

Anticoagulation and cerebral small vessel disease

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Cardiovascular diseases are usually complex and affect multiple organs simultaneously. Treatments for vascular diseases in the brain may therefore have implications for the treatment of cardiac diseases. It is thus important to understand the respective causes and effects. This study explores the causes of intracerebral hemorrhages and links them to the risk of stroke associated with atrial fibrillation. It suggests a fundamental new assessment of the effects of blood thinning on intracerebral hemorrhages.

About 1,000 patients with intracerebral hemorrhage are treated at <u>stroke</u> units each year in Switzerland. Intracerebral hemorrhages are more often fatal than other forms of strokes, and their incidence has not decreased in the past 30 years. The use of blood thinners was previously considered not only to be a risk factor but potential cause for a intracerebral hemorrhage.

Anticoagulation should not be regarded as primary cause

This publication includes the results of two studies conducted by the team of Prof. Werring. It contrasts the role of blood thinning with that of cerebral small vessel disease (SVD) in intracerebral hemorrhages. A moderate to severe cerebral SVD is shown to be closely associated with the occurrence of cerebral hemorrhages. Dr. David Seiffge summarized the results as follows: "Our results show that SVD is a precondition for intracerebral hemorrhages under anticoagulation. The degree of SVD in the brain may be used to predict intracerebral hemorrhages. Without SVD the occurrence of intracerebral hemorrhage is close to zero. Consequently, anticoagulation should no longer be considered a cause of intracerebral hemorrhages."

Why is this important? Protection against stroke for patients with atrial fibrillation

Blood thinning offers important protection against ischemic stroke in patients with atrial fibrillation. Anticoagulation reduces the risk of ischemic stroke in these cases by two-thirds. In the past, anticoagulation has been discontinued immediately in the event of an intracerebral hemorrhage and patients were left unprotected against the risk of a stroke. The new study results now point to a new path: according to the findings, intracerebral hemorrhages can be prevented etiologically by treating cerebral SVD and protection against stroke can be maintained through an adapted continuation of blood thinning. The exact timing and gradation of the two therapies are the subject of further studies.

A challenging methodological approach: combining two multicentre studies

The publication comprises data originating from two independent studies supervised by Prof. David Werring, UCL. The publication is based on two independent, multicentre observational studies. First, a cross-sectional study was carried out with 1,030 patients with intracerebral hemorrhages. CT and MRI were used to look for markers of SVD in



the brain. 1,447 patients with atrial fibrillation and cerebral circulatory disorders were enrolled in a second, prospective study. In this group, the incidence of cerebral hemorrhages and ischaemic stroke was considered in relation to blood thinning.

Using this approach, it was possible to show that SVD is a prerequisite for intracerebral hemorrhage. Patients without such a condition did not have a single brain hemorrhage within the first 2 years in the study, despite being treated with a blood thinner. In contrast, at 1.56% per year, the risk was significantly increased for moderate to severe SVD.

A new way of looking at the situation is needed

The study results suggest that <u>blood</u> thinning alone can no longer be considered a cause of intracerebral hemorrhages. Prof. Marcel Arnold points out: "As a new approach, microangiopathies should be systematically searched for and treated in a targeted manner in order to prevent intracerebral hemorrhages. Suitable specialist outpatient clinics are now available. This would reduce the risk of intracerebral hemorrhages."

A large, international randomized trial (ENRICH-AF), coordinated in Switzerland by David Seiffge, is currently underway with the aim of aligning anticoagulation and microangiopathy therapies with each other.

More information: David J Seiffge et al, Small vessel disease burden and intracerebral haemorrhage in patients taking oral anticoagulants, *Journal of Neurology, Neurosurgery & Psychiatry* (2021). DOI: 10.1136/innp-2020-325299

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