Retinal imaging to identify patients with atrial fibrillation at increased risk of intracerebral haemorrhage: abridged secondary publication

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KEY MESSAGES

1. In patients with atrial fibrillation receiving oral anticoagulants for stroke prevention, there is an increasing incidence of anticoagulant-associated intracerebral haemorrhage, which carries high risks of morbidity and mortality.
2. The presence of cerebral microbleeds (CMBs) on magnetic resonance imaging (MRI) of the brain is associated with an increased risk of intracerebral haemorrhage.
3. The retina shares an embryological origin and similar pathological characteristics with the brain; thus, changes in retinal vessels may indicate the presence of CMBs. A non-invasive method to evaluate bleeding-prone cerebral small vessel disease in patients with atrial fibrillation could help to identify those at increased risk of anticoagulant-associated intracerebral haemorrhage.
4. We recruited patients with atrial fibrillation to undergo optical coherence tomography-angiography (OCT-A) for examination of the three-dimensional capillary network of the retina. We compared capillary network matrix parameters between patients with and without CMBs on MRI.
5. Alterations in the retinal capillary network across various retina layers were associated with the presence and burden of CMBs on MRI. These findings suggest a role for OCT-A in identifying patients with atrial fibrillation at increased risk of bleeding-prone microangiopathy.

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Introduction

Atrial fibrillation (AF) causes one-third of ischaemic strokes, which have high morbidity and mortality.[1] Oral anticoagulants are effective in reducing the risk of ischaemic stroke by 60% to 70%, but the risk of intracerebral haemorrhage remains, particularly in patients with multiple cerebral microbleeds (CMBs) visible on magnetic resonance imaging (MRI) of the brain.[2] Access to MRI is limited among patients with AF who have no history of stroke or transient ischaemic attacks. Furthermore, many patients with AF have contraindications for MRI (eg, cognitive impairment, severe disability after stroke, or the presence of a pacemaker and/or metallic heart valve). A non-invasive method to evaluate bleeding-prone cerebral small vessel disease in patients with AF could help to customise treatment decisions. The retina shares embryological and anatomical features with the brain; thus, many pathological changes in cerebral vessels are reflected in retinal vessels.[3] Optical coherence tomography-angiography (OCT-A) is a non-invasive technique for visualising the microvasculature of the retina and choroid; it provides three-dimensional images of capillary networks in the eye without requiring intravenous dye injection.[4] Using semi-automated computer software, vascular parameters in different retinal layers can be precisely quantified for analysis. This study aimed to identify changes in retinal vascular parameters on OCT-A that are associated with the presence of CMBs on MRI of the brain among patients with AF.

Methods

Between November 2018 and January 2022, Chinese patients aged ≥18 years with AF or atrial flutter were prospectively recruited from outpatient clinics at Prince of Wales Hospital. Patients were excluded if they had contraindications for MRI of the brain (eg, presence of a pacemaker or metallic heart

valve), poor sitting balance for retinal photography, known intracranial or ocular pathologies, or were pregnant. Additionally, healthy controls aged ≥60 years were recruited from the community. OCT-A was performed within 2 weeks of MRI of the brain.

To determine associations between changes in OTC-A metrics and the longitudinal progression of CMB count, a subgroup of patients with prior MRI from the IPAAC (risk of Intracerebral haemorrhage in Patients taking oral Anticoagulants for Atrial fibrillation with Cerebral microbleeds) study was identified.[5] The CMB counts in the two sets of MRIs were compared to identify new CMB development. OCT-A metrics were compared between patients with and without new CMBs in the follow-up MRI.

Results

Of 135 patients with AF and 65 healthy controls recruited, 99 patients with AF and 60 healthy controls were included in the analysis. Multivariable logistic regression models showed that in both groups changes in the retinal capillary matrix were associated with the presence and burden of CMBs in the superficial capillary plexus, deep capillary plexus, and disc centre, after adjustment for confounders. Among patients with previous MRI of the brain from the IPAAC study, those with new CMBs on follow-up MRI had similar changes on OCT-A.

Discussion

To our knowledge, this is the first study to evaluate associations between retinal capillary network changes and CMBs in patients with AF. Although the exact mechanism underlying these vascular changes remains uncertain, we hypothesise that it involves capillary drop-out and secondary vasodilatation at the capillary layer.

This study was limited by disruptions due to the COVID-19 pandemic and social unrest in Hong Kong, which resulted in more than one-third of patients to have a >2-week interval between retinal imaging and MRI. Although the difference was not significant between patients with and without CMBs, the analysis was adjusted for this confounder.

Conclusions

OCT-A has a role in identifying patients at increased risk of anticoagulant-associated intracerebral haemorrhage. Further studies with larger sample size are needed to determine cut-off values for OCT-A parameters.

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