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Patients with Age-related Macular Degeneration Have Increased Susceptibility to Valvular Heart Disease

Natan Lishinsky-Fischer, Itay Chowers, MD, PhD, Yahel Shwartz, MSc, Jaime Levy, MD

Purpose: Valvular heart disease (VHD) contributes significantly to cardiovascular-related morbidity worldwide. Aortic valve stenosis is the third most common cardiovascular disease in the Western world, after hypertension and coronary artery disease. Recent studies have reported an association between VHD and the presence of subretinal drusenoid deposits (SDDs), a distinct manifestation of age-related macular degeneration (AMD). However, these findings were based on self-reported questionnaires and relatively modest cohort sizes. Our goal was therefore to investigate the putative associations between AMD and VHD and between the presence of SDDs and VHD.

Design: Retrospective case-control study.

Subjects: A total of 945 with AMD and 8275 control patients without AMD from a single tertiary center.

Methods: All patients with AMD underwent spectral-domain OCT (SD-OCT). The SD-OCT scans were annotated by 2 experienced graders. Among the patients with AMD, 547 had drusen and SDDs, and 398 had drusen only with no SDDs. We also extracted data from all 9220 patients' electronic medical records, including demographics and previous heart valve procedures based on International Classification of Diseases, ninth revision codes.

Main Outcome Measures: Heart valve-related diagnoses and procedures performed in both patient groups.

Results: Patients with AMD had a higher prevalence of various VHDs compared with the control group, including increased rates of aortic stenosis (odds ratio [OR], 2.00; 95% confidence interval (CI), 1.40–2.86; $P < 0.001$), aortic regurgitation (OR, 2.41; 95% CI, 1.49–3.91; $P < 0.001$), and mitral valve regurgitation (OR, 1.51; 95% CI, 1.13–2.01; $P = 0.004$). Heart valve procedures were also more prevalent among AMD patients including aortic valve replacement (OR, 1.70; 95% CI, 1.08–2.66; $P = 0.019$) and tricuspid valve replacement (OR, 3.99; 95% CI, 1.03–15.46; $P = 0.03$). Moreover, a supervised machine learning model successfully detected the presence of AMD based solemnly on the patient's history of VHD. In the AMD cohort, we found no significant difference in VHD prevalence between patients with nonneovascular AMD and patients with neovascular AMD, or between patients with SDDs and patients without SDDs.

Conclusions: Patients with AMD have a higher prevalence of VHD and are more likely to undergo a heart valve-related procedure compared with patients without AMD, with no difference between patients with SDDs and patients without SDDs in the AMD cohort.

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Supplemental material available at www.ophthalmologyscience.org.

Valvular heart disease (VHD) is a prevalent group of cardiovascular conditions, accounting for approximately 20% of all cardiovascular surgeries and procedures performed in the United States. Traditionally, VHD is classified into degenerative valve disease and rheumatic valve disease, with degenerative valve disease being the primary cause of valve-related morbidity in the United States. Currently, aortic stenosis (AS) is the third most common cardiovascular disease in the Western world, after hypertension and coronary artery disease. Severe AS can cause obstructed flow out of the left ventricle, leading to compensatory left ventricular hypertrophy. Over time, this pressure overload results in a decline in systolic function. For patients with symptoms or documented left ventricular dysfunction, aortic valve replacement is the current recommended treatment.[1]

The presence of VHD was recently reported to be associated with the presence of subretinal drusenoid deposits (SDDs), a clinically distinguishable manifestation of age-related macular degeneration (AMD).[2,3] However, these studies were based either on self-reported questionnaires

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(n = 200),[2] or on a relatively small cohort consisting of 65 patients.[3] Overall, despite sharing several common risk factors such as age, smoking, hypertension, type 2 diabetes mellitus, high body mass index, dyslipidemia, and a history of cardiovascular disease,[4–7] no clear association has been established between AMD and VHD.

Identifying an association between AMD and VHD may provide important insights to the pathogenesis of AMD, may serve as a biomarker for these diseases, and may potentially assist in revealing new therapeutic targets for these conditions. Here, we examined whether patients with AMD are more likely to have VHD or undergo a valve-related procedure compared with control patients without AMD, based on the patients' electronic medical records (EMRs) and a relatively large cohort of patients with AMD and controls.

