




# Underdiagnosis of glaucoma in patients with exudative age-related macular degeneration

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## Abstract

**Objective** To compare the rate of glaucoma-related diagnoses in patients with exudative or non-exudative age-related macular degeneration (AMD).

**Methods** Patients above the age of 55 with a diagnosis of AMD were identified from billing records from 2015 to 2018. Out of the 3991 patients with AMD, two cohorts with 990 patients in each were formed by randomly age-matching patients with exudative AMD with those with non-exudative AMD; patients within each group were further classified by subtype and severity of glaucoma. Charts of AMD patients without glaucoma-related diagnoses were reviewed to determine potential underdiagnosis. We applied a set of broad clinical criteria that comprised an intraocular pressure  $\geq 22$  mmHg, a cup-to-disc ratio (CDR)  $\geq 0.6$ , and/or CDR difference between eyes of  $\geq 0.2$ .

**Results** The rate of diagnosed, open-angle glaucoma was significantly lower in patients with exudative AMD (6.06%) compared to patients with non-exudative AMD (8.99%,  $P = 0.04$ ). Similarly, the rate of suspected glaucoma was significantly lower in the first group compared to the second (12.12% versus 18.48%, respectively,  $P < 0.001$ ). A greater number of patients with exudative AMD (13.94%,  $n = 138$ ) met clinical risk criteria compared with those having non-exudative AMD (6.97%,  $n = 69$ ,  $P < 0.001$ ). When these at-risk patients were added to their respective groups, the rate of glaucoma, or its suspicion, became similar ( $\chi^2 = 1.24$ ,  $P = 0.539$ ).

**Conclusions** A significantly lower rate of diagnosed glaucoma, or its suspicion, was identified in patients with exudative compared to non-exudative AMD. This apparent underdiagnosis was resolved by the retrospective application of clinical criteria that may represent a risk of glaucoma.

## Introduction

Age-related macular degeneration (AMD) is the leading cause of irreversible central vision loss among individuals 60 years of age and older in western industrialized countries despite anti-vascular endothelial growth factor (anti-VEGF) therapy that revolutionized the treatment of the neovascular form of the disease [1–3]. Although anti-VEGF medications

are extremely well tolerated, repeated intraocular injections risk ocular and systemic side effects [4, 5]. One of the more common side effects is a transient [6, 7] or sustained [7–10] elevation in intraocular pressure (IOP). Several case series have found that repeated anti-VEGF injections for the treatment of chronic neovascular AMD are associated with an increased risk of ocular hypertension (OHT), requiring treatment with IOP-lowering medications, and/or a diagnosis of glaucoma [11, 12].

AMD and glaucoma are among the most common causes of vision loss [13–15], making effective management of these diseases key to the prevention of blindness, especially in the setting of their coexistence. As AMD is a chronic condition that often requires patients to receive treatment over many years, long-term fluctuations in IOP in patients receiving repeated intravitreal injections may be an especially important risk modifier for glaucoma or its progression. While some studies have shown an increased rate of glaucoma [16, 17], or more specifically open-angle

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glaucoma (OAG) [18], among patients with exudative AMD, other studies have shown no significant relationship between glaucoma and AMD [19]. However, these studies focused almost exclusively on the exudative form of AMD and performed limited analysis by glaucoma subtype. Furthermore, they did not systematically evaluate the reasons for the observed difference in the rate of glaucoma among patients with AMD.

In this study, we investigate the rate of glaucoma in patients with exudative or non-exudative AMD and compare this to an age-matched reference group. We also examine the rate of each glaucoma subtype in these groups through a review of billing records. Finally, through an analysis of readily obtainable data extracted from a retrospective chart review, we present evidence that the basis of the lower rate of glaucoma, or its suspicion, in patients with exudative but not non-exudative AMD is likely due to an underdiagnosis of the condition. We propose that eyecare providers should monitor longitudinal IOP and optic nerve health to more accurately determine the presence of glaucoma or its risk in patients with AMD.

