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EFFECT OF CONTINUOUS POSITIVE AIRWAY PRESSURE ON THE RETINAL NERVE FIBER LAYER AND CHOROIDAL PERFUSION IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA: A SYSTEMATIC REVIEW

EFEITO DA PRESSÃO POSITIVA CONTÍNUA EM VIAS AÉREAS NA CAMADA DE FIBRAS NERVOSAS RETINIANAS E PERFUSÃO COROIDAL EM PACIENTES COM APNEIA OBSTRUTIVA DO SONO: UMA REVISÃO SISTEMÁTICA

EFECTO DE LA PRESIÓN POSITIVA CONTINUA EN LAS VÍAS AÉREAS EN LA CAPA DE FIBRAS NERVIOSAS RETINIANAS Y LA PERFUSIÓN COROIDAL EN PACIENTES CON APNEA OBSTRUCTIVA DEL SUEÑO: UNA REVISIÓN SISTEMÁTICA

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ABSTRACT

Introduction: Obstructive sleep apnea exposes the retina, optic nerve head, and choroid to recurrent hypoxemia, sympathetic activation, oxidative stress, and vascular dysregulation. Continuous positive airway pressure (CPAP) corrects upper-airway obstruction, but its effect on retinal neural structure and choroidal circulation remains uncertain. Objective: To systematically evaluate the effect of CPAP on retinal nerve fiber layer (RNFL) thickness and choroidal perfusion-related outcomes in adults with obstructive sleep apnea. Methods: PubMed/MEDLINE, Scopus, Web of Science, the Cochrane Library, LILACS, ClinicalTrials.gov, and the World Health Organization International Clinical Trials Registry Platform were searched for studies published from January 2021 through August 23, 2026. Eligible studies compared CPAP exposure, withdrawal, adherence, or response and reported RNFL, retinal microvascular, choroidal thickness, choroidal vascularity index, or choriocapillaris vessel-density outcomes. Risk of bias was assessed with RoB 2 or ROBINS-I, and certainty was graded with GRADE. Owing to clinical and methodological heterogeneity and overlapping cohorts, a narrative synthesis was undertaken. Results and Discussion:

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Thirteen publications representing 10 independent cohorts were included. Longitudinal studies generally suggested preservation or modest thickening of the RNFL, attenuation of progressive retinal arterial narrowing, and partial normalization of choroidal thickness or vascularity after CPAP. A randomized 14-day CPAP-withdrawal trial found no change in flicker-induced retinal vascular reactivity or daytime retinal oxygen saturation, whereas newer OCT angiography cohorts reported treatment-associated changes in retinal perfusion density and vascular geometry. Direct evidence for choroidal perfusion was limited to choriocapillaris vessel-density or vascularity surrogates and was at high risk of confounding. The certainty of evidence was low for RNFL and retinal vascular caliber and very low for direct choroidal perfusion. Conclusion: CPAP may protect retinal neural and vascular integrity in obstructive sleep apnea, particularly when treatment is sustained and adherent, but definitive reversal of axonal injury has not been demonstrated. Evidence for improved choroidal perfusion is insufficient because most studies measured thickness or vascularity rather than blood flow. Standardized, adequately powered controlled trials are required before OCT or OCT angiography can be used as a treatment-response biomarker.

Keywords: Sleep Apnea. Obstructive. Continuous Positive Airway Pressure. Nerve Fibers. Choroid.

RESUMO

Introdução: A apneia obstrutiva do sono expõe a retina, a cabeça do nervo óptico e a coroide à hipoxemia recorrente, ativação simpática, estresse oxidativo e desregulação vascular. A pressão positiva contínua em vias aéreas (CPAP) corrige a obstrução das vias aéreas superiores, mas seu efeito sobre a estrutura neural retiniana e a circulação coroidal permanece incerto. Objetivo: Avaliar sistematicamente o efeito da CPAP na espessura da camada de fibras nervosas retinianas (CFNR) e nos desfechos relacionados à perfusão coroidal em adultos com apneia obstrutiva do sono. Métodos: PubMed/MEDLINE, Scopus, Web of Science, Biblioteca Cochrane, LILACS, ClinicalTrials.gov e Plataforma de Registro de Ensaios Clínicos Internacionais da Organização Mundial da Saúde foram pesquisados para estudos publicados de janeiro de 2021 a 23 de agosto de 2026. Estudos elegíveis compararam exposição ao CPAP, retirada, aderência ou resposta e relataram CFNR, microvascular retiniana, espessura coroidal, índice de vascularidade coroidal ou desfechos de densidade de vasos da coriocapilar. O risco de viés foi avaliado com RoB 2 ou ROBINS-I, e a certeza foi classificada com GRADE. Devido à heterogeneidade clínica e metodológica e sobreposição de coortes, uma síntese narrativa foi realizada. Resultados e Discussão: Treze publicações representando 10 coortes independentes foram incluídas. Estudos longitudinais sugeriram geralmente preservação ou espessamento modesto da CFNR, atenuação do estreitamento arterial retiniano progressivo e normalização parcial da espessura ou vascularidade coroidal após CPAP. Um ensaio randomizado de retirada de CPAP de 14 dias não encontrou mudanças na reatividade vascular retiniana induzida por cintilação ou saturação de oxigênio retiniano diurno, enquanto coortes mais recentes de angiografia por OCT relataram mudanças associadas ao tratamento na densidade de perfusão retiniana e geometria vascular. A evidência direta de perfusão coroidal foi limitada aos surrogados de densidade de vasos da coriocapilar ou vascularidade e apresentava alto risco de confusão. A certeza da evidência foi baixa para CFNR e calibre vascular retiniano e muito baixa para perfusão coroidal direta. Conclusão: O CPAP pode proteger a integridade neural e vascular retiniana na apneia obstrutiva do sono, particularmente quando o tratamento é sustentado e aderente, mas a reversão definitiva da lesão axonal não foi demonstrada. A evidência de melhoria da perfusão coroidal é insuficiente porque a maioria dos estudos mediu espessura ou vascularidade em vez de fluxo sanguíneo. Ensaios controlados padronizados e adequadamente potencializados são necessários antes que OCT ou angiografia por OCT possam ser usados como um biomarcador de resposta ao tratamento.

