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REVIEW

Vascular changes in optical coherence tomography angiography unveiling the depths of dry age-related macular degeneration: a review

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ABSTRACT

Introduction: Recent advancements in imaging techniques, particularly optical coherence tomography angiography (OCTA), have transformed our understanding of retinal microvascular changes in various ocular diseases, including dry age-related macular degeneration (AMD). Our literature review summarizes key findings on retinal vascular alterations in dry AMD as observed with OCTA, highlighting their implications for disease progression and management.

Areas covered: Studies reveal significant changes in dry AMD patients, affecting the superficial and deep capillary plexuses as well as the choroid. These alterations include decreased vascular and flow density, variations in the foveal avascular zone, reduced choriocapillaris perfusion, and alterations in choroidal vascularity and thickness. Such changes reflect the complex vascular pathology of dry AMD and serve as potential biomarkers for monitoring disease progression. Variability in study results underscores the importance of considering AMD stage, sample size, follow-up duration, imaging protocols, and standardization.

Expert opinion: OCTA in dry AMD is primarily research-focused due to technical and methodological challenges. Its adoption in clinical practice requires standardized protocols and improved software. With future advancements and a better understanding of disease pathology, OCTA could become a routine part of dry AMD management, especially as new therapies emerge that utilize OCTA for assessing dry AMD progression.

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Dry AMD; OCTA; SCP; DCP; choriocapillaris; CVI; ChT; VD

1. Introduction

This review delves into the clinical significance of vascular alterations observed through optical coherence tomography angiography (OCTA) in non-neovascular age-related macular degeneration (AMD). While numerous studies have underscored the utility of OCTA in different retinal vascular disorders such as wet AMD, diabetic retinopathy, retinal vein occlusion, retinal artery occlusion, vessel abnormalities, and even anterior segment neovascularization, there has been relatively less focus on vascular changes associated specifically with dry AMD.

1.1. Technical insights into OCTA

Optical coherence tomography angiography is a novel method that enables the noninvasive detection of vascular changes within the retina and choroid. Although still under development, OCTA represents a promising advancement in imaging technology, providing high-resolution images of blood flow across all layers of the retina in a rapid and noninvasive manner. In comparison to fluorescein angiography, OCTA can visualize even deeper vascular layers, leading to a better understanding of the pathogenesis of vascular diseases and the development of new treatment methods [1–3]. This technique relies on detecting changes over time, allowing for the visualization of blood flow in retinal vessels. In comparison to conventional structural optical coherence tomography (OCT), which acquires 3D volumes through raster scans, OCTA involves repeated imaging of the same retinal area to detect motion and create vascular contrast. These repeated scans are compared pixel by pixel to detect signal changes caused by flowing erythrocytes, resulting in motion contrast images. Volumetric OCTA data are obtained by performing repeated B-scans at successively displaced locations in the retina, enabling 3D visualization of the microvasculature. The OCTA volume is typically displayed by segmenting different retinal layers and projecting an en face view similar to traditional angiography techniques [1,4,5].

It is also worth noting that artifacts may have a tremendous impact on OCTA results [6]. Projection artifacts in OCTA

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Article highlights

- Role of Retinal Vasculature: The retinal vasculature is crucial for maintaining retinal function. Recent advancements in OCTA have enhanced understanding of its alterations in dry age-related macular degeneration.
- Findings from OCTA Studies: Key findings include significant vascular changes in dry AMD such as reduced vascular and flow density in superficial and deep capillary plexuses, altered foveal avascular zone, and decreased choriocapillaris perfusion density.
- Disease Progression and Biomarkers: These vascular changes serve as potential biomarkers for dry AMD progression and provide insights into its pathophysiology.
- Choroidal Thickness: Choroidal thickness is an important parameter in assessing disease severity and predicting progression to wet AMD.
- Choroidal Vascularity Index (CVI): CVI is a relatively stable indicator useful for assessing choroidal vascular changes in dry AMD and has shown biphasic changes across disease progression.
- Challenges and Variability: Variability among studies due to differences in imaging devices and protocols affects the reliability of results. Standardization is essential to enhance diagnostic accuracy.
- Future Research: Emphasis is on standardizing OCTA imaging protocols, investigating reliable biomarkers, and conducting long-term studies to improve understanding of vascular changes and their clinical implications in dry AMD management.
- Clinical Implications: Current applications for OCTA in dry AMD are predominantly research-focused, but they are potentially leading to novel diagnostic and therapeutic strategies.

imaging arise from the interaction of light scattering and coherence gating in the eye, mimicking real vasculature in deeper layers. They pose challenges for accurate measurements and can confound the detection of conditions like macular neovascularization (MNV) in wet AMD [7,8]. Motion artifacts or ocular pulsation can affect OCTA image quality, requiring hardware and software solutions for mitigation [9]. Signal attenuation from factors like defocus and hyperreflective material also challenges OCTA interpretation. Defocus and global signal loss can bias vessel density measurements, while local signal loss may mimic real capillary dropout. Modern machine learning algorithms show promise in distinguishing between shadowing artifacts and true pathology in OCTA images, enhancing diagnostic accuracy [10,11].

1.2. OCTA in AMD

AMD stands as the leading cause of vision loss among individuals aged 50 and above in developed countries, underscoring the critical need for developing effective diagnostic methods [12,13]. Dry age-related macular degeneration (AMD) is characterized by the accumulation of drusen beneath the retinal pigment epithelium and the progressive thinning or atrophy of the retinal pigment epithelium and photoreceptors. This leads to a gradual disturbance in nutrient/waste exchange, contributing to retinal cell death. The exact mechanisms involve both choroidal ischemia, where reduced blood flow affects outer retinal layers, and inflammatory pathways that contribute to disease progression. OCTA has significantly advanced our understanding of dry AMD by providing noninvasive imaging of the retinal and choroidal microvasculature. It allows for the visualization of blood flow without dye injection, helping to identify areas of choroidal ischemia and microvascular changes. Traditional imaging using fluorescein angiography and OCT have been pivotal in this regard, yet they come with limitations. Optical coherence tomography angiography emerged as a promising alternative, leveraging advanced algorithms to visualize blood flow without the need for contrast agents. By providing angiographic images of the fundus, OCTA offers a noninvasive and rapid approach for identifying and monitoring macular neovascularization, a hallmark of wet AMD [14]. Furthermore, fluorescein angiography is not tailored to achieve detailed segmentation of various retinal layers, a critical aspect with significant scientific implications. In contrast, optical coherence tomography angiography presents a notable advantage, effortlessly delivering segmentation of distinct layers, precise localization of neovascularization lesion depth, and accurate delineation of lesion size [15,16].

Present studies indicate that retinal vascular changes occur in dry AMD, affecting both superficial (SCP) and deep capillary plexuses (DCP), choriocapillaris, as well as the foveal avascular zone. These changes include reduced vascular density in the superficial capillary plexus and altered flow density in both SCP and DCP [17–19]. Late-stage AMD, specifically geographic atrophy (GA), exhibits significantly lower vessel density in various retinal layers. Additionally, reduced choriocapillaris perfusion density is observed in various stages of AMD, indicating the significant role of choroidal impairment in disease pathogenesis [20–22]. In the early stages of dry AMD, patchy thinning, and reduced density of the choriocapillaris are common, which can progress to geographic atrophy and impaired blood flow. OCTA can detect loss or asymmetric changes in the choriocapillaris layer in patients with dry AMD, potentially driving further research in disease monitoring and targeted therapies [23]. Choroidal thickness measurements, widely used in researching choroidal diseases, reveal notable alterations in individuals with AMD, serving as crucial indicators of disease severity and progression [24,25].