## Subjects and methods

The research followed the tenets of the Declaration of Helsinki and was approved by the institutional review board of the Lahey Hospital (Burlington, Massachusetts, USA). Three years of longitudinal data based on billing records and chart review were analyzed from a single institution spanning the years 2015–2018. Consecutive age-matched exudative and non-exudative patients with AMD who were above the age of 55 and had relevant ICD-10 billing codes (H35.31 or H35.32) in at least two visits were included as the study group. Age-matched patients with bilateral dry eye syndrome (H04.123) without any AMD diagnosis were included as a reference group. When calculating the rate of each glaucoma subtype within the study period, having the relevant ICD-10 codes in at least one visit was used in the analysis. The study was designed as a per-patient analysis rather than a per-eye analysis.

The primary outcome measure was the rate of glaucoma by subtype. Glaucoma was divided broadly into three groups by ICD-10 code: glaucoma suspects (H40.0) including OHT (H40.05); OAG (H40.1) including primary open-angle glaucoma (POAG) (H40.10 and H40.11), low-tension glaucoma (H40.12), pigmentary glaucoma (H40.13), and pseudoexfoliation glaucoma (H40.14); and primary angle closure glaucoma (PACG) (H40.2). For calculating the rate of glaucoma subtypes in each group, having the relevant ICD-10 code in at least one visit was accepted to be sufficient in order to increase the sensitivity of the assessment. In cases where more than one subtype of glaucoma was coded for a

patient, an analysis of the chart was performed to confirm the most likely diagnosis. In cases of asymmetrical disease, e.g., suspected glaucoma in one eye and diagnosed POAG in the other, the more advanced subtype was selected to classify the patient.

Secondary outcome measures included the potential underdiagnosis of glaucoma, or its suspicion, by reviewing charts of subjects without any glaucoma-related diagnosis to apply broad clinical criteria that comprised an IOP value  $\geq 22$  mmHg, a cup-to-disc ratio (CDR)  $\geq 0.6$ , and/or CDR difference between eyes of  $\geq 0.2$ . Postoperative pressure spikes within the first month after surgery were not accepted as evidence of OHT. The reason for potential underdiagnosis (OHT versus CDR findings, or both) was also evaluated for each group. Another secondary outcome measure included the presence and number of times optic coherence tomography (OCT) imaging of the retinal nerve fiber layer (RNFL) and Humphrey visual field (HVF) testing had been obtained for each patient within the study period. These data were used to understand the pattern of monitoring of glaucoma among three different groups.

## Statistical analysis

A  $\chi^2$  test was used for comparing the ratios among three groups and for the between-group analysis a  $\chi^2$  test with Bonferroni correction was used. For the comparison of the means among the three groups, one-way analysis of variance, followed by post-hoc Tukey test, was utilized in the statistical analysis. All tests were two-sided and *P* values below 0.05 were accepted as statistically significant. SPSS for Windows version 21.0 (SPSS Inc., Chicago, Illinois, USA) was utilized for all of the analyses.

## Results

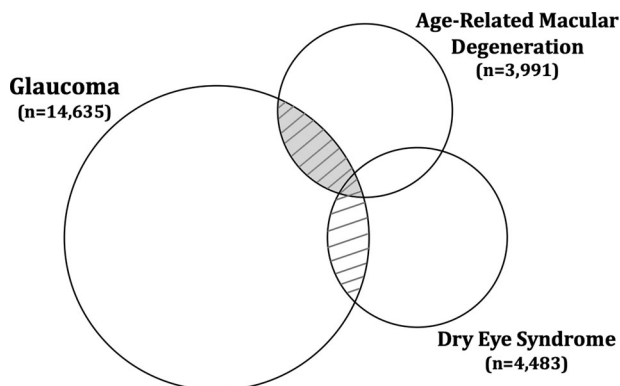
### Demographics

From a total pool of 130,888 unique patients seen in ophthalmology within the study period, 3991 patients with AMD were identified. In all, 1331 patients (1.02%) had a diagnosis of exudative AMD, while 2660 patients (2.03%) were diagnosed with non-exudative AMD; and 4483 patients (3.43%) patients had a diagnosis of bilateral dry eye syndrome (Fig. 1). The demographics of the patients are summarized in Table 1. Next, the patients with exudative AMD were randomly age-matched to patients with non-exudative AMD. This yielded two subgroups each with 990 patients. As a reference group, the study used 990 age-matched patients who had bilateral dry eye syndrome but without a diagnosis of AMD. The mean age of the exudative AMD group was  $81.4 \pm 7.5$  years compared to

