



# Risk of Intermediate Age-Related Macular Degeneration Progression in Patients with Systemic Beta-Blocker Use



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## Introduction

- Age-related macular degeneration (AMD) affects ~12.6% of Americans ≥40 years old.
- Progression from intermediate AMD (iAMD) to advanced neovascular (NV) or non-neovascular (NNV) AMD is influenced by multiple risk factors: age, genetics, cardiovascular disease, smoking, and VEGF-mediated pathways.
- Beta-blockers, commonly used for cardiovascular conditions, may influence VEGF expression and AMD progression.
- Previous studies are conflicting, often limited by design, sample size, or lack of longitudinal follow-up visits.

## Objective

- Improve upon previous studies that included: small sample sizes, cross-sectional designs, variable medication tracking, unclear differentiation between selective and non-selective beta-blockers.
- To determine whether beta-blockers:
- Reduce or increase risk of AMD progression.
  - Affect progression of NV versus NNV AMD differently.

## Methods

- **Study Design:** Prospective cohort study using the University of Colorado AMD Registry (Oct 2014 – Nov 2021).
- **Inclusion Criteria:** iAMD at enrollment, ≥1 month follow-up, documented systemic beta-blocker use at time of enrollment.
- **Data Collection:** Patient demographics, medical history, medication use at baseline and follow-up visits; AMD progression determined via multimodal imaging (OCT, fundus photography, autofluorescence).
- **Outcomes:** Time to conversion from iAMD to advanced NV or NNV AMD.

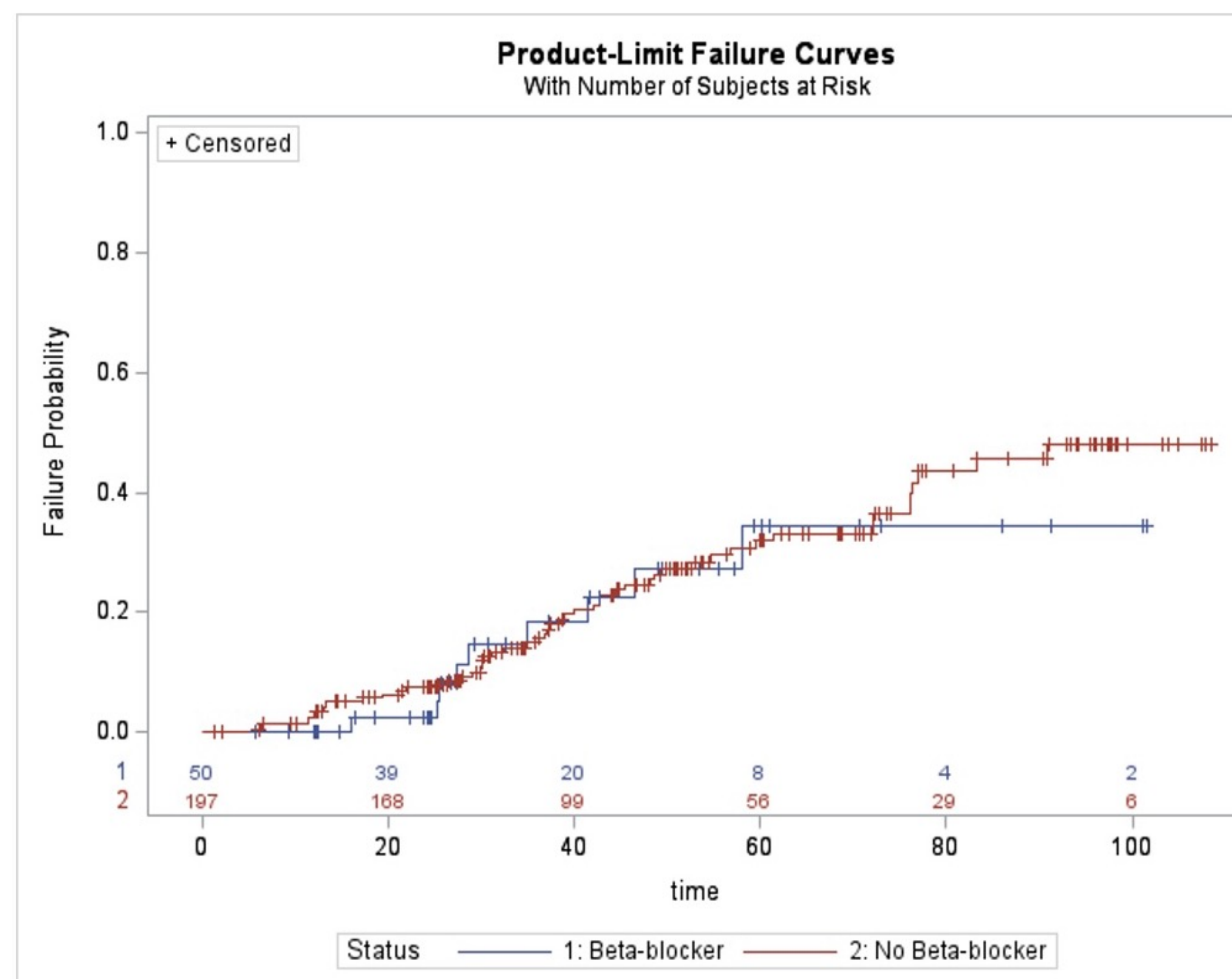
### Analysis:

