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# Changes of the retina and choroid in patients with internal carotid artery stenosis: a systematic review and meta-analysis

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#### ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - Preliminary searches.

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 10 January 2024 and was last updated on 10 January 2024.

## **INTRODUCTION**

Review question / Objective Internal carotid artery stenosis (ICAS) is a prevalent vascular condition associated with ischemic cerebrovascular disease. The ophthalmic artery is the first branch of the ICA. Given the crucial role of ICA in ocular perfusion, we aim to assess the thickness and vessel density of the retina and choroid in individuals with ICAS and healthy controls.

**Rationale** The PubMed and EMBASE databases were searched for studies evaluating retinal and choroidal changes between ICAS and healthy controls using optical coherence tomography (OCT) or optical coherence tomography angiography (OCTA). Data of interest were extracted and analysed using Stata software version 16. The weighted mean difference (WMD) with 95% confidence interval (CI) was pooled for continuous outcomes. The Newcastle-Ottawa Scale (NOS) was used to assess the quality of the included studies.

**Condition being studied** Carotid artery stenosis, which is a common neurological affliction, is responsible for approximately 20% of ischemic strokes . At present, carotid artery stenosis has become a prominent public health concern. It is worth noting that the ophthalmic artery, which provides blood to ocular tissues, takes origin from the internal carotid artery. Carotid artery stenosis, particularly ICAS, frequently causes insufficient ocular blood flow, resulting in chronic ischemic ocular conditions like transient dark haze, ocular ischemic syndrome, ischemic optic neuropathy, optic disc, or retinal neovascularization.

#### **METHODS**

**Search strategy** The PubMed and EMBASE databases were explored for studies assessing the association changes of the retina and choroid in ICAS by using OCT or OCTA. The subsequent mixture of key phrases and unbound ter ms were employed: ("ICAS" OR "carotid artery disease" OR"carotid artery stenosis" OR "ICAS" OR "CAS" OR "carotid stenosis") AND ("optical coherence tomography" OR "OCT" OR "optical coherence tomography angiography" OR "OCT angiography" OR "OCTA").

**Participant or population** Patients with ICAS as the observation group and healthy people as the control.

**Intervention** Observational study. Studies evaluating retinal and choroidal changes between ICAS and healthy controls using optical coherence tomography (OCT) or optical coherence tomography angiography (OCTA).

**Comparator** Patients with ICAS as the observation group and healthy people as the control. And they were both assessed by optical coherence tomography (OCT) or optical coherence tomography angiography (OCTA).

**Study designs to be included** Retrospective or prospective study.

Eligibility criteria The inclusion criteria were as follows: (a) written in English; (b) diagnosis of ICAS was confirmed according to American Heart Association/American Stroke Association(AHA/ ASA) or North American Symptomatic Carotid Endarterectomy Trial(NASCET) (14-15); (c) patients with ICAS as the observation group and healthy people as the control; (d) OCT and OCTA measurements reported as the mean and standard deviation (SD); The exclusion criteria were as follows: (a)duplicate publications, literature reviews, and other unrelated literature; (b) patients with ophthalmic diseases that severely affect the ocular blood flow, such as glaucoma, non-arteritic anterior ischemic neuropathy, diabetic retinopathy, retinal vein occlusion, and age-related macular degeneration;(e) duplicate study populations; (f) studies with incomplete data.

**Information sources** The PubMed and EMBASE databases were explored for studies assessing the association changes of the retina and choroid in ICAS by using OCT or OCTA. TO reduce the possibility of overlooking pertinent studies, we additionally conducted a manual search by

meticulously examining the references cited in the included studies.

**Main outcome(s)** 1. the thickness of pRNFL and choroid:RNFL connects the eyeball and brain, and is an important component of human visual conduction. The thickness of RNFL can represent the number of RGC axons and reflect the survival status of RGC. Choroidal thickness is the distance between the retinal pigment cell layer and the scleral junction of the choroid, and is influenced by choroidal blood flow and vascular filling, and is an important parameter in assessing choroidal perfusion.

2.the vessel density of the superficial capillary plexus (SCP) and the deep capillary plexus (DCP). The superficial capillary plexus (SCP) is located 2.6 times below the inner limiting membrane of the retina  $\mu$  M (15.6 below the inner plexiform layer)  $\mu$  m) The deep capillary plexus (DCP) is 15.6 (70.2) below the inner plexiform layer  $\mu$  M).

**Quality assessment / Risk of bias analysis** Quality and risk of bias were assessed by two investigators using the Newtle-Ottawa Scale (NOS) (16). The quality score was determined by three factors: subject selection, comparability, and exposure. A score of 6 or higher was considered to indicate high qualityresearch.

Strategy of data synthesis Data were analyzed using Stata Software version 16. Weighted Mean difference (WMD) was used as the measure data effect statistic, and both provided their 95% confidence interval (CI). The Cochrane's Q test and I2 statistic were used to assess the statistical heterogeneity. A random-effects or fixed-effects model was applied for the meta-analysis based on the level of heterogeneity. When I2  $\leq$  50%, the fixed effect model was used; when I2>50%, the random effect model was used (17). A P value < 0.05 was regarded to be statistically significant.

**Subgroup analysis** Subgroup analysis was conducted on relevant ICAS patient indicators based on the degree of carotid artery stenosis and type of OCT equipment.

Sensitivity analysis The reliability of the outcomes of this study was confirmed through a sensitivity analysis of the outcome indicators, with each study being removed one by one.

#### Country(ies) involved China.

**Keywords** ICAS, Retina, Choroid, Optical coherence tomography, Optical coherence tomography angiography, Meta-analysis.

#### **Contributions of each author**

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