Study establishes markers and risk stratification model of intracranial aneurysm instability

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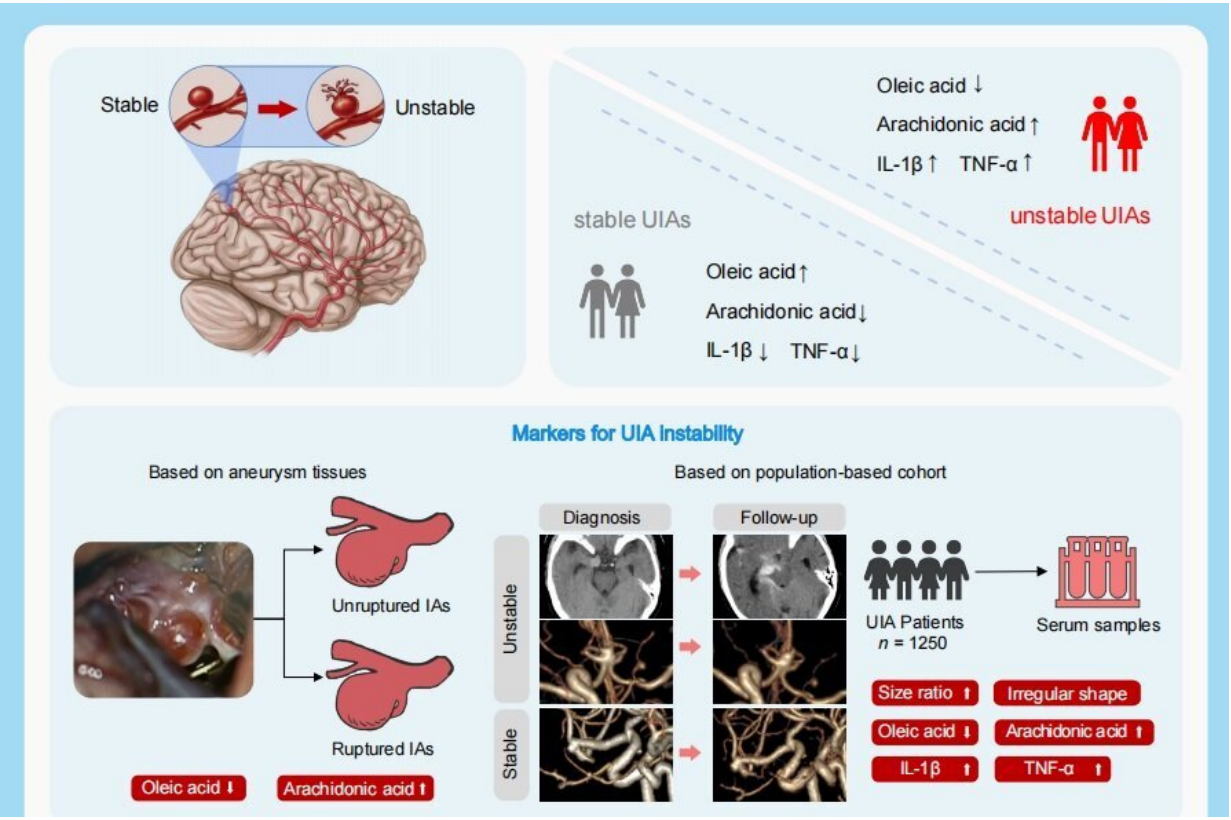

Graphical abstract of the study. This study demonstrated that oleic acid, arachidonic acid, IL-1β, and TNF-α were dysregulated between stable and unstable UIAs. The instability classifier, incorporating radiological features and biomarkers, presents a high accuracy of predicting the risk of UIA instability and contributed to UIA risk stratification, which may help guide treatment decision-making for UIAs. UIA, unruptured intracranial aneurysm; IL-1β,

interleukin 1β; TNF-α, tumor necrosis factor α. Credit: ©Science China Press

Intracranial aneurysm is the leading cause of non-traumatic subarachnoid hemorrhage, with a prevalence of 7% in China. More than 70% of intracranial aneurysms are unruptured intracranial aneurysms (UIAs). Although aneurysm rupture is associated with high morbidity and mortality, previous studies have revealed the rupture rate of UIAs to be as low as 1% per year. Notably, aggressive empirical surgical treatment carries the risk of complications, including ischemic stroke and accidental aneurysm rupture. Evaluating the unstable (rupture and growth) risk of aneurysms is helpful to guide decision making for cases of UIAs.

Metabolites and cytokines influence the environment of the vessels and are essential for the development of cardiovascular and cerebrovascular diseases. However, there are few longitudinal studies on the natural history of UIA rupture or growth, and the relationship between metabolic-cytokine features and UIA instability has been unclear. Moreover, large-scale multi-center longitudinal data in the Chinese population is lacking.

Based on intracranial aneurysm samples and serums from 20 patients, and the dynamic change of metabolites and cytokines during a two-year follow-up, a new study published in *Science Bulletin* has revealed that the abnormity of lipid metabolism is related to intracranial aneurysm rupture, and oleic acid (OA) and arachidonic (AA), interleukin 1β (IL-1β), and tumor necrosis factor-α (TNF-α) are reliable biomarkers to evaluate the risk of UIA instability.

Subsequently, incorporating radiological features and biomarkers related to UIA instability, the research team established a risk stratification

model using a machine-learning algorithm. Based on 1,250 UIA patients who were regularly followed up for two years via radiology, this stratification model performed well with classifying unstable UIAs and stable UIAs [area under curve (AUC) as 0.94 within the derivation cohort, and as 0.89 within the validation cohort], which was superior to the existing clinical models (PHASES score and ELAPSS score).

Finally, the team investigated whether in vivo intervention of OA, IL-1β, and TNF-α could prevent IA from rupture. The in vivo study based on the rat model of intracranial aneurysms showed supplementation of OA and inhibition of IL-1β and TNF-α could prevent aneurysms from rupturing and relieve the inflammation activation in the aneurysm wall.

This study demonstrates the first and largest multi-omics analysis based on two longitudinal multi-center Chinese cohorts, and reveals OA, AA, IL-1β, and TNF-α as biomarkers for UIA instability. These findings could help clinicians to understand the pathological characteristics of ruptured and growing intracranial aneurysms.

This team provided a risk stratification model incorporating radiological features and biomarkers with high accuracy to evaluate the two-year risk of UIA instability, which may guide treatment decision-making for UIAs.

More information: Qingyuan Liu et al, The markers and risk stratification model of intracranial aneurysm instability in a large Chinese cohort, *Science Bulletin* (2023). DOI: 10.1016/j.scib.2023.05.001

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