based cohort study using nationwide Danish medical registries. Patients with risk of thromboembolism surviving the first 30 days after hospitalization because of intracerebral hemorrhage were identified and followed up. We estimated the hazard ratio of all-cause death, thromboembolic events, or major bleeding according to use of AT.

Results—We identified 6369 patients between 2005 and 2013. Among these patients, 2978 (47%) had indication for AT, and during the follow-up, (median: 2.3 year) 1281 (43%) died, 497 (17%) had a thromboembolic event, and 536 (18%) had major bleeding. Postdischarge use of oral anticoagulation therapy among patients with indication for oral anticoagulation therapy was associated with a significant lower risk of death (adjusted hazard ratio, 0.59; 95% confidence interval, 0.43–0.82) and thromboembolic events (adjusted hazard ratio 0.58; 95% confidence interval, 0.35–0.97) and no increased risk of major bleeding (adjusted hazard ratio 0.65; 95% confidence interval, 0.41–1.02). In contrast, use of platelet inhibitors among patients with indication for platelet inhibitors was not related to statistically significantly improved clinical outcome.

Conclusions—Approximately 1 of 2 patients surviving intracerebral hemorrhage had a high risk of thromboembolism. Postdischarge use of oral anticoagulation therapy was associated with a lower risk of all-cause mortality and thromboembolic events and no increased risk of major bleeding. (Stroke. 2016;47:1837-1843. DOI: 10.1161/STROKEAHA.116.012945.)

Key Words: anticoagulants ■ atrial fibrillation ■ epidemiology ■ intracerebral hemorrhage ■ stroke

Clinicians are everyday challenged with the decision of resuming or initiating antithrombotic therapy (AT) among patients with previous hemorrhage, because of a high prevalence of ischemic risk factors or previous thromboembolic events among many of these patients. Patients with intracerebral hemorrhage (ICH) represent a special challenge because of the concerns about the risk of recurrent and potentially catastrophic ICH.1 Within recent years, there has been a remarkable development in the area of AT with introduction of new antithrombotic drugs and increased clinical attention to ensure that guideline recommendations are implemented.

Data on use of AT among patients surviving ICH have until recently been sparse, and there have therefore only been little evidence available for guiding clinical practice. As demonstrated in recent studies, it is therefore not surprising that there has been large variation in clinical practice, and many ICH survivors with a high risk of thromboembolism are not prescribed AT.2,3 The association between use of AT and clinical outcome among patients with previous intracranial hemorrhage/ICH have been examined in a few studies within recent years.4–7 Overall, the findings seem to encourage the use of AT among patients surviving ICH because AT was associated with a lower risk of thromboembolic events without an associated increased risk of major bleeding. However, questions remain, as the available data are primarily restricted to patients with atrial fibrillation...
resuming treatment with vitamin K antagonists. Additional population-based studies with long-term follow-up on well-characterized patient populations, including patients with other indications for AT than atrial fibrillation, are therefore needed to obtain a stronger evidence base for decision making about use of AT (including vitamin K antagonists, non–vitamin K antagonist oral anticoagulants, and platelet inhibitors) among ICH survivors.

We therefore conducted a nationwide follow-up study to examine the effectiveness and safety of AT among these patients.

Methods
The study was based on national Danish registries covering the entire population (~5.6 million). The National Health Service provides tax-financed healthcare to all residents, and unambiguous individual-level linkage between registries is enabled by a unique 10-digit civil registration number, which is assigned to every citizen and used in all registries. According to Statistics Denmark, 89% of the population had Danish ancestry and 11% were immigrants or descendants in 2013.

The study was approved by the Danish Data Protection Agency (ID 1-16-02-371-13). According to Danish law, ethical approval is not required for registry-based studies.

Study Population
The study population consisted of all Danes (≥18 years) admitted with first-time, acute, spontaneous (nontraumatic) ICH and surviving the first 30 days from January 1, 2005, to December 31, 2013.

The patients were identified from the Danish Stroke Registry (DSR). The DSR is a stroke-specific clinical registry. Reporting is mandatory for all hospital departments treating patients with acute stroke.4 The sensitivity and positive predictive value of the registration of patients in the DSR has been estimated to be >90%.9 The registry contains information on the subtype of stroke (ischemic stroke and ICH) and stroke severity but not more detailed information, that is, localization or volume. Information on vital status was obtained from The Danish Civil Registration System, which keeps daily registration number, which is assigned to every citizen and used in all registries. According to Statistics Denmark, 89% of the population had Danish ancestry and 11% were immigrants or descendants in 2013.

The study was approved by the Danish Data Protection Agency (ID 1-16-02-371-13). According to Danish law, ethical approval is not required for registry-based studies.

Outcomes
The following are the major outcomes of this study:

1. All-cause mortality: this was assessed using information from the Danish Civil Registration System.
2. Thromboembolic events: this included hospitalization with myocardial infarction, ischemic stroke, peripheral arterial thrombosis, venous thromboembolism, and pulmonary embolism. Information was obtained from the DNR and the DSR.
3. Major bleeding: this included hospitalization with recurrent ICH and other intracranial bleeding and gastrointestinal, urinary, and airway/lung bleeds. Information was obtained from the DSR and the DNR.
4. Recurrent ICH: this was analyzed as part of the combined end point of major bleeding, but also as an individual end point, because of the serious nature of this type of bleeding.

Antithrombotic Therapy
Information on use of AT was obtained from the Danish National Database of Reimbursed Prescriptions. This registry contains information from 2004 and onward on all reimbursed prescription drugs dispensed at Danish pharmacies. The included antithrombotic medications are available by prescription only, except for low-dose aspirin; however, the potential for identification of individual-level use of low-dose aspirin from prescription data is high in Denmark because the prescribed proportion of individual-level low-dose aspirin sales is >90%.14

Pre-admission use of AT was defined as at least one filled prescription within 90 days before the date of admission with ICH. Post-ICH use was determined using information from all filled prescriptions after the day of admission for each individual. The length of the individual prescriptions was estimated based on information on the package size and the daily defined dose as defined by the World Health Organization.15 Using this information, it was possible to estimate the length of time the individual patient was treated with AT during the follow-up period and to determine whether outcome events occurred during or off treatment. Data on in-hospital use of AT as well as information on the exact timing of potential shorter pauses in treatment (eg, because of dental procedure) was not available and therefore not accounted for.