All these findings prove that understanding vascular changes in non-neovascular age-related macular degeneration is essential for early detection, ongoing monitoring, and effective management of AMD.

2. Methodology

For this review, a comprehensive search strategy was implemented across various databases, including PubMed, Medline, and Embase focusing on articles published within the last 10 years, with particular emphasis on the last 5 years. Keywords related to optical coherence tomography angiography (OCTA), optical coherence tomography (OCT), vascular density (VD), superficial capillary plexus (SCP), deep capillary plexus (DCP), choriocapillaries, choroidal vascularity index (CVI), and choroidal thickness (ChT) were utilized in relation to dry AMD. We took into consideration various study designs, including clinical trials, cross-sectional studies, cohort studies, and meta-analyses. However, we deliberately excluded case–control studies, case reports, letters, editorials, non-human studies, gray literature, and non-English studies (Figure 1). This rigorous approach ensured the inclusion of high-quality evidence while maintaining a focus on relevant clinical findings about optical coherence tomography angiography in dry age-related macular degeneration.

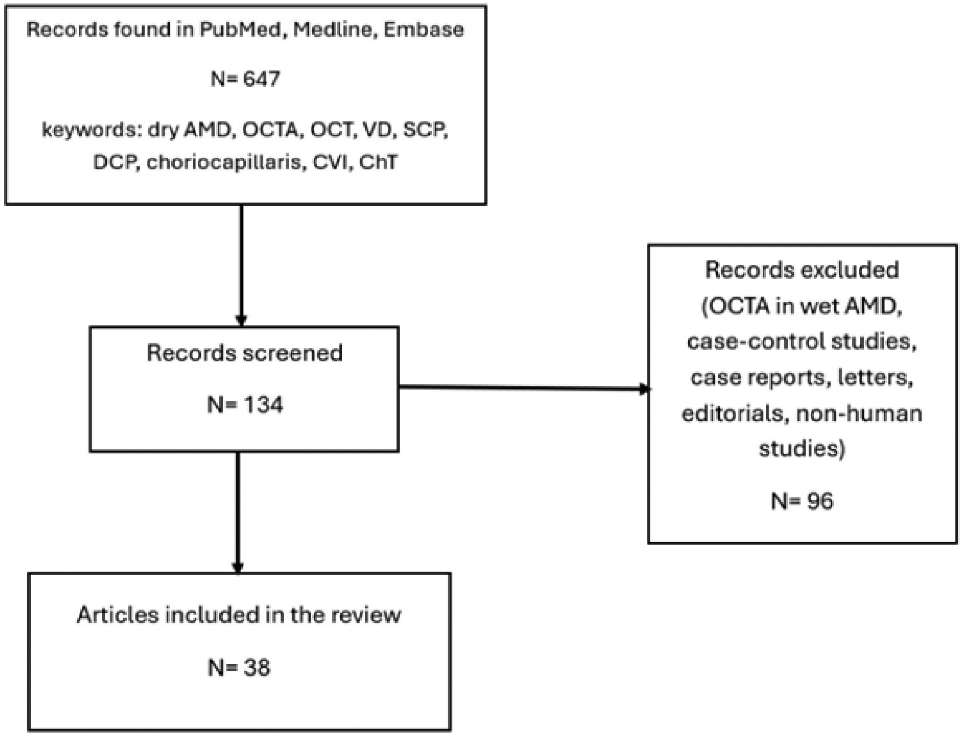

Figure 1. Flowchart of the literature search history.

3. Retinal vasculature

The vascular system of the eye and orbit primarily derives its arterial supply from the ophthalmic artery, a branch of the internal carotid artery within the intracranial region. Other branches of the ophthalmic artery supply the choroidal and anterior eye circulation. Blood drainage from the retina occurs via the central retinal vein, while the choroid drains through the vortex veins. Unlike other veins in the body, those within the eye lack valves and maintain flow against intraocular pressure. Photoreceptors lie between the choroidal and retinal circulation, with their metabolic activity relying on both vascular systems. Projection artifacts previously hindered the clear delineation of retinal plexuses in early OCTA imaging. However, advancements in OCTA algorithms have facilitated the precise visualization of distinct retinal plexuses. Now, we can differentiate four plexuses, including the nerve fiber layer plexus (NFLP) and the ganglion cell layer plexus (GCLP), both forming a superficial vascular plexus (SVP), as well as the intermediate capillary plexus (ICP) and deep capillary plexus (DCP) shown on Figure 2 [26]. The distinct vascular patterns of each plexus reflect their specialized roles in supplying oxygen and nutrients to different retinal layers. Capillary distribution is influenced by oxygen supply, with fewer capillaries near arterioles and venules. These intricate vascular networks play critical roles in maintaining retinal function and integrity [27]. Projection artifacts can hinder the clear delineation of retinal

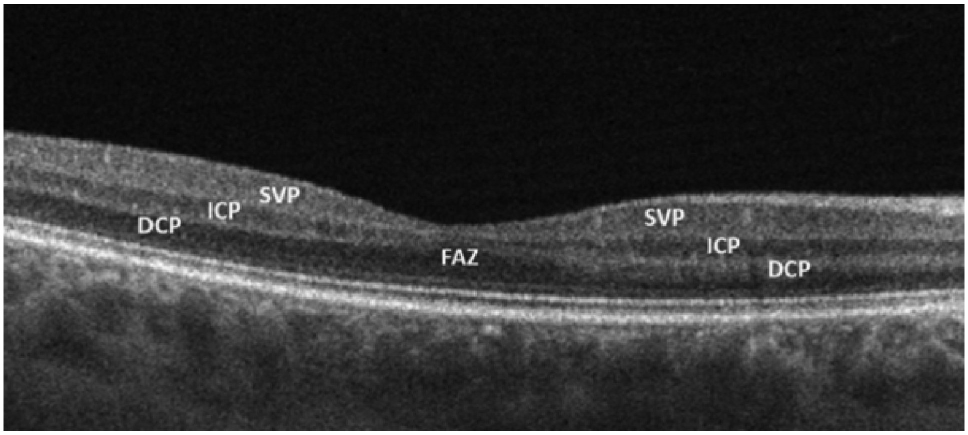

Figure 2. The figure depicts an OCT image using ZEISS PLEX elite 9000 showing retinal vasculature of a healthy individual. The retinal vascular layers consist of the superficial vascular plexus (SVP), followed by the intermediate capillary plexus (ICP), and then the deep capillary plexus (DCP). In the macula, there is an area devoid of retinal vessels known as the foveal avascular zone (FAZ).

plexuses in OCTA imaging. However, advancements in OCTA algorithms have facilitated the precise visualization of distinct retinal plexuses [26]. The NFLP, the most superficial plexus, predominantly perfuses the nerve fiber layer and extends radially along the arcuate nerve fiber bundles. It forms a continuous layer with the GCLP, which resides within the ganglion cell layer (GCL) and supplies the ganglion cell complex. Beneath the NFLP and GCLP lies the deep vascular complex, comprising the ICP and DCP, which are primarily capillary networks distributed within the inner nuclear layer and outer plexiform layer, respectively [28]. In the fovea, the retinal plexuses merge into a single capillary ring encircling the foveal avascular zone (FAZ) [29]. This careful arrangement of vessels along with retina's elevated metabolic demands, might underlie its high sensitivity to vascular damage in such diseases like diabetes or macular degeneration [27].

