Choroidal and retinal imaging biomarkers in Age-related Macular Degeneration and Vitamin D supplementation: a Review

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BACKGROUND

Age-related Macular Degeneration (AMD) is a chronic and multifactorial aging retinal disease that causes irreversible central vision loss. In Europe, AMD represents the main cause of severe visual impairment and blindness in the elderly. Health status, low antioxidant diet, and sedentary lifestyles are modifiable risk factors. Health promotion and preventive medicine are essential to reduce the risk of disease progression and visual impairment.[1] Vitamin D [25(OH)D] (Vit D) deficiency may be a risk factor for AMD [2]. The anti-inflammatory potential of Vit D in AMD and its contribution to improving retinal antioxidant protection has been investigated. A systematic review and meta-analysis conducted by Ferreira et al. showed there was a trend for advanced AMD in people with serum Vit D < 50 nmol/L [3]. Thus, increasing 25(OH)D levels through dietary intake and supplementation may be beneficial [4]. A structural evaluation using SD-OCT and OCT-A seems to be an interesting tool for assessing changes in the retina and choroid after supplementation.

METHODOLOGY

The aim of this review is to summarize quantitative and qualitative imaging biomarkers reported in randomized controlled trials (RCTs) and observational studies (case-control, cohort prospective, and cross-sectional studies) published between 2019 and 2022, related to the association between AMD and Vit D levels and choroidal and retinal outcomes measures after supplementation.

RESULTS

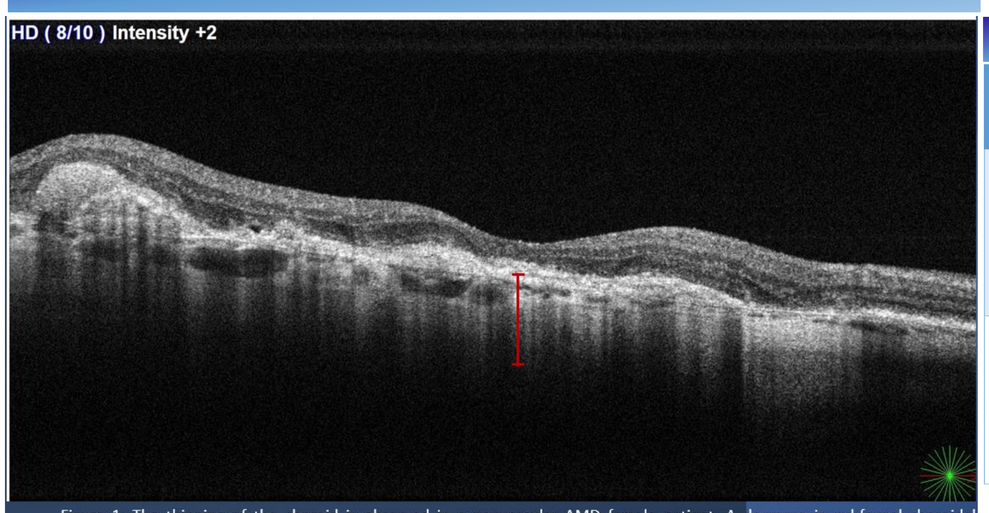

Figure 1: The thinning of the choroid is observed in a neovascular AMD female patient. A decrease in subfoveal choroidal thickness values (less than 250-350 µm) is usually present in advanced stages and could be measured by SD-OCT.

Table 1. Association between vitamin D levels and retinal choroidal structures in AMD.

Study design, country	Author(s) Study, Year	Demographics AMD group	Vitamin D level in AMD group (Mean serum 25(OH)D levels ng/ml)	Association between Vit D and retinal-choroidal structures
Case-Control, Turkey	Kabataş *et al.*, 2022 [5]	N= 114 Median age: 71.5± 7.9 Female: 64	14.4 ± 9.6. (Wet-type AMD=11.4 ± 5.1 dry-type AMD= 15.3 ± 10.9)	The subfoveal choroidal thickness was statistically lower in patients with AMD; there was a weak positive correlation between Vit D level and choroidal thickness.
Cross-sectional, Spain	Serena, *et al. 2022* [6]	N= 93 Median age: 78.96±8.5 Female: 57	15±10 (Early AMD=12.5±7.3 intermediate AMD=15±11 advanced aAMD= 15±8 advanced nAMD= 17±11.5)	There is no statistical difference in central foveal thickness between AMD patients with lower Vit D levels and AMD patients with normal Vit D levels.

SD-OCT: Spectral Domain - Optical Coherence Tomography; Vit D: Vitamin D; AMD – Age Macular Degeneration; aAMD: atrophic Age Macular Degeneration; nAMD: neovascular Age Macular Degeneration; ng/mL: nanograms per milliliter

Table 2. Vitamin D supplementation and retinal-choroidal outcomes in AMD.