Covariates
Information on patient characteristics was obtained from the DSR, the DNR, and the Danish National Database of Reimbursed Prescriptions and included age, sex, admission year, comorbidity (Charlson comorbidity score),16 stroke severity (Scandinavian Stroke Scale score),17 calendar year, CHA2DS2-VASc (Congestive heart failure, Hypertension, Age≥75 years, Diabetes mellitus, previous Stroke/transient ischemic attack, Vascular disease, Age 65–74 years, Sex category, age≥75 years and previous stroke carry doubled risk weight) score, HAS-BLED (Hypertension, Abnormal renal/liver function, Stroke, Bleeding history, Labile international normalized ratio, Elderly >65 years, Drug consumption/alcohol abuse) score, contraindications to oral anticoagulation therapy (OAT), body mass index, smoking habits, and alcohol intake. The CHA2DS2-VASc16 and HAS-BLED13 scores were computed for patients with atrial fibrillation. In the HAS-BLED score, the labile international normalized ratio component of the score was not included, because this information was not available. Both algorithms have been shown to predict thromboembolism and bleeding accurately.16,18 Furthermore, we registered whether the patients had any contraindications to AT that are registered specifically by the physician treating the patients during the initial ICH admission and reflects, for example, one or more of the following contraindications: recent surgery or bleeding, aspirin treatment, uncontrolled hypertension or hemorrhagic diathesis, dementia/alcoholism, lack of patient acceptance, and pregnant in first trimester and other.

Statistical Analysis
We first estimated the prevalence of indication for AT among patients hospitalized with ICH and surviving the first 30 days after admission.

Second, we computed cumulative incidence rates of the clinical outcomes. Patients were followed up from 30 days after admission until the time of the first outcome event (death, thromboembolic event, or major bleeding), date of emigration, and death (in the analyses on thromboembolic events and major bleeding) or the end of the study period, whichever came first.

Third, we examined possible predictors for post-ICH use of AT among all patients with indication for AT. These analyses were performed using separate multivariable logistic regression analyses for treatment with OAT and platelet inhibitors.

We examined the association between postdischarge use of AT and the clinical outcomes using Cox proportional hazards regression, adjusting for the variables presented in Table 1. We separated the patients in 2 groups: group 1 consisted of patients with potential indication for OAT because of atrial fibrillation, artificial heart
Table 1. Characteristics of ICH Patients With Indication for AT According to the Post-ICH Use (Within 180 Days After ICH) of Antithrombotic Therapy