3.1. Retinal vasculature using OCTA in dry AMD

Optical coherence tomography angiography has emerged as a new valuable tool for noninvasive visualization of retinal microvasculature, offering insights into vascular changes associated with dry AMD. This chapter explores recent research investigating retinal vascular alterations in dry AMD using OCTA, focusing on changes in foveal thickness (Table 1), in the superficial and deep capillary plexuses, their vascular density (Table 2), and the foveal avascular zone (Table 3), as well as their implications for disease progression and management. Comparison of angio-OCT between healthy eyes with geographic atrophy is shown on Figures 3 and 4.

Kırıkkaya et al. as the first study in literature observed statistically significant differences between the first and last measurements in both the superficial and deep capillary plexuses and in foveal avascular zone in patients with dry AMD after a 16 month follow-up period [30]. In Toto et al. analysis revealed that the flow density of SVP and DCP was reduced in AMD group. However, there was no significant difference in parafoveal DCP flow density among the groups. They also observed a direct correlation between superficial plexus flow density and parafoveal macular thickness of the inner retina. These findings suggest a potential link between retinal vessel changes and structural alterations detected by OCT in patients with intermediate AMD. Specifically, patients with signs predicting the development of geographic atrophy displayed reduced flow in the SVP and damage to the inner and outer retina [34]. However, not all studies have similar results. The Reiter et al. research aimed to assess vascular changes in SCP and DCP and their relationship with drusen volume changes in intermediate AMD. There was no significant association between changes in drusen volume and flow area or VD after 12 months follow-up. Visual acuity worsened over the study period, while the foveal FA of the SCP increased significantly [36]. According to Trinh et al. the findings revealed a significant reduction in vascular density in the superficial capillary plexus of AMD eyes compared to normal eyes, particularly in the superior quadrant. Although the reduction in the deep capillary plexus was not statistically significant, there was a noticeable trend. Parameters such as total vessel length and average vessel diameter were also decreased in AMD eyes, indicating changes in vessel number and size. Moreover, vascular complexity and the number of branch points were significantly reduced in the deep capillary plexus, suggesting impaired vessel flow [37]. Findings also revealed that eyes affected by both intermediate AMD and reticular pseudodrusen (RPD) exhibited significant thinning in the superior inner and outer macular regions compared to those with intermediate AMD alone. Moreover, eyes with RPD showed thinning in various retinal layers, including the RPE, outer plexiform layer, and inner nuclear layer, compared to eyes with AMD alone. Additionally, the macular deep capillary plexus vessel density was notably reduced in eyes with RPD compared to those with intermediate AMD [38]. In contrary, another study showed that the overall retinal thickness

Table 1. Studies which examined foveal thickness among patients with AMD.

Study	Number of eyes in study group	Number of eyes in control group	AMD type in study group	Mean age in study group	Type of OCT	Projection resolved OCT	FT in study group [μm]	VD in healthy group [μm]
Kırıkkaya and Kaynak [30]	25	NR	early and intermediate	73.3 ± 11.8	OCT Optovue RTVue XR Avanti	ND	231.9 ± 33.8	NR
Wei et al. [31]	33	25	early stage with pseudodrusen	64.33 ± 10.40	OCT Optovue RTVue XR Avanti	used	271.6 ± 14.2	279.0 ± 13.3
Ozcaliskan et al. [32]	58	62	intermediate	72.26 ± 6.72	Heidelberg Spectralis SD OCT	used	260.76 ± 22.94	263.85 ± 24.35
Shin et al. [33]	83	83	intermediate and advanced	68.5 ± 7.9 years	Zeiss HD-OCT 5000 with AngioPlex	not used	243,6 ± 26.70	258.8 ± 15.90
Toto et al. [34]	30	15	intermediate	71.6 ± 7.6	OCT Optovue RTVue XR Avanti	ND	215.2 ± 32,9	268.1 ± 19.2
Yiu et al. [35]	171 eyes	154	intermediate and advanced	72.1 ± 8.6 years	Heidelberg Spectralis SD OCT	ND	260.43 ± 6.29 intermediate AMD 331.96 ± 28.70 advanced AMD	238.74 ± 3.89

AMD – age-related macular degeneration; FT – foveal thickness; OCT – optical coherence tomography; NR – not related; ND – no data.

Table 2. Studies which examined vascular density among patients with AMD.

Study	Number of eyes in study group	Number of eyes in control group	AMD type in study group	Mean age in study group	Type of OCT	Projection resolved OCTA	VD in study group [%]	VD in healthy group [%]
Kırıkkaya and Kaynak [30]	25	NR	early and intermediate combined	73.3 ± 11.8	Optovue RTVue XR Avanti	ND	46.0 ± 7.5	NR
Wei et al. [31]	33	34	early stage with pseudodrusen	64.33 ± 10.40	Optovue RTVue XR Avanti	used	49.5 ± 4.4 SCP 51.8 ± 6.0 DCP	47.6 ± 3.9 SCP 48.3 ± 6.5 DCP
Dereli Can [43]	35	NR	early and early/ intermediate	72.0 ± 8.9	Optovue RTVue XR Avanti	ND	44.84 ± 4.73 SCP 45.35 ± 7.17 DCP	NR
Shin et al. [33]	83	83	intermediate and advanced	68.5 ± 7.9	Zeiss HD-OCT 5000 with AngioPlex	not used	18.61 ± 2.36	20.06 ± 1.52
Ozcaliskan et al. [32]	58	62	intermediate	72.26 ± 6.72	Heidelberg Spectralis SD OCT	used	18.41 ± 4.61 SCP 18.64 ± 5.60 DCP	18.39 ± 3.99 SCP 17.15 ± 4.35 DCP
Reiter et al. [36]	49	NR	intermediate	74.9 ± 5.4	Optovue RTVue XR Avanti	ND	49.88% ± 7.38% SCP 55.43% ± 9.31% DCP	NR
Trinh, Kalloniatis and Nivison-Smith [37]	63	33	intermediate	67,80	Zeiss Cirrus Angioplex OCTA	used	42.4% ± 1.6% SCP	43.2% ± 1.4%
You et al. [41]	10	10	geographic atrophy	>50 years	Optovue RTVue XR Avanti	used	54.8 ± 2.4% SCP 24.4 ± 2.3% DCP	60.8 ± 3.1% SCP 28.0 ± 2.3% DCP
Cicinelli et al. [39]	22	22	intermediate	75.8 ± 6.3	Zeiss AngioPlex CIRRUS HD-OCT 5000	not used	0.390 ± 0.019 SCP 0.406 ± 0.007 DCP	0.406 ± 0.019 SCP 0.425 ± 0.024 DCP

AMD – age-related macular degeneration; OCT – optical coherence tomography; VD – vascular density, SCP – superficial capillary plexus; DCP – deep capillary plexus; NR – not related; ND – no data.

Table 3. Studies which examined FAZ among patients with AMD.

