Study Protocol Systematic Review

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Superb microvascular imaging for detecting neovascularization of carotid plaque compared with contrast-enhanced ultrasound

A protocol for systematic review and meta analysis

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Abstract

Background: Superb microvascular imaging (SMI) is a novel Doppler technique that depicts low velocity blood flow without the use of a contrast agent. Studies suggested that SMI may or may not detect neovascularization of carotid plaque with accuracy comparable to contrast-enhanced ultrasound. To gain clarity, a meta-analysis to systematically review and synthesize relevant data on the SMI for the detection of intraplaque neovascularization was undertaken.

Methods: We will search PubMed, Web of Science, Cochrane Library, and Chinese biomedical databases from their inceptions to the June 31, 2020, without language restrictions. Two authors will independently carry out searching literature records, scanning titles and abstracts, full texts, collecting data, and assessing risk of bias. Review Manager 5.2 and Stata14.0 software will be used for data analysis.

Results: This systematic review will investigate whether SMI is feasible on the detection of intraplaque neovascularization compared with contrast-enhanced ultrasound.

Conclusion: Its findings will provide helpful evidence for the feasibility of SMI on the detection of intraplaque neovascularization.

Systematic review registration: INPLASY202070097.

Abbreviations: CEUS = contrast-enhanced ultrasound, IPN = intraplaque neovascularization, SMI = superb microvascular imaging.

Keywords: carotid plaque, contrast-enhanced ultrasonography, intraplaque neovascularization, meta-analysis, superb microvascular imaging

1. Introduction

Stroke is a common refractory disease that seriously endangers human health. Carotid artery atherosclerosis is a major risk factor for ischemic stroke. Intraplaque neovascularization (IPN) can promote the rapid progress of plaque, induce bleeding, and lead to plaque rupture. Plaque thrombi cause ischemic stroke while IPN is a major risk for plaque-related vascular events.[1] Contrast-enhanced ultrasonography (CEUS) effectively visualizes IPN.[2] Superb microvascular imaging (SMI) is as a novel Doppler technique that depicts low velocity blood flow without the use of a contrast agent.[3] Studies suggested that SMI may or may not detect neovascularization of carotid plaque with accuracy comparable to CEUS.[4–12] To gain clarity, a meta-analysis to assess the feasibility of SMI for the detection of IPN was undertaken compared with contrast-enhanced ultrasound.

2. Materials and methods

This study was conducted in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines and the protocol was registered in the INPLASY (INPLASY202070097).

2.1. Eligibility criteria

2.1.1. Type of study. This study will only include high quality clinical cohort or case control studies that compare SMI with CEUS for evaluating IPN.

2.1.2. Type of patients. The patients should be those who had undergone carotid atherosclerotic plaque formation.

This study was supported by Liaoning Natural Science Foundation Project (20170540256). Provider just financially supports this study, but does not involve all sections of this study, and does not have conflicts interest related to this study.

The authors have no conflicts of interest to disclose.

All data generated or analyzed during this study are included in this published article and its supplementary information files.

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How to cite this article: Zhou Y, Wang C. Superb microvascular imaging for detecting neovascularization of carotid plaque compared with contrast-enhanced ultrasound: a protocol for systematic review and meta analysis. Medicine 2020;99:35(e21907).

Received: 23 July 2020 / Accepted: 24 July 2020

http://dx.doi.org/10.1097/MD.0000000000021907

2.1.3. Intervention and comparison. IPNs of all patients were assessed with SMI and CEUS.

2.1.4. Type of outcomes. The primary outcomes include a semi-quantitative scoring system, through which IPN was graded by means of both SMI and CEUS.

2.2. Search methods

PubMed, Web of Science, Cochrane Library, and Chinese biomedical databases will be searched from their inceptions to the June 31, 2020, without language restrictions. The search strategy for PubMed is shown in Table 1. Other online databases will be used in the same strategy.

2.3. Data extraction and quality assessment

Two authors will independently select the trials according to the inclusion criteria, and import into Endnote X9. Then remove duplicated or ineligible studies. Screen the titles, abstracts, and full texts of all literature to identify eligible studies. All essential data will be extracted using previously created data collection sheet by 2 independent

authors. Discrepancies in data collection between 2 authors will be settled down through discussion with the help of another author. The following data will be extracted from each included research: year of article, first author's surname, sample size, number of intraplaque microvascular flow grades, number of every grade. The quality of selected studies will be independently evaluated according to a tool for the quality assessment of methodological index for non-randomized studies(MINORS). The MINORS criteria included 12 assessment items. Each of these items is scored as "yes" (2), "no" (0), or "unclear"(1). MINORS score ranged from 0 to 24; and score≥17 indicate a good quality. Any disagreements between 2 investigators will be solved through discussion or consultation by a 3rd investigator.

2.4. Statistical Analysis

The STATA version 15.1 software (Stata Corporation, College Station, TX) will be used for meta-analysis. We calculated the pooled summary odds ratio and its 95% confidence interval (CI). The Cochran Q-statistic and I^2 test will be used to evaluate potential heterogeneity between studies.[13] If the Q-test shows a $P < .05$ or I^2 test exhibits $> 50\%$, indicating significant heterogeneity, and the random effect model will be employed or if heterogeneity is not significant, the fixed-effects model was used. If it is possible, we will perform meta-analysis to analyze the pooled outcome data when acceptable homogeneity has been identified. Otherwise, we will conduct subgroup analysis to investigate potential causes for substantial heterogeneity among eligible studies. Sensitivity analysis will be performed to evaluate the influence of a single study on the overall estimate. We will use Begger funnel plots and Egger linear regression test to investigate publication bias.[14]

Table 1

Search strategy sample of PubMed.

Number	Search terms
1	carotid
2	plaques or plaque or fatty streak or fibroatheroma
3	contrast-enhanced ultrasound or contrast-enhanced ultrasonography or contrast ultrasonography or ultrasound contrast imaging or CEUS
4	vulnerability or stability or neovascularization
5	superb microvascular imaging
6	and 1–5

CEUS = contrast-enhanced ultrasound.

2.5. Ethics and dissemination

We will not obtain ethic documents because this study will be conducted based on the data of published literature. We expect to publish this study on a peer-reviewed journal.

3. Discussion

Atherosclerotic plaque formation occurs simultaneously with intraplaque angiogenesis.[15] The development of summarized vascularity increases the probability of plaque-associated cardiovascular and cerebrovascular complications. Hemorrhage from intraplaque blood vessels can destabilize the plaque to promote rupture, further thrombosis, and cardiovascular events.[16] Plaque neovascularization is a marker of plaque instability and predictor of cardiovascular and cerebrovascular diseases.[17] Convenient, safe, and reproducible imaging methods to detect vulnerable arterial plaques provide crucial information supporting therapeutic interventions. Studies suggested that SMI may or may not detect neovascularization of carotid plaque with accuracy comparable to contrast-enhanced ultrasound. To gain clarity, in this study, we will perform a systematic review to summarize high-quality studies and to provide evidence on the evidence-based medical support for clinical practice.

Author contributions

Conceptualization: Cong Wang.
Data curation: Cong Wang and Yang Zhou.
Methodology: Cong Wang.
Writing – original draft: Yang Zhou.
Writing – review & editing: Cong Wang.

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