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>OAT (N=160)</th>
<th>Platelet Inhibitors (N=799)</th>
<th>Combination (N=63)</th>
<th>No AT (N=1956)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, distribution</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;65</td>
<td>35 (21.9)</td>
<td>156 (19.5)</td>
<td>15 (23.8)</td>
<td>526 (26.9)</td>
</tr>
<tr>
<td>65–74</td>
<td>58 (36.3)</td>
<td>209 (26.2)</td>
<td>16 (25.4)</td>
<td>487 (24.9)</td>
</tr>
<tr>
<td>≥85</td>
<td>67 (41.8)</td>
<td>434 (54.3)</td>
<td>32 (50.8)</td>
<td>943 (48.2)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>99 (61.9)</td>
<td>452 (56.6)</td>
<td>42 (66.7)</td>
<td>1086 (55.5)</td>
</tr>
<tr>
<td>Comorbidity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>114 (71.3)</td>
<td>539 (67.5)</td>
<td>42 (66.7)</td>
<td>1178 (60.2)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>23 (14.4)</td>
<td>134 (16.8)</td>
<td>10 (15.9)</td>
<td>243 (12.4)</td>
</tr>
<tr>
<td>Charlson comorbidity index</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No comorbidity, 0</td>
<td>50 (31.3)</td>
<td>187 (23.4)</td>
<td>13 (20.6)</td>
<td>629 (32.2)</td>
</tr>
<tr>
<td>Moderate comorbidity, 1–2</td>
<td>71 (44.4)</td>
<td>391 (48.9)</td>
<td>31 (49.2)</td>
<td>873 (44.6)</td>
</tr>
<tr>
<td>Severe comorbidity, ≥3</td>
<td>39 (24.4)</td>
<td>221 (27.7)</td>
<td>19 (30.2)</td>
<td>454 (23.2)</td>
</tr>
<tr>
<td>Body mass index, distribution</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;18.5</td>
<td>2 (1.3)</td>
<td>22 (2.8)</td>
<td>2 (3.2)</td>
<td>81 (4.1)</td>
</tr>
<tr>
<td>18.5–&lt;25</td>
<td>46 (28.9)</td>
<td>268 (33.5)</td>
<td>18 (28.6)</td>
<td>650 (33.2)</td>
</tr>
<tr>
<td>≥25</td>
<td>57 (35.6)</td>
<td>293 (36.7)</td>
<td>26 (41.3)</td>
<td>618 (31.6)</td>
</tr>
<tr>
<td>Missing</td>
<td>55 (34.4)</td>
<td>216 (27.0)</td>
<td>17 (27.0)</td>
<td>607 (31.0)</td>
</tr>
<tr>
<td>Drinks per week</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤14 women/≤21 for men</td>
<td>123 (76.9)</td>
<td>582 (72.8)</td>
<td>45 (71.4)</td>
<td>1393 (71.2)</td>
</tr>
<tr>
<td>&gt;14 women/&gt;21 for men</td>
<td>18 (11.3)</td>
<td>75 (9.4)</td>
<td>5 (7.9)</td>
<td>193 (9.9)</td>
</tr>
<tr>
<td>Missing</td>
<td>19 (11.9)</td>
<td>142 (17.8)</td>
<td>13 (20.6)</td>
<td>370 (19.9)</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daily</td>
<td>25 (15.6)</td>
<td>205 (25.7)</td>
<td>12 (19.0)</td>
<td>435 (22.2)</td>
</tr>
<tr>
<td>Former</td>
<td>34 (21.3)</td>
<td>201 (25.2)</td>
<td>18 (28.6)</td>
<td>422 (21.6)</td>
</tr>
<tr>
<td>Never</td>
<td>77 (48.1)</td>
<td>239 (29.9)</td>
<td>22 (34.9)</td>
<td>613 (31.3)</td>
</tr>
<tr>
<td>Missing</td>
<td>24 (15.0)</td>
<td>154 (19.3)</td>
<td>11 (17.5)</td>
<td>486 (24.8)</td>
</tr>
<tr>
<td>Scandinavian Stroke Scale score</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–29 point</td>
<td>32 (20.0)</td>
<td>158 (19.8)</td>
<td>11 (17.5)</td>
<td>589 (30.1)</td>
</tr>
<tr>
<td>30–58 point</td>
<td>115 (71.9)</td>
<td>551 (69.0)</td>
<td>50 (79.4)</td>
<td>1076 (55.0)</td>
</tr>
<tr>
<td>Missing</td>
<td>13 (8.1)</td>
<td>90 (1.1)</td>
<td>2 (3.2)</td>
<td>291 (14.9)</td>
</tr>
<tr>
<td>Year of admission</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2005</td>
<td>8 (5.0)</td>
<td>67 (8.4)</td>
<td>3 (4.8)</td>
<td>256 (13.1)</td>
</tr>
<tr>
<td>2006</td>
<td>10 (6.3)</td>
<td>63 (7.9)</td>
<td>3 (4.8)</td>
<td>222 (11.3)</td>
</tr>
<tr>
<td>2007</td>
<td>14 (8.8)</td>
<td>87 (10.9)</td>
<td>10 (15.9)</td>
<td>239 (12.2)</td>
</tr>
<tr>
<td>2008</td>
<td>11 (6.9)</td>
<td>105 (13.1)</td>
<td>7 (11.1)</td>
<td>227 (11.6)</td>
</tr>
<tr>
<td>2009</td>
<td>15 (9.4)</td>
<td>103 (12.9)</td>
<td>6 (9.5)</td>
<td>250 (12.8)</td>
</tr>
<tr>
<td>2010</td>
<td>13 (8.1)</td>
<td>114 (14.3)</td>
<td>4 (6.3)</td>
<td>212 (10.8)</td>
</tr>
<tr>
<td>2011</td>
<td>23 (14.4)</td>
<td>91 (11.4)</td>
<td>16 (25.4)</td>
<td>191 (9.8)</td>
</tr>
<tr>
<td>2012</td>
<td>32 (20.0)</td>
<td>93 (11.6)</td>
<td>9 (14.3)</td>
<td>193 (9.9)</td>
</tr>
<tr>
<td>2013</td>
<td>34 (21.3)</td>
<td>78 (9.8)</td>
<td>5 (7.9)</td>
<td>166 (8.5)</td>
</tr>
</tbody>
</table>

(Continued)
valve, or venous thromboembolism and group 2 consisted of patients with potential indication for resumption of platelet inhibitors, including previous acute myocardial infarction, ischemic stroke (without atrial fibrillation), and peripheral arterial disease. We used multiple imputations to impute the missing values among the covariates assuming that data were missing at random (Markov chain Monte Carlo method). We created 20 data sets based on the aforementioned covariates. The outcome measures were averaged across the 20 imputations correcting for between- and within-imputation variation. Postdischarge use of AT was included as a time-dependent variable. Using this approach, the patients were only considered exposed during the exact number of days of available treatment provided by the individual filled prescriptions.

Furthermore, we repeated the analysis with the follow-up period beginning at 1 year after admission, to counteract any delayed influence on the outcome from their primary ICH admission, and we also repeated the analysis with restriction to patients who were treated with AT before their ICH event. In addition, we made an analysis examining the association of time between first filled prescription for AT after ICH and the clinical outcome to explore when it is safe to resume AT therapy. Finally, we did a propensity score–matched sensitivity analysis on the association between post-ICH major bleeding types can be seen in Table I (adjusted hazard ratio [HR], 0.59; 95% confidence interval).

Clinical Outcomes
Among patients having indication for AT and surviving the first 30 days after their initial ICH event, 1281 (43%) died, 497 (17%) developed a thromboembolic event, and 536 (18%) had a major bleeding during a median follow-up period of 2.3 years. Among patients receiving post-ICH AT, 91 (6.1%) experienced a recurrent ICH as their first major bleeding event, whereas 113 patients (7.6%) who did not receive any AT post-ICH also experienced a recurrent ICH. The distribution of post-ICH major bleeding types can be seen in Table I in the online-only Data Supplement.

Postdischarge use of AT among patients with indication for OAT was associated with a significant lower risk of death (adjusted hazard ratio [HR], 0.59; 95% confidence interval.

Post-ICH use of OAT was primarily initiated within the first 3 to 6 months during which time ≥34% had reimbursed their AT prescription. Within 5 years, ∼48% of all patients had filled at least one prescription for AT. Previous use of OAT, a high Scandinavian Stroke Scale score, and smoking history were significant predictors for resumption of OAT (Table 3). Significant predictors of resumption of platelet inhibitors included pre-ICH use of platelet inhibitors and a high Scandinavian Stroke Scale score.