Study	Number of eyes in study group	Number of eyes in control group	AMD type in study group	Mean age in study group	Type of OCT	Projection resolved OCTA	FAZ in study group [mm^2]	VD in healthy group [mm^2]
Kırıkkaya and Kaynak [30]	25	NR	early and intermediate combined	73.3 ± 11.8	OCTA Optovue RTVue XR Avanti	ND	0.275 ± 0.118	NR
Dereli Can [43]	35	NR	early and early/ intermediate	72.0 ± 8.9	RTVue XR Avanti OCT	ND	0.305 ± 0.11	NR
Shin et al. [33]	83	83	Intermediate and GA combined	68.5 ± 7.9	Zeiss HD-OCT 5000 with AngioPlex	not used	0.29 ± 0.09	0.23 ± 0.06
Ozcaliskan et al. [32]	58	62	intermediate	72.26 ± 6.72	Spectralis spectral-domain OCT	used	297.355 μm^2 ±130.442 SCP 206.271 μm^2 ±105.407 DCP	–270.367 μm^2 ±101.182 SCP 211.669 μm^2 ±100.982 DCP
Cicinelli et al. [39]	22	22	intermediate	75.8 ± 6.3	Zeiss AngioPlexCIRRUS HD-OCT 5000	not used	0.728 ± 0.192	0.550 ± 0.133
Stavrev, Sivkova and Koleva-Georgieva [44]	89	66	early and intermediate	67.8 ± 6.4	Zeiss AngioPlexCIRRUS HD-OCT 5000	ND	0.27 ± 0.09 early AMD 0.28 ± 0.08 intermediate AMD	0.24 ± 0.08

AMD – age-related macular degeneration; OCT – optical coherence tomography; FAZ – foveal avascular zone; SCP – superficial capillary plexus; DCP – deep capillary plexus; NR – not related; ND – no data.

in eyes with RPD was significantly reduced compared to healthy controls, indicating a potential decrease in cellular density. Interestingly, the vessel densities of the DCP in RPD eyes were notably increased globally, as well as in the parafoveal and perifoveal quadrants. However, there were minimal increases in vessel densities observed in the SCP of RPD eyes. The findings suggest that RPD may lead to retinal thinning, possibly reflecting a decrease in cellular components. Moreover, the increased vessel density in the DCP of RPD implies a higher demand for blood supply, which could be a compensatory response to hypoxia induced by RPD in the outer retina [31]. Results also revealed that at the superficial capillary plexus, both RPD and RPD with outer retinal atrophy (ORA) exhibited lower vessel density compared to controls. Similarly, at the deep capillary plexus, all study groups showed significant differences in vessel density compared to healthy subjects. Additionally, the ganglion cell layer was thinner in patients with RPD, RPD with ORA, or drusen compared to controls [39]. According to Ozcaliskan et el. the parafoveal SCP vessel density was reduced in intermediate AMD eyes, with a surprisingly non-significant decrease observed in DCP vessel density. There was a significant correlation between

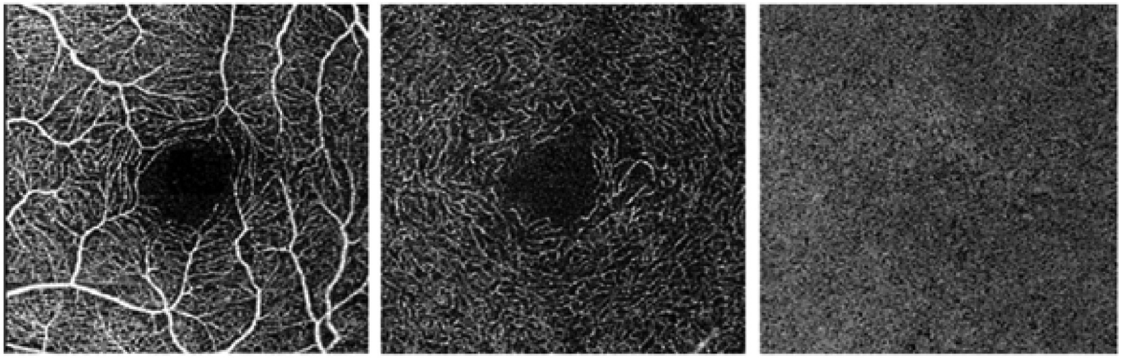

Figure 3. Image of retinal vasculature in a healthy patient. From left to right: superficial capillary plexus, deep capillary plexus, choriocapillaris.

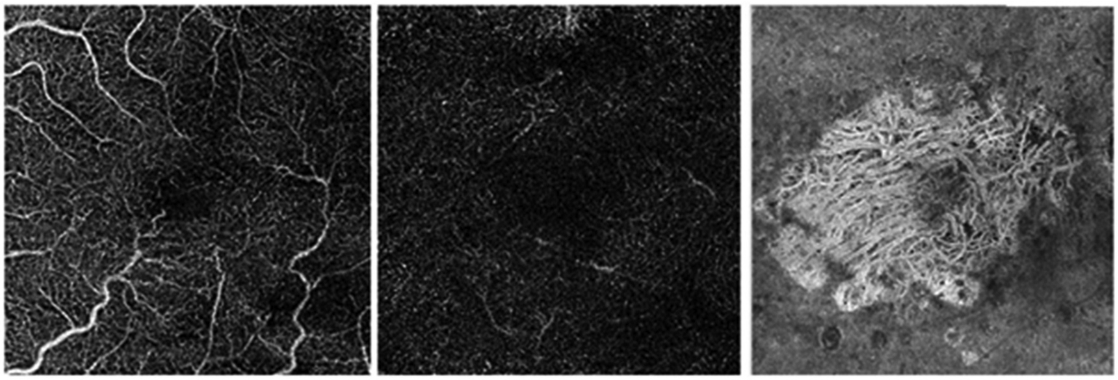

Figure 4. Image of retinal vasculature in a patient with geographic atrophy. From left to right: superficial capillary plexus, deep capillary plexus, choriocapillaris. The superficial and deep capillary plexuses may show no substantial changes in geographic atrophy, but there is a complete loss of the choriocapillaris in the foveal region.

ganglion cell complex thickness and SCP vessel density in intermediate AMD eyes [32]. In contrary, Vaghefi et al. results showed that vascular density was consistently higher in the deep capillary plexus compared to the superficial capillary plexus in all sectors, but there was no significant difference between healthy and intermediate AMD eyes [40]. In late-stage AMD, You et al. came to interesting results showing that eyes with GA had significantly lower vessel density in SVC, ICP, and DCP compared to control eyes but not in the non-GA regions. As expected, vessel density within the GA region decreased significantly in all plexuses, while the GA rim region showed decreases in SCP and ICP but not in DCP [41]. There was also a study aimed to investigate retinal vascular measurements in eyes with nonexudative and exudative age-related macular degeneration using OCTA. Results showed that VD decreased with age in all regions examined. Eyes with exudative AMD displayed lower VD, particularly in the parafoveal and macular regions, compared to nonexudative AMD eyes. It may suggest a potential role of retinal vascular changes in the pathogenesis of AMD, independent of anti-VEGF treatments [42]. There were also studies focusing on FAZ region, but their results vary. Patients with neovascular-exudative age-related macular degeneration in one eye and from early to intermediate nonexudative AMD in the fellow eye were diagnosed using OCTA. The study suggests that while FAZ area may not differ significantly between both groups, alterations in the FAZ circularity index may be observed [43]. Stavrev et al. compared three quantitative indexes – FAZ area, FAZ perimeter, and FAZ circularity in patients with early and intermediate nonexudative AMD and healthy subjects using OCTA. There were no statistically significant differences in all three assessed indexes between the early and intermediate AMD subgroups and the control group. Macular perfusion remains relatively unchanged in the nonexudative stages of AMD [44]. In contrary, another study revealed that dry AMD patients had a FAZ area and FAZ perimeter larger than in age-matched healthy eyes, while the FAZ circularity index was smaller [33].