Palavras-chave: Apneia do Sono. Obstrutiva. Pressão Positiva Contínua em Vias Aéreas. Fibras Nervosas. Coroide.

RESUMEN

Introducción: La apnea obstructiva del sueño expone la retina, la cabeza del nervio óptico y la coroides a hipoxemia recurrente, activación simpática, estrés oxidativo y desregulación vascular. La presión positiva continua en las vías aéreas (CPAP) corrige la obstrucción de las vías aéreas superiores, pero su efecto sobre la estructura neural retiniana y la circulación coroidal sigue siendo incierto. Objetivo: Evaluar sistemáticamente el efecto de la CPAP en el grosor de la capa de fibras nerviosas retinianas (CFNR) y los resultados relacionados con la perfusión coroidal en adultos con apnea obstructiva del sueño. Métodos: Se buscaron en PubMed/MEDLINE, Scopus, Web of Science, la Biblioteca Cochrane, LILACS, ClinicalTrials.gov y la Plataforma de Registro de Ensayos Clínicos Internacionales de la Organización Mundial de la Salud estudios publicados de enero de 2021 a 23 de agosto de 2026. Los estudios elegibles compararon la exposición a CPAP, la retirada, la adherencia o la respuesta e informaron sobre CFNR, microvascular retiniana, grosor coroidal, índice de vascularidad coroidal o resultados de densidad de vasos de la coriocapilar. El riesgo de sesgo se evaluó con RoB 2 o ROBINS-I, y la certeza se calificó con GRADE. Debido a la heterogeneidad clínica y metodológica y a la superposición de cohortes, se realizó una síntesis narrativa. Resultados y Discusión: Se incluyeron trece publicaciones que representaban 10 cohortes independientes. Los estudios longitudinales generalmente sugirieron preservación o engrosamiento modesto de la CFNR, atenuación del estrechamiento arterial retiniano progresivo y normalización parcial del grosor o vascularidad coroidal después de CPAP. Un ensayo aleatorizado de retirada de CPAP de 14 días no encontró cambios en la reactividad vascular retiniana inducida por parpadeo ni en la saturación de oxígeno retiniano diurno, mientras que las cohortes más nuevas de angiografía por OCT informaron cambios asociados al tratamiento en la densidad de perfusión retiniana y la geometría vascular. La evidencia directa de perfusión coroidal se limitó a surrogados de densidad de vasos de la coriocapilar o vascularidad y presentó un alto riesgo de confusión. La certeza de la evidencia fue baja para CFNR y calibre vascular retiniano y muy baja para la perfusión coroidal directa. Conclusión: El CPAP puede proteger la integridad neural y vascular retiniana en la apnea obstructiva del sueño, particularmente cuando el tratamiento es sostenido y adherente, pero no se ha demostrado la reversión definitiva del daño axonal. La evidencia de mejoría de la perfusión coroidal es insuficiente porque la mayoría de los estudios midieron grosor o vascularidad en lugar de flujo sanguíneo. Se requieren ensayos controlados estandarizados y adecuadamente potencializados antes de que OCT o la angiografía por OCT puedan usarse como biomarcador de respuesta al tratamiento.

Palabras clave: Apnea del Sueño. Obstructiva. Presión Positiva Continua en las Vías Aéreas. Fibras Nerviosas. Coroides.

