Prescription of cardiovascular medication in Vascular Dementia.

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A Few cerebrovascular lesions here!
Major mechanisms underlying vascular cognitive impairment (VCI)

(A, Vascular causes. B, Brain parenchymal lesions associated with VCI)

Circ Res. 2017;120:573-591
It is a potential missed opportunity when active patients in the community, still driving, caring for grandchildren or even working; are diagnosed with mild vascular cognitive impairment, but perhaps are not considered for secondary cardiovascular investigations and treatment.

These mild vascular cognitive impairment patients have potentially the most to benefit from timely secondary cardiovascular risk reduction including cardiovascular investigations to exclude cardiac causes, atrial fibrillation, hypercholesterolemia, diabetes, and hypertension. They are most likely to benefit from lifestyle changes.

The main role of interventions in the treatment of vascular dementia is in preventing further ischemic events.
Usual Management after TIA

- Lifestyle
- Antiplatelet/anticoagulant
- Antihypertensive(s)
- Lipid lowering
- Optimise management of other conditions e.g. diabetes
Treatment considerations following diagnosis of VCI or vaD

- Lifestyle
- Antiplatelet/anticoagulant
- Antihypertensive(s)
- Lipid lowering
- Optimise management of other conditions eg diabetes
• PROGRESS

• If you prevent the occurrence of further stroke you reduce dementia and cognitive decline

• Indapamide and perindopril based regimen
Antiplatelets
Silent Cerebrovascular disease

• Approximately 25% of people >80 years of age have ≥1 silent brain infarcts

• It is not clear whether WMH alone, in the absence of other risk factors, is a sufficient reason for aspirin therapy.

AHA & ASA Stroke. 2017;48:e44-e71
Aspirin in Alzheimer’s Disease Increased Risk of Intracerebral Hemorrhage: Cause for Concern?

- AD2000 (AD + CVD): EVA (AD + CVD)

- In case of a conventional indication for aspirin as a secondary prevention measure (e.g., after stroke or myocardial infarction), aspirin should be prescribed also in patients with AD.

- However, with the results of our study suggesting an increased risk for ICH, we want to stress that aspirin should not be prescribed for AD patients to slow cognitive decline if no clear cardiovascular indication exists.
Aspirin in Alzheimer’s Disease Increased Risk of Intracerebral Hemorrhage: Cause for Concern?

**Table.** Numbers of ICHs and Numbers of Patients Randomized in Each Group, Mean Time of Follow-Up per Patient, and HR With 95% CI

<table>
<thead>
<tr>
<th></th>
<th>ICH in Aspirin Group</th>
<th>ICH in Control Group</th>
<th>Mean Time of Follow-Up (Months)</th>
<th>HR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n of Events</td>
<td>%</td>
<td>n of Events</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>EVA</td>
<td>3/65</td>
<td>4.6</td>
<td>0/58</td>
<td>0</td>
<td>22</td>
</tr>
<tr>
<td>AD2000</td>
<td>4/156</td>
<td>2.6</td>
<td>0/154</td>
<td>0</td>
<td>29</td>
</tr>
<tr>
<td>Pooled</td>
<td>7/221</td>
<td>3.2</td>
<td>0/212</td>
<td>0</td>
<td>27</td>
</tr>
</tbody>
</table>

Interesting Observation: Not significant

Stroke. 2010;41:2690-2692
Anticoagulants
AF and dementia share common risk factors. Additional mechanisms (horizontal arrows) might explain risk noted beyond that associated with coronary artery disease, heart failure, hypertension, diabetes and age.

Cumulative event rate of dementia in patients with or without AF. Log rank test demonstrated significantly different risk of dementia between two groups. As the cumulative incidence curve showed, AF patients had a higher risk of dementia compared to non-AF subjects. AF= atrial fibrillation.
Relationship of Anticoagulant Therapy With Cognitive Impairment Among Patients With Atrial Fibrillation: A Meta-Analysis and Systematic Review