81.6 ± 7.8 years for the non-exudative AMD group and 81.7 ± 7.4 years for the dry eye group ( $P = 0.4$ ). After age-matching, 60.7% of the exudative AMD patients were female compared to 59.9% of the non-exudative AMD patients ( $\chi^2 = 0.135$ ,  $P = 0.713$ ). In contrast, females were overrepresented in the reference population of patients with dry eye syndrome at 72.5% ( $\chi^2 = 31.09$ ,  $P < 0.001$ ).

### Dry eye syndrome as an appropriate reference group

To evaluate whether the patients with bilateral dry eye syndrome were an appropriate reference group, the rate of dry eye syndrome in non-exudative AMD patients without glaucoma was compared to the rate in age-matched patients with POAG who did not have any diagnosis of AMD. Glaucoma patients, e.g., may have a higher rate of dry eye due to chronic topical medication use [20]. To test this hypothesis, the 1343 patients with POAG without a diagnosis of AMD were age-matched to an identical number of patients with non-exudative AMD without a diagnosis of POAG. The rate of dry eye syndrome among patients with non-exudative AMD (7.07%) was found to be higher than



**Fig. 1** Venn diagram of the study group patients with glaucoma-related diagnoses, AMD, and bilateral dry eye syndrome (reference group). The overlap between the cohort of patients with both glaucoma-related diagnoses and AMD (dark, blue area,  $n = 768$ , 17.13%) was compared to the patients with both glaucoma-related diagnoses and bilateral dry eye (red, light area,  $n = 828$ , 20.75%) after age-matching.

**Table 1** Demographics.

	Exudative AMD ( $n = 1331$ )	Non-exudative AMD ( $n = 2660$ )	Dry eye syndrome ( $n = 5071$ )	$P$ value
Age (mean ± SD)	83.9 ± 8.5	80.3 ± 9.5	67.1 ± 14.4	<0.001
Gender ( $n$ , %)				
Female	817 (61.4%)	1609 (60.5%)	3823 (75.4%)	<0.001
Male	514 (38.6%)	1051 (39.5%)	1248 (24.6%)	

SD standard deviation.

the rate of dry eye in patients with POAG (3.05%,  $\chi^2 = 22.58$ ,  $P < 0.001$ ). This indicates that using dry eye as a reference group is not likely to overrepresent patients with POAG.

### Rate of glaucoma in patients with exudative compared to non-exudative AMD

The rate of each glaucoma subtype among the three groups is summarized in Table 2. For the groups having a statistically significant difference, between-group  $\chi^2$  testing with Bonferroni correction was performed. The rate of suspected glaucoma was significantly lower in the patients with exudative (12.12%) compared to the non-exudative (18.48%,  $\chi^2 = 13.4$ ,  $P < 0.001$ ) AMD and the reference group (16.67%,  $\chi^2 = 6.33$ ,  $P = 0.012$ ). Similarly, the rate of OAG was significantly lower in the patients with exudative (6.06%) compared to non-exudative (8.99%,  $\chi^2 = 4.2$ ,  $P = 0.04$ ) AMD and the reference group (9.29%,  $\chi^2 = 5.35$ ,  $P = 0.021$ ). However, the rate of POAG was significantly lower in the exudative AMD patients (4.34%) only compared to the reference group (6.97%,  $\chi^2 = 4.48$ ,  $P = 0.034$ ). Finally, the rate of all glaucoma subtypes was significantly lower in the patients with exudative (18.48%) compared to non-exudative (27.78%,  $\chi^2 = 21.93$ ,  $P < 0.001$ ) AMD and in the reference group (26.57%,  $\chi^2 = 16.43$ ,  $P < 0.001$ ). No significant difference was found in the rate of other glaucoma subtypes among three groups (Table 2). Nor was any significant difference found between glaucoma-related diagnoses in the patients with non-exudative AMD compared to the reference population across all of the glaucoma subtypes.