Clinical Outcomes
Among patients having indication for AT and surviving the first 30 days after their initial ICH event, 1281 (43%) died, 497 (17%) developed a thromboembolic event, and 536 (18%) had a major bleeding during a median follow-up period of 2.3 years. Among patients receiving post-ICH AT, 91 (6.1%) experienced a recurrent ICH as their first major bleeding event, whereas 113 patients (7.6%) who did not receive any AT post-ICH also experienced a recurrent ICH. The distribution of post-ICH major bleeding types can be seen in Table I in the online-only Data Supplement.

Postdischarge use of OAT among patients with indication for OAT was associated with a significant lower risk of death (adjusted hazard ratio [HR], 0.59; 95% confidence interval.

Results
We identified 6369 incident ICH patients surviving at least 30 days, of whom 2978 (47%) had indication for AT at the time of admission. Of these, 2298 (77%) had only a single indication for AT, whereas the rest had ≥2 indications. Patient characteristics are presented in Table 1. Among patients with atrial fibrillation, 94% had a CHA2DS-VASc score ≥2 and 50% had a HAS-BLED score ≥4.

Use of AT
The proportion of patients who filled a prescription for OAT within 180 days after ICH admission was reduced by >55% compared with the proportion of patients using OAT at the time of admission for ICH (Table 2).

Table 1. Continued

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>OAT (N=160)</th>
<th>Platelet Inhibitors (N=799)</th>
<th>Combination (N=63)</th>
<th>No AT (N=1956)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indication for AT*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischemic stroke</td>
<td>67 (41.9)</td>
<td>610 (76.3)</td>
<td>32 (50.8)</td>
<td>1430 (73.1)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>115 (71.9)</td>
<td>289 (36.2)</td>
<td>47 (74.6)</td>
<td>581 (29.7)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>12 (7.5)</td>
<td>100 (12.5)</td>
<td>9 (14.3)</td>
<td>143 (7.3)</td>
</tr>
<tr>
<td>Venous thromboembolism</td>
<td>25 (15.6)</td>
<td>51 (6.4)</td>
<td>5 (7.9)</td>
<td>155 (7.9)</td>
</tr>
<tr>
<td>Artificial heart valve</td>
<td>24 (15.0)</td>
<td>16 (2.0)</td>
<td>12 (19.0)</td>
<td>26 (1.3)</td>
</tr>
<tr>
<td>Peripheral arterial disease</td>
<td>3 (1.9)</td>
<td>4 (0.5)</td>
<td>1 (1.6)</td>
<td>22 (1.1)</td>
</tr>
</tbody>
</table>

AT indicates antithrombotic therapy; ICH, intracerebral hemorrhage; and OAT, oral anticoagulation therapy.

*The patients could have more than one indication.

Table 2. Preadmission and Post-ICH Hospitalization Use of AT Among ICH Survivors With Indication for Antithrombotic Therapy

<table>
<thead>
<tr>
<th>Antithrombotic Drug</th>
<th>Preadmission Use (90 d Before; N=2978), (%)</th>
<th>Post-ICH Use (180 d After; N=2543), (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any OAT</td>
<td>421 (14.1)</td>
<td>160 (6.3)</td>
</tr>
<tr>
<td>Vitamin K oral anticoagulants</td>
<td>410 (13.8)</td>
<td>105 (4.1)</td>
</tr>
<tr>
<td>NOACs</td>
<td>11 (0.4)</td>
<td>55 (2.2)</td>
</tr>
<tr>
<td>Any platelet inhibitor</td>
<td>926 (31.1)</td>
<td>799 (31.4)</td>
</tr>
<tr>
<td>ASA</td>
<td>565 (19.0)</td>
<td>461 (18.1)</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>103 (3.5)</td>
<td>201 (7.9)</td>
</tr>
<tr>
<td>Combination (OAT+platelet inhibitor)</td>
<td>153 (5.1)</td>
<td>63 (3.4)</td>
</tr>
</tbody>
</table>

ASA indicates acetylsalicylic acid (or aspirin); AT, antithrombotic therapy; ICH, intracerebral hemorrhage; NOAC, non–vitamin K antagonist oral anticoagulant; and OAT, oral anticoagulation therapy.
Table 3. Predictors of Resumption of Platelet Inhibitors and OAT

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Platelet Inhibitors, Mutually Adjusted OR (95% CI)</th>
<th>Oral Anticoagulants, Mutually Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous treatment with platelet inhibitors</td>
<td>2.54 (1.98–3.26)</td>
<td>…</td>
</tr>
<tr>
<td>Previous treatment with OAT</td>
<td>…</td>
<td>7.15 (4.68–10.92)</td>
</tr>
<tr>
<td>Age</td>
<td>1.01 (1.00–1.02)</td>
<td>0.97 (0.95–0.99)</td>
</tr>
<tr>
<td>Sex (male vs female)</td>
<td>1.13 (0.89–1.45)</td>
<td>1.06 (0.73–1.53)</td>
</tr>
<tr>
<td>BMI</td>
<td>0.75 (0.41–1.36)</td>
<td>1.11 (0.37–3.27)</td>
</tr>
<tr>
<td>Low vs normal</td>
<td>1.13 (0.88–1.47)</td>
<td>0.97 (0.67–1.41)</td>
</tr>
<tr>
<td>High vs normal</td>
<td>1.84 (1.40–2.41)</td>
<td>1.86 (1.22–2.84)</td>
</tr>
<tr>
<td>SSS score (high vs low)</td>
<td>1.23 (0.91–1.65)</td>
<td>0.51 (0.32–0.83)</td>
</tr>
<tr>
<td>Smoking</td>
<td>1.08 (0.79–1.47)</td>
<td>0.64 (0.42–0.97)</td>
</tr>
<tr>
<td>Smoker vs nonsmoker</td>
<td>1.10 (0.77–1.56)</td>
<td>1.28 (0.69–2.37)</td>
</tr>
<tr>
<td>Alcohol</td>
<td>0.97 (0.76–1.24)</td>
<td>0.96 (0.67–1.39)</td>
</tr>
<tr>
<td>Civil status</td>
<td>1.11 (0.61–2.03)</td>
<td>0.54 (0.12–2.48)</td>
</tr>
<tr>
<td>Other vs married</td>
<td>0.82 (0.62–1.09)</td>
<td>1.08 (0.73–1.62)</td>
</tr>
<tr>
<td>Comorbidity level</td>
<td>0.80 (0.87–1.12)</td>
<td>1.09 (0.70–1.70)</td>
</tr>
<tr>
<td>Moderate vs no comorbidity</td>
<td>1.08 (0.81–1.43)</td>
<td>0.99 (0.71–1.39)</td>
</tr>
</tbody>
</table>