These studies reviewed suggest that retinal vascular changes occur in dry AMD, with alterations observed in both the superficial and deep capillary plexuses, as well as in the foveal avascular zone, but results may vary depending mainly on the AMD stage, amount of participants and follow-up period. These changes include reduced vascular density in the SCP, particularly in the superior quadrant, and changes in flow density in both SCP and DCP. Additionally, eyes affected by both intermediate AMD and reticular pseudodrusen display thinning in the superior macular regions and reduced vessel density in the macular DCP, although some studies report increased vessel densities in the DCP of RPD eyes. In late-stage AMD, eyes with geographic atrophy exhibit significant vessel changes in various retinal layers compared to control eyes, particularly within the GA region. Studies investigating the foveal avascular zone in dry AMD using OCTA have also yielded varying results. However, contrasting findings indicated that patients with dry AMD exhibited larger FAZ area and perimeter compared to healthy controls, along with a smaller FAZ circularity index, suggesting potential changes in macular perfusion in AMD.

4. Choroidal vasculature

The choroid is a critical structure in the eye with diverse functions, including supplying the outer retina with blood, thermoregulation, and the production of growth factors, all of which play significant roles in ocular pathologies like macular degeneration. Understanding its anatomy is essential for ophthalmologists to comprehend the pathological mechanisms underlying related diseases. Histologically, the choroid consists of five layers, spanning from the sclera to the retina: Bruch's membrane, the choriocapillaris, Haller's and Sattler's layers, and the suprachoroidal space (Figure 5). The choroidal blood supply is complex, characterized by variable numbers of posterior ciliary arteries branching from the ophthalmic artery [45,46].

The choriocapillaris, an intricate network of capillaries within the choroid, lies adjacent to Bruch's membrane and is characterized by a thin sheet structure. It exhibits regional variations in thickness, being approximately 10 µm thick at the fovea and thinner at about 7 µm in the retinal periphery. Originating from arterioles in Sattler's layer, these capillaries form hexagonal-shaped domains, giving the choriocapillaris a patch-like appearance [47]. Fenestrated and relatively large in diameter, the capillaries facilitate the movement of fluids and nutrients. Adjacent to Sattler's layer, a fibrous layer linked to Bruch's membrane by collagen fibers stabilizes capillary diameters. Bruch's membrane, forming the innermost layer of the choroid, consists of five sublayers, playing a crucial role in supporting the choriocapillaris and retinal pigment epithelium. It is worth noting that OCTA imaging is not influenced by xanthophyll pigment. The choriocapillaris display characteristic lobular filling patterns, which may vary with age and diseases like age-related macular degeneration. The choriocapillaris play vital role in providing nutrients and oxygen to the retinal pigment epithelium and photoreceptors while removing metabolic waste products. Its health is closely intertwined with the functioning of outer retinal and retinal pigment epithelium layers, emphasizing the importance of vascular endothelial growth factor (VEGF) signaling [45].

The choroid's vascular region between choriocapillaris and sclera comprises Haller's outer layer, housing large blood vessels, and Sattler's inner layer, hosting medium and small arteries and arterioles that nourish the capillary network and veins. Within the stroma, which is the extravascular tissue, collagen and elastic fibers, fibroblasts, non-vascular smooth muscle cells, and numerous large melanocytes are closely associated with blood vessels. This tissue also houses mast cells, macrophages, and lymphocytes, typical of connective tissue. Deeper into the choroid there is a suprachoroidal space which serves as a transitional zone between the choroid and sclera, containing elements from both, such as collagen fibers, fibroblasts, and melanocytes. The lamina fusca, found at the outermost layer of the suprachoroid comprises flattened fusiform melanocytes which functional implications remain unclear and fibroblast-like cells, interspersed with myelinated axon bundles [45,48].

4.1. Choroidal vasculature using OCTA in dry AMD

The evaluation of choroidal changes is crucial in understanding the pathogenesis of age-related macular degeneration. Improving our understanding of the choroidal vasculature opens up new possibilities for better assessing the choroid, leading to more precise diagnoses and treatments in the future [49].

Reduced choriocapillaris (CC) perfusion density has been reported in patients with drusen, subretinal drusenoid deposits (SDD), and geographic atrophy, indicating the significant role of whole choroidal impairment in AMD pathogenesis [50]. In OCT findings choroidal vascularity index (CVI) demonstrates changes in both the vascular and stromal components of the choroid [49]. Numerous studies have explored CVI's potential applications in healthy eyes and various chorioretinal diseases, suggesting it exhibits lower variability and is influenced by fewer physiological factors compared to choroidal thickness. Therefore, CVI serves as a relatively stable parameter for

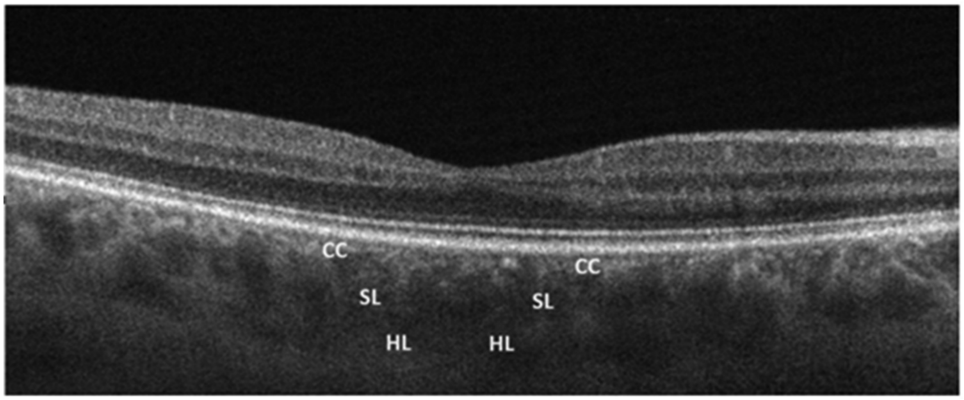

Figure 5. The figure depicts OCT image of the choroidal vasculature below the macula. Below the choriocapillaris (CC) lies Sattler's layer (SL), which contains medium and small arteries. Beneath Sattler's layer is Haller's layer (HL), which accommodates large blood vessels.

