Is the demonstration of high number of cerebral microbleeds (CMB) a contraindication to anticoagulant treatment?

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Both iv. thrombolysis and long-term anticoagulation can be associated with bleeding complications. The HAS-BLED score is useful in daily practice, but having a more sensitive biomarker would be optimal before starting long-term anticoagulation. The cerebral microbleed is one of the promising candidates. The cerebral microbleeds (CMB) are small, 5-10 mm areas of signal loss on MRI susceptibility-weighted sequences (1,2). A metaanalysis performed by Liang et al (3) found increased risk of microbleeds associated- and anticoagulation-related ICH (OR:4.01 P=0.001). It was significant for warfarin (OR:8.02 P=0.015). The META-MICROBLEEDS Initiative (4) (four studies, 990 ischemic pts, follow up 17-37 months) observed an ICH rate of 1.6%, for sICH while recurrent ischaemic stroke rate was 5.9%. Baseline CMB presence was a marker for significant risk of sICH compared to patients without CMBs (OR:4.16 p=0.005). The same author's group (META-MICROBLEEDS) in an other paper (5) concluded, that CMBs were associated also with increased risk of ischemic stroke (OR:2.14 CI: 1.58–2.89 but the relative increase in future intracerebral hemorrhage risk was greater (OR:4.65 95% CI: 2.68–8.08). The cerebral microbleeds were an independent predictor of all-cause mortality (5). The CROMIS-2 study (1490 pts, 2 years follow up), was performed in AF patients with anticoagulation after recent ischaemic stroke or transient ischaemic attack (6). The cerebral microbleed presence was independently associated with symptomatic intracranial haemorrhage risk: sICH 9.8/1000 patient-years in MB pts and 2.6/1000 patient-years (95% CI 1.1-5.4) in those without cerebral microbleeds. Orken et al determined the frequency of new CMBs in 200 ischemic stroke patients who had been receiving warfarin treatment for 2 years. New CMBs on gradient-echo MRI were found in 10% of patients. Of 35 patients who had CMBs at baseline, 26% developed new CMBs after 2 years, compared with 12%, who did not have CMBs (p=0.03). In the Rotterdam Study (8), from 3069 participants 5.9% used coumarin anticoagulants before follow-up MRI. The prevalence of microbleeds was 19.4%, and the incidence was 6.9% during a mean follow-up of 3.9 years. Compared with never users, coumarin users had a higher prevalence of deep or infratentorial microbleeds and a higher incidence of any microbleeds, although statistical significance was not reached in the latter. A higher maximum INR was associated with deep or infratentorial microbleeds. Among coumarin users, a greater variability in INR was associated with a higher prevalence of microbleeds (8). An other observation stressed, that not only the presence but also the number of microbleeds counts: thousand chinese postischemic pts. were followed (9). Having ≥5 microbleeds was independently associated with prior antiplatelet and anticoagulant use, whereas microbleeds of mixed location were independently associated with hypertension and prior anticoagulant use (all P<0.05). Microbleed burden was associated with an increased risk of ICH (microbleed burden versus no microbleeds:1 microbleed: multivariate hazard ratio: 0.59 [95% confidence interval, 0.07–5.05]; 2–4 microbleeds: multivariate hazard ratio: 2.14 [95% confidence interval, 0.50–9.12]; ≥5 microbleeds: multivariate hazard ratio:9.51 [95% confidence interval, 3.25–27.81]; Ptrend<0.0001), but the relationship of microbleed burden and risk of recurrent ischemic stroke was not significant (Ptrend=0.054)(9). The RASUNOA Investigators (10) identified differences between patients suffering ischemic stroke (IS) or intracerebral hemorrhage (ICH) while taking novel (non-vitamin K antagonists) oral anticoagulants (290 NOAC-IS, 61 NOAC-ICH). The proportion of patients with at least one CMB was higher in NOAC-ICH than in NOAC-IS (79%) vs (37%), P < .001), as was the absolute number of CMBs (median 5[IQR 1-24] vs 0 [0-1], P < 0.001). The odds of NOAC-ICH in patients with CMB than without, OR 5.60 P = 0.006. Although the Scientific Statement of AHA/ASA in 2017 (2) found ".. reasonable to provide anticoagulation therapy to patients with microbleeds when there is an indication (eg, AF)" and "MRI screening for microbleeds is not needed before the initiation of antithrombotic therapies"(2), but the listed observations prove, the microbleeds-anticoagulation problem needs further clarification. The "Yes" and "No" lecturers will try to clarify…

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References

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