1 INTRODUCTION

Obstructive sleep apnea (OSA) is a highly prevalent sleep-related breathing disorder that affects hundreds of millions of adults and carries substantial cardiovascular, cerebrovascular, metabolic, and neurocognitive burden.[1] Recurrent complete or partial upper-airway collapse produces intermittent hypoxemia, sleep fragmentation, intrathoracic pressure swings, and sympathetic surges that vary considerably among patients with the same apnea-hypopnea index (AHI).[1] Consequently, hypoxic burden, event duration, arousal intensity, and cardiometabolic phenotype may characterize tissue risk more accurately than event frequency alone.[1] Continuous positive airway pressure (CPAP) is the reference treatment for symptomatic or clinically significant OSA because pneumatic splinting of the upper airway prevents obstructive respiratory events.[2] Effective treatment improves respiratory indices and symptoms, although its biological effect is strongly modified by nightly use, residual disease, mask leak, and treatment pressure.[2]

International recommendations therefore place adherence assessment and longitudinal clinical monitoring at the center of CPAP management rather than equating prescription with effective exposure.[2] The eye is a plausible target organ of OSA because the retina and optic nerve head combine high metabolic demand with terminal microvascular beds that are sensitive to changes in oxygen delivery and autoregulation.[3] Intermittent hypoxia, oxidative stress, endothelial dysfunction, inflammation, and altered vasoactive signaling have all been proposed as mechanisms connecting OSA with retinal vascular disease, glaucoma, and ischemic optic neuropathy.[3] The choroid may also respond to hypoxemia and autonomic imbalance through changes in stromal volume, vascular caliber, permeability, and regional flow.[3]

Clinical reviews consistently associate OSA with several ocular disorders, but the strength and direction of individual associations remain heterogeneous.[4] Evidence is strongest for floppy eyelid syndrome and nonarteritic anterior ischemic optic neuropathy, while findings for glaucoma, central serous chorioretinopathy, and other posterior-segment disorders are less uniform.[4] Claims that OSA treatment prevents ocular disease remain especially uncertain because well-controlled longitudinal treatment studies are scarce.[4] Retinal studies nevertheless describe thinner peripapillary RNFL, altered macular thickness, vascular narrowing, tortuosity, and reduced parafoveal or peripapillary vessel density in more severe OSA.[5]

These abnormalities support the concept that retinal imaging may act as an accessible marker of neural and microvascular injury caused by nocturnal hypoxemia.[5] CPAP could theoretically interrupt this process by stabilizing oxygenation, reducing sympathetic

activation, and improving vascular homeostasis.[5] Optical coherence tomography angiography (OCTA) has expanded this field by providing depth-resolved, dye-free estimates of perfused vessel density in superficial, deep, peripapillary, and choriocapillaris slabs.[6] OCTA measurements, however, are influenced by device algorithms, scan quality, projection artifacts, segmentation error, axial length, systemic blood pressure, and signal strength.[6] Moreover, vessel density is a perfusion-related surrogate and does not directly quantify volumetric blood flow or oxygen delivery.[6]

Structural OCT studies also require cautious interpretation because small short-term increases in RNFL thickness cannot be assumed to represent axonal regeneration.[7] In newly diagnosed OSA, average and superior RNFL thickness may be lower with increasing disease severity and may correlate inversely with the AHI.[7] Yet age, obesity, diabetes, hypertension, glaucoma susceptibility, refractive error, and baseline disc anatomy may generate or amplify these associations.[7] Swept-source OCTA data further suggest that moderate-to-severe OSA is associated with lower peripapillary, macular, and choroidal-layer vascular density than simple snoring or mild disease.[8]

The observed vascular-density reductions correlate with AHI in several retinal and choroidal slabs, supporting a dose-response relationship.[8] Because these data are predominantly cross-sectional, they cannot establish whether hypoxemia causes the abnormality or whether CPAP reverses it.[8] A broad meta-analysis of ocular manifestations found increased risks of glaucoma, retinal vein occlusion, nonarteritic ischemic optic neuropathy, and other eye disorders among patients with OSA.[9] The same synthesis highlighted extensive heterogeneity and did not establish that CPAP modifies posterior-segment disease.[9]

This distinction is clinically important because an association between untreated OSA and ocular damage does not prove that a treatment-induced imaging change is beneficial.[9] A recent meta-analysis of OCTA studies found lower radial peripapillary capillary density in mild-to-moderate and severe OSA compared with controls.[10] The authors proposed optic nerve head vessel density as a potential severity biomarker, while acknowledging the small number and heterogeneity of available studies.[10] A focused synthesis of CPAP-exposed cohorts is therefore required to separate structural RNFL outcomes from retinal perfusion, choroidal morphology, and direct choriocapillaris perfusion.[10]

2 OBJECTIVES

2.1 PRIMARY OBJECTIVE

To determine the effect of CPAP therapy on RNFL thickness and choroidal perfusion-related parameters in adults with OSA.

2.2 SECONDARY OBJECTIVES

1. To assess whether CPAP modifies macular retinal thickness, ganglion cell–inner plexiform layer measurements, or optic nerve head structural parameters.
2. To evaluate changes in retinal vascular caliber, vessel density, perfusion density, vascular reactivity, and retinal oxygen saturation after CPAP initiation, continuation, withdrawal, or differing adherence.
3. To distinguish direct choriocapillaris perfusion measures from indirect choroidal surrogates, including choroidal thickness and choroidal vascularity index.
4. To examine whether treatment duration, OSA severity, hypoxic burden, CPAP adherence, diabetes, intraocular pressure, or imaging methodology modifies the ocular response.
5. To appraise risk of bias, certainty of evidence, clinical applicability, and priorities for future research.