[CI], 0.43–0.82) and thromboembolic events (adjusted HR, 0.58; 95% CI, 0.35–0.97) and a no increased risk of major bleeding (adjusted HR, 0.65; 95% CI, 0.41–1.02), including no increased risk of recurrent ICH (adjusted HR, 0.90; 95% CI, 0.44–1.82; Table 4). In contrast, use of platelet inhibitors among patients with indication for platelet inhibitors was not related to statistically significantly improved clinical outcome, including death (adjusted HR, 0.96; 95% CI, 0.80–1.15), thromboembolic events (adjusted HR, 0.99; 95% CI, 0.75–1.31), and major bleeding (adjusted HR, 0.89; 95% CI, 0.68–1.16). In the land mark analysis in which the follow-up period started 1 year after ICH admission, postdischarge use of OAT was also associated with improved clinical outcome; however, the difference only reached statistical significance for major bleeding (see Table II in the online-only Data Supplement). In contrast, post-ICH OAT use among pre-ICH OAT users was associated with significantly reduced risk of both death (adjusted HR, 0.51; 95% CI, 0.33–0.78) and thromboembolic events (adjusted HR, 0.45; 95% CI, 0.22–0.90) and no increased risk of major bleeding (adjusted HR, 0.71; 95% CI, 0.40–1.26; see Table III in the online-only Data Supplement).

Table IV in the online-only Data Supplement presents the results on the association between time of first filled prescription for AT after ICH and the clinical outcome. Both early (within 30 days from inclusion) and late (>180 days from inclusion) initiation of OAT after ICH was associated with a significantly lower risk of death. Similar patterns were found for thromboembolic events and major bleeding, although the statistical precision was modest in some of the analyses. Initiation of OAT within 31 to 180 days was not associated with a favorable outcome, which may be a chance finding because of the few patients starting OAT within this timeframe.

To further test the robustness of the primary analyses, we also performed a propensity score-matched analysis including 192 patients who started OAT therapy within 180 days after ICH and 192 matching nonusers of OAT. The characteristics of the OAT users and the matched nonusers were well balanced (Figures I and II in the online-only Data Supplement). Use of OAT was associated with a lower risk of death (adjusted HR, 0.48; 95% CI, 0.30–0.75) and thromboembolic events (adjusted HR, 0.48; 95% CI, 0.25–0.96) and no increased risk of major bleeding (adjusted HR, 0.65; 95% CI, 0.35–1.20).

Discussion

Almost half of the patients surviving the first 30 days after their ICH event had indication for AT in our nationwide study. The outcome for this population was in general poor and included a high absolute risk of all-cause mortality as well as ischemic and major bleeding events. Overall, the use of AT post ICH, in particular OAT, was associated with a lower risk of death and thromboembolic events and no increased risk of major bleeding, including recurrent ICH, although not reaching statistical significance in all analyses. Early start/resumption of AT after ICH seemed to be safe.

The high proportion of patients with indication for AT in our study confirms and extends recent findings. Pasquini et al reported that 44% of ICH patients in their study used AT at the time of admission, whereas Pennlert et al in a nationwide Swedish study found that 39% of the patients, who eventually were discharged alive after ICH, were using AT at the time of admission. The high absolute risk of thromboembolic events and death among the ICH survivors with indication for AT in our study is also in accordance with other recent studies.

A high proportion of the patients receiving AT at the time of ICH did not resume AT despite their high risk of thromboembolic events. This is in accordance with the low proportion of OAT use among ICH survivors with atrial fibrillation, which has been reported in other studies. The proportion receiving OAT post ICH varies somewhat between the studies, which may both reflect differences between the studies with regard to definition of study population and follow-up period and reflect variation in clinical practice. Worth noting in our study was the marked relative increase in the use of non–vitamin K antagonist oral anticoagulants when comparing the post- and pre-ICH period. This likely reflects that some of the patients...
who had previously been treated with vitamin K oral anticoagulants were shifted to non–vitamin K antagonist oral anticoagulants in anticipation of a lower risk of recurrent ICH. However, although the relative increase was large (5-fold), the proportion of ICH survivors who used non–vitamin K antagonist oral anticoagulants remained low.

The association between post-ICH use of OAT and the clinical outcome observed in our study is in accordance and extend findings from other recent studies linking OAT with an improved clinical outcome among patients surviving intracranial hemorrhage and traumatic brain injury.4–7,12 The studies differ in design, type of patients included, sample size, and level of details of the available data on patient characteristics and care (including drug use) and outcomes. The individual studies have specific set of strengths and limitations and are therefore complimentary from a methodological point of view. It is consequently remarkable, how consistent the results are across the studies. Altogether, the studies provide support for the hypothesis that depending on appropriate patient selection, OAT therapy can be used safely in patients with high risk of thromboembolism and also in patients at increased risk of ICH or other intracranial hemorrhage. The studies furthermore indicate that early start of OAT therapy can be used without offsetting patient safety.6,12 Still, it is essential to be aware that all of the data presented to date are observational, and although the studies indicate that a nihilistic therapeutic approach is not warranted, they should not be interpreted as a recommendation for unreflected and aggressive use of OAT in all patients with a high predicted risk of thromboembolism surviving ICH. The decision of whether to use or avoid OAT should in any case depend on a thorough assessment of the individual patient’s thrombohemorrhagic risk and should reflect the patient’s preferences and informed choice.