Using dry eye as a reference group for the purposes of calculating the odds ratio for having a glaucoma-related diagnosis reveals that patients with exudative AMD have a

**Table 2** Comparison of the rate of glaucoma by subtype.

	Exudative AMD ( $n = 990$ )		Non-exudative AMD ( $n = 990$ )		Control group ( $n = 990$ )		$P$ value
	$n$	%	$n$	%	$n$	%	
Glaucoma suspect	120	12.12	183	18.48	165	16.67	<0.001 <sup>a</sup>
Open-angle glaucoma	60	6.06	89	8.99	92	9.29	0.014 <sup>a</sup>
POAG	43	4.34	63	6.36	69	6.97	0.034 <sup>a</sup>
LTG	2	0.2	2	0.2	5	0.51	0.37
Pigmentary glaucoma	0	0.0	5	0.51	1	0.1	–
PXG	15	1.51	19	1.92	17	1.72	0.79
PACG	1	0.1	3	0.3	1	0.1	0.45
Other glaucoma	2	0.2	0	0.0	5	0.51	–
All glaucoma subtypes	183	18.48	275	27.78	263	26.57	<0.001 <sup>a</sup>

POAG primary open-angle glaucoma, LTG low-tension glaucoma, PXG pseudoexfoliation glaucoma, PACG primary angle closure glaucoma.

<sup>a</sup> $P < 0.05$ , statistically significant.

**Table 3** Odds ratios for glaucoma-related diagnoses in AMD versus the reference group.

	Exudative AMD versus reference group			Non-exudative AMD versus reference group		
	OR	95% CI	<i>P</i> value	OR	95% CI	<i>P</i> value
Glaucoma suspect	0.69	0.53–0.89	0.004 <sup>a</sup>	1.13	0.90–1.43	0.288
Open-angle glaucoma	0.63	0.45–0.88	0.007 <sup>a</sup>	0.96	0.71–1.31	0.815
Primary open-angle glaucoma	0.61	0.41–0.90	0.012 <sup>a</sup>	0.91	0.64–1.29	0.589
All glaucoma subtypes	0.63	0.51–0.78	<0.001 <sup>a</sup>	1.06	0.87–1.30	0.544

CI confidence interval, OR odds ratio.

<sup>a</sup>*P* < 0.05.

combined 37% lower risk of having a diagnosis of any type of glaucoma (odds ratio, 0.63 [95% CI, 0.51–0.78], *P* < 0.001). Similarly, the risk of having a diagnosis of any of the individual subtypes of glaucoma was also lower in patients with exudative AMD. There was a 31% lower risk of being diagnosed as a glaucoma suspect (odds ratio, 0.69 [95% CI, 0.53–0.89], *P* = 0.004), a 37% lower risk of being diagnosed with OAG (RR, 0.63 [95% CI, 0.45–0.88], *P* = 0.007), and a 39% lower risk of specifically being diagnosed with POAG (odds ratio, 0.61 [95% CI, 0.41–0.90], *P* = 0.012). Sample size was too small to permit an analysis of the other subtypes of OAG or PACG. In sharp contrast, patients with non-exudative AMD did not show any significantly higher or lower odds of being diagnosed with any subtype of glaucoma (odds ratio, 1.06 [95% CI, 0.87–1.30], *P* = 0.544), or its suspicion (odds ratio, 1.13 [95% CI, 0.90–1.43], *P* = 0.288) (Table 3).