3 METHODOLOGY

3.1 DESIGN AND REPORTING

This systematic review was structured according to PRISMA 2020. A review protocol specifying the population, intervention, comparators, outcomes, and analytical plan was prepared before eligibility assessment but was not prospectively registered. Because the included evidence used incompatible imaging platforms, follow-up intervals, treatment definitions, and statistical units, quantitative pooling was not planned unless at least three independent cohorts reported a sufficiently uniform outcome.

3.2 INFORMATION SOURCES AND SEARCH STRATEGY

Electronic searches covered PubMed/MEDLINE, Scopus, Web of Science, the Cochrane Library, and LILACS, supplemented by ClinicalTrials.gov, the World Health Organization International Clinical Trials Registry Platform, backward citation searching, and forward citation tracking. The search period was January 1, 2021, through August 23, 2026, reflecting the prespecified recent-evidence window. Controlled vocabulary and free-text terms combined concepts for obstructive sleep apnea, continuous positive airway pressure or

positive airway pressure, retinal nerve fiber layer, optical coherence tomography, OCT angiography, retina, optic nerve head, choroid, choriocapillaris, vascularity, vessel density, perfusion, oxygen saturation, and vascular reactivity. No language restriction was imposed at the search stage.

3.3 ELIGIBILITY CRITERIA

Eligible studies enrolled adults with polysomnography- or validated sleep-test–defined OSA and evaluated CPAP initiation, ongoing CPAP versus no CPAP, CPAP continuation versus withdrawal, dose or adherence, or treatment response. Outcomes had to include peripapillary RNFL, macular or ganglion cell structure, optic nerve head morphology, retinal vascular caliber or function, OCTA vessel or perfusion density, choroidal thickness, choroidal vascularity index, choriocapillaris vessel density, or another explicitly defined posterior-segment perfusion-related measure. Randomized trials, prospective or retrospective cohorts, and controlled before–after studies were eligible. Cross-sectional studies without analyzable CPAP exposure, case reports, conference abstracts, non-peer-reviewed preprints, pediatric-only studies, and studies restricted to a specific retinal disease without an eligible RNFL or choroidal perfusion outcome were excluded.

3.4 STUDY SELECTION AND DATA EXTRACTION

Two reviewers independently screened titles and abstracts, assessed full texts, and extracted study design, sample, OSA definition and severity, treatment assignment, CPAP adherence, follow-up, ocular exclusions, imaging platform, statistical unit, numerical outcomes, adjustment variables, and adverse or competing ocular effects. Disagreements were resolved by consensus with a third reviewer. Reports from the same cohort were linked and were not treated as independent evidence in certainty assessment or any contemplated pooling.

3.5 RISK OF BIAS AND CERTAINTY OF EVIDENCE

Randomized evidence was assessed with RoB 2, and nonrandomized intervention evidence with ROBINS-I. Particular attention was given to confounding by indication, healthy-adherer effects, baseline imbalance, attrition, use of both eyes without adequate correlation modeling, selective reporting, multiple comparisons, device-dependent segmentation, and lack of an untreated longitudinal comparator. Certainty was rated with GRADE for RNFL structure, retinal vascular caliber or reactivity, and choroidal perfusion-related outcomes.

Evidence was synthesized narratively by anatomical compartment and measurement type; statistical significance was not interpreted as equivalent to clinical importance.

4 RESULTS

4.1 STUDY SELECTION

The electronic and supplementary searches were deduplicated before title and abstract screening. Twenty-one reports proceeded to full-text assessment. Eight were excluded: two were outside the prespecified publication window, three did not provide a comparative or longitudinal CPAP effect, one assessed a disease-specific retinal outcome without an eligible RNFL or choroidal-perfusion endpoint, one relied on diagnostic codes without relevant ocular imaging, and one was a non-peer-reviewed preprint. Thirteen publications were included, representing 10 independent cohorts. Two publications arose from the same Australian cohort, two from the same Spanish cohort, and two randomized reports evaluated different outcomes in the same CPAP-withdrawal trial.

4.2 STUDY CHARACTERISTICS AND PRINCIPAL FINDINGS

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
Wong et al., 2021	79 participants reassessed at approximately 24 months; 25 initiated CPAP; severe OSA with CPAP compared with severe untreated OSA and other severity groups	Central retinal artery and vein equivalents, arteriovenous ratio, vascular pulsation	Severe untreated OSA showed progressive arterial narrowing, whereas severe OSA treated with CPAP showed slight arterial widening; venous caliber and pulsatility findings were not significant.
Rodrigues et al., 2026	39 participants from the Wong cohort reassessed at 7 years; severe OSA with CPAP (n=9) versus severe untreated OSA (n=8), other OSA groups, and controls	Retinal arterial and venous caliber; global and sectoral RNFL	CPAP-treated severe OSA showed slower apparent vascular narrowing, but global RNFL thinning rates were similar and sectoral RNFL differences were not statistically significant.
Naranjo-Bonilla et al., 2021	40 newly diagnosed patients; CPAP (n=28) versus untreated OSA (n=12); 3-month follow-up	Peripapillary RNFL, total retinal thickness, choroidal thickness	CPAP was associated with thickening in multiple RNFL and retinal subfields and temporal choroidal thinning interpreted as normalization; treatment was not randomized.
Naranjo-Bonilla et al., 2022	28 CPAP-treated patients from the preceding cohort;	Peripapillary RNFL, total retina, choroidal	Limited retinal thickening persisted at 12 months and temporal choroidal thickness remained lower than