assessing choroidal vascular changes [51]. Results indicate that as AMD progresses, CVI demonstrates biphasic changes, initially increasing during early drusen formation but subsequently decreasing. Notably, eyes with subretinal drusenoid deposits exhibit marked reductions in CVI, highlighting its potential as a sensitive biomarker for assessing AMD progression and its underlying choroidal vascular changes [52]. GA patients exhibited significantly lower CVI values, along with reduced total choroid area, luminal area, and subfoveal choroidal thickness compared to controls. Best-corrected visual acuity correlated significantly only with choroidal thickness. Over the follow-up period, GA patients experienced a decrease in subfoveal choroidal thickness, an increase in stromal area, and a further decline in CVI [53]. This study explored choroidal changes in different types of dry age-related macular degeneration using the choroidal vascularity index. Four groups were analyzed: dry AMD patients with drusen, reticular pseudodrusen, and geographic atrophy, alongside healthy controls. There were notable variations in choroidal characteristics. RPD patients had lower CVI than controls, while GA patients had the lowest CVI compared to drusen, RPD, and controls. These findings suggest distinct impairments in choroidal features across different dry AMD types [54] Cicinelli et al. found significant reductions in vessel density and vascular/stromal (V/S) ratio at the choriocapillaris, the Sattler and Haller's layers, and the whole choroid layer in all patient groups compared to healthy controls [55]. However, evaluating the CC in AMD patients can be challenging due to shadow artifacts caused by overlying structures like drusen and MNV. Consequently, many studies have focused on evaluating the CC outside drusen areas rather than directly under them [49]. Drusen causing signal loss in structural en-face OCT CC images exhibited larger dimensions compared to those without signal loss. Additionally, areas with signal loss showed reduced CC decorrelation signal index compared to healthy controls. These findings highlight the importance of considering drusen morphology in OCT-A image analysis, as both signal attenuation and segmentation errors are common artifacts in patients with soft drusen [56]. The study found a significant reduction in the CC perfusion in the SDD group. Although there was a trend of reduced vessel density in both groups, with SDD or drusen only, this trend did not reach statistical significance [57]. Li et al. results showed that eyes with macular RPD exhibited higher macular choriocapillaris (CC) flow deficits, decreased CC thickness, and thinner choroidal thickness (ChT) compared to normal and soft drusen eyes. These findings suggest that macular RPD may arise from impaired choroidal perfusion. However, no significant differences were observed in outer retinal layer thickness and choroidal vascularity index measurements among the groups [58]. Results also showed that eyes with RPD exhibited focal dark regions without flow signal on OCTA, indicating choriocapillaris nonperfusion. The areas of nonperfusion were significantly greater in RPD eyes compared to drusen eyes. A correlation was found between these areas and visual acuity in the entire dataset, which was stronger in eyes with RPD but lost significance in eyes with drusen alone. This suggests that larger areas of choriocapillaris nonperfusion in RPD eyes may explain the compromised vision observed in this condition compared to other forms of drusen in AMD [59]. On the other hand, other results indicated that the presence of RPD did not significantly affect choriocapillaris flow deficit parameters or choroidal structural parameters, regardless of adjustments for potential confounders. Although increasing drusen volume was associated with a higher percentage of flow deficits and larger flow deficit size, RPD did not show a significant association with these parameters. Similarly, no significant differences were observed in choroidal thickness and choroidal vascularity index between eyes with and without RPD. These findings suggest that while drusen volume may impact choriocapillaris blood flow, the presence of RPD does not seem to exacerbate vascular changes in intermediate AMD [60]. The absence of detectable choroidal vascular insufficiency in eyes with RPD may be attributed to the constraints of current imaging modalities and analytical methods, rather than indicating a genuine absence of such vascular abnormalities. In geographic atrophy results showed pronounced (CC) flow impairment within the GA region in all eyes examined. Moreover, OCTA revealed milder CC flow impairment extending beyond the GA margin in most cases, with CC flow detected even in regions of foveal sparing [61]. Nassisi et al. aimed to assess the relationship between CC flow alterations around GA and the GA yearly growth rate (yGR) in patients with AMD. Retrospective analysis of spectral domain optical coherence tomography and OCTA images was conducted on patients with GA. The fundus images were used to delineate the GA area, and the CC flow alterations were quantified using OCT angiography. The study found a significant correlation between CC flow impairment around the atrophic lesions and their yGR, particularly in the para- and periatrophy regions. These findings suggest that assessing CC flow alterations may provide useful prognostic information for patients with GA. The reduction in CVI could be associated with the gradual decline in choroidal thickness observed across the three investigated study groups [58]. In contrary, Zhou et al. proved in their study that choroidal thickness, choroidal vessel volume, and choroidal stroma volume exhibited age-related declines, CVI remained relatively stable across all age groups and regions [62]. Breher et al. results indicated that while choroidal thickness decreased toward the peripheral choroid, CVI remained relatively stable across subfields [63]. Reduced choriocapillaris perfusion density has been observed in various stages of age-related macular degeneration, including drusen, subretinal drusenoid deposits (SDD), and geographic atrophy, indicating the significant role of choroidal impairment in AMD pathogenesis. Studies have reported reductions in vessel density and vascular/stromal ratio at the CC and other choroidal layers in AMD patients compared to healthy controls. Evaluating the CC in AMD is challenging due to artifacts caused by overlying structures like drusen. However, recent studies have shown that eyes with macular reticular pseudodrusen exhibit higher CC flow deficits and decreased CC thickness compared to those with soft drusen, suggesting impaired choroidal perfusion in RPD. The vascular theory of reticular pseudodrusen postulates that RPD formation is related to choroidal vascular impairment. OCTA has enhanced our understanding by revealing sharply demarcated areas of nonperfusion in the choriocapillaris, supporting this theory by demonstrating the reduced blood flow associated with RPD [64]. Despite this, the presence of RPD does not always significantly affect choriocapillaris flow parameters or choroidal structural parameters, indicating a complex relationship between RPD and choroidal vascular changes in AMD. Additionally, pronounced CC flow impairment within the GA region has been observed, with milder impairment extending beyond the GA margin in most cases. Furthermore, a significant correlation has been found between CC flow impairment around GA lesions and their growth rate, highlighting the potential utility of assessing CC flow alterations as a prognostic marker for GA progression. Further research is needed to confirm these findings and explore their clinical implications in AMD management.

5. Choroidal thickness in dry AMD

Choroidal thickness after the introduction of OCT has become a more standardized parameter and started being widely used in researching choroidal diseases. Measurements can be taken directly under the fovea or at varying distances from it, allowing for comprehensive mapping of choroid across the region of interest. Despite its extensive application in clinical and research settings for diagnosing and managing ocular conditions, it can be affected by age, intraocular pressure or even time of the day [49,65]. In individuals affected by age-related macular degeneration, numerous studies have highlighted notable alterations in choroidal thickness (Table 4), which serve as a crucial indicator of disease severity and progression. The comprehension of these changes holds paramount importance for the early detection, ongoing monitoring, and effective management of AMD [35,46,66].

Typically, choroidal thickness in AMD patients tends to be thinner when compared to individuals without the condition, signifying a distinct characteristic of the disease. Interestingly, while individuals with early AMD may not exhibit significant differences in ChT compared to normal controls, more pronounced alterations are often observed in advanced stages of the disease. This observation underscores the potential of ChT measurements as valuable indicators of disease progression, offering valuable insights for clinicians and researchers alike. [35,67]. Salehi et al. conducted one of the most comprehensive meta-analyses in this topic including 25 studies comprising 1,632 cases and 1,445 controls. The average macular ganglion cell complex thickness was significantly reduced in AMD patients compared to controls, as was the average peripapillary retinal nerve fiber layer thickness. However, choroidal thickness measurements at different locations showed mixed results, with significant decreases observed at certain locations but not at others. Subsequent analyses included assessments of macular GCL, IPL, and RNFL thickness, with no significant differences found between AMD cases and controls. This study also revealed that the average macular GCC thickness was significantly associated with the sample size of the studies, but other factors such as participant demographics and visual acuity did not show significant correlations [68]. According to Linder et al., the study revealed that the mean subfoveal choroidal thickness was significantly thinner in GA eyes compared to controls. Similar findings were observed in the mean overall choroidal thickness measurements. There was a trend

Table 4. Studies which examined choroidal thickness among patients with AMD.