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log[Hazard Ratio]</th>
<th>SE</th>
<th>Weight</th>
<th>Hazard Ratio IV, Random, 95% CI</th>
<th>Hazard Ratio IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1.1 ≤25% vs &gt;75%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bunch.T 2016</td>
<td>0.6523</td>
<td>0.2314</td>
<td>55.6%</td>
<td>1.92 [1.22, 3.02]</td>
<td></td>
</tr>
<tr>
<td>Jacobs 2014</td>
<td>1.6752</td>
<td>0.4123</td>
<td>44.4%</td>
<td>5.34 [2.38, 11.98]</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>100.0%</td>
<td></td>
<td></td>
<td>3.02 [1.12, 8.19]</td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Tau² = 0.41; Chi² = 4.68, df = 1 (P = 0.03); I² = 79%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 2.18 (P = 0.03)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| 1.1.2 26-50% vs >75% |                  |     |        |                                |                                |
| Bunch.T 2016        | 0.4511           | 0.1909 | 54.3%  | 1.57 [1.08, 2.28]              |                                |
| Jacobs 2014         | 1.411            | 0.3389 | 45.7%  | 4.10 [2.11, 7.97]              |                                |
| Subtotal (95% CI)   | 100.0%           |     |        | 2.44 [0.95, 6.22]              |                                |
| Heterogeneity: Tau² = 0.39; Chi² = 6.09, df = 1 (P = 0.01); I² = 84% | | |
| Test for overall effect: Z = 1.86 (P = 0.06) | | |

| 1.1.3 51-75% vs >75% |                  |     |        |                                |                                |
| Bunch.T 2016        | 0.2624           | 0.16  | 56.4%  | 1.30 [0.95, 1.78]              |                                |
| Jacobs 2014         | 0.9439           | 0.292 | 43.6%  | 2.57 [1.45, 4.55]              |                                |
| Subtotal (95% CI)   | 100.0%           |     |        | 1.75 [0.90, 3.39]              |                                |
| Heterogeneity: Tau² = 0.18; Chi² = 4.19, df = 1 (P = 0.04); I² = 76% | | |
| Test for overall effect: Z = 1.66 (P = 0.10) | | |

Comparison of the indexes between the low TTR group and the high TTR group

Relationship of Anticoagulant Therapy With Cognitive Impairment Among Patients With Atrial Fibrillation: A Meta-Analysis and Systematic Review

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log[Hazard Ratio]</th>
<th>SE</th>
<th>Weight</th>
<th>Hazard Ratio</th>
<th>IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1.1 OAC vs No OAC</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Barber. M 2004</td>
<td>-0.6539</td>
<td>0.3537</td>
<td>0.3%</td>
<td>0.52 [0.26, 1.04]</td>
<td></td>
</tr>
<tr>
<td>Friberg L 2017</td>
<td>-0.3425</td>
<td>0.022</td>
<td>84.1%</td>
<td>0.71 [0.68, 0.74]</td>
<td></td>
</tr>
<tr>
<td>Hu.T.Y 2016</td>
<td>-0.2357</td>
<td>0.1074</td>
<td>3.5%</td>
<td>0.79 [0.64, 0.98]</td>
<td></td>
</tr>
<tr>
<td>Liao.MT 2013</td>
<td>-0.2618</td>
<td>0.3122</td>
<td>0.4%</td>
<td>0.77 [0.42, 1.42]</td>
<td></td>
</tr>
<tr>
<td>Viscogliosi. G 2017</td>
<td>-0.3147</td>
<td>0.0592</td>
<td>11.6%</td>
<td>0.73 [0.65, 0.82]</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td></td>
<td>100.0%</td>
<td>0.71 [0.69, 0.74]</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.00; Chi² = 1.95, df = 4 (P = 0.74); I² = 0%
Test for overall effect: Z = 16.66 (P < 0.00001)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log[Hazard Ratio]</th>
<th>SE</th>
<th>Weight</th>
<th>Hazard Ratio</th>
<th>IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1.2 NOAC vs Wafarin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Friberg L 2017</td>
<td>-0.0305</td>
<td>0.67</td>
<td>6.2%</td>
<td>0.97 [0.26, 3.61]</td>
<td></td>
</tr>
<tr>
<td>Jacobs 2016</td>
<td>-0.7133</td>
<td>0.1717</td>
<td>93.8%</td>
<td>0.49 [0.35, 0.69]</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td></td>
<td>100.0%</td>
<td>0.51 [0.37, 0.71]</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.00; Chi² = 0.97, df = 1 (P = 0.32); I² = 0%
Test for overall effect: Z = 4.04 (P < 0.00001)

Comparison of the OAC group and no OAC group and group NOAC and group warfarin

Effect of apixaban on brain infarction and microbleeds: AVERROES-MRI assessment study

Baseline MRI scans revealed brain infarct(s) in 26.2% and microbleed(s) in 10.5%. The rate of the primary outcomes was 2.0% in the apixaban group and 3.3% in the aspirin group (hazard ratio [HR] 0.55; 0.27-1.14) from baseline to follow-up MRI scan (mean duration of follow-up: 1 year).