Study design, country	Author(s), Year	Demographics studied group	AMD Stage	Compounds	Vit D Dose / Follow-up	Outcomes Measurements / Summary of Findings
Prospective Switzerland	Öncül *et al. 2020* [2]	N= 65 Median age: 28.4± 6.74 Female: 48 Mean Vit D level: 10.94± 3.88 ng/mL	No AMD	Vit D3 (cholecalciferol)	300.000 IU / month Follow-up: 3 months	SD-OCT: A positive correlation between Vit D and subfoveal choroidal thickness values was found with a significant increase in structure after Vit D supplementation. No significant changes were observed in central macular thickness pre- and post-supplementation.
RCT Italy	Parravano *et al. 2019* [7]	N= 30 Median age: 68.5± 8.79 Female: 21	Intermediate AMD	Macuprev® (Vit D3, lutein, zeaxanthin, N-acetylcysteine, bromelain, Vit B12, alpha lipoic acid, rutin, Vit C, zinc oxide, *Vaccinium myrtillus*, *Ganoderma lucidum*)	Vit D3 - 800 IU / day Follow-up: 6 months	SD-OCT: there were no significant retinal and choroidal structural changes during and after the supplementation follow-up period.
RCT Italy	D´Aloisio *et al.* 2022[8]	N= 15 Median age: 70.20± 8.13 Female: 8	Intermediate AMD	Astazin 10® (Astaxanthin, Bromelain, Vit D3, Folic Acid, Lutein, Vit E, Zin gluconate, Copper gluconate)	Vit D3 – 1000 IU / day Follow-up: 6 months	SD-OCT: there was a significant increase in choroidal thickness after supplementation. OCT-A: there was a significant increase in choriocapillaris vessel density after supplementation.

RCT: Randomized clinical trial; SD-OCT: Spectral Domain - Optical Coherence Tomography; OCT-A: Optical Coherence Tomography Angiography; Vit D: Vitamin D; Vit: Vitamin; AMD – Age Macular Degeneration; mg: milligram; IU-International Unit; ng/mL: nanograms per milliliter

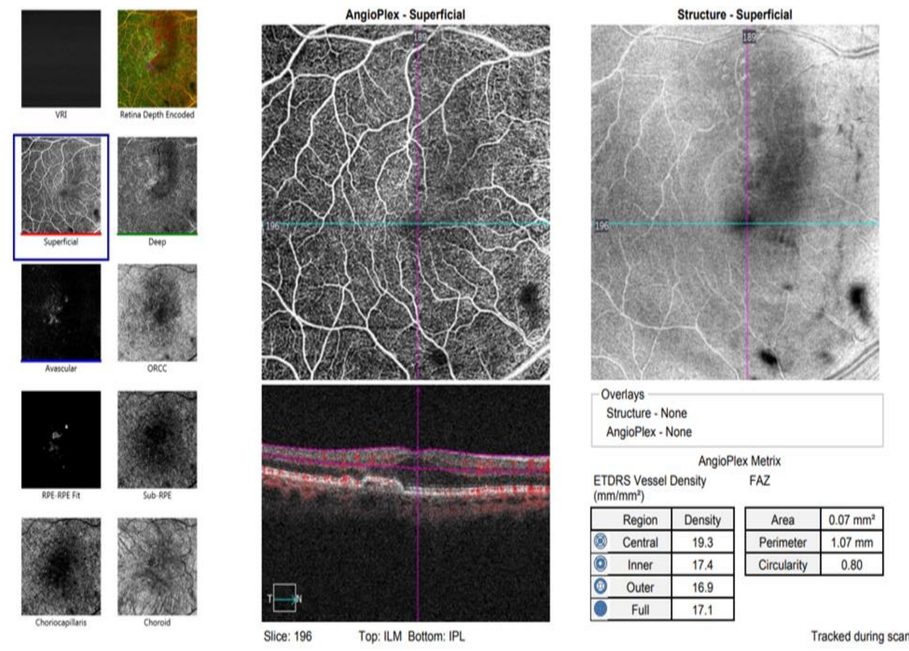

Figure 2: OCTA could play an important role in different stages of AMD, allowing the evaluation of blood flow perfusion through vessel density. Exploring the choriocapillaris map could be important in follow-up after vitamin D supplementation.

CONCLUSIONS

The present review summarized choroidal and retinal imaging biomarkers after vitamin D supplementation in AMD patients and our findings suggest that choroidal thickness (mainly subfoveal) and choriocappilary vessel density (blood perfusion of the choriocapillaris) measured by SD-OCT and OCT-A, respectively, may be highlighted as outcomes measurements post-supplementation. Future research with longer follow-ups is necessary to confirm these results, as well as the role of each compound in the multivitamin formulation and their impact on the retinal-choroidal structure.

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