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
	baseline, 3 months, and 12 months	thickness, intraocular pressure	baseline; intraocular pressure was higher at 12 than at 3 months.
Altinel et al., 2022	22 patients with OSA and 26 controls; OSA eyes reassessed after 12 months of regular CPAP	Choroidal vascularity index, luminal area, stromal area	Baseline choroidal vascularity index was lower in OSA; after CPAP it approached the control value while stromal area decreased, suggesting reduced stromal edema rather than proven increased blood flow.
Tejero-Garcés et al., 2022	52 patients with OSA; CPAP or upper-airway surgery; 6-month follow-up	Macular thickness and volume, peripapillary RNFL, optic nerve head	Macular thickness decreased in mild-to-moderate OSA and foveal thickness increased in severe OSA; no difference between treatment modalities was demonstrated, and CPAP-specific effects were not separable.
Turnbull et al., 2022	Double-blind trial in 37 established CPAP users with moderate-to-severe OSA; sham withdrawal (n=19) versus continued CPAP (n=18) for 14 nights	Flicker-induced retinal arteriolar and venular reactivity	CPAP withdrawal did not significantly alter retinal microvascular reactivity; the experiment addressed short-term functional change rather than chronic structural remodeling.
Turnbull et al., 2023	Same randomized withdrawal trial	Daytime retinal arterial and venous oxygen saturation	Stopping CPAP caused marked recurrence of OSA but did not alter daytime retinal arterial or venous oxygen saturation.
Giarratano et al., 2025	44 newly treated patients; OCTA before and after CPAP; longitudinal adherence analyses after approximately 4 months	Foveal vessel density, foveal avascular zone, vessel radius, tortuosity, RNFL and macular volume	Greater CPAP use was associated with lower foveal vessel density, larger avascular zone, and larger vessel radius; findings were exploratory and did not establish that every directional change represented benefit.
Díaz de Terán et al., 2025	37 patients, 72 eyes; baseline and 12 months of CPAP	RNFL, Bruch membrane opening–minimum rim width, hypoxic burden	Overall RNFL change was not significant; superotemporal rim width increased significantly, and hypoxic burden and diabetes predicted greater damage.
Wang et al., 2025	245 patients with severe OSA treated with CPAP; good response (n=164) versus poor response (n=81)	Subfoveal choroidal thickness, choroidal vascularity index, choriocapillaris vessel density	Post-treatment choroidal indices discriminated response groups, but absent baseline change estimates and reporting inconsistencies limited causal interpretation.
Zhou et al., 2026	97 patients with OSA and 60 controls; longitudinal CPAP subset of 26 patients	RNFL, ganglion cell–inner plexiform layer, total retinal thickness, foveal	The treated subset showed improved structural and retinal perfusion-density parameters and smaller foveal avascular-zone measurements;

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
		avascular zone, retinal perfusion and vessel density	replication in controlled cohorts is required.
Gemici et al., 2026	38 severe OSA patients and 19 controls; 30 adherent patients reassessed after 6 months of CPAP	OCTA vascular parameters, standard and macular visual fields	Average and inferior RNFL and visual-field indices improved after correction for multiple testing, whereas OCTA vascular changes did not remain significant.

Source: Prepared by the authors.

4.3 RISK OF BIAS AND CERTAINTY

The randomized withdrawal trial had low risk of bias for its short-term objective outcomes, although precision was limited by its sample size and brief intervention. The nonrandomized studies generally had serious risk of bias because CPAP assignment or adherence was not randomized, attrition was frequent, residual confounding was plausible, and several analyses tested numerous imaging variables without full multiplicity control. The response-stratified choroidal study had serious-to-critical concerns owing to unclear temporality, absent baseline change estimates, and internal reporting inconsistencies. GRADE certainty was low for RNFL and retinal vascular-caliber outcomes and very low for choroidal perfusion because few independent cohorts measured a direct choriocapillaris endpoint.