- Kaplan-Meier survival curves of time to conversion.
- Cox proportional hazards models (univariate and multivariable, adjusting for age and hypertension).
- Time-varying covariate analysis for beta-blocker exposure.

## Results

- **Cohort:** 292 patients; 66 (22.6%) on beta-blockers at enrollment.
- **Baseline differences:** Beta-blocker users were older (78.3 vs 75.6 years,  $p = 0.006$ ) and more likely to have treated hypertension (78.8% vs 47.4%,  $p < 0.0001$ ); sex distribution similar.
- **AMD progression:** Overall conversion to advanced AMD was 36.6%, with no significant difference between beta-blocker users and non-users (37.9% vs 36.3%,  $p = 0.813$ ).
- **Subtype analysis:** Trend toward higher conversion to neovascular AMD among beta-blocker users (24.2% vs 12.8%,  $p = 0.062$ ); no significant difference in conversion to advanced non-neovascular AMD (13.6% vs 23.4%,  $p = 0.195$ ).

### Kaplan-Meier curve of conversion to any advanced AMD by beta-blocker use at time of enrollment.



### Type of medication among the 82 patients on a beta-blocker during the study period.

Selective	n	Non-Selective	n
Metoprolol succinate	29	Carvedilol	12
Metoprolol tartrate	22	Propranolol	5
Atenolol	9	Sotalolol	2
Nebivololol	6	Labetalol	1

Note: 86 total medications since some patients were on more than one beta-blocker medication during the study period.

## Discussion

- **Systemic beta-blocker use was not significantly associated with progression to advanced AMD** after adjusting for age and treated hypertension.
- Findings are consistent with prior studies showing **inconsistent effects of beta-blockers** on AMD progression.
- Preclinical models show beta-blockers may have **anti-VEGF and anti-angiogenic effects**, but systemic use in humans does **not appear to meaningfully modify AMD risk**.
- **No significant differences** were observed by beta-blocker type or time-varying exposure.
- **Limitations:** modest sample size, potential misclassification of medication use, incomplete dose-response capture.
- **Strengths:** longitudinal design, detailed multimodal imaging review, integration of visit-by-visit medication data.

## Conclusion

- No significant association between systemic beta-blocker use and risk of progression from iAMD to advanced NV or NNV AMD after adjusting for age and hypertension.
- Findings suggest beta-blocker use alone is unlikely to alter AMD progression risk.
- **Future directions:** larger cohorts and prospective monitoring of beta-blocker dose/subtype may clarify any potential role in AMD prevention or progression.

## References

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