Methods

This single center, retrospective, case-control study was approved by the Hadassah Medical Center's Internal Review Board (approval number: HMO 382-19) and adhered to the principles of the Declaration of Helsinki. We collected anonymized information from patients' EMRs.

The data set consisted of 6 × 6-mm OCT volumes acquired using the Heidelberg Spectralis system (HRA+OCT SPECTRALIS; Heidelberg Engineering, Inc). The imaging data were transferred to the Reading Center for detailed analysis, where structural OCT biomarkers and AMD staging were annotated.

Study Cohorts

Exclusion Criteria. Cases presenting with additional macular pathologies or suboptimal imaging quality were excluded from the analysis.

Inclusion Criteria. Consecutive groups of AMD patients and unaffected controls were recruited to the study. Only subjects >60 years of age were included in both the AMD and non-AMD groups. AMD patients included cases with a diagnosis of AMD in the electronic medical records (EMR) and OCT biomarkers indicating early, intermediate, or late AMD. Unaffected controls (non-AMD patients) consisted of cases evaluated at our Ophthalmology Department without an AMD diagnosis in the EMR. Medical information obtained from the patients' EMR data included demographics (age and gender), VHD diagnosis, and valve-related procedures performed based on International Classification of Diseases, ninth revision codes. All VHD diagnoses and procedures are presented in Table S1 (available at www.ophthalmologyscience.org) with their respected *International Classification of Diseases, ninth revision* codes.

Data Preprocessing

Python Programming Interpreter (version 3.10, Python Software Foundation) and Jupyter Notebook (version 7.0.6, NumFOCUS) were used to parse the data and perform the calculations. We also used Excel 2016 (Microsoft) to assemble the data, and Prism (version 9, GraphPad) for statistical analyses and to generate the graphs. Using the Python Pandas package, we divided the total cohort into 4 groups: patients without AMD, all patients with AMD, patients with dry (nonneovascular) AMD, and patients with wet (neovascular) AMD in ≥1 eye. Each patient was assigned a score of 1 for each diagnosis and procedure noted in their EMR.

Statistical Analysis

We report the odds ratio with 95% confidence interval for the patients with AMD compared with the control patients without AMD. The number (%) of patients who underwent each procedure is reported for both groups. Categorical variables were analyzed using a univariate chi-square test. A multivariate logistic regression analysis with stepwise backward selection was used to control for covariates, including age, gender, hypertension, diabetes, and hyperlipidemia. Differences were considered significant at $P < 0.05$.

Machine Learning

We used the following 4 supervised classification machine learning models: random forest, support vector machine, decision tree classifier, and neural network. The patient's history regarding VHD was set as a list of features, and the patient's AMD status was set as the label. The area under the curve and F1 score are reported for each model.

Results

Descriptive Statistics and Statistical Analysis

Our cohort consisted of 945 patients with AMD and 8725 control patients without AMD. The general characteristics of this cohort are summarized in Table 2. Figure 1 shows a forest plot of the odds ratio for the prevalence of various VHDs and heart valve procedures in patients with AMD versus control patients without AMD. Aortic stenosis, aortic regurgitation, and mitral regurgitation were significantly more prevalent in the patients with AMD compared with the control group ($P < 0.001$, $P < 0.001$, and $P = 0.004$, respectively). With respect to heart valve procedures, both aortic valve replacement and tricuspid valve replacement were more prevalent among the patients with AMD compared with control group ($P = 0.02$ and $P = 0.03$, respectively).

Table 3 summarizes the prevalence of various valve-related diagnoses and procedures in unaffected controls, and in the patients with AMD, as well as in patients with nonneovascular AMD and patients with exudative AMD. There was higher prevalence of VHD among patients with AMD compared with control patients without AMD. However, there was no difference between patients with nonexudative AMD and patients with exudative AMD.

The prevalence of valve-related procedures was compared between patients with subretinal drusenoid deposits (SDDs) and patients without SDDs (i.e., with drusen only) in the AMD cohort. No diagnoses or procedures which were evaluated showed variable prevalence among the patients with SDDs compared with the patients without SDDs (Table 4).