5 RESULTS AND DISCUSSION

The most reproducible treatment signal concerned retinal vascular caliber rather than direct capillary flow: a prospective cohort suggested that CPAP may arrest progressive arterial narrowing in severe OSA.[11] Untreated severe OSA showed a decline in central retinal artery equivalent from 171.3 to 165.1 µm, whereas the CPAP-treated severe group changed from 171.2 to 174.0 µm, with a significant between-group trajectory.[11] The arteriovenous ratio also diverged, but venous caliber and dynamic pulsation did not show a consistent treatment effect, indicating a selective rather than universal vascular response.[11] The seven-year extension of the same cohort retained only 39 participants, including nine with severe OSA using CPAP and eight with severe untreated OSA.[12] Retinal arterial and venous calibers appeared larger and narrowed more slowly with CPAP, but global RNFL thinning rates were similar and the sectoral RNFL difference was not statistically significant.[12] Marked attrition, very small subgroups, and nonrandom treatment uptake make the long-term vascular pattern hypothesis-generating rather than causal.[12]

At three months, a Spanish cohort comparing 28 CPAP-treated with 12 untreated patients found increased peripapillary RNFL thickness in five of six sectors, increased total retinal thickness in seven of nine subfields, and temporal choroidal thinning.[13] These changes may represent resolution of hypoxia-related edema or vascular-volume shifts rather than the generation of new axons.[13] The small nonrandomized groups, short follow-up, and multiplicity of OCT outcomes create serious risks of confounding and false-positive findings.[13] In the 12-month report from the same Spanish cohort, thickening persisted in only two of six RNFL sectors and two of nine retinal subfields, while temporal choroidal thickness remained lower than baseline.[14] Because the 12-month analysis contained only the 28 CPAP-treated participants, it could not distinguish treatment from aging, regression to the mean, repeat-scan variability, or secular change.[14] Intraocular pressure was also higher at 12 months than at three months, illustrating that favorable and potentially unfavorable ocular effects can coexist.[14]

In another cohort, 22 patients with OSA had a lower baseline choroidal vascularity index than 26 controls, and 12 months of regular CPAP increased the index toward the control value while reducing stromal area.[15] The investigators interpreted this pattern as improvement of OSA-associated choroidal stromal edema.[15] Nevertheless, the choroidal vascularity index is a binarized structural ratio and should not be described as a direct measure of blood flow, especially without an untreated longitudinal comparator.[15]

The largest choroidal study divided 245 CPAP-treated patients with severe OSA into good-response and poor-response groups and reported significant between-group differences in subfoveal choroidal thickness, choroidal vascularity index, and choriocapillaris vessel density.[16] The reported areas under the receiver-operating-characteristic curve were 0.835 for subfoveal thickness, 0.805 for choriocapillaris vessel density, and 0.910 for choroidal vascularity index.[16] These findings are prognostic associations after treatment, not evidence of within-person perfusion improvement, and unclear temporality, absent baseline changes, and internal reporting inconsistencies impose a high risk of bias.[16]

The strongest experimental design produced a neutral short-term result: 37 established CPAP users with moderate-to-severe OSA were randomized to 14 nights of sham withdrawal or continued treatment.[17] CPAP withdrawal did not significantly change flicker-induced arteriolar reactivity, with a between-group difference in response area under the curve of 3.8 arbitrary units and a 95% confidence interval from −10.6 to 18.2.[17] The null result may reflect genuine short-term stability, but it cannot exclude chronic remodeling, effects in treatment-naïve patients, or a smaller difference than the trial could detect.[17] A second report from the same randomized experiment found no change in daytime retinal arterial or venous

oxygen saturation after CPAP was stopped.[18] The result supports short-term stability of daytime retinal oxygenation despite marked recurrence of OSA.[18] It does not address nocturnal oxygen extraction, choroidal circulation, or the cumulative consequences of years of intermittent hypoxemia.[18]

In an exploratory OCTA cohort of 44 patients, greater CPAP use over approximately four months was associated with lower foveal vessel density, a larger foveal avascular zone, and a larger retinal vessel radius.[19] A lower vessel-density value after treatment should not automatically be labeled deterioration because edema, capillary recruitment, image segmentation, and vascular remodeling can change the metric in different directions.[19] The absence of an untreated comparator, adherence self-selection, and numerous uncorrected or exploratory comparisons substantially reduce certainty.[19]

A 2026 study compared 97 patients with OSA with 60 controls and reassessed a subset of 26 patients after CPAP, reporting improvements in average RNFL, ganglion cell–inner plexiform layer, total retinal thickness, retinal perfusion density, vessel density, and foveal avascular-zone measurements.[20] This integrated structural and OCTA signal is compatible with partial reversibility of hypoxia-related neural and microvascular dysfunction.[20] The small treated subset, nonrandom selection, multiple severity strata, and device-dependent segmentation require independent replication before thresholds can be used clinically.[20]

In a separate severe-OSA cohort, 30 adherent patients completed six months of CPAP after baseline comparison of 38 patients with 19 controls.[21] Average and inferior RNFL thickness and visual-field indices improved after false-discovery-rate correction, whereas OCTA vascular changes did not remain significant after correction.[21] The discordance suggests that structural or functional change may occur without a detectable perfusion-density change, but the uncontrolled longitudinal design cannot establish the mechanism.[21]

A 12-month study of 37 patients and 72 eyes found no significant overall RNFL improvement, although superotemporal Bruch membrane opening–minimum rim width increased significantly.[22] Greater hypoxic burden and diabetes predicted greater retinal or optic nerve damage, supporting risk stratification beyond the AHI.[22] The authors' protective interpretation should be tempered by the absence of an untreated comparator, possible within-person correlation between eyes, and predominantly nonsignificant RNFL changes.[22]

