

## EDITORIAL



# An association between atrial fibrillation and age-related macular degeneration: looking beyond mere coincidence

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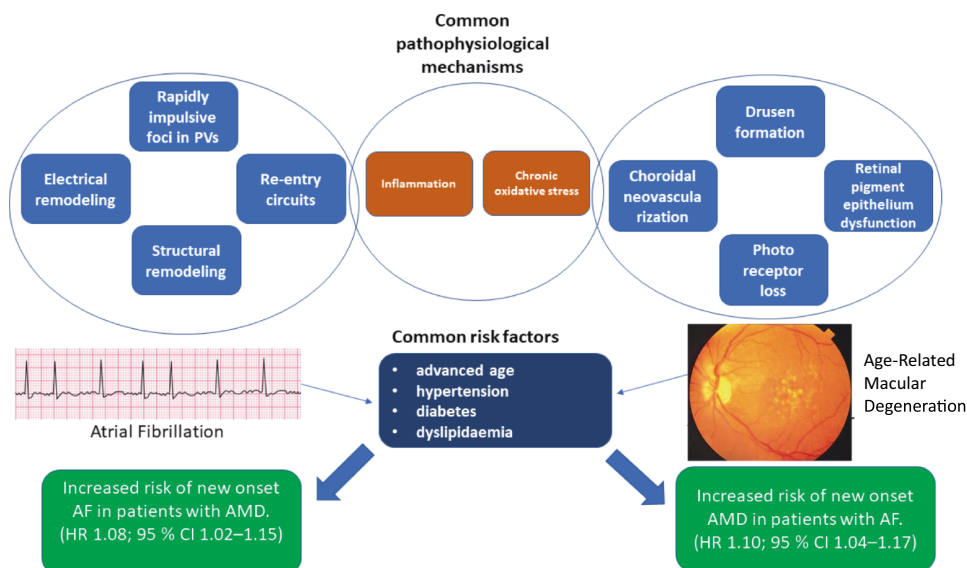
Age-related macular degeneration (AMD) is a leading cause of visual loss in developed countries [1]. Advanced age, smoking, and cardiovascular disorders such as hypertension, coronary artery disease, and hypercholesterolemia are among the significant risk factors for AMD [2]. Loss of vision is often due to destruction of normal macular structure from acute choroidal neovascularisation development (wet AMD) or progressive macular atrophy (dry AMD). Pathophysiological mechanisms of AMD are indeed complex, initiated by drusen formation, chronic oxidative stress, and inflammation leading to retinal pigment epithelium dysfunction, photoreceptor loss, and hypoxia-induced VEGF secretion, eventual development of choroidal neovascularisation [3]. In addition, abnormal markers of angiogenesis (VEGF), hemorheological factors, haemostasis, and endothelial dysfunction have been reported in AMD with an interaction with the components of Virchow's triad for thrombogenesis [4].

Atrial fibrillation (AF), the most common arrhythmia worldwide, is associated with increased mortality and morbidity [5]. Age, hypertension, structural heart disease, sleep apnoea, and metabolic disorders are among the risk factors for AF [6]. Oxidative stress and inflammation also play an important role in aforementioned pathophysiological mechanisms [7], as well as abnormal endothelial damage/dysfunction and angiogenic factors [8].

Given the above, AMD and AF share common features in terms of both risk factors and pathophysiological mechanisms (Fig. 1). Some studies have tried to shed light on the associations between these two conditions [9, 10]. The question is whether these disorders occur concomitantly in individuals of advancing age and comorbidities such as hypertension, diabetes, and dyslipidaemia.

In Table 1, findings of the studies evaluating association between AF and AMD are summarised. One cross-sectional study in participants undergoing coronary angiography reported a significant association was observed between early AMD (dry AMD, drusen formation only) and AF on univariate analysis, but not after adjustment for covariates [9]. Analysis of the prospective angiography INSPIRE database demonstrated that the long-term rate of AMD in the patients with AF over a mean 5.9 years of follow-up was significantly higher compared to those without AF (2.1% vs. 1.2%) [10]. After adjustment for components of CHA<sub>2</sub>DS<sub>2</sub>-VASc score and cardiovascular medications, there was no significant association between AF and subsequent AMD at 1- or 5-years evaluation [10].