The strength of our study include the prospective population-based design with complete follow-up, limiting the risk of bias and the large sample size.

Table 4. Crude and Adjusted HRs with 95% CIs of Death, Thromboembolic Events, and Major Bleeding According to Time-Dependent Use of OAT and Platelet Inhibitors

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Patients With Indication for OAT</th>
<th>Patients With Indication for Platelet Inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Crude HRs (95% CI)</td>
<td>Adjusted HRs (95% CI)*</td>
</tr>
<tr>
<td>Death</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OAT</td>
<td>0.41 (0.30–0.56)</td>
<td>0.59 (0.43–0.82)</td>
</tr>
<tr>
<td>Vitamin K oral anticoagulants</td>
<td>0.43 (0.31–0.60)</td>
<td>0.64 (0.46–0.90)</td>
</tr>
<tr>
<td>NOACs</td>
<td>0.31 (0.13–0.75)</td>
<td>0.36 (0.15–0.88)</td>
</tr>
<tr>
<td>Platelet inhibitors</td>
<td>0.79 (0.66–0.95)</td>
<td>0.81 (0.67–0.98)</td>
</tr>
<tr>
<td>Thromboembolic event</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OAT</td>
<td>0.59 (0.36–0.97)</td>
<td>0.58 (0.35–0.97)</td>
</tr>
<tr>
<td>Vitamin K oral anticoagulants</td>
<td>0.51 (0.29–0.89)</td>
<td>0.48 (0.27–0.86)</td>
</tr>
<tr>
<td>NOACs</td>
<td>1.04 (0.42–2.53)</td>
<td>1.25 (0.49–3.17)</td>
</tr>
<tr>
<td>Platelet inhibitors</td>
<td>1.13 (0.84–1.53)</td>
<td>1.03 (0.75–1.41)</td>
</tr>
<tr>
<td>Major bleeding</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OAT</td>
<td>0.66 (0.42–1.02)</td>
<td>0.65 (0.41–1.02)</td>
</tr>
<tr>
<td>Vitamin K oral anticoagulants</td>
<td>0.68 (0.43–1.08)</td>
<td>0.68 (0.42–1.10)</td>
</tr>
<tr>
<td>NOACs</td>
<td>0.54 (0.17–1.71)</td>
<td>0.48 (0.15–1.55)</td>
</tr>
<tr>
<td>Platelet inhibitors</td>
<td>0.90 (0.66–1.22)</td>
<td>0.96 (0.70–1.31)</td>
</tr>
<tr>
<td>Recurrent ICH</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OAT</td>
<td>0.90 (0.46–1.77)</td>
<td>0.90 (0.44–1.82)</td>
</tr>
<tr>
<td>Vitamin K oral anticoagulants</td>
<td>0.96 (0.47–1.94)</td>
<td>0.96 (0.46–2.01)</td>
</tr>
<tr>
<td>NOACs</td>
<td>0.57 (0.08–4.16)</td>
<td>0.56 (0.07–4.19)</td>
</tr>
<tr>
<td>Platelet inhibitors</td>
<td>1.18 (0.72–1.92)</td>
<td>1.24 (0.75–2.05)</td>
</tr>
</tbody>
</table>

The analyses are separated according to indication for OAT (patients with atrial fibrillation, artificial heart valve, or venous thromboembolism) and platelet inhibitors (patients with a history of acute myocardial infarction, ischemic stroke, or peripheral arterial disease). AT indicates antithrombotic therapy; BMI, body mass index; CI, confidence interval; HR, hazard ratio; ICH, intracerebral hemorrhage; NOAC, non–vitamin K antagonist oral anticoagulant; and OAT, oral anticoagulant therapy.

*Adjusted for sex, age, admission year, stroke severity, indication for AT, contraindications to OAT, BMI, alcohol consumption, smoking status, and civil status.
level of the patients (eg, modified Rankin Scale); however, except for data on stroke severity at the time of admission, data on these factors were not available. Furthermore, the data available did not fully allow that the definitions of bleeding proposed by the Bleeding Academic Research Consortium were used; however, the definition used in our study did closely resemble a type 2 bleeding or higher as defined by Bleeding Academic Research Consortium.23

Conclusions
In conclusion, indication for AT was found among almost half of all surviving ICH patients. Postdischarge initiation or resuming of OAT among patients with indication was associated with lower mortality and lower risk of thromboembolic events and was not associated with an increased risk of major bleeding, including recurrent ICH. Randomized clinical trial data are warranted to confirm these findings.

Sources of Funding
This study was partly supported by a research grant from Bristol-Myers Squibb (BMS) and Pfizer to Aarhus University.

Disclosures
Drs Hansen, Brandes, and Husted are members of an advisory board for BMS/Pfizer. Dr Damgaard has received speaker’s honoraria from Bayer, Boehringer-Ingelheim, BMS, and Pfizer. Dr Johnsen is member of advisory boards for BMS/Pfizer and Bayer and has received speaker’s honoraria from Bayer, Boehringer-Ingelheim, BMS, and Pfizer. The other authors report no conflicts.

References

Ottosen et al ICH and Indication for Antithrombotic Therapy 1843
Use of Antithrombotic Therapy and Long-Term Clinical Outcome Among Patients Surviving Intracerebral Hemorrhage
Tobias Pilgaard Ottosen, Miriam Grijota, Morten Lock Hansen, Axel Brandes, Dorte Damgaard, Steen Elkjær Husted and Søren Paaske Johnsen

Stroke. 2016;47:1837-1843; originally published online June 14, 2016;
doi: 10.1161/STROKEAHA.116.012945
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

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Table I. Distribution of subtypes of major bleeding, after admission with ICH.

