Presence of cerebral microbleeds on MRI: what are the therapeutic implications?

Cerebral microbleeds (CMB) on gradient-recalled echo (GRE) T2-weighted MRI are considered a biomarker for micrangiopathy or bleeding-prone small-vessel diseases. Identifying high-risk patients before treatment with antiplatelet or antithrombotic agents could potentially reduce the hazard of Intracerebral Haemorrhage (ICH).

What do we know about the association between the use of antithrombotics or anticoagulation, ICH and CMBs?

Gregoire et al investigated the association of CMB with (ICH) with respect to use of antiplatelet agent. They found that CMBs were more frequent, more lobar in location and were more numerous in antiplatelet-users with ICH than in antiplatelet users without lobar ICH. The number of CMBs was associated with the risk of antiplatelet-related ICH with (adjusted OR 1.33 per additional CMB). The authors concluded that in patients with a large number of lobar CMBs, the risk of ICH could outweigh the benefits of antiplatelet therapy.

Sang et al observed, in 107 patients with primary ICH, that primary ICH with CMBs was more common in elderly patients with prominent ischemic change and frequent use of antithrombotics or anticoagulants. Wong at al analyzed aspirin use with and without ICH and its association with presence of CMBs with 21 patients in each group. The authors observed that both the presence and the number of CMBs were more common in aspirin-users with ICH. Fan et al studied prospectively a Chinese cohort of 121 acute ischaemic stroke patients for stroke recurrence and ICH in association with CMBs. Of the 43 (35%) patients having CMBs, 16 developed recurrent stroke. No difference in the 11 patients with ischaemic stroke was seen in association with presence of CMBs. Of the 5 patients who had ICH, 4 patients had CMBs.

In a cohort of 106 Japanese patients with ICH, the prevalence of CMB was found to be 54.7% which was significantly associated with advanced age, white matter hyperintensity and previous ICH or ischaemic stroke. Nonetheless, no association was found between the presence of CMBs and regular use of antiplatelet agent irrespective of previous history of stroke.

What is the data on association of thrombolytic use, ICH and CMBs?

Kidwell investigated the presence of CMBs in pretreatment MRI of 41 patients undergoing intra-arterial thrombolytic therapy for acute ischaemic stroke. Five patients demonstrated CMBs. Only 1 patient had a haemorrhagic transformation and the symptomatic haemorrhage occurred at the site of a prior CMB opposite to the site of ischaemia. Major symptomatic haemorrhage occurred in 1 of 5 patients with CMBs compared to 4 of 36 patients without CMBs.

Derex et al conducted a retrospective analysis of pre-treatment T2-weighted MRI of 44 patients who underwent thrombolysis (intravenous Alteplase) for acute ischaemic stroke. CMBs were found on pretreatment MRI in 18.2% patients. Neither symptomatic nor asymptomatic ICH had any significant association with CMBs till day 7 of follow-up. Interestingly, no ICH was seen to occur at the site of CMB while all patients had ICH within the ischaemic area.

Kakuda et al prospectively evaluated MRI of 77 patients with acute ischaemic stroke treated with intravenous Alteplase on day 1 and day 30 (mean age, 71 years; 31 men). CMBs were identified in 15.7% patients. They also reported that no significant difference was observed in the frequency of either symptomatic or asymptomatic haemorrhagic complications after thrombolysis between patients with and without CMBs at baseline. None of the patients with CMBs at baseline had a symptomatic ICH. Therefore, the presence of CMBs on gradient echo imaging does not appear to substantially increase the risk of either symptomatic or asymptomatic brain haemorrhage following intravenous Alteplase.

Conclusion

Current data is insufficient to support the hypothesis that CMBs are associated with a higher risk of ICH or haemorrhagic transformation after thrombolytic therapy in patients with stroke. Larger prospective studies are required to investigate the predictive value and therapeutic implication of CMBs with regard to the use of antithrombotic agents, anticoagulation or thrombolytic therapy and associated risk of ICH; however the current data suggests caution in the use of these agents for stroke prevention in patients with CMB on MRI.
References