In a retrospective observational study published in this journal, Tsai et al. [11] analysed the National Health Insurance Research Database of Taiwan to evaluate whether the incidence of AF was associated according to the AMD and vice versa. They reported the risk of developing AF was higher among AMD patients compared to those without AMD (incidence rate 9.85% vs 8.95%).



**Fig. 1** Shared pathophysiological mechanisms and risk factors between atrial fibrillation and age-related macular degeneration.





**Table 1.** Summary of the studies evaluating association of atrial fibrillation and age-related macular degeneration.

First author, publication year	Study population, AF and AMD patients, and follow-up	Study design	Country	Main finding	Comments
Phan [9], 2014	1576 Australian participants aged $\geq 75$ y; Among total study population, 147 AF patients and 1521 patients without AF, and 107 patients had AMD.	Cross-sectional	Australia	Early AMD is not independently associated with AF on a multivariable logistic regression (OR 0.66; 95% CI 0.23–1.87).	No follow-up Limited sample size No sub-group analysis for wet vs dry AMD
Bunch [10], 2025	38,746 patients without prior AMD; among them 7187 had prevalent AF and 4600 developed AF; 312 developed AMD; mean follow-up of 6.4 years.	Retrospective longitudinal	USA	Unadjusted AF–AMD association was significant (HR 1.80; 95% CI 1.52–2.12) but didn't remain significant after adjustment (HR 1.03; 95% CI 0.86–1.23)	Diagnoses according to ICD 9/10 codes No sub-grouping AF patients to different AF sub types No sub-group analysis for wet vs dry AMD
Tsai [11], 2025	Adults $\geq 50$ y from Taiwan's NHIRD; AMD cohort $n = 31,726$ and non-AMD $n = 31,997$ ; AF cohort $n = 33,958$ and non-AF $n = 35,827$ ; mean follow-up of 6.40–6.46 years.	Retrospective longitudinal	Taiwan	AF is associated with developing new-onset AMD (HR 1.10; 95% CI 1.04–1.17) and AMD is associated with developing new-onset AF (HR 1.08; 95% CI 1.02–1.15)	Diagnoses according to ICD 9/10 codes No sub-grouping AF patients to different AF sub types

Similarly, the risk of developing AMD was higher among AF patients compared to those without (incidence rate 11.98% vs 10.88%). Although dry AMD was associated with developing AF (HR 1.09; 95% CI 1.02–1.16), this trend was not observed in patients with wet AMD (HR 0.94; 95% CI 0.74–1.19).

Although this study had a large population-based cohort (31,766 patients in the AF cohort and 34,236 in the AMD cohort) with a follow-up of 6.4 years, the development of AMD, especially the dry type, can take much longer. Patients with AF have more comorbidities and more clinical visits; consequently, they have a higher likelihood of being diagnosed with AMD and vice versa. Also, the reported HRs for developing AMD/AF and developing AF/AMD indicate an absolute risk increase of 1.0–1.1 extra case(s) in 1000 patient-years, which is a small and perhaps not a clinically significant increased risk. Another important factor is that this study analysed east Asian patients and the generalisability of the results for other ethnicities remains limited, given the reported differences between Asians and non-Asians in terms of cardiovascular clinical epidemiology and complications [12–14].

Given the above, it would not be unreasonable to regularly monitor visual acuity of older patients with AF and comorbidities and advise self-check symptoms of metamorphopsia or blurry central vision which would be highly indicative of early development of wet AMD. Further studies should evaluate the beneficial effect of risk-based screening for AF patients who are at higher risk of developing AMD. Lifestyle modification, healthy diet, smoking cessation, and management of comorbidities such as hypertension, diabetes, and dyslipidaemia might be beneficial for both conditions since they share common pathophysiological mechanisms and risk factors. Holistic, integrated approach should be implemented in clinically complex patients with advanced ages and social risk factors who are at higher risk of developing AF or AMD. Management of modifiable risk factors, and closer follow-ups, and checking early sign of AMD in clinically complex AF patients are recommended.

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#### **AUTHOR CONTRIBUTIONS**

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The authors declare no competing interests.