Multivariate Analysis

A backward elimination multivariate analysis was performed to control for potential confounding variables based on the general characteristics of the cohort. The confounding variables were entered in the first step using the VHDs from Table 3. The model revealed that AS, aortic

Table 2. Summary of the General Characteristics of the Study Cohort

Characteristic	Non-AMD (n = 8725)	AMD		
		All AMD (n = 945)	*Nonexudative AMD (n = 314)*	*Exudative AMD (n = 631)*
Age, yrs	79.3 ± 10.31	82.97 ± 6.95	81.85 ± 7.33	83.52 ± 6.7
Female	4810 (55.13%)	557 (58.94%)	201 (64.01%)	356 (56.42%)
Hypertension	4276 (49.01%)	529 (56.34%)	184 (58.6%)	345 (55.2%)
Hyperlipidaemia	2540 (29.11%)	343 (36.53%)	127 (40.45%)	216 (34.56%)
Hypercholesterolemia	1052 (12.06%)	106 (11.29%)	38 (12.1%)	68 (10.88%)
Diabetes	2051 (23.51%)	215 (22.9%)	77 (24.52%)	138 (22.08%)

Data are presented as the mean ± standard deviation or n (%). AMD = age-related macular degeneration.

regurgitation, hypertension, hyperlipidemia, age, and diabetes were significant for AMD patients versus non-AMD patients after termination ($P < 0.001$, $P = 0.007$, $P = 0.001$, $P = 0.005$, $P = 0.003$, and $P < 0.001$, respectively). The results of each iteration of the model are summarized in Table S5 (available at www.ophthalmologyscience.org).

Machine Learning

An attempt to generate a supervised machine learning model that could predict whether a patient has AMD based on their valve-related history was then conducted (Fig 2). Patients with ≥1 valve-related diagnosis or procedure were included in the learning process. We used a random forest algorithm to classify patients with AMD and patients without AMD according to a binary representation of the heart valve procedure they underwent. Figure 2A shows the receiver operating characteristic curves, with the corresponding area under the curve and F1 score for each of the following machine learning models: random forest, support vector machine, decision tree classifier, and neural network. Figure 2B summarizes the importance of each feature for the random forest and decision tree classifier models' architecture in descending order, showing that mitral regurgitation and AS together account for nearly 50% of the total importance.

Discussion

Here, we examined the overall association between AMD and VHD. Our findings indicate that a higher percentage of patients with AMD were diagnosed with a major VHD such as AS, aortic regurgitation, or mitral regurgitation compared with unaffected controls. Moreover, a higher percentage of patients with AMD underwent replacement of the aortic or tricuspid valve compared with the control group patients. We also developed a supervised machine learning model than can predict if an individual has AMD based on the patient's history of VHD, suggesting that a patient's valvular status is at least partly indicative of the patient's risk of developing AMD.

Collectively, VHDs constitute a significant percentage of cardiovascular morbidity and mortality cases worldwide. Approximately 61% of VHD-related deaths are linked to

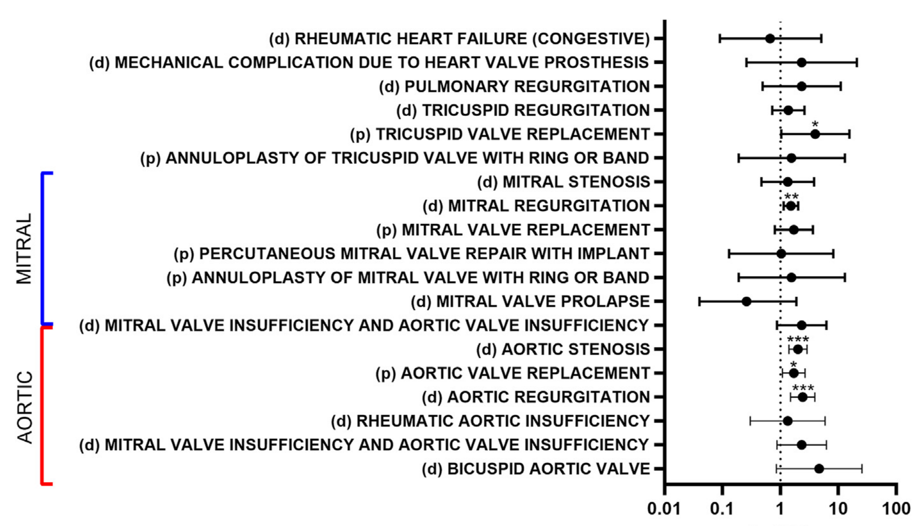

Figure 1. Forest plot summarizing the odds ratio (OR) for the prevalence of valve-related diagnoses and procedures in patients with AMD versus patients without AMD. Note that the *x*-axis is a log scale. $^*P < 0.05$, $^{**}P < 0.01$, and $^{***}P < 0.001$. AMD = age-related macular degeneration; d = diagnosis; p = procedure.

