Global cortical atrophy – but not enlarged perivascular spaces – are associated with an unfavorable outcome in stroke patients on oral anticoagulation for atrial fibrillation.

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Background

Oral anticoagulation (OAC) is the treatment of choice for patients following ischemic stroke (IS) related to atrial fibrillation (AF). Cerebral small vessel disease (SVD), another important cause of IS and intracerebral hemorrhage (ICH), is frequently concomitantly observed in these patients. Upon MR-imaging, SVD is associated with various imaging measures, such as white matter hyperintensities (WMH) and cerebral microbleeds (CMB). These markers of SVD have recently been shown to be related to an unfavorable clinical course in stroke patients on OAC, with the presence of SVD being associated with an increased risk for both, IS and ICH. Other MRI-markers of SVD comprise enlarged perivascular spaces (PVS). Also, SVD is known to eventually lead to secondary brain atrophy, which can be operationalized by assessment of global cortical atrophy (GCA). To date, the role of PVS and GCA on the prognosis in stroke patients on OAC is unclear.

Methods

This observational study is based on the prospective, ongoing registry on stroke patients on OAC conducted at the stroke center of the University Hospital of Basel (Novel Oral Anticoagulants in Ischemic Stroke Patients (NOACISP)-LONGTERM). Patients with sufficient MRI quality to assess PVS and GCA and a minimal follow-up period of 3 months were included in this study (03/2011-11/2017).

We measured the load of PVS and the degree of GCA based on established visual rating scales: PVS were rated in two brain regions of their occurrence: (i) basal ganglia and (ii) centrum semiovale; they were categorized in five groups: (0) no PVS, (I) 1-10 PVS, (II) 11-20 PVS, (III) 21 – 40 PVS, (IV) > 40 PVS.

The GCA scale compromises 4 stages and is based on an overall assessment of cortical atrophy (0: no atrophy with normal brain volume, 1: mild atrophy, sulcal opening; 2: moderate atrophy, gyral volume loss, 3: severe atrophy: gyral thinning with a knife like appearance). Using adjusted logistic and Cox regression analysis we investigated the association of PVS and GCA using a composite outcome measure, comprising: (i) recurrent IS; (ii) ICH; and (iii) death. We adjusted our analysis for age, hypertension, gender, antiplatelet use , diabetes and SVD neuroimaging markers.

Results

In total, (overall n=320, mean age of 78.2 years SD 9.2) during the median follow up period of 754 days (IQR 708-828), there were 22 IS, 8 ICH and fifty-three patients died. The presence and load of PVS in both localizations were not associated with the composite outcome. GCA was associated with an increased risk for the composite outcome in all three degrees of atrophy (grade 1: OR 3.74 95 % CI 1,397 - 10.0; p = 0.009); this risk increased with the severity of the GCA (grade 2: OR 4.5 95 % CI 1,579 - 12.854 p = 0.005, grade 3: OR 4.86 95 % CI 1,52 - 15.5, p = 0.008). This association remained significant also after adjusting for WMH and CMBs. Also, in time to event analysis the hazard ratio for the composite outcomes were increased in patients with GCA (grade 1: HR 4.138 95 % CI 1.412 – 12.122, p = 0.01, grade 2: 4.454 95 % CI 1.437, 13.811, p=0.01, grade 3: 5.023 95 % CI 1.434 – 17.589, p =0.012)

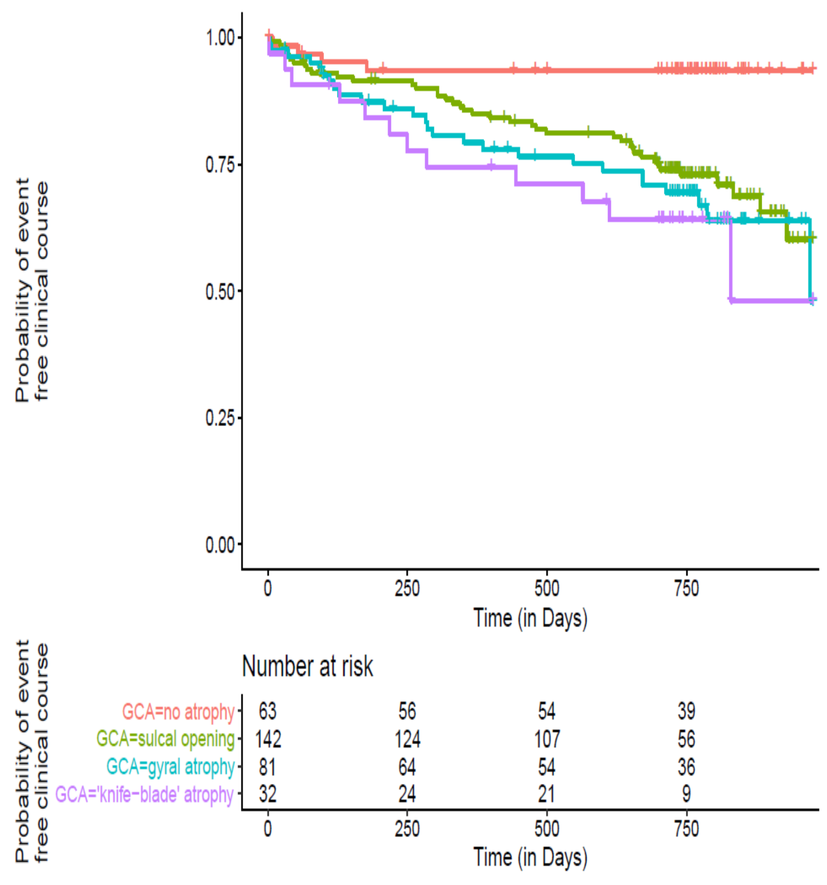

Figure 1: Kaplan Meier curve for the composite outcome (i.e. ICH, AIS, death) by the degree of global cortical atrophy. The patients are represented in different color: In red patients with no atrophy (grade 0), in green patients with mild atrophy (grade 1: sulcal opening), in blue with moderate atrophy (grade 2: gyral atrophy and in violet with severe atrophy (grade 3: knife-blade appearance)

Conclusion

The presence of global cortical atrophy, but not PVS, was associated with an unfavorable outcome in stroke patients treated with OAC for AF. This association was independent of other imaging markers of SVD, indicating that GCA potentially reflects both vascular as well as neurodegenerative processes in these patients.