A 52-patient study combining CPAP and upper-airway surgery reported reduced macular thickness in mild-to-moderate OSA and increased foveal thickness in severe OSA after six months.[23] No significant difference between treatment modalities was demonstrated, and the published results did not isolate a CPAP-specific effect.[23] The severity-dependent

direction of change also warns that thickening can signify recovery from atrophy in one context but edema or measurement variability in another.[23]

Intraocular pressure is a clinically relevant competing pathway because a 2025 systematic review and meta-analysis found a significant increase after long-term CPAP in pooled analyses, although component studies were heterogeneous.[24] Higher nocturnal or sustained intraocular pressure can reduce ocular perfusion pressure and confound interpretation of RNFL and choroidal changes.[24] Periodic intraocular-pressure and glaucoma-risk assessment is therefore reasonable for susceptible patients, without diminishing the established respiratory indication for CPAP.[24]

Across outcomes, GRADE certainty was low for RNFL preservation and retinal vascular caliber and very low for direct choroidal perfusion because almost all choroidal studies measured thickness or vascularity rather than flow.[25] CPAP should continue to be prescribed for standard sleep-medicine indications, while OCT and OCTA remain adjunctive research or surveillance tools rather than validated treatment targets.[25] Future trials should randomize treatment strategy when ethical, predefine one eye or use hierarchical eye-level models, quantify objective adherence and residual AHI, standardize scan timing and segmentation, and measure nocturnal ocular perfusion, choriocapillaris flow deficit, RNFL, ganglion cell complex, intraocular pressure, and visual function together.[25]

6 CONCLUSION

The contemporary evidence suggests that sustained CPAP may attenuate retinal vascular narrowing and may preserve selected RNFL or optic nerve head measurements in adults with OSA. The direction of effect is generally favorable, but the magnitude is small, inconsistent across sectors, and uncertain because most data come from uncontrolled or nonrandomized cohorts.

An increase in RNFL thickness after CPAP cannot be interpreted automatically as axonal regeneration. It may reflect resolution of hypoxia-related swelling, altered vascular volume, segmentation variability, regression to the mean, or true preservation of tissue that would otherwise have thinned. The most defensible conclusion is possible structural protection, not proven neural restoration.

Evidence for improved choroidal perfusion is substantially weaker. Choroidal thickness and choroidal vascularity index describe morphology, while OCTA vessel density is a perfusion-related surrogate rather than a measurement of volumetric blood flow. Only limited high-risk evidence directly evaluated the choriocapillaris, so a causal perfusion benefit has not been established.

Clinically, CPAP should be continued according to respiratory and cardiovascular indications, with attention to objective adherence and residual OSA. Baseline and longitudinal ophthalmic assessment may be considered in patients with severe hypoxic burden, diabetes, glaucoma risk, optic neuropathy, or unexplained retinal findings. Intraocular pressure should be monitored when clinically indicated because CPAP-related pressure effects may coexist with vascular benefits.

Future research should use adequately powered controlled designs, standardized OCT and OCTA acquisition, prespecified primary endpoints, eye-level correlation methods, and simultaneous assessment of hypoxic burden, treatment pressure, adherence, intraocular pressure, ocular perfusion pressure, and visual function. Until such studies are available, RNFL and choroidal imaging should be viewed as promising mechanistic biomarkers rather than validated criteria for judging CPAP effectiveness.

REFERENCES

1. Malhotra A, Ayappa I, Ayas N, Collop N, Kirsch D, McArdle N, *et al.* Metrics of sleep apnea severity: beyond the apnea-hypopnea index. Sleep. 2021;44(7):zsab030.

10. Ji K, Yang Y, Zhang Q, Xing Y, Wan W. Meta-analysis: characteristics of retinal vasculature in obstructive sleep apnea syndrome humans. J Ophthalmol. 2024;2024:4600428.

11. Wong B, Tong JY, Schulz AM, Graham SL, Farah CS, Fraser CL. The impact of continuous positive airway pressure treatment on retinal vascular changes in obstructive sleep apnea. J Clin Sleep Med. 2021;17(5):983-991.

12. Rodrigues D, Schulz AM, Britton A, Wong B, Tong J, Farah CS, *et al.* Impact of continuous positive airway pressure treatment on retinal vasculature in obstructive sleep apnea: a 7-year follow-up. Invest Ophthalmol Vis Sci. 2026;67(10):7.

13. Naranjo-Bonilla P, Muñoz-Villanueva MC, Giménez-Gómez R, Jurado-Gámez B. Retinal and choroidal thickness measurements in obstructive sleep apnea: impacts of continuous positive airway pressure treatment. Graefes Arch Clin Exp Ophthalmol. 2021;259(11):3381-3393.

14. Naranjo-Bonilla P, Giménez-Gómez R, Muñoz-Villanueva MDC, Jurado-Gámez B. Retinal and choroidal effects of continuous positive airway pressure as treatment for sleep apnea: results at 12 months. Int J Environ Res Public Health. 2022;19(19):12637.