Table 3. Summary of the Prevalence of Valve-Related Diagnoses and Procedures in Patients with AMD and Patients without AMD

		AMD		
Diagnosis/Procedure	**Non-AMD (n = 8725)**	*All AMD (n = 939)*	*Nonexudative AMD (n = 314)*	*Exudative AMD (n = 625)*
(d) Bicuspid aortic valve	4 (0.05%)	2 (0.21%)	1 (0.32%)	1 (0.16%)
(d) Mitral valve insufficiency and aortic valve insufficiency	20 (0.23%)	5 (0.53%)	1 (0.32%)	4 (0.64%)
(d) Rheumatic aortic insufficiency	14 (0.16%)	2 (0.21%)	0 (0.0%)	2 (0.32%)
(d) ST post repair of aortic aneurysm	4 (0.05%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
(d) ST post thoracic endovascular aortic repair	4 (0.05%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
(d) Aortic regurgitation	82 (0.94%)	21 (2.24%)	11 (3.5%)	10 (1.6%)
(p) Aortic valve replacement	127 (1.46%)	23 (2.45%)	6 (1.91%)	17 (2.72%)
(d) Aortic stenosis	180 (2.06%)	38 (4.05%)	15 (4.78%)	23 (3.68%)
(d) Mitral valve prolapse	36 (0.41%)	1 (0.11%)	0 (0.0%)	1 (0.16%)
(p) Annuloplasty of mitral valve with ring or band	6 (0.07%)	1 (0.11%)	0 (0.0%)	1 (0.16%)
(p) Percutaneous mitral valve repair with implant	9 (0.1%)	1 (0.11%)	0 (0.0%)	1 (0.16%)
(p) Mitral valve replacement	44 (0.5%)	8 (0.85%)	1 (0.32%)	7 (1.12%)
(d) Mitral regurgitation	365 (4.18%)	58 (6.18%)	24 (7.64%)	34 (5.44%)
(d) Mitral stenosis	28 (0.32%)	4 (0.43%)	1 (0.32%)	3 (0.48%)
(d) Diseases of the tricuspid valve	19 (0.11%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
(d) Replaced tricuspid valve	2 (0.02%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
(d) ST post tricuspid valve repair	7 (0.08%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
(p) Annuloplasty of tricuspid valve with ring or band	6 (0.07%)	1 (0.11%)	0 (0.0%)	1 (0.16%)
(p) Tricuspid valve replacement	7 (0.08%)	3 (0.32%)	1 (0.32%)	2 (0.32%)
(d) Tricuspid regurgitation	75 (0.86%)	11 (1.17%)	2 (0.64%)	9 (1.44%)
(d) Tricuspid stenosis	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
(d) Pulmonary regurgitation	8 (0.09%)	2 (0.21%)	0 (0.0%)	2 (0.32%)
(d) Pulmonary stenosis	1 (0.01%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
(d) Mechanical complication due to heart valve prosthesis	4 (0.05%)	1 (0.11%)	0 (0.0%)	1 (0.16%)
(d) Rheumatic heart failure (congestive)	14 (0.16%)	1 (0.11%)	1 (0.32%)	0 (0.0%)

Data are presented as n (%). AMD = age-related macular degeneration; d = diagnosis; p = procedure; ST = status.

issues with the aortic valve; the mitral valve accounts for another 15% of VHD-related fatalities, while the pulmonary and tricuspid valves are responsible for the remaining 24%.[8] The mortality rate due to AS is highest in Western Europe, (averaging 4/100 000; 95% confidence interval, 3.4—4.5), followed closely by North America (3.6/100 000; 95% confidence interval, 3.0—4.0).[8] The natural progression of AS is slow, with an annual increase of 7 mmHg accompanied by a decrease of 0.1 cm^2 in valve area. However, once AS progresses to the severe or symptomatic stage, the prognosis is relatively poor, with a 5-year mortality rate reaching 60% after the first hospitalization and a 1-year mortality rate of 50% if left untreated.[9] Thus, identifying AMD as a biomarker for predicting VHD could be highly beneficial. Based on our findings, patients recently diagnosed with AMD should undergo an assessment of their valvular health, and any major cardiovascular conditions identified should be addressed proactively to reduce risk associated with these conditions.