In those who completed baseline and follow-up MRI scans, the rate of new infarction detected on MRI was 2.5% in the apixaban group and 2.2% in the aspirin group (HR 1.09; 0.47-2.52), but new infarcts were smaller in the apixaban group (P = .03). There was no difference in proportion with new microbleeds on follow-up MRI (HR 0.92; 0.53-1.60) between treatment groups.

Antihypertensives
Impact of Hypertension on Cognitive Function: A Scientific Statement From the American Heart Association

• Chronic arterial hypertension is a well-established risk factor for both types of dementia, but the link between hypertension and its treatment and cognition remains poorly understood.

• There is strong evidence of a deleterious influence of midlife hypertension on late-life cognitive function, but the cognitive impact of late-life hypertension is less clear. Observational studies demonstrated a cumulative effect of hypertension on cerebrovascular damage, but evidence from clinical trials that antihypertensive treatment improves cognition is not conclusive.
The group concluded that there were insufficient data to make evidence-based recommendations. However, judicious treatment of hypertension, taking into account goals of care and individual characteristics (eg, age and comorbidities), seems justified to safeguard vascular health and, as a consequence, brain health.
Lipid lowering
There is no evidence to recommend the use of statin therapy for the treatment of AD or VaD.
Statin induced cognitive impairment

There is no significant evidence to suggest that statins cause cognitive impairment


Kelley, B.J. and Glasser, S. Cognitive effects of statin medications. CNS Drugs 2014:28;411–419

In the absence of evidence to guide clinical practice, it seems appropriate to treat those patients with vascular risk factors that meet criteria for lipid-lowering therapy, in terms of primary and secondary prevention of cardiovascular and cerebrovascular events, in line with current guidelines.

Management of the individual patient in a holistic manner according to their own vascular risk profile is recommended.

Overall, there is no evidence to support lipid-lowering therapy in patients for the management of VaD or AD. Giving statins in later life to prevent or treat dementia is not recommended, whilst in midlife data are lacking.
Treatments for diabetes

Warning!!!!

Hypoglycaemia!!!!
Practical Advice

- **Ensure Diagnosis and subtype**

- **If evidence of infarct**
  - Aspirin
  - Statin
  - Blood pressure control

- **Subcortical disease**
  - No evidence for/against aspirin (cerebral haemorrhage???)
  - No evidence for cholesterol or blood pressure control
  - Check for any other history of cardiovascular disease (CHD, TIA? PVD)

- **No evidence for routine use of aspirin/anticoagulation/statins/blood pressure control for the treatment of vascular dementia per se**
Cerebral Microbleeds
Probability of symptomatic intracranial haemorrhage according to the presence or absence of cerebral microbleeds: CROMIS-2
Our prospective, observational, multicentre cohort of patients anticoagulated after recent ischaemic stroke or transient ischaemic attack associated with atrial fibrillation shows that baseline cerebral microbleed presence is independently associated with an increased risk of symptomatic intracranial haemorrhage, but not of recurrent ischaemic stroke.

However, the absolute rate of recurrent ischaemic stroke was much higher than the absolute rate of intracranial haemorrhage, even in those with cerebral microbleeds. We also show that the addition of a neuroimaging biomarker (cerebral microbleed presence) improves the predictive ability of a clinical bleeding risk score (HAS-BLED), which could help clinicians better identify patients at high risk of intracranial haemorrhage.
Anticoagulation and other therapies in patients with silent microbleeds

- It is reasonable to provide anticoagulation therapy to patients with microbleeds when there is an indication (eg, AF).
- When anticoagulation is needed, a novel oral anticoagulant is preferred over warfarin.
- Percutaneous closure of the left atrial appendage could be considered as an alternative to anticoagulation.
- It is reasonable to provide antiplatelet therapy to patients with microbleeds when there is an indication.
- MRI screening for microbleeds is not needed before the initiation of antithrombotic therapies.
- Individuals with silent microbleeds are at increased future risk of both ischemic stroke and ICH.
- Implement preventive care recommended by AHA/ASA guidelines for primary prevention of ischemic stroke.
- It is reasonable to provide preventive care recommended by AHA/ASA guidelines for prevention of ICH.