### Underdiagnosis of glaucoma

Charts of subjects without a glaucoma-related diagnosis were reviewed and a standard set of clinical criteria applied to assess for the potential underdiagnosis. We found that the rate of these risk factors was significantly higher in patients with exudative AMD (13.94%, *n* = 138) compared to non-exudative AMD (6.97%, *n* = 69, *P* < 0.001), and in the reference group (6.67%, *n* = 66, *P* < 0.001). When these potentially underdiagnosed patients were added back to each group, the rate of glaucoma suspicion became 26.06% (*n* = 258) for exudative AMD patients, 25.45% (*n* = 252) for non-exudative AMD patients, and 23.33% (*n* = 231) for the reference group ( $\chi^2 = 2.17$ , *P* = 0.34). A  $\chi^2$  analysis showed that the addition of these patients significantly increased the rate of glaucoma suspects in all three groups ( $\chi^2 = 62.27$ ,  $\chi^2 = 14.03$ ,  $\chi^2 = 13.75$ , respectively, *P* < 0.001). Including these patients also equalized the overall rate of all glaucoma-related diagnoses across all three groups in our study, yielding 32.42% (*n* = 321) for patients with exudative AMD, 34.75% (*n* = 344) for patients with non-exudative AMD, and 33.23% (*n* = 329) for the

**Table 4** Distribution of the reasons for potential underdiagnosis.

	Exudative AMD		Non-exudative AMD		Reference group	
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
	CDR $\geq$ 0.6 or CDR difference $\geq$ 0.2	72	52.18	33	47.83	44
IOP $\geq$ 22 mmHg	53	38.40	27	39.13	8	12.12
Both (CDR risk + OHT)	13	9.42	9	13.04	14	21.21
Total	138	100	69	100	66	100

AMD age-related macular degeneration, IOP intraocular pressure, CDR cup-to-disc ratio, OHT ocular hypertension.

reference group ( $\chi^2 = 1.24$ , *P* = 0.539). This change in rate was significant across all groups ( $\chi^2 = 50.69$ ,  $\chi^2 = 11.19$ ,  $\chi^2 = 10.50$ , respectively, *P* < 0.001). The specific risk criteria identified as the potential reasons for underdiagnosis of glaucoma, or its suspicion, are shown in Table 4.

When the underdiagnosed patients in each group were compared in terms of having either a RNFL-OCT or HVF testing within the study period, the patients with exudative AMD had similar rates of testing compared to the non-exudative AMD patients (38.40% versus 27.54%, *P* = 0.122). However, even though they did not have any glaucoma-related diagnosis, the at-risk patients identified in the reference group were found to have a significantly higher rate of RNFL imaging (72.73%, *n* = 48) compared to at-risk patients with exudative (38.40%, *n* = 53, *P* < 0.001) and non-exudative (27.54%, *n* = 19, *P* < 0.001) AMD.

### Rate of testing in patients with glaucoma-related diagnoses

The rate of RNFL-OCT and HVF testing for all patients with a glaucoma-related diagnosis was compared among the three different study groups. RNFL imaging was significantly less commonly performed in patients with exudative AMD (70.49%, *n* = 129) compared to the reference group (80.6%, *n* = 212, *P* = 0.04), but not to the patients with non-exudative AMD (79.27%, *n* = 218, *P* = 0.095).

Similarly, the rate of HVF testing in patients with exudative AMD (46.45%,  $n = 85$ ) was lower than the reference group (63.12%,  $n = 166$ ,  $P = 0.001$ ), whereas there was no significant difference compared to patients with non-exudative AMD (56.78%,  $n = 155$ ,  $P = 0.09$ ). Furthermore, the mean number of HVF tests per patient within the study period was significantly lower in the patients with exudative AMD ( $1.09 \pm 1.48$ ) compared to the reference group ( $1.54 \pm 1.53$ ,  $P < 0.001$ ). However, there was no significant difference in the mean number of HVF tests in the patients with non-exudative ( $1.3 \pm 1.51$ ) compared to exudative ( $P = 0.31$ ) AMD or the reference group ( $P = 0.15$ ), respectively. Among the same patient cohorts, the mean number of RNFL-OCT tests per patient within the study period was  $1.42 \pm 1.31$  for the patients with exudative AMD compared to  $1.54 \pm 1.13$  for patients with non-exudative AMD and  $1.6 \pm 1.15$  for the reference group ( $P = 0.28$ ).