Common Pathologic Factors in VHD and AMD

The shared underlying factors for AMD and VHD are unknown. Collagen, proteoglycans, and elastin form the 3 main components of the extracellular matrix (ECM) and are essential for maintaining the biomechanical stability of heart valves. In addition to the ECM, heart valves consist of valvular interstitial cells and valvular endothelial cells, and healthy, stable communication between valvular interstitial cells and valvular endothelial cells is essential for proper valvular function. Degenerative processes that affect these ECM components and valvular cells can cause the gradual deposition of lipids in the subendothelium, as well as oxidation, inflammation, ECM remodeling, differentiation of fibroblasts, and, finally, valvular calcification, which in turn leads to impaired valvular function.[10] Activation of the complement pathway, particularly complement 3a and complement 5a, was reported in AS.[11] With respect to AMD, calcification, inflammation and dysregulation of lipid metabolism were associated with the disease and the breakdown of collagen and elastin have been reported in Bruch's membrane in patients with AMD.[12] Moreover, studies suggest that atherosclerosis contributes to the pathogenesis of both VHD and AMD.[10,12] Genetic variants in genes encoding protein involved in ECM metabolism were associated with AMD. It is unknown if the same variants are also associated with VHD.

Table 4. Summary of the Prevalence of Valve-Related Diagnoses and Procedures in the AMD Cohort, with Corresponding ORs for Patients with SDDs versus Patients without SDDs

Diagnosis/Procedure	No SDDs (n = 396)	SDDs (n = 543)	OR	95% CI	*P* Value
(d) Bicuspid aortic valve	0 (0.0%)	2 (0.37%)	0.5	0.03–8.05	0.62
(d) Mitral valve insufficiency and aortic valve insufficiency	2 (0.51%)	3 (0.55%)	2.02	0.22–18.11	0.52
(d) Rheumatic aortic insufficiency	1 (0.25%)	1 (0.18%)	NA	NA	NA
(d) ST post repair of aortic aneurysm	0 (0.0%)	0 (0.0%)	NA	NA	NA
(d) ST post thoracic endovascular aortic repair	0 (0.0%)	0 (0.0%)	NA	NA	NA
(d) Aortic regurgitation	7 (1.77%)	14 (2.58%)	0.45	0.19–1.07	0.06
(p) Aortic valve replacement	6 (1.52%)	17 (3.13%)	1.44	0.56–3.68	0.45
(d) Aortic stenosis	13 (3.28%)	25 (4.6%)	0.76	0.39–1.48	0.42
(d) Mitral valve prolapse	1 (0.25%)	0 (0.0%)	NA	NA	NA
(p) Annuloplasty of mitral valve with ring or band	0 (0.0%)	1 (0.18%)	NA	NA	NA
(p) Percutaneous mitral valve repair with implant	1 (0.25%)	0 (0.0%)	NA	NA	NA
(p) Mitral valve replacement	5 (1.26%)	3 (0.55%)	3.55	0.43–28.94	0.21
(d) Mitral regurgitation	19 (4.8%)	39 (7.18%)	0.7	0.4–1.19	0.19
(d) Mitral stenosis	0 (0.0%)	4 (0.74%)	1.51	0.16–14.57	0.72
(d) Diseases of the tricuspid valve	0 (0.0%)	0 (0.0%)	NA	NA	NA
(d) Replaced tricuspid valve	0 (0.0%)	0 (0.0%)	NA	NA	NA
(d) ST. Post tricuspid valve repair	0 (0.0%)	0 (0.0%)	NA	NA	NA
(p) Annuloplasty of tricuspid valve with ring or band	0 (0.0%)	1 (0.18%)	NA	NA	NA
(p) Tricuspid valve replacement	2 (0.51%)	1 (0.18%)	1	0.09–11.12	1
(d) Tricuspid regurgitation	5 (1.26%)	6 (1.1%)	2.28	0.49–10.61	0.28
(d) Tricuspid stenosis	0 (0.0%)	0 (0.0%)	NA	NA	NA
(d) Pulmonary regurgitation	2 (0.51%)	0 (0.0%)	NA	NA	NA
(d) Pulmonary stenosis	0 (0.0%)	0 (0.0%)	NA	NA	NA
(d) Mechanical complication due to heart valve prosthesis	0 (0.0%)	1 (0.18%)	NA	NA	NA
(d) Rheumatic heart failure (congestive)	0 (0.0%)	1 (0.18%)	NA	NA	NA

Data are presented as n (%). CI, confidence interval; d = diagnosis; NA = not applicable; OR, odds ratio; p = procedure; SDD = subretinal drusenoid deposit; ST = status.