AHA & ASA Stroke. 2017;48:e44-e71
Thank You

Questions?
There is good evidence that statins given in late life to people at risk of vascular disease do not prevent cognitive decline or dementia.
McGuinness, Craig, Bullock, Passmore. Cochrane Database Syst Rev. 2016 Jan 4;(1)

We found no studies assessing role of statins in treatment of VaD.

Blood pressure lowering in patients without prior cerebrovascular disease for prevention of cognitive impairment and dementia. No effect but not relevant to VCI/VaD.
STROKOG (stroke and cognition consortium): An international consortium to examine the epidemiology, diagnosis, and treatment of neurocognitive disorders in relation to cerebrovascular disease.
Cholesterol lowering medications, such as statins, are used to prevent first and recurrent vascular events including MI and IS. Reducing stroke occurrence by lowering cholesterol may, as a consequence, reduce the incidence of post-stroke dementia.

The Finnish Cardiovascular Risk Factors, Aging and Dementia (CAIDE) study found that midlife total cholesterol predicted cognitive impairment 21 years later, an effect that was attenuated following adjustment for statin usage.

Similarly, raised midlife cholesterol was associated with an increased risk of developing VaD over a 30-year period in a study based on medical records.

In contrast, results from cohorts involving those in later-life vary with some finding higher levels of cholesterol to be associated weakly with a higher risk [37], and others finding a relationship with a lower risk of VaD.

These inconsistencies probably represent the timing of cholesterol measurement in relation to age and clinical onset of dementia. Indeed, pravastatin in older people at risk of CVD had no effect on multiple cognitive outcomes when compared with placebo.
Statins prevention

• Trials of statins assessing outcomes relevant to cognition, dementia and SVD are lacking

• First, inclusion of those with advanced dementia or very elderly people, who carry multiple vascular risk factors and are therefore at risk of vascular disease.

• Second, different markers of dementia were used including a variety of cognitive tests and diagnostic definitions.

• Third, different statin types were assessed including lipophilic and hydrophilic subtypes.

• Fourth, the duration of treatment and timing of assessment in relation to the former varied considerably.

• Fifth, patients from lower socioeconomic class are less likely to be prescribed statins. Last, the pathophysiology of VaD is heterogeneous with significant overlap with AD [
<table>
<thead>
<tr>
<th>Symptomatic intracranial haemorrhage</th>
<th>Absolute event rate*</th>
<th>Rate per 1000 patient-years (95% CI)</th>
<th>Absolute rate increase per 1000 patient-years (95% CI)</th>
<th>Univariable hazard ratio (95% CI)</th>
<th>Adjusted hazard ratio (95% CI)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>No cerebral microbleeds</td>
<td>7/2654</td>
<td>2.6 (1.1 to 5.4)</td>
<td>1 (ref)</td>
<td>1 (ref)</td>
<td>1 (ref)</td>
</tr>
<tr>
<td>Cerebral microbleeds present</td>
<td>7/712</td>
<td>9.8 (4.0 to 20.3)</td>
<td>7.2 (2.9 to 14.9)</td>
<td>3.73 (1.31 to 10.64)</td>
<td>3.67 (1.27 to 10.60)</td>
</tr>
<tr>
<td>1 cerebral microbleed</td>
<td>2/367</td>
<td>5.4 (0.7 to 19.7)</td>
<td>2.8 (–0.4 to 14.3)</td>
<td>2.04 (0.42 to 9.84)</td>
<td>2.03 (0.42 to 9.83)</td>
</tr>
<tr>
<td>≥2 cerebral microbleeds</td>
<td>5/345</td>
<td>14.4 (4.7 to 33.8)</td>
<td>11.8 (3.6 to 28.4)</td>
<td>5.58 (1.77 to 17.58)</td>
<td>5.46 (1.70 to 17.51)</td>
</tr>
<tr>
<td>Recurrent ischaemic stroke</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No cerebral microbleeds</td>
<td>39/2608</td>
<td>15.0 (10.6 to 20.4)</td>
<td>1 (ref)</td>
<td>1 (ref)</td>
<td>1 (ref)</td>
</tr>
<tr>
<td>Cerebral microbleeds present</td>
<td>17/704</td>
<td>24.1 (14.1 to 38.7)</td>
<td>9.1 (3.5 to 18.3)</td>
<td>1.62 (0.92 to 2.87)</td>
<td>1.53 (0.85 to 2.76)</td>
</tr>
<tr>
<td>1 cerebral microbleed</td>
<td>9/362</td>
<td>24.9 (11.4 to 47.2)</td>
<td>9.9 (0.8 to 32.2)</td>
<td>1.68 (0.82 to 3.47)</td>
<td>1.75 (0.84 to 3.65)</td>
</tr>
<tr>
<td>≥2 cerebral microbleeds</td>
<td>8/341</td>
<td>23.4 (10.1 to 46.2)</td>
<td>8.4 (–0.5 to 25.8)</td>
<td>1.56 (0.73 to 3.35)</td>
<td>1.32 (0.60 to 2.93)</td>
</tr>
</tbody>
</table>