Study	Number of eyes in study group	Number of eyes in control group	AMD type in study group	Mean age in study group	Type of OCT	Projection resolved OCTA	Choroidal thickeness in study group [μm]	Choroidal thickeness in control group [μm]
Fukuda et al. [76]	172	NR	intermediate	72.8 ± 10.4	Heidelberg Spectralis SD OCT	ND	233.1 ± 78.0	NR
Kırıkkaya and Kaynak [30]	25	NR	early and intermediate combined	73.3 ± 11.8	OCTA Optovue RTVue XR Avanti	ND	177.5 ± 46.9	NR
Viggiano et al. [77]	84	30	pseudodrusen and intermediate	76.0 ± 6.26	Heidelberg Spectralis SD OCT	used	254.43 ± 92.99	264.38 ± 49.57
Sato et al. [78]	29	41	early	77.0 ± 6.5	Heidelberg Spectralis SD OCT	ND	238.3 ± 108.3	187.2 ± 66.8
Abdolrahimzadeh et al. [79]	48	42	intermediate	77.5 ± 5.7	Heidelberg Spectralis SD OCT	used	193.0 ± 61.8	234.9 ± 60.9
Fan et al. [72]	55	NR	early and intermediate	80 ± 8.4 years	Heidelberg Spectralis SD OCT	ND	151.4 ± 58.3	NR
Koh et al. [80]	63	30	intermediate	56.50 ± 5.50	Zeiss Cirrus HD-OCT (SD)	used	314.02 ± 78.80	278.5 ± 65.31
Lindner et al. [69]	72	37	geographic atrophy	75.97 ± 7.09	Heidelberg Spectralis SD OCT	used	173.03 ± 90.22 GA	253.95 ± 69.19
Yiu et al. [35]	171	154	intermediate and advanced	72.1 ± 8.6	Heidelberg Spectralis SD OCT	ND	236.61 ± 10.16 intermediate AMD 220.47 ± 15.52 advanced AMD	237.01 ± 15.52

AMD – age-related macular degeneration; OCT – optical coherence tomography; NR – not related; ND – no data.

toward thinner choroids in eyes with larger GA lesions, the correlation was not statistically significant. The study's conclusions suggest that the choroidal thickness in GA eyes is thinner compared to age-matched normal eyes [69]. What's more, choroidal thickness changes can be also a predictive factor for a progression from dry to wet AMD. In Bouteleux et al. study, initially comprising 134 eyes followed up for 9 months 95 patients experienced at least one episode of recurrence, with a total of 119 episodes analyzed. Notably, a significant increase in choroidal thickness (ChT) was observed during recurrence, particularly in the subfoveal area. However, no significant change in ChT was seen in the fellow eye between baseline and recurrence. The study also found no significant difference in ChT change between various treatments or associations with the number of IVIs received or blood pressure [70]. However, in a meta-analysis by Trinh et al. examined the relationship between choroidal thickness, and the progression of AMD. Choroidal thickness was one of the OCT biomarkers analyzed in relation to the risk of progression to late AMD, geographic atrophy, and neovascularization. The findings indicated that choroidal thickness was not significantly associated with the risk of progression to late-stage age macular degeneration including geographic atrophy [71]. There is also an association between subfoveal choroidal thickness (SCT) and macular atrophy (MA) progression, with thinner choroids predicting faster MA progression. In a study involving 88 eyes, baseline SCT was assessed in relation to the presence and development of macular atrophy. Eyes with MA had significantly thinner choroids compared to those without dry AMD. Importantly, eyes with baseline SCT ≤124 µm were more likely to develop MA compared to those with SCT >124 µm. However, predictive factors for incident MA development in eyes without baseline MA remain unclear [72].

6. Variability in study results

In examining vascular changes in dry AMD through OCTA, significant variability in study results has been observed. This variability is influenced by several critical factors, including differences in OCTA devices, patient demographics, and imaging protocols.

6.1. Variability in OCTA devices

Different optical coherence tomography angiography devices can significantly affect study outcomes by providing variations in image acquisition and analysis. For instance, the studies reviewed used devices such as the Optovue RTVue XR Avanti, Heidelberg Spectralis SD OCT, and Zeiss HD-OCT 5000. Each device might differ in its sensitivity and resolution, leading to variability in measurements such as foveal thickness vascular density. As shown in the data, the FT in study groups using Optovue devices ranged from 215.2 µm to 271.6 µm. In FAZ area, measurements using Zeiss HD-OCT 5000 differed from 0.728 to 0.29 mm^2, compared to the Optovue RTVue XR Avanti indicating values around 0.275 mm^2 to 0.305 mm^2 in the study group.

6.2. Impact of patient demographics

Patient demographics such as age and sample size can also influence outcomes. For example, the mean age of participants in the studies ranged from around 64 to 76 years. These demographic differences can impact the generalizability of results, especially when comparing studies with variations in control group sizes and participant ages.

6.3. Imaging protocols and standardization

The lack of standardized imaging protocols across studies poses challenges in achieving consistent results. Variations in scanning areas, resolution settings, and data processing techniques can lead to discrepancies in findings. For example, VD percentages in study groups differed widely, with values from 18.61% to 49.5% being reported for similar patient demographics and capillary plexuses, highlighting the impact of different OCTA analysis methodologies.

These differences between OCTA devices underscore the need for standardized protocols and methodologies to reduce variability, enhance the reliability of comparative analyses in future research and develop more accurate diagnostic and monitoring

7. Study limitations

In this review of vascular alterations observed through optical coherence tomography angiography in non-neovascular age-related macular degeneration, several limitations are notable. First, varying methods of assessing vascular density across different studies can introduce inconsistencies, as measurements heavily depend on the software and algorithms used, which may affect comparability. Different OCTA devices and software might employ various segmentation techniques and algorithms for calculating vascular density, resulting in potential discrepancies in reported outcomes.

Artifacts in OCTA imaging, such as projection and motion errors, along with signal attenuation, could skew vascular measurements. The diversity in technical methodologies across included studies, including differences in OCTA device settings, adds another layer of variability. It is worth mentioning that drusen may impact OCTA's ability to segment retinal capillary layers due to the shadowing effect and signal attenuation they cause, complicating the visualization of the vasculature underneath. The presence of drusen can lead to segmentation errors in defining the boundaries of the capillary plexuses, potentially affecting diagnostic accuracy [56].

Additionally, small sample sizes and short follow-up durations limit the statistical power and generalizability of the findings. The study might also not fully capture stage-specific changes in dry AMD due to variability in results depending on the AMD stage.

By addressing these limitations in the future research, we can aim for a more consistent and comprehensive understanding of vascular changes in dry AMD, allowing for improved clinical application and progress in the field.

8. Future research directions

To advance the role of optical coherence tomography angiography in studying dry age-related macular degeneration, it is essential to focus on specific research areas that enhance understanding and clinical application.