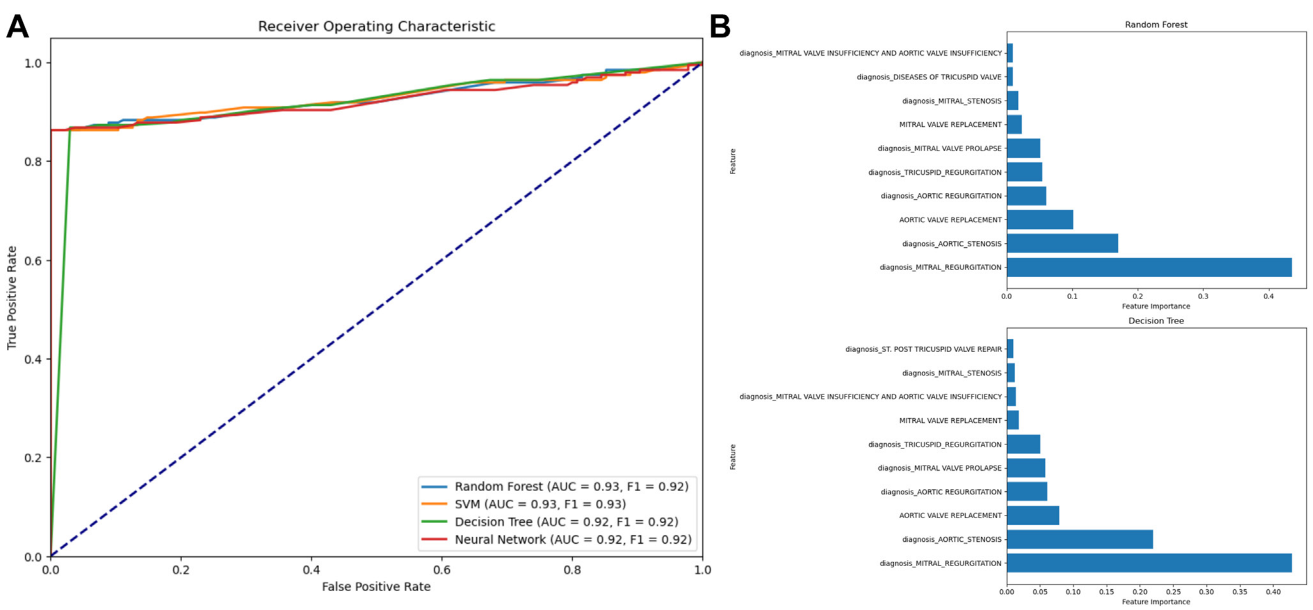

Figure 2. A, True positive rate plotted against false positive rate for predicting AMD based on a patient's valvular history. The corresponding receiver operating characteristic curves were analyzed using the random forest classifier, support vector machine (SVM), decision tree classifier, and neural network models. **B,** Summary of the relative importance of the indicated valve-related diagnoses and procedures in the random forest and decision tree classifier models. AMD = age-related macular degeneration; AUC = area under the curve.

SDDs and VHD

Ledesma-Gil et al[2] and Fei et al[3] previously described a possible connection between the presence of SDDs and the development of VHD by focusing on AMD with SDDs versus AMD without SDDs, reporting that approximately 82% of patients with a valvular defect also presented with SDDs. In our cohort, there was no difference in valve-related diagnoses and procedures between patients with SDDs and patients without SDDs. Ledesma-Gil et al[2] included only cases with intermediate AMD, and SDDs were diagnosed with multimodal imaging. In our study, we included early, intermediate and late AMD cases, with SDDs diagnosed based solely on OCT, without fundus photography or autofluorescence imaging. However, this does not necessarily contradict the previous findings. As noted above, valvular defects can vary widely, and not all defects are diagnosed at early stages or require valve replacement; therefore, a higher prevalence of VHD may still exist among patients with SDDs who do not undergo a valve-related procedure. As shown in Table 3, certain VHDs, such as mitral stenosis and tricuspid regurgitation, were indeed more common in the SDD group, while other conditions were not. Nonetheless, these differences were not statistically significant enough to warrant reporting. The variations may be due to differences in imaging modalities and inclusion criteria. Additionally, they could arise from the use of EMRs versus cardiologist examinations, as well as significant variability in the timing of VHD detection.