## Discussion

This study aimed to compare the rate of glaucoma by subtype in patients with exudative and non-exudative AMD. We also compared this rate to a reference population consisting of individuals with bilateral dry eye, an unrelated condition common in older age [20]. We found that OAG and suspected glaucoma were both less commonly diagnosed in patients with exudative compared to non-exudative AMD, as well as in a reference population. OAG and POAG as a specific subtype were also less common in patients with exudative AMD, but only compared to the reference group. Furthermore, the rate of potential underdiagnosis of glaucoma appears to be twice as likely in patients with exudative compared with non-exudative AMD and is similar to the rate in our reference population. Adding these at-risk patients, identified by applying glaucoma risk factors, to their respective groups resolved the difference in the overall rate of glaucoma. In fact, only 26% of the patients identified as potentially underdiagnosed based upon these clinical criteria would need to be confirmed as having glaucoma to equalize the rate across all three groups. This strongly suggests that there may indeed be a problem of underdiagnosis of glaucoma-related conditions in the population of patients with exudative AMD.

Previous reports regarding the rate of glaucoma in patients with AMD vary widely [17–19]. The rate of OAG in the present study (6.06%) is similar to the rate of OAG in exudative AMD patients reported by Hu et al. [18] (5.06%) ( $\chi^2 = 1.53$ ,  $P = 0.217$ ). Contrary to the higher rate of OAG found among patients in our reference group (9.29%), they found a significantly lower rate of OAG (1.92%) in their control group. However, these patients were selected

without any specific diagnoses and included patients less than 40 years of age who are unlikely to manifest glaucoma. Recently, a nationwide review of claims-based data in a large Medicare population found a significantly higher rate of glaucoma-related diagnoses in patients with exudative AMD compared to the rate in our study (24.8% versus 18.48%,  $\chi^2 = 20.5$ ,  $P < 0.001$ ) [17]. This difference may at least be partially due to the less-specific study inclusion criteria; as well, cases in this study were not further differentiated by glaucoma subtype. Our study population, in contrast, is derived from a hospital-based outpatient clinic that serves as a glaucoma and retina referral center where both types of subspecialists are well represented. This may reduce variability in diagnosis coding, but might be expected to introduce a referral bias, and yet our rate of glaucoma-related diagnoses is still lower than some studies.

The reason for choosing dry eye syndrome as a reference group is because like AMD, it is an age-related condition that often requires longitudinal follow-up with frequent visits over many years. One potential bias from using patients with dry eye syndrome might be a higher rate of OAG due to the well-known association of dry eye with treatment for glaucoma [20]. Interestingly, non-exudative AMD patients actually showed a significantly higher rate of dry eye syndrome (7.05%) in comparison with the POAG patients (3.04%) ( $\chi^2 = 22.58$ ,  $P < 0.001$ ). This finding suggests that the lower rate of suspected glaucoma and OAG was not related to a higher frequency of dry eye in POAG patients. However, one study [21] showed that up to 60% of the glaucoma patients who use topical glaucoma medications have ocular surface disease. Another study by Ali et al. [20] showed that 11% of the dry eye patients had coexisting glaucoma. Although there might be undercoding-related bias in the present study to explain the lower rate of dry eye in patients with POAG, this alone would not explain the difference in the rate of glaucoma risk that we identified, since most patients with glaucoma-related diagnoses are not on glaucoma medications.

In the present study, we chose to assess the potential underdiagnosis of glaucoma, or its suspicion, by applying broad clinical criteria typical of those used to define risk in routine clinical practice, as well as in some previous studies [22, 23]. However, the diagnosis of glaucoma requires a comprehensive evaluation of the patient beyond characterizing the structure of the optic disc or observing an elevated IOP. Most importantly, functional testing is needed to identify the characteristic defects indicative of a glaucomatous optic neuropathy. A chart review cannot establish the presence of glaucoma, but it can give a general idea of the potential for underdiagnosis, though the predictive value of such criteria is limited [24]. Newman et al. [25] examined the diagnostic outcome of referral to a glaucoma specialist

for elevated IOP with and without a suspicious disc and found that the positive predictive value of an elevated IOP alone was 43%, compared to only 25% for a suspicious disc alone or to more than 50% when both were combined. The most common reason for potential underdiagnosis of glaucoma in the present study was a suspicious disc, followed by an increased IOP, or both (Table 4). Ideally a patient with any of these risk criteria would be evaluated for potential glaucoma.

