Risk of recurrent intracerebral haemorrhage and ischaemic stroke after intracerebral haemorrhage: multicenter prospective cohort study

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Background

Intracerebral haemorrhage (ICH) is a devastating condition with mortality over 50% at 1 year. In ICH survivors identifying clinical and imaging risk factors associated with IS and recurrent ICH could help clinicians with difficult antithrombotic decisions.

Whilst there is some data on the risk of recurrent ICH (estimated between 1.3% and 7.4% annually), which might be highest for patients with lobar ICH, there is less data on the risk of subsequent IS and associated risk factors.

This study therefore investigated the incidence and the demographic, clinical and imaging associations of stroke events (both IS and recurrent ICH) in ICH survivors. We hypothesized that participants with lobar ICH would have a higher risk of recurrent ICH and a lower risk of IS than those with non-lobar ICH (defined as ICH in the basal ganglia, thalamus, caudate, capsular structures, deep white matter, or brainstem, but not including cerebellar ICH).

Methods

All data was collected as part of CROMIS-2 ICH, a prospective multicentre observational study of adult ICH survivors. Our outcome events of interest were recurrent ICH or IS. Follow up was collected from patients and GPs via a questionnaire, nominally at 6 months.

Scans were rated for leukoaraiosis by a trained research fellow using a validated scale. A scan was classified as “positive” for small vessel disease in the presence of either lacunar infarction or moderate/severe leukoaraiosis. Haematoma location was defined using a published scale, then subdivided into lobar or deep excluding the cerebellar

Cox regression analysis was undertaken due to variable follow up. Multivariable Cox regression was then performed, due to the low number of events we adjusted for variables identified as significant ($p<0.05$) in the univariable analyses. In sensitivity analysis, we additionally included variables significant at the 20% level one by one in turn

Results

CROMIS-2 ICH recruited 1094 patients. The mean age was 73 years (SD 12 years) and 463 (43%) were female. 372 (35%) had atrial fibrillation. 440 (41%) patients were on anticoagulation at the time of their ICH, 274 (25%) on anti-platelets and 444 (43%) on statins at the time of their ICH. When considering ICH location, 447 (41%) were lobar and 581 (53%) were deep or located in the brainstem and 65 (6%) were located in the cerebellum.

1058 (97%) patients had follow up during which 60 patients had 62 stroke events: 35 recurrent ICH events over 1648 patient-years (2.1%/year) and 27 IS events over 1608 patient-years (1.7%/year). Two patients had recurrent IS events whilst one patient had an IS followed later by a recurrent ICH.

Recurrent ICH rate by ICH location and risk

24 patients with lobar ICH had a recurrent ICH over 665 patient-years (3.6%/year) vs. 11 patients with non-lobar ICH over 982 patient-years, a rate of (1.1%/year)

In multivariable analysis (adjusting for antiplatelet use and previous ICH), lobar ICH location (HR 3.25, 95% CI 1.49 to 7.07) and previous antiplatelet use (HR 2.22, 95% CI 1.09 to 4.54) were significantly associated with recurrent ICH risk

New IS rate by ICH location and risk

6 patients with lobar ICH location had a new IS over 654 patient-years of follow-up, (0.9% per year) vs. 19 patients with non-lobar ICH over 953 patients years of follow-up (2.0% per year).

In multivariable analysis adjusting for AF at time of index ICH and previous IS or TIA . Atrial fibrillation presence at time of baseline ICH was significantly associated with IS occurrence (HR 2.59; 95% CI 1.13 to 5.92 $p=0.025$). Lobar ICH location was inversely associated with IS occurrence but this was not statistically significant (HR 0.40; 95% CI 0.16 to 1.02 $p=0.055$).

Recurrent ICH risk

Ischaemic stroke risk

Conclusion

Lobar ICH survivors have a higher rates and risk of recurrent ICH than non-lobar ICH survivors. The rate of IS was lower in lobar ICH survivors than in non-lobar ICH survivors as was the risk although this did not reach statistical significance in adjusted analyses. Further studies are needed to define whether treatment effects (e.g. antithrombotic drugs for IS prevention) differ according to ICH location.