One major limitation of the study by Ledesma-Gil et al[2] was the use of self-reported questionnaires, which has been shown to lead to substantial overreporting or underreporting of cardiac incidents.[13] Fei el al[3] validated their patients' diagnoses by performing a transthoracic echocardiogram; however, their cohort was relatively small (n = 65 patients). By contrast, we use a relatively large cohort of 945 patients with AMD and 8275 unaffected controls with EMR-derived valve-related diagnoses and procedures.

Machine Learning

Here, we examined whether a patient's valvular history can provide any insights into their AMD status, using 4 common classification techniques suitable for binary data.[14,15] Interestingly, even though these models are based on different underlying algorithms, all 4 models yielded relatively consistent performance, suggesting that these models are both robust and reliable.

Study Limitations

Our study has several limitations that warrant discussion. This is a retrospective study focused on identifying previously unknown associations. The presented correlation is not sufficient to deduce any causal connection between VHD and AMD. The cohort consisted exclusively of patients who were diagnosed or underwent valve-related procedures at our hospital, Hadassah Medical Center; therefore, some of the patients in our cohort may have undergone a valve-related procedure at another medical center to which we did not have access. This issue could be mitigated by requesting the entire medical profile from the patients' health maintenance organizations or insurance companies. In addition, the control group included cases that underwent ophthalmic examinations without an AMD diagnosis in the EMR; however, OCT scans were not evaluated. Lastly, SDDs were diagnosed based solely on OCT, without the use of multimodal imaging.

Conclusions

Our results indicate that a higher percentage of patients with AMD undergo a heart valve procedure compared with patients without AMD. Moreover, the presence of a valvular condition may indicate a predisposition to developing AMD. These findings may suggest the importance of cross-referral between ophthalmologists and cardiologists for patients who present with any form of VHD or AMD. The findings also may suggest the potential existence of a common pathogenic pathways for AMD and VHD. Identifying this factor may help to identify novel therapeutic targets for these conditions.

Footnotes and Disclosures

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Ophthalmology Department, Hadassah Medical Center, Faculty of Medicine, The Hebrew University of Jerusalem, Jerusalem, Israel.

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The authors have made the following disclosures:

I.C.: Support − Israel Science Fund Grant; Consultant − Orsight Pharma, Roche; Patents − Sensinject, AISEE; Participation on a Data Safety Monitoring or Advisory Board − Kriya; Stock or stock options − Ocutrack, Remepy.

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The other authors have no proprietary or commercial interest in any materials discussed in this article.

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HUMAN SUBJECTS: Human subjects were included in this study. This single center, retrospective, case-control study was approved by the Hadassah Medical Center's Internal Review Board (approval number: HMO 382-19) and adhered to the principles of the Declaration of Helsinki. The requirement for informed consent was waived due to the retrospective nature of the study.

No animal subjects were included in this study.

Author Contributions:

Conception and design: Lishinsky-Fischer, Chowers, Shwartz, Levy

Data collection: Lishinsky-Fischer, Chowers, Shwartz, Levy

Analysis and interpretation: Lishinsky-Fischer, Chowers, Shwartz, Levy

Obtained funding: N/A.

Overall responsibility: Lishinsky-Fischer, Chowers, Shwartz, Levy

Abbreviations and Acronyms:
AMD = age-related macular degeneration; **AS** = aortic stenosis; **CI** = confidence interval; **ECM** = extracellular matrix; **EMR** = electronic medical record; **OR** = odds ratio; **SDD** = subretinal drusenoid deposit; **SD-OCT** = spectral-domain OCT; **VHD** = valvular heart disease.

Keywords:
Age-related macular degeneration, Electronic medical records, OCT, Valvular heart disease.

Correspondence:
Jaime Levy, MD, Kiryat Hadassah, PO Box 12000, 91120 Jerusalem, Israel. E-mail: levjaime@gmail.com.

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