<table>
<thead>
<tr>
<th>Type of bleeding</th>
<th>No N, (%)</th>
<th>Yes N, (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intracranial</td>
<td>230 (15.6)</td>
<td>215 (14.3)</td>
</tr>
<tr>
<td>- (Subtype intracerebral)</td>
<td>113 (7.6)</td>
<td>91 (6.1)</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>23 (1.6)</td>
<td>18 (1.2)</td>
</tr>
<tr>
<td>Urinary or lung bleeding</td>
<td>24 (1.6)</td>
<td>26 (1.7)</td>
</tr>
<tr>
<td>None</td>
<td>1201 (81.3)</td>
<td>1241 (82.7)</td>
</tr>
<tr>
<td>Total</td>
<td>1478 (100.0)</td>
<td>1500 (100.0)</td>
</tr>
</tbody>
</table>
Use of antithrombotic therapy and long-term clinical outcome among patients surviving intracerebral hemorrhage

**Supplementary Table II** Crude and adjusted hazard ratios (HRs) with 95% confidence intervals (95% CI) of death, thromboembolic events and major bleeding according to time-dependent use of oral anticoagulant therapy (OAT) (including vitamin K oral anticoagulants and non-vitamin K oral anticoagulants (NOAC)) and platelet inhibitors. The analyses includes patients who survive the 1 year after admission and post-discharge have indication for OAT due to either atrial fibrillation, artificial heart valve or venous thromboembolism.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Patients with indication for OAT</th>
<th>Patients with indication for platelet inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Crude HRs (95% CI)</td>
<td>Adjusted HRs (95% CI)*</td>
</tr>
<tr>
<td><strong>Death</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OAT</td>
<td>0.54 (0.38-0.76)</td>
<td>0.79 (0.55-1.14)</td>
</tr>
<tr>
<td>-Vitamin K oral anticoagulants</td>
<td>0.56 (0.39-0.80)</td>
<td>0.85 (0.67-1.08)</td>
</tr>
<tr>
<td>-NOACs</td>
<td>0.38 (0.12-1.19)</td>
<td>0.51 (0.16-1.65)</td>
</tr>
<tr>
<td>Platelet inhibitors</td>
<td>0.82 (0.65-1.03)</td>
<td>0.85 (0.67-1.08)</td>
</tr>
<tr>
<td><strong>Thromboembolic event</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OAT</td>
<td>0.66 (0.33-1.32)</td>
<td>0.74 (0.36-1.55)</td>
</tr>
<tr>
<td>-Vitamin K oral anticoagulants</td>
<td>0.52 (0.24-1.14)</td>
<td>0.59 (0.26-1.34)</td>
</tr>
<tr>
<td>-NOACs</td>
<td>4.51 (1.10-18.46)</td>
<td>5.28 (1.09-25.45)</td>
</tr>
<tr>
<td>Platelet inhibitors</td>
<td>5.95 (3.98-8.91)</td>
<td>5.52 (3.61-8.43)</td>
</tr>
<tr>
<td><strong>Major bleeding</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OAT</td>
<td>0.54 (0.31-0.94)</td>
<td>0.47 (0.26-0.88)</td>
</tr>
<tr>
<td>-Vitamin K oral anticoagulants</td>
<td>0.61 (0.35-1.06)</td>
<td>0.55 (0.31-1.00)</td>
</tr>
<tr>
<td>-NOACs</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Platelet inhibitors</td>
<td>0.84 (0.58-1.22)</td>
<td>0.89 (0.60-1.31)</td>
</tr>
</tbody>
</table>

* Adjusted for the following variables: sex, age, admission year, stroke severity, indication for AT, contraindications to OAT, BMI, alcohol consumption, smoking status, civil status.
Supplementary Table III Crude and adjusted hazard ratios (HRs) with 95% confidence intervals (95% CI) of death, thromboembolic events and major bleeding according to time-dependent use of oral anticoagulant therapy (OAT) (including vitamin K oral anticoagulants and non-vitamin K oral anticoagulants (NOAC)). This analysis includes patients with pre-ICH treatment use of OAT, who survive the first 30-days after admission and post-discharge have indication for OAT due to either atrial fibrillation, artificial heart valve or venous thromboembolism.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Patients with indication for OAT</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Crude HRs (95% CI)</td>
<td>Adjusted HRs (95% CI)*</td>
<td></td>
</tr>
<tr>
<td><strong>Death</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OAT</td>
<td>0.38 (0.25-0.58)</td>
<td>0.51 (0.33-0.78)</td>
<td></td>
</tr>
<tr>
<td>-Vitamin K oral anticoagulants</td>
<td>0.36 (0.23-0.57)</td>
<td>0.49 (0.31-0.78)</td>
<td></td>
</tr>
<tr>
<td>-NOACs</td>
<td>0.51 (0.21-1.24)</td>
<td>0.60 (0.24-1.51)</td>
<td></td>
</tr>
<tr>
<td>Platelet inhibitors</td>
<td>0.66 (0.49-0.88)</td>
<td>0.66 (0.49-0.90)</td>
<td></td>
</tr>
<tr>
<td><strong>Thromboembolic event</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OAT</td>
<td>0.47 (0.24-0.92)</td>
<td>0.45 (0.22-0.90)</td>
<td></td>
</tr>
<tr>
<td>-Vitamin K oral anticoagulants</td>
<td>0.38 (0.18-0.85)</td>
<td>0.35 (0.15-0.79)</td>
<td></td>
</tr>
<tr>
<td>-NOACs</td>
<td>0.94 (0.29-3.04)</td>
<td>1.23 (0.35-4.26)</td>
<td></td>
</tr>
<tr>
<td>Platelet inhibitors</td>
<td>1.38 (0.88-2.15)</td>
<td>1.33 (0.83-2.11)</td>
<td></td>
</tr>
<tr>
<td><strong>Major bleeding</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OAT</td>
<td>0.70 (0.41-1.20)</td>
<td>0.71 (0.40-1.26)</td>
<td></td>
</tr>
<tr>
<td>-Vitamin K oral anticoagulants</td>
<td>0.67 (0.38-1.21)</td>
<td>0.69 (0.37-1.27)</td>
<td></td>
</tr>
<tr>
<td>-NOACs</td>
<td>0.84 (0.26-2.71)</td>
<td>0.84 (0.25-2.83)</td>
<td></td>
</tr>
<tr>
<td>Platelet inhibitors</td>
<td>1.17 (0.76-1.79)</td>
<td>1.20 (0.77-1.86)</td>
<td></td>
</tr>
</tbody>
</table>

