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Predictive Value of Contrast-Enhanced Carotid Ultrasound Features for Stroke Risk: A Systematic Review and Meta-Analysis

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ADMINISTRATIVE INFORMATION

Support - No.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 2 April 2025 and was last updated on 2 April 2025.

INTRODUCTION

Review question / Objective To elucidate the contrast-enhanced ultrasound (CEUS) features of carotid artery plaques in patients who have experienced an ischemic stroke (IS).

Condition being studied A computerized search was conducted in databases such as Pub-Med, EMSCO, and Ovid to identify studies reporting CEUS findings of carotid artery plaques. Patients were categorized as IS and non-IS based on clinical and radiological diagnosis, and the quantitative and semi-quantitative CEUS data were analyzed for differences between the two groups.

METHODS

Participant or population The following predefined eligibility criteria were utilized for study inclusion: (1) Participants: Patients diagnosed with carotid artery atherosclerotic plaques were enrolled. All patients underwent CEUS prior to carotid endarterectomy. Based on the North American Symptomatic Endarterectomy Trial criteria (NASCET), the patients were categorized into two groups: those with asymptomatic and those with symptomatic internal carotid artery stenosis attributable to plaques. Symptomatic internal carotid artery stenosis was defined as the onset of neurological manifestations associated with the ipsilateral carotid artery within the preceding 120 - day period. Other potential etiologies of stroke, such as cardioembolism, were strictly excluded. Notably, none of the patients with asymptomatic internal carotid artery stenosis due to plaques had a history of ischemic events resulting from carotid artery stenosis. (2) Intervention: All participants underwent CEUS examination. (3) Outcome measures: Quantitative or semi-quantitative CEUS characteristics of carotid artery plaques, with clinical and imaging diagnoses of IS and non-ischemic stroke (non-IS). (4) Study design: No restrictions on study type. Research with fewer than 10 participants, along with individual case reports and case series, were omitted from consideration. Two separate

evaluators screened the collected articles independently, with any disparities being reconciled by a third reviewer.

Intervention Intervention: All participants underwent CEUS examination.

Comparator CEUS plaque enhancement, plaque enhanced intensity was calculated by subtracting baseline from peak intensities in the core, plaque shoulder, and vessel lumen.

Study designs to be included No restrictions on study type. Research with fewer than 10 participants, along with individual case reports and case series, were omitted from consideration. Two separate evaluators screened the collected articles independently, with any disparities being reconciled by a third reviewer.

Eligibility criteria We conducted a literature search in the Embase, PubMed, and Ovid electronic databases to screen studies that reported the CEUS features of carotid artery plaques in patients with IS. The search terms used included "stroke," "carotid plaque," and "contrast-enhanced ultrasound." The search was limited to publications up to June 1, 2024, without any language restrictions. Next, we conducted a thorough manual search through the bibliographies of the chosen articles to uncover any supplementary studies that could bear relevance to the subject matter.

Information sources We conducted a literature search in the Embase, PubMed, and Ovid electronic databases to screen studies that reported the CEUS features of carotid artery plaques in patients with IS.

Main outcome(s) After the computerized search, a total of 13 eligible studies, comprising 3,092 participants (1,953 with stroke), were included for analysis. IS patients exhibited significantly higher plaque enhancement intensity versus control group (SMD = 0.71, 95% CI: 0.32, 1.11). The positive rate of plaque enhancement within the plaques was significantly higher in IS patients versus non-IS patients (OR = 3.25, 95% CI: 1.86, 5.68). The sensitivity of hyperintense lesion-based diagnosis of stroke was 0.68 (95% CI: 0.54, 0.80), and the specificity was 0.61 (95% CI: 0.47, 0.73), with an area under the curve (AUC) of 0.697.

Quality assessment / Risk of bias analysis A systematic data extraction process was carried out using an Excel spreadsheet to collect the following information from the included studies: publication year, first author, study design, participant count, and outcomes. Two reviewers independently extracted the data and verified the information, with any disagreements addressed with a third reviewer.

Strategy of data synthesis The heterogeneity across the included studies was evaluated utilizing the corrected p-value and the I-squared (I^2) statistic. Studies were deemed to exhibit negligible heterogeneity when the I^2 statistic was below 50%, prompting the use of a fixed-effects meta-analytic model. Conversely, an I^2 value of 50% or greater was interpreted as indicative of substantial heterogeneity, leading the authors to employ a random-effects approach to provide a more conservative statistical description of the effect sizes.

Subgroup analysis The heterogeneity across the included studies was evaluated utilizing the corrected p-value and the I-squared (I^2) statistic. Studies were deemed to exhibit negligible heterogeneity when the I^2 statistic was below 50%, prompting the use of a fixed-effects meta-analytic model. Conversely, an I^2 value of 50% or greater was interpreted as indicative of substantial heterogeneity, leading the authors to employ a random-effects approach to provide a more conservative statistical description of the effect sizes.

Sensitivity analysis The heterogeneity across the included studies was evaluated utilizing the corrected p-value and the I-squared (I^2) statistic. Studies were deemed to exhibit negligible heterogeneity when the I^2 statistic was below 50%, prompting the use of a fixed-effects meta-analytic model. Conversely, an I^2 value of 50% or greater was interpreted as indicative of substantial heterogeneity, leading the authors to employ a random-effects approach to provide a more conservative statistical description of the effect sizes.

Country(ies) involved China.

Keywords Carotid artery plaque, Contrast-enhanced ultrasound, Ischemic stroke, Carotid stenosis, Meta-analysis.

Contributions of each author
Author 1 - Shili Zhou.
Author 2 - Pinjing Hui.