INTRODUCTION

Review question / Objective Currently, the 5-year risk of rupture in UIA could be evaluated by the PHASES score, which is based on geographic location, hypertension, age, history of aSAH, aneurysm size, and location. However, additional risk factors should be identified for further preventing the risk of aneurysm rupture. We therefore performed this systematic review and meta-analysis to identify the risk factors for aneurysm rupture in UIA patients.

Condition being studied Rupture of an intracranial aneurysm could cause aneurysmal subarachnoid hemorrhage (aSAH), and the annual incidence nearly 9 per 100,000 of UIA, with 1.4% of UIA rupture annually. Considering aSAH was a serious complication after UIA, and the mortality rate reached 67%, with nearly 50% of the survivors are left disabled, thus the clinician should explain the actual risk of rupture.

METHODS

Search strategy (intracranial aneurysm(s) OR cerebral aneurysm(s)) AND (risk of rupture OR aneurysm rupture OR risk factors OR rupture OR unruptured OR subarachnoid hemorrhage) AND (follow-up OR natural history OR natural course).

Participant or population All of patients diagnosed with UIA.

Intervention The predictors for aneurysm rupture reported ≥ 3 times.

Comparator Reference group.

Study designs to be included No restriction for study design, including prospective or retrospective study.

Eligibility criteria Study was included if they met: (1) Patients: all of patients diagnosed with UIA; (2) Exposure: the predictors for aneurysm rupture
reported ≥ 3 times; (3) Outcomes: the study should reported the effect estimate for the risk of aneurysm rupture or data could transform into effect estimate; and (4) Study design: no restriction for study design, including prospective or retrospective study.

**Information sources** PubMed, EmBase, Cochrane library, and manually search reference lists of relevant review and original article.

**Main outcome(s)** Age, gender, smoking status, hypertension, diabetes mellitus, hyperlipidemia, history of SAH, family history of SAH, size of aneurysm, multiple aneurysm, and aneurysm location.

**Quality assessment / Risk of bias analysis** The methodological quality of included studies were assessed using the Newcastle-Ottawa Scale (NOS), which was partially validated for assessing the quality of observational studies in meta-analysis. The NOS contained selection (4 items), comparability (1 item), and outcome (3 items), and the “star system” for each study ranged from 0-9.

**Strategy of data synthesis** The risk factors for aneurysm rupture in each study was assigned as the odds ratio (OR) with 95% confidence interval (CI), and the pooled analysis was calculated using the random-effects model with considering the underlying varies among included studies.

**Subgroup analysis** Subgroup analyses were performed according to region, study design, follow-up, and study quality, and the differences between subgroups were compared using interaction P test.

**Sensitivity analysis** The robustness of pooled conclusion was assessed using a sensitivity analysis through sequential removing single study.

**Language restriction** No restriction were placed on published language.

**Country(ies) involved** China.

**Keywords** risk factors; rupture; intracranial aneurysm; systematic review; meta-analysis.

**Contributions of each author**
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