8.1. Standardizing OCTA protocols

A critical step is establishing standardized imaging protocols across different OCTA devices, such as Optovue RTVue XR Avanti, Heidelberg Spectralis SD, and Zeiss HD-OCT 5000. This includes developing universal calibration and scanning protocols to ensure consistent image acquisition and analysis. Collaboration among device manufacturers and researchers is necessary to create standardized algorithms that minimize variability in data interpretation.

8.2. Addressing current limitations

Efforts should continue to improve hardware and software solutions to mitigate artifacts, such as motion and projection errors, which pose significant challenges in OCTA imaging. Additionally, comprehensive studies utilizing diverse population samples are needed to understand better how factors like age, ethnicity, and disease progression impact OCTA measurements, thereby improving the generalizability of findings.

8.3. Potential clinical applications

Future research should concentrate on identifying reliable biomarkers for disease progression and severity in dry AMD, aiding in early diagnosis and the development of personalized treatment strategies. Vascular changes differ mainly in the SCP and choriocapillaris, indicating that AMD pathology should be explored more extensively in these regions in the current research. Implementing long-term longitudinal studies to monitor changes over time can enhance the ability to predict and manage the transition from dry to wet AMD, ultimately improving patient outcomes. OCTA can also track changes in the vascular structure of the retina and choroid, which is useful in assessing the efficacy of new treatments such as complement inhibitors. For instance, OCTA can measure the area of geographic atrophy before and after treatment intervention, helping to evaluate the success of complement inhibitors in slowing GA progression [73]. Complement inhibitors are new medications targeting the immune pathways involved in AMD's pathogenesis, aiming to slow the progression of GA by reducing inflammation and complement system activation. This class of drugs, including those like pegcetacoplan, has shown promise in clinical trials [74]. A complement inhibition therapy for GA allows clinicians to monitor patients with a single OCTA scan, identifying persistent hypertransmission defects and predicting treatment outcomes based on OCT biomarkers. A key biomarker is the double-layer sign, which indicates nonexudative MNV, because such eyes are prone to developing new exudation when treated with complement inhibition What is more, OCTA's ability to non-invasively monitor microvascular changes offers a promising endpoint for clinical trials in dry AMD. It could potentially serve as a biomarker for the efficacy of interventions aimed at modifying disease progression by providing quantitative data on capillary density and perfusion [75].

9. Conclusions

In conclusion, optical coherence tomography angiography has significantly advanced the understanding of retinal and choroidal vascular changes in dry age-related macular degeneration. This technology provides valuable insights into the disease's pathogenesis by allowing detailed, noninvasive visualization of retinal microvasculature across different stages of dry AMD. Studies illustrate the presence of considerable alterations in the superficial and deep capillary plexuses, choriocapillaris, and choroidal thickness. These changes have the potential to serve as biomarkers for disease progression and suggest novel pathways for intervention. However, discrepancies in imaging outcomes across studies underline the necessity for standardized OCTA protocols to enhance result reliability and diagnostic accuracy. Furthermore, while current applications of OCTA in dry AMD are predominantly research-focused, ongoing technological advancements and future longitudinal studies may facilitate its clinical implementation, potentially leading to improved diagnostic and therapeutic strategies for managing dry AMD.

10. Expert opinion

The advent of Optical Coherence Tomography Angiography has heralded a new era in the diagnosis and management of retinal vascular disorders, particularly age-related macular degeneration. The primary utility of OCTA lies in its ability to provide rapid, noninvasive, and high-resolution imaging of retinal and choroidal vasculature.

The integration of OCTA into clinical practice holds immense promise for improving the early detection, diagnostic accuracy, and personalized management of dry AMD. Unlike traditional imaging methods, OCTA allows for detailed visualization of the retinal and choroidal microvasculature without the need for dye injection. This capability will be pivotal in predicting the onset of geographic atrophy and understanding its timeline, providing clinicians with a tool to intervene proactively. The economic implications are significant, as early and accurate diagnosis can potentially reduce the burden of patient management and visual impairment associated costs.

However, the transition from research to clinical application faces challenges. A crucial barrier is the lack of standardized imaging protocols and interpretations. The variability in OCTA outcomes, often due to differences in device algorithms and scanning protocols, hinders its widespread adoption. Additionally, OCTA is currently hampered by limitations such as motion artifacts, projection artifacts, and difficulties in obtaining scans from patients with significant vision impairment.

For OCTA to achieve its full potential in AMD management, standardization across devices and methodologies is imperative. Developing universal scanning and interpretation guidelines could minimize variability, thereby enhancing both diagnostic accuracy and comparability of clinical findings. Addressing the technical limitations through advancements in image processing algorithms will also improve the reliability of OCTA. Moreover, a deeper understanding of the pathophysiological changes in AMD at a molecular level is required. This includes identifying new molecular targets and exploring how genetic and environmental factors contribute to disease progression. These could unveil further therapeutic targets.

Future research should focus on refining OCTA imaging to capture early vascular changes predictive of disease progression. Machine learning algorithms hold potential for automating the detection of these changes, integrating data from OCTA, genetic markers, and other diagnostic tools to provide a comprehensive risk assessment for AMD progression.

Additionally, exploring the relationship between these vascular changes and potential therapeutic interventions, like complement inhibitors, could lead to significant breakthroughs in treatment strategies. Longitudinal studies and large-scale clinical trials will be critical in validating the use of OCTA-derived biomarkers for disease progression and therapeutic response.

In the next 5–10 years the primary gain of adopting OCTA in standard procedures will be the ability to preemptively manage AMD progression, improving patient quality of life while potentially alleviating healthcare system burdens.

In conclusion, while OCTA in dry AMD currently exists within a research-focused niche, its trajectory toward integration in routine clinical practice will depend on overcoming technical and methodological barriers, validating its use in diverse settings, and scaling its application to encompass comprehensive AMD management strategies.

Abbreviations

AMD	Age-Related Macular Degeneration
CC	Choriocapillaris
ChT	Choroidal Thickness
CVI	Choroidal Vascularity Index
DCP	Deep Capillary Plexus
dAMD	Dry Age-Related Macular Degeneration
FA	Flow Area
FAZ	Foveal Avascular Zone
GA	Geographic Atrophy
GCC	Ganglion Cell Complex
GCL	Ganglion Cell Layer
GCLP	Ganglion Cell Layer Plexus
HD-OCT	High-Definition Optical Coherence Tomography
ICP	Intermediate Capillary Plexus
IPL	Inner Plexiform Layer
IVIs	Intravitreal Injections
MA	Macular Atrophy
MNV	Macular Neovascularization
NFL	Nerve Fiber Layer
NFLP	Nerve Fiber Layer Plexus
OCT	Optical Coherence Tomography
OCTA	Optical Coherence Tomography Angiography
OPL	Outer Plexiform Layer
ORA	Outer Retinal Atrophy
RPD	Reticular Pseudodrusen
RPE	Retinal Pigment Epithelium
RNFL	Retinal Nerve Fiber Layer
SCP	Superficial Capillary Plexus
SCT	Subfoveal Choroidal Thickness
SD OCT	Spectral Domain Optical Coherence Tomography
SDD	Subretinal Drusenoid Deposits
SVP	Superficial Vascular Plexus
VD	Vascular Density
VEGF	Vascular Endothelial Growth Factor
yGR	Yearly Growth Rate

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