15. Altinel MG, Uslu H, Kanra AY, Dalkilic O. Effect of obstructive sleep apnoea syndrome and continuous positive airway pressure treatment on choroidal structure. Eye. 2022;36(10):1977-1981.

16. Wang C, Yu J, Gu Y, Wu Z, Xia Y. Choroidal vascular and oropharyngeal morphological indicators in predicting CPAP treatment efficacy in severe OSAS patients: a prospective cohort study. Head Face Med. 2025;21:64.

17. Turnbull CD, Stockley JA, Madathil S, Huq SSA, Cooper BG, Ali A, *et al.* Effect of obstructive sleep apnoea on retinal microvascular function: a randomised controlled trial. Graefes Arch Clin Exp Ophthalmol. 2022;260(7):2129-2139.

18. Turnbull CD, Stradling JR, Heitmar R. The effect of obstructive sleep apnea on retinal arterial and venous oxygen saturations: further evidence from a randomised study. Graefes Arch Clin Exp Ophthalmol. 2023;261(6):1757-1759.

19. Giarratano Y, Hill EA, Hamid C, Wiseman S, Gray C, Chappell FM, *et al.* Retinal microvascular phenotypes can track small vessel disease burden and CPAP treatment effectiveness in obstructive sleep apnea. J Cereb Blood Flow Metab. 2025;45(4):690-702.

2. Mediano O, González Mangado N, Montserrat JM, Alonso-Álvarez ML, Almendros I, Alonso-Fernández A, *et al.* International consensus document on obstructive sleep apnea. Arch Bronconeumol. 2022;58(1):52-68.

20. Zhou R, Li Y, Wang H, Hu J, Gong W, Hu J, *et al.* OCTA-based evaluation of retinal microvascular and structural changes in patients with obstructive sleep apnea-hypopnea syndrome before and after treatment. Sleep Med. 2026;144:108955.

21. Gemici YI, Ozturk U, Erdogan M, Ilker SS, Yilmaz H, Kisabay Ak A. Multimodal neuro-ophthalmologic changes and the impact of CPAP therapy in severe obstructive sleep apnea: a prospective OCT, OCTA, and visual field study. Doc Ophthalmol. 2026. Epub ahead of print.

22. Díaz de Terán T, Boira I, Cerveró A, Casado A, López-de-Eguileta A, Fonseca S, *et al.* Benefit of continuous positive airway pressure on optic nerve damage in patients with obstructive sleep apnea. Sleep Breath. 2025;29:173.

23. Tejero-Garcés G, Ascaso FJ, Casas P, Adiego MI, Baptista P, O'Connor-Reina C, *et al.* Assessment of the effectiveness of obstructive sleep apnea treatment using optical coherence tomography to evaluate retinal findings. J Clin Med. 2022;11(3):815.

24. Kongchan P, Banhiran W, Chirapapaisan N, Kasemsuk N. The effect of continuous positive airway pressure therapy on intraocular pressure in patients with OSA: a systematic review and meta-analysis. J Clin Sleep Med. 2025;21(5):907-915.

25. Kaštelan S, Kozina L, Alaber M, Tomić Z, Andrešić M, Bakija I, *et al.* Neuro-ophthalmological disorders associated with obstructive sleep apnoea. Int J Mol Sci. 2025;26(14):6649.

3. Liu PK, Chiu TY, Wang NK, Levi SR, Tsai MJ. Ocular complications of obstructive sleep apnea. J Clin Med. 2021;10(15):3422.

4. Lee SSY, Nilagiri VK, Mackey DA. Sleep and eye disease: a review. Clin Exp Ophthalmol. 2022;50(3):334-344.

5. Nakayama LF, Tempaku PF, Bergamo VC, Polizelli MU, Santos da Cruz NF, Bittencourt LRA, *et al.* Obstructive sleep apnea and the retina: a review. J Clin Sleep Med. 2021;17(9):1947-1952.

6. Christou EE, Kostikas K, Asproudis C, Zafeiropoulos P, Stefaniotou M, Asproudis I. Retinal microcirculation characteristics in obstructive sleep apnea/hypopnea syndrome evaluated by OCT-angiography: a literature review. Int Ophthalmol. 2022;42(12):3977-3991.

7. Devi TS, Agrawal A, Gupta N, Gupta R, Samanta R, Nishant P. Retinal nerve fiber layer thickness in patients with obstructive sleep apnea. J Glaucoma. 2023;32(5):347-354.

8. Lin PW, Lin HC, Chang CT, Lin MC, Friedman M, Salapatas AM. Decreased peripapillary and macular vascular densities in patients with moderate/severe obstructive sleep apnea/hypopnea syndrome. Nat Sci Sleep. 2023;15:1-12.

9. Bulloch G, Seth I, Zhu Z, Sukumar S, McNab A. Ocular manifestations of obstructive sleep apnea: a systematic review and meta-analysis. Graefes Arch Clin Exp Ophthalmol. 2024;262(1):19-32.