Data are calculated on the 1447 participants with follow-up data available. *Calculated as number of events/patient-years. †Adjusted for age and hypertension for symptomatic intracranial haemorrhage, and adjusted for age, sex, hypertension, diabetes, previous ischaemic stroke, and age-related white matter hyperintensities score for recurrent ischaemic stroke.

Table 3: Absolute event rates, absolute risks, and univariable and multivariable hazard ratios for symptomatic intracranial haemorrhage and recurrent ischaemic stroke during follow-up, according to baseline presence and burden of cerebral microbleeds.

Lancet Neurol 2018; 17: 539–47
Lifelong antiplatelet treatment is recommended after ischaemic vascular events, on the basis of trials done mainly in patients younger than 75 years. Upper gastrointestinal bleeding is a serious complication, but had low case fatality in trials of aspirin and is not generally thought to cause long-term disability. Consequently, although coprescription of proton-pump inhibitors (PPIs) reduces upper gastrointestinal bleeds by 70–90%, uptake is low and guidelines are conflicting. We aimed to assess the risk, time course, and outcomes of bleeding on antiplatelet treatment for secondary prevention in patients of all ages.

We did a prospective population-based cohort study in patients with a first transient ischaemic attack, ischaemic stroke, or myocardial infarction treated with antiplatelet drugs (mainly aspirin based, without routine PPI use) after the event in the Oxford Vascular Study from 2002 to 2012, with follow-up until 2013. We determined type, severity, outcome (disability or death), and time course of bleeding requiring medical attention by face-to-face followup for 10 years. We estimated age-specific numbers needed to treat (NNT) to prevent upper gastrointestinal bleeding with routine PPI co-prescription on the basis of Kaplan–Meier risk estimates and relative risk reduction estimates from previous trials.

3166 patients (1582 [50%] aged ≥75 years) had 405 first bleeding events (n=218 gastrointestinal, n=45 intracranial, and n=142 other) during 13 509 patient-years of follow-up. Of the 314 patients (78%) with bleeds admitted to hospital, 117 (37%) were missed by administrative coding. Risk of non-major bleeding was unrelated to age, but major bleeding increased steeply with age (≥75 years hazard ratio [HR] 3·10, 95% CI 2·27–4·24; p<0·0001), particularly for fatal bleeds (5·53, 2·65–11·54; p<0·0001), and was sustained during long-term follow-up. The same was true of major upper gastrointestinal bleeds (≥75 years HR 4·13, 2·60–6·57; p<0·0001), particularly if disabling or fatal (10·26, 4·37–24·13; p<0·0001). At age 75 years or older, major upper gastrointestinal bleeds were mostly disabling or fatal (45 [62%] of 73 patients vs 101 [47%] of 213 patients with recurrent ischaemic stroke), and outnumbered disabling or fatal intracerebral haemorrhage (n=45 vs n=18), with an absolute risk of 9·15 (95% CI 6·67–12·24) per 1000 patient years.

The estimated NNT for routine PPI use to prevent one disabling or fatal upper gastrointestinal bleed over 5 years fell from 338 for individuals younger than 65 years, to 25 for individuals aged 85 years or older.