* Adjusted for the following variables: sex, age, admission year, stroke severity, indication for AT, contraindications to OAT, BMI, alcohol consumption, smoking status, civil status.
Table IV. Crude and adjusted hazard ratios (HRs) with 95% confidence intervals (95% CI) of death, thromboembolic events and major bleeding according to timing of post-ICH initiation of antithrombotic therapy, including oral anticoagulant therapy (OAT) (including vitamin K oral anticoagulants and non-vitamin K oral anticoagulants) and platelet inhibitors.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Death</th>
<th>Thromboembolic event</th>
<th>Major bleeding</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Crude HRs (95% CI)</td>
<td>Adjusted HRs (95% CI)*</td>
<td>Crude HRs (95% CI)</td>
</tr>
<tr>
<td>OAT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-30 days</td>
<td>0.48 (0.30 - 0.77)</td>
<td>0.56 (0.33 - 0.94)</td>
<td>0.72 (0.38 - 1.34)</td>
</tr>
<tr>
<td>31-60 days</td>
<td>0.73 (0.27 - 1.94)</td>
<td>0.59 (0.15 - 2.41)</td>
<td>-</td>
</tr>
<tr>
<td>61-180 days</td>
<td>1.34 (0.60 - 3.00)</td>
<td>0.78 (0.25 - 2.45)</td>
<td>-</td>
</tr>
<tr>
<td>&gt; 180 days</td>
<td>0.71 (0.49 - 1.05)</td>
<td>0.61 (0.40 - 0.92)</td>
<td>0.91 (0.50 - 1.66)</td>
</tr>
<tr>
<td>Platelet inhibitors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-30 days</td>
<td>0.91 (0.75 - 1.11)</td>
<td>0.78 (0.63 - 0.97)</td>
<td>0.87 (0.63 - 1.19)</td>
</tr>
<tr>
<td>31-60 days</td>
<td>0.90 (0.54 - 1.51)</td>
<td>0.88 (0.51 - 1.54)</td>
<td>1.10 (0.52 - 2.33)</td>
</tr>
<tr>
<td>61-180 days</td>
<td>1.42 (1.07 - 1.89)</td>
<td>1.47 (1.08 - 2.01)</td>
<td>1.91 (1.18 - 3.08)</td>
</tr>
<tr>
<td>&gt; 180 days</td>
<td>0.91 (0.78 - 1.06)</td>
<td>0.94 (0.79 - 1.12)</td>
<td>1.06 (0.82 - 1.36)</td>
</tr>
</tbody>
</table>

* Adjusted for the following variables: sex, age, admission year, stroke severity, indication for AT, contraindications to OAT, BMI, alcohol consumption, smoking status, civil status.
Supplementary Figure I: Standardized differences in variables included in the propensity score for the entire study population (blue dots) and for the propensity score-matched patients (red dots).
Supplementary Figure II: Variance ratios of variables included in the propensity score for the entire study population (blue dots) and for the propensity score-matched patients (red dots).
非アジア系コホートのもやもや血管障害鑑別における血管壁MRIの付加価値

Added Value of Vessel Wall Magnetic Resonance Imaging in the Differentiation of Moyamoya Vasculopathies in a Non-Asian Cohort

Mahmud Mossa-Basha, MD1; Adam de Havenon, MD3; Kyra J. Becker, MD2, et al.

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背景および目的: これまでにもやもや病とアテローム性動脈硬化症を鑑別する画像を評価する研究は行われていたが、血管壁MRIの付加価値を調査した研究はない。そこで本研究では、もやもや病、アテローム性もやもや症候群（atherosclerotic-moyamoya syndrome: A-MMS）、血管炎性もやもや症候群（vasculitic-mMSS: V-MMS）の鑑別におけるマルチコントラストプロトコールによる血管壁MRIの診断的付加価値を評価した。

方法: 血管障害（もやもや病、アテローム性動脈硬化症、血管炎）および頭蓋内動脈の狭窄閉塞性疾患と臨床的に判断される患者の頸動脈領域を後向きに調査した。臨床データを知らされていない2名の神経放射線科医が各頸動脈の内腔画像を見て側副血管の範囲を評価し、推定診断と診断の確信度を判断した。3週間後に読影者2名が頸動脈の内腔画像および血管壁MRI画像で造影後の増強の有無・パターン・強度、T2信号の特徴、病変のパターン、推定診断および確信度を検討した。

結果: A-MMS 10例、V-MMS 3例、もやもや病8例の頸動脈病変38ヶ所を対象とした。内腔画像のみに比べ、内腔画像+血管壁MRIにより診断精度は有意に改善された（32% vs. 87%, P < 0.001）。もやもや病で最も多かった血管壁MRI所見は、増強、リモデリング、T2不均一性のいずれも認められない病変であった。A-MMSの場合は偏心性、リモデリング、T2不均一性が多かったが、増強は軽度/中等度かつ均一/不均一であった。V-MMSの場合は均一な中等度に増強した偏心性病変が多くあった。読影者間の一致度は、血管壁MRIの全特徴が「中~高」（κ=0.46~0.86）、側副血管のグレードが「やや低」（κ=0.35）であった。内腔画像の診断に対する読影者間一致度は11%であったが、内腔画像+血管壁MRIの場合は82%であった（P<0.001）。

結論: 血管壁MRIと従来の画像法を組み合わせることにより、もやもや血管障害の鑑別精度を大きく改善することができる。