Effect of Statins on the Onset of Age-related Macular Degeneration

Durga Ganesh[1,3], Jeffrey N. Chiang[2], Eran Halperin[2], Srinivas R. Sadda[3]

[1]David Geffen School of Medicine, University of California - Los Angeles, Los Angeles, CA;
[2]Department of Computational Medicine, University of California - Los Angeles, Los Angeles, CA; [3]Doheny Eye Institute, University of California - Los Angeles, Los Angeles, CA

Background

- Age-related macular degeneration (AMD) affects about 10 million individuals in the United States, and is the third-largest cause of vision loss worldwide.[1] AMD can be further subdivided into Geographic Atrophy and Choroidal Neovascularization.[1]
- Although there are a variety of treatments under investigation for AMD, AMD does not currently have an effective treatment or cure.[1,2]
- Known risk factors for AMD include aging and smoking most significantly, as well as obesity, sex, ethnicity, exposure to sunlight, and cardiovascular disease.[3]
- High dietary fat intake has been implicated as a risk factor for vascular and retinal diseases, fueling a hypothesis that high levels of cholesterol may be related to AMD progression.[3]
- Although many studies have evaluated whether statins (which lower serum cholesterol levels) will influence AMD onset and progression, the studies' overall findings remain inconclusive.[3]
- We investigated the effect of statins on the age of onset of AMD.

Methods

- Data on 38,176 patients seen at UCLA Stein Eye who were referred to retina specialists was extracted from the Electronic Health Record.
- These parameters were analyzed: sex, ethnicity, smoking history, statin use, obesity, Diabetic Retinopathy (DR), and Diabetes Mellitus (DM).
- The following statins were screened: Simvastatin, Atorvastatin, Pravastatin, Fluvastatin, Lovastatin, Pitavastain, Rosuvastatin, and Cerivastatin.
- Survival analysis was performed using a proportional hazards regression model (*statsmodel* package in Python), to determine the effect of statins on the age of onset for AMD.
- Kaplan Meier survival curves were generated to visualize the effect of statins on AMD onset (*lifelines* package in Python).

Results

Table 1: Demographic information and medical history of patients diagnosed with AMD. Patients' sex and histories of smoking, statin use, obesity, Diabetic Retinopathay (DR), Diabetes Mellitus (DM) with complications, and DM without complications are represented as percentages of all patients with AMD (n = 5,387).

	Female	History of Smoking	History of Statin Use	History of Obesity	History of DM (Uncomplicated)	History of DM (Complicated)	History of DR
Percentage of Patients with AMD	60%	53%	44%	7%	15%	3%	0.5%

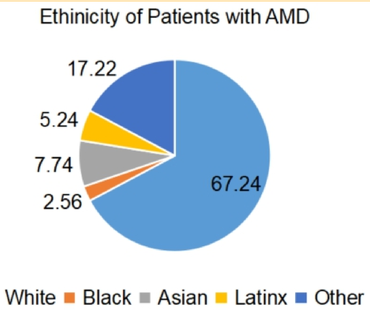


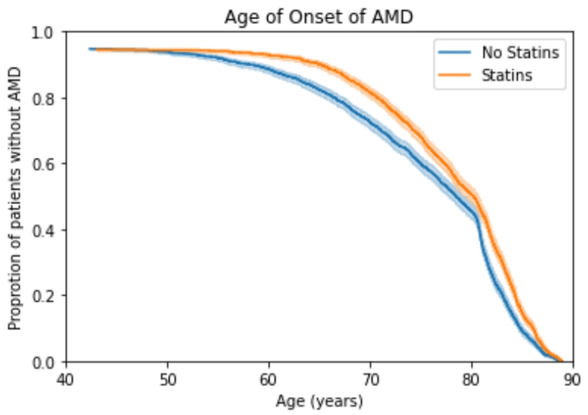
Figure 1: Ethnicity breakown of patients diagnosed with AMD. n = 5,387.

White: 67.24%
Black: 2.56%
Asian: 7.74%
Latinx: 5.24%
Other: 17.22%

Table 2: Survival analysis of age of onset of AMD with respect to statins and other covariates. The hazard ratio, p-value, and 95% confidence interval are provided for smoking status, sex, ethnicity, statin use, obesity, history of DR, history of DM without complications, and history of DM with complications. Significant covariates are highlighted in purple, with $p<0.0045$ after Bonferroni correction (n = 5,387).

	Hazard Ratio	P-value	95% Confidence Interval
Never Smoker	0.89	0.0000	[0.84, 0.94]
Female	1.07	0.0001	[1.01, 1.13]
White	0.83	0.0000	[0.77, 0.89]
Black	0.67	0.000	[0.56, 0.79]
Asian	0.88	0.0197	[0.78, 0.98]
Latnix	0.78	0.0001	[0.69, 0.88]
Statin Use	0.89	0.0001	[0.84, 0.94]
Obesity	1.12	0.0476	[1.00, 1.24]
Diabetic Retinopathy	1.51	0.0292	[1.04, 2.20]
Diabetes Mellitus (Uncomplicated)	0.92	0.0556	[0.84, 1.00]
Diabetes Mellitus (Complicated)	0.99	0.9222	[0.84, 1.17]

Figure 2: Kaplan Meier survival curves of age of onset of AMD, stratified by statin status. Among patients with AMD, 2,370 patients were on statins and 3,017 patients had no history of statin use. Confidence intervals are displayed as the shaded region around each curve.



Discussion

- Statins appear to provide a protective effect in delaying the onset of AMD. The protective effects of lowering serum cholesterol levels should be further explored.
- Beyond the strong evidence in the literature that smoking is a risk factor for AMD[3], we show that smoking appears to hasten the onset of AMD.
- Female patients had a significantly higher risk for developing AMD earlier on, compared to men.
- Exposure to sunlight is a risk factor for AMD, with White patients traditionally associated with having the highest risk due to paler irises. Interestingly, White, Black, and Latinx patients all appeared to have a delayed onset of AMD, although White patients experienced the shortest delay.
- The comorbidities we explored did not have a significant effect on the onset of AMD.
- As patients in our dataset were referred to a retina specialist, this could inflate the raw rate of AMD diagnosis.

Conclusion

- When controlling for demographic factors and specific comorbidities, statins appear to delay the onset of AMD in patients referred to retina specialists at Stein Eye.
- Rather than merely being a risk factor, patients' sex, ethnicity, and smoking status appear to affect the age of onset of AMD.

References

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