To understand the reasons for the potential underdiagnosis of glaucoma, we assessed the presence and number of RNFL imaging studies and HVF tests among our three groups. We found that both the rate of HVF testing and RNFL imaging were significantly lower in patients with exudative AMD compared to the reference group. As exudative AMD can affect the inner retinal layers including the ganglion cell complex, this could affect the central visual field causing misinterpretation of the test results when comorbid glaucoma is present [26]. The lower rate of HVF testing in the exudative AMD patients might also be explained by the loss of central visual acuity in these patients, which might make the test more difficult for some patients to perform or impact the accuracy of the results [27]. In contrast to HVF testing, which may be limited by the AMD disease process, the utility of RNFL imaging has been shown to effectively differentiate glaucoma in exudative AMD patients [26]. Therefore, RNFL imaging may be a better option to screen and follow glaucoma in patients with AMD. However, RNFL imaging was also less commonly performed in the exudative AMD patients in our study. Providers may be less likely to order this test in patients with macular edema or significant atrophy that could make it harder to interpret, even if providers suspect glaucoma. The higher frequency of RNFL imaging in the reference population might signal that a greater proportion of these patients were actually screened by providers for a risk of glaucoma even if they were ultimately not given an associated diagnosis.

Our study, similar to previous studies, is limited by the constraints imposed by a retrospective analysis based on billing records supplemented by a chart review. Both a larger sample size and additional data beyond a clinic-based population are necessary for external validation of our findings. Studies utilizing billing records have been reported to have high specificity and low sensitivity [28]. Combining ICD-10 codes with an analysis of charts increases the accuracy of the clinical classification of each patient [28]. However, this lack of precision should have a similar effect on each of the groups in our study. In addition, a study of billing records of patients with diabetic macular edema showed that these patients can be accurately identified utilizing only the ICD diagnosis codes [29]. However, to date no study has investigated the accuracy of the diagnosis of

AMD or glaucoma based on a comparison of ICD-10 coding. Doing a per-patient analysis was preferred over a per-eye analysis to reduce the complexity of the data. However, a more in-depth study using a per-eye analysis should be performed to increase our understanding of the relationship between AMD and glaucoma. Finally, only patients above the age of 55 were included in our study, and age-matching was performed to limit age-related bias. Although both AMD and glaucoma are age-related diseases [30], patients outside of this cohort were not assessed in our analysis.

In conclusion, within the limitations of this retrospective study, we found that OAG, POAG, and suspected glaucoma were recognized at a significantly lower rate in patients with exudative AMD, suggesting the possibility of underdiagnosis of glaucoma in such patients. This implies that a sizable fraction of patients with exudative AMD may be experiencing a delay in the recognition of glaucoma, whose early detection is crucial for preventing vision loss. Although no specific guidelines have been published regarding the screening of patients with AMD for glaucoma, both the American Academy of Ophthalmology [31] and European Glaucoma Society [32] recommend screening populations at high risk for glaucoma. Despite disagreement over the rate of glaucoma in patients with AMD, it is not uncommon for these age-related conditions to occur together. Since treatments for exudative AMD may even contribute to the onset of glaucoma in some patients, eyecare providers have an added responsibility not to miss this important diagnosis. We recommend that eyecare providers regularly monitor IOP and CDR, together with other glaucoma risk factors, to detect more accurately the presence of glaucoma in patients with AMD over the course of follow-up.

## Summary

### What was known before

- There is a controversy over the rate of glaucoma in patients with age-related macular degeneration (AMD), and the rate of glaucoma in patients with non-exudative AMD is unknown.

### What this study adds

- Diagnosed glaucoma, or its suspicion, in patients with exudative AMD was significantly lower when compared to those with non-exudative AMD or those in an age-matched reference group.
- Reviewing charts for clinical risk criteria suggests that the reason for the seemingly lower numbers of

glaucoma patients or suspects in exudative AMD may be underdiagnosis.

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**Author contributions** BM was responsible for the chart review, extracting and analyzing the data, figure development, and writing of the manuscript. DJR was responsible for the study hypothesis and design, the development of electronic medical record reporting tools, reviewing and analyzing the data, interpreting the results, and writing of the manuscript.

## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

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