In patients receiving aspirin-based antiplatelet treatment without routine PPI use, the long-term risk of major bleeding is higher and more sustained in older patients in practice than in the younger patients in previous trials, with a substantial risk of disabling or fatal upper gastrointestinal bleeding. Given that half of the major bleeds in patients aged 75 years or older were upper gastrointestinal, the estimated NNT for routine PPI use to prevent such bleeds is low, and co-prescription should be encouraged.
ICH and Dementia

- Of the 738 people with ICH recruited, 279 (37.8%) developed dementia during the median follow-up of 47.4 months.
- 140 patients developed dementia within 6 months, with the remaining 139 being diagnosed more than 6 months post-ICH.
- An important question to address in those with delayed dementia following ICH is whether cognitive impairment is secondary to the ICH, or are the bleed and cognitive impairment both sequelae of the same underlying disease process.

Biffi et al. Risk factors associated with early vs delayed dementia after intracerebral hemorrhage. JAMA Neurol. 73, 969–976
• Traditional vascular risk factors – diabetes, hypercholesterolaemia, hypertension and smoking – are implicated as risk factors for VaD.

• The associations between cholesterol and small vessel disease (SVD), stroke, cognitive impairment and subsequent dementia are complex and as yet not fully understood.

• Similarly, the effects of lipids and lipid-lowering therapy on preventing or treating dementia remain unclear; the few trials that have assessed lipid-lowering therapy for preventing (two trials) or treating (four trials) dementia found no evidence to support the use of lipid-lowering therapy for these indications.

• It is appropriate to treat those patients with vascular risk factors that meet criteria for lipid-lowering therapy for the primary and secondary prevention of cardiovascular and cerebrovascular events, and in line with current guidelines.

• Managing the individual patient in a holistic manner according to his or her own vascular risk profile is recommended. Although
• Statin therapy protects against stroke in terms of both primary and secondary prevention

• HPS, TnT study

• Meta-analysis of 31 trials revealed no increased risk of ICH in people taking statins (odds ratio [OR] 1.08, 95% CI 0.88–1.32) [138]
As discussed previously, stroke and its recurrence are predictors of dementia. In addition, other vascular diseases – namely coronary artery disease, peripheral arterial disease, AF, renal disease and cardiac failure – have all been associated with cognitive impairment and VaD.

In addition to hypercholesterolaemia, modifiable vascular risk factors comprise diabetes, hypertension, obesity, physical inactivity and smoking, which are all independently associated with cognitive impairment and dementia in later life.
Medications potentially used in VCI

• Antiplatelets*
• Anticoagulation*
• Antihypertensives
• Lipid lowering*
• Hypoglycaemics
• Non pharm: weight, exercise, smoking
Dementia in Patients with and without AF

Forest plot showing the individual and pooled adjusted hazard ratios (HR) of dementia in patients with and without AF. Square boxes denote HR, dimension of each square box denotes weight of random effect analysis, and horizontal lines represent 95% confidence interval.

Cerebral microbleeds and intracranial haemorrhage risk in patients anticoagulated for atrial fibrillation after acute ischaemic stroke or transient ischaemic attack (CROMIS-2): a multicentre observational cohort study

- Cerebral microbleeds are a potential neuroimaging biomarker of cerebral small vessel diseases that are prone to intracranial bleeding. We aimed to determine whether presence of cerebral microbleeds can identify patients at high risk of symptomatic intracranial haemorrhage when anticoagulated for atrial fibrillation after recent ischaemic stroke or transient ischaemic attack.

- 1447 recruited over a mean period of 850 days (366 patient-years).

- The symptomatic intracranial haemorrhage rate in patients with cerebral microbleeds was 9.8 per 1000 patient-years (95% CI 4.0–20.3) compared with 2.6 per 1000 patient-years (95% CI 1.1–5.4) in those without cerebral microbleeds (adjusted hazard ratio 3.67, 95% CI 1.27–10.60).

- Compared with HAS-BLED score alone (C-index 0.41, 95% CI 0.29–0.53), models including cerebral microbleeds and HAS-BLED (0.66, 0.53–0.80) and cerebral microbleeds, diabetes, anticoagulant type, and HAS-BLED (0.74, 0.60–0.88) predicted symptomatic intracranial haemorrhage significantly better (difference in C-index 0.25, 95% CI 0.07–0.43, p=0.0065; and 0.33, 0.14–0.51, p=0.00059, respectively).

- In patients with atrial fibrillation anticoagulated after recent ischaemic stroke or transient ischaemic attack, cerebral microbleed presence is independently associated with symptomatic intracranial haemorrhage risk and could be used to inform anticoagulation decisions.

Lancet Neurol 2018; 17: 539–47